Pharmacodynamic studies of SB 11285, a systemically bioavailable STING agonist in orthotopic tumor models

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INTRODUCTION

The activation of innate and adaptive immunity via Stimulator of Interferon Genes (STING) signaling is a potentially transformative immuno-therapeutic strategy in cancer. We have previously reported that the cyclic dinucleotide SB 11285 administered by IT, IP and IV routes has demonstrated potent anti-tumor activity, immune memory, abscopal effect and is synergistic with other anti-cancer agents including checkpoint inhibitors. We report here the anti-tumor and pharmacodynamic studies of SB 11285 in multiple orthotopic and subcutaneous syngeneic mouse tumor models.

SB 11285 self-assembles to form nanostructures

IV administration of SB 11285 resulted in potent anti-tumor activity in Orthotopic NBT-II syngeneic rat bladder cancer model

SB 11285 induces significant CD8+ T cells infiltration in tumor tissues

SB 11285 inhibits tumor growth and metastasis in orthotopic 4T1 breast cancer model after intraperitoneal (IP) administration

Summary: We have discovered highly potent first-in-class STING agonists that can be administered by systemic routes. The lead STING agonist SB 11285 has demonstrated potent Type I IFN and CD8+ T cell-dependent anti-tumor activity in multiple subcutaneous and orthotopic tumor models. As a novel agonist, SB 11285 also showed inhibition of tumor metastasis. SB 11285 is being evaluated in IND-enabling studies for the initiation of clinical trials.