Introduction

- Somatostatin receptor 2 (SSTR2), a GPCR, is highly over-expressed in neuroendocrine tumors (NETs) and small cell lung cancer (SCLC).
- Somatostatin analogs and radionuclide therapies have clinical liabilities including short half-life, modest efficacy, administration challenges, and adverse side effects due to non-selective inhibition of other SSTRs.
- To exploit the potent mechanism of T cell immunotherapy for SSTR2+ cancers, we designed XmAb18087, a humanized and affinity-optimized anti-SSTR2 × anti-CD3 bispecific antibody that possesses a full Fc domain to maintain long serum half-life and facilitate efficient manufacturing.
- XmAb18087 eliminates SSTR+ tumor cells by stimulating redirected T cell-mediated cytotoxicity (RTCC) in vitro and in a mouse model.
- In monkeys, XmAb18087 stimulates T cell redistribution and activation and cytokine induction via an SSTR2 target-dependent mechanism.

Summary

The anti-SSTR2 × anti-CD3 bispecific antibody XmAb18087:

- Is humanized and contains a human Fc domain for long serum half-life.
- Effectively recruits T cells to kill SSTR2+ cancer cell lines in vitro.
- Induces anti-tumor activity in human PBMC-engrafted NSCLC mice.
- Stimulates SSTR2-dependent T cell activation, T cell maturation, and cytokine release in monkeys.
- Is efficiently manufactured using standard antibody production methods.

These results support clinical development of XmAb18087 as a therapeutic for neuroendocrine tumors and NSCLC.