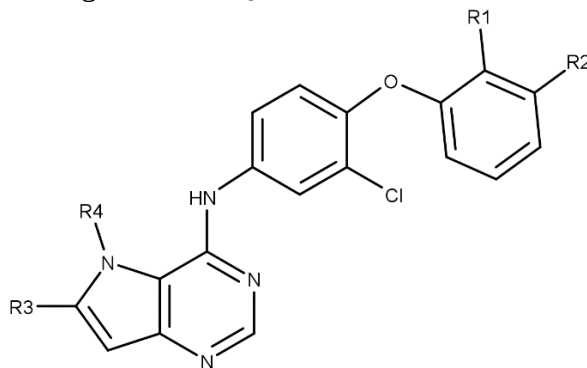


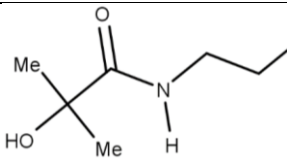
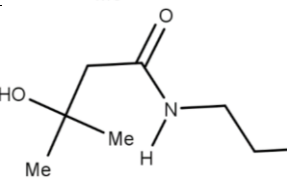
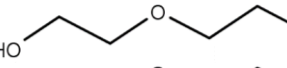
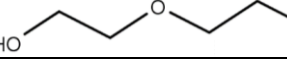
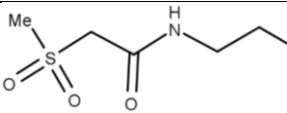
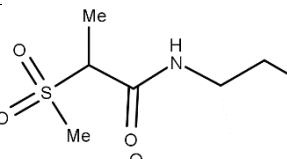
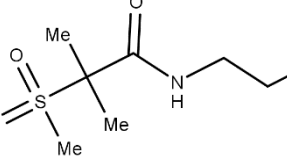
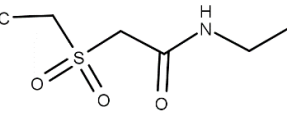
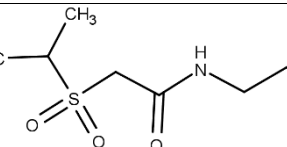
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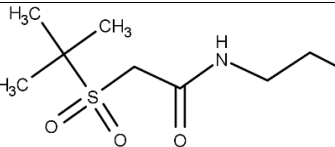
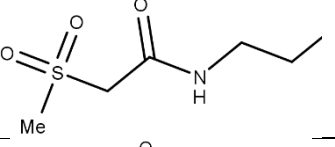
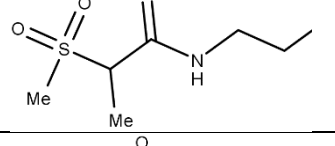
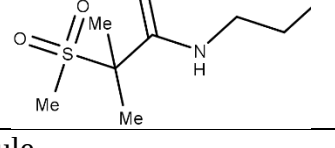
Supplementary Tables

Table S1. Structure of pyrrolo[3,2-d]pyrimidine derivatives with their experimental dual activities (EGFR/HER2) used to generate G-QSAR model.



Comp Id	R1	R2	R3	R4	IC ₅₀ (EGFR) (nM)	IC ₅₀ (HER2) (nM)	pIC ₅₀ (EGFR)	pIC ₅₀ (HER2)
C1	H	-Cl	H		9.5	4.1	8.02	8.39
C2	H	-CF ₃	H		34	12	7.47	7.92
C3	H	-OCF ₃	H		110	29	6.96	7.54
C4	H	-Cl	H		5.7	2.1	8.24	8.68
C5	H	-CF ₃	H		15	5.1	7.82	8.29
C6	H	-OCF ₃	H		49	8.4	7.31	8.08
C7	H	-CF ₃	H		33	15	7.48	7.82
C8	H	-CF ₃	H		22	7.7	7.66	8.11
C9	H	-CF ₃	H		44	9.4	7.36	8.03
C10	H	-CF ₃	H		31	12	7.51	7.92
C11	H	-CF ₃	H		40	12	7.40	7.92
C12*	H	-CF ₃	H		15	5.7	7.82	8.24

C13	H	-CF ₃	H		35	15	7.46	7.82
C14	H	-CF ₃	H		23	17	7.64	7.77
C15	H	-CF ₃	-CH ₃		38	12	7.42	7.92
C16	H	-CF ₃	-CN		230	19	6.64	7.72
C17*	H	H	H	H	110	16	6.96	7.80
C18	F	H	H	H	61	9.3	7.21	8.03
C19	H	F	H	H	150	20	6.82	7.70
C20	-Cl	H	H	H	27	11	7.57	7.96
C21	H	-Cl	H	H	35	8.3	7.46	8.08
C22	-CN	H	H	H	51	8	7.29	8.10
C23	H	-CN	H	H	150	8.2	6.82	8.09
C24	-CF ₃	H	H	H	150	120	6.82	6.92
C25	H	-CF ₃	H	H	67	30	7.17	7.52
C26	-OCF ₃	H	H	H	210	55	6.68	7.26
C27	H	-OCF ₃	H	H	220	41	6.66	7.39
C28	H	-OCH ₃	H	H	290	26	6.54	7.59
C29	H	-Cl	H	-CH ₃	9.2	3.3	8.04	8.48
C30*	H	-CF ₃	H	-CH ₃	27	11	7.57	7.96
C31	H	-OCF ₃	H	-CH ₃	50	17	7.30	7.77
C32	H	-CF ₃	H		15	6.3	7.82	8.20
C33*	H	-CF ₃	H		18	7.1	7.74	8.15
C34	H	-CF ₃	H		47	17	7.33	7.77
C35*	H	-CF ₃	H		31	8.5	7.51	8.07
C36	H	-CF ₃	H		53	11	7.28	7.96

C37*	H	-CF ₃	H		56	14	7.25	7.85
C38	H	-Cl	H		6.7	2.9	8.17	8.54
C39*	H	-Cl	H		9.8	4.1	8.01	8.39
C40	H	-Cl	H		11	11	7.96	7.96

* Asterisk showing test set molecule

Table S2. Observed and predicted activity along with residuals for dual inhibitors (EGFR/HER2) activities of the single as well as dual response of G-QSAR models

Comp Id	EGFR					HER2				
		Single		Dual			Single		Dual	
	Actual pIC ₅₀	Pred.	Residual	Pred.	Residual	Actual pIC ₅₀	Pred.	Residual	Pred.	Residual
C1	8.02	8.15	-0.13	8.13	-0.11	8.39	8.34	0.05	8.51	-0.12
C2	7.47	7.55	-0.08	7.51	-0.04	7.92	7.88	0.04	8.03	-0.11
C3	6.96	7.15	-0.19	7.34	-0.38	7.54	7.67	-0.13	7.86	-0.32
C4	8.24	8.15	0.09	8.13	0.11	8.68	8.53	0.15	8.51	0.17
C5	7.82	7.55	0.27	7.51	0.31	8.29	8.06	0.23	8.03	0.26
C6	7.31	7.15	0.16	7.34	-0.03	8.08	7.86	0.22	7.86	0.22
C7	7.48	7.50	-0.02	7.42	0.06	7.82	8.06	-0.24	7.97	-0.15
C8	7.66	7.53	0.13	7.47	0.19	8.11	8.06	0.05	8.00	0.11
C9	7.36	7.42	-0.06	7.45	-0.09	8.03	8.06	-0.03	7.99	0.04
C10	7.51	7.45	0.06	7.51	0.00	7.92	8.01	-0.09	8.03	-0.11
C11	7.4	7.48	-0.08	7.56	-0.16	7.92	8.01	-0.09	8.06	-0.14
C12*	7.82	7.55	0.27	7.50	0.32	8.24	7.98	0.26	8.02	0.22
C13	7.46	7.54	-0.08	7.42	0.04	7.82	7.71	0.11	7.67	0.15
C14	7.64	7.53	0.11	7.42	0.22	7.77	7.83	-0.06	7.75	0.02
C15	7.42	7.55	-0.13	7.51	-0.09	7.92	7.90	0.02	8.03	-0.11
C16	6.64	6.60	0.04	6.60	0.04	7.72	7.74	-0.02	7.78	-0.06
C17*	6.96	7.18	-0.22	7.25	-0.29	7.8	7.88	-0.08	8.00	-0.20
C18	7.21	7.18	0.03	7.25	-0.04	8.03	7.88	0.15	8.00	0.03
C19	6.82	6.78	0.04	7.18	-0.36	7.7	7.67	0.03	7.93	-0.23

C20	7.57	7.18	0.39	7.25	0.32	7.96	7.88	0.08	8.00	-0.04
C21	7.46	7.77	-0.31	7.43	0.03	8.08	8.34	-0.26	8.06	0.02
C22	7.29	7.18	0.11	7.25	0.04	8.1	7.88	0.22	8.00	0.10
C23	6.82	7.18	-0.36	7.01	-0.19	8.09	7.88	0.21	7.76	0.33
C24	6.82	6.85	-0.03	6.68	0.14	6.92	6.96	-0.04	6.98	-0.06
C25	7.17	7.18	-0.01	6.81	0.36	7.52	7.88	-0.36	7.58	-0.06
C26	6.68	6.68	0.00	6.82	-0.14	7.26	7.19	0.07	7.24	0.02
C27	6.66	6.78	-0.12	6.64	0.02	7.39	7.67	-0.28	7.41	-0.02
C28	6.54	6.78	-0.24	6.85	-0.31	7.59	7.67	-0.08	7.61	-0.02
C29	8.04	8.05	-0.01	7.94	0.10	8.48	8.34	0.14	8.39	0.09
C30*	7.57	7.45	0.12	7.33	0.24	7.96	7.88	0.08	7.91	0.05
C31	7.3	7.05	0.25	7.15	0.15	7.77	7.67	0.10	7.74	0.03
C32	7.82	7.52	0.30	7.54	0.28	8.2	8.12	0.08	8.05	0.15
C33*	7.74	7.46	0.28	7.52	0.22	8.15	8.01	0.14	8.03	0.12
C34	7.33	7.39	-0.06	7.45	-0.12	7.77	7.69	0.08	7.70	0.07
C35*	7.51	7.46	0.05	7.52	-0.01	8.07	8.06	0.01	8.03	0.04
C36	7.28	7.39	-0.11	7.51	-0.23	7.96	8.04	-0.08	8.02	-0.06
C37*	7.25	7.34	-0.09	7.46	-0.21	7.85	7.74	0.11	7.82	0.03
C38	8.17	8.11	0.06	8.16	0.01	8.54	8.58	-0.04	8.53	0.01
C39*	8.01	8.05	-0.04	8.14	-0.13	8.39	8.47	-0.08	8.52	-0.13
C40	7.96	7.99	-0.03	8.06	-0.10	7.96	8.15	-0.19	8.18	-0.22

where,

Pred. = Predicted activity

Residual = Actual – Predicted activity

* Asterisk showing test set molecules

Table S3. Statistical results of the various fragment based dual QQSAR models

Statistical parameter	PLS-SWFB		PLS-SA		PLS-GA		MLR-SWFB		MLR-GA		PCR-SWFB		PCR-SA		PCR-GA	
	EGFR	HER2	EGFR	HER2	EGFR	HER2	EGFR	HER2	EGFR	HER2	EGFR	HER2	EGFR	HER2	EGFR	HER2
r²	0.50	0.50	0.83	0.84	0.66	0.59	0.60	0.40	0.71	0.68	0.47	0.47	0.76	0.76	0.67	0.67
q²	0.42	0.36	0.64	0.76	0.35	0.37	0.46	0.04	0.49	0.49	0.14	0.14	0.58	0.58	0.28	0.28
pred_r²	0.39	0.47	0.64	0.71	0.29	0.49	0.36	0.42	0.42	0.52	-0.13	-0.13	0.49	0.49	-0.02	-0.02
r²_se	0.33	0.26	0.20	0.16	0.28	0.24	0.30	0.29	0.27	0.23	0.35	0.35	0.24	0.24	0.29	0.29
q²_se	0.35	0.29	0.30	0.19	0.38	0.30	0.35	0.37	0.36	0.29	0.45	0.45	0.32	0.32	0.42	0.42
F-test	30.91	31.02	26.73	29.29	28.75	21.33	14.48	6.45	10.50	9.12	6.33	6.33	17.37	17.37	10.89	10.89
Zscore_r²	12.54	7.25	9.93	6.44	7.63	4.10	16.29	16.43	8.13	7.64	3.79	3.79	6.59	6.59	6.12	6.12
Zscore_q²	5.98	4.29	3.69	4.74	2.64	3.40	4.47	3.07	2.67	2.03	1.61	1.61	4.39	4.39	3.56	3.56