

Product Data Sheet

Product Name: LDC8201

Cat. No.: GC79456

Chemical Properties

Cas. No. 2411873-31-7

Formula C₂₈H₂₈ClN₅O

M.Wt 486.02

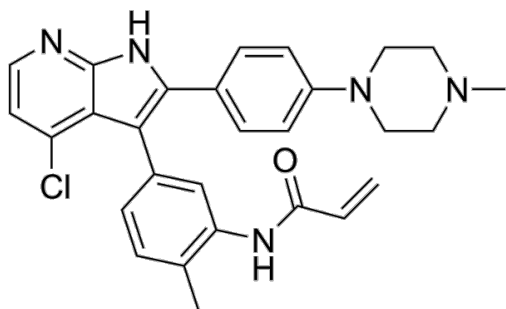
Solubility

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

LDC8201 is a selective, orally active, covalent inhibitor that targets EGFR and Her2 exon 20 insertion mutants. LDC8201 induces tumor shrinkage and regression. LDC8201 is applicable to research related to non-small cell lung cancer carrying EGFR or Her2 exon 20 insertion mutations [1] [2].

In Vivo, LDC8201 (90 mg/kg; p.o.; BID for 6 days then QD for 8 days; 14 days) induces 89% tumor shrinkage in Balb/c nude mice bearing EGFR^{L858R+T790M} mutant NCI-H1975 tumors after 14 days of oral treatment at 90 mg/kg^[2]. LDC8201 (30-90 mg/kg; p.o.; QD; up to 21 days) induces dose-dependent tumor shrinkage (9%, 41%, and 50% at 30, 60, and 90 mg/kg respectively) in RJ:NMRI-

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

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Foxn1nu/nu nude mice bearing EGFRH773_V774insNPH mutant Cuto17 tumors after 21 days of once-daily oral treatment, with no associated toxicity^[2].

In Vitro, LDC8201 (14 nM to 30 μ M; 72 h) potently inhibits cell viability in EGFRH773_V774insNPH and Her2A775_G776insYVMA Ba/F3 cells (GI₅₀ = 48 nM and 59 nM, respectively), EGFRV769_D770insASV Cuto 14 cells (GI₅₀ = 39 nM), and EGFRH773_V774insNPH Cuto 17 cells (GI₅₀ = 23 nM), with moderate selectivity (6-fold) over EGFR wild-type A431 cells (GI₅₀ = 303 nM)^[1]. LDC8201 exhibits moderate in vitro ADME properties, including moderate microsomal and hepatocyte clearance, high plasma protein binding, moderate Caco-2 permeability, low hERG inhibition, and low cytotoxicity in normal cells^[1]. LDC8201 (8 decreasing concentrations; 72 h) potently inhibits the growth of Ba/F3-EGFR-H773_V774insNPH cells with a GI₅₀ of 48 nM and an EC₅₀ of 53 nM^[2]. LDC8201 (8 decreasing concentrations; 72 h) potently inhibits the growth of Ba/F3-Her2A775_G776insYVMA cells with a GI₅₀ of 59 nM and an EC₅₀ of 86 nM^[2]. LDC8201 (8 decreasing concentrations; 72 h) potently inhibits the growth of H1975 cells with a GI₅₀ of 18 nM^[2]. LDC8201 (0.01-1 μ M) inhibits EGFR activation and downstream ERK signaling in Cuto 17 cells at concentrations as low as 10 nM^[2]. LDC8201 (0.01-1 μ M) inhibits EGFR activation and downstream ERK signaling in A431 cells at concentrations of 100 nM and above, demonstrating wild-type-sparing activity^[2]. LDC8201 (1 μ M) has moderate metabolic stability in mouse liver microsomes with an intrinsic clearance of 93 μ L/min/mg^[2]. LDC8201 (10 μ M; 2 h) has moderate permeability across Caco-2 cell monolayers with an apical-to-basolateral Papp of 51 nm/s^[2].

References:

- [1]. Tumbrink H L. 3.3 MIZ1- Δ POZ shapes treatment response in small cell lung cancer[J]. Exploiting molecular vulnerabilities in genetically defined lung cancer models, 2023: 45.
- [2]. Lategahn J, et al. Insight into Targeting Exon20 Insertion Mutations of the Epidermal Growth Factor Receptor with Wild Type-Sparing Inhibitors. Journal of medicinal chemistry. 2022 May 12;65(9):6643-6655.

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