Defeating primary checkpoint resistance: SRK-181 is a first-in-class, fully human antibody that renders resistant tumors sensitive to anti-PD-1 (Abstract 4090)

### Introduction

Despite the prominent reliance on primary checkpoint resistance in cancer therapies, there is a significant need for new approaches in checkpoint blockade that can overcome resistance. Serine/threonine kinase family exchangeable receptor (SRK) is a human protein that may represent a novel target for checkpoint blockade. Through an in vitro and in vivo evaluation of SRK-181, a first-in-class fully human antibody, we demonstrate its potential as a checkpoint inhibitor in resistant tumors.

### Methodology

**Experimental Design:** We conducted in vitro and in vivo experiments to evaluate the effects of SRK-181 on tumor growth and checkpoint activation. In vitro, we measured the inhibition of tumor cell proliferation and the activation of checkpoint pathways. In vivo, we performed tumor growth inhibition studies in a murine model.

### Results

- **Inhibition of Tumor Growth:** SRK-181 significantly inhibited the growth of resistant tumors in the murine model, demonstrating its efficacy in overcoming checkpoint resistance.
- **Checkpoint Activation:** SRK-181 blocked the activation of checkpoint pathways, including PD-1/PD-L1, in resistant tumors.

### Conclusion

SRK-181 represents a promising new checkpoint inhibitor that shows potential in overcoming resistance to primary checkpoint blockade. Further studies are needed to confirm its clinical efficacy in resistant tumors.