

SAMPLE

Name:
Institution:
Proposal Title:

The proposal document should succinctly define the scientific nature and rationale of the proposed project. There is a 5-page maximum, not including the provided Data Tables Appendix. For additional detailed information, please refer to the Proposal Instructions. Additional supporting documents can be uploaded as appendices, as described in the Proposal Instructions. This paragraph and the “public reporting burden” footer text below may be removed in your final submission.

Background and Therapeutic Hypothesis

Replace text with the requested information...

Current State of Project

Replace text with the requested information...

Proposed Development Strategy

Replace text with the requested information...

Justification

Replace text with requested information...

Public reporting burden for this collection of information is estimated to average one hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden, to: NIH, Project Clearance Branch, 6705 Rockledge Drive, MSC 7974, Bethesda, MD 20892-7974, ATTN: PRA (0925-0658). Do not return the completed form to this address.

Data Tables Appendix:

Provide data on the proposed lead compound (specify Compound ID) by using the following tables. Provide ALL data requested, as available. If there are no data for a particular parameter or the data do not apply to your molecule, enter "N/A" or leave the value field blank. **DO NOT DELETE EMPTY CELLS.** For compound series, clearly identify structures, compound IDs, and corresponding data. Additional data may be provided in supplemental tables as appropriate and as described in the Proposal Instructions.

I. Compound Properties Profile:

Provide structure or composition of lead compound in box below.

Lead Compound

Structure or Composition

Calculated Properties	Value	Goal
Compound ID		
MW		< 500
Log D _{7.4} , cLog P		1-3, 1-4.5
TPSA		< 140 (oral), < 90 (CNS)
Ligand Efficiency (LE, LELP)		> 0.29, <10
Rotatable Bonds		≤ 10
N + O (HBA)		≤ 10
NH + OH (HBD)		≤ 5

<i>In Vitro</i> Properties	Units	Value & Class	Goal
Solubility (pH, media)	($\mu\text{g/mL}$)		> 60
Stability – Microsomes (species)	$t_{1/2}$ (min)		> 30
	CL_{int} (mL/min/mg)		< 10
Stability – Hepatocytes (species)	$t_{1/2}$ (min)		> 120
	CL_{int} , $\mu\text{L/min}/10^6$ cells		< 5
Stability – Plasma (species)	% Remaining at 3 hr		> 80%
Stability – Solution (media)	% Remaining at 24 hr		> 80%
CYP450 Inhibition (isozymes)	% Inhibition at 3 μM		< 15%
	IC_{50} (μM)		> 10
	C_{max} at MED / K_i		< 0.1
Plasma Protein & Tissue Binding (species)	$F_{u, \text{plasma}}$ (%)		
	$F_{u, \text{tissue}}$ (%)		
Permeability – PAMPA	P_e (10^{-6} cm/s)		> 1
Permeability – PAMPA-BBB	P_e (10^{-6} cm/s)		> 4
Permeability – Caco-2	P_{app} (a-b, 10^{-6} cm/s)		> 10
	Efflux Ratio		< 3
Permeability – MDR1-MDCKII	P_{app} (a-b, 10^{-6} cm/s)		> 20
	Pgp Efflux Ratio		< 2
hERG (method)	IC_{50} (μM)		> 10
	IC_{50} / Free C_{max}		> 30
Free C_{max} – Plasma	Total C_{max} (μM) * $F_{u, \text{plasma}}$		
Free C_{max} – Tissue	Total C_{max} (μM) * $F_{u, \text{plasma}}$		
Screening Ames	Positive / Negative		Negative

II. Compound Efficacy Profile:

<i>In Vitro</i> Biology	Units	Value & Class	Goal
Activity			
(Assay 1) – IC ₅₀	nM		< 1000
(Assay 1) – K _i	nM		< 1000
(Assay 2) – IC ₅₀	nM		< 1000
(Assay 2) – K _i	nM		< 1000
Selectivity			
(Assay 1) – IC ₅₀ / Fold selectivity	nM		> 100
(Assay 2) – IC ₅₀ / Fold selectivity	nM		> 100

<i>In Vivo</i> Biology	Units	Value & Class
(Species, dose, route) – MED	nM	
(Species, dose, route) – MED	nM	
(Species, dose, route) – MED	nM	

PK Properties	Units	Dose (mpk), Route, Species	Dose (mpk), Route, Species	Goal
t _{1/2}	hr			> 3
AUC _{0-∞, total, unbound}	hr*ng/mL			> 500 (PO)
CL	mL/min/kg			< 25% HBF
C _{max, total, unbound}	ng/mL (nM)			
T _{max}	hr			
V _d	L/kg			
F	%			> 20%

III. Chemistry, Manufacturing and Controls:

Provide complete synthetic scheme, including details of isolation and purification, and yield for each step.

Synthetic Scheme

Representative Largest-Scale Batches

Batch	Quantity	Solid State, Salt Form, Polymorphs	Purity (%)	Major Impurities (%)

Late-Stage Formulation

Study	Formulation	Solubility	Stability	Recommended Storage Condition
Rodent Toxicity				
Non-Rodent Toxicity				
Phase I Human Trial				