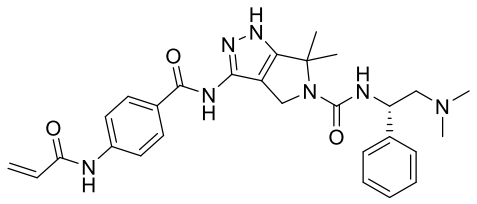
Product data sheet

MedKoo Cat#: 558735 Name: YKL-5-124 CAS#: 1957203-01-8 (free base) Chemical Formula: $C_{28}H_{33}N_7O_3$ Exact Mass: 515.2645 Molecular Weight: 515.62	
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:
YKL-5-124 is a potent and highly selective covalent CDK7 inhibitor which causes arrest at the G1/S transition and inhibition of E2F-driven gene expression. This results in no change to RNA polymerase II C-terminal domain phosphorylation.

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

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	1.94 mL	9.70 mL	19.39 mL
5 mM	0.39 mL	1.94 mL	3.88 mL
10 mM	0.19 mL	0.97 mL	1.94 mL
50 mM	0.04 mL	0.19 mL	0.39 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

Olson CM, Liang Y, Leggett A, Park WD, Li L, Mills CE, Elsarrag SZ, Ficarro SB, Zhang T, Düster R, Geyer M, Sim T, Marto JA, Sorger PK, Westover KD, Lin CY, Kwiatkowski N, Gray NS. Development of a Selective CDK7 Covalent Inhibitor Reveals Predominant Cell-Cycle Phenotype. Cell Chem Biol. 2019 Jun 20;26(6):792-803.e10. doi: 10.1016/j.chembiol.2019.02.012. Epub 2019 Mar 21. PMID: 30905681; PMCID: PMC6588464.

In vivo study

Zhang H, Christensen CL, Dries R, Oser MG, Deng J, Diskin B, Li F, Pan Y, Zhang X, Yin Y, Papadopoulos E, Pyon V, Thakurdin C, Kwiatkowski N, Jani K, Rabin AR, Castro DM, Chen T, Silver H, Huang Q, Bulatovic M, Dowling CM, Sundberg B, Leggett A, Ranieri M, Han H, Li S, Yang A, Labbe KE, Almonte C, Sviderskiy VO, Quinn M, Donaghue J, Wang ES, Zhang T, He Z, Velcheti V, Hammerman PS, Freeman GJ, Bonneau R, Kaelin WG Jr, Sutherland KD, Kersbergen A, Aguirre AJ, Yuan GC, Rothenberg E, Miller G, Gray NS, Wong KK. CDK7 Inhibition Potentiates Genome Instability Triggering Anti-tumor Immunity in Small Cell Lung Cancer. Cancer Cell. 2020 Jan 13;37(1):37-54.e9. doi: 10.1016/j.ccell.2019.11.003. Epub 2019 Dec 26. PMID: 31883968; PMCID: PMC7277075.

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7. Bioactivity

Biological target:

CDK7 inhibitor

In vitro activity

The discovery of a highly selective covalent CDK7 inhibitor. YKL-5-124 causes arrest at the G1/S transition and inhibition of E2F-driven gene expression; these effects are rescued by a CDK7 mutant unable to covalently engage YKL-5-124, demonstrating on-target specificity. Unlike THZ1, treatment with YKL-5-124 resulted in no change to RNA polymerase II C-terminal domain phosphorylation; however, inhibition could be reconstituted by combining YKL-5-124 and THZ531, a selective CDK12/13 inhibitor, revealing potential redundancies in CDK control of gene transcription. These findings highlight the importance of CDK7/12/13 polypharmacology for anti-cancer activity of THZ1 and posit that selective inhibition of CDK7 may be useful for treatment of cancers marked by E2F misregulation.

Reference: Olson CM, Liang Y, Leggett A, Park WD, Li L, Mills CE, Elsarrag SZ, Ficarro SB, Zhang T, Düster R, Geyer M, Sim T, Marto JA, Sorger PK, Westover KD, Lin CY, Kwiatkowski N, Gray NS. Development of a Selective CDK7 Covalent Inhibitor Reveals Predominant Cell-Cycle Phenotype. Cell Chem Biol. 2019 Jun 20;26(6):792-803.e10. doi: 10.1016/j.chembiol.2019.02.012. Epub 2019 Mar 21. PMID: 30905681; PMCID: PMC6588464.

In vivo activity

Cyclin-dependent kinase 7 (CDK7) is a central regulator of the cell cycle and gene transcription. However, little is known about its impact on genomic instability and cancer immunity. Using a selective CDK7 inhibitor, YKL-5-124, it was demonstrated that CDK7 inhibition predominately disrupts cell-cycle progression and induces DNA replication stress and genome instability in small cell lung cancer (SCLC) while simultaneously triggering immune-response signaling. These tumor-intrinsic events provoke a robust immune surveillance program elicited by T cells, which is further enhanced by the addition of immune-checkpoint blockade. Combining YKL-5-124 with anti-PD-1 offers significant survival benefit in multiple highly aggressive murine models of SCLC, providing a rationale for new combination regimens consisting of CDK7 inhibitors and immunotherapies.

Reference: Zhang H, Christensen CL, Dries R, Oser MG, Deng J, Diskin B, Li F, Pan Y, Zhang X, Yin Y, Papadopoulos E, Pyon V, Thakurdin C, Kwiatkowski N, Jani K, Rabin AR, Castro DM, Chen T, Silver H, Huang Q, Bulatovic M, Dowling CM, Sundberg B, Leggett A, Ranieri M, Han H, Li S, Yang A, Labbe KE, Almonte C, Sviderskiy VO, Quinn M, Donaghue J, Wang ES, Zhang T, He Z, Velcheti V, Hammerman PS, Freeman GJ, Bonneau R, Kaelin WG Jr, Sutherland KD, Kersbergen A, Aguirre AJ, Yuan GC, Rothenberg E, Miller G, Gray NS, Wong KK. CDK7 Inhibition Potentiates Genome Instability Triggering Anti-tumor Immunity in Small Cell Lung Cancer. Cancer Cell. 2020 Jan 13;37(1):37-54.e9. doi: 10.1016/j.ccell.2019.11.003. Epub 2019 Dec 26. PMID: 31883968; PMCID: PMC7277075.