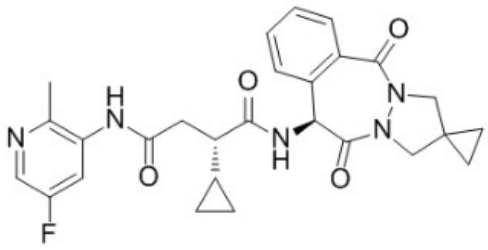
FT-B4G460

SPL-707

Potent, selective and orally available signal peptide peptidase-like 2a (SPPL2a) inhibitor with an IC 50 of 80 nM.

Product Description

Catalog #:	B4G460, 10 mg		
Name:	**SPL-707**		
CAS:	1537032-82-8		
Molecular Formula:	$C_{27}H_{28}FN_5O_4$		
Molecular Weight :	505.54		
IC_{50} & Target :	IC50: 80 nM (SPPL2a) [1]		
Storage:	Powder:	-20°C	3 years
		4°C	2 years
	In solvent:	-80°C	6 months
		-20°C	1 month



For Research Use Only

Introduction

Avelumab is a fully human IgG1 anti-PD-L1 monoclonal antibody with potential antibody-dependent cell-mediated cytotoxicity.

Directions for use

In Vitro

SPL-707 shows 25-fold selectivity over SPP with an IC 50 of 3.7 µM and some preference for SPPL2a over SPPL2b with a 3-fold selectivity, comparing IC 50 values generated with comparable assay formats for the different proteases [1].

In Vivo

SPL-707 significantly inhibits processing of the SPPL2a substrate CD74/p8 fragment in rodents at doses ≤10 mg/kg b.i.d. po. Oral dosing of SPL-707 for 11 days at ≥10 mg/kg b.i.d. recapitulates the phenotype seen in Sppl2a knockout (ko) and ENU mutant mice (reduced number of specific B cells and myeloid dendritic cells) [1].

Cell Assay [1]

DNA vectors encoding human Notch1-VP16-Gal4 fusion protein and a Gal4-luciferase reporter for the γ-secretase RGA, or human SPPL2a, VP16-TNFa(aa1-76)-NTF substrate, and the Gal4-luciferase reporter plasmid for the SPPL2a RGA, are transiently transfected in HEK293 cells using FuGENE. After transfection, the cell suspensions are diluted and distributed to white solid 384-well plate at 10000 cells/50 µL/well. After 3 h, 200 nL of SPL-707 in DMSO is stamped into the wells in concentration response covering final inhibitor concentrations of 10 µM to 0.3 nM in triplicate.

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Subsequently, plates are incubated for 24 h at 37°C, 5% CO 2 in a humidified incubator before the addition of 30 µL Bright Glo. After incubation for 5 min at rt, luminescence is measured and IC 50 values are determined by plotting compound concentration vs normalized luminescence values [1].

References

[1]. **Velcicky J**, *et al*. Discovery of the First Potent, Selective, and Orally Bioavailable Signal Peptide Peptidase-Like 2a (SPPL2a) Inhibitor Displaying Pronounced Immunomodulatory Effects In Vivo. *J Med Chem*. 61(3):865-880 (2018)

Ordering information

Catalog size quantities and prices may be found at http://www.interchim.com.
Please inquire for higher quantities (availability, shipment conditions).

Please contact InterBioTech – Interchim for any other information
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