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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 to Present Results from Multiple Clinical Studies of olverembatinib and APG-2575 at the 2023 American Society of Hematology (ASH) Annual Meeting, two of which have been Selected for Oral Reports

Ascentage Pharma Group International (the "**Company**" or "**Ascentage Pharma**") is pleased to announce that results from multiple clinical studies of olverembatinib and APG-2575 (lisaftoclax) have been selected for presentations, including two oral reports, at the 65th American Society of Hematology (ASH) Annual Meeting. Olverembatinib was selected for oral reports at the ASH Annual Meeting for the sixth consecutive year, underscoring the significant interest in the drug's efficacy and safety by the global hematology community.

Olverembatinib has broad therapeutic potential for the treatment of multiple solid tumors and hematologic malignancies. Through an oral report, Ascentage Pharma will present the latest results from a randomized, controlled registrational Phase II study in patients with first- and second-generation tyrosine kinase inhibitor (TKI)-resistant chronic myeloid leukemia in the chronic-phase (CML-CP). The data show that, in patients with CML-CP who were resistant/intolerant to TKIs, olverembatinib demonstrated statistically significant and clinically meaningful improvement in event-free survival (EFS), compared with the best available therapy (BAT), meeting the primary endpoint of the study. The other Oral Report featuring early results from a Phase II study of olverembatinib combined with venetoclax and reduced-intensity chemotherapy in treatment-naïve patients with Ph+ ALL, led by Prof. Xiaoyuan Gong of the Institute of Hematology and Blood Diseases Hospital, the Chinese Academy of Medical Sciences

Also at this year's ASH Annual Meeting, Ascentage Pharma will release updated results from a US study of olverembatinib in a Poster Presentation. These data demonstrate the favorable potential clinical benefit of olverembatinib monotherapy and combination regimens in patients with heavily pretreated CML or Philadelphia chromosome-positive acute lymphoblastic leukemia (Ph+ ALL) and show the drug's therapeutic effect in patients who had failed prior treatment with ponatinib or asciminib, further demonstrating the drug's potential as a new treatment option to patients with CML or Ph+ ALL worldwide.

In addition, multiple other studies of olverembatinib were also selected for Poster Presentations, including one featuring a case series study of liposome mitoxantrone combined with venetoclax, homoharringtonine, and olverembatinib (the MVHO regimen) in pediatric patients with refractory or recurrent acute myeloid leukemia (AML), carried out by a team of investigators including Wenting Hu and Prof. Shuhong Shen of the Department of Hematology & Oncology, Shanghai Children's Medical Center of Shanghai Jiao Tong University School of Medicine (see the table below for details).

Developed by Ascentage Pharma, APG-2575 (lisaftoclax) is an orally available Bcl-2 inhibitor promising a wide therapeutic window in multiple hematologic malignancies and solid tumors. The investigational clinical data of lisaftoclax in patients with chronic lymphocytic leukemia (CLL), to be presented at the ASH Annual Meeting this year, once again demonstrate the drug's promising efficacy and favorable tolerability in patients with CLL who were heavily-pretreated and had prior exposure to BTK inhibitors. In two other abstracts on lisaftoclax, results were disclosed from clinical studies of the drug as a single agent and in combination regimens in multiple hematologic malignancies including relapsed/refractory (R/R) multiple myeloma (MM) and AML.

The ASH Annual Meeting is one of the largest gatherings of the international hematology community, bringing together the latest and most cutting-edge scientific research in the pathogenesis and clinical treatment of hematologic diseases. The 65th ASH Annual Meeting will take place on December 9, 2023 to December 12, 2023, both online and in-person in San Diego, the United States.

Studies of Ascentage Pharma's Drug Candidates to be presented at ASH 2023 include but not limited to:

Drug Candidate	Title	PI/Presenter	Institution	Abstract#	Format
Olverembatinib	Olverembatinib (HQP1351) Demonstrates Efficacy Vs. Best Available Therapy (BAT) in Patients (Pts) with Tyrosine Kinase Inhibitor (TKI)-Resistant Chronic Myeloid Leukemia Chronic-Phase (CML-CP) in a Registrational Randomized Phase 2 Study	Qian Jiang Xiaojun Huang	The Peking University People's Hospital	#869	Oral Report
	Olverembatinib Combined with Venetoclax and Reduced-Intensity Chemotherapy for Patients with Newly Diagnosed Philadelphia Chromosome-Positive Acute Lymphoblastic Leukemia: Early results from a phase II study	Xiaoyuan Gong	Institute of Hematology and Blood Diseases Hospital, the Chinese Academy of Medical Sciences	#827	Oral Report
	Update of Olverembatinib (HQP1351) Overcoming Ponatinib and/or Asciminib Resistance in Patients (Pts) with Heavily Pretreated/Refractory Chronic Myeloid Leukemia (CML) and Philadelphia Chromosome-Positive Acute Lymphoblastic Leukemia (Ph+ ALL)	Elias Jabbour Hagop Kantarjian	MD Anderson Cancer Center	#1798	Poster Presentation
	Combination of Liposome Mitoxantrone, Venetoclax, Homoharringtonine, and Olverembatinib (HQP1351) (MVHO) in Pediatric Patients with Refractory or Recurrent Acute Myeloid Leukemia (AML): Case Series	Wenting Hu Shuhong Shen	Department of Hematology & Oncology, Shanghai Children's Medical Center of Shanghai Jiao Tong University School of Medicine	#2840	Poster Presentation
	Combination of Olverembatinib and VP Regimen As First-Line Therapy for Adult Patients with Philadelphia Chromosome-Positive Acute Lymphoblastic Leukemia	Gaixiang Xu Jie Jin	The First Affiliated Hospital, Zhejiang University School of Medicine	#4205	Poster Presentation
	Olverembatinib(HQP1351)-Based Therapy in Adults with Relapsed or Refractory Philadelphia Chromosome-Positive Acute Lymphoblastic Leukemia or Advanced Chronic Myeloid Leukemia: Results of the Real-Life Study	Na Xu	Nanfang Hospital of Southern Medical University	#4538	Poster Presentation
	Frontline Combination of 3 Generation TKI Olverembatinib and Blinatumomab for Ph+/Phlike ALL Patients	Hongsheng Zhou	Nanfang Hospital of Southern Medical University	#1504	Poster Presentation

Drug Candidate	Title	PI/Presenter	Institution	Abstract#	Format
Lisaftoclax APG-2575	Updated Efficacy and Safety Results of Lisaftoclax (APG-2575) in Patients (pts) with Heavily Pretreated Chronic Lymphocytic Leukemia (CLL): Pool Analysis of Two Clinical Trials	Keshu Zhou Jianyong Li Jianxiang Wang	Henan Cancer Hospital, Jiangsu Province Hospital Institute of Hematology and Blood Diseases Hospital, the Chinese Academy of Medical Sciences	#1900	Poster Presentation
	Safety and Efficacy of Lisaftoclax (APG-2575), a Novel BCL-2 Inhibitor (BCL-2i), in Relapsed or Refractory (R/R) or Treatment-Naïve (TN) Patients (Pts) with Acute Myeloid leukemia (AML), Myelodysplastic Syndrome (MDS), or Other Myeloid Neoplasms	Huafeng Wang Jie Jin	The First Affiliated Hospital, Zhejiang University School of Medicine	#2925	Poster Presentation
	First Report on the Effects of Lisaftoclax (APG-2575) in Combination with Novel Therapeutic Regimens in Patients with Relapsed or Refractory Multiple Myeloma (R/R MM) or Immunoglobulin Light-Chain (Amyloid Light-Chain AL) Amyloidosis	Sikander Ailawadhi Asher A. Chanan-Khan	Mayo Clinic	#2016	Poster Presentation

The abstracts of Olverembatinib (HQP1351) and lisaftoclax presented at the 2023 ASH Annual Meeting are as follows:

Olverembatinib (HQP1351) Demonstrates Efficacy Vs. Best Available Therapy (BAT) in Patients (Pts) with Tyrosine Kinase Inhibitor (TKI)-Resistant Chronic Myeloid Leukemia Chronic-Phase (CML-CP) in a Registrational Randomized Phase 2 Study

- **Format:** Oral Report
- **Abstract:** #869
- **Session:** 632. Chronic Myeloid Leukemia: Clinical and Epidemiological: Mechanisms of resistance and expanded therapies
- **Time:** December 11, 2023, Monday, 3:45 PM (Pacific Time)/December 12, 2023, Tuesday, 7:45 AM (Beijing Time)
- **Highlights:**
  - ➢ This is a multicenter, randomized, registrational Phase II study designed to assess the efficacy and safety of olverembatinib compared with the BAT in patients with CML-CP.
  - ➢ As of April 30, 2023, a total of 144 patients were enrolled, of whom 69.4% were male and 30.6% were female. The median (range) age of these patients was 49 (18-77) years.
    - ✧ A total of 96 patients were treated with olverembatinib and 48 patients were treated with BAT.
    - ✧ The median (range) duration of follow-up for the olverembatinib and BAT arms were 12.67 (0-40.9) months and 2.94 (0-40.4) months, respectively. 66 (45.8%) patients had ≥1 BCR::ABL1 mutations and 39 (27.1%) had the BCR::ABL1^{T315I} mutation.
    - ✧ A total of 97 patients discontinued therapies (56 58.3% from the olverembatinib arm, 41 85.4% from the BAT arm) due to disease progression, treatment failure, adverse events (AEs), consent withdrawal, poor compliance, or death.
  - ➢ Safety results: 82/96 (85.4%) patients receiving olverembatinib and 31/46 (67.4%) patients receiving BAT experienced grade ≥3 AEs. AEs with an incidence >20% included thrombocytopenia; leukopenia; anemia; neutropenia; elevated creatine phosphokinase (CPK), alanine aminotransferase (ALT), and aspartate aminotransferase (AST); and hypertriglyceridemia. Serious AEs (SAEs) with an incidence >5% included thrombocytopenia. Common AEs (≥10%) that led to discontinuation, dose reduction, or treatment withdrawal were thrombocytopenia, neutropenia, and leukopenia.

- ➢ Efficacy results:

  - ✧ Data showed that in patients with CML-CP resistant/intolerant to prior treatment with TKIs, the olverembatinib arm, compared with the BAT arm, achieved statistically significant improvement in event-free survival (EFS), therefore meeting the primary endpoint of the study. The median (range) EFS was 21.22 (95% CI: 10.15 to not reached) months in the olverembatinib arm compared to 2.86 (95% CI 2.53-4.73) months in the BAT arm. Compared with the BAT control arm, olverembatinib reduced the risk of events by 65%. In the olverembatinib arm, the estimated EFS at 6, 12, and 24 months was 73% (95% CI, 62.5-81.0), 58.7% (95% CI, 47.5-68.2), and 46.9% (95% CI, 35.9-57.2), respectively. In the BAT group, it was 32.6% (95% CI,19.7-46.2), 26.1% (95% CI, 14.5-39.3), and 16.9% (95% CI, 7.7-29.2) at 6, 12 and 24 months, respectively.

  - ✧ Neither the olverembatinib nor the BAT arm reached the median overall survival (OS). As of the data cutoff date, 34 (71%) patients in the BAT control arm were crossed-over to be treated with olverembatinib after reaching the EFS endpoint.

  - ✧ The olverembatinib arm showed significantly better efficacy and higher response rates than the BAT control arm.

  - ✧ Conclusions: This study represents the largest sample of patients with CML-CP resistant or intolerant to both first- and second-generation TKIs. Olverembatinib was observed to be better tolerated and more effective than BAT in treating these patients.

Update of Olverembatinib (HQP1351) Overcoming Ponatinib and/or Asciminib Resistance in Patients (Pts) with Heavily Pretreated/Refractory Chronic Myeloid Leukemia (CML) and Philadelphia Chromosome-Positive Acute Lymphoblastic Leukemia (Ph+ ALL)

- **Format:** Poster Presentation
- **Abstract:** #1798
- **Session:** 632. Chronic Myeloid Leukemia: Clinical and Epidemiological: Poster I
- **Time:** December 9, 2023, Saturday, 5:30 PM-7:30 PM (Pacific Time)/December 10, 2023, Sunday, 9:30 AM-11:30 AM (Beijing Time)
- **Highlights**

  - ➢ Olverembatinib, a novel, potent BCR::ABL1 tyrosine kinase inhibitor (TKI), has shown strong antitumor activity in patients with CML and Ph+ ALL. This abstract reports on the safety, efficacy, and pharmacokinetics (PK) of olverembatinib in patients with CML and Ph+ ALL outside China, particularly in patients previously treated with third-generation TKI ponatinib and/or allosteric STAMP inhibitor asciminib.

- Methods: Olverembatinib was administered orally once every other day (QOD) in 28-day cycles. In the monotherapy cohort, patients were enrolled after treatment failures on at least 2 prior TKIs and randomized to receive olverembatinib QOD at 30, 40, or 50 mg. In the combination cohort, patients with Ph+ B-cell precursor ALL (BCP ALL) or lymphoid CML-BP (CML-LBP) resistant to at least 1 TKI were enrolled and administered olverembatinib (30 or 40 mg) QOD in combination with blinatumomab.

- As of June 30, 2023, 76 patients were enrolled, including 57 with CML-CP and 19 with advanced Ph+ leukemia. The median (range) age was 54.5 (21-80) years and 56.6% of patients were male.

  - 11 (14.5%), 23 (30.3%) and 39 (51.3%) patients had received 2, 3, and ≥4 TKIs, respectively.

  - A total of 52.6% of patients were previously treated with ponatinib, of whom 67.5% were resistant and 25.0% were intolerant to the drug, and 7.5% of patients failed for other reasons.

  - A total of 27.6% of patients were previously treated with asciminib, of whom 71.4% were resistant and 19.1% were intolerant to the agent, and 9.5% failed for other reasons.

  - At baseline, 32% of patients had T315I mutations, 38% had hypertension, and 17.1% had other cardiovascular comorbidities.

- The median (range) duration of treatment was 24.1 (0-134) weeks. PK analysis showed that western patients had a PK profile similar to historical data on Chinese patients.

- Safety results: 12 patients with CML-CP and 7 with advanced Ph+ ALL discontinued treatment for reasons including AEs (n = 4), disease progression (n = 7), and other reasons (n = 8). A total of 54 (83.1%) patients experienced treatment-related AEs (TRAEs) of any grade after receiving olverembatinib. Grade ≥3 AEs occurring in ≥3 patients (≥ 4.6% incidence) included thrombocytopenia (17%), neutropenia (13.8%), elevated blood creatine phosphokinase (13.8%), leukopenia (7.7%), anemia (4.6%), and elevated lipase (4.6%). 10 (15.4%) patients experienced olverembatinib treatment-related serious AEs (SAEs). 2 (3.1%) patients discontinued the study due to TRAEs and no TRAE-related deaths were reported.

- Efficacy results:

  - Among 50 efficacy-evaluable patients with CML-CP, 57% (25/44) achieved a complete cytogenetic response (CCyR), 43% (21/49) achieved a major molecular response (MMR), and the efficacy continued to improve over time. The rate of MMR in patients with CML-CP treated for 6 months and 12 months was 66% and 88%, respectively. At 24 months, the rate of progression-free survival (PFS) was 75% (95% CI: 56.1%-86.7%) and the OS was 97.6% (95% CI: 90.8%-99.4%).

    - Among patients whose disease failed ≥4 prior TKIs, CCyR and MMR rates were 57% (13/23) and 42% (11/26), respectively.

- In patients with CML-CP harboring the T315I mutation, CCyR and MMR rates were 60% (9/15) and 44% (7/16), respectively.

- In patients without the T315I mutation, CCyR and MMR rates were 55% (16/29) and 42% (14/33), respectively.

- In patients who had failed treatment with ponatinib, CCyR and MMR rates were 53% (8/15) and 38% (6/16), respectively.

- In patients who had failed treatment with asciminib, CCyR and MMR rates were 43% (3/7) and 38% (3/8), respectively. Among the 8 patients who were resistant/intolerant to both ponatinib and asciminib, 2 achieved MMR.

✧ Among the 13 efficacy-evaluable patients with advanced Ph+ ALL, 3 (23%) achieved MMR, of whom 1 patient harbored the T315I mutation and 2 were T315I mutation negative and resistant to ponatinib.

✧ In the combination cohort, 2 patients with Ph+ BCP ALL received olverembatinib 30 mg QOD in combination with blinatumomab. Both patients achieved CCyR and 1 achieved negative minimal residual disease (MRD) status after 1 treatment cycle.

➢ Conclusions: Olverembatinib alone or combined with blinatumomab was efficacious and well-tolerated in heavily pretreated patients with CML or Ph+ ALL. The efficacy of olverembatinib was not affected by prior exposure to ponatinib or asciminib, and the status of the T315I mutation. Olverembatinib may provide an effective treatment option for patients with CML or Ph+ ALL who have failed 2 or more TKIs.

Olverembatinib Combined with Venetoclax and Reduced-Intensity Chemotherapy for Patients with Newly Diagnosed Philadelphia Chromosome-Positive Acute Lymphoblastic Leukemia: Early results from a phase II study

- **Format:** Oral Report

- **Abstract:** #827

- **Session:** 614. Acute Lymphoblastic Leukemia: Therapies, Excluding Transplantation and Cellular Immunotherapies: Optimal Frontline Treatment for ALL

- **Time:** December 11, 2023, Monday; 2:45 PM-4:15 PM (Pacific Time)/December 12, 2023, Tuesday; 6:45 AM-8:15 AM (Beijing Time)

- **Highlights:**

  - ➢ Background: The combination of olverembatinib (HQP1351), a novel third-generation tyrosine kinase inhibitors (TKIs), with venetoclax generated high response rates in patients with relapsed/refractory Philadelphia chromosome-positive acute lymphoblastic leukemia (Ph ALL). However, the efficacy and safety of these two agents-based regimens as frontline treatment remains unknown.

  - ➢ Methods: This is a single-arm phase II study (NCT05594784) that enrolled patients (pts) ≥ 14 years (yrs) of age with newly diagnosed Ph + ALL. Pts were treated with a combination of venetoclax (100 mg d1, 200 mg d2, 400 mg d3-28), olverembatinib 40 mg once every continuously other day, vincristine 1.4 mg/m2 (maximum dose 2 mg) on day 1, 8, 15, 22, and prednisone 60 mg/m2 on day 1-14; 40 mg/m2 on day 15-28 in cycle 1. In cycle 2-3, oral treatment with venetoclax 400 mg × 7 days, olverembatinib once every other day continuously and prednisone 60 mg/m × 7 days were administrated. Cycles were repeated every 28 days. During cycle 1, The dose of olverembatinib was reduced to 30 mg once every other day for pts achieving a complete molecular response (CMR). The primary endpoint of this study was the CMR rate at 3 months. CMR was defined as undetectable BCR:ABL1 transcripts by using the RT-PCR method with sensitivity of 0.001%. MMR was defined as more than 3-log reduction of BCR:ABL1 transcripts.

  - ➢ From August 2022 to April 2023, a total of 31 pts were enrolled. All pts completed 3 cycles of treatment and could be assessed for the primary endpoint. The data cutoff date was July 25, 2023 with a median follow-up time of 5.8 months. The median age was 40 years (range, 20-66 years) and males accounted for 58.1%. Twenty-three pts (74.2%) expressed the p190 transcript and 8 pts (25.8%) expressed the p210 transcript. The median expression level of BCR:ABL1 was 96.33% (range, 70.79%-175.39%).

  - ➢ Efficacy results: All patients achieved CR at the end of cycle 1 and no TLS or treatment-related deaths occurred. Molecular response at the end of cycle 1 was CMR in 17 patients (54.8%), and MMR in 8 (25.8%). Molecular response at 3 months was CMR in 19 patients (61.3%) and MMR in 10 (32.3%). No patients developed relapses or deaths at the last follow-up.

  - ➢ Safety results: The regimen was well-tolerated and safe. Most side effects were grade 1-2. The demand for transfusion and the incidence of infections significantly decreased compared to our historic data. No patient discontinued olverembatinib or venetoclax due to toxicity.

  - ➢ Conclusions: The combination of olverembatinib and venetoclax with reduced-intensity chemotherapy is a safe and effective regimen in patients with newly diagnosed Ph ALL. The regimen results in high rates of CMR in the absence of intensive chemotherapy or immunotherapy.

Combination of Liposome Mitoxantrone, Venetoclax, Homoharringtonine, and Olverembatinib (HQP1351) (MVHO) in Pediatric Patients with Refractory or Recurrent Acute Myeloid Leukemia (AML): Case Series

- **Format:** Poster Presentation
- **Abstract:** #2840
- **Session:** 613. Acute Myeloid Leukemias: Clinical and Epidemiological: Poster II
- **Time:** December 10, 2023, Sunday; 6:00 PM-8:00 PM (Pacific time)/December 11, 2023, Monday; 10:00 PM-12:00AM (Beijing Time)
- **Highlights:**

  ➢ Background: AML accounts for up to 25% of new pediatric acute leukemia cases. Although the overall survival (OS) in pediatric AML has increased to approximately 70% in recent years because of enhanced risk stratification strategies and therapeutics, approximately 30% of patients experience relapse, and 5% to 10% die because of disease complications or untoward medication effects. Hence, pediatric AML continues to represent an unmet medical need. This study investigated the efficacy and safety of the MVHO therapy in pediatric patients with refractory or recurrent AML.

  ➢ Methods: The study enrolled patients with recurrent or newly diagnosed AML with poor prognosis secondary to related molecular abnormalities, including NUP98 rearrangements, FUS-ERG, CBFA2T3-GLIS2, and del(7q), who did not achieve complete remission (CR) after first-line induction therapy (i.e., DA, DAE, DAH, MAG, and CLAG). Patients were administered the MVHO regimen, which included 1 dose of liposome mitoxantrone at 8 mg/m^2; venetoclax at 300 to 350 mg/m^2 once daily on days (D) 1 through 7 (with dose escalation if high tumor burden); homoharringtonine at 2 mg/m^2 once daily on D1 through 7; and olverembatinib at 20-30 mg/m^2 every other day on D1, 3, 5, and 7. The remission rate after 1 cycle (28-35 days, depending on hematopoietic recovery), total remission rate, recurrence rate, event-free survival (EFS), hematologic toxicity, and infection rate of the MVHO protocol were evaluated.

  ➢ A total of 18 patients were enrolled (9 boys and 9 girls), with a median (range) age of 7.3 (4 months-13 years) years, and underwent a total of 27 cycles of the MVHO therapy. Half of the patients underwent 1 cycle and the other half underwent 2 cycles. Per French-American-British (FAB) classification criteria: patients had myelodysplastic syndrome (n = 2); mixed-phenotype acute leukemia (n = 2); and AML subtypes M7 (n = 4), M2 (n = 4), M5 (n = 4), M4 (n = 1), and M0 (n = 1).

- ➢ Efficacy results: The median (range) follow-up time was 131 (26-256) days. The total response rate (CR + complete remission with incomplete hematological recovery Cri + partial response) was 83.3%, and the remission rate (CR + Cri) after 1 cycle was 72.2%. A total of 8 patients were minimum residual disease negative. For the 6 patients with recurrent AML, the remission rate after 1 cycle was 66.7%. A total of 3 patients discontinued because of no response or disease progression, and 12 patients underwent hematopoietic stem cell transplantation, after which 1 patient relapsed. The rate of recurrence was 6.7% (1/15). The 8-month mean (± SD) EFS was 60.1% (± 19%) and the OS was 100%.

- ➢ Safety results: Among the 26 cycles of treatment evaluated for toxicity, there were no associated fatal infections or bleeding events. Prophylactic levofloxacin and posaconazole were administered orally (or intravenously in the case of emergent fever) during myelosuppression in each cycle. No breakthrough infection was observed in 5 of 26 cycles of MVHO. There was 1 case of septic shock, and the incidence of grade ≥3 infection was 80.7%, which included pneumonia and bloodstream infections. Common grade 4 treatment-related adverse events (TRAEs) were neutropenia, which was experienced by 100% of patients, and grade 4 thrombocytopenia, which was experienced by 46.1% of patients. Platelets did not decrease to below 100,000/μL after 5 of 26 cycles of MVHO treatment.

- ➢ Conclusions: MVHO therapy was effective and reasonably well tolerated in pediatric patients with refractory or recurrent AML, suggesting that it may comprise a suitable first-line treatment option for pediatric patients with AML.

Updated Efficacy and Safety Results of Lisaftoclax (APG-2575) in Patients (pts) with Heavily Pretreated Chronic Lymphocytic Leukemia (CLL): Pool Analysis of Two Clinical Trials

- **Format:** Poster Presentation
- **Abstract:** #1900
- **Session:** 642. Chronic Lymphocytic Leukemia: Clinical and Epidemiological: Poster I
- **Time:** Saturday, December 9, 2023; 5:30 PM-7:30 PM (Pacific Time)/Sunday, December 10, 2023; 9:30 AM-11:30 AM (Beijing Time)
- **Highlights:**

  - ➢ This abstract reported updated data from long-term follow-ups in two Phase 1b/2 studies of lisaftoclax (APG-2575-CN001 NCT03913949 and APG-2575-CC101 NCT04494503) in patients with CLL.

  - ➢ In the 2 studies, lisaftoclax was administered orally once daily in 28-day cycles, in 100 mg, 200 mg, 400 mg, 600 mg, and 800 mg dose cohorts. Under close monitoring for prevention and early detection of tumor lysis syndrome (TLS), patients were treated (with a daily dose ramp-up schedule) until disease progression, intolerable toxicity, death, or any other reason for termination.

- ➢ As of April 27, 2023, a total of 47 patients with CLL were enrolled. The median (range) duration of follow-up was 14.06 (0.7-30.2) months. The median (range) age was 58 (34-80) years. At enrollment, 53.2% of patients were in Rai stage III/IV, and 48.9% of patients were in Binet stage C. 44.7% of patients had received ≥3 lines of treatment; 66.0% of patients had received ≥2 lines of treatment; 23.4% of patients were treated with Bruton tyrosine kinase inhibitors (BTKis); and 55.3% were treated with a CD20 monoclonal antibody. 68.1% (32) of patients discontinued the study due to disease progression (51.1%), consent withdrawal (6.4%), adverse events (AEs) (2.1%), investigator's decision (2.1%), poor compliance (2.1%), protocol deviation (2.1%), and other reasons (2.1%).

- ➢ The overall response rate (ORR) in patients with CLL was 73.3% (33/45), and the complete response (CR)/incomplete hematological recovery (Cri) rate was 24.4% (11/45).

- ➢ In total, 76.6% (36) of patients experienced grade ≥3 treatment-emergent adverse events (TEAEs); 27.7% (13) experienced serious AEs (SAEs). Treatment-related adverse events (TRAEs) were observed in 95.7% (45) of patients, of whom 68.1% (32) experienced grade ≥3 TRAEs and 14.9% (7) experienced SAEs. One case of tumor lysis syndrome (TLS) was reported.

- ➢ Conclusion: Lisaftoclax demonstrated significant efficacy and favorable tolerability in patients with CLL who were heavily pretreated and had prior exposure to BTKis.

Safety and Efficacy of Lisaftoclax (APG-2575), a Novel BCL-2 Inhibitor (BCL-2i), in Relapsed or Refractory (R/R) or Treatment-Naïve (TN) Patients (Pts) with Acute Myeloid leukemia (AML), Myelodysplastic Syndrome (MDS), or Other Myeloid Neoplasms

- **Format:** Poster Presentation

- **Abstract:** #2925

- **Session:** 616. Acute Myeloid Leukemias: Investigational Therapies, Excluding Transplantation and Cellular Immunotherapies

- **Time:** December 10, 2023, Sunday, 6:00 PM-8:00 PM (Pacific Time)/December 11, 2023, Monday, 10:00 AM-12:00 PM (Beijing Time)

- **Highlights:**

  - ➢ This multicenter, open-label, Phase I study in China evaluated the efficacy and safety of lisaftoclax alone or combined with azacitidine (AZA) or homoharringtonine (HHT) in patients with treatment-naïve or R/R AML, MDS, or other myeloid neoplasms.

  - ➢ Trial design:

    - ✧ In part one, lisaftoclax as a single agent was orally administered once daily at 200, 400, 600, or 800 mg, using a "3 + 3" dose escalation design.

- ✧ In part two, patients with R/R AML, mixed-phenotype acute leukemia (MPAL), blastic plasmacytoid dendritic cell neoplasm (BPDCN), or chronic myelomonocytic leukemia (CMML) were enrolled in Cohorts A, B, and C; while patients with higher-risk MDS were enrolled in Cohort D; and older or chemotherapy-ineligible (unfit) patients with treatment-naïve AML were enrolled in Cohort E. Lisaftoclax was administered orally once daily in 28-day cycles (or 14-day cycles for patients with MDS). A daily ramp-up schedule was adopted to prevent tumor lysis syndrome (TLS). Cohort A was treated with lisaftoclax combined with low-dose HHT (1 mg daily on days d 1-14); Cohort B was treated with lisaftoclax combined with standard-dose HHT (2 mg/m^2 daily on d1-7); Cohort C, D, E were treated with lisaftoclax combined with AZA (75 mg/m^2 daily on d1-7). Dose-limiting toxicity(DLT) was assessed during the first cycle.

- ➢ As of July 19, 2023, a total of 115 patients were enrolled, including 89 patients with AML (64 R/R; 25 TN older/unfit), 22 with MDS (7 R/R MDS; 15 TN MDS), 2 MPAL, 1 CMML, and 1 BPDCN. A total of 13 patients received lisaftoclax monotherapy, and 102 patients received combination regimens.

- ➢ Efficacy results:

  - ✧ In patients treated with lisaftoclax monotherapy, the ORR and composite remission rate (CRc = complete remission CR + CR with incomplete blood count recovery CRi) were each 8.3% (1/12).

  - ✧ Lisaftoclax at 600 mg and 800 mg were chosen as exploratory doses for combination therapies.

    - – Among the 21 efficacy evaluable patients with TN AML in Cohort E, the ORR and CRc were 71.4% and 47.6%, respectively.

    - – Among the 36 efficacy evaluable patients with R/R AML or myeloid neoplasm in Cohort C, the ORR and CRc were 75.0% and 44.4%, respectively. The PFS was 10.22 months.

    - – Among patients in Cohort B, the ORR and CRc were both 75.0%.

    - – Among patients in Cohort D, the ORR was 70.0%, the CR/marrow CR rate was 60.0%.

- ➢ Safety results: Common TEAEs included hematologic toxicity, electrolyte imbalance, and diarrhea. No TLS was reported during the study and dose-limiting toxicities (DLTs; pneumonia, respiratory failure, and heart failure) were observed in 1 patient in Cohort C. 13 patients who received lisaftoclax monotherapy have experienced TEAEs and grade ≥3 TEAEs and 4 (30.8%) patients experienced SAEs. In patients treated with lisaftoclax combined with HHT, 12 (85.7%) experienced TEAEs and grade ≥3 TEAEs, and 2 (14.3%) experienced SAEs. In the 75 patients treated with lisaftoclax combined with AZA, 100% of patients experienced TEAEs, including 55 (73.3%) who experienced grade ≥3 TEAEs and 18 (24.0%) SAEs.

- ➢ Increased systemic exposure of lisaftoclax was discerned as the dosage escalated from 200 mg to 800 mg. Compared to lisaftoclax monotherapy, no significant difference was observed in the pharmacokinetic (PK) profile of lisaftoclax combined with AZA or HHT.

- ➢ Conclusions: Lisaftoclax, in monotherapy or combination regimens, showed encouraging efficacy and favorable tolerability profiles in patients with R/R AML or MDS and older/unfit patients with TN AML.

First Report on the Effects of Lisaftoclax (APG-2575) in Combination with Novel Therapeutic Regimens in Patients with Relapsed or Refractory Multiple Myeloma (R/R MM) or Immunoglobulin Light-Chain (Amyloid Light-Chain AL) Amyloidosis

- **Format:** Poster Presentation

- **Abstract:** #2016

- **Session:** 653. Multiple Myeloma: Prospective Therapeutic Trials: Poster I

- **Time:** December 9, 2023, Saturday; 5:30 PM-7:30 PM (Pacific time)/December 10, 2023, Sunday; 9:30 PM-11:30 PM (Pacific time)

- **Highlights:**

  - ➢ This multicenter study was designed to evaluate the safety and efficacy of lisaftoclax combination regimens in patients with R/R MM or R/R AL amyloidosis.

  - ➢ This study has three treatment arms that included Arm A: lisaftoclax combined with pomalidomide and dexamethasone in patients with R/R MM; Arm B: lisaftoclax combined with daratumumab, lenalidomide, and dexamethasone in patients with R/R MM; and Arm C: lisaftoclax combined with pomalidomide and dexamethasone in patients with R/R amyloidosis. Lisaftoclax was administered orally once daily (QD) at 5 dose levels (400 mg, 600 mg, 800 mg, 1,000 mg, and 1,200 mg) without ramp-up in 28-day cycles. Pomalidomide, daratumumab, and lenalidomide were administered per label use. Dexamethasone 40 mg (20 mg for patients aged >75 years) was administered on Days 1, 8, 15, and 22 of 28-day cycles.

  - ➢ As of July 3, 2023, a total of 30 patients were enrolled. Among them, 22, 3, and 5 patients were enrolled into Arm A, B, and C, respectively. 66.7% of patients were male and the median (range) age was 70.5 (24-88) years. All patients were previously exposed to multiple lines of treatment, with a median (range) line of prior therapies of 4 (1-19). 18 patients were triple-class-exposed, including 7 who had received pomalidomide and 3 who harbored the t(11;14) chromosomal abnormality.

  - ➢ Safety results: A total of 19 patients experienced lisaftoclax treatment related AEs, including nausea (16.7%), neutropenia (16.7%); thrombocytopenia, leukopenia, abdominal distension, constipation, or diarrhea (6.7% each). A total of 7 patients experienced grade ≥3 TRAEs, including neutropenia (10.0%), febrile neutropenia (3.3%), iron deficiency anemia (3.3%), thrombocytopenia (3.3%), prolonged electrocardiogram QT interval (3.3%), and acute kidney injury (3.3%). Two patients experienced lisaftoclax-related SAEs, including 1 acute kidney injury and 1 febrile neutropenia.

- ➢ Efficacy results:
  - ✧ In Arm A, 21 patients with R/R MM were efficacy evaluable, with an ORR (partial response PR+ very good partial response VGPR) of 66.7%.
  - ✧ In Arm B, 1 patient with R/R MM achieved PR and another achieved VGPR.
  - ✧ In Arm C, 3 patients with R/R amyloidosis achieved a hematologic VGPR. The ORR was 60% and 1 patient experience organ function improvement.
- ➢ Conclusions: Lisaftoclax combination regimens were well tolerated and demonstrated potent antitumor activity in patients with R/R MM and R/R amyloidosis.

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 successfully.

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

Suzhou, People's Republic of China, November 3, 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.