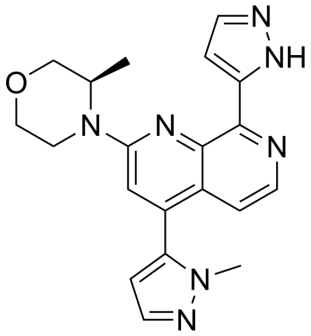
Elimusertib

Cat. No.:	HY-101566
CAS No.:	1876467-74-1
Molecular Formula:	$C_{20}H_{21}N_7O$
Molecular Weight:	375.43
Target:	ATM/ATR
Pathway:	Cell Cycle/DNA Damage; PI3K/Akt/mTOR
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 5.4 mg/mL (14.38 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.6636 mL	13.3181 mL	26.6361 mL
5 mM	0.5327 mL	2.6636 mL	5.3272 mL
10 mM	0.2664 mL	1.3318 mL	2.6636 mL

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

In Vivo

1. Add each solvent one by one: 0.5% CMC-Na/saline water
   Solubility: 4 mg/mL (10.65 mM); Suspended solution; Need ultrasonic and adjust pH to 3 with HCl
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 1.09 mg/mL (2.90 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: 0.89 mg/mL (2.37 mM); Suspended solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

Elimusertib (BAY-1895344) is a potent, orally active and selective ATR inhibitor with an IC_{50} of 7 nM. Elimusertib has anti-tumor activity[1][2]. Elimusertib can be used for the research of solid tumors and lymphomas[3].

IC_{50} & Target

ATR
7 nM (IC_{50})

In Vitro

Elimusertib potently inhibits the proliferation of a broad spectrum of human tumor cell lines with a median IC_{50} of 78 nM[1].

?Elimusertib potently suppresses hydroxyurea-induced H2AX phosphorylation (IC_{50}: 36 nM)[1].
?Elimusertib shows good selectivity against mTOR (ratio of IC_{50} values: mTOR/ATR 61)[3].
?Elimusertib reveals high selectivity against other related kinases, such as DNA-PK (IC_{50}: 332 nM), ATM (IC_{50}: 1420 nM), and PI3K (IC_{50}: 3270 nM)[3].
?Elimusertib has potent antiproliferative activity against various cancer cell lines in vitro, 25 for example in the CRC cell lines HT-29 (IC_{50}: 160 nM) and LoVo (IC_{50}: 71 nM), and in the B-cell lymphoma cell line SU-DHL-8 (IC_{50}: 9 nM)[3].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

Elimusertib shows potent anti-tumor efficacy in monotherapy in a variety of xenograft models of ovarian and colorectal cancer, and causes complete tumor remission in mantle cell lymphoma models[2].
?Elimusertib (50 mg/kg; p.o.; b.i.d.; 3 days on/4 days off; for 11 days) exhibits strong antitumor efficacy in the ATM-mutated SU-DHL-8 (ATM K1964E) human GCB-DLBCL cell line derived xenograft model in mice[3].
?Elimusertib (20 mg/kg, and 10 mg/kg from day 14; p.o.; daily; 2 days on/5 days off; for 42 days) in combination with Carboplatin (40 mg/kg; i.p.; daily; 1 day on/6 days off) results in synergistic antitumor activity in the platinum-resistant ATM protein low expressing CR5038 human CRC PDX model in NOD/SCID mice[3].
?Elimusertib exhibits moderate oral bioavailability (rat 87%, dog 51%) following oral administration (rat and dog 0.6-1 mg/kg)[3].
?Elimusertib exhibits terminal elimination half-lives (mouse 0.17 h, rat 1.3 and, dog 1.0 h) due to? plasma clearance (3.5, 1.2, and 0.79 L/h/kg respectively) following intravenous administration (mouse, rat and dog 0.3-0.5 mg/kg)[3].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Female C.B-17 SCID mice, SU-DHL-8 GCB-DLBCL xenograft model[3]
Dosage:	50 mg/kg
Administration:	Oral administration, b.i.d., 3 days on/4 days off, for 11 days
Result:	Inhibited tumor area.

Animal Model:	Male Wistar rats[3]
Dosage:	0.3-0.5 mg/kg for i.v.; 0.6-1 mg/kg for oral (Pharmacokinetic Analysis)
Administration:	Intravenous injection and oral administration
Result:	Oral bioavailability (87%), $T_{1/2}$ (1.3 h).

Animal Model:	Female beagle dogs[3]
Dosage:	0.3-0.5 mg/kg for i.v.; 0.6-1 mg/kg for oral (Pharmacokinetic Analysis)
Administration:	Intravenous injection and oral administration
Result:	Oral bioavailability (51%), $T_{1/2}$ (1.0 h).

CUSTOMER VALIDATION

- Cancer Res. 2022 Jan 12;canres.1707.2021.
- Biochem Pharmacol. 2023 Mar 14;115494.
- Research Square Preprint. 2023 Nov 20.

- Research Square Preprint. 2023 Jun 9.
- Research Square Preprint. 2023 May 17.

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REFERENCES

[1]. Ulrich T. Luecking, et al. Abstract 983: Identification of potent, highly selective and orally available ATR inhibitor BAY 1895344 with favorable PK properties and promising efficacy in monotherapy and combination in preclinical tumor models. Cancer Research. July 2017 Volume 77, Issue 13 Supplement.

[2]. Antje Margret Wengner, et al. Abstract 836: ATR inhibitor BAY 1895344 shows potent anti-tumor efficacy in monotherapy and strong combination potential with the targeted alpha therapy Radium-223 dichloride in preclinical tumor models. Cancer Research. July 2017 Volume 77, Issue 13 Supplement

[3]. Ulrich Lücking, et al. Damage Incorporated: Discovery of the Potent, Highly Selective, Orally Available ATR Inhibitor BAY 1895344 with Favorable Pharmacokinetic Properties and Promising Efficacy in Monotherapy and in Combination Treatments in Preclinical Tumor Models. J Med Chem. 2020 Jul 9;63(13):7293-7325.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA