

Supplementary Material

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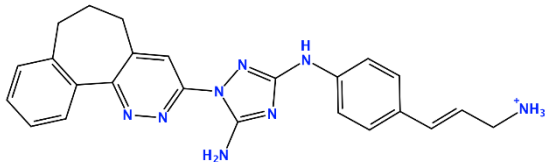
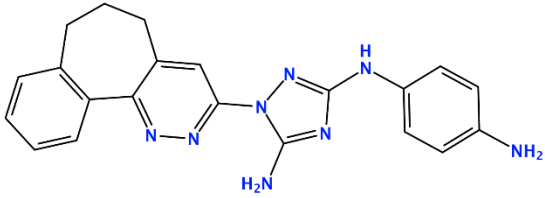
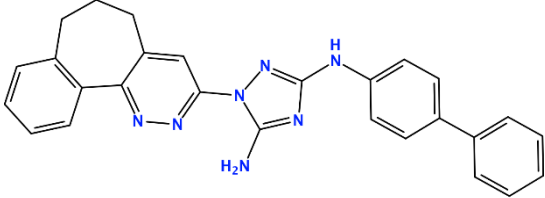
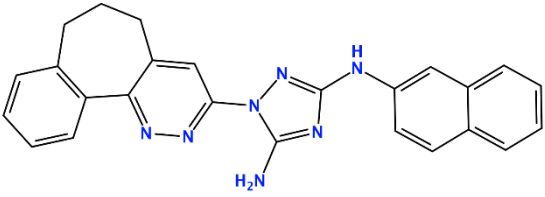
Figure S1. 2D interaction diagrams of designed compound R5 with the binding pockets of Axl, Tyro3, ABL1 and Met kinases.

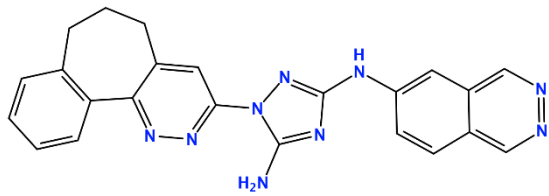
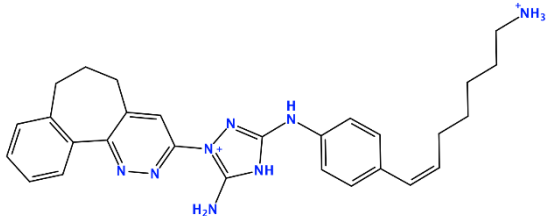
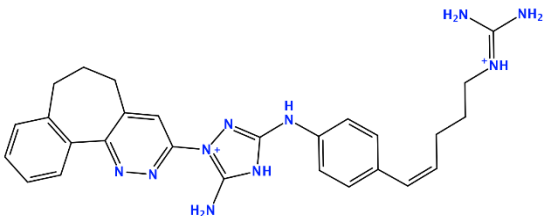
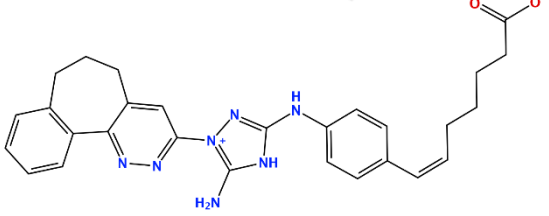
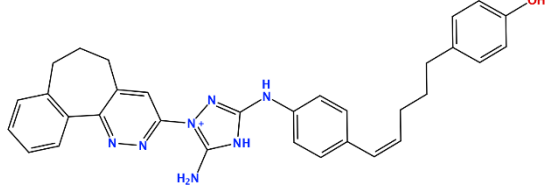
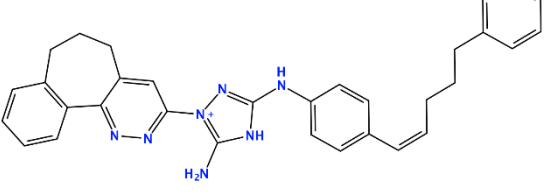
PubChem CIDs for R428 patented analogs

PubChem CIDs for Crizotinib patented analogs

Table S1. Docking scores according to GOLD, MOE and AutoDock for modifications of R428_2, R428_3 and R428_4 compounds.¹

¹The modifications of R428_2, R428_3 and R428_4 corresponding to the following PubChem CIDs: 67104254, 67106757 and 67103760, respectively.

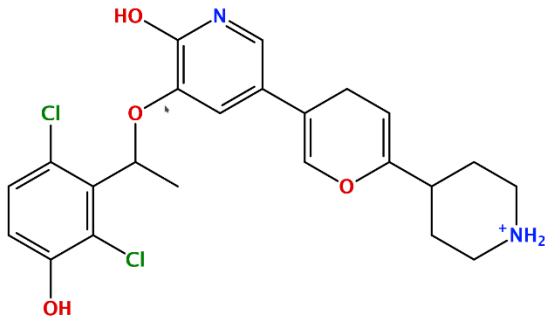
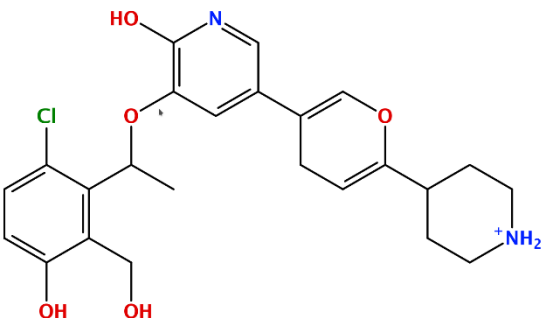
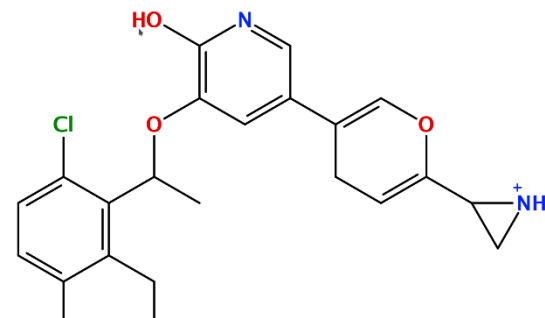
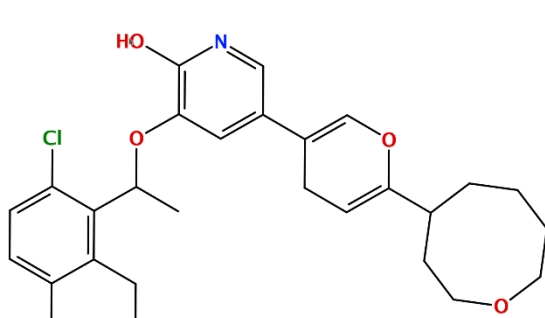
Compound No.	2D Structure	Score (GOLD)	Score, kcal/mol (MOE)	ΔG , kcal/mol
R1'		67	-6.42	-9.99
R2'		57	-6.71	-8.56
R3'		67	-7.10	-10.24
R4'		65.2	-7.17	-11.49

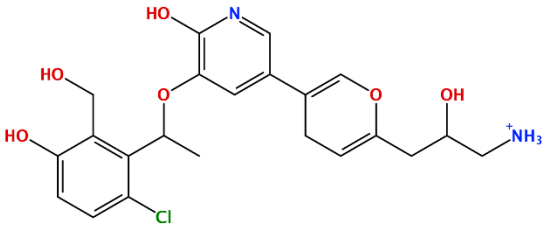
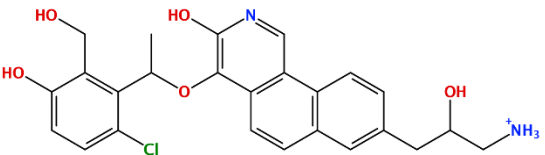
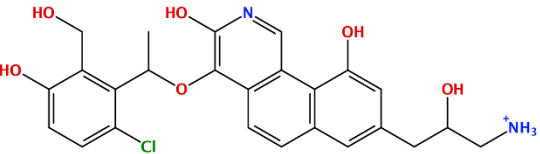
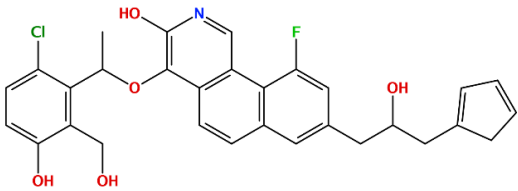
R5'		58.55	-6.97	-10.84
R6'		83.3	-7.61	-9.11
R7'		83.46	-7.77	-8.94
R8'		82.35	-7.41	-7.76
R9'		85.27	-8.01	-9.92
R10'		85.28	-8.29	-10.34

R11'	The chemical structure of R11' features a fluorene system. The fluorene's 9-position is connected to a 1,2,4-triazole ring. The triazole has an amino group (-NH ₂) at the 3-position and is linked via its 4-position to a 4-((E)-3-(indol-3-yl)prop-1-en-1-yl)phenyl group.	84.75	-7.52	-9.76
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Table S2. Docking scores according to GOLD, MOE and Autodock for the new designed compounds from Crizotinib.

Compound No.	2D Structure	Score (GOLD)	Score, kcal/mol (MOE)	ΔG , kcal/mol
C1	The chemical structure of C1 consists of a 2,6-dichlorophenol moiety (with the hydroxyl group in red) connected via an isopropyl ether linkage to a 4-amino-2-pyridyl group. This pyridine ring is further connected to a 1-(piperidin-4-yl)-1H-imidazole moiety, where the piperidine ring is shown with a positive charge (+NH ₂).	62.04	-7.41	-9.32
C2	The chemical structure of C2 is similar to C1, but the pyridine ring has a hydroxyl group (-OH in red) at the 3-position instead of an amino group. It is connected to the same 1-(piperidin-4-yl)-1H-imidazole moiety.	64.33	-7.67	-9.82

C3		59.25	-7.05	-9.39
C4		65.78	-6.9	-8.92
C5		60.34	-7.24	-8.62
C6		62.75	-7.97	-8.27

C7		63.06	-7.21	-8.09
C8		63.41	-7.22	-8.76
C9		62.09	-7.23	-8.66
C10		68.35	-7.44	-8.46

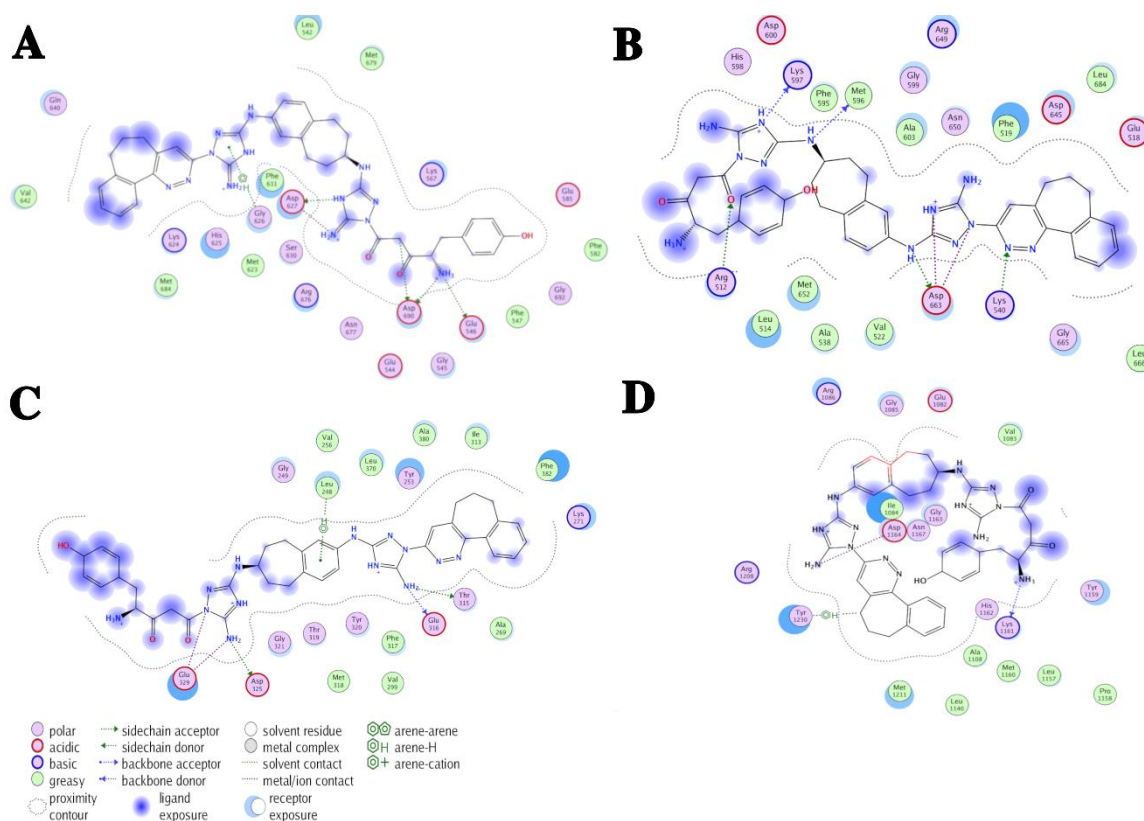


Figure S1. 2D interaction diagrams of designed compound R5 with the binding pockets of Axl (A), Tyro3 (B), ABL1 (C) and Met (D) kinases.

PubChem CIDs for R428 patented analogs:

25123113, 25123764, 25123765, 25123766, 25124093, 25124412, 25124413, 25124416, 25124748, 25126438, 25126441, 25126768, 25126769, 25126770, 25126771, 25127082, 25127084, 25127085, 25127087, 25127411, 25127412, 25127413, 25127729, 25127732, 25128065, 25242518, 44555405, 44608272, 44608274, 44608478, 46843554, 46843555, 46843556, 46843635, 46843636, 46843709, 46843710, 46843711, 46843712, 46843713, 46843779, 46843780, 46843781, 46843782, 46843783, 46843846, 46843849, 46843914, 46843915, 46843916, 46843917, 46843983, 46843984, 46843985, 46844040, 46844043, 46844099, 46844156, 46844158, 46844160, 58247200, 59276159, 66694799, 66694824, 66694833, 66694842, 66694868, 66694872, 66694875, 66694882, 66694895, 66694908, 66694911, 66694913, 66694927, 66694944, 66694947, 66694949, 66694955, 66695119, 66695125, 66695128, 37103757, 67103760, 67103793, 67103828, 67103831, 67103892, 67103902, 67103980,

67103984, 67104015, 67104024, 67104046, 67104110, 67104115, 67104119, 67104124, 67104128, 67104199, 67104235, 67104240, 67104245, 67104254, 67104256, 67104272, 67104274, 67104292, 67104295, 67104296, 67104297, 67104298, 67104308, 67104314, 67104315, 67104323, 67104329, 67104341, 67104351, 67104364, 67104375, 67104390, 67201090, 67201627, 67202616, 67202697, 67202721, 67203099, 67262438, 67262504, 67300667, 67537244, 67537596, 68729332, 76714002, 90974101.

PubChem CIDs for Crizotinib patented analogs:

11575401, 11576617, 11597571, 11612136, 11625675, 11647759, 11647760, 11654090, 11656580, 11662380, 11667754, 117071753, 21110756, 21110757, 44256053, 44256477, 54579455, 56671814, 56671943, 66548953, 71621328, 71664254, 71664255, 72199381, 73386634, 76322034.