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Ascentage Pharma presents new clinical data of apoptosis targeted drug candidates

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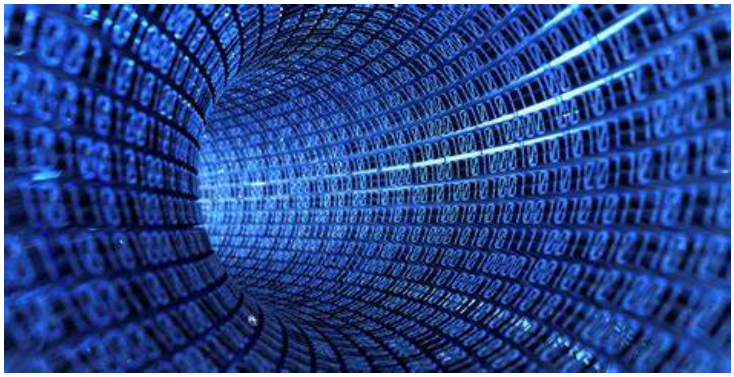
Ascentage Pharma presented the data from its most recent clinical trials of APG-115 in China and U.S.



Ascentage Pharma, a globally-focused, clinical-stage biotechnology company engaged in developing novel therapies for cancers, hepatitis B virus and age-related diseases has announced that the company presented new data of two apoptosis-targeted drug candidates APG-115 (a novel MDM2-p53 inhibitor) and APG-1387 (a novel IAP inhibitor) at the 55th Annual Meeting of the American Society of Clinical Oncology (ASCO).

With the theme "Caring for Every Patient, Learning from Every Patient", 2019 ASCO Annual Meeting attracted over 40,000 oncologists and researchers globally to present and share the cutting-edge research and achievements in clinical oncology in Chicago from May 31-June 4.

Ascentage Pharma presented the data from its most recent clinical trials of APG-115 in China and U.S. and the data of phase I study of APG-1387 as a monotherapy or in combination with pembrolizumab in treatments of patients with advanced solid tumors (Board #117).

It is encouraging that in the study of APG-115 as a monotherapy, a confirmed PR was observed in 1 patient with liposarcoma (TP53-WT and MDM2Amp), with target lesion decreased 64%.

"Liposarcoma is a common histological type of malignant soft tissue sarcomas, accounting for about 15% of soft tissue sarcomas. There is no effective treatment for it and the probability of recurrence is high. Liposarcoma belongs to the'cold tumor' type and has a poor response to immunotherapy," said Pro. Xing Zhang, Chief physician of Melanoma and Sarcoma Medical Oncology Unit of Sun Yat-sen University Cancer Center. She continued, "We believe APG-115 is an efficient MDM2-p53 inhibitor. The data of Phase I study of APG-115 in Chinese patients with liposarcomas is encouraging. We enrolled 14 patients, 8 with liposarcoma; a confirmed PR was observed in one liposarcoma patient after 4 months of treatment discontinuance. Another 5 patients achieved SD (including 2 liposarcoma patients). Based on clinical trial results, APG-115 is well-tolerated and with acceptable safety profile. We expect further data to address the unmet medical needs."

There have also been promising advances in the Phase I study of a novel IAP inhibitor, APG-1387, as a monotherapy in treatments of patients with advanced solid tumors. Drew W. Rasco, M.D., Associate Director of Clinical Research at the START Center for Cancer Care in San Antonio commented: "Among 10 mPC (metastatic pancreatic cancer) patients treated

with APG-1387 monotherapy, 3 patients achieved SD. One patient at MTD received SD for >9 cycles (3-wk a cycle) with the best response +6%, still ongoing; one patient achieved SD for > 8 months with best response of -16.7% tumor shrinkage. This preliminary result is worth mentioning, because mPC patients in general have only 3-6 months survival time, and overall survival rate of one year is 8.8%. Currently there is no effective treatment. We look forward to additional data from the on-going studies."

"APG-115 and APG-1387 are two apoptosis targeting products in clinical development of Ascentage Pharma. These results show our further progress in clinical development of targeting apoptosis. We are working hard to provide more therapy options for patients as soon as possible,"said Dr. Dajun Yang, Chairman and CEO of Ascentage Pharma.

- **A Phase I Study of a Novel MDM2-P53 Antagonist APG-115 in Chinese Patients with Advanced Solid Tumors**

- Through April 23, 2019, 14 patients with advanced solid tumors (8 LPSs) received APG-115 ranging from 100-200mg, QOD, 3 weeks on 1 week off, in a 4-week cycle.
- Two DLTs judged by investigator at 200mg (thrombocytopenia and febrile neutropenia). APG-115 was well-tolerated across all dose levels tested and the MTD was 150mg, due to the late onset thrombocytopenia, safety expansion was ongoing at 100mg. The most common Grade ?3 AEs were hematologic toxicities, particularly thrombocytopenia, which were predictable as the activation of p53 in the bone marrow.
- APG-115 displayed approximately linear pharmacokinetics over 100-200mg range.
- A confirmed PR was observed in 1 patient with liposarcoma (TP53-WT and MDM2Amp) at the 150mg, and the duration of response has lasted after 4 months of treatment discontinuance.

- **A Phase I study of a Novel MDM2 Antagonist APG-115 in Patients with Advanced Solid Tumors**

- Through April 19, 2019, total 29 patients were treated with APG-115 at various doses range from 10-300mg.
- Most common TRAEs (>10%): fatigue, nausea, vomiting, decreased appetite, diarrhea, neutrophil count decreased, platelet count decreased, white blood cell count decreased.
- Platelet count decreased, fatigue, and nausea were determined as DLTs.
- APG-115 at 100mg QOD (3 weeks on, 1 week off) was well-tolerated. The MTD/RP2D of APG-115 monotherapy was determined as 100mg.
- Base on the preliminary anti-tumor data, APG-115 is active. Nine patients achieved SD among 19 response evaluable patients. 50% (5/10) patients at MTD achieved SD among response evaluable patients.
- PK analyses have shown that AUC and Cmax generally increase dose proportionally over the dose range of 20-300mg.
- Serum MIC-1 (biomarker of TP53 activation) increase was exposure dependent within the dose range tested in patients with solid tumors.
- Further evaluation of APG-115 in combination with pembrolizumab in patients with advanced solid tumors is ongoing.

- **A Phase I Study of a Novel IAP Inhibitor APG-1387 as a Monotherapy or in Combination with Pembrolizumab in Treatments of Patients with Advanced Solid Tumors**

- Through April 19, 2019, 24 patients had been treated with APG-1387 and 5 patients had been treated with APG-1387 plus pembrolizumab.
- APG-1387 was well tolerated and had manageable adverse events. Most common TRAEs (>10%) are fatigue.
- Two DLTs were observed at 60mg including lipase increase and facial nerve disorder, MTD of APG-1387 monotherapy was determined as 45mg.
- Three out of 10 mPC patients in APG-1387 monotherapy (at 45mg) achieved SD, one of them at 45 mg has been treated > 9 cycles with confirmed SD (+6%).
- Preliminary PK data of APG-1387 showed a dose proportionality in exposure (Cmax and AUC) over the dose range of 20-45 mg.
- APG-1387 treatment induced significant XIAP suppression in PBMCs and cytokine (especially IL-12p40 and IL-10) release in serum, suggesting a potential pharmacodynamics and host immunomodulation effects.
- The potential effects of APG-1387 alone or in combination with pembrolizumab deserve further exploration in patients with advanced pancreatic cancer.

APG-115 is an orally administered, selective, small molecule inhibitor of the MDM2-p53 PPI. APG-115 has strong binding affinity to MDM2 and is designed to activate p53 tumor suppression activity by blocking the MDM2-p53 PPI. APG-115 is currently in Phase I clinical trials in China and the United States in patients with ACC (Adenoid cystic carcinoma) and other sarcomas. APG-115 is in Phase Ib/II combination study with pembrolizumab in the U.S.

APG-1387 is a novel small molecule IAP inhibitor (Inhibitor of Apoptosis Protein). Ascentage Pharma is developing APG-1387 globally, and has completed dose escalation Phase I clinical trials in advanced solid tumors in China and Australia, and a Phase I clinical trial of APG-1387 and pembrolizumab combination is currently ongoing in the U.S. APG-1387 is also being investigated for the treatment of patients with chronic hepatitis B virus in China.