Product Data Sheet

Product Name: BLU-945
Cat. No.: GC63910

Chemical Properties

Cas. No.	2660250-10-0		
Formula	$C_{28}H_{37}FN_6O_3S$	M.Wt	556.7
Solubility		Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ 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	BLU-945		

Protocol

Cell experiment [1]:

Cell lines	Ba/F3 cells, PC9, PC9_DC, YU-1182, and YU-1097
Preparation Method	Cells were seeded and incubated for 3 days for Ba/F3 cells, PC9, PC9_DC, YU-1182, and YU-1097. Cells were treated with BLU-945, osimertinib, or gefitinib at 10 different concentrations ranging from 0.095 to 25,000nM. 0.1% dimethyl sulfoxide (DMSO) and 25,000nM staurosporine were used as negative and positive controls, respectively. After 4h of treatment, cells were processed using the PhosphoEGFR (Tyr1068) AlphaLISA SureFire Ultra Detection Kit according to the manufacturer’s instructions. Viability was measured using CellTiter-Glo® assay.

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Reaction Conditions	0.095 to 25,000nM; 4h
Applications	BLU-945 inhibited EGFR phosphorylation,cell viability and growth.

Animal experiment [1]:

Animal models	Female nu/nu mice; female NOD-SCID mice
Preparation Method	To generate YU-1097 PDCderived tumor xenograft models, cells (5×10^6 in 100μL) were implanted subcutaneously into the flanks of 6-week-old female nu/nu mice. To generate an EGFR_L858R/C797S-expressing Ba/F3 syngeneic injection model, cells (3×10^6 in 200μL) were implanted into the flank of female NOD-SCID mice. Prior to the onset of drug treatment, mice were measured for tumor size in two dimensions and the tumor volume (mm^3) was calculated using formula $V=0.5\ a \times b^2$ where a and b are the long and short diameters of the tumor in mm, respectively. Mice were randomly grouped when the tumor volume reached $200mm^3$ and allocated to the following treatment groups: vehicle, osimertinib (25mg/kg once daily [QD]), BLU-945 (100mg/kg twice daily [BID]), and combinations of osimertinib with BLU-945. BLU-945 and osimertinib were formulated in 20% Solutol HS 15 with 0.5% methylcellulose and dosed orally for 30 days. Tumor size and body weight were measured twice weekly. Tumor samples were harvested and snap-frozen for subsequent analysis.

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Dosage form	100mg/kg/day for 30 days; bid; p.o.
Applications	Treatment of BLU-945 demonstrated tumor shrinkage and inhibition of the EGFR pathway both as monotherapy and in combination with osimertinib.

References:
[1] Lim, S. M., Schalm, S. S., Lee, E. J., Park, S., Conti, C., Millet, Y. A., Woessner, R., Zhang, Z., Tavera-Mendoza, L. E., Stevison, F., Albayya, F., Dineen, T. A., Hsieh, J., Oh, S. Y., Zalutskaya, A., Rotow, J., Goto, K., Lee, D. H., Yun, M. R., & Cho, B. C. (2024). BLU-945, a potent and selective next-generation EGFR TKI, has antitumor activity in models of osimertinib-resistant non-small-cell lung cancer. *Therapeutic advances in medical oncology*, *16*, 17588359241280689.

Background

BLU-945 is a potent, highly selective, reversible and orally active epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor (TKI)[1]. EGFR plays a crucial role in cell

proliferation, differentiation, survival, and migration, and its gene mutations are one of the key drivers of non-small cell lung cancer (NSCLC)[2]. BLU-945 can effectively inhibit EGFR with L858R and/or exon 19 deletion mutation, T790M mutation and C797S mutation[3]. The IC_{50} value of BLU-945 for EGFR L858R/C797S is 28.9nM, and for EGFR ex19del/C797S is 108.8nM[3]. BLU-945 is usually used for the research of lung cancer including non-small cell lung cancer (NSCLC)[4-7].

In vitro BLU-945 (0-10mM; 4h) inhibited EGFR phosphorylation in cell lines harboring EGFR L858R/T790M/C797S and EGFR ex19del/T790M/C797S mutations and inhibited cell viability and growth of EGFR mutant/osimertinib-resistant cell lines[3].

In vivo, in osimertinib-resistant models of NSCLC (osimertinib second line: EGFR_L858R/C797S and third line: EGFR_ex19del/T790M/C797S and L858R/T790M/C797S), treatment of BLU-945(orally; 100mg/kg; bid; 30d) alone or combinated with osimertinib demonstrated tumor shrinkage and inhibition of the EGFR pathway[3].

References:
[1] John Emmerson Campbell, et al. Inhibitors of mutant forms of egfr. Patent WO2021133809A1.
[2] Melosky, B., Kambartel, K., Häntschel, M., Bennetts, M., Nickens, D. J., Brinkmann, J., Kayser, A., Moran, M., & Cappuzzo, F. (2022). Worldwide Prevalence of Epidermal Growth Factor Receptor Mutations in Non-Small Cell Lung Cancer: A Meta-Analysis. *Molecular diagnosis & therapy*, *26*(1), 7–18.
[3] Lim, S. M., Schalm, S. S., Lee, E. J., Park, S., Conti, C., Millet, Y. A., Woessner, R., Zhang, Z., Tavera-Mendoza, L. E., Stevison, F., Albayya, F., Dineen, T. A., Hsieh, J., Oh, S. Y., Zalutskaya, A., Rotow, J., Goto, K., Lee, D. H., Yun, M. R., & Cho, B. C. (2024). BLU-945, a potent and selective next-generation EGFR TKI, has antitumor activity in models of osimertinib-resistant non-small-cell lung cancer. *Therapeutic advances in medical oncology*, *16*, 17588359241280689.
[4] Eno, M. S., Brubaker, J. D., Campbell, J. E., De Savi, C., Guzi, T. J., Williams, B. D., Wilson, D., Wilson, K., Brooijmans, N., Kim, J., Özen, A., Perola, E., Hsieh, J., Brown, V., Fetalvero, K., Garner, A., Zhang, Z., Stevison, F., Woessner, R., Singh, J., … Dineen, T. A. (2022). Discovery of BLU-945, a Reversible, Potent, and Wild-Type-Sparing Next-Generation EGFR Mutant Inhibitor for Treatment-Resistant Non-Small-Cell Lung

Cancer. *Journal of medicinal chemistry*, *65*(14), 9662–9677.
[5] Kannan, K., & Mohan, S. (2025). Targeting exon mutations in NSCLC: clinical insights into LAG-3, TIM-3 pathways, and advances in fourth-generation EGFR-TKIs. *Medical oncology (Northwood, London, England)*, *42*(6), 196.
[6] Shum E, Elamin Y, Piotrowska Z, Spigel DR, Reckamp KL, Rotow J, et al. (2022). EP08.02–045 phase 1/2 study of BLU-945 in patients with common activating EGFR-mutant non-small cell lung cancer. *Journal of Thoracic Oncology*. 2022;17(9):S418.
[7] Elamin Y, Nagasaka M, Shum E, Bazhenova L, Camidge D, Cho B, et al. BLU-945 monotherapy and in combination with osimertinib (OSI) in previously treated patients with advanced EGFR -mutant (EGFRm) NSCLC in the phase 1/2 SYMPHONY study. J Clin Oncol. 2023;41:9011–9011.