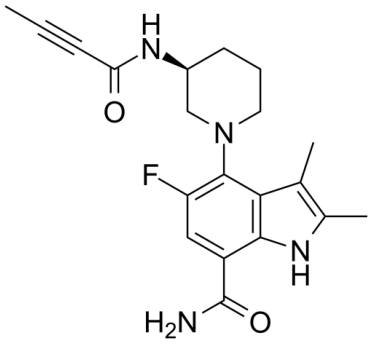
Data Sheet

Product Name:	Branebrutinib
Cat. No.:	CS-0043577
CAS No.:	1912445-55-6
Molecular Formula:	C20H23FN4O2
Molecular Weight:	370.42
Target:	Btk
Pathway:	Protein Tyrosine Kinase/RTK
Solubility:	DMSO : ≥ 100 mg/mL (269.96 mM)



BIOLOGICAL ACTIVITY:

Branebrutinib (BMS-986195) is a highly potent, selective covalent, irreversible inhibitor of Bruton's tyrosine kinase **(BTK)**, with an **IC_{50}** of 0.1 nM[1][2]. IC50 & Target: IC50: 0.1 nM (BTK)[1]. **In Vitro:** BMS-986195 is a potent and highly selective inhibitor of BTK, which acts by covalently modifying an active-site cysteine residue. BMS-986195 is more than 5000-fold selective for BTK over all kinases outside of the Tec family, and selectivity ranges from 9- to 1010-fold within the Tec family. BMS-986195 inactivates BTK in human whole blood with a rapid rate of inactivation ($3.5\times10^{-4}nM^{-1}\bullet min^{-1}$) and potently inhibits antigen-dependent interleukin-6 production, CD86 expression and proliferation in B cells (IC_{50}<1 nM) without effect on antigen-independent measures in the same cells. A similar potency is measured against FcγR-dependent TNF-α production in human cells[1]. **In Vivo:** In mice, BMS-986195 demonstrates robust efficacy in murine models of RA including CIA and CAIA, protecting against clinically evident disease, histologic joint damage and bone mineral density loss. In both mice and monkeys, maximal efficacy is observed at doses ≤0.5 mg/kg PO QD, which achieves ≥95% inactivation of BTK in vivo. At similar doses, BMS-986195 is also highly protective against nephritis in the NZB/W mouse model of lupus. To investigate the dynamics of BTK inactivation and resynthesis of BTK, cynomolgus monkeys are given single or multiple doses of BMS-986195. 100% peak inactivation of BTK is obtained with a single administration of BMS-986195 at 0.5 mg/kg PO[1].

References:

[1]. JR Burke, et al. BMS-986195 Is a Highly Selective and Rapidly Acting Covalent Inhibitor of Bruton's Tyrosine Kinase with Robust Efficacy at Low Doses in Preclinical Models of RA and Lupus Nephritis. 2017 ACR/ARHP Annual Meeting, September 18, 2017.

[2]. Watterson SH, et al. Discovery of Branebrutinib (BMS-986195): A Strategy for Identifying a Highly Potent and Selective Covalent Inhibitor Providing Rapid in Vivo Inactivation of Bruton's Tyrosine Kinase (BTK). J Med Chem. 2019 Apr 11;62(7):3228-3250.

CAIndexNames:

1H-Indole-7-carboxamide, 5-fluoro-2,3-dimethyl-4-[(3S)-3-[(1-oxo-2-butyn-1-yl)amino]-1-piperidinyl]-

SMILES:

O=C(C1=CC(F)=C(N2C[C@@H](NC(C#CC)=O)CCC2)C3=C1NC(C)=C3C)N

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

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