Fenebrutinib

Cat. No.: HY-19834

CAS No.: 1434048-34-6

Molecular Formula: $C_{37}H_{44}N_8O_4$

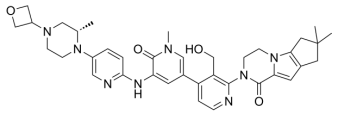
Molecular Weight: 664.8

Target: Btk

Pathway: Protein Tyrosine Kinase/RTK

Storage: 4°C, stored under nitrogen

* In solvent : -80°C, 6 months; -20°C, 1 month (stored under nitrogen)



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 23 mg/mL (34.60 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.5042 mL	7.5211 mL	15.0421 mL
5 mM	0.3008 mL	1.5042 mL	3.0084 mL
10 mM	0.1504 mL	0.7521 mL	1.5042 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: ≥ 1 mg/mL (1.50 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 1 mg/mL (1.50 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 1 mg/mL (1.50 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Fenebrutinib (GDC-0853) is a potent, selective, orally available, and noncovalent bruton's tyrosine kinase (Btk) inhibitor with K_is of 0.91 nM, 1.6, 1.3, 12.6, and 3.4 nM for WT Btk, and the C481S, C481R, T474I, T474M mutants. Fenebrutinib has the potential for rheumatoid arthritis and systemic lupus erythematosus research[1].

IC_{50} & Target

Ki: 0.91 nM (Btk WT), 1.6 nM (Btk C481S), 1.3 nM (Btk C481R), 12.6 nM (Btk T474I), and 3.4 nM (Btk T474M)[1]

In Vitro

Fenebrutinib (GDC-0853) inhibits CD69 expression on $CD19^+$ B cells in human whole blood with an IC_{50} of 8.4±5.6 nM. Fenebrutinib inhibits CD63 expression on basophils with an IC_{50} of 30.7±4.1 nM[2].

	Fenebrutinib suppresses anti-IgM induced Btk Y223 autophosphorylation in human whole blood (IC_{50}=11 nM)[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Fenebrutinib (GDC-0853) dose-dependently reduces ankle thickness following once (0.06, 0.25, 1, 4, and 16 mg/kg QD; orally) or twice (0.125, 0.5, and 2 mg/kg BID; orally) daily in female Lewis rats with developing collagen-induced arthritis[2]. Fenebrutinib (0.2 mg/kg IV and 1.0 mg/kg PO; for rats) and (0.2 mg/kg IV and 0.5 mg/kg PO for dogs) demonstrates the half-lives ($t_{1/2}$s) of 2.2 and 3.8 h In rats, and dogs, respectively[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Female Lewis rats with developing collagen-induced arthritis (CIA)[2]
Dosage:	0.06, 0.25, 1, 4, and 16 mg/kg once daily (QD); 0.125, 0.5, and 2 mg/kg twice daily (BID)
Administration:	Dosed orally; for 16 days
Result:	Dose-dependently reduced ankle thickness following QD and BID dosing regimens.

CUSTOMER VALIDATION

- Leukemia. 2021 Feb 1.
- JCI Insight. 2019 Jun 20;4(12). pii: 127566.
- Int J Mol Sci. 2022, 23(1), 76.
- Molecules. 2023 May 22, 28(10), 4225.
- Separations. 2023 May 9, 10(5), 302.

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REFERENCES

[1]. Erickson RI , et al. Bruton's Tyrosine Kinase Small Molecule Inhibitors Induce a Distinct Pancreatic Toxicity in Rats. J Pharmacol Exp Ther. 2017 Jan;360(1):226-238.

[2]. Crawford JJ, et al. Discovery of GDC-0853: A Potent, Selective, and Noncovalent Bruton's Tyrosine Kinase Inhibitor in Early Clinical Development. J Med Chem. 2018 Mar 22;61(6):2227-2245.

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