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# Phase 1 Study of DLL3-targeted CAR-T Cells Armored With dnTGFBR2 in Small-Cell Lung and Large-Cell Neuroendocrine Cancers

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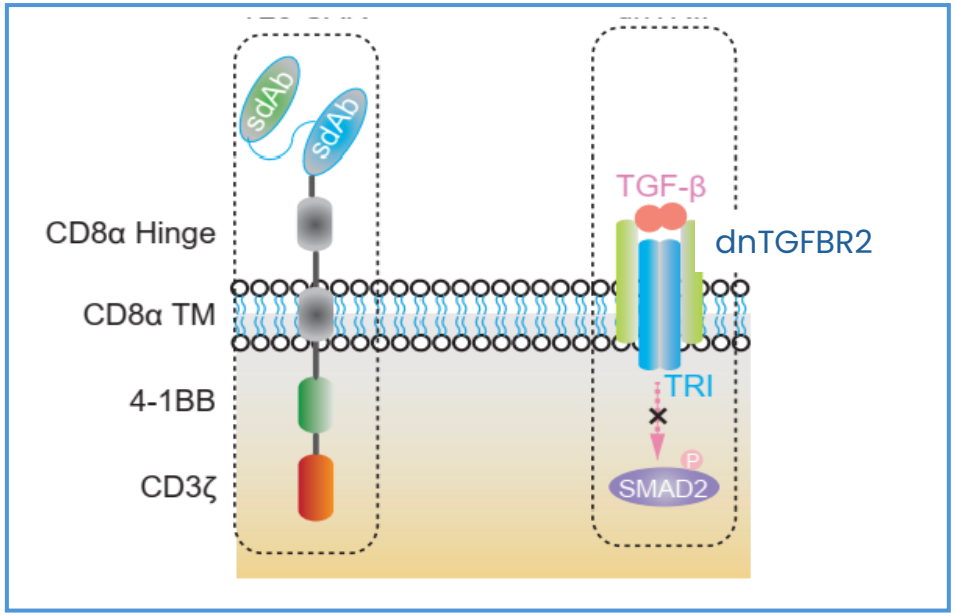
# LB2102 CAR-T Cell Design

- DLL3 Targeting CAR-T: No cross-reactivity with DLL1, DLL4, or other membrane proteins
- Dominant-negative TGF-β receptor 2 (dnTGFBR2): non-signaling receptor that blocks TGF-β–mediated SMAD signaling
- Increases CAR-T cell proliferation and reduces exhaustion




# LB2102-1001 Phase 1 Study

- Data presented from 15 subjects with metastatic, relapsed or refractory SCLC (n=13) or LCNEC (n=2) that progressed following ≥1 prior line of standard treatment
- ECOG ≤1
- 9 (60.0%) subjects with history of brain metastases (none untreated or symptomatic)
- Median age, 56 years (20-68 years)
- 8 men (53.3%)
- Median 1 line of priory therapy (1-7 lines)
- Study ongoing, at Dose Level 7 (16 x$10^6$ CAR+ T cells/kg)

## Part A: Dose Escalation (i3+3) Study Design ($N_{max}$=36)

**Dose level 1**
0.3 x $10^6$ CAR+ T cells/kg

**Dose Level 2**
1.0 x $10^6$ CAR+ T cells/kg

**Dose Level 3**
2.0 x $10^6$ CAR+ T cells/kg

**Dose Level 4**
4.0 x $10^6$ CAR+ T cells/kg

**Dose Level 5**
8.0 x $10^6$ CAR+ T cells/kg

**Data presented up to DL5**

**Dose Level 6***
12.0 x $10^6$ CAR+ T cells/kg
(skipped if no or minimal drug-related adverse events observed at the preceding dose level

**Dose Level 7**
16.0 x $10^6$ CAR+ T cells/kg

Decision Point:
Optimal Dose or RDE

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# LB2102 Safety and Pharmacokinetics (PK)

- No dose-limiting toxicities (DLTs), ICANS, delayed hypersensitivity reactions, or neurotoxicities have been observed
- There were 10 subjects with TEAEs related to LB2102, distributed across all dose levels (DLs)
- The most common TEAEs were hematopoietic (anemia, neutrophil and white blood cell decreases) and related to lymphodepletion (LD)
- There were 2 cases of Grade 1 cytokine-release syndrome; only one of them (at DL4) was an SAE
- CAR-T cell expansion, measured by qPCR analysis of the CAR transgene, was observed in all subjects starting at DL3 ($2x10^6$ CAR-T cells/kg)

| | Dose Level 1<br>$0.3 \times 10^6$<br>CAR-T cells/kg<br>(N=3) | Dose Level 2<br>$1.0 \times 10^6$<br>CAR-T cells/kg<br>(N=3) | Dose Level 3<br>$2.0 \times 10^6$<br>CAR-T cells/kg<br>(N=3) | Dose Level 4<br>$4.0 \times 10^6$<br>CAR-T cells/kg<br>(N = 3) | Dose Level 5<br>$8.0 \times 10^6$<br>CAR-T cells/kg<br>(N = 3) |
|---|---|---|---|---|---|
| PK-evaluable subjects | 1 | 1 | 3 | 3 | 3 |
| $C_{max}$ (copies/ug DNA) median (range) | 647<br>(647, 647) | 2509<br>(2509, 2509) | 694<br>(46, 2257) | 581<br>(564, 1126) | 527<br>(251, 538) |
| Tmax (day) median (range) | 28<br>(28, 28) | 13<br>(13, 13) | 15<br>(10, 29) | 15<br>(5, 20) | 6<br>(6, 10) |
| $AUC_{last}$ (day*copies/ug DNA) median (range) | 5656<br>(5656, 5656) | 6973<br>(6973, 6973) | 8997<br>(138, 47329) | 6728<br>(2883, 15873) | 3351<br>(1661, 9298) |

# Efficacy

**Disease control rate (CR+PR+SD): 73.3%** (n=11/15)

- At higher DLs: 88.9%

**Objective response rate (CR+PR): 13.3%** (n=2/15)

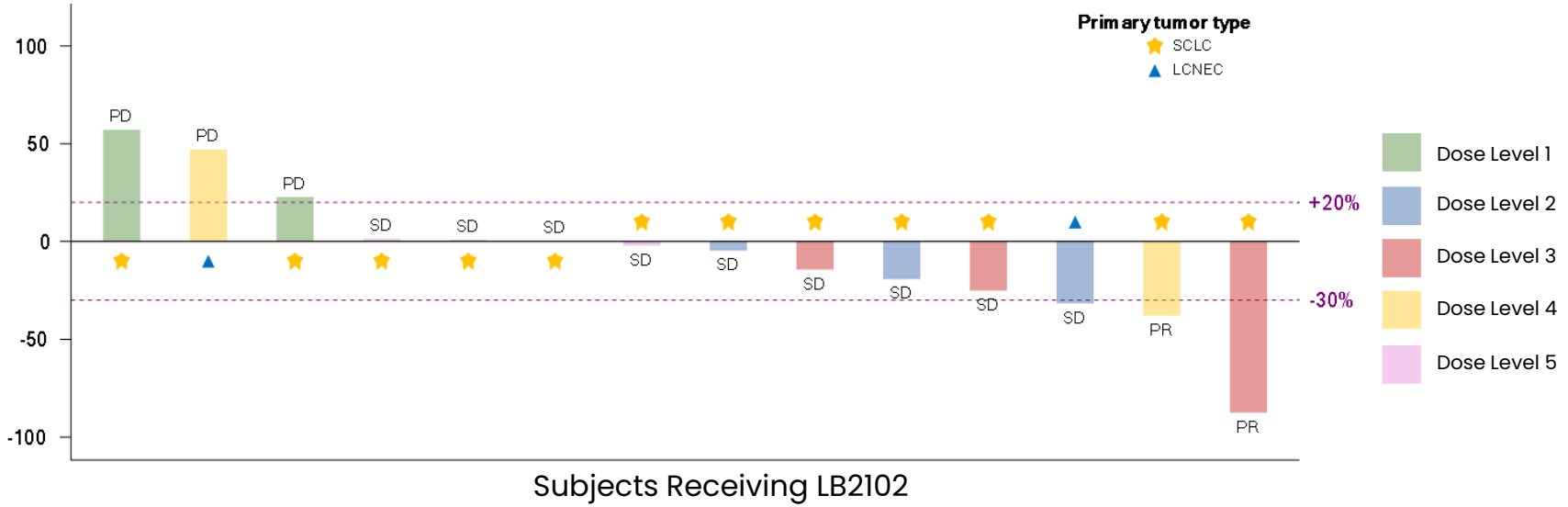
- At higher DLs: 22.2%

CR, complete responses; none at any dose

## Best Overall Responses (per RECIST 1.1 criteria)

| Dose level (DL) | Partial Response | Stable Disease | Progressive Disease | Objective Response Rate | Disease Control Rate |
|---|---|---|---|---|---|
| **DL 1-2** (≤ 1.0 x $10^6$ CAR T cells/kg) N=6, n (%) | **0** | **3 (50.0%)** | 3 (50.0%) | **0** | **3 (50.0%)** |
| **DL 3–5** (2.0–8.0 x $10^6$ CAR T cells/kg) N=9, n (%) | **2 (22.2%)** | **6 (66.7%)** | 1 (11.1%) | **2 (22.2%)** | **8 (88.9%)** |
| **Total** N=15, n (%) | **2 (13.3%)** | **9 (60.0%)** | 4 (26.7) | **2 (13.3%)** | **11 (73.3%)** |

## Best Overall Response and Percent Change From Baseline in Target Tumor Lesion Size




Subjects Receiving LB2102

PR, partial response; SD, stable disease; PD, progressive disease

Note: Percent change from baseline was not evaluable in 1 subject due to non-measurable disease at baseline per RECIST 1.1 criteria, so not presented in the figure.

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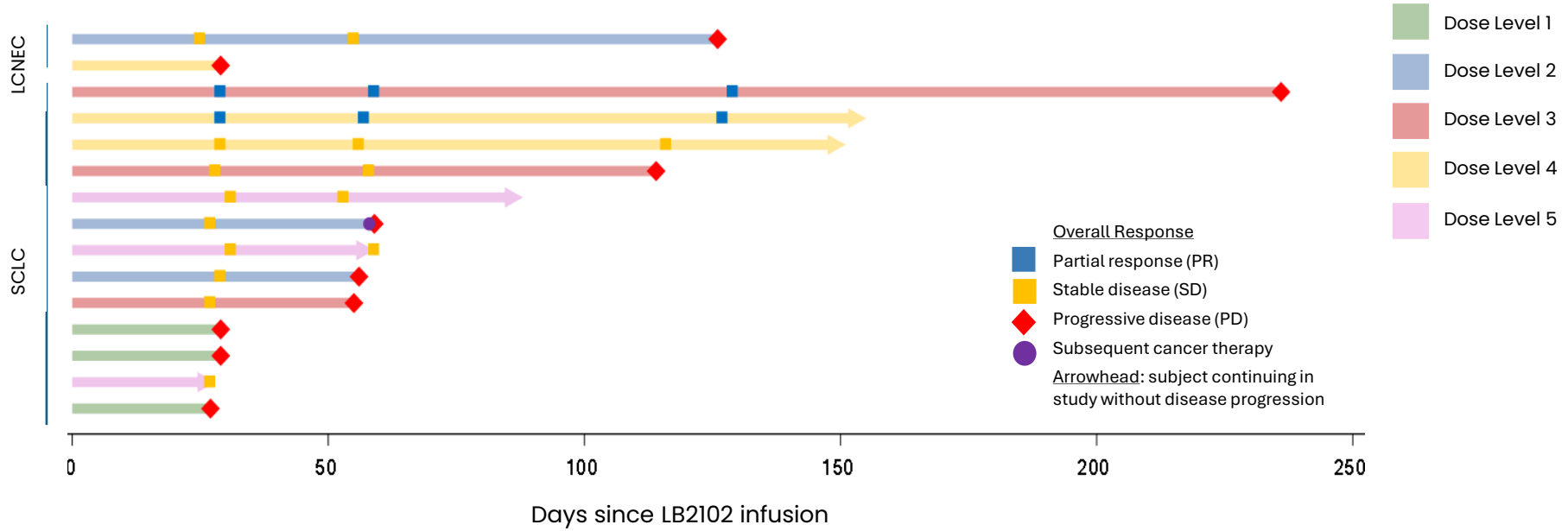
# Efficacy (cont)

## Responses Over Time in Subjects Who Received LB2102




- **3 subjects** (1 SD at DL2, PR DL3; PR at DL4) had **sustained tumor shrinkage** over time
- Two patients at DL4 continue to respond at **5+ months (1 PR and 1 SD)**
- One patient at DL3 had **PR until month 8**.

Not specified in above figures/efficacy summary: an additional subject treated off-protocol at DL3 also achieved durable PR, up to Month 8. Ref: WCLC 2025 E-poster EP.13.29 Hao et al.

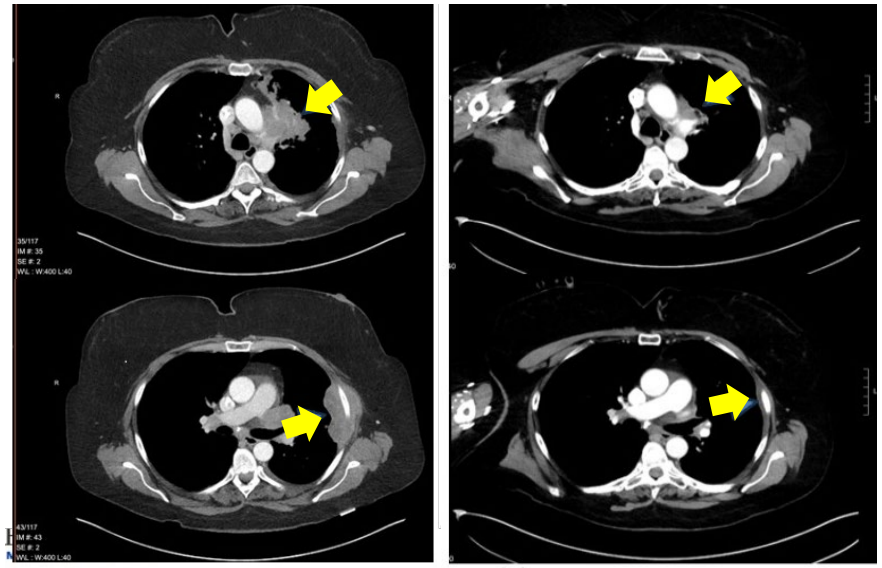
# CT Scans From 2 Subjects at DL3 (2.0 x 106 CAR+ T cells/kg) at Time of Best Response

## Subject # 8 in LB2102 Study

- Subject had Partial Response **(PR) through Month 4 (target lesion reduced by 69.8% from baseline**) with subsequent negative PET scan at Month 6

Baseline (before LD chemotherapy and LB2102)

4 months After LB2102



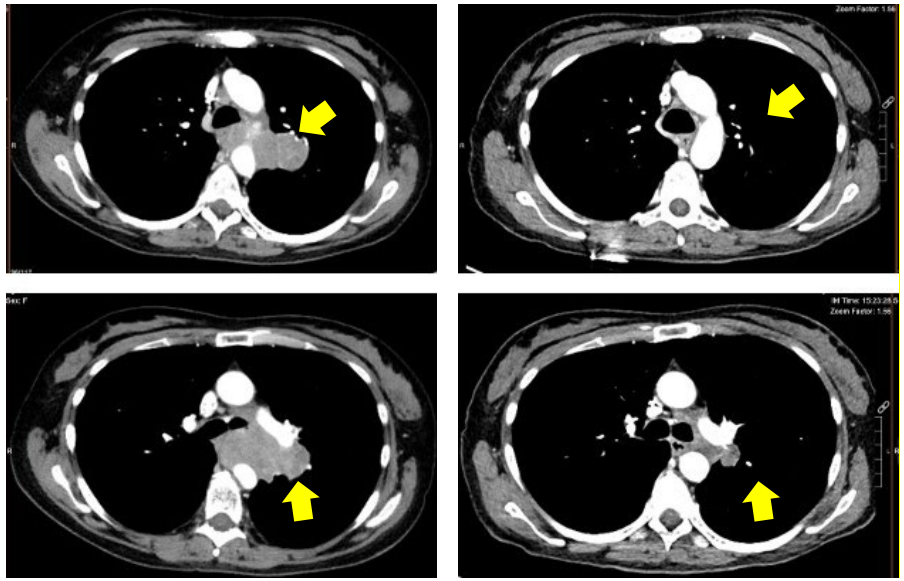
- **At month 8,** despite continued target lesion shrinkage of 87.5%, disease progressed due to new lesions
- Subject is now receiving tarlatamab

## 1 Subject Treated Off Protocol*

- Subject had a **PR through Month 6 (lesion reduced by 76% from baseline)***

Baseline (before LD chemotherapy and LB2102)

6 months After LB2102



- **At month 8** subject continues PR and is pain- and treatment-free with ECOG-1*

Yellow arrows indicate tumor mass

CT images from Dr Z Hao, Markey Cancer Center, Lexington, KY

*Ref: WCLC 2025 E-poster Ref: WCLC 2025 E-poster EP.13.29 Hao et al.

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# Target Expression Persists Post-treatment

## DLL3 Expression in Lung and Adrenal Gland Tumor Biopsy (Subject # 8 at DL3)

**At Screening**

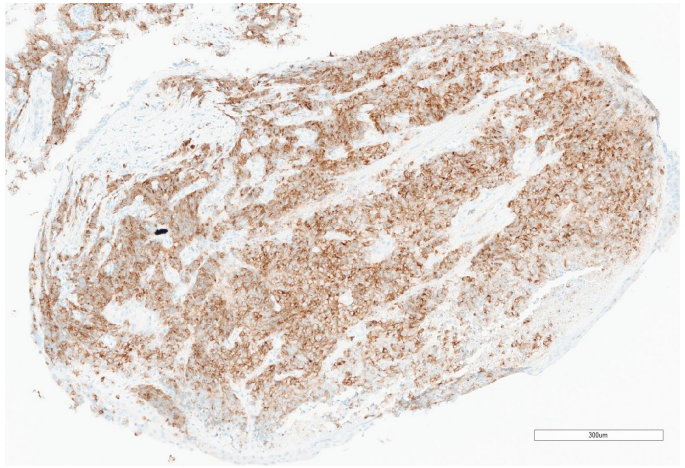
- Lung tumor tissue is 99% DLL3 positive (brown)

**At Month 4/5**

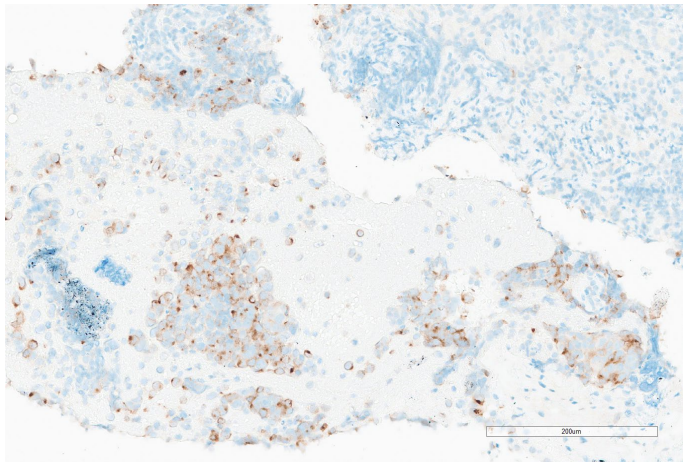
- Subject had PR (CT scan) at 4 months with negative PET result at 5 months

**At Month 8**

- Subject developed a new lesion in right adrenal gland
- 94% of new tumor lesion is DLL3-positive (brown)

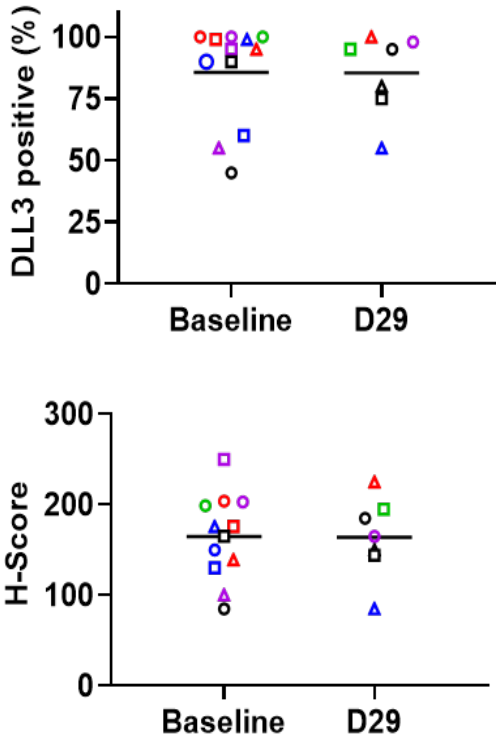


Scale bar 300 μm



Scale bar 200 μm

## No Difference in Mean DLL3 Expression Before and After LB2102




- DLL3 expression was evaluable in tumor tissues from 80% (12 of 15) subjects in the LB2102-1001 study at **baseline** and 54% (7 of 13) LB2102-treated subjects at **Day 29.**
- Mean DLL3 expression and H-score were 86% and 165 at **baseline** and 85% and 164 at **Day 29**

Note: data for 1 patient (red triangle) is from Day 65 because no Day 29 biopsy was available

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# Conclusions

- LB2102 demonstrated **favorable safety profile** with no DLTs, ICANS or other safety signal up to DL5 (8.0 x $10^6$ cells/kg)
- TEAEs were mainly **cytopenias,** co-related to lymphodepletion
- **Only 2 cases of cytokine-release syndrome (both Grade 1) were reported**
- Early signal for efficacy with partial responses starting at DL3.
  - **At DL3 or above, the overall respose rate (ORR) was 22.2% and the disease control rate (DCR) was 88.9%;** across all DLs the ORR was 13.3% and DCR was 73.3%.
- Additionally, 1 subject treated off-protocol at DL3 also achieved **durable PR lasting 8+ months***
- High DLL3 expression persisted post-treatment
- Dose escalation is ongoing, at Dose Level 7 (16.0 x$10^6$ CAR+ T cells/kg)

*Ref: See WCLC 2025, E-poster Ref: WCLC 2025 E-poster EP.13.29 Hao et al.

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