

Supplementary

Table S1 Kinase inhibitory profiling studies of CB538 on Axl and other tyrosine kinases

Kinase inhibition(%) at 0.5 μ M CB538	
Kinase	Kinase inhibition(%)
Abl	0
B-Raf	0
cSRC	5
EGFR	0
Flt	0
Fms	4
FGFR	0
cKit	0
KDR	7
PDGFR	0
RET	0
Syk	12
DDR1	48
AxL	68
Ron	76
Mer	100

The in vitro ability of CB538 to inhibit kinases in biochemical formats was conducted by Eurofins Pharma Discovery Service (Dundee, UK), and the inhibition potency of CB538 was incubated with a fixed concentration of recombinant human enzyme at the K_m value of ATP.

Table S2 Kinase inhibitory effect of CB538 on MET kinases

Kinase, IC ₅₀ (nM)	CB538	Glesatinib	Type I inhibitor	
			Capmatinib	Crizotinib
MET	0.5	10.2	55.5	261.6
MET exon14del	17.1	7.4	31.9	34.1
MET D1228N	2.1	7.3	6,901	107.5
MET D1228Y	0.2	N/A	N/A	N/A
MET Y1230H	0.7	1.5	>10,000	145.9

The in vitro kinase assay was measured by 10-point concentration-response using the ADP-Glo™ luminescent kinase and the c-Met enzyme inhibition potency of MET-TKIs was determined using recombinant human c-Met protein. IC₅₀ was evaluated at 10 μ mol/L ATP. N/A, not applicable.