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 Releases Latest Results from Multiple Clinical Studies of Its Lead Drug Candidates in 2024 European Hematology Association Hybrid Congress (EHA 2024)

Ascentage Pharma Group International (the "**Company**" or "**Ascentage Pharma**") is pleased to announce that it has released updated results from three studies of olverembatinib (HQP1351), the first China-approved third-generation BCR-ABL inhibitor and updated data of lisaftoclax (APG-2575), one of its key drug candidates, combined with novel therapeutic regimens in patients with relapsed/refractory (R/R) multiple myeloma (MM) or immunoglobulin light-chain (AL) amyloidosis, in poster presentations at the 2024 European Hematology Association Hybrid Congress (EHA 2024), taking place in Madrid, Europe.

The EHA Hybrid Congress is the largest gathering of the hematology field in Europe. It showcases the most cutting-edge research and state-of-the-art innovative therapies, attracting over 10,000 clinical experts and researchers from more than 100 countries every year. This year, in addition to the latest data of lisaftoclax, Ascentage Pharma also released those of the third-generation BCR-ABL1 inhibitor olverembatinib (HQP1351) and the EED inhibitor APG-5918.

Highlights of the Latest Results from Multiple Clinical Studies of Ascentage Pharma presented at EHA 2024 are as follows:

Olverembatinib Overcomes Ponatinib and Asciminib Resistance in Patients (Pts) with Heavily Pretreated Chronic Myeloid Leukemia (CML) and Philadelphia-Positive Acute Lymphoblastic Leukemia (Ph+ ALL)

Highlights:

- Background: Existing preclinical and clinical data show that olverembatinib, an investigational, novel, potent BCR::ABL1 TKI, has strong antitumor activity in CML or Ph+ ALL.

- Introduction: This multicenter, open-label study was designed to assess the safety, efficacy, and pharmacokinetic (PK) profiles of olverembatinib in patients with heavily TKI (including ponatinib and asciminib) pretreated CML or Ph+ ALL.

- Patient enrollment and methods: As of January 2, 2024, a total of 80 heavily TKI pretreated patients, including 62 patients with CML-CP and 18 patients with advanced Ph+ leukemia (CML-AP, CML-BP, Ph+ ALL), were enrolled. These patients were randomly assigned to receive orally administered olverembatinib at 30, 40, or 50 mg once every other day (QOD) in 28-day cycles.

- Efficacy results:

  1) In patients with CML-CP:

     – 31/51 (60.8%) patients achieved a complete cytogenetic response (CCyR), and 25/59 (42.4%) achieved a major molecular response (MMR). No differences in the response rates of patients with/without the T315I mutation were observed.

     – In patients who failed prior treatment with ponatinib, 15/26 (57.7%) achieved a CCyR (including 10/19 [52.6%] patients with prior resistance to ponatinib and 3/4 [75.0%] with prior intolerance of ponatinib), and 11/30 (36.7%) patients achieved an MMR (including 9/21 [42.9%] patients with prior resistance to ponatinib and 1/6 [16.7%] with prior intolerance of ponatinib).

     – In patients who were asciminib-resistant, 4/8 (50.0%) achieved a CCyR, and 4/12 (33.3%) achieved an MMR.

  2) In patients with advanced Ph+ leukemia:

     – 3/14 (21.4%) patients achieved a CCyR, and 3/17 (17.6%) patients achieved an MMR.

- Safety results:

  – 72 (90.0%) patients experienced treatment emergent adverse events (TEAEs) during their treatment with olverembatinib. Most of the TEAEs were mild to moderate in severity.

  – Common grade ≥3 TEAEs included thrombocytopenia (17.5%), neutropenia (12.5%), and increases in blood creatine phosphokinase (12.5%). Serious adverse events occurring in ≥3 (3.8%) patients included atrial fibrillation, COVID-19 infection, febrile neutropenia, and intestinal obstruction. No treatment-related adverse events (TRAE) led to death. Two (2.5%) patients experienced Grade 1 treatment-related arterial occlusive events, one each with angina pectoris and cardiac failure.

- Conclusions: Olverembatinib was efficacious and well tolerated in patients with heavily TKI pretreated CML-CP and advanced Ph+ leukemias, including ponatinib- or asciminib-resistant/intolerant disease.

Combination of Third Generation TKI Olverembatinib and Chemotherapy or Blinatumomab for New Diagnosed Adult Ph+ ALL Patients

Highlights:

- Background: TKIs have improved the long-term outcomes of patients with Ph+ ALL, but resistance to TKIs remains a challenge. Previous reports showed that third-generation TKI ponatinib, combined with chemotherapy, results in modest rates of complete molecular response (CMR) of 75% in 3 months. Our recent study, a front-line combination of olverembatinib and the PDT-ALL-2016 regimen in Ph+ ALL, had shown a promising outcome, achieving a CMR rate of 84.6% at day 90. Furthermore, the combination of TKI and blinatumomab (BITE) as a chemotherapy-free treatment approach has demonstrated safety and effectiveness.

- Introduction: This study explored the clinical efficacy of the front-line combination of olverembatinib and chemotherapy (TKI+chemotherapy) or olverembatinib and blinatumomab (TKI+BITE) for the treatment of Ph+ ALL.

- Patient enrollment and methods: From Jan 2022 to Dec 2023, 31 patients with newly diagnosed Ph+ ALL treated with olverembatinib (40mg once every other day) with pediatric-inspired chemotherapy (n=19; PDT-ALL-2016 protocol) or blinatumomab (n=12; administered for a total of 2 weeks followed by 2 weeks of break) were enrolled. The median age was 40 years old, 15 (48.4%) patients had one comorbid disease, and 8 (25.81%) patients had ≥2 comorbid diseases.

- Efficacy results: With a median follow-up of 16 months, all patients achieved a complete remission (CR) after one cycle of treatment. For the entire cohort, 28 (90.3%) patients achieved a CMR within 3 months. Among them, 16 (84.2%) and 12 (100.0%) patients in the TKI + chemotherapy and TKI + BITE cohorts achieved a CMR within 3 months, respectively. The 1-year overall survival (OS) rate was 93.1% and event-free survival (EFS) rate was 78.4% in the entire cohort. For the TKI + chemotherapy cohort, the 1-year OS rate was 96.2% and the EFS rate was 71.5%. In the TKI + BITE cohort, the 1-year OS rate was 100.0% and the EFS rate was 90.0%.

- Safety results: Adverse events were observed in 10 (32.3%) patients: 3 patients (9.6%) developed septic shock during treatment, 2 patients (6.4%) experienced mild pancreatitis, 2 patients (6.4%) experienced Pneumocystis jirovecii pneumonia, 2 patients (6.4%) experienced grade 2 cytokine release syndrome (CRS), and 1 patient (3.2%) developed pulmonary embolism.

- Conclusions: This study showed the combination of olverembatinib and chemotherapy or blinatumomab for treating adult patients with Ph+ ALL. Among the 31 patients enrolled, a notable rate of 1-year survival and CMR was observed, which holds promise for improved long-term survival. Both the TKI + chemotherapy and TKI+BITE cohorts showed good clinical outcomes, although the TKI + BITE cohort exhibited better survival than the TKI + chemotherapy cohort. It is important to note that, although 74.19% of enrolled patients had at least one comorbid disease and the median age was 40 years, the safety profile was acceptable.

Patient Reported Outcomes in Adults with TKI-Resistant Chronic Myeloid Leukemia Receiving Olverembatinib-Therapy

Highlights:

- Background: Third-generation (3G) TKIs have improved the outcomes of patients with TKI-resistant CML. However, there are very limited data on patient reported outcomes in adults receiving 3G TKIs such as olverembatinib.

- Introduction: The aim of this study was to assess health-related quality of life (HRQoL), anxiety and depression symptoms and identify variables associated with them in patients with TKI-resistant CML receiving olverembatinib-therapy.

- Patient enrollment and methods:

  – Subjects with TKI-resistance receiving olverembatinib in the multicenter study were invited to complete the European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire (QLQ-C30), the Self-Rating Anxiety Scale (SAS) and the Self-Rating Depression Scale (SDS) questionnaires at baseline and regularly during the study treatment. The time trends of the patient reported outcomes were estimated by a linear model using the generalized estimating equation based on the independent working correlation matrix. The generalized estimating equation model was utilized to assess the impact of patients' characteristics at baseline and treatment response during olverembatinib therapy on HRQoL, SAS, and SDS.

  – A total of 159 patients in CP or AP CML were included in this study. Median (range) age was 42 (20-74) years. 104 (65%) patients were male. Interval from diagnosis of CML to initiation of olverembatinib therapy was 5 (0.3-23) years. 77 (48%) patients received olverembatinib therapy within 5 years from the diagnosis of CML. All patients completed the QLQ-C30 questionnaire; and 115 completed the SAS and SDS questionnaires.

- Survey results:

  – Assessed by the EORTC QLQ-C30 questionnaire, the top 3 severe symptom burdens at baseline were financial difficulties, fatigue, and insomnia. Eight scale items including global health, physical functioning, emotional functioning, fatigue, pain, dyspnea, diarrhea and financial difficulties improved significantly during olverembatinib therapy. No scale deteriorated significantly. In multivariate analysis, age < 40 years was associated with better improvement of social functioning ($p = 0.021$); CP (vs. AP), better improvement of dyspnea ($p = 0.028$) and diarrhea ($p = 0.042$); achieving MMR, better improvement of global health ($p = 0.005$), nausea and vomiting ($p = 0.009$), and diarrhea ($p = 0.001$).

  – At baseline, 96 (84%) patients were normal according to the SAS score; and 19 (16%) had mild or moderate anxiety symptoms. 64 (56%) patients were normal according to the SDS score; 37 (32%) had mild depression symptoms; and 14 (12%), moderate or severe depression symptoms. SAS score was decreased significantly during olverembatinib therapy over time ($p < 0.001$) while the SDS score did not change significantly. At 36 months on olverembatinib therapy, 78 (95%) and 48 (59%) patients had no anxiety and depression symptoms assessed by SAS and SDS questionnaires, respectively. There was no variable identified that impacted the change of SAS score during olverembatinib therapy.

- Conclusions: HRQoL and anxiety symptoms significantly improved over time during olverembatinib therapy in patients with TKI-resistant CML. Younger age, CP than AP, and achieving MMR on olverembatinib therapy were associated with better improvements of HRQoL.

Lisaftoclax (APG-2575) Combined with Novel Therapeutic Regimens in Patients (Pts) with Relapsed or Refractory (R/R) Multiple Myeloma (MM) or Immunoglobulin Light-Chain (AL) Amyloidosis

Highlights:

- Background: R/R MM is incurable, with virtually inevitable relapse without appropriate therapeutic intervention. AL amyloidosis is a rare disease that may cause serious organ damage or death. Lisaftoclax is a novel, potent, selective BCL-2 inhibitor with clinical benefits in hematologic malignancies and solid tumors and a low reported incidence of adverse events (AEs).

- Introduction: The aim of this multicenter study was to evaluate the safety and efficacy of lisaftoclax combined with pomalidomide and dexamethasone (Arms A and C) or daratumumab, lenalidomide, and dexamethasone (Arm B) in patients with R/R MM (Arm A and B) or R/R AL amyloidosis (Arm C).

- Patient enrollment and methods: Patients with an Eastern Cooperative Oncology Group (ECOG) performance status ≤2 were administered lisaftoclax daily in repeated 28-day cycles. Pomalidomide, daratumumab, and lenalidomide were administered per label use. Dexamethasone was administered at 40 mg/day, and patients aged >75 were administered at the reduced dose of 20 mg/day.

  – As of January 25, 2024, 44 patients that included 36 patients with R/R MM and 8 patients with R/R AL amyloidosis were enrolled in the 3 arms of the study (Arms A, B, and C) to receive lisaftoclax at various doses.

  – The median (range) age of patients was 70.5 (24-88) years, 68.2% were male, and 65.9% were older than 65 years.

  – The median (range) number of lines of prior therapies was 3 (1-19), median (range) time from diagnosis to the first dose of study drug was 5.5 (1-29) years, and median (range) number of treatment cycles was 4 (1-26).

- Efficacy results:

  – In Arm A, 27 patients with R/R MM were efficacy evaluable. Among them, 10 had partial response (PR), 7 had very good PR (VGPR), and 2 had complete response (CR). The overall response rate (ORR [PR+VGPR+CR]) was 70.4%.

  – In Arm B, 2 patients with R/R MM achieved CR.

  – In Arm C, 7 patients with R/R AL amyloidosis were efficacy evaluable, and the ORR was 85.7% (4 VGPRs, 2 CR).

- Safety results:

  – Of the 42 patients included in safety analysis, ten patients experienced Grade ≥3 TRAEs, including neutropenia (14.3%), febrile neutropenia (2.4%), etc. 3 patients experienced serious TRAEs that included febrile neutropenia, acute kidney injury, and diarrhea with electrolyte imbalance (1 each).

  – A total of 24 patients discontinued treatment because of disease progression (n=15), TEAE (n=3), nonadherence (n=1), or investigator/patient decision (n=5).

- Conclusions: Lisaftoclax plus novel therapeutic regimens was well tolerated and demonstrated preliminary antitumor activity in patients with either R/R MM or AL amyloidosis.

* *Lisaftoclax and APG-5918 are investigational drug that has not been approved in any country and region.*

* *Olverembatinib is an investigational drug that has not been approved for any indication outside the Chinese mainland.*

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 and APG-5918 successfully.

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

Suzhou, People's Republic of China, June 17, 2024

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, Mr. Ren Wei and Dr. David Sidransky as independent non-executive Directors.