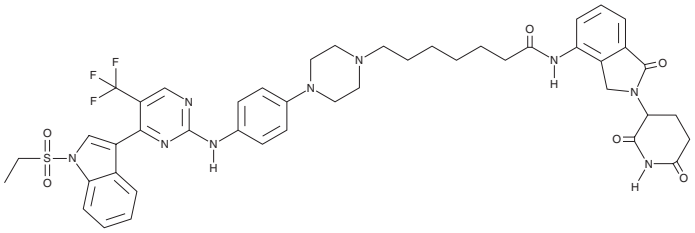
PRODUCT INFORMATION

PROTAC EGFR Degrader 9

Item No. 45393



CAS Registry No.: 2992670-33-2
Formal Name: N-[2-(2,6-dioxo-3-piperidinyl)-2,3-dihydro-1-oxo-1H-isoindol-4-yl]-4-[4-[[4-[1-(ethylsulfonyl)-1H-indol3-yl]-5-(trifluoromethyl)-2-pyrimidinyl]amino]phenyl]-1-piperazineheptanamide
Synonyms: Proteolysis-targeting Chimera EGFR Degrader-9, Proteolysis-targeting Chimera Epidermal Growth Factor Receptor Degrader-9
MF: $C_{45}H_{48}F_3N_9O_6S$
FW: 900.0
Purity: ≥95%
Supplied as: A solid
Storage: -20°C
Stability: ≥4 years

Information represents the product specifications. Batch specific analytical results are provided on each certificate of analysis.

Laboratory Procedures

PROTAC EGFR Degrader 9 is supplied as a solid. A stock solution may be made by dissolving the PROTAC EGFR Degrader 9 in the solvent of choice, which should be purged with an inert gas. PROTAC EGFR Degrader 9 is sparingly soluble (1-10 mg/ml) in DMSO and slightly soluble (0.1-1 mg/ml) in acetonitrile.

Description

PROTAC EGFR degrader 9 is a proteolysis-targeting chimera (PROTAC) containing the mutant $EGFR^{T790M/C797S}$-binding compound D51 conjugated to the cereblon (CRBN) ligand lenalidomide (Item No. 14643) *via* an alkyl linker.[1] It selectively induces degradation of mutant EGFRs over wild-type EGFR with half-maximal degradation concentration (DC_{50}) values of 10.2, 36.5, 88.5, 75.4, and >300 nM for $EGFR^{L858R/T790M/C797S}$, $EGFR^{\Delta19/T790M/C797S}$, $EGFR^{L858R/T790M}$, $EGFR^{\Delta19}$, and wild-type EGFR, respectively. PROTAC EGFR degrader 9 inhibits the growth of H1975 non-small cell lung cancer (NSCLC) cells expressing mutant $EGFR^{L858R/T790M/C797S}$ (IC_{50} = 10.3 nM) and induces cell cycle arrest at the G_0/G_1 phase and apoptosis in the same cells. It reduces tumor size in an H1975 xenograft mouse model when administered at doses of 25 and 100 mg/kg.

Reference

1. Zhu, Y., Ye, X., Wu, Y., *et al.* Design, synthesis, and biological evaluation of novel EGFR PROTACs targeting C797S mutation. *J. Med. Chem.* **67(9)**, 7283-7300 (2024).

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