SBI-0640756

Cat. No.: HY-19560

CAS No.: 1821280-29-8

Molecular Formula: $C_{23}H_{14}ClFN_2O_2$

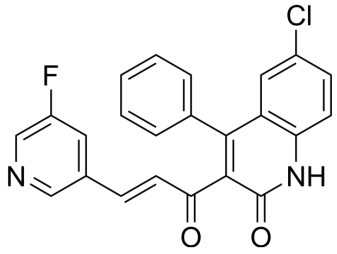
Molecular Weight: 404.82

Target: Eukaryotic Initiation Factor (eIF); Autophagy

Pathway: Cell Cycle/DNA Damage; Autophagy

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 26 mg/mL (64.23 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.4702 mL	12.3512 mL	24.7023 mL
5 mM	0.4940 mL	2.4702 mL	4.9405 mL
10 mM	0.2470 mL	1.2351 mL	2.4702 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 50% PEG300 >> 50% saline
   Solubility: 5 mg/mL (12.35 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 0.5% CMC-Na/saline water
   Solubility: 2.5 mg/mL (6.18 mM); Suspended solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

SBI-0640756 (SBI-756) is an inhibitor of eIF4G1 and disrupts the eIF4F complex.

IC_{50} & Target

eIF4

In Vitro

SBI-0640756 (SBI-756) is a water soluble inhibitor of eIF4G1. SBI-0640756 (SBI-756) (0-1 μM) disrupts eIF4F complex in parent and BRAFi-resistant melanoma. SBI-0640756 (SBI-756) shows inhibitory effect on human melanoma lines, and also suppresses AKT, NF-κB and AKT/mTORC1 activity[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo	SBI-0640756 (SBI-756) (0.5 mg/kg, i.p.) delays tumor onset and reduces tumor incidence by 50% in $Nras^{Q61K}$/$Ink4a^{-/-}$ genetic model. SBI-0640756 (SBI-756) (1 mg/kg, 2 times per week, i.p.) in combination with BRAF inhibitor potently suppresses growth of established tumors and does not resume tumor growth in immunodeficient mice bearing A375 tumors[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	WM793, Lu1205, WM1346 and WM1366 melanoma cells are seeded at 1500 cells in 50 µL per well in 384-well plates. Cells are allowed to attach overnight. SBI-0640756 (SBI-756) or derivatives analogs are serially diluted 2-fold with media from stock solutions and added to cells. Tests are performed in triplicate, and each microplate included media and DMSO control wells. Cell viability is assessed using ATPlite after 48 or 72 h. Cell growth inhibition is calculated as a percentage of DMSO-treated controls and plotted against the log drug concentration. IC_{50} values are interpolated from the resulting linear regression curve fit[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice[1] Six-week-old female nu/nu mice are allowed to acclimatize for 1 week. A375 cells (1×10^6, suspended in 200 µL sterile PBS) are injected into subcutaneous flank tissue. When the xenograft size reach -250 mm^3, mice are sorted into different groups. For PLX4720 and SBI-0640756 (SBI-756) combination experiments, mice are either fed PLX4720-containing chow alone (AIN76A Roden Diet with 417 mg PLX4720/kg) for the control group or PLX4720-containing chow plus an IP injection of 1 mg/kg SBI-0640756 twice a week. For MEKi plus SBI-0640756 (SBI-756) experiments, PD0325901 at 20 mg/kg (formulated in 0.5% hydroxypropyl methylcellulose plus 0.2% Tween-80) is administered by oral gavage twice a week (Monday and Thursday) for the control group, or PD035901 plus IP injection of 1 mg/kg SBI-0640756 (SBI-756) is administered twice a week (Tuesday and Friday)[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Front Pharmacol. 2024 Feb 9:15:1346383.

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REFERENCES

[1]. Feng Y et al. SBI-0640756 Attenuates the Growth of Clinically Unresponsive Melanomas by Disrupting the eIF4F Translation Initiation Complex. Cancer Res, 2015 Dec 15, 75(24):5211-8.

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