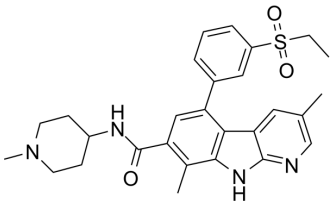
TAK-901

Cat. No.:	HY-12201
CAS No.:	934541-31-8
Molecular Formula:	$C_{28}H_{32}N_4O_3S$
Molecular Weight:	504.64
Target:	Aurora Kinase
Pathway:	Cell Cycle/DNA Damage; Epigenetics
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 : 65 mg/mL (128.80 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.9816 mL	9.9081 mL	19.8161 mL
	5 mM	0.3963 mL	1.9816 mL	3.9632 mL
	10 mM	0.1982 mL	0.9908 mL	1.9816 mL

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

BIOLOGICAL ACTIVITY

Description

TAK-901 is a multi-targeted aurora inhibitor with IC_{50}s of 21 and 15 nM for aurora A and B, respectively.

IC_{50} & Target

Aurora A	Aurora B
21 nM (IC_{50})	15 nM (IC_{50})

In Vitro

TAK-901 exhibits time-dependent, tight-binding inhibition of Aurora B, but not Aurora A. Consistent with Aurora B inhibition, TAK-901 suppresses cellular histone H3 phosphorylation and induces polyploidy. In various human cancer cell lines, TAK-901inhibits cell proliferation with effective concentration values from 40 to 500 nM. Examination of a broad panel of kinases in biochemical assays reveals inhibition of multiple kinases. However, TAK-901 potently inhibits only a few kinases other than Aurora B in intact cells, including FLT3 and FGFR2[1].

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

In Vivo

In rodent xenografts, TAK-901 exhibits potent activity against multiple human solid tumor types, and complete regression is observed in the ovarian cancer A2780 model. TAK-901 also displayed potent activity against several leukemia models. TAK-901 induces pharmacodynamic responses consistent with Aurora B inhibition and correlating with retention of TAK-901 in

	tumor tissue[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	Enzyme activities of Aurora A/TPX2 and Aurora B/INCENP complexes are assayed at room temperature in buffer containing serially diluted TAK-901, and the product is quantified using IMAP detection reagents. Aurora A/TPX2 (2 nM) is assayed with 100 nM FL-Kemptide and 1 mM ATP. Aurora B/INCENP (0.8 nM) is assayed with 100 nM 5-carboxy-fluorescein-GRTGRRNSI-NH2 (FL-PKAtide) and 10 mM ATP. For time-dependent inhibition, Aurora B/INCENP is incubated with TAK-901 for 1 hour at room temperature followed by addition of 150 mM ATP to initiate the reaction[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Cell Assay [1]	Cells are plated in 96-well microtiter plates and incubated with serial dilutions of TAK-901 for 72 hours. Cell proliferation is determined by ELISA analysis of bromodeoxyuridine (BrdUrd) incorporation into DNA. IMR-90 immortalized lung fibroblasts are seeded in 96-well microtiter plates and cultured for 3 to 4 days until confluent. Cells are then incubated with serial dilutions of TAK-901 for 72 hours. The MTS assay is conducted[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice: Tumor-bearing mice or rats are treated intravenously twice daily (b.i.d.) with either vehicle or TAK-901 on 2 consecutive days per week or every other day for 2 or 3 cycles. The antitumor activity of TAK-901 in human tumor and leukemia xenograft models are monitored[1]. Nude rats bearing A2780 tumors averaging 250 to 500 mg receive an intravenous dose of TAK-901. Plasma samples are collected by terminal cardiac puncture under CO_2 anesthesia. Tumors are dissected and snap-frozen at -80°C[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- EBioMedicine. 2021 Jan 30;64:103220.
- Technical University of Munich. 24.01.2018.

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REFERENCES

[1]. Farrell P, et al. Biological characterization of TAK-901, an investigational, novel, multitargeted Aurora B kinase inhibitor. Mol Cancer Ther. 2013 Apr;12(4):460-70.

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