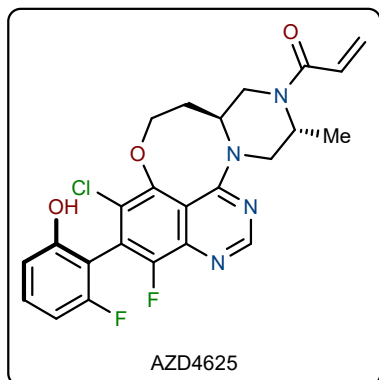


Discovery and Bioactivities



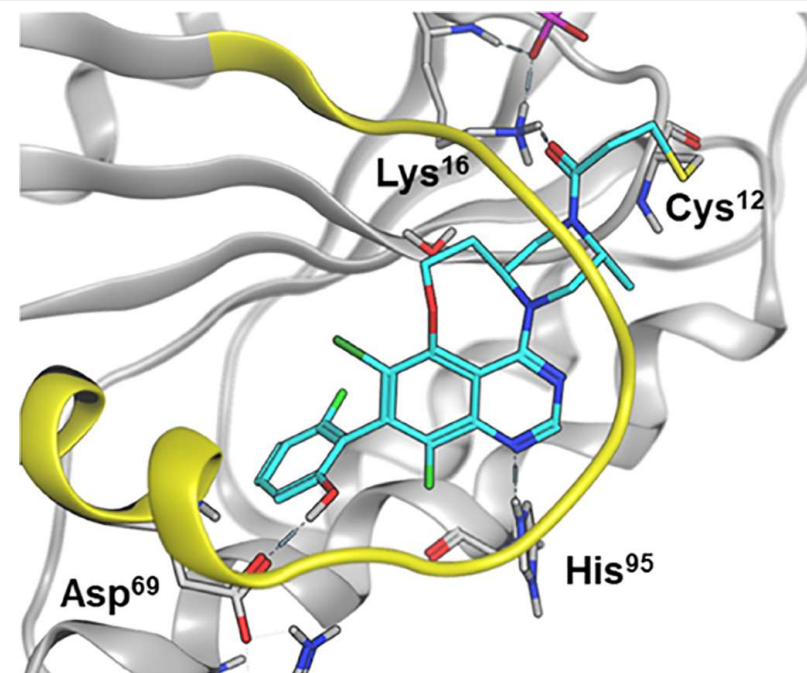
AstraZeneca

Discovered by structure-based drug design

Highly selective for reaction with the cysteine in KRAS^{G12C} over other cysteine-containing proteins

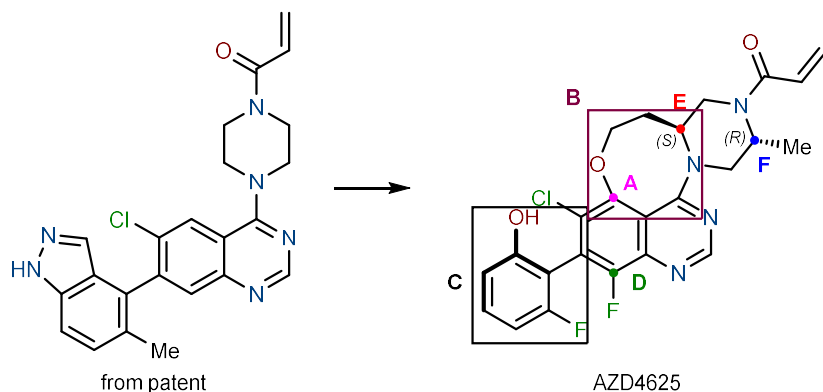
Selective antiproliferative phenotype in cancer cells bearing the G12C mutation

Clinical development candidate for the treatment of KRAS^{G12C} positive tumors



Kettle, J. G.; Bagal, S. K.; Bickerton, S.; Bodnarchuk, M. S.; Boyd, S.; Breed, J.; Carbajo, R. J.; Cassar, D. J.; Chakraborty, A.; Cosulich, S.; Cumming, I.; Davies, M.; Davies, N. L.; Eatherton, A.; Evans, L.; Feron, L.; Fillery, S.; Gleave, E. S.; Goldberg, F. W.; Hanson, L.; Harfinger, S.; Howard, M.; Howells, R.; Jackson, A.; Kemmitt, P.; Lamont, G.; Lamont, S.; Lewis, H. J.; Liu, L.; Niedbala, M. J.; Phillips, C.; Polanski, R.; Raubo, P.; Robb, G.; Robinson, D. M.; Ross, S.; Sanders, M. G.; Tonge, M.; Whiteley, R.; Wilkinson, S.; Yang, J.; Zhang, W., *J. Med. Chem.* **2022**, *65* (9), 6940 <https://doi.org/10.1021/acs.jmedchem.2c00369>

Logic of Design



Synthesis

