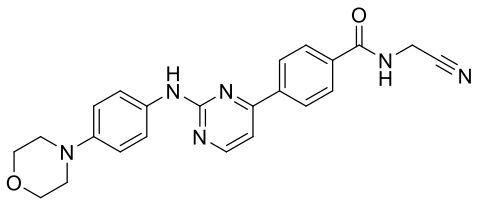
Product data sheet

MedKoo Cat#: 200786 Name: Momelotinib free base CAS#: 1056634-68-4 (free base) Chemical Formula: $C_{23}H_{22}N_6O_2$ Exact Mass: 414.18042 Molecular Weight: 414.46	
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:
Momelotinib, also known as CYT387, is an inhibitor of Janus kinases JAK1 and JAK2, acting as an ATP competitor with IC50 values of 11 and 18 nM, respectively. The inhibitor is significantly less active towards other kinases, including JAK3 (IC50 = 0.16 μM). As of 2011, CYT387 is being developed as a drug for myelofibrosis and currently undergoes Phase I/II clinical trials. Additional potential treatment indications for CYT387 include other myeloproliferative neoplasms, cancer (solid and liquid tumors) and inflammatory conditions.

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	16.0	38.6

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.41 mL	12.06 mL	24.13 mL
5 mM	0.48 mL	2.41 mL	4.83 mL
10 mM	0.24 mL	1.21 mL	2.41 mL
50 mM	0.05 mL	0.24 mL	0.48 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. Hofland T, de Weerdt I, Ter Burg H, de Boer R, Tannheimer S, Tonino SH, Kater AP, Eldering E. Dissection of the Effects of JAK and BTK Inhibitors on the Functionality of Healthy and Malignant Lymphocytes. J Immunol. 2019 Oct 15;203(8):2100-2109. doi: 10.4049/jimmunol.1900321. Epub 2019 Sep 11. PMID: 31511358.
2. Giordano G, Parcesepe P, D'Andrea MR, Coppola L, Di Raimo T, Remo A, Manfrin E, Fiorini C, Scarpa A, Amoreo CA, Conciatori F, Milella M, Caruso FP, Cerulo L, Porras A, Pancione M. JAK/Stat5-mediated subtype-specific lymphocyte antigen 6 complex, locus G6D (LY6G6D) expression drives mismatch repair proficient colorectal cancer. J Exp Clin Cancer Res. 2019 Jan 22;38(1):28. doi: 10.1186/s13046-018-1019-5. PMID: 30670049; PMCID: PMC6343337.

In vivo study

1. Schwartz BE, Rajagopal V, Smith C, Cohick E, Whissell G, Gamboa M, Pai R, Sigova A, Grossman I, Bumcrot D, Sasidharan K, Romeo S, Sehgal A, Pingitore P. Discovery and Targeting of the Signaling Controls of PNPLA3 to Effectively Reduce Transcription, Expression, and Function in Pre-Clinical NAFLD/NASH Settings. Cells. 2020 Oct 7;9(10):2247. doi: 10.3390/cells9102247. PMID: 33036387; PMCID: PMC7600576.

2. Yogev O, Almeida GS, Barker KT, George SL, Kwok C, Campbell J, Zarowiecki M, Kleftogiannis D, Smith LM, Hallsworth A, Berry P, Möcklinghoff T, Webber HT, Danielson LS, Buttery B, Calton EA, da Costa BM, Poon E, Jamin Y, Lise S, Veal GJ, Sebire N, Robinson SP, Anderson J, Chesler L. In Vivo Modeling of Chemoresistant Neuroblastoma Provides New Insights into Chemorefractory Disease and Metastasis. Cancer Res. 2019 Oct 15;79(20):5382-5393. doi: 10.1158/0008-5472.CAN-18-2759. Epub 2019 Aug 12. PMID: 31405846.

7. Bioactivity

Biological target:

Momelotinib (CYT387) is an ATP-competitive inhibitor of JAK1/JAK2 with IC50a of 11 nM and 18 nM, respectively.

In vitro activity

Momelotinib showed the strongest inhibition of proliferation of CLL cells. JAK, BTK, and PI3Kδ inhibitors did not induce cell death in CLL cells (Fig. 1B). As expected, JAK inhibitors were not able to reduce resistance to venetoclax and fludarabine after coculture of CLL cells on CD40L-fibroblasts because CD40 signaling is not mediated by JAKs (Fig. 1C). Treatment with both JAK inhibitors but not BTK or PI3Kδ inhibitors led to a reduction in p-STAT6 induced by IL-4 (Fig. 1D). Surprisingly, momelotinib treatment also led to a reduction in IgM-induced p-Akt and p-S6 levels, although not as strong as both BTK inhibitors or idelalisib. Ruxolitinib did not affect BCR signaling to Akt or S6, demonstrating different modes of action of these JAK inhibitors. These results demonstrate that JAK inhibitors are not cytotoxic for CLL cells by themselves, but are able to influence signaling of prosurvival cytokines like IL-4 and IL-21 that induce proliferation and IgM expression, and momelotinib was able to partially block BCR signaling.

Reference: J Immunol. 2019 Oct 15;203(8):2100-2109. https://www.jimmunol.org/content/203/8/2100.long

In vivo activity

In order to more precisely establish the in vivo efficacy of CYT387 in a treatment resistant setting, this study used subcutaneous allografts of cells excised from Th-MYCN or Th-MYCNCPM32 tumors in 129 × 1/SvJ (immunocompetent, strain-matched) mice. As expected, Th-MYCNCPM32 allografts were refractory to CPM treatment with a 160% mean growth at 7 days after treatment (Fig. 6A), while Th-MYCN allografts underwent complete regression at a dose of 32 mg/kg CPM. In contrast, treatment with 32 mg/kg CPM (once per week) together with 50 mg/kg CYT387 (administered 5 days on 2 days off) significantly reduced tumor volume at day 5 in the treatment resistant Th-MYCNCPM32 allografts from a mean of 152% ± 21% to 82% ± 20% (Fig. 6B). Furthermore, this study observed an increase in survival of 6 days (representing of 37%) from a median of 16 days to a median of 22 days (Fig. 6C). These results establish that the acquisition of chemoresistance following treatment with CPM is transplantable, therefore cell-intrinsic, and that in vivo treatment with the JAK STAT inhibitor CYT387 reduces tumor growth and extends survival in CPM chemoresistant neuroblastoma.

Reference: Cancer Res. 2019 Oct 15;79(20):5382-5393. https://cancerres.aacrjournals.org/content/79/20/5382.long

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.