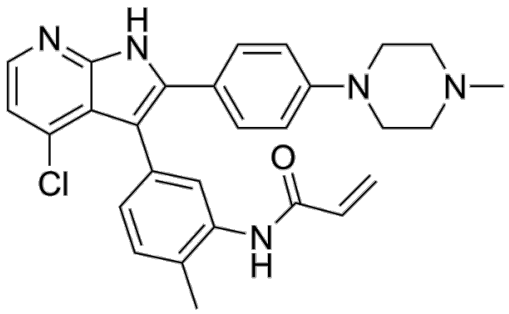
Product Data Sheet

Product Name: LDC8201
Cat. No.: GC79456

Chemical Properties

Cas. No.	2411873-31-7		
Formula	$C_{28}H_{28}ClN_5O$	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 EGFRL858R+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-

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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 μM; 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 μM) inhibits EGFR activation and downstream ERK signaling in Cuto 17 cells at concentrations as low as 10 nM[2]. LDC8201 (0.01-1 μM) 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 μM) has moderate metabolic stability in mouse liver microsomes with an intrinsic clearance of 93 μL/min/mg[2]. LDC8201 (10 μM; 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.

Caution: Product has not been fully validated for medical applications. For research use only.
Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com
Address: 10292 Central Ave. #205, Montclair, CA, USA