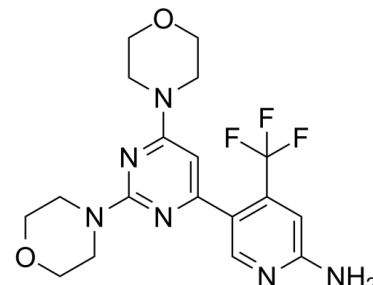


## Data Sheet

<b>Product Name:</b>	Buparlisib
<b>Cat. No.:</b>	CS-0089
<b>CAS No.:</b>	944396-07-0
<b>Molecular Formula:</b>	C <sub>18</sub> H <sub>21</sub> F <sub>3</sub> N <sub>6</sub> O <sub>2</sub>
<b>Molecular Weight:</b>	410.39
<b>Target:</b>	Apoptosis; PI3K
<b>Pathway:</b>	Apoptosis; PI3K/Akt/mTOR
<b>Solubility:</b>	DMSO : ≥ 100 mg/mL (243.67 mM)



### BIOLOGICAL ACTIVITY:

Buparlisib (NVP-BKM120) is a pan-class I **PI3K** inhibitor, with **IC<sub>50</sub>s** of 52, 166, 116 and 262 nM for **p110α**, **p110β**, **p110δ** and **p110γ**, respectively. **IC<sub>50</sub> & Target:** IC<sub>50</sub>: 52 nM (p110α), 166 nM (p110β), 116 nM (p110δ), 262 nM (p110γ)<sup>[1]</sup> **In Vitro:** Buparlisib (NVP-BKM120) exhibits 50-300 nM activity for class I PI3K's, including the most common p110α mutants. Additionally, NVP-BKM120 exhibits lower potency against class III and class IV PI3K's, where 2, 5, >5, and >25 μM biochemical activity is observed for inhibition of VPS34, mTOR, DNAPK, and PI4K, respectively<sup>[1]</sup>. Buparlisib (NVP-BKM120) induces multiple myeloma (MM) cell apoptosis in both dose- and time-dependent manners. Buparlisib (NVP-BKM120) at concentrations ≥10 μM induces significant apoptosis in all tested MM cell lines at 24 h (P<0.05, compares with control). Therefore, 10 μM Buparlisib (NVP-BKM120) and 24-h treatment are chosen in the following experiments if not stated otherwise. Buparlisib (NVP-BKM120) treatment results in a dose-dependent growth inhibition in all tested MM cell lines. Buparlisib (NVP-BKM120) **IC<sub>50</sub>** varies among tested MM cells. At 24 h treatment, **IC<sub>50</sub>** for ARP-1, ARK, and MM.1R is between 1 and 10 μM, while **IC<sub>50</sub>** for MM.1S is <1 μM, and **IC<sub>50</sub>** for U266 is between 10 and 100 μM. In summary, NVP-BKM120 treatment results in MM cell growth inhibition and apoptosis in dose- and time-dependent manners<sup>[2]</sup>. **In Vivo:** In A2780 xenograft tumors, oral dosing of Buparlisib (NVP-BKM120) at 3, 10, 30, 60, and 100 mg/kg results in a dose dependent modulation of pAKT<sup>Ser473</sup>. Partial inhibition of pAKT<sup>Ser473</sup> is observed at 3 and 10 mg/kg, and near complete inhibition is observed at doses of 30, 60, or 100 mg/kg, respectively. Inhibition of pAKT (normalized to total AKT) tracked well with both plasma and tumor drug exposure<sup>[1]</sup>. Mice receiving Buparlisib (NVP-BKM120) (5 μM per kg per day for 15 days) treatment has significantly smaller tumor burdens as compared with control mice, which are measured as tumor volume (P<0.05) and level of circulating human kappa chain (P<0.05). In addition, NVP-BKM120 treatment significantly prolongs the survival of tumor-bearing mice (P<0.05)<sup>[2]</sup>.

### PROTOCOL (Extracted from published papers and Only for reference)

**Cell Assay:** NVP-BKM120 is dissolved in DMSO and stored, and then diluted with appropriate media before use<sup>[1]</sup>.<sup>[1]</sup> A2780 cells are cultured in DMEM supplemented with 10% FBS, L-glutamine, sodium pyruvate, and antibiotics. Cells are plated in the same medium at a density of 1000 cells per well, 100 μL per well into black-walled-clear-bottom plates and incubated for 3-5 hours. Buparlisib (NVP-BKM120) supplied in DMSO (20 mM) are diluted further into DMSO (7.5 μL of 20 mM Buparlisib (NVP-BKM120) in 22.5 μL DMSO. Mix well, transfer 10 μL to 20 μL DMSO, repeat until 9 concentrations have been made). The diluted Buparlisib (NVP-BKM120) solution (2 μL), is then added to cell medium (500 μL) cell medium. Equal volumes of this solution (100 μL) are added to the cells in 96 well plates and incubated at 37°C for 3 days and developed using Cell Titer Glo. Inhibition of cell proliferation is determined by luminescence read using Trilux<sup>[1]</sup>. **Animal Administration:** NVP-BKM120 is dissolved in DMSO/PBS (Mice)<sup>[2]</sup>.<sup>[2]</sup> Mice<sup>[2]</sup> Six- to eight-week-old female severe combined immunodeficiency (SCID) mice are used. SCID mice are subcutaneously inoculated in the right flank with 1 million ARP-1 or MM.1S cells suspended in 50 μL phosphate-buffered saline (PBS). After palpable tumor developed (tumor diameter ≥5 mm), mice are treated with intraperitoneal injection of DMSO/PBS or Buparlisib (NVP-BKM120) (5 μM

per kg per day) for 15 days. Tumor sizes are measured every 5 days, and blood samples are collected at the same period. Tumor burdens are evaluated by measuring tumor size and detecting circulating human kappa chain or lambda chain.

### References:

- [1]. Burger MT, et al. Identification of NVP-BKM120 as a Potent, Selective, Orally Bioavailable Class I PI3 Kinase Inhibitor for Treating Cancer. ACS Med Chem Lett. 2011 Aug 26;2(10):774-9.
- [2]. Zheng Y, et al. Novel phosphatidylinositol 3-kinase inhibitor NVP-BKM120 induces apoptosis in myeloma cells and shows synergistic anti-myeloma activity. J Mol Med (Berl). 2012 Jun;90(6):695-706.
- [3]. Ni J, et al. Combination inhibition of PI3K and mTORC1 yields durable remissions in mice bearing orthotopic patient-derived xenografts of HER2-positive breast cancer brain metastases. Nat Med. 2016 Jul;22(7):723-6.
- [4]. Liu H, et al. Identifying and Targeting Sporadic Oncogenic Genetic Aberrations in Mouse Models of Triple Negative Breast Cancer. Cancer Discov. 2018 Mar;8(3):354-369.

### CAIndexNames:

2-Pyridinamine, 5-(2,6-di-4-morpholinyl-4-pyrimidinyl)-4-(trifluoromethyl)-

### SMILES:

FC(F)(C1=C(C2=CC(N3CCOCC3)=NC(N4CCOCC4)=N2)C=NC(N)=C1)F

**Caution: Product has not been fully validated for medical applications. For research use only.**

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