Discovery and Development of an Anti-CD40 Agonistic Antibody for Cancer Immunotherapy

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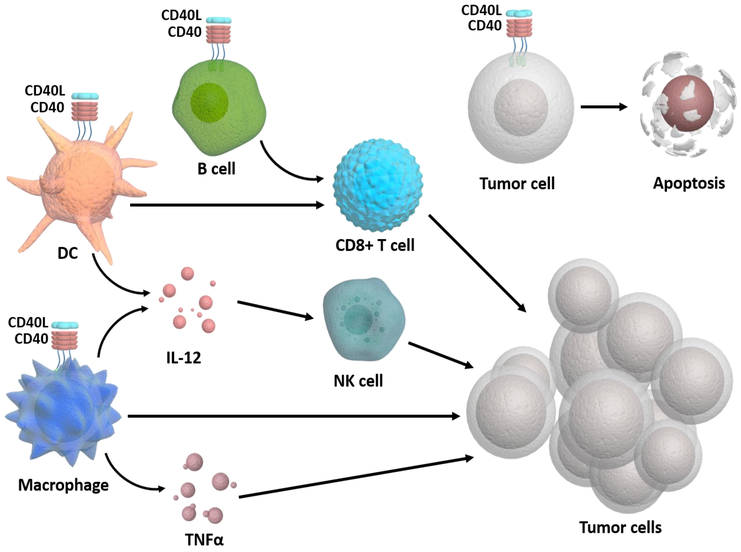
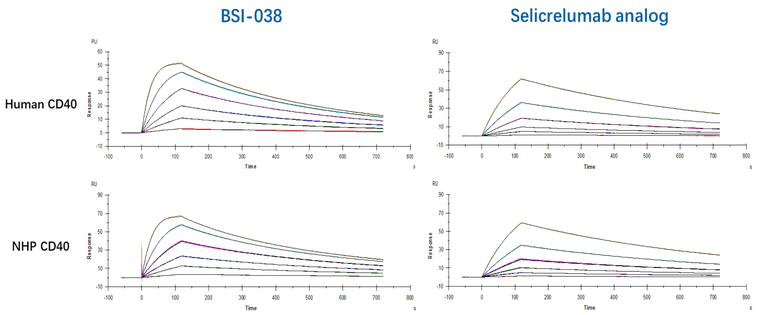
Introduction

CD40 agonism is able to promote anti-tumor immunity by stimulation of both innate and adaptive immune responses. A superior anti-CD40 agonistic antibody, BSI-038, was identified with enhanced binding affinity and bioactivity than Selicrelumab analog. It exhibited potent and dose-dependent anti-tumor activity in animal models. It was well-tolerated in pre-clinical studies with the highest non-severely toxic dose of 150 mg/kg in monkeys. Phase I trial was ongoing in China.

Effects of CD40-CD40L Signaling

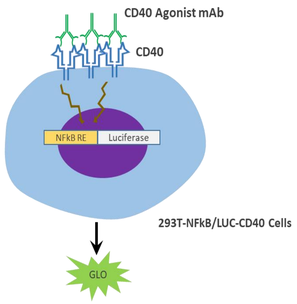


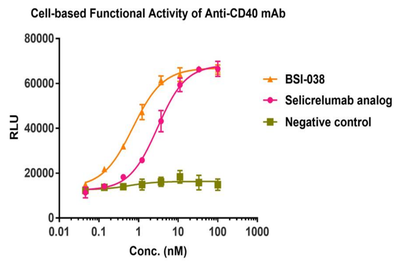
BSI-038 Exhibits Higher Binding Affinity



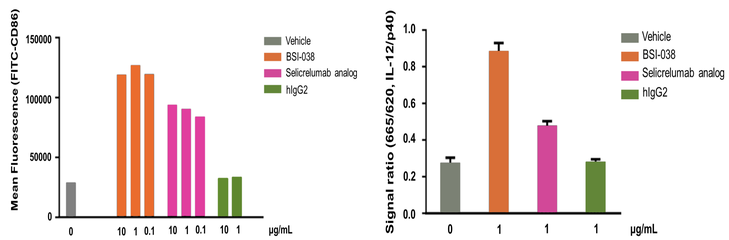
Antibody	Human CD40			NHP CD40		
	k_a (1/Ms)	k_d (1/s)	K_D (M)	k_a (1/Ms)	k_d (1/s)	K_D (M)
BSI-038	2.31E+06	2.70E-03	**1.17E-09**	2.56E+06	2.74E-3	**1.07E-09**
Selicrelumab analog	2.06E+05	1.62E-03	7.84E-09	1.73E+05	1.51E-3	8.73E-09

BSI-038 Shows Higher Cellular Bioactivity

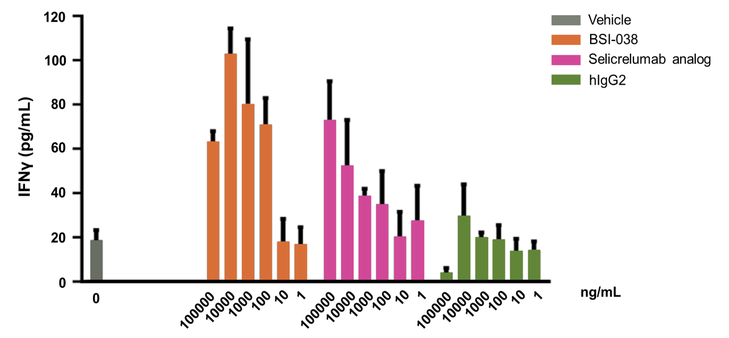




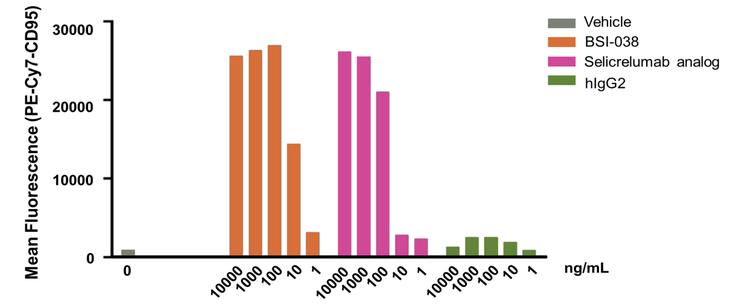
BSI-038 Significantly Activates Monocyte-Derived DCs



BSI-038 Significantly Promotes IFNγ Secretion in MLR

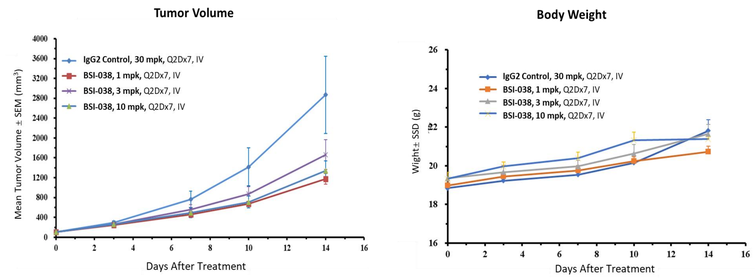


BSI-038 Significantly Stimulates CD95 On Ramos Cells

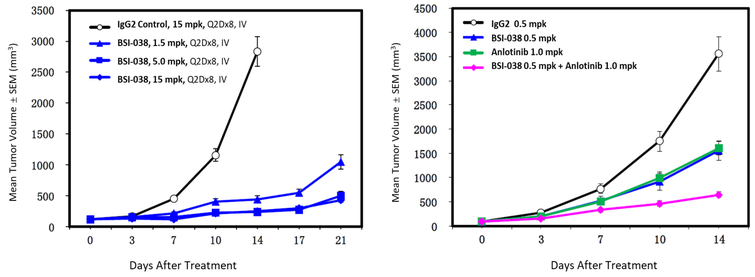


BSI-038 Shows Potent Anti-Tumor Activity *In Vivo*

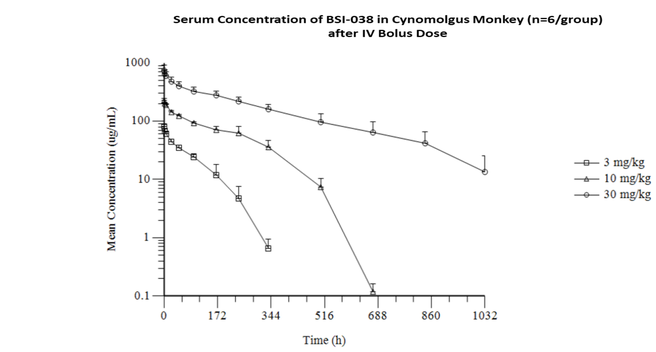
Subcutaneous hCD40/MC38 in hCD40 Knock-in Mice



Subcutaneous Ramos Xenograft in NOD/SCID Mice



BSI-038 Shows Good PK Profile in Cynomolgus Monkey



Parameters	Unit	Low Dose (3 mg/kg)	Medium Dose (10 mg/kg)	High Dose (30 mg/kg)
$t_{1/2}$	h	39.6±8.41	93.0±26.7	173±91.0

Summary

- Higher binding affinity and higher *in vitro* and *ex vivo* bioactivity than Selicrelumab analog;
- Potent *in vivo* anti-tumor activity in multiple animal models;
- Well-tolerated in pre-clinical studies with the highest non-severely toxic dose of 150 mg/kg in monkeys;
- Phase I trial ongoing in China and data expected in Q3 of 2023