

Product Data Sheet

Product Name: A-1155463

Cat. No.: GC17512

Chemical Properties

Cas. No. 1235034-55-5

Chemical Name 2-(8-(benzo[d]thiazol-2-ylcarbonyl)-3,4-dihydroisoquinolin-2(1H)-yl)-5-(3-(4-(3-(dimethylamino)prop-1-yn-1-yl)-2-fluorophenoxy)propyl)thiazole-4-carboxylic acid

SMILES O=C(C1=C(CCCOC2=CC=C(C#CCN(C)C)C=C2F)SC(N3CC4=C(C=CC=C4C(NC5=NC6=CC=CC=C6S5)=O)CC3)=N1)O

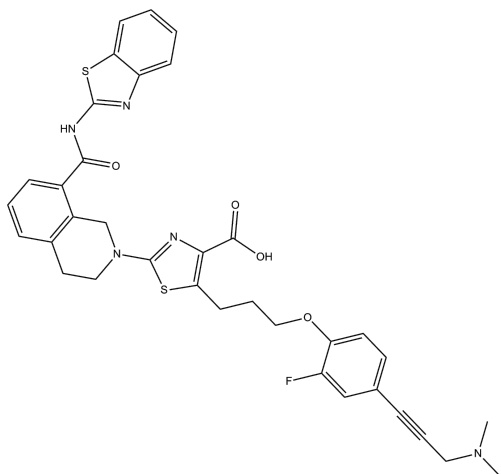
Formula $C_{35}H_{32}FN_5O_4S_2$ M.Wt 669.79

Solubility $\geq 67\text{mg/mL}$ in DMSO Storage Store at -20°C

General tips For obtaining a higher solubility, please warm the tube at 37°C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°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

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

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Animal experiment: Mice: Following a single 5 mg/kg IP dose of A-1155463 in nontumor bearing SCID-Beige mice, platelet counts fell dramatically as measured at 6 h postdose and then rebounded to normal levels within 72 h. A-1155463 is then administered to SCID-Beige mice that had been inoculated with BCL-XL-dependent H146 tumor cells with a daily dose at 5 mg/kg IP for 14 days[2].

References:

- [1]. Levenson JD, et al. Exploiting selective BCL-2 family inhibitors to dissect cell survival dependencies and define improved strategies for cancer therapy. *Sci Transl Med*. 2015 Mar 18;7(279):279
- [2]. Tao ZF, et al. Discovery of a Potent and Selective BCL-XL Inhibitor with in Vivo Activity. *ACS Med Chem Lett*. 2014 Aug 26;5(10):1088-93.
- [3]. Zhang H, et al. Genomic analysis and selective small molecule inhibition identifies BCL-X(L) as a critical survival factor in a subset of colorectal cancer. *Mol Cancer*. 2015 Jul 2;14:126.

Background

K_i=19 nM

A-1155463 is a potent and selective BCL-XL inhibitor.

BCL-2 plays a key role in the survival of lymphoid malignancies, while BCL-XL overexpression has been associated with drug resistance and disease progression of various solid tumors and hematological malignancies.

In vitro: A-1155463 was identified via nuclear magnetic resonance fragment screening and structure-based design to be a highly potent and selective BCL-XL inhibitor. A-1155463 was found to be substantially more potent against BCL-XL-dependent cell lines relative to the previously reported inhibitor, WEHI-539 [1].

In vivo: Animal study showed that following a single IP dose of A-1155463 at 5 mg/kg in nontumor bearing SCID-Beige mice, platelet counts dramatically decreased at 6 h postdose and then rebounded to normal levels within 72 h. Such platelet depletion and recovery kinetics were similar to

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those of the dual inhibitor navitoclax. Moreover, in order to give additional evidence that A-1155463 was conferring on-target in-vivo activity, A-1155463 was then administered to SCIDBeige mice that had been inoculated with BCL-XL-dependent H146 tumor cells. Results showed that the daily IP dosing of A-1155463 at 5 mg/kg for 14 days caused a statistically significant inhibition of tumor growth, which was alleviated upon cessation of dosing [1].

Clinical trial: Up to now, A-1155463 is still in the preclinical development stage.

Reference:

[1] Tao ZF et al. Discovery of a Potent and Selective BCL-XL Inhibitor with in Vivo Activity. ACS Med Chem Lett. 2014 Aug 26;5(10):1088-93.

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