PROOF OF CONCEPT OBTAINED

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

Data demonstrates that product has expected Mechanism of Action and has potential to meet cTPP.

Drug candidate has demonstrated initial clinical efficacy Proof of Concept.

(*Flexible milestone that may be evaluated at the end of phase 1, phase 2 or phase 3)

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Clinical safety aligns with TPP criteria (includes clinical and laboratory abnormalities)	Satisfactory safety profile using validated assays and adequate statistical analyses a) Safety signal detection (e.g., drug candidate-related adverse events (AEs) which may include serious adverse events (SAEs)) b) Management of any adverse events (reporting of the events to the applicable ethical committees and regulatory agencies)	▪ Summary of data and rationale
▪ Efficacy proof-of-concept completed and aligns with TPP criteria	Initial clinical efficacy proof-of-concept demonstrated using qualified/standardized clinical endpoint assays and adequate statistical analyses	▪ Summary of data and rationale
▪ Exposure-Response characterized to support selection of optimal dosage, regimen, and route of administration for Phase 2 trials defined	a) Exposure-Response characterized b) Dose, regimen, and route of administration studies c) Recommendations for Phase 2 studies	▪ Summary of data and rationale
▪ TPP achievement assessed	a) Probability assessment of whether candidate will meet target product profile	▪ Use cTPP template