Supplementary information S1 | **Sample MIABE file exemplifying data extracted from PMID: 20568778**

Responsible Person or Role			
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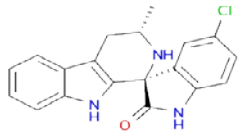
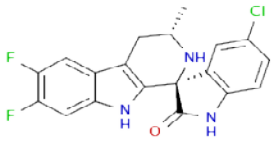
MIABE Criteria	Mapping 9a	Mapping 20a	Data Source (Page No or Database) (MI:0444)	Comments
Molecule properties				
Primary Name	Compound 9a	Compound 20a	p. 5158	Novel compounds, no common name available
ChEBI AC No.	CHEBI:731077	CHEBI:730276	ChEBI (MI:0474)	
ChEMBL AC No.	CHEMBL1083769	CHEMBL1082725	ChEMBL (MI:0967)	
Molecule type (MI:0313)	Small molecule (MI:0328)	Small molecule (MI:0328)		
IUPAC Name (MI:2007)	(1R,3S)-50 -Chloro-3-methyl-2,3,4,9-tetrahydrospiro[β-carboline-1,30 -indol-20 (10 H)-one	(1R,3S)-50 -Chloro-6,7-difluoro-3-methyl-2,3,4,9-tetrahydrospiro-[β-carboline-1,30 -indol]-20 (10 H)-one	p. 5162	
Chemical structure (MI:2009)			p. 5158 (Table 3)	Drawn in full with stereochemistry specified
InChi Key (MI:0970)	QGMFKGFHTXZZHX-APBUJDDRSA-N (standard), QGMFKGFHTXZZHX-APBUJDDRBH (non-standard)	JZCVYBQWYSYJEA-WPCRTTGESA-N (standard), JZCVYBQWYSYJEA-WPCRTTGEBH (non-standard)		Not specified in paper
Chemical Salt	None	None		
Prodrug	No	No		

Molecule production				
Chemical Synthesis	Synthesis described fully on page 5161-2	Synthesis described fully on page 5162	p. 5162	
% Purity	Determined by LC/MS and HPLC to be > 95%	Determined by LC/MS and HPLC to be > 95%	P5160	

Physicochemical properties				
Molecular weight (MI:2025)	337.80283	373.78376	ChEMBL	Not specified in paper
Water solubility (MI:2027)	194mg/mL (pH 6.8)	170mg/mL (pH 6.8)	5157 (Table 2)	experimentally determined, method not described
LogP (MI:2029)	experimental logP = 3.4 (calculated logD pH7.4 = 3.5)	experimental logP = 4 (calculated logD pH7.4 = 3.9)	5157 (Table 2)	experimentally determined, method not described

In Vitro Assays				
Primary target	Human CYP2C9	Human CYP2C9	5158 (Table 3)	No accession given but species/name clearly stated and unambiguous
Assay details	Inhibition of CYP2C9 in human liver microsomes, using diclofenac as a measure of activity, and monitoring the reduction in CYP activity as a function of compound concentration, quantified by product formation using ESI + LC-MS/MS.	Inhibition of CYP2C9 in human liver microsomes, using diclofenac as a measure of activity, and monitoring the reduction in CYP activity as a function of compound concentration, quantified by product formation using ESI + LC-MS/MS.	S5 + supplementary reference 3d	Details for standard assays given in supplementary reference 3d
Assay parameters			Supplementary reference 3d	Not given, assumed to be as in supplementary references 3b/3d
Delivery systems	Liver microsomes	Liver microsomes	S5 + supplementary reference 3b	Compound preparation assumed to be as in supplementary reference 3b
Results	IC50 = 1.51μM	IC50 = 7.35μM	p. 5158 (Table 3)	
Secondary targets	Inactive against CYP 3A4 + 2D6	Inactive against CYP 3A4 + 2D6	p. 5158	

In vitro assays (2)				
Primary target	Liver enzymes	Liver enzymes	p. 5158 (Table 3)	Intrinsic clearance in liver microsomes
Assay details	Metabolic stability in liver microsomes, measured using a compound depletion approach and quantified by LC/MS	Metabolic stability in liver microsomes, measured using a compound depletion approach and quantified by LC/MS	S4-5 + supplementary reference 1b	Details for standard assay given in supplementary reference 1b
Assay parameters			Supplementary reference 1b	Not given, assumed to be as in supplementary reference 1b
Delivery systems	Liver microsomes	Liver microsomes	S4 and supplementary reference 1b	Compound preparation assumed to be as in supplementary reference 1b
Results	Intrinsic clearance = high (mouse), high (human)	Intrinsic clearance = low (mouse), low (human)	p. 5158 (Table 3)	
Secondary targets	N/A	N/A		

Cellular Assays				
Cell type	Human erythrocytes, infected with Plasmodium falciparum NF54	Human erythrocytes, infected with Plasmodium falciparum NF54	S7-8	Screen described in more detail in supplementary information of reference 3a
Culture conditions	Parasites cultivated in medium consisting of RPMI 1640 supplemented with 0.5% ALBUMAX II, 25mM Hepes, 25mM NaHCO3 (pH7.3), 0.36mM hypoxanthine and 100mg/mL neomycin (described more fully in reference 17). Cultures maintained in atmosphere of 3% O2, 4% CO2, 93% N2 in humidified modular chambers at 37ºC.	Parasites cultivated in medium consisting of RPMI 1640 supplemented with 0.5% ALBUMAX II, 25mM Hepes, 25mM NaHCO3 (pH7.3), 0.36mM hypoxanthine and 100mg/mL neomycin (described more fully in reference 17). Cultures maintained in atmosphere of 3% O2, 4% CO2, 93% N2 in humidified modular chambers at 37ºC.	S7-8 + reference 17	Test of blood quality described in reference 3a
Agonists/antagonists	Compounds dissolved in DMSO (10mM) and diluted in hypoxanthine-free culture medium. Titrated in duplicates over a 64-fold range in 96 well plates.	Compounds dissolved in DMSO (10mM) and diluted in hypoxanthine-free culture medium. Titrated in duplicates over a 64-fold range in 96 well plates.	S8	

Results	IC50 = 9nM	IC50 = 0.2nM	5156 (Figure 2) + 5158 (Table 3)	
Secondary cellular assay	N/A	N/A		
Toxicological observations	N/A	N/A		

Cellular Assays (2)				
Cell type	Human erythrocytes, infected with Plasmodium falciparum K1			
Culture conditions	Parasites cultivated in medium consisting of RPMI 1640 supplemented with 0.5% ALBUMAX II, 25mM Hepes, 25mM NaHCO3 (pH7.3), 0.36mM hypoxanthine and 100mg/mL neomycin (described more fully in reference 17). Cultures maintained in atmosphere of 3% O2, 4% CO2, 93% N2 in humidified modular chambers at 37ºC.		S7-8 + reference 17	Test of blood quality described in reference 3a
Agonists/antagonists	Compounds dissolved in DMSO (10mM) and diluted in hypoxanthine-free culture medium. Titrated in duplicates over a 64-fold range in 96 well plates.		S8	
Results			p. 5156 (Figure 2)	
Secondary cellular assay	N/A	N/A		
Toxicological observations	N/A	N/A		

Whole Organism Studies				
Animal studies	In vivo antimalarial activity. Female NMRI mice (20-22g).	In vivo antimalarial activity. Female NMRI mice (20-22g).	S8	Age not given, all other conditions assumed normal
Plant studies	N/A	N/A		
Fungal studies	N/A	N/A		
Disease models	Plasmodium berghei infected mouse model (strain GFP ANKA)	Plasmodium berghei infected mouse model (strain GFP ANKA)	S8 and supplementary reference 6	
Dosing route	Intravenous infection with parasite, oral dosing with compound	Intravenous infection with parasite, oral dosing with compound	S8	
Dosing schedule	Compounds formulated with 10% ethanol, 30% PEG400 and 6% vitamin E TPGS and administered in a volume of 10mL/kg as either a single dose (24h post infection) or three consecutive daily doses (24, 48 + 72h post infection)	Compounds formulated with 10% ethanol, 30% PEG400 and 6% vitamin E TPGS and administered in a volume of 10mL/kg as either a single dose (24h post infection) or three consecutive daily doses (24, 48 + 72h post infection)	S8	
Results	Single dose: reduced parasitemia on day 3 by 99.9%, prolonged survival time to 10.7 days; Multiple dose: reduced parasitemia on day 4 by 99.9%, prolonged survival time to 14.6 days	Single dose: reduced parasitemia on day 3 by 99.6%, prolonged survival time to 12.0 days; Multiple dose: reduced parasitemia on day 4 by 99.8%, prolonged survival time to 17.2 days	p. 5159 (Table 5+6)	
Toxicological observations	No toxicity or behavioural changes observed at any dose	No toxicity or behavioural changes observed at any dose	5160	
Drug-drug interactions				

Pharmacokinetic Studies				
Absorption	AUC = 3.88μM/h	AUC = 71.44μM/h	5159 (Table 4), S5-7	
Protein binding	ND	ND		Not measured
Dosing route	Oral and IV	Oral and IV	5159 (Table 4), S5-7	
Dosing schedule	Single dose at 25mg/kg (oral) and 5mg/Kg (iv)	Single dose at 25mg/kg (oral) and 5mg/Kg (iv)	5159 (Table 4), S5-7	Sampling timepoints described in S5/6

T1/2	0.66 h (oral), 0.42 h (iv)	3.18 h (oral), 2.94 h (iv)	5159 (Table 4), S5-7	
Cmax	3.58μM (Tmax 0.25 h)	8.32μM (Tmax 2 h)	5159 (Table 4), S5-7	
Volume of distribution	Vss = 0.91 L/kg (iv)	Vss = 1.60 L/kg (iv)	5159 (Table 4), S5-7	
Bioavailability	F = 13% (oral)	F = 53% (oral)	5159 (Table 4), S5-7	
Metabolism	IC50 = 1.51μM Human CYP2C9	IC50 = 7.35μM Human CYP2C9	5159 (Table 4), S5-7	
Metabolites	ND	ND		
Excretion	CL = 49.66 mL/min/kg (iv)	CL = 8.53 mL/min/kg (iv)	5159 (Table 4), S5-7	