

## The pharmacodynamic and mechanistic foundation for the antineoplastic effects of GFH009, a potent and highly selective CDK9 inhibitor for the treatment of hematologic malignancies

### SUPPLEMENTARY MATERIALS

**Supplementary Table 1: Inhibitory action of GFH009 on other CDK family members**

Various CDK/ cognate cyclin pairs tested	Remaining enzymatic activity (%) after exposure to GFH009 at a concentration of 1 $\mu$ M/10 $\mu$ M	Selectivity vs. CDK9
Cdc7/cyclinB1	75/47	>100
CDK1/cyclin B	97/50	>1000
CDK2/cyclin A	80/51	>1000
CDK2/cyclin E	63/27	>100
CDK3/cyclin E	74/39	>100
CDK4/cyclin D3	70/41	>100
CDK5/p25	79/43	>100
CDK5/p35	66/43	>100
CDK6/cyclin D3	85/58	>1000
CDK7/cyclin H/MAT1	67/19	>100
CDK12/cyclin K	94/86	>1000
CDK13/cyclin K	93/88	>1000
CDK14/cyclin Y	70/39	>100
CDK16/cyclin Y	23/5	<100
CDK17/cyclin Y	30/7	<100
CDK18/cyclin Y	53/12	>100

**Supplementary Table 2: Results of GPCR agonist action testing of GFH009 administered at a maximum dose of 12  $\mu$ M**

Agonist action against GPCR type shown below

<b>Target</b>	<b>% Agonist Effect @ Max Dose (12 <math>\mu</math>M)</b>
5-HT1A (serotonin)	-0.33
5-HT1B (serotonin)	-51.01
5-HT2A (serotonin)	-1.68
5-HT2B (serotonin)	4.55
$\alpha$ 1a (adrenoceptor)	4.58
$\alpha$ 2a (adrenoceptor)	-3.87
AD2 (adenosine)	21.7
b1 (adrenoceptor)	4.53
b2 (adrenoceptor)	-0.6
CB1 (cannabinoid)	-0.7
CB2 (cannabinoid)	0.23
CCKa	-0.4
D1 (dopamine)	-1.49
D2 (dopamine)	3.66
ETA (endothelin)	-0.08
H1 (histamine)	1.55
H2 (histamine)	-0.03
M1 (muscarinic Ach)	-2.18
M2 (muscarinic Ach)	-0.63
M3 (muscarinic Ach)	0.49
op-d (opioid)	-0.98
op-k (opioid)	21.57
op-m (opioid)	0.71
V1A (vasopressin)	0.59

**Supplementary Table 3: Results of off-target inhibitory action testing of GFH009 administered at a maximum dose of 10  $\mu$ M****Competitive antagonist activity against GPCR type shown below**

<b>Target</b>	<b>% Inhibitory Effect @ Max Dose (10 <math>\mu</math>M)</b>
5-HT1A (serotonin)	12.31
5-HT1B (serotonin)	4.71
5-HT2A (serotonin)	-7.10
5-HT2B (serotonin)	-24.98
a1a (adrenoceptor)	68.39
a2a (adrenoceptor)	5.16
AD2 (adenosine)	-13.58
b1 (adrenoceptor)	30.48
b2 (adrenoceptor)	-3.46
CB1 (cannabinoid)	-9.21
CB2 (cannabinoid)	-8.86
CCKa	16.26
D1 (dopamine)	1.10
D2 (dopamine)	10.34
ETA (endothelin)	-0.32
H1 (histamine)	12.37
H2 (histamine)	-18.49
M1 (muscarinic Ach)	98.78
M2 (muscarinic Ach)	95.69
M3 (muscarinic Ach)	99.12
op-d (opioid)	-15.46
op-k (opioid)	11.54
op-m (opioid)	20.94
V1A (vasopressin)	-1.57