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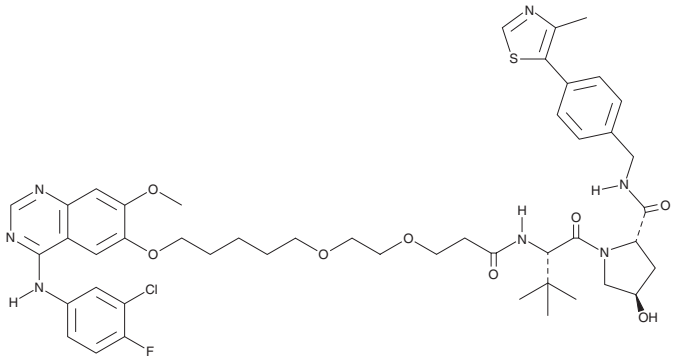
PRODUCT INFORMATION

Gefitinib-based PROTAC 3

Item No. 28597

CAS Registry No.:	2230821-27-7
Formal Name:	(2S,4R)-1-((S)-2-(3-(2-((5-((4-((3-chloro-4-fluorophenyl)amino)-7-methoxyquinazolin-6-yl)oxy)pentyl)oxy)ethoxy)propanamido)-3,3-dimethylbutanoyl)-4-hydroxy-N-(4-(4-methylthiazol-5-yl)benzyl)pyrrolidine-2-carboxamide
Synonym:	Gefitinib-based Proteolysis-targeting Chimera 3
MF:	$C_{47}H_{57}ClFN_7O_8S$
FW:	934.5
Purity:	≥98%
UV/Vis.:	λ_{max}: 252, 332 nm
Supplied as:	A crystalline solid
Storage:	-20°C
Stability:	≥2 years



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

Laboratory Procedures

Gefitinib-based PROTAC 3 is supplied as a crystalline solid. A stock solution may be made by dissolving the gefitinib-based PROTAC 3 in the solvent of choice, which should be purged with an inert gas. Gefitinib-based PROTAC 3 is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide (DMF). The solubility of gefitinib-based PROTAC 3 in these solvents is approximately 10, 16, and 25 mg/ml respectively.

Gefitinib-based PROTAC 3 is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, gefitinib-based PROTAC 3 should first be dissolved in DMF and then diluted with the aqueous buffer of choice. Gefitinib-based PROTAC 3 has a solubility of approximately 0.25 mg/ml in a 1:3 solution of DMF:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

Description

Gefitinib-based PROTAC 3 is a proteolysis-targeting chimera (PROTAC) comprised of the EGF receptor (EGFR) inhibitor gefitinib (Item No. 13166) linked to the von Hippel-Lindau (VHL) E3 ubiquitin ligase ligand VHL ligand 1 (Item No. 21591).[1] In cell-based assays, gefitinib-based PROTAC 3 induces degradation of EGFR containing the activating mutation L858R or an exon 19 deletion with half-maximal degradation (DC_{50}) values of 22.3 and 11.7 nM, respectively, but does not induce degradation of wild-type EGFR at concentrations up to 10 µM.

Reference

1. Burslem, G.M., Smith, B.E., Lai, A.C., *et al.* The advantages of targeted protein degradation over inhibition: an RTK case study. *Cell Chem. Biol.* **25(1),** 66-77 (2018).

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