Figure S1. Active (blue text) and inactive compounds from the Published Kinase Inhibitor Set within the 'furopyrimidines and related' chemotype series that were selected from the phenotypic and viability screen of MCF7-CXCR4-ΔCTD compared with MCF7-fulvestrant-resistant cells. Representative images captured using brightfield microscopy are shown (magnification, x4). ΔCTD, truncated COOH-terminal domain; CXCR4, chemokine receptor 4.

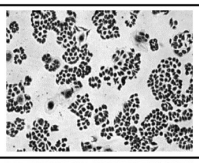
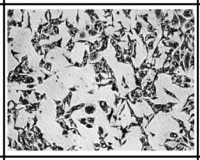
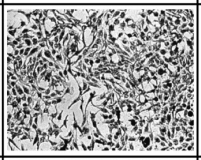
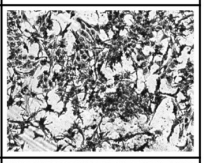
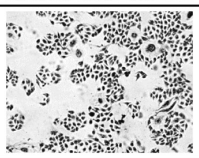
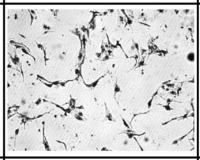
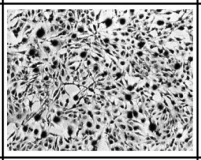
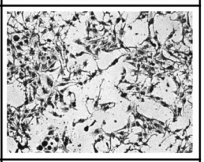
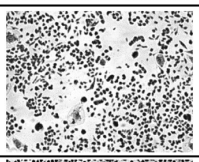
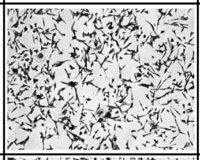
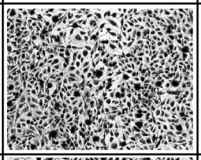
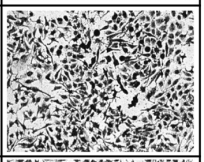
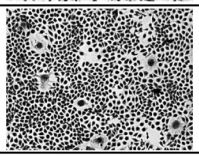
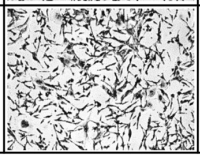
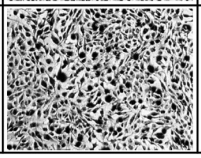
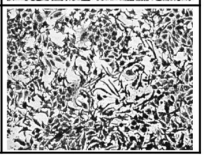
	Chemotype	**MCF7-CXCR4-ΔCTD**	**MDA-MB-231**	**MDA-MB-157**	**BT549**
GW856804X	Furopyrimidines_and_related				
GW795486X	Furopyrimidines_and_related				
GW642125X	Furopyrimidines_and_related				
GW642138X	Furopyrimidines_and_related				

Figure S2. Active (blue text) and inactive compounds from the Published Kinase Inhibitor Set within the '4-hydrazinly pyrazolopyrimidine' chemotype series that were selected from the phenotypic screen of MCF7-CXCR4-ΔCTD compared with triple-negative breast cancer cell lines (MDA-MB-231, BT-549 and MDA-MB-157). Representative images captured using brightfield microscopy are shown. ΔCTD, truncated COOH-terminal domain; CXCR4, chemokine receptor 4.

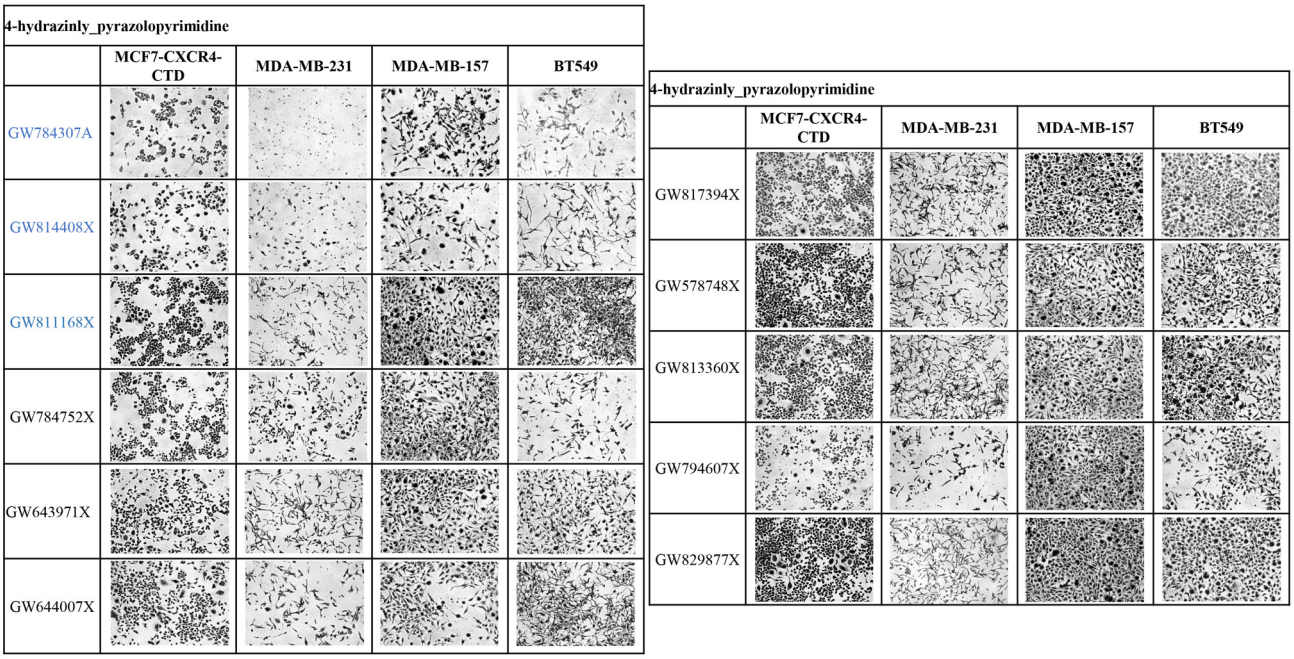


Figure S3. Active (blue text) and inactive compounds from the Published Kinase Inhibitor Set within the 'oxindole' chemotype series that were selected from the phenotypic screen of MCF7-CXCR4-ΔCTD compared with triple-negative breast cancer cell lines (MDA-MB-231, BT-549 and MDA-MB-157). Representative images captured using brightfield microscopy are shown. ΔCTD, truncated COOH-terminal domain; CXCR4, chemokine receptor 4.

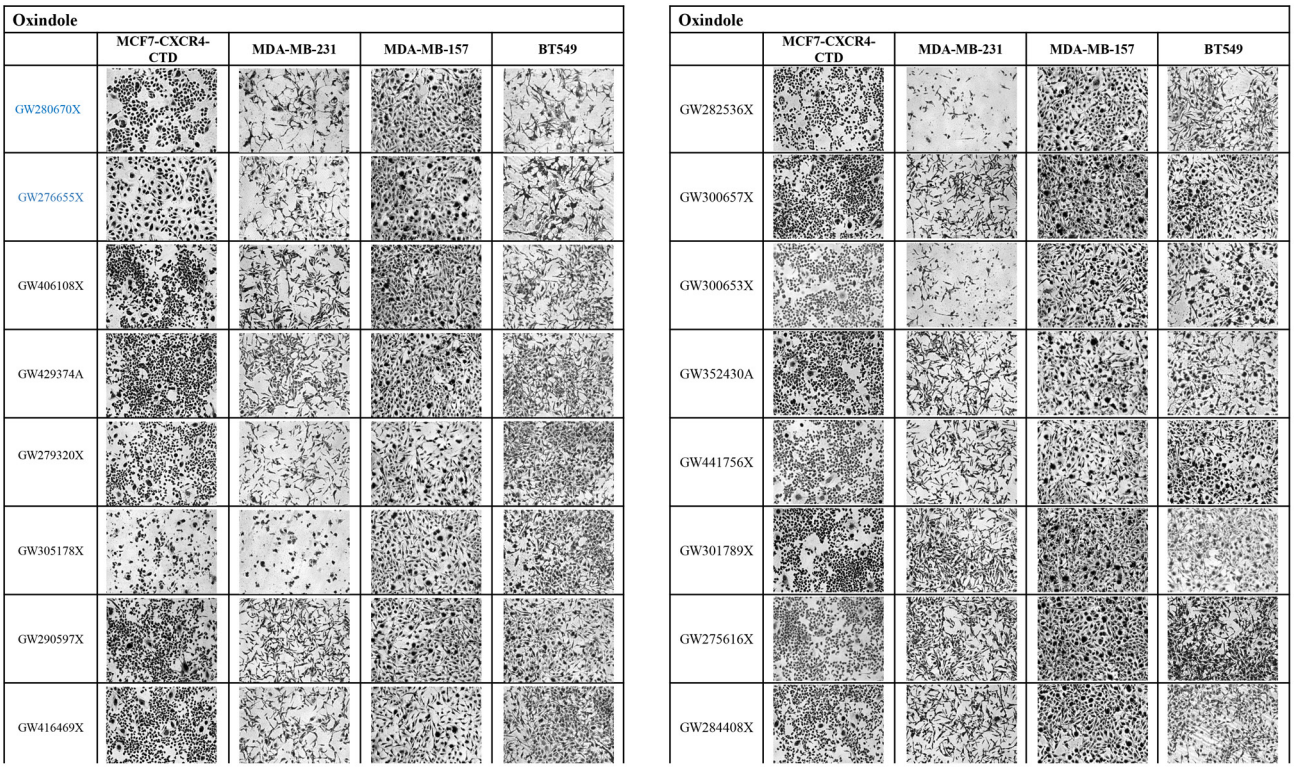


Figure S4. Active (blue text) and inactive compounds from the Published Kinase Inhibitor Set within the '2,4-dianilino pyrrolopyrimidines' chemotype series that were selected from the phenotypic and viability screen of MCF7-CXCR4-ΔCTD compared with MCF7-FR cells. Representative images captured using brightfield microscopy are shown. ΔCTD, truncated COOH-terminal domain; CXCR4, chemokine receptor 4; FR, fulvestrant-resistant.

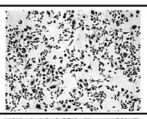
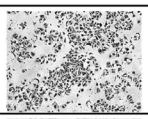
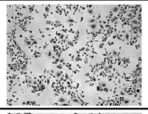
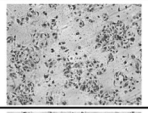
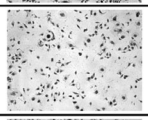
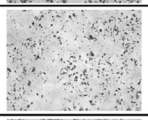
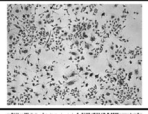
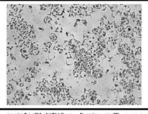
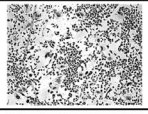
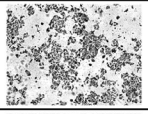
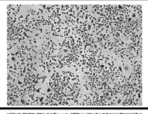
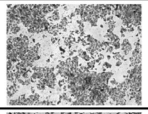
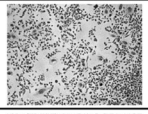
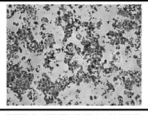
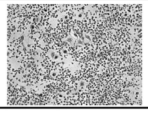
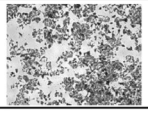
	MCF7-CXCR4-ΔCTD	**MCF7-FR**
GSK1173862A		
GSK994854A		
GSK2213727A		
GSK2163632A		
GSK1392956A		
GSK2219385A		
GSK1511931A		
GSK1819799A		

Figure S5. Active (blue text) and inactive compounds from the Published Kinase Inhibitor Set within the '2-aryl 3-pyridimidinyl pyrazolopyridazines' chemotype series that were selected from the phenotypic and viability screen of MCF7-CXCR4-ΔCTD compared with MCF7-FR cells. Representative images captured using brightfield microscopy are shown. ΔCTD, truncated COOH-terminal domain; CXCR4, chemokine receptor 4; FR, fulvestrant-resistant.

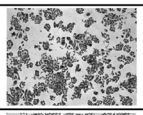
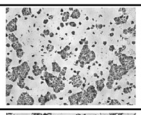
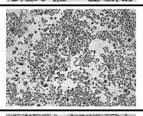
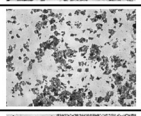
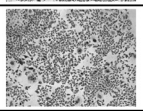
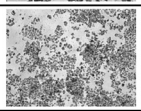
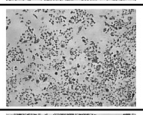
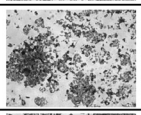
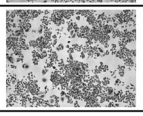
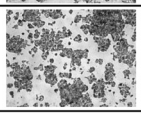
	MCF7-CXCR4-ΔCTD	**MCF7-FR**
GW827099X		
GW827396X		
GW829055X		
GW828525X		
GW829906X		

Figure S6. Active (blue text) and inactive compounds from the Published Kinase Inhibitor Set within the '3-amino pyrazolopyridines' chemotype series that were selected from the phenotypic and viability screen of MCF7-CXCR4-ΔCTD compared with MCF7-FR cells. Representative images captured using brightfield microscopy are shown. ΔCTD, truncated COOH-terminal domain; CXCR4, chemokine receptor 4; FR, fulvestrant-resistant.

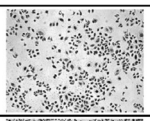
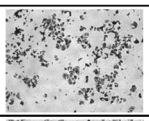
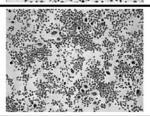
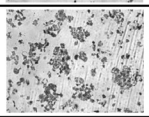
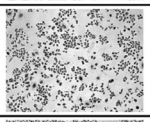
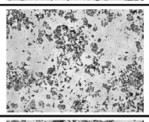
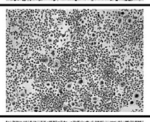
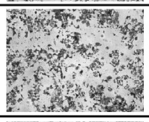
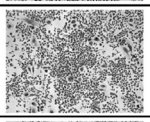
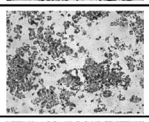
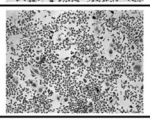
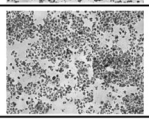
	MCF7-CXCR4-ΔCTD	**MCF7-FR**
SB-725317		
SB-711237		
SB-732881-H		
SB-739452		
SB-739245-AC		
SB-743899		

Figure S7. Active (blue text) and inactive compounds from the Published Kinase Inhibitor Set within the 'maleimide' chemotype series that were selected from the phenotypic and viability screen of MCF7-CXCR4-ΔCTD compared with MCF7-FR cells. Representative images captured using brightfield microscopy are shown. ΔCTD, truncated COOH-terminal domain; CXCR4, chemokine receptor 4; FR, fulvestrant-resistant.

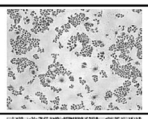
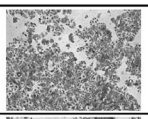
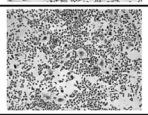
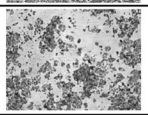
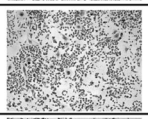
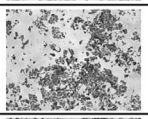
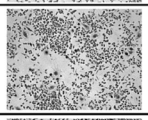
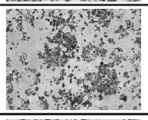
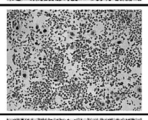
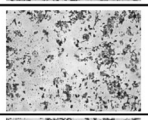
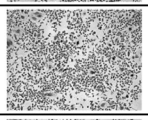
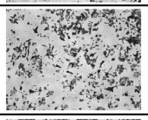
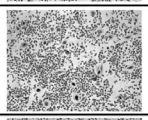
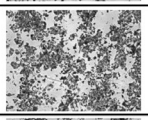
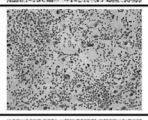
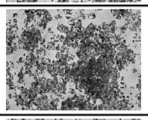
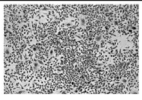
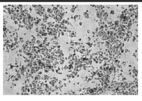
	MCF7-CXCR4-ΔCTD	**MCF7-FR**
GW296115X		
SB-409514		
SB-409513		
SKF-62604		
SB-333612		
SB-361058		
SB-360741		
SB-390523		
SB-390527		

Figure S8. Active (blue text) and inactive compounds from the Published Kinase Inhibitor Set within the 'furopyrimidines and related' chemotype series that were selected from the phenotypic and viability screen of MCF7-CXCR4-ΔCTD compared with MCF7-FR cells. Representative images captured using brightfield microscopy are shown. ΔCTD, truncated COOH-terminal domain; CXCR4, chemokine receptor 4; FR, fulvestrant-resistant.

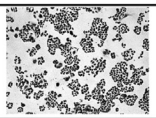
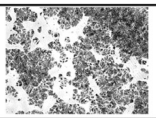
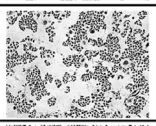
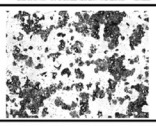
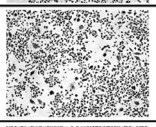
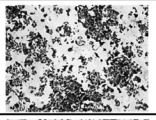
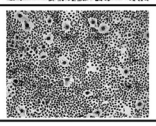
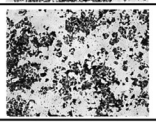
	MCF7-CXCR4-ΔCTD	**MCF7-FR**
GW856804X		
GW795486X		
GW642125X		
GW642138X		

Figure S9. Kinases selectively inhibited by ‘active’ compounds alone compared with ‘inactive’ compounds in the same chemotype. Heat map of (A) the maleimide chemotype and (B) the 3-amino-pyrazolopyridines chemotype classes. Percent kinase activity is represented in the heat maps, with green indicating high activity and red low activity. Compounds in blue were identified as ‘hits’ in the screen. All cells were treated at 1 μM inhibitor for 72 h.

A **Chemotype: Maleimide**

	GW296115X	SB-409514	SB-409513	SKF-62604	SB-333612	SB-361058	SB-360741	SB-390523	SB-390527	SB-376719
ABL-Q	72	3	5	7	4	6	2	5	2	17
HCK	76	3	4	15	13	10	4	8	5	16
PYK2	81	9	7	14	7	16	3	13	9	13
LTK	78	0	3	8	2	5	0	5	1	3
ROS	79	7	1	6	14	10	3	4	6	10
RET	77	8	4	10	10	6	3	6	8	12
RET-V791F	82	1	8	9	9	7	-1	17	3	13
KIT	80	-3	5	15	12	15	0	12	1	5
KIT-D	75	-7	6	8	2	3	-3	6	3	1
FLT3	79	1	0	4	5	3	2	5	3	2
FLT3-D	93	4	-4	3	15	4	3	3	4	3
PDGFRa	84	15	10	19	15	16	7	15	10	14
PDGFRa-D	96	6	2	5	7	8	3	1	-1	3
PDGFRa-T	94	1	6	10	7	11	1	7	3	7
PDGFRa-V	97	9	0	5	7	7	3	0	2	1
PDGFRb	85	11	9	14	9	12	7	14	3	10
TNK1	89	9	11	9	0	14	1	12	3	16
MAP4K4	88	7	8	20	10	13	1	5	7	11
MINK	85	8	8	18	10	11	-1	5	6	8
PDK1	76	5	2	2	1	6	2	1	3	3
RSK1	82	8	3	10	0	4	-1	4	4	5
RSK2	80	14	2	12	1	2	-2	2	4	5
RSK4	88	21	3	9	1	4	-1	1	7	11
RSK3	92	20	2	10	2	4	-1	3	6	11
P70S6K1	84	1	2	2	2	3	-1	0	1	3
PIM3	83	1	0	10	-2	1	0	4	-1	1
BRSK1	102	13	0	9	5	3	1	2	6	7
BRSK2	95	19	2	11	3	3	-2	4	9	12
QIK	78	20	5	14	5	11	-3	0	11	28
SIK	77	9	5	13	7	8	-5	6	6	18
AURORAC	87	13	-1	-1	16	-4	-4	-3	7	-1
CHEK2	83	2	3	2	9	4	-2	4	2	-2

B

Chemotype:3-amino_pyrazolopyridines

	SB-725317	SB-711237	SB-732881-H	SB-739452	SB-739245-AC
ABL-H	81	28	14	26	8
ABL-M	81	27	10	30	5
ABL-Q	82	14	16	32	12
ABL-T	88	21	16	27	23
LTK	92	1	36	1	1
ALK	72	2	45	4	-1
KDR	72	3	23	15	16
MAP4K4	75	33	22	9	10
RSK3	71	2	6	3	0
BRSK2	70	11	27	11	19
PIM2	75	0	16	0	1
PIM3	74	1	45	-3	6
CDK2/cyclin E	73	5	33	9	5