亞盛醫藥
Ascentage Pharma

ASCENTAGE PHARMA GROUP INTERNATIONAL
亞盛醫藥集團

(Incorporated in the Cayman Islands with limited liability)

(Stock Code: 6855)

Voluntary Announcement

Ascentage Pharma Presents Results from Four Studies at 2023 American Society of Clinical Oncology (ASCO) Annual Meeting

Ascentage Pharma Group International (the "**Company**" or "**Ascentage Pharma**") is pleased to announce that the abstracts on the four of the Company's studies selected for presentations at the 2023 American Society of Clinical Oncology (ASCO) Annual Meeting have been published on ASCO's official website. These studies evaluated four of the Company's lead drug candidates, namely the first and only China-approved third-generation BCR-ABL inhibitor olverembatinib (HQP1351), Bcl-2 selective inhibitor lisaftoclax (APG-2575), MDM2-p53 inhibitor alrizomadlin (APG-115), and FAK/ALK/ROS1 inhibitor (APG-2449).

APG-2449

FAK inhibition with novel FAK/ALK inhibitor APG-2449 could overcome resistance in NSCLC patients who are resistant to second-generation ALK inhibitors

- Highlights

  - This open-label, multicenter, Phase I dose-escalation and dose-expansion study was designed to evaluate the safety/tolerability, pharmacokinetics (PK), pharmacodynamics (PD), and efficacy of ATG-2449 in patients with ALK/ROS1^{+} NSCLC or other solid tumors.

  - As of December 9, 2022, 130 patients were enrolled and treated with APG-2449 at doses ranged from 900-1,500 mg. The median age of those patients was 53 (21-78) years and 53.8% of them were female. After 1,200 mg daily (QD) was determined as the recommended Phase II dose (RP2D), patients with NSCLC were enrolled into 2 dose-expansion cohorts. Among them, Cohort 1 included patients who were resistant to second-generation ALK/ROS1^{+} tyrosine kinase inhibitors (TKIs), Cohort 2 included those who were ALK/ROS1^{+} TKI-naïve.

- Efficacy Results: In the subgroup of patients with TKI-naïve NSCLC (n = 33; 31 were efficacy evaluable), the overall response rate (ORR) and disease control rate (DCR = complete response (CR) rate + partial response (PR) rate + stable diseases (SD) rate) were 70.6% (12/17) and 88.2% (15/17), respectively, in $ROS1^+$ treatment-naïve patients; and were 78.6% (11/14) and 100% (14/14) in ALK^+ treatment-naïve patients. Among the 27 patients with ALK^+ NSCLC who were resistant to second-generation ALK inhibitors, 7 achieved PR (7/27; 25.9%) when treated with APG-2449 at the RP2D.

- Analysis of FAK Expressions: Among the 27 patients with ALK^+ NSCLC who were resistant to second-generation ALK inhibitors, compared to the baseline, those who experienced PR showed lower phosphorylated FAK (pFAK) levels in peripheral blood mononuclear cells (PBMCs) by Day 28 (24 hours after dosing on Day 28) than patients who experienced SD. Furthermore, patients with progressive disease showed an increase of PBMC pFAK levels on Day 28 compared to baseline, indicating APG-2449 could inhibit FAK phosphorylation. Meanwhile, patients with higher pFAK expression in tumor tissues at baseline tended to achieve better clinical responses than those with lower pFAK expression post APG-2449 treatment.

- Safety Results: A total of 117 (90%) patients experienced treatment-related adverse events (TRAEs) with the most frequent TRAEs being elevated blood creatinine (43.8%), alanine aminotransferase (ALT) (40.8%), and aspartate aminotransferase (AST) (33.1%) levels, as well as gastrointestinal disorders that included nausea (25.4%), vomiting (21.5%), and diarrhea (21.5%). A total of 17 (13.1%) TRAEs were grade≥3.

- Conclusions: APG-2449 showed a favorable preliminary safety profile and antitumor efficacy in patients with NSCLC. Preliminary efficacy was observed in patients who were TKI-naïve and resistant to second-generation ALK inhibitors. FAK inhibition could be a novel approach to overcome ALK resistance in patients with NSCLC who are resistant to second-generation ALK inhibitors.

olverembatinib

Antitumor activity of olverembatinib (HQP1351) in patients (pts) with tyrosine kinase inhibitor-(TKI)- resistant succinate dehydrogenase- (SDH-) deficient gastrointestinal stromal tumor (GIST)

- Highlights

  - This open-label, multicenter Phase Ib/II study in China was designed to evaluate the safety, tolerability, PK, and antitumor activity of olverembatinib in patients with TKI-resistant locally advanced or metastatic GIST.

  - As of January 15, 2023, a total of 20 patients with SDH-deficient GIST were enrolled in the study. The median age of those patients was 30 years (14-56). Olverembatinib, at doses ranged from 20-50 mg (50 mg cohort n=6; 40 mg cohort n=8; 30 mg cohort n=6), was administered once every other day (QOD) in 28-day cycles.

- Efficacy Results: The median duration of treatment in the 20 patients with SDH-deficient GIST was 7.8 (1.81-42.3) months. A total of 5 of these patients experienced PRs. Of the 16 evaluable patients who were treated with olverembatinib for more than 16 weeks, the clinical benefit rate (CBR=CR+PR+SD>16 weeks) was 93.8% (15/16) and the longest treatment duration was 42 months.

- Safety Results: All patients experienced at least one treatment-emergent adverse event (TEAE), most of which were grade 1 or 2; 2 patients experienced grade 3 AEs; and the only hematologic AE with an incidence rate≥20% was anemia (55%). A total of 15 (75%) patients experienced TRAEs, among them 1 experienced a grade 3 TRAE (neutropenia). No serious TRAEs were reported during the study.

- Conclusions: Olverembatinib was well-tolerated up to 50 mg QOD and showed antitumor activity in patients with TKI-resistant SDH-deficient GIST. A total of 5 (25%) PRs were reported among 20 evaluable patients; the 16 patients treated for≥16 weeks achieved a CBR of 93.8%. These promising findings warrant further investigation.

APG-2575

Lisaftoclax

Preliminary data of a phase 1b/2 study of BCL-2 inhibitor lisaftoclax (APG-2575) alone or combined with ibrutinib or rituximab in patients (pts) with Waldenström macroglobulinemia (WM).

- Highlights

  - This open-label, multicenter, global Phase Ib/II study was designed to evaluate the safety, tolerability, efficacy, and PK of the orally-administered high-selectivity novel Bcl-2 inhibitor lisaftoclax as monotherapy or in combination with ibrutinib or rituximab in patients with WM.

  - As of January 25, 2023, a total of 46 patients were enrolled in the study and later enrolled into 3 arms as follows:

    Arm A: lisaftoclax monotherapy in patients resistant/intolerant to Bruton tyrosine kinase inhibitors (BTKi) (n=14)

    Arm B: lisaftoclax plus ibrutinib in treatment-naïve patients (n=24)

    Arm C: lisaftoclax plus rituximab in ibrutinib and other BTKi-naïve relapsed/refractory patients (n=8)

    Lisaftoclax was escalated from 400 to 1,200 mg using a modified toxicity probability interval-2 (mTPI-2) design. Arm A, B, and C were escalated to up to 1,000 mg, 1,200 mg, and 800 mg, respectively.

- Efficacy Results: The ORR and median time to response (MTTR) for Arm A, Arm B, and Arm C were 25%, 90.9%, and 37.5%; and 4.3, 1.9, and 4.4 months, respectively. The study did not observe any significant difference between patients with and without the CXCR4 mutation.

- Safety Results: At 1,200 mg, 1 grade 3 dose-limiting toxicity (DLT) (grade 3 tumor lysis syndrome TLS) due to pre-existing renal impairment was observed in Arm B. At 1,000 mg, 1 grade 3 laboratory TLS occurred in Arm B due to dehydration and active symptomatic recurrence. The abnormal electrolytes in this patient was resolved after 1 day of drug intervention and the AE did not reoccur in the patient. Grade≥3 lisaftoclax-related AEs included neutropenia (13%), leukocytopenia (4.3%), anemia (2.2%), weight loss (2.2%), and septic shock (2.2%). Ventricular arrhythmias were not observed. The PK data indicated no drug-to-drug interaction (DDI) between lisaftoclax and ibrutinib.

- Conclusions: Lisaftoclax alone or combined with ibrutinib/rituximab demonstrated measurable effects in patients with treatment-naïve or BTKi-refractory WM.

APG-115

Alrizomadlin

A phase 2 study of alrizomadlin (APG-115) in combination with pembrolizumab in patients with unresectable or metastatic cutaneous melanoma that has failed immuno-oncologic (IO) drugs.

- Highlights

  - This open-label, multicenter Phase Ib/II study conducted in the U.S. and Australia was designed to evaluate the safety, tolerability, PK, and antitumor activity of alrizomadlin plus pembrolizumab in patients with unresectable or metastatic cutaneous melanoma or advanced solid tumors. At the meeting, the study released the latest Phase II efficacy and safety results from the cutaneous melanoma subgroup.

  - As of December 12, 2022, a total of 31 patients with cutaneous melanoma that had progressed on PD-1/PD-L1 immunotherapy were enrolled in the study. The median age of these patients was 65 years (27-84) and 21 of these patients were male, and 10 (32.3%) were female. Alrizomadlin 150 mg was administered QOD for 2 consecutive weeks, with 1 week off, in 21-day cycles. Pembrolizumab 200 mg was administered intravenously on day 1 of the treatment cycles.

  - Efficacy Results: In 26 efficacy-evaluable patients, 2 achieved CR, 4 achieved PR, resulting in a confirmed ORR (ORR=CR+PR) of 23.1%. The initial analysis indicated that the ORR observed in patients whose disease had failed IO treatment was primarily attributable to the alrizomadlin plus pembrolizumab regimen, not the delayed effect of prior immunotherapy.

- Safety Results: 30 (96.8%) patients reported TRAEs, with the most frequent TRAEs (>10%) being nausea (71%), vomiting (38.7%), fatigue (35.5%), thrombocytopenia (32.3%), diarrhea (25.8%), neutropenia (19.4%), decreased appetite (16.1%), and decreased leukocyte count (12.9%). 4 (12.9%) patients reported serious TRAEs, including anemia, thrombocytopenia, deep vein, thrombosis, joint effusion, pulmonary embolism, and vomiting.

- Conclusions: Alrizomadlin combined with pembrolizumab is well tolerated and demonstrates clinical efficacy in these patients with cutaneous melanoma that had progressed on PD-1/PD-L1 immunotherapy.

Cautionary Statement required by Rule 18A.05 of the Rules Governing the Listing of Securities on The Stock Exchange of Hong Kong Limited: We cannot guarantee that we will be able to obtain further approval for, or ultimately market, APG-2575, APG-115 and APG-2449 successfully.

By order of the Board
Ascentage Pharma Group International
Dr. Yang Dajun
Chairman and Executive Director

Suzhou, People's Republic of China, May 28, 2023

As at the date of this announcement, the Board of Directors of the Company comprises Dr. Yang Dajun as Chairman and executive Director, Dr. Wang Shaomeng and Dr. Lu Simon Dazhong as non-executive Directors, and Mr. Ye Changqing, Dr. Yin Zheng, Mr. Ren Wei and Dr. David Sidransky as independent non-executive Directors.