

SAMPLE

Name & Degrees:
Institution:
Address:
E-mail:
Proposal Title:

This proposal should outline the scientific nature and rationale of the project. Refer to the BrIDGs Proposal Instructions for detailed descriptions of information requested in each section of this proposal. **The research description is limited to a maximum of 5 pages** (Arial 11pt, single-spaced, 1" margins). Figures and tables must be placed in-line with your text and will count against the page limit. The Data Collection Tables in the enclosed Appendix **do not** count against the limit. Required supporting materials are to be uploaded as described in the Instructions.

Background

Replace text with the requested information.

Available Data

Replace text with the requested information.

Development Plans

Replace text with the requested information.

Justification

Replace text with the 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.

Principal Investigator's Last
Name, First Initial

Abbreviated Title

Submission Date

REMINDER: There is a 5-page maximum to the preceding written portion of the proposal, inclusive of figures / tables you have included in-line with the above text. The Data Collection Tables in the following Appendix do not count against the 5-page maximum. They are meant to facilitate efficient data collection across a range of important values. Judicious use of the following tables and required uploaded Reference PDFs can allow provision of key data (e.g., supplemental figures) that otherwise may not fit into the page limits above.

Appendix: Data Collection Tables

Use the following tables to provide data, as available and applicable, on the proposed lead agent (specify Compound ID). If there are no data for a particular parameter, or the data do not apply to your molecule, leave the value field blank, or enter "N/A". **Do not delete empty cells.** Additional data may be provided in supplemental tables, as appropriate.

I. Compound Properties Profile:

Provide structure or composition of lead compound in box below (required).

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)	($\mu\text{g}/\text{mL}$)		> 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} , $\mu\text{L}/\text{min}/10^6$ 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 (required).

Synthetic Scheme

Representative Largest-Scale Batches

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

Late-Stage Formulation

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