702 PHASE 1 STUDY OF DLL3-DIRECTED CHIMERIC ANTIGEN RECEPTOR T-CELLS IN SUBJECTS WITH EXTENSIVE STAGE SMALL CELL LUNG CANCER

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Background Extensive Stage Small Cell Lung Cancer (ES-SCLC) and Large Cell Neuroendocrine of the lung (LCNEC) are aggressive neuroendocrine carcinomas with an exceptionally poor prognosis.[1] [2] Although the majority of patients experience response to first line of therapy, the durability of response is often limited. Delta-like ligand 3 (DLL3) is an inhibitory Notch ligand that is highly expressed on the cell surface in SCLC (~85% of the patients having positive staining in >25% tumor cells) and LCNEC (74% having positive staining in at least 1% of tumor cells).[3] [4] Preclinical studies of LB2102, an autologous DLL3-directed CAR-T cell, have demonstrated DLL3-specific antitumor effects with a low risk of on-target/off-tumor toxicities and off-target/off-tumor toxicities.

Methods This phase 1, open-label, multicenter, dose-escalation and cohort expansion study of LB2102 will treat up to 41 subjects with ES-SCLC or LCNEC (NCT05680922). Part A will enroll and treat 12–24 subjects, and Part B will treat 11–17 subjects (figure 1). Subjects will be pooled from Part A and Part B to a total of 23 subjects treated at the recommended dose for expansion. The patient population is adult subjects with histologically/cytologically confirmed unresectable small cell lung carcinoma (SCLC), large cell neuroendocrine lung carcinoma (LCNEC), combined SCLC, or combined LCNEC as per WHO 2021 criteria. Patients enrolled have received at least one prior line of standard treatment with progression or insufficient response, and for whom standard treatment is intolerable, unlikely to confer significant clinical benefit, is no longer effective, or the subject declines further standard treatment. Other key criteria include ECOG PS 0 or 1; life expectancy > 4 months per investigator judgment; available archival or fresh biopsy tissue, presence of ≥ 1 radiologically measurable lesion per RECIST 1.1, and adequate organ function per protocol. No prior DLL3 targeted therapy is allowed. LB2102 will be manufactured from autologous T cells collected from peripheral mononuclear blood cell apheresis. Subjects may receive optional bridging therapy followed by lymphodepletion chemotherapy with fludarabine and cyclophosphamide for 3 days. The subject will then receive one infusion of LB2102 and will be followed post-infusion for safety and disease assessments. The objectives of the study include characterization of safety and tolerability, evaluation of the recommended phase 2 dose, and assessment of preliminary antitumor activity. US sites will begin enrollment in fall 2023.

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Trial Registration Registered on Clinicaltrial.gov (NCT05680922).

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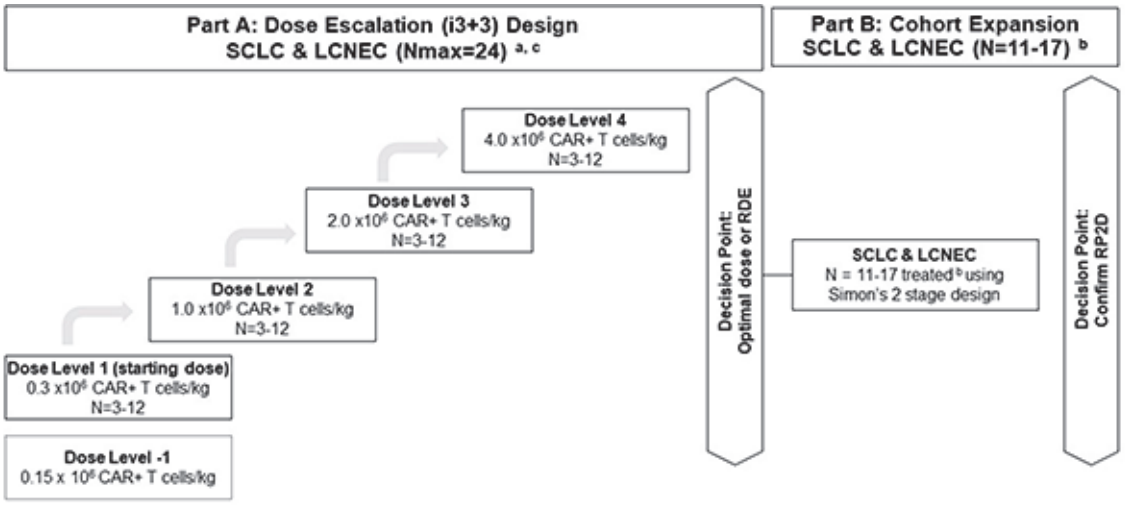

[a] treated subjects will range from 12 to 24 based on recommendations from DEC guided by statistical modeling using i3+3 design

[b] at least 6 subjects will be required to be treated at the RDE in part A, and the maximum number treated will be 12. These subjects will be pooled with the subjects in part B to make the total number of subjects of 23, therefore it is expected that 11-17 additional subjects will be enrolled a the RDE in the cohort expansion.

[c] Dose Stagger: 1st and 2nd subjects in the dose level 1 will be staggered for at least 4 weeks and the subsequent subjects will be staggered for at least 2 weeks. Prior to each dose escalation, there will be an observation period of at least 4 weeks between the final subject of one dose level and the first subject at the next dose level. At dose level 2 and higher all subjects will be staggered at least 2 weeks

Abstract 702 Figure 1 LB2102-1001 Study Design