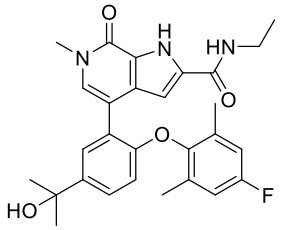
Product data sheet

MedKoo Cat#: 206981 Name: ABBV-744 CAS#: 2138861-99-9 Chemical Formula: $C_{28}H_{30}FN_3O_4$ Exact Mass: 491.222 Molecular Weight: 491.5634	
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:
ABBV-744 is a BDII-selective BET bromodomain inhibitor that is being investigated to treat AML and metastic castration-resistant prostate cancer.

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	33.57	68.29
DMSO:PBS (pH 7.2) (1:3)	0.25	0.51
DMF	30.0	61.03

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	**1 mg**	**5 mg**	**10 mg**
1 mM	2.03 mL	10.17 mL	20.34 mL
5 mM	0.41 mL	2.03 mL	4.07 mL
10 mM	0.20 mL	1.02 mL	2.03 mL
50 mM	0.04 mL	0.20 mL	0.41 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. Fakhar Z, Khan S, AlOmar SY, Alkhuriji A, Ahmad A. ABBV-744 as a potential inhibitor of SARS-CoV-2 main protease enzyme against COVID-19. Sci Rep. 2021 Jan 8;11(1):234. doi: 10.1038/s41598-020-79918-3. PMID: 33420186; PMCID: PMC7794216.
2. Sheppard GS, Wang L, Fidanze SD, Hasvold LA, Liu D, Pratt JK, Park CH, Longenecker K, Qiu W, Torrent M, Kovar PJ, Bui M, Faivre E, Huang X, Lin X, Wilcox D, Zhang L, Shen Y, Albert DH, Magoc TJ, Rajaraman G, Kati WM, McDaniel KF. Discovery of N-Ethyl-4-[2-(4-fluoro-2,6-dimethyl-phenoxy)-5-(1-hydroxy-1-methyl-ethyl)phenyl]-6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-2-carboxamide (ABBV-744), a BET Bromodomain Inhibitor with Selectivity for the Second Bromodomain. J Med Chem. 2020 May 28;63(10):5585-5623. doi: 10.1021/acs.jmedchem.0c00628. Epub 2020 May 7. PMID: 32324999.

In vivo study

1. Sheppard GS, Wang L, Fidanze SD, Hasvold LA, Liu D, Pratt JK, Park CH, Longenecker K, Qiu W, Torrent M, Kovar PJ, Bui M, Faivre E, Huang X, Lin X, Wilcox D, Zhang L, Shen Y, Albert DH, Magoc TJ, Rajaraman G, Kati WM, McDaniel KF. Discovery of N-Ethyl-4-[2-(4-fluoro-2,6-dimethyl-phenoxy)-5-(1-hydroxy-1-methyl-ethyl)phenyl]-6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-2-carboxamide (ABBV-744), a BET Bromodomain Inhibitor with Selectivity for the Second Bromodomain. J Med Chem. 2020 May 28;63(10):5585-5623. doi: 10.1021/acs.jmedchem.0c00628. Epub 2020 May 7. PMID: 32324999.

2. Faivre EJ, McDaniel KF, Albert DH, Mantena SR, Plotnik JP, Wilcox D, Zhang L, Bui MH, Sheppard GS, Wang L, Sehgal V, Lin X, Huang X, Lu X, Uziel T, Hessler P, Lam LT, Bellin RJ, Mehta G, Fidanze S, Pratt JK, Liu D, Hasvold LA, Sun C, Panchal SC, Nicolette JJ, Fossey SL, Park CH, Longenecker K, Bigelow L, Torrent M, Rosenberg SH, Kati WM, Shen Y. Selective inhibition of the BD2 bromodomain of BET proteins in prostate cancer. Nature. 2020 Feb;578(7794):306-310. doi: 10.1038/s41586-020-1930-8. Epub 2020 Jan 22. PMID: 31969702.

7. Bioactivity

Biological target:

ABBV-744 is a highly BDII-selective BET bromodomain inhibitor.

In vitro activity

Compound 46 (ABBV744) was tested for binding against the first and second bromodomains of BRD2, BRD3, and BRDt in the TR-FRET binding assay and displayed similarly potent and selective binding to that observed with BRD4 (Table 9). Whereas potent dual-bromodomain BET inhibitors such as 5 show potent antiproliferative effects against a wide range of cancer cell lines,46 shows substantially higher relative potency against cell lines derived from prostate cancer and AML, implying that BD1 inhibition is not required to inhibit proliferation in a subset of cancer indications.

Reference: J Med Chem. 2020 May 28;63(10):5585-5623. https://pubmed.ncbi.nlm.nih.gov/32324999/

In vivo activity

In a mouse xenograft model using LNCaP cells, treatment with 4.7 mg kg^{-1} ABBV-744 (1/16 of the maximum tolerated dose (MTD)) caused a delay in tumour growth that was equivalent to ABBV-075 treatment at the MTD dose of 1 mg kg^{-1} (Fig. 4a). Comparing efficacious exposure levels of ABBV-744 in LNCaP tumour-bearing mice (4.7 mg kg^{-1}; area under the curve, 1.1 μg h ml^{-1}) and MTD (75 mg kg^{-1}; area under the curve, 13.1 μg h ml^{-1}) demonstrated that ABBV-744 was able to produce significant antitumour activity at 1/12 of the highest tolerable exposure of ABBV-744 (Extended Data Fig. 8a). The activity exhibited by ABBV-744 at 1/16 of the MTD of ABBV-744 was superior to the activities achieved using JQ1 and iBET at their respective MTDs or, in the case of RVX-208, at the highest feasible dose in this model (Extended Data Fig. 8b, c). Similarly, ABBV-744 at 1/16 MTD also displayed equivalent or better antitumour activity compared with ABBV-075 at MTD in the enzalutamide-resistant MDA-PCa-2b xenograft model (Fig. 4b).

Reference: Nature. 2020 Feb;578(7794):306-310. https://pubmed.ncbi.nlm.nih.gov/31969702/

Note: The information listed here was extracted from literature. MedKoo has not independently retested and confirmed the accuracy of these methods. Customer should use it just for a reference only.