BACKGROUND

- AST-008 is a toll-like receptor 9 (TLR9) agonist oligonucleotide in a proprietary spherical nucleic acid (SNA) format with immune-stimulatory properties
- SNAs are dense, radial arrangements of nucleic acids that have useful properties as compared to linear oligonucleotides (i.e., oligonucleotides not in the SNA format), notably increased cellular uptake and an optimal presentation of the oligonucleotides for TLR9 agonism
- AST-008 is designed to enter into and activate immune cells to elicit an immune response to treat solid tumours in combination with a checkpoint inhibitor
- AST-008 has potent antitumour activity as a monotherapy and synergizes with anti-PD-1 antibody therapy in several preclinical tumour models

OBJECTIVES

- Primary
  ➢ To evaluate the safety and tolerability of AST-008 after single subcutaneous (SC) doses
- Secondary
  ➢ To recommend a dose and regimen for further development
  ➢ To determine the pharmacokinetics (PK) of AST-008 in plasma and urine
  ➢ To determine the pharmacodynamics (PD) of AST-008 after SC doses
  ➢ To determine the effect of AST-008 on QTc interval

METHODS

- AST-008 was evaluated in a Phase 1a study under protocol AST-008-101
- Four dose levels of AST-008 were evaluated in four cohorts. Each cohort included four volunteers, and all received a single dose of AST-008. The dose levels were 5, 10, 12.5 and 18.8 µg/kg
- Peripheral blood cytokine concentrations and cell activation were measured with a Random Evidence Investigator or ELISA, and a Beckman Coulter Navios flow cytometer, respectively
- Plasma and urine concentrations of AST-008 were assessed with a peptide nucleic acid probe/liquid chromatography assay

POPULATION

- Healthy volunteers aged 18 to 40 with body mass index of 18 to 25 kg/m²
- Subjects with a recent history of tobacco, drugs of abuse, prescription medications including corticosteroids or other immunosuppressive drugs, or other investigational products were excluded

CONCLUSIONS

- AST-008 was well tolerated and elicited no serious adverse events or dose limiting toxicity at the doses tested
- AST-008 is a potent innate immune activator and exhibits pharmacodynamic properties that are expected to result in anti-tumour effects in patients with cancer
- AST-008 was not detected in the plasma or urine of any subject
- Preparation of a Phase 1b/2 study of AST-008 in combination with pembrolizumab in cancer patients is ongoing