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 Updated Results from Multiple Clinical Studies Demonstrating Rapid Progress in Global Clinical Development

Ascentage Pharma Group International (the "**Company**" or "**Ascentage Pharma**") is pleased to announce that the seven clinical abstracts selected for presentations at the 2022 American Society of Clinical Oncology (ASCO) Annual Meeting were published on the ASCO's website today. These abstracts are related to seven clinical studies of the company's five novel drug candidates, including the third-generation tyrosine kinase inhibitor (TKI), olverembatinib (HQP1351); the Bcl-2 inhibitor, lisaftoclax (APG-2575); the MDM-p53 inhibitor, alrizomadlin (APG-115); the ALK inhibitor, APG-2449; and the dual Bcl-2/Bcl-xL inhibitor, pelcitoclax (APG-1252).

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. This year's ASCO Annual Meeting will take place both online and in-person at the McCormick Place in Chicago from June 3, 2022 to June 7, 2022 (US time).

The seven abstracts to be presented by Ascentage Pharma at this year's ASCO Annual Meeting are as follows:

Drug Candidate	Abstract Title	Abstract number	Format
Olverembatinib (HQP1351)	Promising antitumor activity of olverembatinib (HQP1351) in patients (pts) with tyrosine kinase inhibitor- (TKI-) resistant succinate dehydrogenase- (SDH-) deficient gastrointestinal stromal tumor (GIST).	#11513	Poster discussion
Lisaftoclax (APG-2575)	A phase Ib/II study of lisaftoclax (APG-2575), a novel BCL-2 inhibitor (BCL-2i), in patients (pts) with relapsed/refractory chronic lymphocytic leukemia or small lymphocytic lymphoma (R/R CLL/SLL).	#7543	Poster presentation
	Phase Ib/II study of BCL-2 inhibitor lisaftoclax (APG-2575) safety and tolerability when administered alone or combined with a cyclin-dependent kinase 4/6 (CDK4/6) inhibitor in patients with estrogen receptor-positive (ER^+) breast cancer or advanced solid tumors.	#TPS1122	Poster presentation
Alrizomadlin (APG-115)	Newly updated activity results of alrizomadlin (APG-115), a novel MDM2/p53 inhibitor, plus pembrolizumab: Phase 2 study in adults and children with various solid tumors.	#9517	Poster discussion

Drug Candidate	Abstract Title	Abstract number	Format
APG-2449	First-in-human phase I results of APG-2449, a novel FAK and third-generation ALK/ROS1 tyrosine kinase inhibitor (TKI), in patients (pts) with second-generation TKI-resistant ALK/ROS1 non-small-cell lung cancer (NSCLC) or mesothelioma.	#9071	Poster presentation
Pelcitoclax (APG-1252)	Updated study results of pelcitoclax (APG-1252) in combination with osimertinib in patients (pts) with EGFR-mutant non-small-cell lung cancer (NSCLC).	#9116	Poster presentation
	First-in-human study of pelcitoclax (APG-1252) in combination with paclitaxel in patients (pts) with relapsed/refractory small-cell lung cancer (R/R SCLC).	e20612	Online Publication

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

Format:	Poster Discussion
Abstract number:	#11513
Time:	Sunday, June 5, 2022	11:30 AM–1:00 PM CDT/Monday, June 6, 2022	12:30 AM–2:00 AM Beijing Time
Track:	Sarcoma

Highlights:

- This is an open-label, multicenter Phase Ib/II study designed to evaluate the safety, tolerability, pharmacokinetics (PK) and antitumor activity of olverembatinib in Chinese patients with locally advanced or metastatic GIST whose disease was resistant or failed to respond to imatinib or other TKIs.

- As of January 30, 2022, 39 patients had been enrolled. Olverembatinib was administered orally once every other day (QOD) in 28-day repeated cycles. After 3 patients were treated at 20 mg, other patients were randomly allocated in a 1:1:1 ratio to 30, 40, and 50 mg regimens.

- Efficacy Results:

  - ➢ In the 8 patients with KIT wild-type GIST, 6 were confirmed as SDH-deficient: 2 had partial responses (PRs), 1 patient's tumor shrunk by 35.9% and lasted for 16 cycles, and another patient's tumor shrunk by 54.2% at the first evaluation. 4 patients had stable disease as the best response for 2, 6, 14, and 36 cycles.

  - ➢ 31 patients had KIT or PDGFRA mutations, 13 had stable disease for at least 2 cycles as the best response, 8 withdrew early, and 10 had progressive disease before Cycle 3.

- A total of 36 (92.3%) patients experienced treatment-emergent adverse events, most of which were mild or moderate. Common treatment-related adverse events (≥ 20%) included increased leukocyte (59.0%) and neutrophil (46.2%) counts, anemia (20.5%), constipation or asthenia (35.9% each), hyperuricemia (25.6%), hypoalbuminemia (23.1%), and elevated aspartate aminotransferase (AST) or alanine aminotransferase (ALT) (20.5% each).

- Conclusions: olverembatinib was well tolerated and showed antitumor activity in patients with TKI-resistant SDH-deficient GIST. These promising findings warrant further investigation.

A phase Ib/II study of lisaftoclax (APG-2575), a novel BCL-2 inhibitor (BCL-2i), in patients (pts) with relapsed/refractory chronic lymphocytic leukemia or small lymphocytic lymphoma (R/R CLL/SLL)

Format:	Poster Presentation
Abstract number:	#7543
Time:	Saturday, June 4, 2022	8:00 AM–11:00 AM CDT/ Saturday, June 4, 2022	9:00 PM–12:00 AM Beijing Time
Track:	Hematologic Malignancies — Lymphoma and Chronic Lymphocytic Leukemia

Highlights:

- The aim of this multicenter, open-label study was to evaluate the safety, antitumor activity, and PK of lisaftoclax in patients with R/R CLL/SLL.

- As of January 25, 2022, 45 patients had been enrolled. Lisaftoclax was administered orally once daily at 3 dose cohorts (400, 600, or 800 mg) in 28-day cycles, with 15 patients in each cohort.

- Lisaftoclax monotherapy demonstrated favorable safety profiles in all three dose cohorts, and no dose-limiting toxicity (DLT) was observed during the Phase I study.

- The risk of tumor lysis syndrome (TLS) in patients on daily dose ramp-up was extremely low, which was consistent with the observations of the Phase I study. The median duration of treatment was 7 cycles and the objective response rate (ORR) in patients with R/R CLL/SLL was 68.29%.

- BCL-2i lisaftoclax was well tolerated up to 800 mg/day. There were no significant new or unmanageable safety findings. The recommended Phase II dose (RP2D) of lisaftoclax was determined as 600 mg. Lisaftoclax may offer a treatment alternative for patients with R/R CLL/SLL, with a daily ramp-up schedule that may be more convenient and "user friendly".

Phase Ib/II study of BCL-2 inhibitor lisaftoclax (APG-2575) safety and tolerability when administered alone or combined with a cyclin-dependent kinase 4/6 (CDK4/6) inhibitor in patients with estrogen receptor-positive (ER^+) breast cancer or advanced solid tumors

Format:	Poster Presentation
Abstract number:	#TPS1122
Time:	Monday, June 6, 2022	8:00 AM–11:00 AM CDT/ Monday, June 6, 2022	9:00 PM–12:00 AM Beijing Time
Track:	Breast Cancer — Metastatic

Highlights:

- This global multicenter, open-label, dose-escalation and dose-expansion study assesses the safety of lisaftoclax monotherapy in patients with histologically or cytologically confirmed advanced solid tumors that have progressed on standard therapy, and the safety and efficacy of lisaftoclax in combination with the CDK4/6 inhibitor palbociclib in physiologically postmenopausal women with $ER^+/HER2^-$ metastatic breast cancer that has progressed or relapsed after treatment with a CDK4/6 inhibitor.

- This trial consists of two parts:

  - A Phase Ib dose-escalation phase using a standard 3+3 design to determine the maximum tolerated dose (MTD) of lisaftoclax as a single agent in patients with solid tumors, as well as both the MTD and RP2D of lisaftoclax when combined with palbociclib in women with $ER^+/HER2^-$ metastatic breast cancer.

  - The Phase II part of this study is a signal-seeking expansion of lisaftoclax at the RP2D combined with palbociclib in women with ER^+/HER2 metastatic breast cancer. This phase is conducted using Simon's Minimax two-stage design. The primary objective for the Phase II part is to determine clinical benefit response rate, and secondary efficacy endpoints include ORR, duration of response (DOR), time to response, and progression-free survival.

Newly updated activity results of alrizomadlin (APG-115), a novel MDM2/p53 inhibitor, plus pembrolizumab: Phase 2 study in adults and children with various solid tumors

Format:	Poster Discussion
Abstract number:	#9517
Time:	Monday, June 6, 2022	4:30 PM–6:00 PM CDT/Tuesday, June 7, 2022	5:30 AM–7:00 AM Beijing Time
Track:	Melanoma/Skin Cancers

Highlights:

- This US/Australian multicenter trial evaluated the safety, tolerability, PK, PD, and antitumor activity of alrizomadlin in combination with pembrolizumab in patients with advanced solid tumors.

- As of November 3, 2021, 130 patients had been enrolled in the Phase II study. Alrizomadlin was orally administered QOD at the RP2D of 150 mg in combination with intravenously administered pembrolizumab. This study consists of 6 cohorts: PD-1/PD-L1-refractory melanoma (n=44), non-small cell lung cancer (NSCLC, n=26), ATM-mutant solid tumors (n=18), liposarcoma (n=17), urothelial cancer (n=13), and malignant peripheral nerve sheath tumour (MPNST, n=12).

- Efficacy Results:

  ➢ In the 38 efficacy evaluable (EE) patients with melanoma progressed on PD-1/PD-L1 inhibitors, the confirmed ORR was 13% (2 complete responses CRs+3PRs/38EEs). In the cutaneous and uveal melanoma sub-cohorts, confirmed ORRs were 24% (2CRs+2PRs/17EEs) and 9% (1PR/11EEs), respectively.

  ➢ In the MPNST cohort, the clinical benefit rate, defined by PR, CR and stable disease (SD) of > 4 cycles, was 40% (4 SDs/10 EEs).

  ➢ The PD-1/PD-L1-refractory NSCLC, urothelial, and liposarcoma cohorts each reported 1 confirmed PR.

- Common treatment-related adverse events (TRAEs; ≥ 10%) of any grade were nausea, thrombocytopenia, vomiting, fatigue, decreased appetite, diarrhea, neutropenia, and anemia.

- Conclusions: alrizomadlin, combined with pembrolizumab, was well tolerated and demonstrated preliminary antitumor activity in multiple tumor types and may restore antitumor effects in patients with cancer resistant or intolerant to immuno-oncologic (I-O) drugs.

First-in-human phase I results of APG-2449, a novel FAK and third-generation ALK/ROS1 tyrosine kinase inhibitor (TKI), in patients (pts) with second-generation TKI-resistant ALK/ROS1 non-small-cell lung cancer (NSCLC) or mesothelioma

Format:	Poster Presentation
Abstract number:	#9071
Time:	Monday, June 6, 2022, 8:00 AM–11:00 AM CDT/Monday, June 6, 2022, 9:00 PM–12:00 AM, Beijing Time
Track:	Lung Cancer — Non-Small Cell Metastatic

Highlights:

- This dose-escalation and dose-expansion study was designed to assess the safety, tolerability, RP2D, PK, PD, and efficacy of APG-2449 in patients with second-generation TKI-resistant/naïve ALK/ROS1$^+$ NSCLC or mesothelioma.

- As of December 30, 2021, 84 patients with NSCLC or mesothelioma enrolled were treated with APG-2449 at doses ranging from 150 to 1,500 mg. APG-2449 was administered orally once daily on a 28-day cycle using a "3+3" dose escalation design.

- 4 PRs were observed in 14 ALK$^+$ patients resistant to second-generation TKIs treated at the RP2D. Among 8 patients with brain metastases, 1 CR and 3 PRs were observed intracranially. In 10 TKI-naïve patients, the ORR was 80% (ALK$^+$, 6/8; ROS1$^+$, 2/2) and the disease control rate (DCR) was 100%.

- In addition, AGP-2449 demonstrated a favorable safety profile. The preliminary biomarker data showed decreased FAK phosphorylation in peripheral blood mononuclear cells and increased IFN-γ levels in serum after multiple doses of APG-2449.

- Conclusion: APG-2449 has a favorable safety and PK profile. Preliminary efficacy was observed in patients whose disease was resistant to second-generation or TKI-naïve. Biomarker data indicated potential target engagement on FAK and the immunomodulatory effects of APG-2449.

Updated study results of pelcitoclax (APG-1252) in combination with osimertinib in patients (pts) with EGFR-mutant non-small-cell lung cancer (NSCLC)

Format:	Poster Presentation
Abstract number:	#9116
Time:	Monday, June 6, 2022, 8:00 AM–11:00 AM CDT/Monday, June 6, 2022, 9:00 PM–12:00 AM, Beijing Time
Track:	Lung Cancer — Non-Small Cell Metastatic

Highlights:

- In preclinical models, the dual Bcl-2/Bcl-xL inhibitor pelcitoclax enhanced the antitumor effects of osimertinib. A report presented at the 2021 World Conference on Lung Cancer (WCLC) demonstrated that the combination of pelcitoclax and osimertinib at the RP2D was safe, with preliminary efficacy observed in some patients whose disease failed prior osimertinib or other third-generation EGFR-TKI treatments.

- After the RP2D was determined to be pelcitoclax 160 mg per week plus osimertinib 80 mg QD, patients were enrolled into 3 expansion cohorts of 20 patients each: Cohort 1 included those with disease resistant to third-generation EGFR-TKIs; Cohort 2 included those who were osimertinib-naïve, EGFR-sensitive or with T790M-positive mutations; and Cohort 3 (EC-3) included those with the EGFR exon 20 insertion mutation.

- As of January 6, 2022, 61 patients had been treated with pelcitoclax plus osimertinib. Among the 20 efficacy evaluable patients in EC-2, 17 PRs (85%) were observed. The median (range) time to response was 1.4 (1.2–7.0) months, and the median DOR was not reached. The DOR rate at 9 months after first response was 71.4% (95% CI 25.8–92.0). Among the 7 patients who had brain metastases at baseline in EC-2; 2 CRs and 3 PRs were observed intracranially.

- Conclusions: pelcitoclax plus osimertinib was well tolerated and showed comparable efficacy in TKI-naïve patients. Further randomized control trials are warranted to elucidate the role of pelcitoclax when combined with osimertinib.

First-in-human study of pelcitoclax (APG-1252) in combination with paclitaxel in patients (pts) with relapsed/refractory small-cell lung cancer (R/R SCLC)

Format: Publication Only

Abstract number: #e20612

Highlights:

- The primary aim of this study was to determine the safety and preliminary efficacy of pelcitoclax combined with paclitaxel in patients with R/R SCLC. Patients received pelcitoclax IV infusion on Days 1, 8, and 15 plus paclitaxel 80 mg/m^2 on Days 1 and 8 of a 21-day cycle.

- The primary endpoint of the Phase Ib part of this study was to characterize the safety and tolerability of the combination. The primary endpoint of the Phase II part was the ORR of pelcitoclax at the RP2D plus paclitaxel.

- As of December 20, 2021, 28 patients had been enrolled. The RP2D of pelcitoclax was determined to be 240 mg. 5 of 20 evaluable patients reported PR, the ORR was 25%, and no DLT was reported.

- Conclusions: weekly treatment with pelcitoclax at 240 mg in combination with paclitaxel at 80 mg/m^2 demonstrated favorable tolerability and modest antitumor activity in patients with R/R SCLC.

About Ascentage Pharma

Ascentage Pharma is a China-based, globally focused, clinical-stage biotechnology company engaged in developing novel therapies for cancers, CHB (Chronic hepatitis B), and age-related diseases. On October 28, 2019, Ascentage Pharma became listed on the Main Board of The Stock Exchange of Hong Kong Limited with the stock code: 6855.HK.

Ascentage Pharma has its own platform for developing therapeutics that inhibit protein-protein interactions to restore apoptosis or programmed cell death. The Company has built a pipeline of eight type I small molecule clinical drug candidates which have entered the clinical development stage, including novel, highly potent Bcl-2, and dual Bcl-2/Bcl-xL inhibitors, as well as candidates aimed at IAP and MDM2-p53 pathways, and next-generation tyrosine kinase inhibitors (TKIs). Ascentage Pharma is also the only company in the world with active clinical programs targeting all three known classes of key apoptosis regulators. The Company is conducting more than 50 Phase I/II clinical trials in China, the US, Australia and Europe. Olverembatinib, the Company's core drug candidate developed for the treatment of drug-resistant chronic myeloid leukemia (CML), was granted Priority Review status and a Breakthrough Therapy Designation (BTD) by the Center for Drug Evaluation (CDE) of China National Medical Products Administration (NMPA), and is already approved for the indication. In addition, Olverembatinib has also been granted an Orphan Drug Designation (ODD) and a Fast Track Designation (FTD) by the US FDA, and an Orphan Designation by the EU. As at the date of this announcement, Ascentage Pharma has obtained a total of 15 ODDs from the US FDA and 1 ODD from the EU for four of the Company's investigational drug candidates. The Company has been designated for multiple major national R&D projects in China, including five Major New Drug Development Projects, one Enterprise Innovative Drug Incubator Base status, four Innovative Drug Research and Development Programs, and one Major Project for the Prevention and Treatment of Infectious Diseases.

Leveraging its robust research and development capabilities, Ascentage Pharma has built a portfolio of global intellectual property rights, and entered into global partnerships with numerous leading biotechnology and pharmaceutical companies and research institutes such as UNITY Biotechnology, MD Anderson Cancer Center, Mayo Clinic, Dana-Farber Cancer Institute, MSD, AstraZeneca and Pfizer. The Company has built a global and talented team with experience in the research and development of innovative drugs and clinical development, and is setting up its commercial manufacturing and sales and marketing teams with high standards. Ascentage Pharma aims to continuously strengthen its research and development capabilities and accelerate the clinical development progress of its product pipeline to fulfil its mission of 'addressing unmet clinical needs of patients in China and around the world' for the benefit of more patients.

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-1252, APG-2449 and APG-115 successfully.

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

Suzhou, People's Republic of China, May 27, 2022

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.