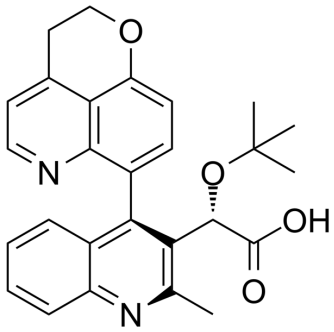
BI 224436

Cat. No.:	HY-18595
CAS No.:	1155419-89-8
Molecular Formula:	$C_{27}H_{26}N_2O_4$
Molecular Weight:	442.51
Target:	HIV; HIV Integrase
Pathway:	Anti-infection; Metabolic Enzyme/Protease
Storage:	Powder -20°C 3 years 4°C 2 years * The compound is unstable in solutions, freshly prepared is recommended.



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 50 mg/mL (112.99 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.2598 mL	11.2992 mL	22.5984 mL
	5 mM	0.4520 mL	2.2598 mL	4.5197 mL
	10 mM	0.2260 mL	1.1299 mL	2.2598 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (5.65 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.65 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.65 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

BI 224436 is a novel HIV-1 noncatalytic site integrase inhibitor with EC_{50} values of less than 15 nM against different HIV-1 laboratory strains.

IC_{50} & Target

EC50: 15 nM (HIV-1)[1]

In Vitro

BI 224436 has cellular cytotoxicity of more than 90 μM. BI 224436 has a low, 2.1-fold decrease in antiviral potency in the presence of 50% human serum. BI 224436 retains full antiviral activity against recombinant viruses encoding INSTI

	resistance substitutions N155S, Q148H, and E92Q. BI 224436 displays an additive effect in combination with most approved antiretrovirals, including INSTIs. BI 224436 has drug-like in vitro absorption, distribution, metabolism, and excretion (ADME) properties, including Caco-2 cell permeability, solubility, and low cytochrome P450 inhibition[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	BI 224436 exhibits excellent pharmacokinetic profiles in rat (clearance as a percentage of hepatic flow [CL], 0.7%; bioavailability [F], 54%), monkey (CL, 23%; F, 82%), and dog (CL, 8%; F, 81%)[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	BI 224436 is dissolved in acetonitrile-methanol (50:50, vol/vol) to achieve a concentration of 1.5 mM. Phosphate buffer (pH 7.4), cofactor, and test substance or isoform-selective inhibitors are added to 96-well plates and are prewarmed to 37°C for 10 min. Cofactor concentrations are 1.3 mM NADP, 3.3 mM glucose-6-phosphate, and 0.4 U/mL glucose-6-phosphate dehydrogenase. Reactions are initiated by the addition of prewarmed (37°C) enzyme and substrate. Reaction mixtures are incubated at 37°C and terminated by the addition of 0.038 ml of 40:40:20 (vol/vol) methanol–acetonitrile–0.5 M Tris buffer. Formation of the fluorescent metabolites is measured using a microplate spectrofluorometer at specific excitation and emission wavelengths. The IC_{50} is determined using the 96-well 32 procedure supplied with the SAS software[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Rats: For oral PK studies, BI 224436 is administered in a suspension of 0.5% (wt/vol) methyl cellulose (MC), 0.3% (vol/vol) Tween 80, and 1% (vol/vol) N-methyl-2-pyrrolidine (MP) in water. For i.v. dosing, BI 224436 is dissolved in 70% PEG 400–30% water (vol/vol). The appropriate amount of BI 224436 is dissolved in PEG 400 with sonication. The rats receive a single i.v. dose of 0.2 mg/kg of body weight (1 mL/kg) via the jugular vein as a bolus or received a single oral dose of 0.4 mg/kg (10 mL/kg) administered by gavage. Blood samples are obtained at 0, 0.25, 0.5, 1, 1.5, 2, 3, 4, 6, 8, 12, 24, and 32 h after dosing for analysis[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Elife. 2019 May 23;8:e46344.
- J Virol. 2020 Sep 15;94(19):e00486-20.
- J Biol Chem. 2017 Dec 1;292(48):19814-19825.
- Retrovirology. 2020 Aug 31;17(1):28.
- Ann Med Res. 2022 Dec;54(1):1590-1600.

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REFERENCES

[1]. Fenwick C, et al. Preclinical profile of BI 224436, a novel HIV-1 non-catalytic-site integrase inhibitor. Antimicrob Agents Chemother. 2014 Jun;58(6):3233-44.

Caution: Product has not been fully validated for medical applications. For research use only.

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