

Product Data Sheet

Product Name: PIK-III
Cat. No.: GC14679

Chemical Properties

Cas. No. 1383716-40-2

Chemical Name 4'-(cyclopropylmethyl)-N2-(pyridin-4-yl)-[4,5'-bipyrimidine]-2,2'-diamine

SMILES NC1=NC=C(C2=NC(NC3=CC=NC=C3)=NC=C2)C(CC4CC4)=N1

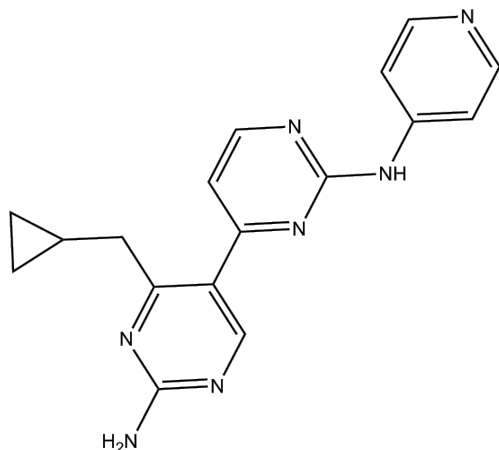
Formula $C_{17}H_{17}N_7$ M.Wt 319.36

Solubility $\geq 31.9\text{mg/mL}$ in DMSO Storage Store at -20°C

General tips For obtaining a higher solubility, please warm the tube at 37°C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C 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



Background

IC50: 18 nM for VPS34

PIK-III is a VPS34 inhibitor and is able to inhibit autophagy.

VPS34 kinase has been found to be responsible for synthesis and deposition of phosphatidylinositol-3-phosphate at autophagosome formation sites, resulting in the recruitment of PtdIns(3)P-binding

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

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proteins.

In vitro: In previous study, PIK-III was identified as a selective inhibitor of VPS34 binding in a hydrophobic pocket. In addition, PIK-III could acutely inhibit the autophagy and lipidation of LC3, which led to the stabilization of autophagy substrates. Moreover, substrates such as NCOA4 were identified by conducting ubiquitin-affinity proteomic assay on PIK-III-treated cells, which accumulated in cells with ATG7 deficiency and co-localized with autolysosomes. NCOA4 could bind ferritin heavy chain-1 directly to target the iron-binding ferritin complex following starvation or iron depletion [1].

In vivo: Animal study showed that PIK-III-treated Ncoa4^{-/-} mice had a profound accumulation of iron in splenic macrophages that were important for iron reutilization from engulfed red blood cells. In summary, such in vivo results provided a novel mechanism for selective autophagy of ferritin and revealed a previously untouched role for autophagy and NCOA4 in the control of in-vivo iron homeostasis [1].

Clinical trial: Up to now, PIK-III is still in the preclinical development stage.

Reference:

[1] Dowdle WE et al. Selective VPS34 inhibitor blocks autophagy and uncovers a role for NCOA4 in ferritin degradation and iron homeostasis in vivo. Nat Cell Biol. 2014 Nov;16(11):1069-79.

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