Discovery of pyrazolo[1,5-a]pyrimidin B-cell lymphoma 6 (BCL6) binders and optimisation to high affinity macrocyclic inhibitors

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Virtual screen

Fragment hit $K_d = 689 \mu M$

Medchem optimisation: $10^5$ affinity increase!

$K_d = 0.0065 \mu M$

Cell probes to test BCL6 hypothesis in DLBCL cancer

SBDD

Conformational prediction

Slow-off kinetics

Selectivity

SAR

Macrocyclisation

"Snack" synthesis

IMED Biotech Unit I IMED Oncology chemistry