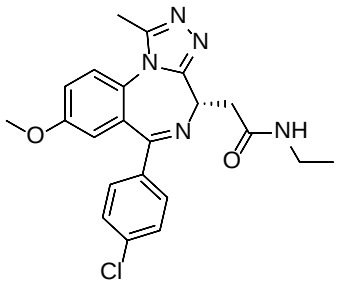
Product data sheet

MedKoo Cat#: 205967 Name: Molibresib CAS#: 1260907-17-2 Chemical Formula: $C_{22}H_{22}ClN_5O_2$ Exact Mass: 423.1462 Molecular Weight: 423.90	
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:
Molibresib, also known GSK525762A, I-BET-762 and GSK525762 , is a small molecule inhibitor of the BET (Bromodomain and Extra-Terminal) family of bromodomain-containing proteins with potential antineoplastic activity. Upon administration, the BET inhibitor GSK525762 binds to the acetylated lysine recognition motifs on the bromodomain of BET proteins, thereby preventing the interaction between the BET proteins and acetylated histone peptides. This disrupts chromatin remodeling and gene expression. Prevention of the expression of certain growth-promoting genes may lead to an inhibition of tumor cell growth.

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	53.57	126.37
Ethanol	63.70	150.27
Water	11.0	25.95

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.36 mL	11.80 mL	23.59 mL
5 mM	0.47 mL	2.36 mL	4.72 mL
10 mM	0.24 mL	1.18 mL	2.36 mL
50 mM	0.05 mL	0.24 mL	0.47 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. Ma S, Chen C, Zhu J, Li Y, Wang X, Song X, Cao J, Xu K. [In vitro study of BRD4 inhibitor GSK525762A against primary adult common B-cell acute lymphoblastic leukemia cells in vitro]. Zhonghua Xue Ye Xue Za Zhi. 2015 Jul;36(7):563-9. Chinese. doi: 10.3760/cma.j.issn.0253-2727.2015.07.007. PMID: 26304078; PMCID: PMC7342640.
2. Wang X, Qi N, Ma S, Yan ZL, Wu QY, Wang L, Chen C, Xu KL. [Effect of BRD4 Inhibitor GSK525762A on Proliferation and Apoptosis of SUP-B15 Cells In Vitro and Its Possible Mechanism]. Zhongguo Shi Yan Xue Ye Xue Za Zhi. 2016 Dec;24(6):1654-1658. Chinese. doi: 10.7534/j.issn.1009-2137.2016.06.008. PMID: 28024472.

In vivo study

1. Xie F, Huang M, Lin X, Liu C, Liu Z, Meng F, Wang C, Huang Q. The BET inhibitor I-BET762 inhibits pancreatic ductal adenocarcinoma cell proliferation and enhances the therapeutic effect of gemcitabine. Sci Rep. 2018 May 25;8(1):8102. doi: 10.1038/s41598-018-26496-0. PMID: 29802402; PMCID: PMC5970200.

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7. Bioactivity

Biological target: Molibresib (I-BET762; GSK525762) is a BET bromodomain inhibitor with IC50 of 32.5-42.5 nM.

In vitro activity

The effects of bromodomain-containing protein 4 (BRD4) inhibitor GSK525762A on the proliferation and apoptosis of primary common B-cell acute lymphoblastic leukemia (common B-ALL) cells were investigated. GSK525762A inhibited the proliferation of leukemia cells in a dose-dependent manner, the median value of IC50 was 256.25 (90.64-1 378.39)nmol/L. GSK525762A promoted cells apoptosis of B-ALL leukemia cells in a dose-dependent manner, the median apoptosis rates respectively were 45.17%(9.38%-70.91%), 66.02% (24.36%-96.34%) and 89.29% (39.29%-99.37%) after treated by 500, 1 000 and 2 500 nmol/L GSK525762A. GSK525762A had a similar effect on Ph^+ ALL and Ph^- B-ALL, but the effect of proliferation inhibition and apoptosis enhancement on Ph+ B-ALL was weaker than that on Ph^- B-ALL. Compared with vehicle control group, the levels of c-MYC, Bcl-2 and CDK6 transcripts in leukemic cells were reduced after treatment for 24 h and 48 h by 1 000 nmol/L GSK525762A, and there were no significant differences in the downregulation of c-MYC and CDK6 mRNA between Ph^+ and Ph^- B-ALL; however, the inhibitory effect on Bcl-2 transcription was weaker in Ph^+ B-ALL cells than that in Ph^- B-ALL cells. Moreover, c-MYC, Bcl-2 and CDK6 protein levels decreased in GSK525762A treated group.

Reference: Zhonghua Xue Ye Xue Za Zhi. 2015 Jul;36(7):563-9. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7342640/

In vivo activity

In Panc-1 tumor-bearing mice, GEM (Gemcitabine) and I-BET762 decreased the tumor weight and volume. The combination of GEM and I-BET762 triggered a remarkable decline in tumor weight and volume compared with that of either agent alone (Fig. 6A). TUNEL and Ki67 assays indicated that I-BET762 and GEM induced less apoptosis when used alone than did the combination treatment (Fig. 6B and C). In contrast, compared with the parental tumors, Bim-KD tumors showed noticeably weaker growth suppression in response to the combination therapy (Fig. 6A–C).

Reference: Sci Rep. 2018 May 25;8(1):8102. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5970200/