

Template for a Preclinical Research Proposal

Preclinical Research Proposals should be brief and focus on novel research which advances the understanding of the target biology and mechanism(s) of action. The output of the research should provide further insight into pharmacological effects on the target that may relate to disease pathophysiology and therefore may support the development of potential new translational assessments or therapies.

Please complete this template below and enlarge each section as needed. Include published references to support the proposal.

- 1. Preclinical Research Proposal Title :** *Descriptive Title*
- 2. Hypothesis:** *Statement of the hypothesis for the compound and biological target in human disease. Brief evidence why this biological pathway may be important in the disease area under investigation.*
- 3. Outline of Research Plan**
 - *Specific aims including scientific rationale*
 - *Overview of the experimental plans including rationale for choice of in vitro cell/tissue assay and/or animal model with a clear study design and details of endpoints being measured. For in vitro cell assays, provide details on any cell lines that will be used. For in vivo studies justify choice of species, animal numbers and group size (e.g. using statistics/power analysis for primary endpoints). For studies using transgenic mouse, tissue or cells include details of the genetic background with appropriate published references.*
 - *Include approximate timelines for completing the work.*
 - *Anticipated outcome of results and describe the impact of the results (e.g. progressing this compound as a therapy or increasing understanding of mechanisms in disease).*
- 4. Operational feasibility** What has/has not been done before by you or members of your team? (Note: Innovative, novel approaches are welcome).
- 5. References:** *List of key publications used in your proposal.*
- 6. Project Decision Tree or Scheme of Work Flow Plan:** *Including estimated timelines.*

Notes

Out of scope: Standalone experiments that only look at pharmacokinetic or safety parameters, screening assays using multiple compounds and clinical studies should not be included in these preclinical research proposals.

Confidential information: Please include only **non-confidential information** in the concept proposal. If confidential data exists that would strengthen the proposal, the author may indicate that confidential information is available to share under a Confidential Disclosure Agreement (CDA). If AstraZeneca finds the non-confidential Concept Proposal sufficiently interesting, we will discuss about executing a CDA.

Additional details: During the submission process, additional details regarding the use of human tissue and/or animals will be requested.

7. Animal Use Risk Assessment for non-AZ funded external animal studies: *please complete if your research proposal includes the use of animals. Put a check (X) in each category that most accurately represents the animal model in the proposal.*

Species

- Invertebrates, fish, birds, fetal/larval forms, reptiles
- Mice, rats, hamsters
- Guinea pigs, rabbits, ferrets, mini pigs, genetically altered animals, other species
- Farm animals, equines, dogs, cats, harmful mutants, surgically prepared animals (any species)
- Non-human primates (NHPs)

Sensitivity

- Ex vivo studies, terminal studies, or studies on conscious animals with appropriate mitigation of pain/distress, but not involving any of the criteria in sensitivity selections below
- Studies use not humanely established or unconventional methods of euthanasia
- Models involve major surgery and/or repeated surgery, prolonged restraint, juvenile or neonatal animals
- Models of public concern, smoking, brain surgery/instrumentation, drug dependency in NHPs, unalleviated pain, or with death required as an endpoint

Potential for pain and distress

- Ex vivo or terminal studies
- Studies involve no more than minor or transient discomfort or stress (routine dosing/sampling) or have the potential to cause prolonged pain or distress but the use of anesthetics/analgesics provides appropriate mitigation
- Studies involve some pain or distress but with appropriate mitigation (most toxicity tests, surgery) or the potential to cause high degrees of pain or distress but procedures are terminated before pain or distress occurs
- Studies involve potential for significant pain or distress which cannot be alleviated but are scientifically justified (acute tox studies with significant morbidity or death as an endpoint, pain models)

Past engagement with AstraZeneca

- AstraZeneca and the external facility have had previous agreements over the last 5 years
- AstraZeneca and the external facility have had no previous agreements in the last 5 years

Name and Location* of external facility:

Reputation of facility

- Facility has external regulatory oversight, AAALAC accreditation or equivalent, and no history of security/media issues in last 3 years
- Facility has no external regulatory oversight, AAALAC accreditation, and no history of security/media issues in last 3 years
- Facility has no external regulatory oversight, no AAALAC accreditation, and no history of security/media issues in last 3 years
- Facility has no external regulatory oversight, no AAALAC accreditation and/or has a history of security/media issues in last 3 years

Please note the questions below. You will be required to provide responses to these questions in the online form.

- Can your institute assure AstraZeneca that any *in vivo* studies using animals, conducted under this proposal, will be performed in a manner consistent with the principles of AstraZeneca's Bioethics policy?
(<https://www.astrazeneca.com/sustainability/resources.html#global-policies-and-positions-0>)
- Please list species, estimated numbers, and length of study.
- Please give details of the specific procedure the animals will undergo.
- Please indicate if this is a terminal procedure under anaesthetic, and if so, the anaesthetic used.
- Please indicate if recovery anaesthesia will be used as part of any procedures, if so, please provide details of the anaesthetic regime.
- If surgery is involved, please include details of the procedure.
- Will the animals be imaged as part of the procedure? Please indicate frequency and length of each procedure. How will the animal be monitored?
- What endpoint criteria will be used to ensure that animals under study do not suffer unduly?
- Does your institute have an ethical welfare body e.g. IACUC/ERP? If so, please give brief details on remit, membership and meeting frequency.