

Product Data Sheet

Product Name: GNE-7915

Cat. No.: GC12121

Chemical Properties

Cas. No. 1351761-44-8

Chemical Name (4-((4-(ethylamino)-5-(trifluoromethyl)pyrimidin-2-yl)amino)-2-fluoro-5-methoxyphenyl)(morpholino)methanone

SMILES CCNC1=C(C(F)(F)F)C=NC(NC2=CC(F)=C(C(N3CCOCC3)=O)C=C2OC)=N1

Formula $C_{19}H_{21}F_4N_5O_3$

M.Wt 443.4

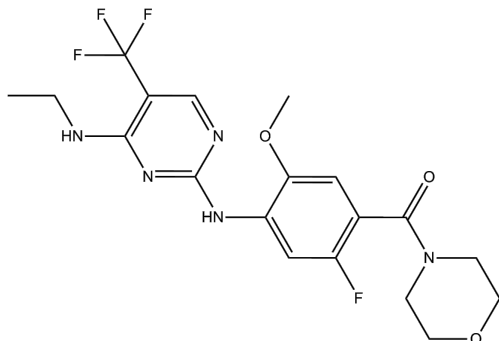
Solubility $\geq 22.15\text{mg/mL}$ in DMSO

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

GNE-7915 is a highly potent, selective, and brain-penetrable leucine-rich repeat kinase2 (LRRK2) inhibitor, with K_i and IC_{50} of 1 nM and 9 nM, respectively.

GEN-7915 is extensive inhibitor across 187 screened kinases, except TTK kinase. In an extended profile across 392 kinases, GNE-7915 only bound to 10 enzymes to a significant extent ($>50\%$ probe displaced at 100 nM). GNE-7915 and its progenitors are the first selective LRRK2 inhibitors to penetrating the brain barrier. [1]

GEN-7915 has been shown to induce dephosphorylation of LRRK2 in the brain of transgenic mice.

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

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GNE-7915 is not reported to cause cellular or genetic toxicity, and has progressed into preclinical studies in cynomolgus monkeys [3]. The use of in silico modelling, extensive in vitro assays and resource-efficient in vivo techniques to produce GNE-7915, reflects a trend towards the concerted optimisation of potency, selectivity and pharmacokinetic properties in early-stage drug development [1]. GNE-7915 can inhibit TNF α and CXCL10 at higher concentrations ($\geq 3 \mu\text{M}$) in both WT and LRRK2 KO experiments [2].

References:

1. Kavanagh ME, Doddareddy MR, Kassiou M. The development of CNS-active LRRK2 inhibitors using property-directed optimisation. *Bioorg Med Chem Lett*. 2013 Jul 1;23(13):3690-6. doi: 10.1016/j.bmcl.2013.04.086. Epub 2013 May 9.
2. Luerman GC, Nguyen C, Samaroo H et al. Phosphoproteomic evaluation of pharmacological inhibition of leucine-rich repeat kinase 2 reveals significant off-target effects of LRRK-2-IN-1. *J Neurochem*. 2014 Feb;128(4):561-76. doi: 10.1111/jnc.12483. Epub 2013 Nov 11.
3. Estrada AA, Liu X, Baker-Glenn C et al. Discovery of highly potent, selective, and brain-penetrable leucine-rich repeat kinase 2 (LRRK2) small molecule inhibitors. *J Med Chem*. 2012 Nov 26;55(22):9416-33. doi: 10.1021/jm301020q. Epub 2012 Oct 15.

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