Vecabrutinib

Cat. No.: HY-109078

CAS No.: 1510829-06-7

Molecular Formula: $C_{22}H_{24}ClF_4N_7O_2$

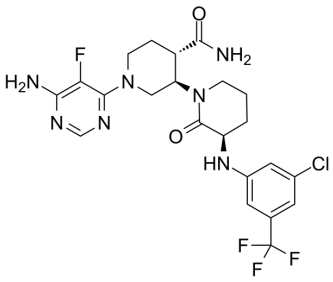
Molecular Weight: 529.92

Target: Btk; Itk

Pathway: Protein Tyrosine Kinase/RTK

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 : 125 mg/mL (235.88 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.8871 mL	9.4354 mL	18.8708 mL
	5 mM	0.3774 mL	1.8871 mL	3.7742 mL
	10 mM	0.1887 mL	0.9435 mL	1.8871 mL

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

In Vivo

1. Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline
   Solubility: ≥ 2.5 mg/mL (4.72 mM); Clear solution
2. Add each solvent one by one: 5% DMSO >> 95% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (4.72 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (3.93 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (3.93 mM); Clear solution
5. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (3.93 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Vecabrutinib (SNS-062) is a potent, noncovalent BTK and ITK inhibitor, with K_d values of 0.3 nM and 2.2 nM, respectively. Vecabrutinib shows an IC_{50} of 24 nM for ITK[1][2].

IC_{50} & Target	IC50: 24 nM (ITK)[2] Kd: 0.3 nM (BTK), 2.2 nM (ITK)[1]
In Vitro	Vecabrutinib inhibits pBTK in human whole blood with an average IC_{50} of 50 nM. Vecabrutinib inhibits WT and C481S BTK with similar IC_{50}s (pBTK IC_{50}s: WT BTK 2.9 nM, C481S BTK 4.4 nM)[1]. In a recombinant kinase assay, IC_{50}s of Vecabrutinib against WT BTK and C481S BTK are 4.6 nM and 1.1 nM. Vecabrutinib retains activity against the mutated BTK variant. Vecabrutinib is six times more potent than PCI-32765 and greater than 640 times more potent than acalabrutinib against C481S BTK. Vecabrutinib demonstrates dose-dependent inhibition of BTK in primary patient CLL cells comparable to PCI-32765 via immunoblot for BTK phosphorylation. Vecabrutinib decreases viability of primary CLL cells in the presence of HS5 stromal protection by 5.5%[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Vecabrutinib has good oral bioavailability in rat and dog (%F ≥ 40%) and a terminal half-life of 5 to 6 hours. Vecabrutinib is well tolerated with continuous drug levels and at exposures much greater than those achieved for PCI-32765[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Proc Natl Acad Sci U S A. 2022 Oct 25;119(43):e2207280119.
- JCI Insight. 2019 Jun 20;4(12). pii: 127566.

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REFERENCES

[1]. Minke E. Binnerts, et al. Abstract C186: SNS-062 is a potent noncovalent BTK inhibitor with comparable activity against wild type BTK and BTK with an acquired resistance mutation. Molecular Cancer Therapeutics. December 2015 Volume 14, Issue 12 Supplement

[2]. Catherine A. Fabian, et al. Abstract 1207: SNS-062 demonstrates efficacy in chronic lymphocytic leukemia in vitro and inhibits C481S mutated Bruton tyrosine kinase. Cancer Research July 2017 Volume 77, Issue 13 Supplement

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