SB 11312, an active metabolite of SB 11285, is a potent and systemically bioavailable STING agonist

Interimmunotherapy 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. Herein, we describe the discovery of the highly potent metabolite of SB 11285, designated as SB 11312 for application in immuno-oncology. SB 11312 is a mixture of two diastereomers of which SB 11312-A is the more active isomer. Both SB 11312 & SB 11312-A have potent immune-modulating, as well as, anti-tumor activities in tumor models. Comparative single-dose pharmacokinetic profiles of SB 11285 and SB 11312 following intravenous (IV) and intratumoral (IT) administration of SB 11285 in the CT26 tumor model is also described.

**INTRODUCTION**

**RESULTS**

SB 11312 & SB 11312-A showed potent induction of IFN-β from bone marrow derived dendritic cells (mBMDCs).

Intratumorally administered SB 11312 in A20 Murine Lymphoma Model and CT26 Murine Colon Carcinoma Model show potent antitumor activity.

**Summary:** We have discovered a highly potent first-in-class STING agonist SB 11285 that can be administered by systemic routes. SB 11312 (an active metabolite of SB 11285) and SB 11312-A (the single isomer of SB 11312) has demonstrated potent CD8+ T cell dependent anti-tumor activity in multiple subcutaneous tumor models. As a novel agonist, SB 11312-A also potently enhanced anti-tumor activity of the anti-PD1 antibody.