Product Data Sheet

Product Name: RNK08954
Cat. No.: GC79243

Chemical Properties

Cas. No.	3032602-44-8		
Formula	$C_{36}H_{36}F_2N_6O_3$	M.Wt	638.71
Solubility		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

RNK08954 is an orally active KRAS G12D inhibitor with a K d of 0.0395 nM. RNK08954 selectively binds the inactive GDP-bound KRAS G12D form, suppresses downstream KRAS-mediated signaling pathways p-ERK1/2 experssion. RNK08954 inhibits KRAS G12D -mutant cell proliferation, induces G0-G1 cell cycle arrest, and inhibits tumor growth in mouse xenograft models. RNK08954 can be used for the research of non-small cell lung cancer, pancreatic ductal adenocarcinoma [1].

In Vivo, RNK08954 (3-200 mg/kg; p.o.; once or twice daily; 30-35 days) induces dose-dependent tumor growth inhibition and regression in GP2d colorectal cancer xenografts mice, with 70% tumor

regression at 60 mg/kg once daily and near-complete regression at higher twice-daily doses[1]. RNK08954 (10-200 mg/kg; p.o.; once daily for 5 days) dose-dependently inhibits KRAS downstream signaling (p-ERK, p-S6, DUSP6) in GP2d xenografts mice, with significantly higher drug exposure in tumor tissue compared to plasma[1]. RNK08954 (25-100 mg/kg; p.o.; once daily, twice daily; 28 days) potently inhibits tumor growth in SW1990 pancreatic cancer xenografts mice, with near-complete tumor regression observed at 100 mg/kg twice daily[1]. RNK08954 (25-100 mg/kg; p.o.; once daily, twice daily; 42 days) achieves complete tumor regression in Panc 04.03 pancreatic cancer xenografts mice at a dose of 100 mg/kg twice daily[1]. RNK08954 (50-200 mg/kg; p.o.; twice daily; 35 days) drives dose-dependent tumor growth inhibition in A427 non-small cell lung cancer xenografts mice[1]. RNK08954 (100-200 mg/kg; p.o.; once daily, twice daily; 35 dyas) potently inhibits tumor growth in multiple KRASG12D-mutant pancreatic cancer PDX mice models[1]. RNK08954 (200 mg/kg; p.o.; once daily; 28 dyas) induces significant tumor shrinkage in an orthotopic HPAF-II-luc pancreatic cancer mice models at 200 mg/kg once daily[1]. RNK08954 (100 mg/kg; p.o.; once daily) inhibits tumor growth and modulates the tumor immune microenvironment by expanding CD8+ T cells in CT-26 syngeneic mice models, with enhanced efficacy when combined with anti-PD-1[1].

In Vitro, RNK08954 potently and selectively binds to inactive GDP-bound KRASG12D with a Kd of 39.5 pM, with significantly lower affinity for other KRAS variants and wild-type KRAS[1]. RNK08954 (5-1250 nM; 6-72 h) potently inhibits KRAS downstream signaling in KRASG12D-mutant SW1990 cells, with an IC_{50} of <5.14 nM for p-ERK1/2 inhibition at 6 hours, and sustained inhibition through 72 hours[1]. RNK08954 (72 h) potently inhibits viability of KRASG12D-mutant human tumor cell lines with a median IC_{50} of 10.8 nM, and shows high selectivity against KRAS wild-type and non-G12D KRAS-mutant cells[1]. RNK08954 induces G0-G1 cell cycle arrest and cell death in KRASG12D-mutant SW1990 cells[1].

References:

[1]. Xie L, et al. Preclinical Characterization and Clinical Activity of RNK08954, a Highly Selective and Orally Bioavailable KRASG12D Inhibitor. Cancer Discov. 2026;16(5):895-910.