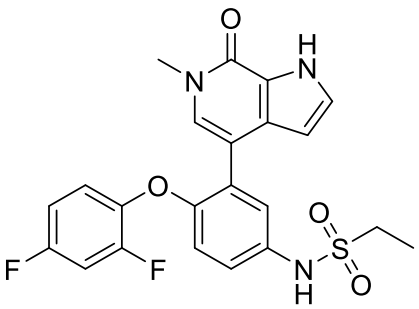
Product data sheet

MedKoo Cat#: 206520 Name: Mivebresib CAS#: 1445993-26-9 Chemical Formula: $C_{22}H_{19}F_2N_3O_4S$ Exact Mass: 459.1064 Molecular Weight: 459.4678	
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:

bresib, also known as ABBV-075, is a potent BET inhibitor (bromodomain (BRD)-containing proteind) with potential antineoplastic activity. Upon administration, the bromodomain inhibitor ABBV-075 binds to the acetyl-lysine binding site in the BRD of certain BRD-containing protein(s), thereby preventing the interaction between those proteins and acetylated histones. This disrupts chromatin remodeling, prevents the expression of certain growth-promoting genes, and leads to an inhibition of cell growth in susceptible tumors.

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	60.0	130.59

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.18 mL	10.88 mL	21.76 mL
5 mM	0.44 mL	2.18 mL	4.35 mL
10 mM	0.22 mL	1.09 mL	2.18 mL
50 mM	0.04 mL	0.22 mL	0.44 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. Bui MH, Lin X, Albert DH, Li L, Lam LT, Faivre EJ, Warder SE, Huang X, Wilcox D, Donawho CK, Sheppard GS, Wang L, Fidanze S, Pratt JK, Liu D, Hasvold L, Uziel T, Lu X, Kohlhapp F, Fang G, Elmore SW, Rosenberg SH, McDaniel KF, Kati WM, Shen Y. Preclinical Characterization of BET Family Bromodomain Inhibitor ABBV-075 Suggests Combination Therapeutic Strategies. Cancer Res. 2017 Jun 1;77(11):2976-2989. doi: 10.1158/0008-5472.CAN-16-1793. Epub 2017 Apr 17. PMID: 28416490.
2. Faivre EJ, Wilcox D, Lin X, Hessler P, Torrent M, He W, Uziel T, Albert DH, McDaniel K, Kati W, Shen Y. Exploitation of Castration-Resistant Prostate Cancer Transcription Factor Dependencies by the Novel BET Inhibitor ABBV-075. Mol Cancer Res. 2017 Jan;15(1):35-44. doi: 10.1158/1541-7786.MCR-16-0221. Epub 2016 Oct 5. PMID: 27707886.

In vivo study

1 Lin X, Huang X, Uziel T, Hessler P, Albert DH, Roberts-Rapp LA, McDaniel KF, Kati WM, Shen Y. HEXIM1 as a Robust Pharmacodynamic Marker for Monitoring Target Engagement of BET Family Bromodomain Inhibitors in Tumors and Surrogate Tissues. Mol Cancer Ther. 2017 Feb;16(2):388-396. doi: 10.1158/1535-7163.MCT-16-0475. Epub 2016 Nov 30. PMID: 27903752.

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2. Faivre EJ, Wilcox D, Lin X, Hessler P, Torrent M, He W, Uziel T, Albert DH, McDaniel K, Kati W, Shen Y. Exploitation of Castration-Resistant Prostate Cancer Transcription Factor Dependencies by the Novel BET Inhibitor ABBV-075. Mol Cancer Res. 2017 Jan;15(1):35-44. doi: 10.1158/1541-7786.MCR-16-0221. Epub 2016 Oct 5. PMID: 27707886.

7. Bioactivity

Biological target:

Mivebresib (ABBV-075) is a potent bromodomain and extraterminal domain (BET) bromodomain inhibitor that binds to BRD4 with a Ki of 1.5 nM

In vitro activity

To determine whether the noted apoptotic response to ABBV-075 can be recapitulated in primary patient-derived samples, we focused on AML, where patient-derived cells are readily available. Similar to what was observed in AML cell lines, patient-derived AML cells were also highly sensitive to ABBV-075 (IC50 < 0.1 μmol/L), and eight out of nine patient samples exhibited >30% apoptosis (Fig. 3D). It is noteworthy that many patient-derived AML cells appeared to be resistant to cytarabine, a first-line therapy for AML (e.g., pts 3027, 3235, 3012, and 3085, all with IC50s ⩾ 3 μ mol/L), but remained responsive to ABBV-075, suggesting that ABBV-075 may provide benefit in the resistant/refractory setting of AML. As controls, no high degrees of apoptosis was observed in PBMCs from healthy donors, and ABBV-075 or MS417 did not trigger apoptosis in CD34+ cells from cord blood (Supplementary Fig. S3). ABBV-075 also downregulated both BCL-XL and BCL-2 in SKM-1 cells and downregulated BCL-XL in AML-2 and OCI-Ly3 cells (Supplementary Fig. S5), indicating that modulating the intrinsic apoptotic machinery may be a common mechanism underlying apoptosis induced by BET inhibitors.

Reference: Cancer Res. 2017 Jun 1;77(11):2976-2989. https://pubmed.ncbi.nlm.nih.gov/28416490/

In vivo activity

To identify potential pharmacodynamic markers for BET inhibitors in skin, we determined transcriptional alterations in skin samples from ABBV-075–treated mice. Hexim1 and Lrg1 were significantly up- or downregulated, respectively, in skin samples from ABBV-075–treated mice (Supplementary Fig. S4). Similar to what was observed in tumor and blood, Hexim1 was upregulated by ABBV-075 at 6 hours and returned to baseline at 24 hours (Fig. 5A). ABBV-075 treatment caused significant upregulation of Hexim1 but not the housekeeping genes B2m and Hprt1 in these FFPE samples (Fig. 5B). The response of Hexim1 to ABBV-075 in FFPE skin samples was further verified using the RNA ISH method. As shown in Fig. 5C, ABBV-075 treatment resulted in a significant increase of Hexim1 expression in the skin section.

Reference: Mol Cancer Ther. 2017 Feb;16(2):388-396. https://pubmed.ncbi.nlm.nih.gov/27903752/

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.