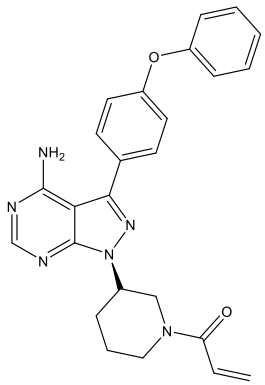
Catalog # 10-4757
Ibrutinib

CAS# 936563-96-1

1-[(3*R*)-3-[4-amino-3-(4-phenoxyphenyl)pyrazolo[3,4-d]pyrimidin-1-yl]piperidin-1-yl]prop-2-en-1-one; PCI-32765

Lot # FBS2145



Ibrutinib is a very potent (IC_{50} = 0.5nM) irreversible inhibitor of Bruton tyrosine kinase (BTK) that blocks activation of the B-cell antigen receptor (BCR).[1] Ibrutinib also potently inhibits several other kinases including BLK, BMS, FGR, EGFR, and ITK. It is a clinically useful drug to treat B cell cancers. It inhibits CLL cell migration and survival[2,3] and downregulates expression of CD20[4]. It enhanced antitumor immune responses in combination with anti PD-L1 blockade *via* its inhibition of ITK (IL2-inducible T-cell kinase).[5] BTK has also been shown to have a role in modulating the innate immune system, especially in dendritic cells and macrophages, suggesting a possible role in immunotherapy.[6]

1) Honigberg *et al*. (2010), *The Bruton tyrosine kinase inhibitor PCI-32765 blocks B-cell activation and is efficacious in models of autoimmune disease and B-cell malignancy;* Proc.Natl.Acad.Sci.USA **107** 13075
2) Ponader *et al*. (2012), *The Bruton tyrosine kinase Inhibitor PCI-32765 thwarts chronic lymphocytic leukemia cell survival and tissue homing in vitro and in vivo*; Blood **119** 1182
3) De Rooij *et al*. (2012), *The clinically active BTK inhibitor PCI-32765 targets B-cell receptor- and chemokine-controlled adhesion and migration in chronic lymphocytic leukemia*; Blood **119** 2590
4) Pavlasova *et al*. (2016), *Ibrutinib inhibits CD20 upregulation on CLL B cells mediated by the CXCR4/SDF-1 axis*; Blood **128** 1609
5) Sagiv-Barfi *et al.* (2015) *Therapeutic antitumor immunity by checkpoint blockade is enhanced by ibrutinib, an inhibitor of both BTK and ITK*; Proc.Natl.Acad.Sci.USA **112** E966
6) Weber *et al.* (2017), *Bruton's Tyrosine Kinase: An Emerging Key Player in Innate Immunity*; Front.Immunol. **8** 1454

PHYSICAL DATA

Molecular Weight:	440.51
Molecular Formula:	$C_{25}H_{24}N_6O_2$
Purity:	99% by HPLC
	NMR: (Conforms)
Solubility:	DMSO (>25 mg/ml)
Physical Description:	White to Off-white solid
Storage and Stability:	Store as supplied desiccated at -20°C for up to 1 year from the date of purchase. Solutions in DMSO may be stored at -20°C for up to 1 month.

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