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 Results from Three Studies at the 2023 American Association of Cancer Research Annual Meeting

Ascentage Pharma Group International (the "**Company**" or "**Ascentage Pharma**") is pleased to announce that it had released results from three preclinical studies of the Company's China-approved type 1 novel third-generation BCR-ABL inhibitor olverembatinib (HQP1351), and the key investigational apoptosis-targeted drug candidates of Ascentage Pharma, the Bcl-2 inhibitor lisaftoclax (APG-2575) and the MDM2-p53 inhibitor alrizomadlin (APG-115), in poster presentations at the 2023 American Association of Cancer Research Annual Meeting (AACR 2023).

The details of these posters presented at AACR 2023 are as follows:

Olverembatinib (HQP1351) enhances antitumor effects of immunotherapy in renal cell carcinoma (RCC)

- Abstract number: 5071

- In solid tumors, resistance to checkpoint inhibitors (CPIs) is frequently observed, partially due to upregulation of vascular endothelial growth factor A (VEGFA) and programmed death-ligand 1 (PD-L1). This culminates in an immunosuppressive tumor microenvironment and immune escape. Inhibitors against VEGF and the VEGF receptor (VEGFR) foster tumor vessel normalization and immunostimulatory reprogramming, in turn promoting treatment effects of immunotherapies. In recent years, TKIs plus immunotherapy have been approved to treat advanced RCC. Currently under clinical development for relapsed or refractory chronic myeloid leukemia and gastrointestinal tumor, olverembatinib is a new-generation multikinase inhibitor with targets including VEGFR, fibroblast growth factor receptor (FGFR), SRC, BCR-ABL1, c-KIT, and platelet-derived growth factor receptor. The aim of this study was to assess whether olverembatinib combined with immunotherapy can promote inhibitory effects on RCC.

- Our results demonstrate that combining olverembatinib with a CPI confers synergistic antitumor effects in an RCC cancer mouse model by targeting tumor growth, angiogenesis, and immune regulation. This novel combination may provide an alternative approach to enhance treatment effects with CPIs in renal cancers.

Combination of olverembatinib (HQP1351) with Bcl-2 inhibitor lisaftoclax (APG-2575) overcomes resistance in gastrointestinal stromal tumors (GISTs)

- Abstract number: 1631

- GISTs are common malignant mesenchymal tumors that occur in the GI tract, with an estimated incidence rate of 1% to 2%. About 75% to 80% of patients with GIST have mutations in the KIT gene, while 5% to 10% have mutations in the platelet-derived growth factor receptor α (PDGFRA) gene. Tyrosine kinase inhibitors (TKIs) offer patients an improved quality of life but increased pharmacological resistance to TKIs is often observed. Bcl-2 is expressed in >80% of GISTs, and amplification of Bcl-2 and Bcl-xL are common features associated with disease progression. One approach to enhance GIST eradication is to concurrently inhibit oncogenic KIT signaling while actively engaging apoptotic pathways. Olverembatinib (HQP1351) is a new, third-generation TKI that targets BCR-ABL1, KIT and PDGFRA and is currently in development for relapsed or refractory chronic myeloid leukemia and GIST. Lisaftoclax (APG-2575) is a selective Bcl-2 inhibitor under development for hematologic malignancies. The purpose of this study was to evaluate whether combining a Bcl-2 inhibitor, lisaftoclax, with olverembatinib enhances treatment effect on imatinib-resistant GISTs.

- Our results demonstrate that olverembatinib and Bcl-2 inhibitor lisaftoclax have synergistic antitumor effects in imatinib-resistant GIST. Considering that the resistance mechanisms are similar for most TKIs, this novel dual approach may have the potential for treating patients with GISTs whose disease has progressed after treatment with imatinib or other TKIs.

MDM2 inhibitor alrizomadlin (APG-115) promotes antitumor activity of mitogen-activated protein kinase (MAPK) inhibitors in uveal melanoma

- Abstract number: 1632

- Uveal melanoma (UM) is the commonest primary intraocular malignancy, yet its molecular pathogenesis is poorly understood. Most UM cases have activating mutations in genes encoding G protein subunits alpha Q or 11, leading to activation of downstream effectors. These include protein kinase C, mitogen-activated protein kinases (MAPK1/3; also termed extracellular signal-regulated kinase 2/1 [ERK2/ERK1], respectively), and yes-associated protein, suggesting a rationale for therapeutically targeting these related pathways. Genetic analyses show that TP53 is infrequently mutated in UM, but associated pathways may be functionally inactivated. Ubiquitination-mediated degradation of p53 activates MAPK signaling, such that, active p53 may promote suppression of MAPK signaling. Alrizomadlin (APG-115) is a small molecule targeting p53/MDM2 that is in clinical development for solid and hematologic cancers. This study evaluated the antitumor effect of alrizomadlin, alone or combined with other targeted therapies, in preclinical models of UM.

- Our results demonstrate the potential utility of combining alrizomadlin with MAPK pathway inhibitors to treat patients with UM.

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-115 successfully.

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

Suzhou, People's Republic of China, April 18, 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.