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Results from the Phase 1 study of LB2102, a dnTGFBR2-armored, DLL3-targeted autologous CAR-T cell therapy, in patients with relapsed or refractory SCLC or LCNEC

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Key Takeaway Points

LB2102 has a favorable safety profile across 6 dose levels tested in 20 heavily pretreated subjects with relapsed/refractory SCLC or LCNEC

No DLTs; CRS and ICANS are manageable

Encouraging anti-tumor activity were seen at Dose Levels ≥ 3 (2.0-16 x 10^6 CAR+ T cells/kg)

Objective Response Rate of 28.6% and Disease Control Rate of 78.6%

Responses are durable at a median 12.5 month follow up

Median Duration of Response 6.5 months, with ongoing responses

Median Duration of Disease Control 6.1 months at Dose Levels ≥ 3 , supporting further investigation

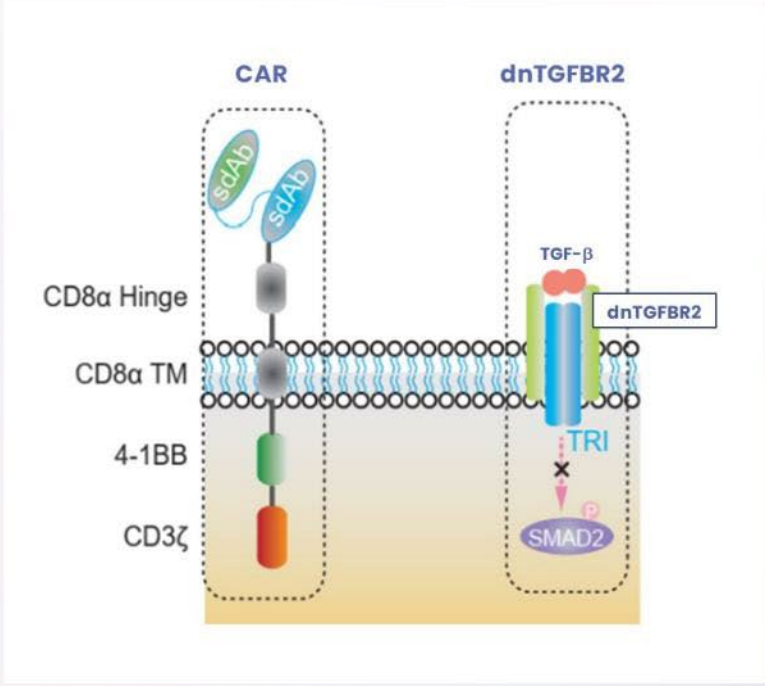
LB2102 : DLL3-targeted Autologous CAR-T Cells With dnTGFBR2 Armor

DLL3

- An inhibitory Notch ligand highly expressed on the cell surface in SCLC and other neuroendocrine tumors
- Minimal expression in normal tissues

LB2102 CAR-T Cell Design

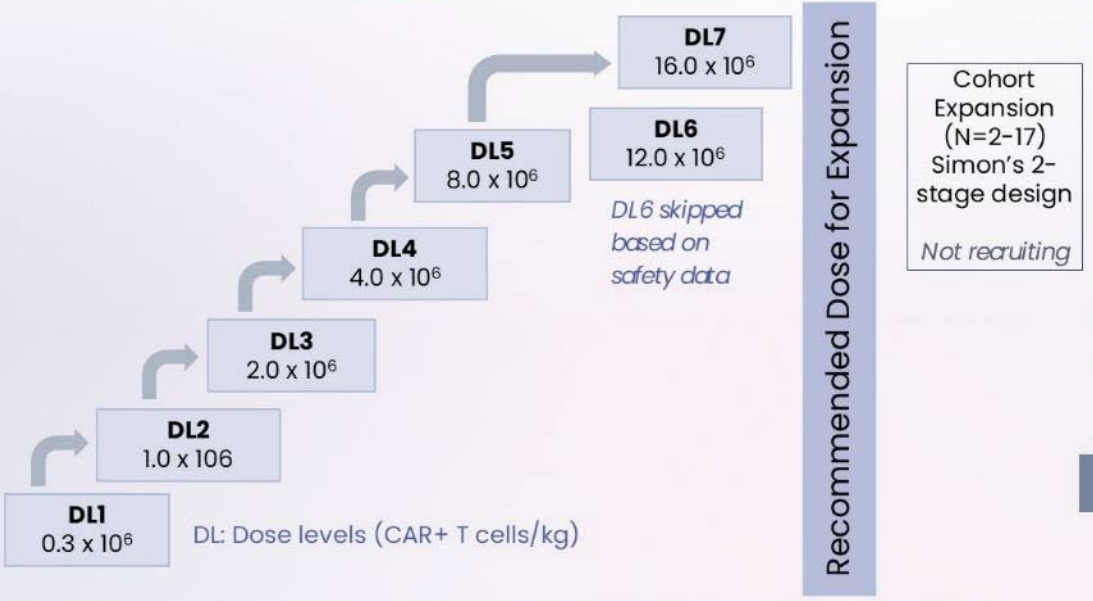
- Chimeric antigen receptor (CAR): dual single-domain antibodies (sdAb) with high-affinity binding for DLL3
- **dnTGFBR2** blocks TGF-β mediated signaling to SMAD2
- dnTGFBR2 removes the inhibitory effects of TGF-β on the CAR-T cells, leading to their increased activation, proliferation, and anti-tumor effector functions



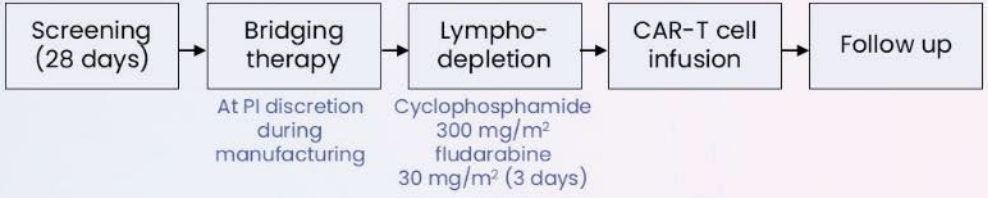
Oral abstract, **no. 339** ASCGT Congress 2026

LB2102 First-in-human Phase 1, Open Label, Multi- Center Study

Part A: Dose escalation i3+3 Design (Nmax=36)



Study Flow Diagram



Key Eligibility Criteria

- Unresectable small cell lung carcinoma (SCLC), large cell neuroendocrine lung carcinoma (LCNEC)
- ≥ 1 prior line of systemic treatment and have progressed after or have had an insufficient response
- Presence of ≥ 1 radiologically measurable lesion
- ECOG 0 or 1 and adequate organ function
- No prior CAR-T or DLL3-targeted therapy
- No symptomatic brain metastases. Subjects with treated and stable brain metastasis are allowed

Study Objectives for Part A

Primary Objective: To characterize the safety and tolerability of LB2102 and determine the recommended dose for expansion (RDE)

Secondary Objective: To evaluate the preliminary efficacy, pharmacokinetics and immunogenicity

Study Enrolled Heavily Treated Subjects with R/R SCLC or LCNEC

- The study population comprised 20 subjects with relapsed and/or refractory (R/R) SCLC or LCNEC
- Most subjects had SCLC, with extensive-stage disease at initial diagnosis
- 70% of subjects had history of brain metastases
- 95% of subjects received bridging therapy while waiting for CAR-T cell manufacturing, including brain radiation in 40% of subjects

Demographic and Disease Characteristics	Total (N=20)
Age: median (range)	56.5 (20, 73)
≥ 60 years	13 (65.0)
Sex: female	10 (50.0)
Primary tumor type	
SCLC	17 (85.0)
LCNEC	3 (15.0)
ECOG: 0	13 (65.0)
1	7 (35.0)
Disease state at initial diagnosis	
Limited	5 (25.0)
Extensive	14 (70.0)
Unknown	1 (5.0)
History of brain metastases	14 (70)
Selected sites of metastases at enrollment	
Liver	8 (40.0)
Bone	8 (40.0)
Prior systemic lines of treatment: median (range)	1.0 (1, 7)
Prior brain radiation	10 (50.0)
Lines of bridging therapy: median (range)	1 (1, 2)
Brain radiation during bridging	8 (40.0)
Follow-up (months): median (range)	12.5 (1.1, 19.5)

Note: n (%) is presented, unless otherwise stated

Safety was Manageable, No DLTs or LB2102-related Deaths

	DL1 and DL2 (N=6)	DL3 (N=3)	DL4 (N=3)	DL5 (N=3)	DL7 (N=5)	Total (N=20)
Any TEAE	6 (100)	3 (100)	3 (100)	3 (100)	5 (100)	20 (100)
Grade ≥ 3	3 (50.0)	3 (100)	3 (100)	2 (66.7)	5 (100)	16 (80.0)
Grade 5	0	0	0	0	0	0
Any TRAE	5 (83.3)	1 (33.3)	3 (100)	2 (66.7)	4 (80.0)	15 (75.0)
Grade ≥ 3*	3 (50.0)	0	2 (66.7)	0	4 (80.0)	9 (45.0)
Any Serious TEAE	2 (33.3)	1 (33.3)	2 (66.7)	1 (33.3)	2 (40.0)	8 (40.0)
Related to LB2102	0	0	1 (33.3)	0	0	1 (5.0)
Any DLT	**0**	**0**	**0**	**0**	**0**	**0**
Adverse Event of Interest	0	1 (33.3)	1 (33.3)	0	4 (80.0)	6 (30.0)
CRS, Any Grade	0	1 (33.3)	1 (33.3)	0	4 (80.0)	6 (30.0)
CRS, Grade ≥ 3	0	0	0	0	0	0
ICANS, Any Grade	0	0	0	0	3 (60.0)	3 (15.0)
ICANS, Grade ≥ 3	0	0	0	0	1 (20.0)	1 (5.0)
Infection, Grade ≥ 4	0	0	0	0	1 (20.0)	1 (5.0)

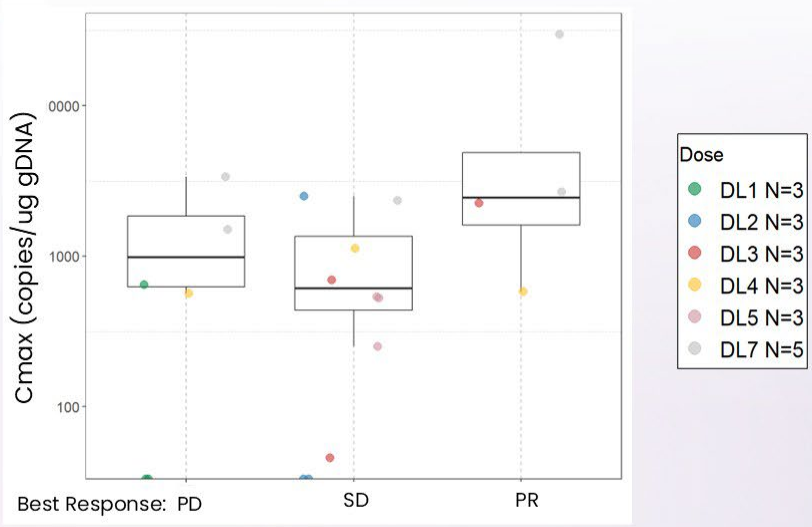
Note: n (%) with at least 1 TEAE is presented
*Grade ≥ 3 non-hematologic LB2102-related TEAEs were ICANS, AST elevation, CRP elevation, dyspnea, prolonged QT, and hypoxia (all n=1)

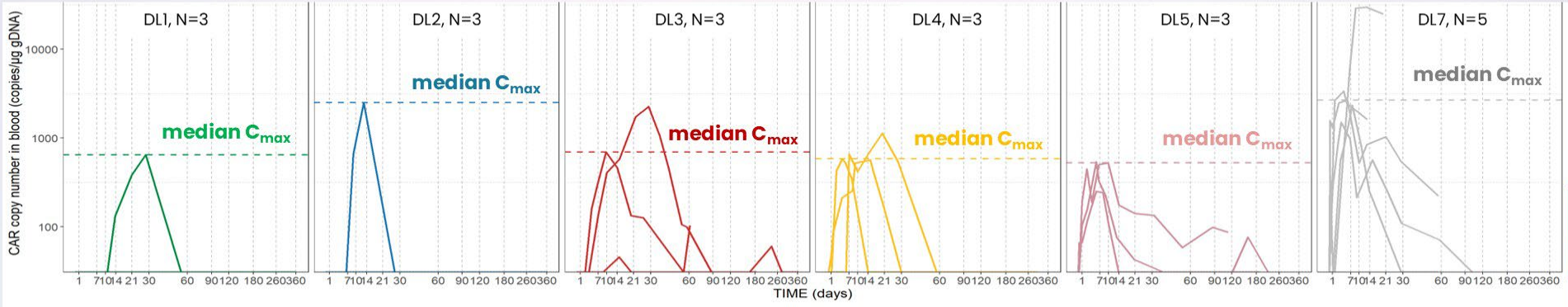
- **CRS** occurred in 6 subjects (30%) all Grade ≤ 2
- **ICANS** occurred in 3 subjects (15%): 2 Grade 1 and 1 Grade 3
- **Most-common** Grade ≥ 3 LB2102-related AEs were hematologic and co-attributed to lymphodepletion

CAR-T Cells Were Measurable in All Subjects at ≥ DL3

- PK analyses were conducted using peripheral blood samples from 20 subjects
- At DL ≥ 3 (2.0-16 x 10^6 CAR-T cells/kg)
  - Median C_{max} values were 694, 581, 527, and 2670 copies/µg gDNA
  - median T_{max} values were 15, 15, 6, and 6 days

Subjects With a PR had Higher PK Exposure

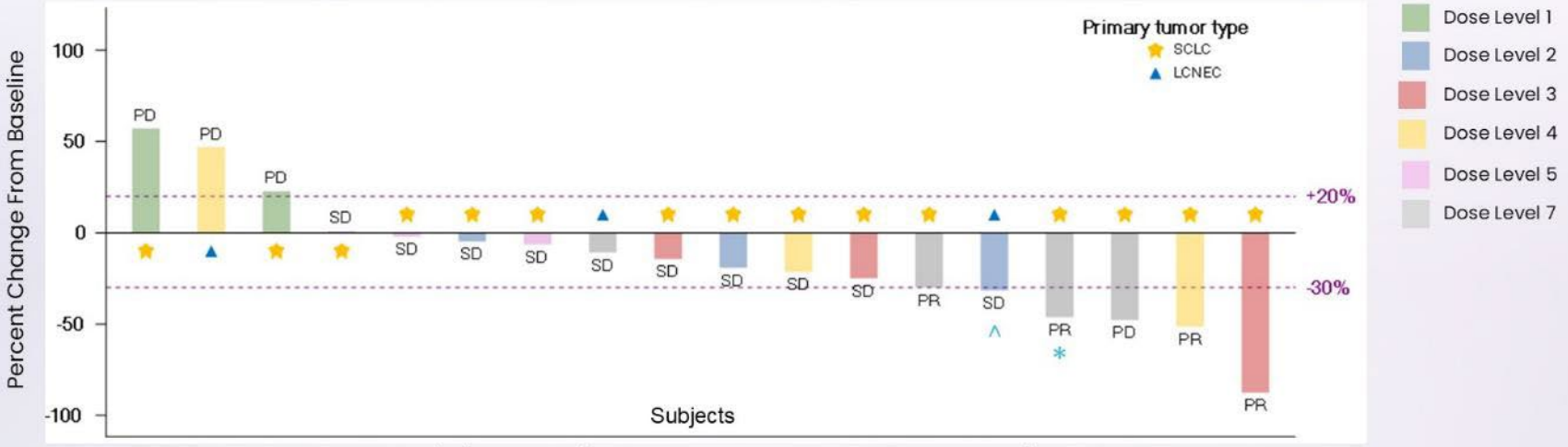




Note: Values below the LLOQ were treated as 0

At DL3 and Above, the Objective Response Rate (ORR) is 28.6% Disease Control Rate (DCR) is 78.6%

Best Responses (per RECIST 1.1)



Note: 2 subjects with progressing disease (PD) not shown (1 non-measurable at baseline; 1 missing TL data) but included in ORR

^ SD as best response; target lesion reduced by 32% but PD due to new lesion

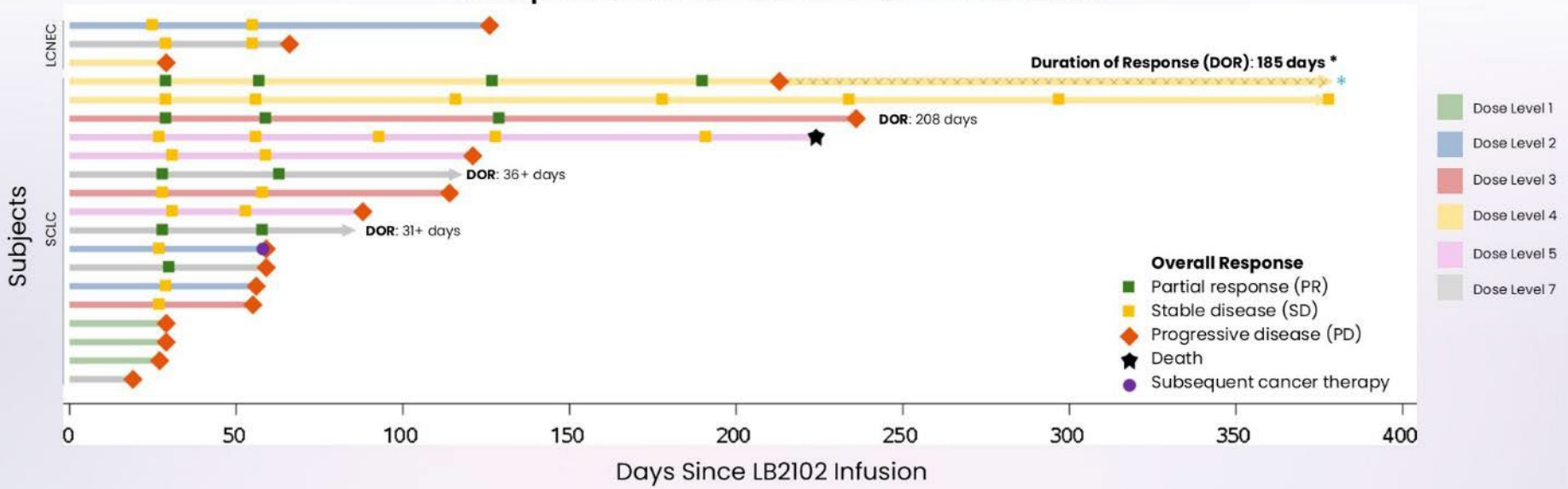
* Unconfirmed PR, tumor lesion reduced by 48%; PD at confirmation

Best Responses Across Dose Levels

	DL1 [N=3] n (%)	DL2 [N=3] n (%)	DL3 [N=3] n (%)	DL4 [N=3] n (%)	DL5 [N=3] n (%)	DL7 [N=5] n (%)	Overall [N=20] n (%)
ORR (PR)	0	0	1 (33.3)	1 (33.3)	0	2 (40.0)	4 (20.0)
DCR (PR+SD)	0	3 (100)	3 (100)	2 (66.7)	3 (100)	3 (60.0)	14 (70.0)

DL, dose level; PR, partial response; SD, stable disease

Responses to LB2101 are Durable

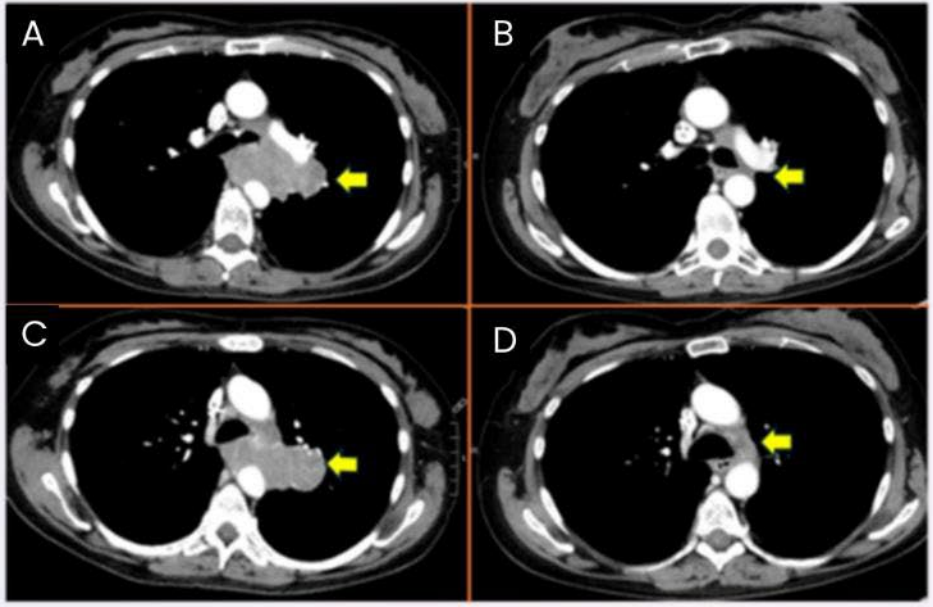


* PD driven by brain metastases and managed with SBRT; no subsequent systemic antineoplastic therapy (cross-hatched part of arrow)

- Data cut-off April 13 (median follow up 12.5 mo; range 1.1-19.5 mo): median **DOR was 6.5 mo** (95% CI, 6.1-NR), ongoing response in 2 subjects
- **At ≥DL3** (median follow up 9.5 mo; range, 1.1-17.6 mo):
  - Median **duration of disease control was 6.1 mo** (95% CI, 1.3-6.8 mo)
  - DCR was 51.9% at 6 mo and 13.0% at 9 mo

Durable PR in a Subject with Refractory SCLC Treated Off-protocol with LB2102

Before LB2102 Infusion Month 12 After Infusion



Mass reduced 80% in size in 1 year (yellow arrow)
Subject had PR per RECIST1.1 criteria

One subject treated off-protocol at DL3 achieved durable PR
(ongoing at 12 mo; data not included in this trial)

Durable ~80% tumor reduction with symptom resolution and sustained ECOG 0 without ongoing cancer therapy

WCLC 2025, LB2102 E-poster EP.13.29 Hao et al

Conclusions

DLL3-targeted CAR-T LB2102 has a favorable safety profile: Phase 1 study (n=20) in patients with R/R SCLC and LCNEC demonstrated no DLTs, with manageable CRS and ICANS

Encouraging anti-tumor activity: at DL ≥ 3, ORR of 28.6% and a DCR of 78.6%

Responses are durable: median DOR 6.5 mo with ongoing responses and median duration of disease control 6.1 mo at DL ≥ 3, supporting sustained clinical benefit

These findings support continued study of DLL3-targeted CAR-T cells in patients with SCLC and LCNEC

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