IOA-244 is a non-ATP-competitive, highly selective, tolerable phosphoinositide 3-kinase delta inhibitor that directly targets solid tumours and breaks immune tolerance

**IOA-244**

**IAO-244 chemical structure**

**IOA-244 key features**

- Unique chemical structure
- Non-ATP competitive
- Excellent PK properties
- Favourable safety profile

**Summary**

Inhibiting PI3Kδ preferentially targets regulatory T cells and myeloid derived suppressor cells, breaking tumour-immune induced tolerance and restoring anti-tumour immunity. Here we report the exploration of IOA-244/MSC323044, a non-ATP competitive PI3Kδ inhibitor, for the treatment of solid tumors. To harness the differentiation of IOA-244 from other PI3Kδ inhibitors, we have performed molecular dynamic and hydrogen-deuterium exchange MS studies, as well as in-cell kinase profiling where we compared structural and selectivity features of IOA-244 to other inhibitors. Then, to investigate the tumor intrinsic and extrinsic activity of IOA-244, we performed in vitro proliferation assays, xenograft, patient-derived xenograft models, and in vivo syngeneic tumor models. Here, we tested IOA-244 in mono-therapy or in combination with checkpoint blockade inhibitors. IOA-244 is currently in clinical Phase I evaluation for lymphoma and solid tumors. In this study, IOA-244 showed unprecedented tolerability and clinical benefit. In conclusion, thanks to its unique structural and selectivity features, IOA-244 represents a best in class PI3Kδ inhibitor, with an exceptional safety profile.

**IOA-244**

**IOA-244 impairs Treg proliferation, while preserving CD8 and CD4 conventional T cells**

**IOA-244 shows direct antitumor activity in PI3Kδ expressing tumors**

**IOA-244 shows best in class clinical safety profile**