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HLX43 First-in-human Study Data Readout

Presenter Dr. Qingyu Wang, General Manager of Clinical Development & China CMO

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Sponsor Shanghai Henlius Biotech, Inc

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HLX43-FIH101 Study Design

cutoff date 2025/03/28

<u>Key inclusion criteria</u>

- $ J H • \ H D U V
- ECOG PS 0 or 1.
- For **phase 1a**, histologically or cytologically confirmed advanced/metastatic malignant **solid tumors**.
- For **phase 1b**, histologically or cytologically confirmed advanced/metastatic **NSCLC** refractory or not amenable to standard therapy.
- Measurable disease according to RECIST v1.1.

Screening

Phase 1a: solid tumor

- **4.0 mg/kg Q3W** N=3-6
- **3.0 mg/kg Q3W** N=3-6
- **2.5 mg/kg Q3W** N=3-6
- **2.0 mg/kg Q3W** N=3-6
- **1.0 mg/kg Q3W** N=3-6
- **0.5 mg/kg Q3W** N=3-6

CN only, 7 sites

Phase 1b: NSCLC

- **3.0 mg/kg Q3W** NSCLC, N=21
- **2.5 mg/kg Q3W** NSCLC, N=22
- **2.0 mg/kg Q3W** NSCLC, N=21

CN only, 14 sites

Leading Principle Investigator:

Dr. Jie Wang

Director of Medical Oncology Department, Cancer Hospital Chinese Academy of Medical Sciences

Tenured Professor at Peking Union Medical College

President of the Shanxi Cancer Hospital

Leading Site: Cancer Hospital Chinese Academy of Medical Sciences

CN, China; ECOG PS, Eastern Cooperative Oncology Group performance status; NSCLC, non-small cell lung cancer; Q3W, every 3 weeks; RECIST, Response Evaluation Criteria in Solid Tumors.

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HLX43 Ph 1a Dose Escalation Efficacy Data

cutoff date 2025/03/28

Median follow-up duration: 9.7 months

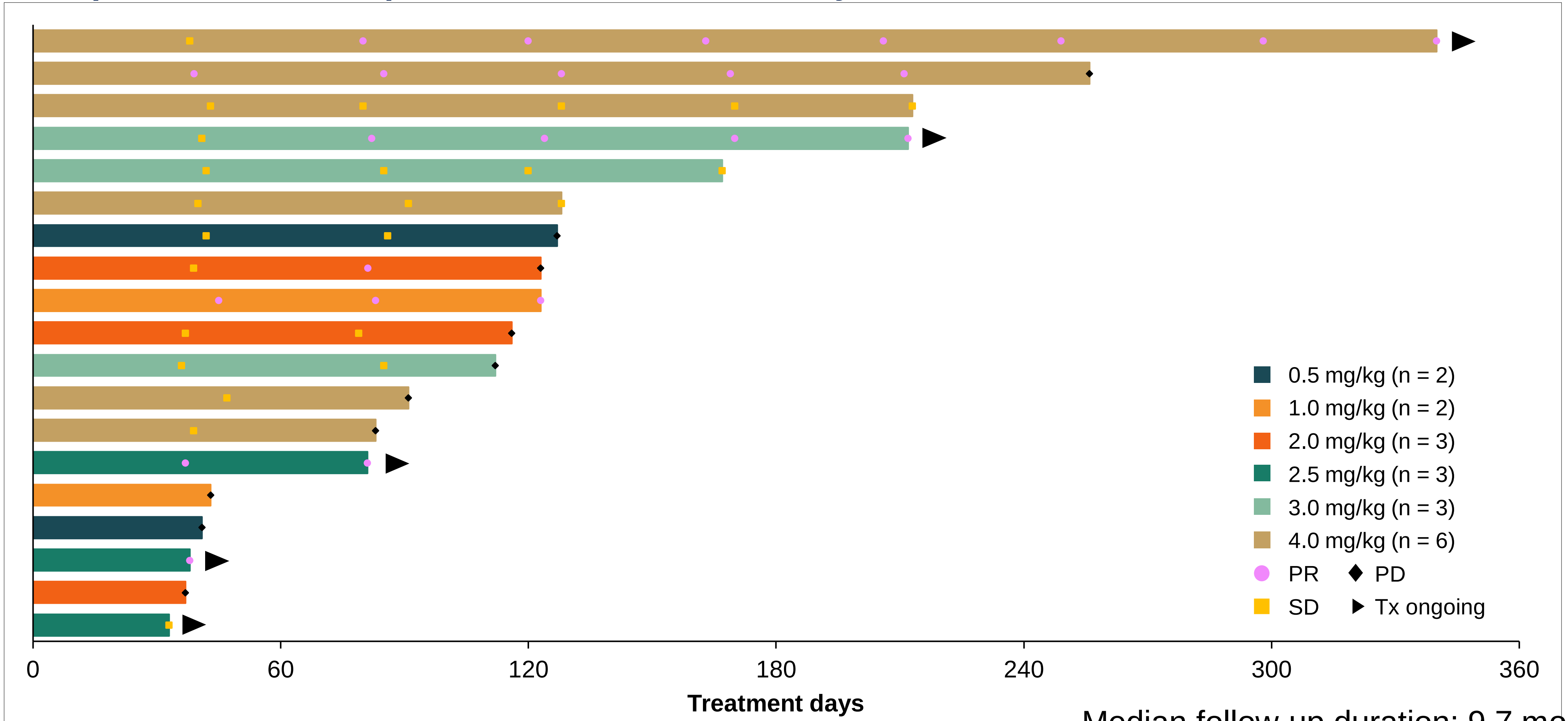
Tumor response per RECIST v1.1[a]	Phase 1a (n = 19)
CR, n (%)	0
PR, n (%)	7 (36.8)
SD, n (%)	7 (36.8)
PD, n (%)	4 (21.1)
NE, n (%)	1 (5.3)
ORR, % (95% CI)	36.8 (16.3–61.6)
DCR, % (95% CI)	73.7 (48.8–90.9)
mDOR, months (95% CI)	7.2 (1.4–NE)
mPFS, months (95% CI)	4.2 (2.7–8.4)
mOS, months (95% CI)	8.9 (6.0–NE)

[a] Unconfirmed tumor response assessed by investigator in the 19 efficacy-evaluable patients; 2 patients did not have post-baseline tumor assessment.
CI, confidence interval; CR, complete response; DCR, disease control rate; mDOR, median duration of response; mPFS, median progression-free survival; mOS, median overall survival; NE, not evaluable; ORR, objective response rate; PD, progressive disease; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease.

HLX43 Ph 1a Dose Escalation Efficacy Data

cutoff date 2025/03/28

Swimmer plot of time to response and duration of study treatment[a]



Median follow-up duration: 9.7 months

[a] In the 19 efficacy-evaluable patients; 2 patients did not have post-baseline tumor assessment.
PD, progressive disease; PR, partial response; SD, stable disease; Tx, treatment.

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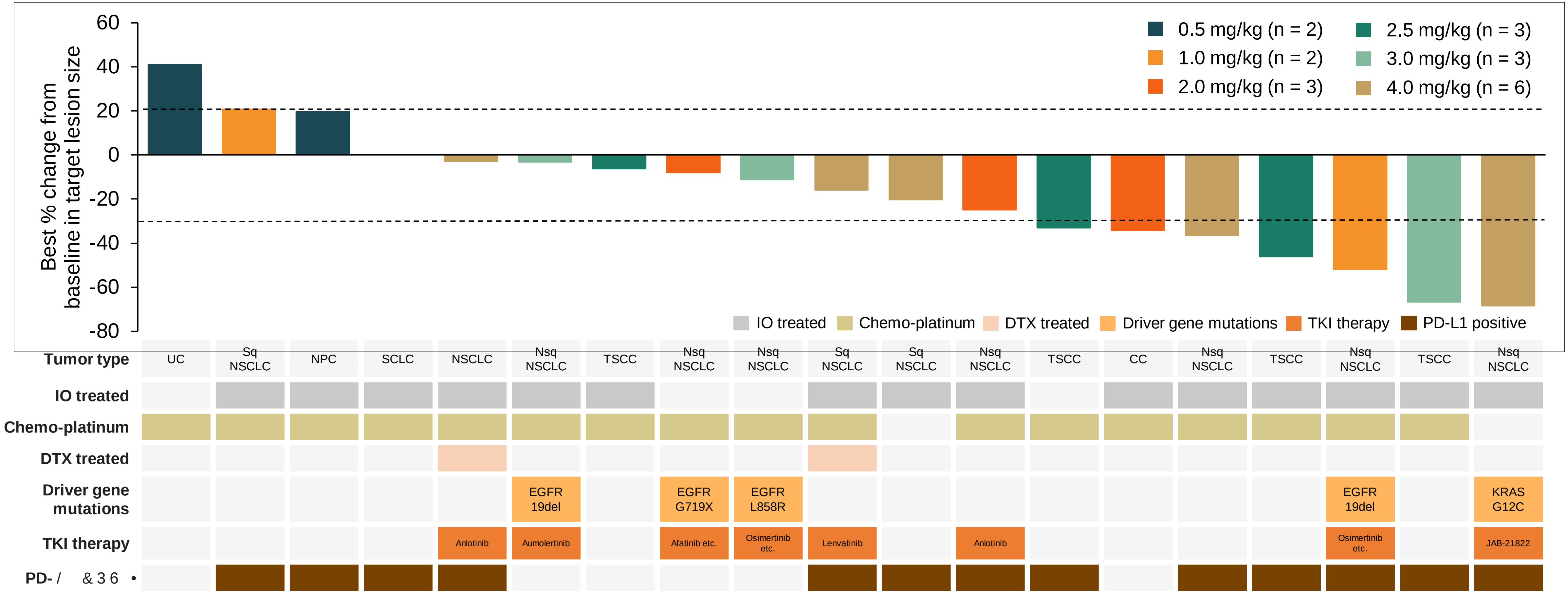
HLX43 Ph 1a Dose Escalation Efficacy Data

cutoff date 2025/03/28

Best percentage change from baseline in target lesion size[a]

Median follow-up duration: 9.7 months



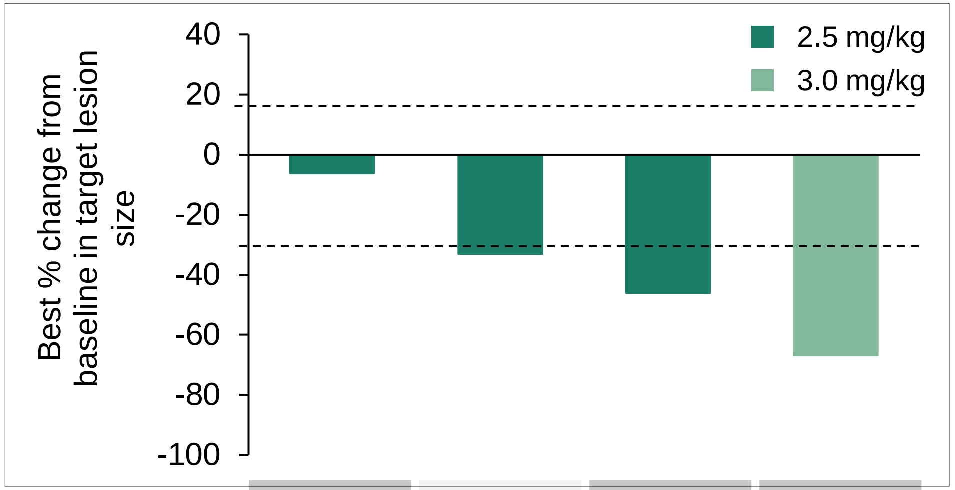
[a] In the 19 efficacy-evaluable patients; 2 patients did not have post-baseline tumor assessment.

CC, cervical carcinoma; chemo, chemotherapy; CPS, combined positive score; DTX, docetaxel; EGFR, epidermal growth factor receptor; IO, immunotherapy; KRAS, Kirsten rat sarcoma viral oncogene homolog; NPC, nasopharyngeal cancer; NSCLC, non-small cell lung cancer; nsqNSCLC, nonsquamous NSCLC; PD-L1, programmed death-ligand 1; SCLC, small cell lung cancer; sqNSCLC, squamous NSCLC; TSCC, thymic squamous cell carcinoma; UC, uterine carcinosarcoma.

HLX43 Ph 1a Efficacy Data in TSCC

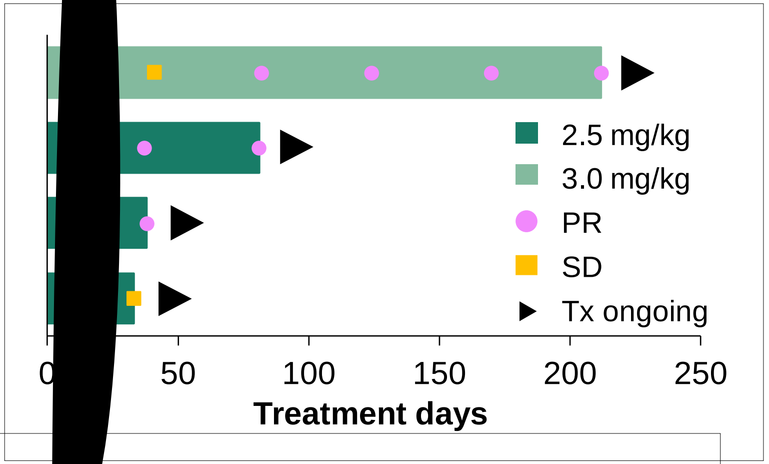
cutoff date 2025/03/28

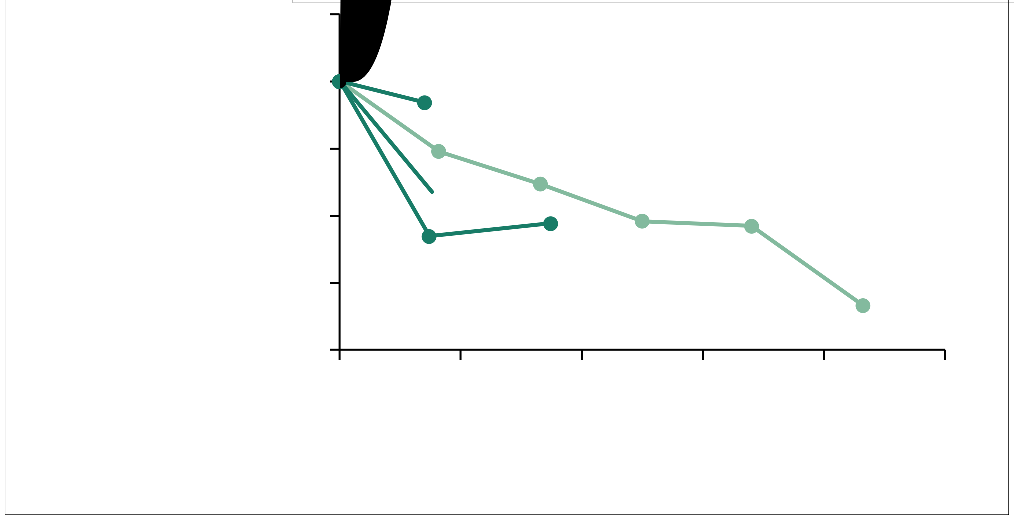
TSCC: ORR 75% (3/4)



IO Treated				
Chemo-Platinum treated				
PD-L1 CPS •1				
Prior lines	1	1	3	6

IO Treated | Chemo-Platinum Treated | PD-L1 Positive





[a] Unconfirmed tumor response assessed by investigator in the 19 efficacy-evaluable patients; 2 patients did not have post-baseline tumor assessment.
CPS, combined positive score; IO, immunotherapy; ORR, objective response rate; PD-L1, programmed death-ligand 1; TSCC, thymic squamous cell carcinoma.

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HLX43 Ph 1a Dose Escalation Safety Data
cutoff date 2025/03/28

Median follow-up duration: 9.7 months

Summary of adverse events, n (%)	**Phase 1a (n = 21)**
Any TEAE*	21 (100)
• * U D 3G H	10 (47.6)
• * U D G H •	
Neutrophil count decreased	5 (23.8)
White blood cell count decreased	5 (23.8)
Anemia	3 (14.3)
Pneumonia	3 (14.3)
Serious	10 (47.6)
Any TRAE	20 (95.2)
• * U D 3G H	6 (28.6)
TEAE leading to Tx interruption	9 (42.9)
TEAE leading to Tx discontinuation	4 (19.0)
TEAE leading to dose reduction	8 (38.1)
TEAE leading to death	4 (19.0)

0 R V W F R P P R Q 7 ($ (V • Q	**Phase 1a (n = 21)**
Anemia	16 (76.2)
Interleukin level increased	13 (61.9)
White blood cell count decreased	11 (52.4)
Neutrophil count decreased	10 (47.6)
Hyponatremia	10 (47.6)
Nausea	9 (42.9)
Hypoalbuminemia	9 (42.9)
Hyperuricemia	8 (38.1)
Aspartate aminotransferase increased	5 (23.8)
Lymphocyte count decreased	5 (23.8)
Hypochloremia	5 (23.8)

* No infusion-related reaction was reported in this study.

TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event; Tx, treatment.

DLT: One patient in the 4 mg/kg dose group in phase 1a experienced DLTs of febrile neutropenia and decreased white blood cell count; MTD was 4 mg/kg.

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HLX43-[illegible]

CN, China; ECOG PS, Eastern Cooperative Oncology Group performance status; NSCLC, non-small cell lung cancer; Q3W, every 3 weeks; RECIST, Response Evaluation Criteria in Solid Tumors.

HLX43 Ph 1b Dose Expansion – Patient Demographics and Baseline Characteristics

cutoff date 2025/03/28

Median follow-up duration: 7.0 months

n (%)	Phase 1b 2.0 mg/kg (n = 21)
Median age (range), years	56 (39–73)
Male	14 (66.7)
ECOG PS	
0	5 (23.8)
1	16 (76.2)
Prior anti-cancer therapy*	
Chemotherapy+immunotherapy	16 (76.2)
Chemotherapy	11 (52.4)
Target therapy	9 (42.9)
Immunotherapy	5 (23.8)
Prior lines of therapy	
1	7 (33.3)
2	1 (4.8)
3	6 (28.6)
•	7 (33.3)
Median (range)	**3.0 (1–7)**

n (%)	Phase 1b 2.0 mg/kg (n = 21)
NSCLC subtype	
Squamous	15 (71.4)
EGFR wild type	100%
Nonsquamous	6 (28.6)
EGFR wild type	100%
Used docetaxel	
Yes	9 (42.9)
No	12 (57.1)
Brain metastasis	
Yes	6 (28.6)
No	15 (71.4)
Liver metastasis	
Yes	3 (14.3)
No	18 (85.7)
PD-L1 expression level**	
& 3 6 •	16 (76.2)
CPS < 1	5 (23.8)

* Patients all received platinum-based treatment previously; ** Detected with SP263.

CPS, combined positive score; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; NSCLC, non-small cell lung cancer; PD-L1, programmed death-ligand 1.

HLX43 Ph 1b 2.0mg/kg Efficacy Data

cutoff date 2025/03/28

Median follow-up duration: 7.0 months

Tumor response per RECIST v1.1[a]	Phase 1b 2.0 mg/kg (n = 21)
CR, n (%)	0
PR, n (%)	8 (38.1)
SD, n (%)	9 (42.9)
PD, n (%)	4 (19.0)
NE, n (%)	0
ORR, % (95% CI)	38.1 (18.1–61.6)
Confirmed ORR, % (95% CI)	33.3 (14.6–57.0)
2 5 5 L Q S D W L H Q W V Z K R K D G • S U L R U lines of therapy, %	38.5 (5/13)
DCR, % (95% CI)	81.0 (58.1–94.6)
mDOR, months (95% CI)	NR (1.4–NE)
mPFS, months (95% CI)	5.4 (4.0–6.3)
mOS, months (95% CI)	NR (6.7–NE)

Subgroup analysis of tumor response per RECIST v1.1[a]	ORR % (95% CI)	DCR % (95% CI)
NSCLC subtype		
Squamous (n = 15)	40.0 (16.3–67.7)	73.3 (44.9–92.2)
Confirmed response	33.3 (11.8–61.6)	73.3 (44.9–92.2)
Nonsquamous (n = 6)	33.3 (4.3–77.7)	100 (54.1–100)
Confirmed response	33.3 (4.3–77.7)	100 (54.1–100)
Used docetaxel		
Yes (n = 9)	33.3 (7.5–70.1)	77.8 (40.0–97.2)
No (n = 12)	41.7 (15.2–72.3)	83.3 (51.6–97.9)
Brain metastasis		
Yes (n = 6)	33.3 (4.3–77.7)	100 (54.1–100)
No (n = 15)	40.0 (16.3–67.7)	73.3 (44.9–92.2)
Liver metastasis		
Yes (n = 3)	33.3 (0.8–90.6)	66.7 (9.4–99.2)
No (n = 18)	38.9 (17.3–64.3)	83.3 (58.6–96.4)
PD-L1 expression		
& 3 6 • Q	37.5 (15.2–64.6)	81.3 (54.4–96.0)
CPS < 1 (n = 5)	40.0 (5.3–85.3)	80.0 (28.4–99.5)

[a] Unconfirmed tumor response assessed by investigator.

CI, confidence interval; CPS, combined positive score; CR, complete response; DCR, disease control rate; mDOR, median duration of response; mPFS, median progression-free survival; mOS, median overall survival; NE, not evaluable; NR, not reached; NSCLC, non-small cell lung cancer; ORR, objective response rate; PD, progressive disease; PD-L1, programmed death-ligand 1; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease.

HLX43 Ph 1b 2.0mg/kg Efficacy Data

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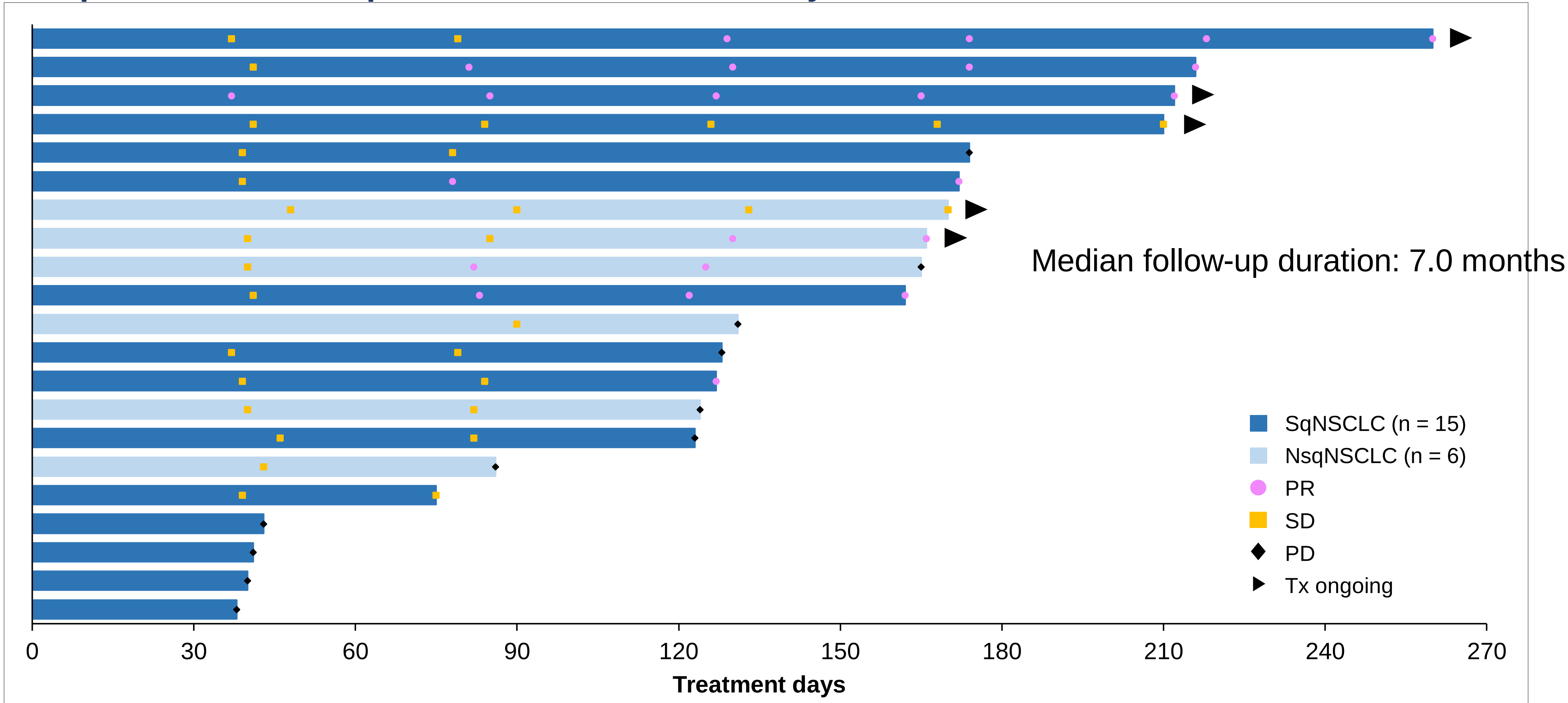
Swimmer plot of time to response and duration of study treatment[a]



[a] In efficacy-evaluable patients.

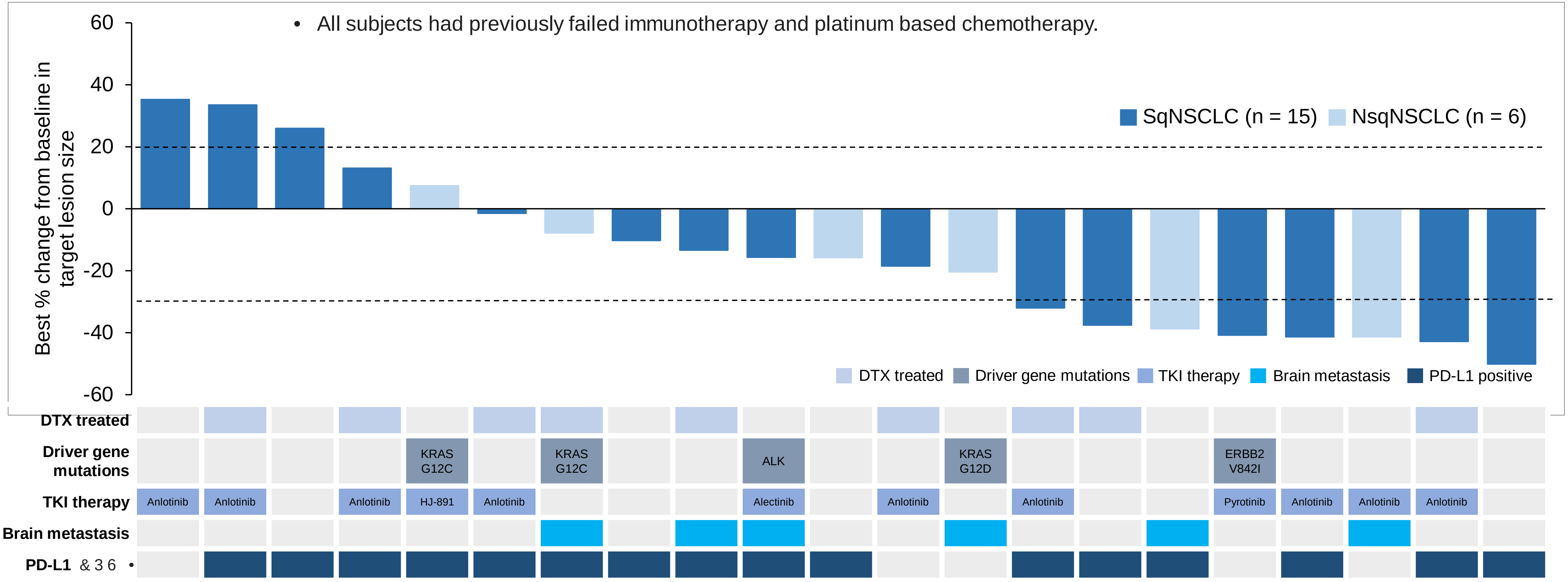
NsqNSCLC, nonsquamous non-small cell lung cancer; PD, progressive disease; PR, partial response; SD, stable disease; sqNSCLC, squamous non-small cell lung cancer; Tx, treatment.

HLX43 Ph 1b 2.0mg/kg — 100% DCR in Patients with Brain Metastasis

cutoff date 2025/03/28

Best percentage change from baseline in target lesion size[a]

Median follow-up duration: 7.0 months



[a] In efficacy-evaluable patients.

ALK, anaplastic lymphoma kinase; CPS, combined positive score; DTX, docetaxel; ERBB2, Erb-B2 receptor tyrosine kinase; KRAS, Kirsten rat sarcoma viral oncogene homolog; NSCLC, non-small cell lung cancer; nsqNSCLC, nonsquamous NSCLC; PD-L1, programmed death-ligand 1; sqNSCLC, squamous NSCLC; TKI, tyrosine kinase inhibitor.

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HLX43 Ph 1b 2.0mg/kg Safety Data

cutoff date 2025/03/28

Median follow-up duration: 7.0 months

Summary of adverse events, n (%)	**Phase 1b 2.0 mg/kg (n = 21)**
Any TEAE*	21 (100)
• * U D G H 3**	11 (52.4)
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Anemia	3 (14.3)
Lymphocyte count decreased	3 (14.3)
Serious	11 (52.4)
Any TRAE	21 (100)
• * U D G H 3	9 (42.9)
TEAE leading to Tx interruption	10 (47.6)
TEAE leading to Tx discontinuation	2 (9.5)
TEAE leading to dose reduction	0
TEAE leading to death	3 (14.3)

0 R V W F R P P R Q 7 ($ (V **n (%)**	**Phase 1b 2.0 mg/kg (n = 21)**
Anemia	16 (76.2)
Decreased appetite	12 (57.1)
Nausea	11 (52.4)
Hypoalbuminemia	8 (38.1)
Neutrophil count decreased	8 (38.1)
White blood cell count decreased	8 (38.1)
Constipation	7 (33.3)
Hyponatremia	7 (33.3)
Vomiting	7 (33.3)
Alanine aminotransferase increased	6 (28.6)
Aspartate aminotransferase increased	6 (28.6)
Interleukin level increased	6 (28.6)
Hypertriglyceridemia	6 (28.6)
Lymphocyte count decreased	6 (28.6)
Hypochloremia	5 (23.8)
Pneumonia	5 (23.8)
Proteinuria	5 (23.8)
Weight decreased	5 (23.8)

* No infusion-related reaction was reported in this study.

** No Grade 3 or higher platelet count decreased was reported; only 3 patients (14.3%, 3/21) experienced Grade 1 platelet count decreased.

TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event; Tx, treatment.

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Conclusion: First Clinical-stage, Biomarker-independent ADC with IO Activity

A

Broad Therapeutic Effects

B

C

Potential of HLX43

HLX43 is an ADC with the potential for comprehensive coverage of cancer treatment and immunotherapy functionality.

Future Plans

HLX43 development in multiple tumor types and the exploration of various combination therapies, including combining it with serplulimab

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Thanks `

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