INITIAL RESULTS FROM PHASE I DOSE ESCALATION TRIAL OF CAN1012 IN PATIENTS WITH SOLID TUMOR MALIGNANCIES

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Background CAN1012 is a selective Toll-like receptor 7 (TLR7) agonist whose receptor locates in intracellular endosomes of plasmacytoid dendritic cells (pDC). Upon binding to TLR7 agonist, pDC secret high levels of type I interferons and other anti-viral cytokines/chemokines.

Methods CAN1012 has been demonstrated to stimulate IFN-alpha release in human PBMC in vitro and to produce anti-tumor effects, when given intratumorally (IT) in various syngeneic mouse tumor models in vivo. Furthermore, it can be used in combination with immune checkpoint inhibitors, anti-angiogenesis inhibitors or chemotherapy agents to enhance the anti-tumor effect. The exposure of CAN1012 in tumor tissues via IT route was over 1,000-fold higher than in blood, resulting in much less systemic toxicity. Pharmacodynamic studies revealed that it increased CD4+ and CD8+ T cell infiltration in the tumor microenvironment (TME), but decreased myeloid-derived suppressor cell (MDSCs) counts. It also has a favorable ADME/PK profile when administered subcutaneously in mice, rats and monkeys, and its pharmaceutical properties have also been optimized for IT administration.

Results Based on the superior safety and efficacy of CAN1012 in preclinical studies, a first in-human Phase I dose-escalation trial for advanced cancer patients was initiated in multi clinical centers both in US (NCT04987112) and China (CTR20222322), using intratumoral administration and a standard 3+3 trial design. Up to now, four dose cohorts were successfully administered in patients. Preliminary results indicated that CAN1012 is well-tolerated with no severe adverse effect documented. In addition, a favorable efficacy is observed in some of treated patients.

Conclusions The trial is still undergoing according to the initial design and is expected to be completed by the end of this year.

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