2. SYNOPSIS

<table>
<tr><td>Name of Sponsor/Company:
Shanghai Henlius Biotech, Inc.</td><td rowspan="3">Individual Study Table Referring to Part of The Dossier:
Volume:
Page:</td><td rowspan="3">(For national authority use only)</td></tr>
<tr><td>Name of Finished Product:
HLX10 (or serplulimab, hereafter referred as HLX10)</td></tr>
<tr><td>Name of Active Ingredient:
HLX10 (Recombinant humanized anti-PD-1 monoclonal antibody)</td></tr>
<tr><td colspan="3">Title of Study:
A Randomized, Double-Blind, Multicenter, Phase III Study to Compare Clinical Efficacy and Safety of HLX10 (Recombinant Humanized Anti-PD-1 Monoclonal Antibody Injection) in Combination with Chemotherapy (Carboplatin-Etoposide) in Previously Untreated Patients with Extensive Stage Small Cell Lung Cancer (ES-SCLC)</td></tr>
<tr><td colspan="3">Principal Investigator:
The global coordinating investigator is Professor Ying Cheng, Department of Oncology, Jilin Province Cancer Hospital, Changchun City, Jilin Province, China.
A list of principal investigators is provided in Appendix 16.1.4.</td></tr>
<tr><td colspan="3">Study Centers:
In this study, sites in eight countries: China, Russia, Ukraine, Poland, Turkey, Georgia, the United States, and Bulgaria were initiated. Subjects were screened from 114 sites across six countries, including China, Russia, Ukraine, Poland, Turkey, Georgia.
A list of study sites is provided in Appendix 16.1.4.</td></tr>
<tr><td colspan="3">Publications (reference):
Cheng Y, Han L, Wu L, et al. Effect of First-Line Serplulimab vs Placebo Added to Chemotherapy on Survival in Patients With Extensive-Stage Small Cell Lung Cancer: The ASTRUM-005 Randomized Clinical Trial. JAMA. 2022;328(12):1223–1232.</td></tr>
<tr><td colspan="2">Studied Period (years):
First patient enrolled date: September 12, 2019
Last patient enrolled date: April 27, 2021</td><td>Phase of Development: III</td></tr>
</table>

Data analysis cutoff date: May 7, 2024 Database lock date: August 16, 2024	

Objectives:

Primary:

- To compare the clinical efficacy of HLX10 in combination with chemotherapy versus placebo in combination with chemotherapy in previously untreated patients with extensive stage small cell lung cancer (ES-SCLC).

Secondary:

- To compare the safety and tolerability of HLX10 in combination with chemotherapy versus placebo in combination with chemotherapy in previously untreated patients with ES-SCLC and evaluate pharmacokinetics (PK), immunogenicity, and biomarkers.

Exploratory:

- CCI [redacted]
  CCI [redacted]

Methodology:

This was a randomized, double-blind, placebo-controlled, multicenter, Phase III study to compare the clinical efficacy, safety, and tolerability of HLX10 (recombinant humanized anti-PD-1 monoclonal antibody injection) with placebo in combination with chemotherapy in patients with previously untreated ES-SCLC, to obtain PK parameters and to investigate the biomarker related to efficacy.

Subjects in this study were randomized to treatment Arm A or B at a 2:1 ratio as follows:

- Arm A (HLX10): HLX10 + chemotherapy (carboplatin-etoposide)
- Arm B (control): placebo + chemotherapy (carboplatin-etoposide)

Randomization was stratified by PD-L1 expression level (negative: tumor proportion scores [TPS] < 1%, positive: TPS ≥ 1%, or not evaluable/not available), brain metastasis (yes versus no), and age (≥ 65 years versus < 65 years).

After screening, subjects who met the inclusion criteria and did not meet any of the exclusion criteria were enrolled. Included subjects were treated with HLX10 or placebo in combination with chemotherapy once every 3 weeks, until disease progression, death, intolerable toxicity, withdrawal of informed consent, or occurrence of other reasons specified in the protocol (whichever occurred first).

Initial treatment was to be discontinued when the subject had evidence of disease progression as assessed per RECIST 1.1. If a subject had the first disease progression and was clinically stable, and intended to receive second-line chemotherapy treatment subsequently (the selection of second-line chemotherapy may refer to the NCCN guidelines or the European Society for

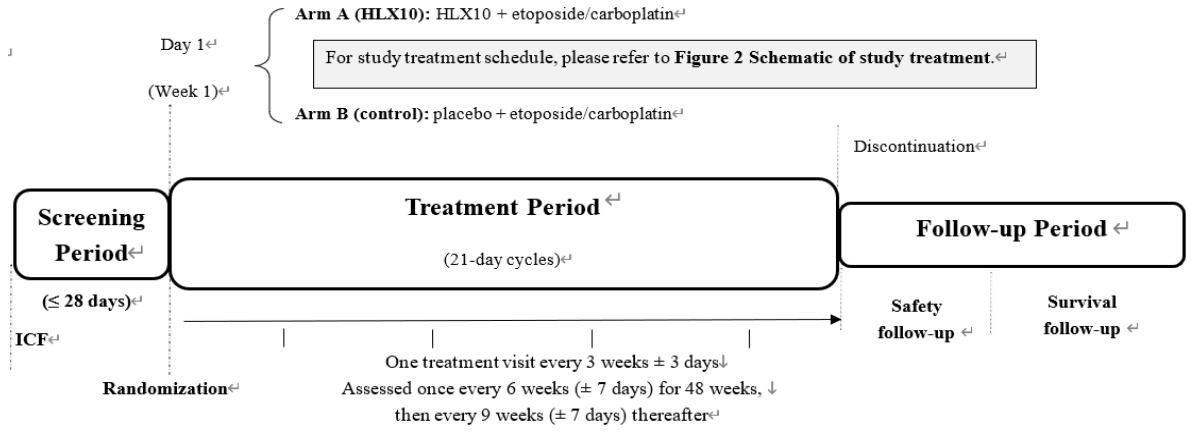
Medical Oncology [ESMO] guidelines), it was at the discretion of the investigator to continue treating the subject with blinded HLX10 or placebo assignment per protocol in addition to the second-line chemotherapy, until the second disease progression, intolerable toxicity, death, withdrawal of consent, or lost to follow-up. Subjects who permanently discontinued initial treatment due to an AE, withdrawal of consent, or for any reason other than disease progression, would not be eligible for the post-progressive disease (PD) treatment.

Subjects who met the following conditions could continue the treatment after appropriate discussion with the subject and obtaining the supplementary informed consent.

1. Subjects who had received HLX10 or placebo in combination with chemotherapy, who might benefit from continuing HLX10/placebo treatment despite progression, could be able to receive HLX10 or placebo therapy in the post-PD treatment.
2. Subjects eligible for continued treatment in the post-PD treatment period, as judged by the investigator.
3. The subject was requested to sign the supplementary informed consent form to receive investigational product with second-line chemotherapy.
4. The subject was clinically stable, defined as:
    a. No clinical signs and/or symptoms (including worsening of laboratory findings) that might indicate disease progression.
    b. A stable Eastern Cooperative Oncology Group (ECOG) performance status score.
    c. No rapid disease progression or tumor progression requiring urgent alternative medical intervention at critical anatomical sites (e.g., spinal cord compression).

The primary endpoint of this study was to compare the OS of HLX10 in combination with chemotherapy versus placebo in combination with chemotherapy.

Overall Study Design Schematics



Stratification factors:

- PD-L1 expression level (negative: TPS <1%, positive: TPS ≥1%, or not evaluable/not available)
- Brain metastasis (yes versus no)
- Age (≥ 65 years versus < 65 years)

TPS = Tumor Proportion Scores.

Screening period: The maximum screening period is 28 days.
Treatment period: Including initial treatment and post-PD treatment (optional)
After finishing the initial treatment period, patients in both arms who had 1st disease progression per RECIST 1.1 and might benefit from their assigned treatment in addition to 2nd line chemotherapy, may be eligible to continue to receive their assigned treatment in the post-PD treatment period (optional) until the 2nd disease progression, intolerable toxicity, death, withdrawal of consent, or lost to follow-up.
Safety follow-up period: 90 days after the last study drug administration. Safety visit is required at the site 30 days (±7 days) after the last study drug administration, and telephone follow-up is required 90 days (±7 days) after the last study drug administration.
Survival follow-up period: Every 12 weeks ± 7 days.

Number of Patients (Planned and Analyzed):

Planned: 567 (HLX10+carboplatin/etoposide group =378; placebo + carboplatin/etoposide group=189)

Analyzed: 585 (HLX10+carboplatin/etoposide group =389; placebo + carboplatin/etoposide group=196)

Inclusion and Exclusion Criteria:

Inclusion Criteria:

1. Voluntary participation in clinical studies; fully understood and was informed about the study, and had signed the informed consent form (ICF); willingness to follow and ability to complete all trial procedures.
2. Male or female aged ≥ 18 years at the time of signing the ICF.
3. Histologically or cytologically diagnosed with ES-SCLC (according to the Veterans Administration Lung Study Group [VALG] staging system).
4. No prior systemic therapy for ES-SCLC (including systemic chemotherapy, molecular targeted therapy, biological therapy, and other investigational therapies).
5. Patients who had received chemoradiotherapy for previous limited stage SCLC had to have been treated with curative intent and had had a treatment-free interval of at least 6 months

from the last course of chemotherapy, radiotherapy, or chemoradiotherapy to the diagnosis of extensive stage SCLC.

6. At least one measurable lesion as assessed by IRRC according to RECIST 1.1 within 4 weeks prior to randomization.

   Note: Measurable lesions were not from previously irradiated sites. If a lesion at the previously irradiated site was the only selectable target lesion, a radiological assessment showing significant progression of the irradiated lesion had to have been provided by the investigator.

7. Patients had to provide tumor tissues that met the requirements for the determination of PD-L1 expression levels. Patients were assessed for an evaluable PD-L1 expression category (negative: TPS < 1%, positive: TPS ≥ 1%, or not evaluable/not available) by the central laboratory for randomization.

   Note: It was recommended to provide formalin-fixed tumor tissue samples, paraffin-embedded tumor specimens (preferred), formalin-fixed paraffin embedded (FFPE), tumor specimens or newly prepared unstained serial tissue sections (preferably adhesive slides) within 6 months prior to the first dose of study medication. A relevant pathology report also had to be provided for the above specimens. Freshly collected specimens, radical resections, core needle biopsy, excisions, incisions, punch or clamp biopsies were acceptable (newly obtained tissues are preferred). Fine-needle aspirations (i.e., samples that lacked a complete tissue structure and provided only cell suspension and/or cell smear), brush biopsies, and cell pellet samples from pleural or peritoneal effusions were unacceptable.

8. Prior antineoplastic therapy had to have been ≥ 2 weeks from the first dose in this study with treatment-related AEs resolved to National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) Grade ≤ 1 (except for Grade 2 alopecia).

9. An Eastern Cooperative Oncology Group (ECOG) Performance Status (PS) score of 0 or 1.

10. An expected survival ≥ 12 weeks.

11. Patients with prior denosumab use who were able and willing to switch to bisphosphonate therapy for bone metastases starting prior to randomization and throughout treatment.

12. Normal major organ functions as defined by the following criteria (no blood transfusions, or treatment with albumin, recombinant human thrombopoietin or colony-stimulating factor within 14 days prior to the first dose in this study):

Hematologic system	
Absolute neutrophil count (ANC)	≥ 1.5×10^9/L
Lymphocyte	≥ 0.5×10^9/L
Platelet (PLT)	≥ 100×10^9/L
Haemoglobin	≥ 90 g/L
Hepatic functions	

Total bilirubin	≤ 1.5×upper limit of normal (ULN); For patients with Gilbert's syndrome, total bilirubin ≤ 3×ULN is acceptable
Alanine transaminase (ALT)	≤ 2.5×ULN; ≤ 5×ULN for patients with liver metastases
Aspartic transaminase (AST)	≤ 2.5×ULN; ≤ 5×ULN for patients with liver metastases
Alkaline phosphatase (ALP)	≤ 2.5×ULN; ≤ 5.0×ULN for patients with liver or bone metastases
Renal functions	
Creatinine	≤ 1.5×ULN; In case of > 1.5×ULN, creatinine clearance ≥ 50 mL/min (calculated from Cockcroft-Gault formula)
Coagulation functions	
Activated partial thromboplastin time (APTT)	≤ 1.5×ULN
Prothrombin time or International normalized ratio (INR)	≤ 1.5×ULN
The above requirements applied only to subjects who were not receiving anticoagulant therapy; subjects who were receiving anticoagulant therapy had to maintain a stable dose of anticoagulants.	

13. Female patients had to meet one of the following conditions:
    a. Menopause (defined as no menses for at least 1 year and no confirmed cause other than menopause), or
    b. Surgically sterilized (removal of the ovaries and/or uterus), or
    c. Of child-bearing potential, but must meet the following:
        - Serum pregnancy test had to be negative within 7 days prior to randomization, and
        - Agreed to use birth control methods with an annual failure rate of < 1% or maintain abstinence (avoid heterosexual intercourse) (from the signing of ICF to at least 6 months after the final dose of study drug) (birth control methods with an annual failure rate of < 1% include bilateral tubal ligation, male sterilization, proper use of hormonal contraceptives that inhibit ovulation, hormone-releasing intrauterine contraceptive devices and copper containing intrauterine contraceptive devices or condoms), and
        - Not breast-feeding.
14. Male patients must: agree to abstinence (avoid heterosexual intercourse) or take contraception measures as follows: male patients with a pregnant partner or a partner of childbearing potential must remain abstinent or use a condom to prevent embryonic exposure during study treatment and for at least 6 months after the last dose of study drug.

Periodic abstinence (e.g., contraceptive methods based on calendar day, ovulation, basal body temperature or post-ovulation) and external ejaculation are ineligible methods of contraception.

Exclusion Criteria:

1. Histologically or cytologically confirmed mixed SCLC.
2. Other active malignancies within 5 years or at the same time. Localized tumors that had been cured, such as basal cell carcinoma, squamous-cell skin cancer, superficial bladder cancer, prostate carcinoma in situ, cervical cancer in situ and breast cancer in situ were acceptable.
3. Patients who were preparing for or had received an organ or bone marrow transplant.
4. Pleural or pericardial effusion requiring clinical intervention, or ascites.
5. Patients with known or documented active central nervous system (CNS) metastases and/or carcinomatous meningitis at screening. However, the following subjects were allowed to be enrolled: 1) Subjects with asymptomatic brain metastases (i.e., no progressive CNS symptoms caused by brain metastases, no requirement for corticosteroids, and lesion size ≤ 1.5 cm) could be included but were required to receive regular brain imaging as a site of lesion. 2) Subjects with treated brain metastases which had been stable for at least 2 months (as confirmed by 2 radiological examinations at least 4 weeks apart after treatment of brain metastases), with no evidence of new or enlarging brain metastases, and with discontinued steroids 3 days prior to study drug administration (Stable brain metastases here had to be confirmed before the first dose of the study drug).
6. Subjects with spinal cord compression that had not been radically treated with surgery and/or radiotherapy.
7. Patients with myocardial infarction within half a year before the first dose of the study drug, poorly controlled arrhythmia (including QTc intervals ≥ 450 ms for males and ≥ 470 ms for females) (QTc intervals were calculated by Fridericia's formula).
8. Class III to IV cardiac insufficiency according to NYHA classification or a left ventricular ejection fraction < 50% by cardiac color Doppler.
9. Subject had uncontrolled or symptomatic hypercalcemia (> 1.5 mmol/L ionized calcium or calcium > 12 mg/dL or corrected serum calcium > ULN).
10. Subject with peripheral neuropathy ≥ Grade 2 by CTCAE.
11. Human immunodeficiency virus (HIV) infection, positive test for HIV antibody.
12. Active or latent pulmonary tuberculosis.
13. Subjects with previous and concurrent interstitial pneumonia, pneumoconiosis, radiation pneumonitis, drug-related pneumonitis and severe impaired pulmonary function that might interfere with the detection and management of suspected drug-related pulmonary toxicity, as judged by the investigator.

14. Hepatitis B (positive test for HBsAg or HBcAb and positive test for HBV-DNA) or Hepatitis C (positive tests for HCV antibody and HCV-RNA). Hepatitis B and C co-infection (positive test for HBsAg or HBcAb and positive test for HCV antibody).
15. Known active or suspected autoimmune diseases. Subjects in a stable state with no need for systemic immunosuppressant therapy were allowed to enroll.
16. Treatment with live vaccines and all coronavirus disease 2019 (COVID-19) vaccines (fully administered to the required number of doses) within 28 days prior to study drug administration; inactivated viral vaccines for seasonal influenza were allowed.
17. Subjects requiring treatment with systemic corticosteroids (> 10 mg/day prednisone efficacy dose) or other immunosuppressive drugs within 14 days prior to the first dose or during the study. However, in the absence of active autoimmune disease, subjects were allowed to use topical or inhaled steroids and adrenal hormone replacement therapy at doses equivalent to ≤ 10 mg/day of prednisone efficacy.
18. Any active infection requiring systemic anti-infective therapy within 14 days prior to study drug administration or subjects with a positive reverse transcription polymerase chain reaction (RT-PCR) test for SARS-CoV-2 infection at randomization. Subjects with a history of COVID-19 infection had to have a negative RT-PCR test prior to the first dose of the study drug.
19. Major surgery within 28 days prior to the first dose of the study drug, defined as: surgeries requiring at least 3 weeks of recovery to be able to receive treatment in this study.
20. Radical radiation therapy within 3 months prior to study medications.

    Note: Palliative radiotherapy to bone or palliative radiotherapy to superficial lesions was allowed according to local standards 14 days prior to the first dose. Radiotherapy covering more than 30% of the bone marrow area within 28 days prior to the first dose was not allowed.
21. The subject had previously received other antibodies/drugs against immune checkpoints, such as PD-1, PD-L1, CTLA4.
22. Participation in any other ongoing clinical studies, or less than 14 days from the end of the previous clinical study treatment to the start of this trial.
23. Known history of severe allergy to any monoclonal antibody.
24. Known hypersensitivity to carboplatin or etoposide.
25. Pregnant or lactating women.
26. Known history of psychotropics abuse or drug abuse.
27. In the judgment of the investigator, the subject had any other factors that might lead to a premature discontinuation.

Test Product, Dose and Mode of Administration, Batch Number:

HLX10: CCI mg/kg, intravenous (IV) infusion for 30 to 90 minutes, administered on Day 1 of each cycle, once every 3 weeks (21 days).

Batch number(s): CCI CCI CCI CCI CCI CCI CCI

Reference Therapy, Dose and Mode of Administration, Batch Number:

Placebo: IV infusion, administered on Day 1 of each cycle, once every 3 weeks (21 days).

Batch number(s): CCI CCI

Duration of Treatment:

The initial treatment continued until disease progression. Post-PD treatment (blinded HLX10/placebo with second-line chemotherapy) was possible at the investigator's discretion if a subject met prespecified criteria, until the second disease progression, intolerable toxicity, death, withdrawal of consent, or lost to follow-up.

Criteria for Evaluation:

Efficacy:

Computed tomography (CT) or magnetic resonance imaging (MRI) was used for tumor imaging, and the images were assessed by Independent Radiology Review Committee (IRRC) and investigator.

Efficacy variables included overall survival (OS, primary efficacy variable), progression-free survival (PFS), PFS2 (defined as time to the second/subsequent objective tumor progression on the next-line treatment or death from any cause), objective response rate (ORR), and duration of response (DOR). PFS was evaluated based on tumor response assessed by IRRC using RECIST 1.1 and by the investigator using RECIST 1.1 and iRECIST. PFS2 was evaluated based on tumor response assessed by investigator using RECIST 1.1. ORR and DOR were assessed using RECIST 1.1 only. The final results of tumor assessment were determined by IRRC, and the results of the investigator's assessment were used as a reference.

Safety:

Safety assessments variables included AEs (including deaths and other serious adverse events [SAEs], infusion-related reactions [also referred to as injection reactions], and immune-related adverse events [irAEs]), clinical laboratory tests (including routine blood test, blood chemistry test, coagulation test, routine urine test, myocardial enzymogram, BNP/NT-proBNP, and thyroid function test), 12-lead ECG, vital signs, and physical examination.

Pharmacokinetics:

PK and ADA samples of HLX10 or placebo were collected and sent to the central laboratory for analysis. PK and ADA samples from all subjects were collected at the following time points: within 7 days pre-dose in Cycle 1, within 3 days pre-dose in Cycles 2, 4, 6, 8 and every 4 cycles thereafter, within 2 hours after the end of dosing in Cycles 1 and 8 of treatment period (for PK only), and at EOT visit and safety follow-up.

Biomarkers:

Biomarkers analyzed in this study included PD-L1 expression, microsatellite instability (MSI), and tumor mutation burden (TMB) in tumor tissue.

Quality of Life:

Subjects were assessed for quality of life using the following instruments: CCI [redacted] CCI [redacted] and CCI [redacted]

Statistical Methods:

Sample Size Determination:

The randomization ratio for the active treatment and placebo was 2:1. The sample size was estimated based on the assumption that the median OS for treatment with placebo + chemotherapy (carboplatin + etoposide) was 10 months and the hazard ratio (HR) of (HLX10 + chemotherapy) group versus the placebo group was 0.7. It was further assumed that when the enrollment period was 24 months and the whole study period was 34 months, to achieve a confidence level of 85% at an overall significance level of $\alpha = 0.05$ (two-sided), at least 342 OS events had to have been observed. Considering a dropout rate of 20%, a total of 567 subjects (378 in treatment arm and 189 in control arm) needed to be enrolled in the 2 arms.

Primary Efficacy Analyses:

The comparison of the time-to-event between the HLX10 and placebo groups was performed by a two-sided stratified log-rank test and the prespecified stratification factors. Time-to-event distributions were estimated using the Kaplan-Meier (KM) product-limit method. If median event time was evaluated, the corresponding two-sided 95% CI was to be computed using the Brookmeyer-Crowley approach. The standard error of the survival rate at a fixed time point (e.g., PFS rate at 6 months) was estimated using Greenwood's formula. The HR and its 95% CI were estimated by stratified Cox proportional hazards model. Efron's method was used to handle ties. All CIs were presented to one more decimal place than the point estimate.

For binomial proportions endpoints (e.g., ORR), considering the stratified randomization, the stratified Cochran-Mantel-Haenszel method is used to test the between-group variation in the ORR and to estimate the odds ratio and its 95% CI. For each single arm, the 95% CI for the proportion was derived using Clopper-Pearson method.

Considering the stratified randomization, the stratified Cochran-Mantel-Haenszel method was used to test the between-group variation in the ORR and to estimate the odds ratio and its 95%

CI. The estimate for ORR and 95% Clopper-Pearson CI was presented. Efficacy analyses were performed primarily in the Intent-To-Treat Population (ITT), supported by the Per Protocol Set (PPS).

Safety Analyses:

Safety analyses were primarily based upon summaries of the data rather than formal statistical inference. All safety summaries and analyses used the Safety Set.

Pharmacokinetics and Immunogenicity Analyses:

HLX10 concentrations and ADA status were listed by individual subjects and summarized in tables and figures. The accumulation index (R_{Cmax} and $R_{Ctrough}$, ratio of HLX10 drug cumulation) following multiple HLX10 dosing were calculated by the nominal sampling time, listed, and summarized by descriptive statistics.

Biomarker Analyses:

The OS and PFS, assessed by IRRC and by the investigator based on RECIST 1.1, were analyzed in view of their relationship with biomarkers.

Results:

Subject Disposition:

A total of 585 subjects were randomized, including 389 subjects who were randomly assigned to the HLX10+carboplatin and etoposide group (hereafter referred to as the HLX10 group) and 196 who were randomly assigned to the placebo + carboplatin and etoposide group (hereafter referred to as the placebo group).

As of May 7, 2024, all 585 (100%) subjects discontinued the study treatment. The most common reason for discontinuing the study treatment was progressive disease, which occurred in a higher proportion of subjects in the placebo group (74.5%) than in the HLX10 group (61.4%). Furthermore, 10.3% of subjects in the HLX10 group and 8.7% in the placebo group withdrew from study treatment, and 9.3% of subjects in the HLX10 group and 6.1% in the placebo group discontinued study treatment due to AEs.

As of the data cutoff date, 89 (15.2%) subjects completed the study, 496 (84.8%) subjects discontinued the study. The most common reason for discontinuing the study was death (76.4%), which occurred in a higher proportion of subjects in the placebo group (84.7%) than in the HLX10 group (72.2%).

Demographic and Baseline Characteristics:

The mean age was 61.1 years, 82.2% of the subjects were male, and 68.5% were Asian. Non-Asian (all Caucasian) subjects consisted 31.5% of the overall population. The mean BMI was 24.324 kg/m^2. The distribution of each characteristic was similar between the HLX10 and placebo groups.

The median duration since the first SCLC diagnosis was 0.23 months, and 97.3% of subjects

were diagnosed within 6 months before study entry. At study entry, 99.8% of the subjects had extensive stage SCLC and 81.0% were classified as Stage IV. Nearly all subjects (96.6%) had metastasis, including 13.3% of subjects with CNS metastasis. The distribution of each characteristic was similar between the HLX10 and placebo groups.

Efficacy Results:

Interim Analysis Data (Cutoff Date: October 22, 2021)

- As of October 22, 2021, when 246 OS events had occurred, the median (95% CI) OS was 15.38 (13.273, NA) months in the HLX10 group and 10.91 (9.955, 14.324) months in the placebo group. The stratified HR (95% CI) was 0.63 (0.489, 0.818) with $p < 0.001$. Thus, treatment with HLX10 reduced the risk of death by 37% and prolonged the median OS by 4.47 months. The OS rate at 2 years was 43.1% in the HLX10 group and 7.9% in the placebo group. Treatment with HLX10 was associated with significantly longer OS in subjects with ES-SCLC. The prespecified stopping boundary for OS (alpha = 0.012) was met.
- In the non-Asian (all Caucasian) population, the median (95% CI) OS was 12.55 (11.335, NA) months in the HLX10 group and 10.51 (8.148, 14.620) months in the placebo group. The stratified HR (95% CI) was 0.70 (0.413, 1.176) with $p = 0.176$. This could be attributed to the shorter duration of follow-up in the non-Asian population (median 9.13 months) than the overall population (median 12.32 months) by the cutoff date (October 22, 2021). Nevertheless, the OS benefit observed with the addition of HLX10 in the non-Asian population was consistent with that in the overall population.
- In the Asian population, the median (95% CI) OS was 16.03 (13.339, NA) months in the HLX10 group and 11.10 (9.955, 14.522) months in the placebo group. The stratified HR (95% CI) was 0.62 (0.458, 0.845) with $p = 0.002$. Thus, treatment with HLX10 reduced the risk of death by 38% and prolonged the median OS by 4.93 months. The OS benefit observed with the addition of HLX10 in the Asian population was consistent with that in the overall population.
- Subgroup analysis showed consistent OS benefit of HLX10 treatment over placebo regardless of age, sex, race, ethnicity, baseline ECOG performance status, brain metastasis, and baseline PD-L1 expression levels.
- The median (95% CI) PFS assessed by IRRC according to RECIST 1.1 was 5.72 (5.520, 6.899) months in the HLX10 group and 4.34 (4.205, 4.501) months in the placebo group. The stratified HR (95% CI) was 0.48 (0.383, 0.590) ($p < 0.001$). Thus, treatment with HLX10 reduced the risk of progressive disease or death by 52%.
- The median (95% CI) PFS assessed by investigator according to RECIST 1.1 was 5.49 (4.994, 5.684) months in the HLX10 group and 4.34 (4.205, 4.435) months in the placebo group. The stratified HR (95% CI) was 0.58 (0.476, 0.707) ($p < 0.001$). Thus, treatment with HLX10 reduced the risk of progressive disease or death by 42%.
- The median (95% CI) PFS assessed by investigator according to iRECIST was 5.68 (5.454,

6.867) months in the HLX10 group and 4.37 (4.238, 4.600) months in the placebo group. The stratified HR (95% CI) was 0.56 (0.454, 0.681) ($p < 0.001$).

- The median (95% CI) PFS2 assessed by investigator according to RECIST 1.1 was 11.04 (9.758, 12.945) months in the HLX10 group and 8.28 (7.556, 8.969) months in the placebo group. The stratified HR (95% CI) was 0.61 (0.458, 0.824) ($p = 0.001$).
- According to RECIST 1.1, as assessed by IRRC, 0.8% and 79.4% of subjects in the HLX10 group had unconfirmed CR and PR, respectively, compared to 0 and 70.4% in the placebo group. The unconfirmed ORR was 80.2% in the HLX10 group and 70.4% in the placebo group, resulting in an odds ratio (95% CI) of 1.71 (1.150, 2.544). In the HLX10 group, 0.8% and 66.6% of subjects had confirmed CR and PR, respectively, compared to 0 and 58.7% in the placebo group. The confirmed ORR was 67.4% in the HLX10 group and 58.7% in the placebo group, resulting in an odds ratio (95% CI) of 1.46 (1.022, 2.093).
- According to RECIST 1.1, as assessed by investigator, 2.8% and 74.0% of subjects in the HLX10 group had unconfirmed CR and PR, respectively, compared to 0.5% and 68.4% in the placebo group. The unconfirmed ORR was 76.9% in the HLX10 group and 68.9% in the placebo group, resulting in an odds ratio (95% CI) of 1.51 (1.027, 2.227). In the HLX10 group, 2.3% and 63.0% of subjects had confirmed CR and PR, respectively, compared to 0 and 55.1% in the placebo group. The confirmed ORR was 65.3% in the HLX10 group and 55.1% in the placebo group, resulting in an odds ratio (95% CI) of 1.55 (1.090, 2.214).
- As assessed by IRRC, the median (95% CI) duration of response in subjects who had an unconfirmed objective response was 5.55 (4.238, 6.801) months in the HLX10 group and 3.22 (2.924, 4.172) months in the placebo group. The stratified HR (95% CI) was 0.48 (0.369, 0.616) ($p < 0.001$). The median (95% CI) duration of response in subjects who had a confirmed objective response was 5.78 (5.158, 7.524) months in the HLX10 group and 4.14 (3.023, 4.205) months in the placebo group. The stratified HR (95% CI) was 0.44 (0.331, 0.582) ($p < 0.001$).
- As assessed by investigator, the median (95% CI) duration of response in subjects who had an unconfirmed objective response was 4.37 (4.172, 5.552) months in the HLX10 group and 3.02 (2.924, 3.975) months in the placebo group. The stratified HR (95% CI) was 0.51 (0.404, 0.649) ($p < 0.001$). The median (95% CI) duration of response in subjects who had a confirmed objective response was 5.55 (4.370, 6.669) months in the HLX10 group and 3.98 (3.023, 4.205) months in the placebo group. The stratified HR (95% CI) was 0.49 (0.372, 0.634) ($p < 0.001$).
- All secondary efficacy endpoints consistently favored the HLX10 group over the placebo group.
- The trends of efficacy benefits in the non-Asian population and Asian population were consistent with those in the overall population.
- Analyses in the PPS produced consistent results with the ITT set.

Updated Analysis Data (Cutoff Date: June 13, 2022)

- As of June 13, 2022, when 363 OS events (death events was 364, CCI [redacted] CCI [redacted] had occurred, the median (95% CI) OS was 15.80 (14.127, 17.577) months in the HLX10 group and 11.10 (9.955, 12.353) months in the placebo group. The stratified HR (95% CI) was 0.62 (0.496, 0.763) with $p < 0.001$. Thus, treatment with HLX10 reduced the risk of death by 38% and prolonged the median OS by 4.70 months. The OS rate at 2 years was 31.7% in the HLX10 group and 18.7% in the placebo group.
- In the non-Asian (all Caucasian) population, the median (95% CI) OS was 15.64 (12.649, 18.464) months in the HLX10 group and 11.20 (8.542, 14.324) months in the placebo group. The stratified HR (95% CI) was 0.51 (0.334, 0.791) with p=0.002. Thus, treatment with HLX10 reduced the risk of death by 49% and prolonged the median OS by 4.44 months. The OS rate at 2 years was 26.3% in the HLX10 group and 10.2% in the placebo group.
- In the Asian population, the median (95% CI) OS was 15.90 (13.864, 17.873) months in the HLX10 group and 11.10 (9.955, 12.945) months in the placebo group. The stratified HR (95% CI) was 0.65 (0.505, 0.840) with $p < 0.001$. Thus, treatment with HLX10 reduced the risk of death by 35% and prolonged the median OS by 4.8 months. The OS rate at 2 years was 33.1% in the HLX10 group and 20.2% in the placebo group.
- Subgroup analysis showed consistent OS benefit of HLX10 treatment over placebo regardless of age, sex, race, ethnicity, baseline ECOG performance status, brain metastasis, and baseline PD-L1 expression levels.
- The median (95% CI) PFS assessed by IRRC according to RECIST 1.1 was 5.75 (5.552, 6.932) months in the HLX10 group and 4.34 (4.205, 4.435) months in the placebo group. The stratified HR (95% CI) was 0.47 (0.381, 0.576) ($p < 0.001$). Thus, treatment with HLX10 reduced the risk of progressive disease or death by 53%.
- The median (95% CI) PFS assessed by investigator according to RECIST 1.1 was 5.49 (5.027, 5.717) months in the HLX10 group and 4.34 (4.205, 4.435) months in the placebo group. The stratified HR (95% CI) was 0.58 (0.480, 0.704) ($p < 0.001$). Thus, treatment with HLX10 reduced the risk of progressive disease or death by 42%.
- The median (95% CI) PFS assessed by investigator according to iRECIST was 5.65 (5.454, 6.735) months in the HLX10 group and 4.37 (4.271, 4.600) months in the placebo group. The stratified HR (95% CI) was 0.58 (0.475, 0.704) ($p < 0.001$).
- The median (95% CI) PFS2 assessed by investigator according to RECIST 1.1 was 11.73 (10.448, 13.010) months in the HLX10 group and 8.90 (7.688, 9.988) months in the placebo group. The stratified HR (95% CI) was 0.59 (0.458, 0.762) ($p < 0.001$).
- According to RECIST 1.1, as assessed by IRRC, 1.8% and 79.2% of subjects in the HLX10 group had unconfirmed CR and PR, respectively, compared to 0 and 70.4% in the placebo group. The unconfirmed ORR was 81.0% in the HLX10 group and 70.4% in the placebo

group, resulting in an odds ratio (95% CI) of 1.80 (1.205, 2.680). In the HLX10 group, 1.5% and 67.4% of subjects had confirmed CR and PR, respectively, compared to 0 and 58.7% in the placebo group. The confirmed ORR was 68.9% in the HLX10 group and 58.7% in the placebo group, resulting in an odds ratio (95% CI) of 1.58 (1.099, 2.260).

- According to RECIST 1.1, as assessed by investigator, 3.3% and 74.3% of subjects in the HLX10 group had unconfirmed CR and PR, respectively, compared to 0.5% and 68.4% in the placebo group. The unconfirmed ORR was 77.6% in the HLX10 group and 68.9% in the placebo group, resulting in an odds ratio (95% CI) of 1.58 (1.072, 2.334). In the HLX10 group, 2.8% and 63.0% of subject had confirmed CR and PR, respectively, compared to 0.5% and 54.6% in the placebo group. The confirmed ORR was 65.8% in the HLX10 group and 55.1% in the placebo group, resulting in an odds ratio (95% CI) of 1.60 (1.120, 2.281).
- As assessed by IRRC, the median (95% CI) duration of response in subjects who had an unconfirmed objective response was 5.55 (4.370, 6.932) months in the HLX10 group and 3.22 (2.924, 4.172) months in the placebo group. The stratified HR (95% CI) was 0.48 (0.378, 0.611) ($p < 0.001$). The median (95% CI) duration of response in subjects who had a confirmed objective response was 6.47 (5.454, 7.524) months in the HLX10 group and 4.17 (3.055, 4.205) months in the placebo group. The stratified HR (95% CI) was 0.45 (0.346, 0.586) ($p < 0.001$).
- As assessed by investigator, the median (95% CI) duration of response in subjects who had an unconfirmed objective response was 4.40 (4.172, 5.552) months in the HLX10 group and 3.02 (2.924, 3.975) months in the placebo group. The stratified HR (95% CI) was 0.52 (0.418, 0.657) ($p < 0.001$). The median (95% CI) duration of response in subjects who had a confirmed objective response was 5.55 (4.402, 6.867) months in the HLX10 group and 4.14 (3.220, 4.205) months in the placebo group. The stratified HR (95% CI) was 0.50 (0.389, 0.647) ($p < 0.001$).
- All secondary efficacy endpoints consistently favored the HLX10 group over the placebo group.
- The trends of efficacy benefits in the non-Asian population and Asian population were consistent with those in the overall population.
- Analyses in the PPS produced consistent results with the ITT set.

End-of-Study Analysis Data (Cutoff Date: May 7, 2024)

- As of May 7, 2024, when 446 OS events (death events was 447, CCI [redacted] CCI had occurred, the median (95% CI) OS was 15.77 (13.897, 17.413) months in the HLX10 group and 11.10 (9.955, 12.353) months in the placebo group. The stratified HR (95% CI) was 0.60 (0.494, 0.730) with $p < 0.001$. Thus, treatment with HLX10 reduced the risk of death by 40% and prolonged the median OS by 4.67 months. The OS rate at 3 years was 25.3% in the HLX10 group and 10.1% in the placebo group.

- In the non-Asian (all Caucasian) population, the median (95% CI) OS was 15.64 (12.649, 17.807) months in the HLX10 group and 11.20 (8.542, 14.324) months in the placebo group. The stratified HR (95% CI) was 0.50 (0.337, 0.738) with $p < 0.001$. Thus, treatment with HLX10 reduced the risk of death by 50% and prolonged the median OS by 4.44 months. The OS rate at 3 years was 22.3% in the HLX10 group and 7.1% in the placebo group.
- In the Asian population, the median (95% CI) OS was 15.77 (13.339, 17.873) months in the HLX10 group and 11.10 (9.955, 12.945) months in the placebo group. The stratified HR (95% CI) was 0.64 (0.508, 0.811) with $p < 0.001$. Thus, treatment with HLX10 reduced the risk of death by 36% and prolonged the median OS by 4.67 months. The OS rate at 3 years was 26.5% in the HLX10 group and 11.3% in the placebo group.
- Subgroup analysis showed consistent OS benefit of HLX10 treatment over placebo regardless of age, sex, race, ethnicity, baseline ECOG performance status, brain metastasis, and baseline PD-L1 expression levels.
- The median (95% CI) PFS assessed by IRRC according to RECIST 1.1 was 5.82 (5.552, 6.932) months in the HLX10 group and 4.34 (4.205, 4.435) months in the placebo group. The stratified HR (95% CI) was 0.47 (0.380, 0.572) ($p < 0.001$). Thus, treatment with HLX10 reduced the risk of progressive disease or death by 53%.
- The median (95% CI) PFS assessed by investigator according to RECIST 1.1 was 5.49 (5.027, 5.717) months in the HLX10 group and 4.34 (4.205, 4.435) months in the placebo group. The stratified HR (95% CI) was 0.57 (0.470, 0.687) ($p < 0.001$). Thus, treatment with HLX10 reduced the risk of progressive disease or death by 43%.
- The median (95% CI) PFS assessed by investigator according to iRECIST was 5.65 (5.454, 6.735) months in the HLX10 group and 4.37 (4.271, 4.600) months in the placebo group. The stratified HR (95% CI) was 0.56 (0.459, 0.674) ($p < 0.001$).
- The median (95% CI) PFS2 assessed by investigator according to RECIST 1.1 was 12.32 (10.908, 13.372) months in the HLX10 group and 8.90 (7.819, 10.185) months in the placebo group. The stratified HR (95% CI) was 0.58 (0.455, 0.738) ($p < 0.001$).
- According to RECIST 1.1, as assessed by IRRC, 2.6% and 78.4% of subjects in the HLX10 group had unconfirmed CR and PR, respectively, compared to 0 and 70.4% in the placebo group. The unconfirmed ORR was 81.0% in the HLX10 group and 70.4% in the placebo group, resulting in an odds ratio (95% CI) of 1.80 (1.205, 2.680). In the HLX10 group, 2.3% and 66.6% of subjects had confirmed CR and PR, respectively, compared to 0 and 58.7% in the placebo group. The confirmed ORR was 68.9% in the HLX10 group and 58.7% in the placebo group, resulting in an odds ratio (95% CI) of 1.58 (1.099, 2.260).
- According to RECIST 1.1, as assessed by investigator, 3.6% and 74.0% of subjects in the HLX10 group had unconfirmed CR and PR, respectively, compared to 0.5% and 68.4% in the placebo group. The unconfirmed ORR was 77.6% in the HLX10 group and 68.9% in the placebo group, resulting in an odds ratio (95% CI) of 1.58 (1.072, 2.334). In the HLX10

group, 3.1% and 62.7% of subjects had confirmed CR and PR, respectively, compared to 0.5% and 54.6% in the placebo group. The confirmed ORR was 65.8% in the HLX10 group and 55.1% in the placebo group, resulting in an odds ratio (95% CI) of 1.60 (1.120, 2.281).

- As assessed by IRRC, the median (95% CI) duration of response in subjects who had an unconfirmed objective response was 5.55 (4.370, 6.998) months in the HLX10 group and 3.22 (2.924, 4.172) months in the placebo group. The stratified HR (95% CI) was 0.48 (0.375, 0.604) ($p < 0.001$). The median (95% CI) duration of response in subjects who had a confirmed objective response was 6.80 (5.520, 8.345) months in the HLX10 group and 4.17 (3.055, 4.205) months in the placebo group. The stratified HR (95% CI) was 0.45 (0.347, 0.582) ($p < 0.001$).
- As assessed by investigator, the median (95% CI) duration of response in subjects who had an unconfirmed objective response was 4.40 (4.172, 5.552) months in the HLX10 group and 3.02 (2.924, 3.975) months in the placebo group. The stratified HR (95% CI) was 0.52 (0.417, 0.652) ($p < 0.001$). The median (95% CI) duration of response in subjects who had a confirmed objective response was 5.55 (4.402, 6.899) months in the HLX10 group and 4.14 (3.220, 4.205) months in the placebo group. The stratified HR (95% CI) was 0.50 (0.388, 0.638) ($p < 0.001$).
- All secondary efficacy endpoints consistently favored the HLX10 group over the placebo group.
- The trends of efficacy benefits in the non-Asian population and Asian population were consistent with those in the overall population.
- Analyses in the PPS produced consistent results with the ITT set.

Taken together, our findings highlighted that HLX10 was superior to placebo when administered in combination with carboplatin and etoposide in previously untreated subjects with ES-SCLC. Data for both the Asian and non-Asian population were consistent with that for the overall population, hence demonstrating the robustness of the results.

Pharmacokinetics and Immunogenicity Results:

- As of May 7, 2024, after multiple doses of HLX10, the mean serum concentration of HLX10 showed mild increase from single dose. The accumulation ratios for C_{max} and C_{trough} were 1.850 and 3.056, respectively. Subjects with positive ADA results had slightly lower exposure compared with ADA-negative subjects, and the difference was too small and had no clinically meaningful effects.
- The exposure and accumulation parameters in non-Asian population were comparable to those of the Asian population and the overall population.
- Two subjects in the HLX10 group were with positive ADA at baseline. A total of 7 (1.8%) of the 389 subjects in the HLX10 group had at least one post-treatment positive ADA result. Of these 7 subjects with post-treatment ADA results, 4 were from the non-Asian population, 3 were from the Asian population. All the positive ADA samples were tested as negative

NAbs.

Safety Results:

- As of May 7, 2024, the overall incidence of TEAEs was comparable between the HLX10 group and the placebo group (96.4% vs 98.0%). TEAEs with incidence ≥ 20% (in the HLX10 group) by PT were anaemia (HLX10 group vs placebo group: 72.2% vs 71.4%), neutrophil count decreased (56.6% vs 51.5%), alopecia (54.2% vs 56.6%), white blood cell count decreased (54.2% vs 51.0%), platelet count decreased (41.6% vs 44.9%), nausea (36.2% vs 43.9%), neutropenia (30.1% vs 32.1%), decreased appetite (28.3% vs 28.6%), hyponatraemia (25.4% vs 13.3%), constipation (24.7% vs 29.6%), leukopenia (24.4% vs 20.4%), and vomiting (20.3% vs 29.6%).
- Grade ≥ 3 TEAEs were reported in 84.8% of subjects in the HLX10 group and 83.2% in the placebo group (80.2% vs 77.0%, when the cases that reported as disease progression or COVID-19 were excluded). The incidence of Grade ≥ 3 TEAEs was comparable between the groups. Grade ≥ 3 TEAEs with incidence ≥ 20% (in the HLX10 group) by PT were neutrophil count decreased (HLX10 group vs placebo group: 42.9% vs 40.3%), white blood cell count decreased (24.4% vs 25.0%), and neutropenia (23.4% vs 20.9%).
- TEAEs related to HLX10 were reported in 71.7% of subjects in the HLX10 group, while TEAEs related to placebo were reported in 57.7% of subjects in the placebo group. TEAEs related to HLX10/placebo with incidence ≥ 10% (in the HLX10 group) by PT were anaemia (HLX10 group vs placebo group: 23.1% vs 18.9%), white blood cell count decreased (20.8% vs 16.8%), neutrophil count decreased (19.8% vs 17.9%), platelet count decreased (16.2% vs 18.4%), hypothyroidism (16.2% vs 2.6%), nausea (13.4% vs 14.3%), alanine aminotransferase increased (12.3% vs 9.7%), hyperthyroidism (12.1% vs 3.1%), aspartate aminotransferase increased (10.0% vs 10.7%), and decreased appetite (10.0% vs 9.7%).
- Grade ≥ 3 TEAEs related to HLX10/placebo were reported in 35.0% of subjects in the HLX10 group and 29.1% in the placebo group, and the incidence was comparable between the groups. Grade ≥ 3 TEAEs related to HLX10/placebo with incidence ≥ 5% (in the HLX10 group) by PT were neutrophil count decreased (HLX10 group vs placebo group: 14.1% vs 13.8%), white blood cell count decreased (8.7% vs 8.7%), platelet count decreased (6.2% vs 8.2%), and anaemia (5.4% vs 5.6%).
- TEAEs leading to death occurred in 10.0% of subjects in the HLX10 group and 13.8% in the placebo group, most frequently associated with disease progression (HLX10 group vs placebo group: 3.9% vs 5.1%). Excluding disease progression, TEAEs leading to death were reported in 6.2% of subjects in the HLX10 group and 8.7% of subjects in the placebo group. Excluding disease progression and COVID-19, TEAEs leading to death were reported in 5.4% of subjects in the HLX10 group and 7.7% of subjects in the placebo group. A total of 6 (1.0%) subjects experienced TEAEs related to HLX10/placebo leading to death, including 5 (1.3%) subjects in the HLX10 group and 1 (0.5%) subject in the placebo group.
- The incidence of serious TEAEs was comparable between the HLX10 group and the placebo

group (39.8% vs 39.3%). Serious TEAEs with incidence ≥ 2% (in the HLX10 group) by PT were platelet count decreased (HLX10 group vs placebo group: 6.7% vs 7.7%), neutrophil count decreased (4.4% vs 9.2%), white blood cell count decreased (4.4% vs 5.6%), disease progression (3.9% vs 5.1%), pneumonia (3.3% vs 3.6%), neutropenia (2.8% vs 2.0%), thrombocytopenia (2.8% vs 2.0%), and leukopenia (2.3% vs 1.5%).

- Serious TEAEs related to HLX10/placebo were reported in 18.8% of subjects in the HLX10 group and 14.3% in the placebo group. Serious TEAEs related to HLX10/placebo with incidence ≥ 2% (in the HLX10 group) by PT were platelet count decreased (HLX10 group vs placebo group: 3.9% vs 5.1%), white blood cell count decreased (2.6% vs 3.1%), and neutrophil count decreased (2.3% vs 5.6%).
- Overall, 45.2% of subjects in the HLX10 group and 41.8% in the placebo group experienced TEAEs leading to interruption of HLX10/placebo. TEAEs leading to interruption of HLX10/placebo with incidence ≥ 5% (in the HLX10 group) by PT were neutrophil count decreased (HLX10 group vs placebo group: 10.0% vs 11.2%), platelet count decreased (9.8% vs 11.2%), neutropenia (9.5% vs 9.7%), anaemia (6.4% vs 7.7%), and white blood cell count decreased (5.9% vs 6.6%).
- A total of 57 (9.7%) subjects experienced TEAEs leading to discontinuation of HLX10/placebo during the study, including 39 (10.0%) subjects in the HLX10 group and 18 (9.2%) in the placebo group. The number of subjects who discontinued HLX10/placebo due to TEAEs related to HLX10/placebo was small, including 6.2% of subjects in the HLX10 group and 4.6% in the placebo group, which suggests that HLX10 was not associated with a substantial risk of treatment discontinuation.
- Treatment-emergent infusion reactions were uncommon and occurred in 2.1% of subjects in the HLX10 group and 0.5% in the placebo group. Immune-related TEAEs occurred in 38.0% of subjects in the HLX10 group and 18.9% in the placebo group. Immune-related TEAEs with incidence ≥ 3% (in the HLX10 group) by PT were hypothyroidism (HLX10 group vs placebo group: 12.3% vs 1.0%), hyperthyroidism (9.8% vs 3.1%), and rash (3.1% vs 1.0%).
- The incidences of injection reactions and immune-related TEAEs reported in the HLX10 group were generally similar to those reported in other marketed anti-PD-1/PD-L1 antibodies and were consistent with the safety results of previous HLX10 studies, respectively.
- Some clinically significant abnormalities were found in clinical laboratory tests, including liver function and thyroid function, as well as in 12-lead ECG results. These findings were consistent with the known safety profile of HLX10.
- In the non-Asian population, the incidence of TEAEs was 89.0% in the HLX10 group and 93.0% in the placebo group. Approximately half of the subjects had Grade ≥ 3 TEAEs (59.8% vs 50.9%, the cases that reported as disease progression or COVID-19 were excluded). The safety profile of HLX10 in the non-Asian population was generally comparable to that in the overall safety population.

- In the Asian population, the incidence of TEAEs was 100% in both groups. The incidence of Grade ≥ 3 TEAEs was comparable between the HLX10 group and the placebo group (90.1% vs 87.8%, the cases that reported as disease progression or COVID-19 were excluded). The safety profile of HLX10 in the Asian population was generally comparable to that in the overall safety population.

Overall, HLX10 treatment in combination with carboplatin and etoposide was well tolerated in ES-SCLC patients. TEAEs related to HLX10 were generally related to the immunological mechanism of action as expected. No new safety signals were identified in this study.

Overall Conclusion:

Efficacy

HLX10 demonstrated meaningful and consistent benefits over placebo in OS, PFS, ORR, and DOR among subjects with previously untreated ES-SCLC when administered in combination with carboplatin and etoposide.

Primary Efficacy Endpoint

- The treatment with HLX10 was associated with significantly longer OS in subjects with previously untreated ES-SCLC compared to the placebo group. The OS benefit observed with the addition of HLX10 in both the non-Asian (all Caucasian) and Asian population was consistent with that in the overall population. Subgroup analysis confirmed consistent OS benefit of HLX10 treatment over placebo across various factors including age, sex, race, ethnicity, baseline ECOG performance status, brain metastasis, and baseline PD-L1 expression levels.

Secondary Efficacy Endpoints

- All secondary efficacy endpoints (PFS, PFS2, ORR, DCR) consistently favored the HLX10 group over the placebo group.
- The efficacy benefits observed in both the non-Asian population and Asian population were consistent with those in the overall population.

Safety

- The incidence and severity of AEs (including serious TEAEs, Grade ≥ 3 TEAEs, TEAEs leading to death, and TEAEs leading to study drug interruption or discontinuation), laboratory tests, vital signs, physical examinations, 12-lead electrocardiogram (ECG), and ECOG score were comparable between the HLX10 group and the placebo group.
- HLX10 was well tolerated, with no new safety signals being identified in this study.

Pharmacokinetics and Immunogenicity

- After multiple doses, the accumulation ratios of C_{max} and C_{trough} for HLX10 was mild. The exposure and accumulation parameters in the non-Asian population were comparable to

those in the Asian population and the overall population. ADA (positive or negative) did not impact on the PK exposure.

- The immunogenic risk of HLX10 was low, with all positive ADA samples being tested negative for NAbs.

Date of the Report: December 19, 2024