

## Product Data Sheet

Product Name: BLZ945  
Cat. No.: GC12539

### Chemical Properties

Cas. No. 953769-46-5

Chemical Name 4-((2-(((1R,2R)-2-hydroxycyclohexyl)amino)benzo[d]thiazol-5-yl)oxy)-N-methylpicolinamide

SMILES O=C(NC)C1=NC=CC(OC2=CC3=C(N=C(N[C@@H]4CCCC[C@H]4O)S3)C=C2)=C1

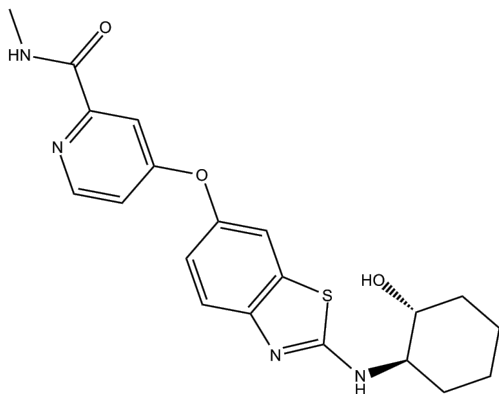
Formula  $C_{20}H_{22}N_4O_3S$  M.Wt 398.48

Solubility  $\geq 19.9\text{mg/mL}$  in DMSO Storage Store at  $-20^{\circ}\text{C}$

General tips For obtaining a higher solubility, please warm the tube at  $37^{\circ}\text{C}$  and shake it in the ultrasonic bath for a while. Stock solution can be stored below  $-20^{\circ}\text{C}$  for several months.

Shipping Condition Evaluation sample solution: ship with blue ice. All other available size: ship with RT, or blue ice upon request.

Structure



### Protocol

#### Cell experiment [1]:

Cell lines BMDM cell line

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

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**Preparation method** The solubility of this compound in DMSO is > 19.9 mg/mL. General tips for obtaining a higher concentration: Please warm the tube at 37 °C for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below - 20 °C for several months.

**Reacting condition** 6.7 ~ 6700 nM; 96 hrs

**Applications** In BMDM cell line, BLZ945 specifically inhibited CSF-1-dependent proliferation (EC<sub>50</sub> = 67 nM), and reduced CSF-1R phosphorylation.

### Animal experiment [2]:

**Animal models** Female MMTV-PyMT transgenic mice

**Dosage form** 200 mg/kg; p.o.; q.d., for 16 days

**Applications** In female MMTV-PyMT transgenic mice, BLZ945 decreased macrophages in tumors and livers, but showed no effect on lung macrophages, circulating monocytes and tumor cell proliferation.

**Other notes** Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.

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### References:

[1]. Pyonteck SM, Akkari L, Schuhmacher AJ, Bowman RL, Sevenich L, Quail DF, Olson OC, Quick ML, Huse JT, Teijeiro V, Setty M, Leslie CS, Oei Y, Pedraza A, Zhang J, Brennan CW, Sutton JC, Holland EC, Daniel D, Joyce JA. CSF-1R inhibition alters macrophage polarization and blocks glioma progression. *Nat Med*. 2013 Oct;19(10):1264-72.

[2]. Strachan DC, Ruffell B2, Oei Y et al. CSF1R inhibition delays cervical and mammary tumor growth in murine models by attenuating the turnover of tumor-associated macrophages and enhancing infiltration by CD8+ T cells. *Oncoimmunology*. 2013 Dec 1;2(12):e26968.

### Background

BLZ945, also named as 4-[2((1R,2R)-2-Hydroxycyclohexylamino)-benzothiazol-6-yloxy]-pyridine-2-carboxylic acid methylamide, is a small molecule inhibitor of CSF-1R kinase with IC<sub>50</sub> value of 1.2 nM. [2]

CSF-1R is the receptor for macrophage colony stimulating factor (M-CSF) which mediates the biological effects of this cytokine. The main biological effects of CSF-1R signaling are differentiation, proliferation, migration and survival of precursor macrophages and osteoclasts from the monocytic lineage [1].

BLZ945 has the potential to treat an array of diseases associated with normal and deregulated function of precursor macrophages and osteoclasts from the monocytic lineage. [14C]BLZ945 metabolites were kinetically and structurally characterized from an in vitro across species comparison study using human hepatocytes and microsomes. Both compounds BLZ945 and M9 have significant anti-proliferative activity against the M-CSF dependent cell line MNFS-60 with EC<sub>50</sub> of 71 and 140 mM, respectively. The biotransformation of BLZ945 in human liver micro-somes and recombinant cytochromes occurred predominantly via oxidative routes with also a secondary reductive pathway. [2]

BLZ945 decreased the growth of malignant cells in the mouse mammary tumor virus-driven polyomavirus middle T antigen (MMTV-PyMT) model of mammary carcinogenesis. BLZ945 prevented tumor progression in the keratin 14-expressing human papillomavirus type 16 (K14-HPV-16) transgenic model of cervical carcinogenesis. [3]

### References:

[1]. Stanley ER, Berg KL, Einstein DB et al. Biology and action of colony--stimulating factor-1. *Mol*

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*Reprod Dev.* 1997 Jan;46(1):4-10.

[2]. Krauser JA, Jin Y, Walles M et al. Phenotypic and metabolic investigation of a CSF-1R kinase receptor inhibitor (BLZ945) and its pharmacologically active metabolite. *Xenobiotica*. 2015 Feb;45(2):107-23.

[3]. Strachan DC, Ruffell B2, Oei Y et al. CSF1R inhibition delays cervical and mammary tumor growth in murine models by attenuating the turnover of tumor-associated macrophages and enhancing infiltration by CD8+ T cells. *Oncoimmunology*. 2013 Dec 1;2(12):e26968.

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