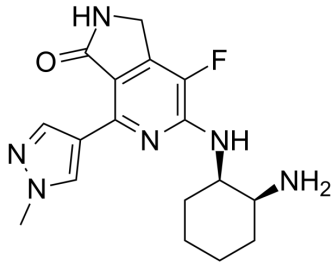
TAK-659

Cat. No.:	HY-100867
CAS No.:	1312691-33-0
Molecular Formula:	$C_{17}H_{21}FN_6O$
Molecular Weight:	344.39
Target:	Syk; FLT3
Pathway:	Protein Tyrosine Kinase/RTK
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	TAK-659 is a highly potent, selective, reversible and orally available dual inhibitor of spleen tyrosine kinase (SYK) and fms related tyrosine kinase 3 (FLT3), with an IC_{50} of 3.2 nM and 4.6 nM for SYK and FLT3, respectively. TAK-659 induces cell death in tumor cells but not in nontumor cells, and with potential for the treatment of chronic lymphocytic leukemia (CLL)[1][2][3][4] .
IC_{50} & Target	IC50: 3.2 nM (Syk), 4.6 nM (FLT3)[1]
In Vitro	TAK-659 inhibits cellular proliferation in SYK-dependent DLBCL and FLT3-dependent AML cell lines[1][3]. TAK-659 (5 μM; 1-24 hours) induces Casp3 activation in the LMP2A/MYC cells which was readily apparent at 4 h and reached maximum levels at 8 h of treatment[4]. TAK-659 (0.01-10 μM; 1 hour) stimulates expression of phospho-Syk at Tyr525 and Tyr352 and phospho-ERK1/2 increased in Ramos cells[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Apoptosis Analysis[4]

Cell Line:	LMP2A/MYC cells
Concentration:	5 μM
Incubation Time:	1 hour, 2 hours, 4 hours, 8 hours, 24 hours
Result:	Induced apoptosis in LMP2A/MYC lymphoma cells.

Western Blot Analysis[2]

Cell Line:	Ramos cells
Concentration:	0.01 μM,0.1 μM,1 μM,10 μM
Incubation Time:	1 hour
Result:	Enhanced expression of phospho-Syk at Tyr525 and Tyr352 and phospho-ERK1/2 in stimulated Ramos cells.

In Vivo	TAK-659 (100 mg/kg/day; p.o.; for 10 days) treatment totally abrogates splenomegaly and tumor development in

LMP2A/MYC mice in both pretumor and tumor cell transfer experiments[4].
TAK-659 treatment kills tumor cells, but not host cells within the spleen and tumors[4].
TAK-659 treatment abrogates metastasis of tumor cells into bone marrow[4].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	LMP2A/MYC double transgenic mice[4]
Dosage:	100 mg/kg/day
Administration:	Oral gavage; for 10 days
Result:	Inhibited LMP2A-induced tumor cell survival in vivo.

REFERENCES

[1]. Lam B, et al. Discovery of TAK-659 an orally available investigational inhibitor of Spleen Tyrosine Kinase (SYK). Bioorg Med Chem Lett. 2016 Dec 15;26(24):5947-5950.

[2]. Purroy N, et al. Inhibition of BCR signaling using the Syk inhibitor TAK-659 prevents stroma-mediated signaling in chronic lymphocytic leukemia cells. Oncotarget. 2017 Jan 3;8(1):742-756.

[3]. Jie Yu, et al. Anti-tumor activity of TAK-659, a dual inhibitor of SYK and FLT-3 kinases, in AML models. Journal of Clinical Oncology 34, no. 15_suppl.

[4]. Cen O, et al. Spleen Tyrosine Kinase Inhibitor TAK-659 Prevents Splenomegaly and Tumor Development in a Murine Model of Epstein-Barr Virus-Associated Lymphoma. mSphere. 2018 Aug 22;3(4).

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