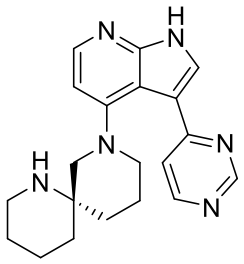
Product data sheet

MedKoo Cat#: 563970 Name: BDP9066 CAS#: 2226507-04-4 Chemical Formula: $C_{20}H_{24}N_6$ Exact Mass: 348.2062 Molecular Weight: 348.45	
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:

BDP9066 is a potent and selective MRCK inhibitor with an IC50 of 64 nM for MRCKβ in SCC12 cells, Ki values of 0.0136 nM . BDP9066 reduced substrate phosphorylation, leading to morphological changes in cancer cells along with inhibition of their motility and invasive character. In over 750 human cancer cell lines tested, BDP9066 displayed consistent anti-proliferative effects with greatest activity in hematological cancer cells. BDP-9066 prevented radiation-driven increases in motility both in vitro and in a clinically relevant orthotopic xenograft model of GBM. Crucially, treatment with BDP-9066 in combination with RT significantly increased survival in this model and markedly reduced infiltration of the contralateral cerebral hemisphere.

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	10.0	28.7

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.87 mL	14.35 mL	28.70 mL
5 mM	0.57 mL	2.87 mL	5.74 mL
10 mM	0.29 mL	1.43 mL	2.87 mL
50 mM	0.06 mL	0.29 mL	0.57 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. Unbekandt M, Belshaw S, Bower J, Clarke M, Cordes J, Crighton D, Croft DR, Drysdale MJ, Garnett MJ, Gill K, Gray C, Greenhalgh DA, Hall JAM, Konczal J, Lilla S, McArthur D, McConnell P, McDonald L, McGarry L, McKinnon H, McMenemy C, Mezna M, Morrice NA, Munro J, Naylor G, Rath N, Schüttelkopf AW, Sime M, Olson MF. Discovery of Potent and Selective MRCK Inhibitors with Therapeutic Effect on Skin Cancer. Cancer Res. 2018 Apr 15;78(8):2096-2114. doi: 10.1158/0008-5472.CAN-17-2870. Epub 2018 Jan 30. PMID: 29382705; PMCID: PMC5901721.

2. Birch JL, Strathdee K, Gilmour L, Vallatos A, McDonald L, Kouzeli A, Vasan R, Qaisi AH, Croft DR, Crighton D, Gill K, Gray CH, Konczal J, Mezna M, McArthur D, Schüttelkopf AW, McConnell P, Sime M, Holmes WM, Bower J, McKinnon HJ, Drysdale M, Olson MF, Chalmers AJ. A Novel Small-Molecule Inhibitor of MRCK Prevents Radiation-Driven Invasion in Glioblastoma. Cancer Res. 2018 Nov 15;78(22):6509-6522. doi: 10.1158/0008-5472.CAN-18-1697. Epub 2018 Oct 2. PMID: 30279244.

In vivo study

1. Unbekandt M, Belshaw S, Bower J, Clarke M, Cordes J, Crighton D, Croft DR, Drysdale MJ, Garnett MJ, Gill K, Gray C, Greenhalgh DA, Hall JAM, Konczal J, Lilla S, McArthur D, McConnell P, McDonald L, McGarry L, McKinnon H, McMenemy C, Mezna M, Morrice NA, Munro J, Naylor G, Rath N, Schüttelkopf AW, Sime M, Olson MF. Discovery of Potent and Selective MRCK

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Inhibitors with Therapeutic Effect on Skin Cancer. Cancer Res. 2018 Apr 15;78(8):2096-2114. doi: 10.1158/0008-5472.CAN-17-2870. Epub 2018 Jan 30. PMID: 29382705; PMCID: PMC5901721.
2. Birch JL, Strathdee K, Gilmour L, Vallatos A, McDonald L, Kouzeli A, Vasan R, Qaisi AH, Croft DR, Crighton D, Gill K, Gray CH, Konczal J, Mezna M, McArthur D, Schüttelkopf AW, McConnell P, Sime M, Holmes WM, Bower J, McKinnon HJ, Drysdale M, Olson MF, Chalmers AJ. A Novel Small-Molecule Inhibitor of MRCK Prevents Radiation-Driven Invasion in Glioblastoma. Cancer Res. 2018 Nov 15;78(22):6509-6522. doi: 10.1158/0008-5472.CAN-18-1697. Epub 2018 Oct 2. PMID: 30279244.

7. Bioactivity

Biological target:

BDP9066 is a potent and selective myotonic dystrophy-related Cdc42-binding kinase MRCK inhibitor with an IC50 of 64 nM for MRCKβ in SCC12 cells, Ki values of 0.0136 nM and 0.0233 nM for MRCKα/β in house determinations, respectively.

In vitro activity

To investigate the effect of BDP9066 on pMLC2 in SCC12 cells, which express MRCK but no detectable DMPK (Supplemental Figure 5), varying BDP9066 concentrations incubated with cells for 2 hours led to dose-dependent inhibition of MLC2 phosphorylation (Figure 6A, left) with an EC50 = 64 nM (Figure 6A, right), corresponding to a 5-fold increase in cellular potency relative to BDP5290 (19). SCC12 cell viability following 24 hour treatment was unaffected by all BDP9066 concentrations up to 0.5 µM (Figure 6B), despite maximal pMLC2 inhibition at this concentration (Figure 6A), with a 25% decrease in viability at 1 µM (Figure 6B). These results indicate that BDP9066 is relatively non-toxic at concentrations that profoundly inhibit substrate phosphorylation. Treatment of SCC12 cells with non-toxic 0.5 µM BDP9066 led to changes in cell morphology, with reduced proportions of regularly (rounded, few protrusions) shaped cells (Figure 6C, green cells), and increased irregularly (greater spreading, increased protrusions) shaped cells (Figure 6C, blue cells) as determined by high content imaging. The collective effect of these BDP9066 induced morphological alterations resulted in increased 2D cell area and decreased roundness (Figure 6E, right panels). In over 750 human cancer cell lines tested, BDP8900 and BDP9066 displayed consistent anti-proliferative effects with greatest activity in hematological cancer cells

Reference: Cancer Res. 2018 Apr 15; 78(8): 2096–2114. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5901721/

In vivo activity

BDP9066 was evaluated for in vivo pharmacological proof-of-concept as an SCC chemotherapeutic agent. Topical application of 25 µg BDP9066 on FVB mouse skin twice per day for 2 days led to 26 µM mean BDP9066 concentration in skin, but only 0.04 µM in blood (Figure 7A). BDP9066 application led to significantly reduced epidermal MRCKα pS1003 positive staining (Figure 7B). To determine how repeated dosing would affect BDP9066 accumulation and distribution, skin and blood concentrations were determined after 10 µg was administered once, or 25 µg was repeated over 4 days (Figure 7C). Although relative to the single 10 µg dose, repeated 25 µg doses did result in 2.8 fold higher concentrations in skin (Figure 7C, left panel), and 4 fold higher concentrations in blood (Figure 7C, right panel), these differences were less than the 10 fold difference in total BDP9066 administered, indicating that compound accumulation was less than additive. These results indicated that it was possible to achieve sustainable BDP9066 levels in mouse skin by repeated topical application, which were sufficient to induce phenotypic responses in squamous cell carcinoma cells in vitro, without significant compound accumulation following sequential administration.

Reference: Cancer Res. 2018 Apr 15; 78(8): 2096–2114. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5901721/