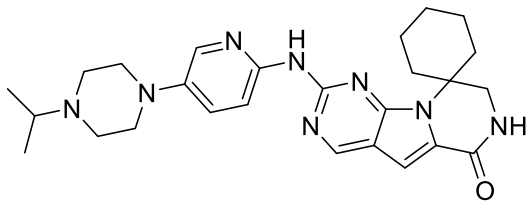
Product data sheet

MedKoo Cat#: 206842 Name: Lerociclib CAS#: 1628256-23-4 (free base) Chemical Formula: $C_{26}H_{34}N_8O$ Exact Mass: 474.2856 Molecular Weight: 474.613	
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:

Lerociclib , also known as G1T38, is an oral, potent and selective CDK4/6 inhibitor for the treatment of Rb competent tumors. Biochemical profiling demonstrates G1T38 is a competitive, nanomolar inhibitor of CDK4/6 with highly selectivity for CDK4-cyclin D1 and CDK6-cyclin D3. G1T38 exhibits a low EC50 (<100 nM) in Rb competent cell lines compared to >3 μM in Rb null cells. In vivo, daily oral treatment with G1T38 causes significant, durable growth inhibition of tumors in a HER2/neu GEMM and in MCF7 xenograft breast cancer models.

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	1.00	2.11

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	**1 mg**	**5 mg**	**10 mg**
1 mM	2.11 mL	10.53 mL	21.07 mL
5 mM	0.42 mL	2.11 mL	4.21 mL
10 mM	0.21 mL	1.05 mL	2.11 mL
50 mM	0.04 mL	0.21 mL	0.42 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. Andreano KJ, Wardell SE, Baker JG, Desautels TK, Baldi R, Chao CA, Heetderks KA, Bae Y, Xiong R, Tonetti DA, Gutgesell LM, Zhao J, Sorrentino JA, Thompson DA, Bisi JE, Strum JC, Thatcher GRJ, Norris JD. G1T48, an oral selective estrogen receptor degrader, and the CDK4/6 inhibitor lerociclib inhibit tumor growth in animal models of endocrine-resistant breast cancer. Breast Cancer Res Treat. 2020 Apr;180(3):635-646. doi: 10.1007/s10549-020-05575-9. Epub 2020 Mar 4. PMID: 32130619; PMCID: PMC7103015.

In vivo study

1. Andreano KJ, Wardell SE, Baker JG, Desautels TK, Baldi R, Chao CA, Heetderks KA, Bae Y, Xiong R, Tonetti DA, Gutgesell LM, Zhao J, Sorrentino JA, Thompson DA, Bisi JE, Strum JC, Thatcher GRJ, Norris JD. G1T48, an oral selective estrogen receptor degrader, and the CDK4/6 inhibitor lerociclib inhibit tumor growth in animal models of endocrine-resistant breast cancer. Breast Cancer Res Treat. 2020 Apr;180(3):635-646. doi: 10.1007/s10549-020-05575-9. Epub 2020 Mar 4. PMID: 32130619; PMCID: PMC7103015.

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7. Bioactivity

Biological target:

Lerociclib (G1T38) is a potent and selective inhibitor of CDK4/6, with IC50s of 1 nM, 2 nM for CDK4/CyclinD1 and CDK6/CyclinD3, respectively.

In vitro activity

To examine the therapeutic potential of G1T48, cell proliferation assays were performed using multiple ER-positive breast cancer cell lines (Fig. 3). G1T48 significantly inhibited estrogen-mediated growth of MCF7 cells demonstrating approximately threefold higher potency when compared to fulvestrant (Fig. 3a, Online Resource 5). Additionally, G1T48 and benchmark antiestrogens also inhibited the estrogen-mediated growth of ER-positive BT474 and ZR-75-1 breast cancer cells, while no growth inhibition was observed in ER-negative MDA-MB-436 breast cancer cells (Fig. 3, Online Resource 5). Furthermore, G1T48 does not impact apoptosis in MCF7 breast cancer cells. Thus, G1T48 selectively inhibits the growth of ER-positive, but not ER-negative, breast cancer cells.

Reference: Breast Cancer Res Treat. 2020; 180(3): 635–646. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7103015/

In vivo activity

The therapeutic potential of G1T48 in ER-positive primary and endocrine refractory breast cancer models was evaluated in vivo. G1T48 was first assessed, as a monotherapy or in combination with the CDK4/6 inhibitor lerociclib, for its impact on the growth of naïve MCF7 xenograft tumors (Fig. 5a). Ovariectomized estrogen-treated female nu/nu mice bearing MCF7 xenograft tumors were randomized to treatment with vehicle, lerociclib (50 mg/kg), and/or G1T48 (30 or 100 mg/kg). G1T48 treatment demonstrated dose-dependent repression of tumor growth. Next, ovariectomized tamoxifen-treated mice bearing TamR xenografts were randomized to treatment with lerociclib (50 mg/kg or 100 mg/kg), G1T48 (30 mg/kg or 100 mg/kg), fulvestrant (200 mg/kg), or CDK4/6 inhibitor palbociclib (100 mg/kg) as monotherapies or a combination of lerociclib (50 mg/kg) and G1T48 (30 or 100 mg/kg). G1T48 was found to demonstrate dose-dependent inhibition of TamR tumor growth (Fig. 5c) albeit with less efficacy than fulvestrant. Interestingly, G1T48 treatment resulted in greater downregulation of intratumoral ER levels than fulvestrant despite less efficient inhibition of tumor growth.

Reference: Breast Cancer Res Treat. 2020; 180(3): 635–646. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7103015/

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.