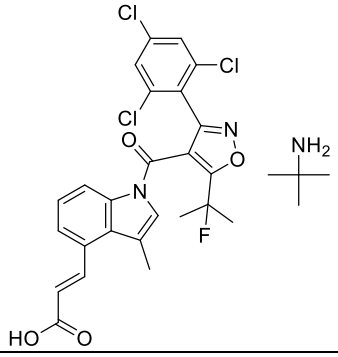
Product data sheet

MedKoo Cat#: 533299 Name: DS-1001B CAS#: 1898207-64-1 (tBuA) Chemical Formula: $C_{29}H_{29}Cl_3FN_3O_4$ Exact Mass: 607.1208 Molecular Weight: 608.9164	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:
DS-1001B is a novel selective mutant IDH1 inhibitor, ameliorating aberrant histone modifications and impairing tumor activity in chondrosarcoma.

2. CoA, QC data, SDS, and handling instruction
SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	14	22.99

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	1.64 mL	8.21 mL	16.42 mL
5 mM	0.33 mL	1.64 mL	3.28 mL
10 mM	0.16 mL	0.82 mL	1.64 mL
50 mM	0.03 mL	0.16 mL	0.33 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator
Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study
In vitro study

1. Nakagawa M, Nakatani F, Matsunaga H, Seki T, Endo M, Ogawara Y, Machida Y, Katsumoto T, Yamagata K, Hattori A, Fujita S, Aikawa Y, Ishikawa T, Soga T, Kawai A, Chuman H, Yokoyama N, Fukushima S, Yahiro K, Kimura A, Shimada E, Hirose T, Fujiwara T, Setsu N, Matsumoto Y, Iwamoto Y, Nakashima Y, Kitabayashi I. Selective inhibition of mutant IDH1 by DS-1001b ameliorates aberrant histone modifications and impairs tumor activity in chondrosarcoma. Oncogene. 2019 Oct;38(42):6835-6849. doi: 10.1038/s41388-019-0929-9. Epub 2019 Aug 12. PMID: 31406254.

In vivo study

1. Nakagawa M, Nakatani F, Matsunaga H, Seki T, Endo M, Ogawara Y, Machida Y, Katsumoto T, Yamagata K, Hattori A, Fujita S, Aikawa Y, Ishikawa T, Soga T, Kawai A, Chuman H, Yokoyama N, Fukushima S, Yahiro K, Kimura A, Shimada E, Hirose T, Fujiwara T, Setsu N, Matsumoto Y, Iwamoto Y, Nakashima Y, Kitabayashi I. Selective inhibition of mutant IDH1 by DS-1001b ameliorates aberrant histone modifications and impairs tumor activity in chondrosarcoma. Oncogene. 2019 Oct;38(42):6835-6849. doi: 10.1038/s41388-019-0929-9. Epub 2019 Aug 12. PMID: 31406254.

2. Machida Y, Nakagawa M, Matsunaga H, Yamaguchi M, Ogawara Y, Shima Y, Yamagata K, Katsumoto T, Hattori A, Itoh M, Seki T, Nishiya Y, Nakamura K, Suzuki K, Imaoka T, Baba D, Suzuki M, Sampetrean O, Saya H, Ichimura K, Kitabayashi I. A Potent Blood-Brain Barrier-Permeable Mutant IDH1 Inhibitor Suppresses the Growth of Glioblastoma with IDH1 Mutation in a Patient-

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Derived Orthotopic Xenograft Model. Mol Cancer Ther. 2020 Feb;19(2):375-383. doi: 10.1158/1535-7163.MCT-18-1349. Epub 2019 Nov 14. PMID: 31727689.

7. Bioactivity

Biological target:

DS-1001b is a selective inhibitor of mutant IDH1 R132X.

In vitro activity

DS-1001b strongly inhibited mutant IDH1 but not wild-type IDH1. The role of mutant IDH1 in chondrosarcoma was investigated by assessing the effects of DS-1001b on chondrosarcoma cell lines with wild-type or mutant IDH. Sanger sequencing was performed to determine the presence of IDH mutations in the different cell lines. The heterozygous IDH mutation was detected in JJ012 (IDH1R132G), L835 (IDH1R132C), and SW1353 (IDH2R172S) cells (Supplementary Fig. 1A), whereas OUMS27 and NDCS-1 cells had no mutation in either allele (data not shown). Measurement of intracellular 2-HG by LC-MS/MS showed that 2-HG levels were significantly higher in IDH-mutated cell lines than in IDH wild-type cell lines, in which 2-HG was barely detectable (Fig. 1b). The levels of 2-HG did not differ significantly between mutant IDH1 and IDH2 cell lines. Exposure to 1 μM DS-1001b for 72 h markedly decreased intracellular 2-HG levels in JJ012 and L835 cells, whereas DS-1001b had no effect in SW1353, OUMS27, and NDCS-1 cells. Intracellular D-2-HG levels measured by LC-TOFMS were 100-fold higher than L-2-HG levels and completely blocked with 1 μM DS-1001b for 72 h in both IDH1-mutated cell lines (Fig. 1c).

Reference: Oncogene. 2019 Oct;38(42):6835-6849. https://doi.org/10.1038/s41388-019-0929-9

In vivo activity

The present study describes a novel, orally bioavailable selective mutant IDH1 inhibitor, DS-1001b. The drug has high blood-brain barrier (BBB) permeability and inhibits IDH1R132H. Continuous administration of DS-1001b impaired tumor growth and decreased 2-HG levels in subcutaneous and intracranial xenograft models derived from a patient with glioblastoma with IDH1 mutation. Moreover, the expression of glial fibrillary acidic protein was strongly induced by DS-1001b, suggesting that inhibition of mutant IDH1 promotes glial differentiation. These results reveal the efficacy of BBB-permeable DS-1001b in orthotopic patient-derived xenograft.

Reference: Mol Cancer Ther. 2020 Feb;19(2):375-383. http://mct.aacrjournals.org/cgi/pmidlookup?view=long&pmid=31727689