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 AMERICAN SOCIETY OF CLINICAL ONCOLOGY ANNUAL MEETING

Ascentage Pharma Group International (the "**Company**" or "**Ascentage Pharma**") is pleased to announce that that its four abstracts selected for presentations at the 2024 American Society of Clinical Oncology (ASCO) Annual Meeting are now available on ASCO's official website. These abstracts report on the Company's three lead drug candidates, including olverembatinib (HQP1351), the first and only China-approved third-generation BCR-ABL inhibitor; lisaftoclax (APG-2575), a BCL-2 selective inhibitor; and APG-2449, a FAK/ALK/ROS1 inhibitor. All lead drug candidates are being studied as they are investigational drugs and not approved in the US.

Updated results from the four studies will be presented in Oral Reports or Posters at the ASCO Annual Meeting taking place during May 31, 2024 to June 4, 2024 (US local time). The ASCO Annual Meeting showcases the most cutting-edge research in clinical oncology and state-of-the-art advanced cancer therapies and is the world's most influential and prominent scientific gathering of the clinical oncology community.

These four clinical studies to be presented by Ascentage Pharma at this year's ASCO Annual Meeting are as follows:

Drug Candidates	Abstract Title	Abstract number	Format
Olverembatinib (HQP1351)	Updated efficacy results of olverembatinib (HQP1351) in patients with tyrosine kinase inhibitor (TKI)-resistant succinate dehydrogenase (SDH)-deficient gastrointestinal stromal tumor (GIST) and paraganglioma.	#11502	Oral Report
Lisaftoclax (APG-2575)	Safety and efficacy of lisaftoclax, a novel BCL-2 inhibitor, in combination with azacitidine in patients with treatment-naïve or relapsed or refractory acute myeloid leukemia.	#6541	Poster Presentation
	Updated efficacy and safety results of BCL-2 inhibitor lisaftoclax (APG-2575) alone or combined with ibrutinib or rituximab in patients (pts) with Waldenström macroglobulinemia (WM).	#7078	Poster Presentation
APG-2449	Updated study results of novel FAK/ALK/ROS1 inhibitor APG-2449 in patients (pts) with non-small-cell lung cancer (NSCLC) resistant to second-generation ALK inhibitors.	#3124	Poster Presentation

Oral Report

Olverembatinib (HQP1351)

Updated efficacy results of olverembatinib (HQP1351) in patients with tyrosine kinase inhibitor (TKI)-resistant succinate dehydrogenase (SDH)-deficient gastrointestinal stromal tumor (GIST) and paraganglioma

Abstract Number: 11502

Session Title: Sarcoma

Date and Time:

June 3, 2024, Monday, 3:00 PM – 6:00 PM (US Central Time)

June 4, 2024, Tuesday. 4:00 AM – 7:00 AM (Beijing Time)

First Author: Haibo Qiu, MD, PhD, Sun Yat-sen University Cancer Center, Guangzhou, Guangdong, China.

Highlights:

Background: SDH-deficient GIST is a rare type of GIST, mainly observed in the stomach of children, adolescents, and young adults under 30 years of age. No active targeted therapies have been identified in this subset of GIST. Olverembatinib, approved in China for the treatment of patients with chronic myeloid leukemia, has shown promising clinical efficacy in SDH-deficient GIST. In this abstract, the study reports updated efficacy data of olverembatinib in SDH-deficient GIST and preliminary efficacy data in paraganglioma, an SDH-deficient-related tumor.

Introduction: The aim of this study was to evaluate the safety and efficacy (per RECIST v1.1) of olverembatinib in patients with SDH-deficient GIST and other solid tumors. Olverembatinib was administered orally once every other day (QOD) in 28-day cycles.

Patient enrollment and methods: As of December 27, 2023, 26 patients with SDH-deficient GIST (confirmed by immunohistochemistry [IHC] assay) had received ≥1 dose of olverembatinib (median [range] age, 30 [13-56] years), and 25 of them had received 1-4 tyrosine kinase inhibitors (TKIs; 42.3% of patients received ≥3 TKIs). Olverembatinib was administered in doses ranging from 30 to 50 mg (30 mg [n = 6]; 40 mg [n = 14]; 50 mg [n = 6]). This study also enrolled 6 patients with paraganglioma.

Efficacy results:

- In the 26 patients with SDH-deficient GIST, the median (range) duration of treatment was 15.6 (1.8-42.3) months. 6 of those patients achieved partial responses (PR); another 18 patients achieved stable diseases (SD) lasting > 4 cycles. The clinical benefit rate (CBR, complete response [CR] + PR + SD > 4 cycles) was 92.3% (24/26) and the longest treatment duration was 40 months. After a median (range) follow-up of 17.0 (4.1-57.5) months, the median (range) progression-free survival (PFS) was 25.7 months (12.1-not reached [NR]).

- Among the 6 patients with paraganglioma, 5 achieved SDs > 4 cycles, with a CBR of 83.3% and a median (range) PFS of 8.25 (1.87-NR) months.

Safety results: The adverse event profile was the same as previously reported (Qiu H, et al, J Clin Oncol 41:11540), with no newly emergent safety issues observed.

Conclusions: Olverembatinib was well tolerated. In patients with SDH-deficient GIST, olverembatinib demonstrated a CBR exceeding 90% and significantly prolonged the estimated median PFS, indicating the potential benefit of this treatment and providing a benchmark for future studies in this rare subtype of GIST.

Poster Presentations

Lisaftoclax (APG-2575)

Safety and efficacy of lisaftoclax, a novel BCL-2 inhibitor, in combination with azacitidine in patients with treatment-naïve or relapsed or refractory acute myeloid leukemia

Abstract Number: 6541

Session Title: Hematologic Malignancies – Leukemia, Myelodysplastic Syndromes, and Allotransplant

Date and Time:

June 3, 2024, Monday, 9:00 AM – 12:00 PM (US Central Time)

June 3, 2024, Monday, 10:00 PM – 01:00 AM on the next day (Beijing Time)

First Author: Huafeng Wang, MD, PhD, The First Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou, Zhejiang, China.

Highlights:

Background and introduction: Early studies showed that lisaftoclax in combination with various agents can synergistically induce apoptosis in acute myeloid leukemia (AML). This poster presents follow-up safety and efficacy data from a Phase Ib/II study of lisaftoclax combined with azacitidine (AZA) in adults with AML.

Patient enrollment and methods:

- This study enrolled elderly (≥75 years)/unfit treatment-naïve (TN) patients with AML who were intolerant of standard induction chemotherapies and patients (≥18 years) with relapsed/refractory (R/R) AML. Lisaftoclax (400/600/800 mg) was administered orally once daily in 28-day cycles. In the first treatment cycle, a daily ramp up schedule was used to prevent tumor lysis syndrome (TLS). AZA was administered once daily on D1-D7 at 75 mg/m^2.

- As of January 25, 2024, 76 patients with AML were enrolled, including 37 patients with R/R AML and 39 elderly/unfit patients with TN AML who were intolerant of standard induction chemotherapies. The median (range) age was 66 (20-81) years, and 61.8% of the patients were male.

Efficacy results:

- In patients with R/R AML treated with lisaftoclax combined with AZA, the overall response rate ([ORR]=CR + CRi + morphologic leukemia-free state [MLFS] + PR) was 72.7%, the composite complete remission rate (CRc = CR + CRi) was 45.5%. In the 600 mg cohort (n=30), the median duration of treatment was 3.8 months, the ORR was 76.7%, the CRc was 50.0%, the median time to CRc was 2.5 months, the median PFS was 10.2 months, and the median overall survival (OS) was 14.7 months.

- Among patients with TN AML treated with lisaftoclax combined with AZA, the ORR was 64.1%, the CRc was 51.3%. In the 600 mg cohort (n=29), the median duration of treatment was 3.3 months, the median time to CRc was 1.9 months. The median PFS was not reached.

- 600 mg lisaftoclax combined with AZA was established as the recommended Phase II dose (RP2D).

Safety results: All patients treated with lisaftoclax combined with AZA reported treatment-emergent adverse events (TEAEs), with 89.5% experiencing Grade 3/4 TEAEs and 43.4% experiencing serious adverse events (SAEs). Common TEAEs included neutropenia (60.5%), thrombocytopenia (60.5%), diarrhea (42.1%), hypokalemia (40.8%), pyrexia (35.5%), and vomiting (30.3%). Grade ≥ 3 TEAEs reported in ≥ 10% of patients included neutropenia (57.9%), thrombocytopenia (50.0%), anemia (27.6%), pneumonia (17.1%), and febrile neutropenia (10.5%). No TLS was reported. The 30-/60-day mortality rates were 1.3% and 3.9%, respectively.

Conclusions: These data support an emerging role for the new Bcl-2 inhibitor lisaftoclax combined with AZA for the treatment of elderly/unfit TN patients with AML and patients with R/R AML, especially demonstrated a potentially favorable safety profile in terms of TLS, a low incidence of neutropenic fever, and low early mortality. A Phase III randomized, double-blind study is being conducted to determine whether lisaftoclax combined with AZA improves the survival of elderly/unfit TN patients with AML intolerant of standard induction chemotherapies.

Updated efficacy and safety results of BCL-2 inhibitor lisaftoclax (APG-2575) alone or combined with ibrutinib or rituximab in patients (pts) with Waldenström macroglobulinemia (WM)

Abstract Number: 7078

Session Title: Hematologic Malignancies – Lymphoma and Chronic Lymphocytic Leukemia

Date and Time:

June 3, 2024, Monday, 9:00 AM – 12:00 PM (US Central Time)

June 3, 2024, Monday, 10:00 PM – 01:00 AM on the next day (Beijing Time)

First Author: Masa Lasica, MBBS, FRACP, FRCPA, St Vincent's Hospital, Melbourne, Victoria, Australia.

Highlights:

Background: Lisaftoclax is a novel, oral, highly selective, potent Bcl-2 inhibitor. Lisaftoclax can overcome resistance to ibrutinib in ibrutinib-insensitive RPCI-WM1 models. In other non-Hodgkin lymphoma (NHL) models (including DOHH2 follicular lymphoma models and OCI-LY1 diffuse large B-cell lymphoma [DLBCL] models), lisaftoclax combined with ibrutinib has a strong synergistic antitumor effect.

Introduction: This is an open-label, multicenter, global Phase Ib/II study designed to evaluate the efficacy, safety, tolerability, and pharmacokinetics (PK) of lisaftoclax monotherapy or in combinations with agents such as ibrutinib/rituximab in patients with WM.

Patient enrollment and methods:

- In this study, patients with WM were enrolled in 3 arms, including Arm A: lisaftoclax monotherapy in patients resistant or intolerant to prior treatment with Bruton's tyrosine kinase inhibitors (BTKis); Arm B: lisaftoclax combined with ibrutinib in treatment-naïve patients with WM; and Arm C: lisaftoclax combined with rituximab in BTKi-naïve patients with relapsed/refractory WM.

- Lisaftoclax was orally administered once daily in 28-day cycles. Lisaftoclax was gradually escalated from the starting dose of 400 mg to 1,200 mg. As of January 25, 2024, a total of 46 patients were enrolled in the study (Arm A [n=14] at doses of up to 1,000 mg; Arm B [n=24] at doses of up to 1,200 mg; Arm C [n=8] at doses of up to 800 mg).

Efficacy results:

- The median (range) durations of treatment were 11 (1-28), 23.5 (1-34), and 11.5 (5-33) months for Arms A, B, and C, respectively.

- The objective response rates (ORRs; PR, very good partial response [VGPR], CR) were 41.7%, 90.9%, and 37.5% for Arms A, B, and C, respectively.

- In Arm A, patients with wild-type *CXCR4* (n =7) had better overall response to lisaftoclax than the *CXCR4*^{mut} group (n = 3).

- In Arms B and C, no significant differences between patients with/without *CXCR4*^{mut} were observed.

Safety results:

- In Arm B, 1 dose-limiting toxicity (DLT, grade 3 clinical TLS), attributed to pre-existing renal impairment, occurred at 1,200 mg; and 1 grade 3 laboratory TLS, primarily attributed to dehydration and concomitant symptomatic therapies, occurred at 1,000 mg. Abnormal electrolytes was resolved without recurrence after 1 day of drug interruption.

- Grade ≥ 3 lisaftoclax-related adverse events (AEs) included neutropenia (15.2%), thrombocytopenia (4.3%), decreased leukocytes (4.3%), TLS (4.3%), anemia (2.2%), weight loss (2.2%), and septic shock (2.2%).

- Ventricular arrhythmia was not observed.

- One patient required dose reduction because of neutropenia.

- The maximum-tolerated dose (MTD) was not reached.

- Lisaftoclax combined with ibrutinib showed a PK exposure comparable to lisaftoclax or ibrutinib alone, indicating no potential drug-drug interactions (DDIs).

Conclusions: Lisaftoclax alone and combined with ibrutinib or rituximab was well tolerated and demonstrated measurable effects in patients with treatment-naïve or BTKi-treatment-failed WM.

APG-2449

Updated study results of novel FAK/ALK/ROS1 inhibitor APG-2449 in patients (pts) with non-small-cell lung cancer (NSCLC) resistant to second-generation ALK inhibitors.

Abstract Number: 3124

Session Title: Developmental Therapeutics – Molecularly Targeted Agents and Tumor Biology

Date and Time:

June 1, 2024, Saturday, 9:00 AM – 12:00 PM (US Central Time)

June 1, 2024, Saturday, 10:00 PM – 01:00 AM on the next day (Beijing Time)

First Author: Yuxiang Ma, MD, PhD, Sun Yat-sen University Cancer Center, Guangzhou, Guangdong, China.

Highlights:

Background: ALK inhibitors increase FAK pathway gene expression in ALK^+ NSCLC cell lines, with the highest induced expression in drug-tolerant persister cells. This suggests that FAK pathway activation is involved in the mechanism that leads to ALK TKI resistance in ALK^+ NSCLC. APG-2449 is an orally active FAK inhibitor and a third-generation ALK/ROS1 TKI that has shown potent antitumor activity in preclinical models and clinical studies. This poster reports further safety and efficacy data of APG-2449.

Patient enrollment and methods:

- This study comprises a dose-escalation portion and a dose-expansion portion. 1,200 mg daily (QD) was determined as the RP2D. There are two cohorts in the dose-expansion portion: Cohort 1 included patients with NSCLC who were resistant to second-generation ALK TKIs; Cohort 2 included patients with NSCLC who were ALK or ROS1 TKI naïve.

- As of December 9, 2023, a total of 144 patients with NSCLC, mesothelioma, or ovarian cancer were treated with APG-2449 at doses ranging from 150 – 1,500 mg. The median (range) age of patients was 53 (21-78) years and 53.5% were female.

Efficacy results:

- The ORRs of APG-2449 in patients with ROS1 and ALK TKI-naïve NSCLC (n=36) were 68.2% (15/22) and 78.6% (11/14), respectively. Of the 22 patients with NSCLC resistant to second-generation ALK inhibitors and without targetable bypass gene mutations (e.g., *KRAS G12C, BRAF V600E*), 9 achieved PRs (9/22; 40.9%). Among the patients treated with RP2D, 12 had brain metastasis at baseline, 9 of whom achieved intracranial PR, resulting in an intracranial ORR of 75.0%.

- Biomarker analysis found that in patients with NSCLC that was resistant to second-generation ALK TKIs, PFS was correlated with phosphorylated FAK (pFAK) levels in the tumor tissue, suggesting that patients with higher pFAK levels were more likely to benefit from APG-2449.

Safety results: A total of 129 (89.6%) patients had treatment-related adverse events (TRAEs), the most frequent of which were elevated serum creatinine (49.3%), increase in alanine aminotransferase (42.4%), increase in aspartate aminotransferase (36.1%); nausea (28.5%); vomiting (23.6%); diarrhea (22.9%); and decreased leukocyte count (22.2%). In all, 20 (13.9%) TRAEs were grade ≥ 3.

Conclusions: APG-2449 demonstrated preliminary efficacy in patients with NSCLC whose disease was TKI naïve and resistant to second-generation ALK inhibitors, especially in brain metastases. Biomarker analysis showed that high pFAK expression levels in baseline tumor tissue correlated with improved APG-2449 treatment responses in patients with NSCLC resistant to second-generation ALK TKIs.

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

* *Lisaftoclax and APG-2449 are investigational drugs that have not been approved in any country and region.*

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