Research paper

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Scaffold hopping identifies 6,8-disubstituted purines as novel anaplastic lymphoma kinase inhibitors

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Abstract: Rearrangements of anaplastic lymphoma kinase (ALK) are associated with several cancer diseases. Due to resistance development against existing ALK-inhibitors, new, structurally unrelated inhibitors are required. By a scaffold hopping strategy, 6,8-disubstituted purines were designed as analogues of similar ALK-inhibiting thieno[3,2-*d*]pyrimidines. While the new title compounds indeed inhibited ALK and several ALK mutants in submicromolar concentrations, they retained poor water solubility.

Abbreviations

ALK: anaplastic lymphoma kinase; cMet, hepatocyte growth factor receptor; DIPEA, *N,N*-Diisopropylethylamine; DMF, *N,N*-Dimethylformamide; EML4, echinoderm microtubule-associated protein-like 4; FDA, Food and Drug Administration; gk, gatekeeper; µW, micro wave; NSCLC, non-small cell lung cancer; pdb, protein data bank; RT: room temperature; TEA, triethly amine; wt, wild type.