RESULTS

SB 11285 inhibits tumor growth and metastasis in orthotopic 4T1 breast cancer model after IP administration. Significant induction of CD8+ T cells in Spleen, Blood and Lymph nodes was also observed.

SB 11285 showed synergistic anti-tumoral activity when combined with the Immune Check Point Inhibitor - anti-CTLA Antibody.

IV administration of SB 11285 is more efficacious than IP administration.

SB 11285 shows synergistic anti-tumoral activity in combined with the Immune Check Point Inhibitor - anti-CTLA Antibody.

We have discovered highly potent first-in-class STING agonists that cause induction of IFN, NF-kB, ISGs, and cytokines. The lead STING agonist SB 11285 administered by IT, IP and IV routes has demonstrated potent antitumor activity in multiple subcutaneous and orthotopic tumor models, and is synergistic with anti-cancer agents. As a novel STING agonist, SB 11285 induces anti-tumor immune memory, shows abscopal anti-tumoral activity and inhibits tumor metastasis. SB 11285 is being advanced for IND-enabling studies for the initiation of clinical trials.

SUMMARY

Pharmacodynamic and preclinical studies of SB 11285, a highly potent, and systemically bioavailable STING agonist as a novel immunotherapeutic agent

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INTRODUCTION

Immunotherapy has emerged as a transformative approach for the treatment of cancer. Recent work has highlighted a major role for Stimulator of Interferon Genes (STING) agonists in immunotherapy. Conceptually, the activation of STING pathway in immune cells and tumor cells in the tumor microenvironment could result in the induction of innate and adaptive immunity through the activation of cytotoxic T cells and NK cells for profound and durable anti-tumor response. We recently reported the discovery of SB 11285 as a potent, first-in-class, STING agonist. Reported here are the pharmacodynamic studies of SB 11285, in multiple syngeneic mouse tumor models, when administered by intravenous (IV), intraperitoneal (IP) and intratumoral (IT) routes.

RESULTS

SB 11285 displayed significant abscopal effect after IT administration in CT26 mouse model.

IV administration of SB 11285 results in potent and durable anti-tumor activity and induces immune memory in the A20 lymphoma mouse model.

Cytokine expression profile after IP administration of SB 11285 in mice.

SB 11285 and SB 11285 + 100 µg/animal IT showed significant induction of CD8+ T cells in the spleen, blood and lymph nodes after IP administration. Significant induction of CD8+ T cells in the spleen, blood and lymph nodes was also observed.

SB 11285 shows synergistic antitumoral activity when combined with the Immune Check Point Inhibitor - anti-CTLA Antibody.

SB 11285 is more efficacious than IP administration.

SB 11285 shows dose-dependent and highly potent anti-tumor activity in the CT26 colon carcinoma model.

We have discovered highly potent first-in-class STING agonists that cause induction of IFN, NF-kB, ISGs, and cytokines. The lead STING agonist SB 11285 administered by IT, IP and IV routes has demonstrated potent antitumor activity in multiple subcutaneous and orthotopic tumor models, and is synergistic with anti-cancer agents. As a novel STING agonist, SB 11285 induces anti-tumor immune memory, shows abscopal anti-tumoral activity and inhibits tumor metastasis. SB 11285 is being advanced for IND-enabling studies for the initiation of clinical trials.