Product Data Sheet

Product Name:	Rapalink-1
Cat. No.:	GC11607

Chemical Properties

Cas. No.	1887095-82-0		
SMILES	O=C(NCCCCN1N=C(C2=CC=C(OC(N)=N3)C3=C2)C4=C(N)N=CN=C41)CCOCCOCCOCCOCCOCCOCCOCCOCCOCCN5C=C(COCCO[C@@H(C[C@H]([C@@H](OC([C@H](CCCC7)N7C(C([C@@]8(O)[C@H](C)CC[C@H](O8)C[C@H](OC)/C(C)=C/C=C/C=C/[C@@H](C)C[C@@H](OC)[C@H](O)/C(C)=C/[C@H]9C)=O)=O		
Formula	$C_{91}H_{138}N_{12}O_{24}$	M.Wt	1784.14
Solubility	≥ 178.4mg/mL in DMSO	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be below -20℃ for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		
Structure	Rapalink-1		

Background

RapaLink-1 is the third-generation mTOR inhibitor exploiting the unique juxtaposition of two drug (first- and second-generation mTOR kinase inhibitors) –binding pockets to create a bivalent interaction that allows inhibition of the mutants which has resistance to the previous TORKi (mTOR kinase inhibitors).

The PIK3CA–AKT–mTOR pathway is one of the most commonly activated pathways in human cancers, which has led to the development of small-molecule inhibitors that target various nodes in the pathway. Two generation of mTOR inhibitor had been developed.

Rapalink-1 is more potent than first- and second- generation mTOR inhibitors. RapaLink-1 could more potently reduce levels of both p-4EBP1 and cell proliferation. Researches compared rapamycin, RapaLink-1, and MLN0128 in LN229 and U87MG. Both growth inhibition and arrest in G0/G1 were more potent in response to RapaLink-1, compared with rapamycin or MLN0128. RapaLink-1 shows potent anti-tumor efficacy in vivo. RapaLink-1 led to initial regression and subsequent stabilization of tumor size in a xenograft model, while tumors treated with vehicle, rapamycin, or MLN0128 grew steadily.

RapaLink-1 could durably block mTORC1. RapaLink-1 is associated with FKBP12, an abundant mTOR-interacting protein, enabling accumulation of RapaLink-1. RapaLink-1 showed better efficacy than rapamycin or TORKi, potently blocking cancer-derived, activating mutants of mTOR.

References:
[1]. Fan Q1, Aksoy O1, Wong RA1, et al, A Kinase Inhibitor Targeted to mTORC1 Drives Regression in Glioblastoma. Cancer Cell. 2017 Mar 13;31(3):424-435. doi: 10.1016/j.ccell.2017.01.014.
[2] Rodrik-Outmezguine VS1, Okaniwa M2, Yao Z1, et al, Overcoming mTOR resistance mutations with a new-generation mTOR inhibitor. Nature. 2016 Jun 9;534(7606):272-6. doi: 10.1038/nature17963. Epub 2016 May 18.

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com
Address: 10292 Central Ave. #205, Montclair, CA, USA