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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 Announce Updated Data of Bcl-2 Inhibitor Lisaftoclax (APG-2575) Demonstrating an Objective Response Rate of Around 80% and Therapeutic Potential in Patients with R/R CLL/SLL in Oral Presentation at the 2021 Annual Meeting of the American Society of Clinical Oncology (ASCO)

Ascentage Pharma Group International (the “**Company**” or “**Ascentage Pharma**”) is pleased to announce that abstracts reporting on four clinical studies evaluating three of the company’s apoptosis-targeted drug candidates which were selected for the 2021 American Society of Clinical Oncology (ASCO) Annual Meeting have been published on the official website of ASCO today. Of these, two abstracts have been accepted as oral presentations. Data from the global Phase I clinical study of the Bcl-2 inhibitor, Lisaftoclax (APG-2575), in patients with relapsed/refractory chronic lymphocytic lymphoma or small lymphocytic lymphoma (R/R CLL/SLL) have demonstrated an encouraging objective response rate (ORR) of 85.7%, and favorable tolerability and safety profiles. Moreover, the Phase II study of MDM2 inhibitor Alrizomadlin (APG-115) in combination with pembrolizumab in patients with unresectable or metastatic melanoma or advanced solid tumors that have failed immuno-oncologic drugs demonstrated favorable results, including a disease control rate (DCR) of 60.9% and an ORR of 17.4% in the PD-1/PD-L1 inhibitor-resistant melanoma cohort.

The updated results from these two studies will be released in oral presentations at the ASCO Annual Meeting convening on June 4 to June 8, 2021. Ascentage Pharma’s two other studies selected by the ASCO Annual Meeting include a Phase I/II study of APG-115 with or without platinum chemotherapy for patients with salivary gland carcinoma and a Phase Ib/II study of Pelcitoclax (APG-1252) in combination with paclitaxel for patients with R/R small-cell lung cancer.

Those abstracts of Ascentage Pharma selected to be presented at this year's ASCO Annual Meeting are as follows:

First-in-human study of Lisaftoclax (APG-2575), a novel Bcl-2 inhibitor (Bcl-2i), in patients (pts) with relapsed/refractory (R/R) CLL and other hematologic malignancies (HMs)

- **Format:** Oral Presentation
- **Abstract:** #7502
- **Time:** 23:30–02:30 BJT, June 7, 2021/11:30–14:30 EDT, June 7, 2021
- **Session Track:** Hematologic Malignancies — Lymphoma and Chronic Lymphocytic Leukemia
- **Highlights:**
 - This first-in-human global Phase I study assessed the safety, pharmacokinetics (PK), pharmacodynamics (PD), efficacy, and maximum tolerated dose (MTD)/recommended Phase II dose (RP2D) of APG-2575 in patients with R/R CLL and other HMs. APG-2575 was orally administered once daily in a 28-day cycle. Patients with CLL or intermediate-high tumor lysis syndrome (TLS) risk were initiated on a daily ramp-up schedule until the dose assigned before the study cycles.
 - As of January 7, 2021, 35 patients had been enrolled and treated with APG-2575 at doses ranging from 20 to 1,200 mg, with a median of 2 (range: 1–13) prior lines of treatment. These patients had been diagnosed with R/R CLL/SLL (n=15), multiple myeloma (MM, n=6), follicular lymphoma (FL, n=5), Waldenström macroglobulinemia (WM, n=4); and either acute myeloid leukemia (AML), mantle cell lymphoma (MCL), diffuse large B-cell lymphoma (DLBCL), myelodysplastic syndromes (MDS), or hairy cell leukemia (HCL) (n=1 each).
 - APG-2575 was well tolerated, with manageable adverse events (AEs). No dose-limiting toxicity (DLT) was observed even at the maximum dose of 1,200 mg. The MTD has not been reached, and no laboratory or clinical TLS has been reported. Hematologic treatment-related adverse events (TRAEs) of any grade in over 10% patients included neutropenia and anemia, while nonhematologic TRAEs included fatigue, diarrhea, and nausea.

- 12 of 14 evaluable patients with R/R CLL/SLL achieved partial response (PR), for an ORR of 85.7% and a median time to response of 3 treatment cycles (range: 2–7). Absolute lymphocyte counts (ALCs) were reduced at APG-2575 doses as low as 20 mg/day.
- The preliminary PK profile showed that exposures increased with APG-2575 doses from 20 to 1,200 mg (average half-life: 4–5 hours). On BH3 profiling, APG-2575 rapidly triggered changes in Bcl-2 complex in CLL/SLL patient samples, which were consistent with rapid clinical reductions in ALCs.
- In conclusion, efficacy and safety data showed that the Bcl-2 inhibitor APG-2575 offers a potential alternative treatment for patients with R/R CLL/SLL and other HMs, with a daily ramp-up schedule that may be more patient-friendly and a favorable preliminary safety profile.

Preliminary results of a phase II study of APG-115, a novel, small-molecule MDM2 inhibitor, in combination with pembrolizumab in patients with unresectable or metastatic melanoma or advanced solid tumors that have failed immuno-oncologic (I-O) drugs

- **Format:** Oral Presentation
- **Abstract:** #2506
- **Time:** 03:00–06:00 BJT, June 8, 2021/15:00–18:00 EDT, June 7, 2021
- **Session Track:** Developmental Therapeutics — Immunotherapy
- **Highlights:**
 - This open-label, multicenter Phase II study in the US assessed the safety, tolerability, PK, PD, and antitumor activity of APG-115 in combination with pembrolizumab in patients with advanced solid tumors.
 - As of December 25, 2020, 84 patients had been enrolled in the Phase II part of the study and treated with APG-115 at the RP2D dose of 150 mg every other day, in combination with pembrolizumab. This study has 6 cohorts, including patients with: PD-1/PD-L1 inhibitor-resistant melanoma, non-small cell lung cancer (NSCLC), and urothelial carcinoma; or malignant peripheral nerve sheath tumor (MPNST), liposarcoma, and ATM mutant solid tumors that had failed any standard therapy.

➤ **Anti-tumor Effects:**

- ✧ In the PD-1/PD-L1 inhibitor-resistant melanoma cohort (n=26), there was 1 confirmed PR out of 5 patients with uveal (ocular) melanoma; 2 PRs (1 confirmed + 1 unconfirmed) of 5 patients with mucosal melanoma; and 1 PR (confirmed) of 11 patients with cutaneous melanoma. The ORR and DCR in the melanoma cohort were 17.4% (4/23) and 60.9% (14/23), respectively.
 - ✧ In the MPNST cohort (n=6), 1 ongoing PR (unconfirmed).
 - ✧ In the PD-1/PD-L1 inhibitor-resistant NSCLC (n=14 evaluable) and urothelial carcinoma (n=5 evaluable) cohorts, 1 patient in each cohort achieved confirmed PR.
- Common treatment-related adverse events (TRAEs) observed in over 10% of patients were nausea, thrombocytopenia, vomiting, fatigue, decreased appetite, diarrhea, neutropenia, and anemia.
- In conclusion, APG-115 in combination with pembrolizumab is well tolerated and may restore antitumor effects in patients with cancer resistant to or intolerant of I-O drugs.

Trial in progress: A phase I/II trial of novel MDM2 inhibitor APG-115, with or without platinum chemotherapy, in patients with p53 wild-type salivary gland carcinoma

- **Format:** Poster Presentation
- **Abstract:** #TPS6094
- **Time:** 21:00 BJT, June 4, 2021/09:00 EDT, June 4, 2021
- **Session Track:** Head and Neck Cancer
- **Highlights:**
 - This open-label, multicenter Phase I/II trial in the US was designed to assess the safety, DLT, MTD, and antitumor activity of APG-115 with or without platinum chemotherapy in patients with p53 wild-type salivary gland carcinoma.

- **This study has two parts:**
 - ✧ **Part One:** a two-arm randomized study (allocated in a ratio of 1:2, n=42)
 - Arm A:** APG-115 as a single agent (n=14)
 - Arm B:** APG-115 plus platinum chemotherapy (n=28)
 - ✧ **Part Two:** a single-arm study (advanced from the most promising arm in Part One, n=20)
- **Study Endpoints:**
 - ✧ DLT based on the TRAEs of grade 3 to 5 (by NCI CTCAE v5.0) within the first 6 weeks of treatments (2 cycles).
 - ✧ MTD based on DLTs over the same treatment period.
 - ✧ ORR based on the proportion of patients with confirmed CR or PR (per RECIST v1.1) at up to 12 months.
- This study was designed to enroll 42 patients. As of January 27, 2021, 11 patients have been enrolled.

Trial in progress: A multicenter phase Ib/II study of APG-1252 in combination with paclitaxel in patients with relapsed/refractory small-cell lung cancer (R/R SCLC)

- **Format:** Poster Presentation
- **Abstract:** #TPS8589
- **Time:** 21:00 BJT, June 4, 2021/09:00 EDT, June 4, 2021
- **Session Track:** Lung Cancer — Non-Small Cell Local-Regional/Small Cell/Other Thoracic Cancers
- **Highlights:**
 - This open-label, multicenter Phase Ib/II study is assessing the safety of preliminary efficacy of APG-1252 in combination with paclitaxel in patients with R/R SCLC.

- APG-1252 is being administered by intravenous (IV) infusion on Days 1, 8, and 15, with paclitaxel at the fixed-dose of 80 mg/m² on Days 1 and 8 of a 21-day cycle.
- The primary endpoints of the Phase Ib part of this study include MTD and RP2D. The efficacy of APG-1252 combined with paclitaxel will be determined in the Phase II part of the study using a Simon two-stage design, with ORR as the primary endpoint. Other endpoints of the Phase II study include PK, progression-free survival, and overall survival.
- This study was designed to enroll 58 patients. As of February 8, 2021, 15 patients have been enrolled.

About APG-2575

APG-2575 is a novel, orally administered small-molecule Bcl-2-selective inhibitor being developed by Ascentage Pharma. APG-2575 is designed to treat hematologic malignancies and solid tumors by selectively blocking antiapoptotic protein Bcl-2 to restore the normal apoptosis process in cancer cells. APG-2575 is the first China-developed Bcl-2 inhibitor entering clinical development in China. At present, lisaftoclax has been cleared and approved to enter multiple Phase Ib/II studies in the US, China, and Australia, and is being developed globally for the treatment of multiple hematologic malignancies.

About APG-115

Being developed by Ascentage Pharma, APG-115 is an orally administered, selective, small-molecule inhibitor of the MDM2 protein. APG-115 has strong binding affinity to MDM2 and is designed to activate tumor suppression activity of p53 by blocking the MDM2-p53 protein-protein interaction. APG-115 is the first MDM2-p53 inhibitor entering clinical development in China and is currently being investigated in multiple studies in solid tumors and hematologic malignancies in China, Australia, and the US.

About APG-1252

APG-1252 is a Bcl-2/Bcl-xL dual inhibitor drug designed to restore apoptosis through selective inhibition of Bcl-2 and Bcl-xL proteins. Multiple Phase Ib/II studies of APG-1252 as a single agent or in combinations for the treatment of a range of advanced tumors, including small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC), are being conducted in China, the US and Australia.

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 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 key apoptosis regulators. The Company is conducting more than 40 Phase I/II clinical trials in China, the US and Australia. HQP1351, the Company's core drug candidate developed for the treatment of drug-resistant chronic myeloid leukemia (CML), has been granted an Orphan Drug Designation (ODD) and a Fast Track Designation (FTD) by the US FDA, and a New Drug Application (NDA) for the drug candidate has been submitted and subsequently granted Priority Review by the Center for Drug Evaluation (CDE) in China. As at the date of this announcement, Ascentage Pharma has obtained a total of eleven ODDs from the US FDA for four of the Company's investigational drug candidates.

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-1252 successfully.

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

Suzhou, People's Republic of China, May 20, 2021

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, Dr. Tian Yuan, Dr. Lu Simon Dazhong and Mr. Liu Qian as non-executive Directors, and Mr. Ye Changqing, Dr. Yin Zheng, Mr. Ren Wei and Dr. David Sidransky as independent non-executive Directors.