PROOF OF CONCEPT OBTAINED

GLOBAL DRUG DEVELOPMENT

Goals/ Definitions

Data demonstrating Proof of Conceptand that product and has potential to meetcTPP

Drug candidate has demonstrated initial clinical efficacy Proof of Concept.
(*Flexible milestone that may be evaluated at the end of phase 1, phase 2a, or phase 2b)

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 adequatestatistical analyses a) Safety signal detection (e.g., drug candidate-related adverseevents (AEs) which may includeserious adverse events (SAEs)) b) Management of any adverse events (reporting of the events to the applicableethical 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 a) Efficacy (either clinical diseaseor infection) in Phase 2a and/or Phase 2b studies in endemic populations b) Superiority or non-inferiority data in comparativestudies against licensed drug (or treatment) control (if applicable)	▪ Summary of data and rationale
▪ Exposure-Response characterized to support selection of optimal dosage, regimen, and route of administration for Phase 3 trials defined	a) Exposure-Response characterized b) Dose, regimen, and route of administration studies c) Recommendations for Phase 3 studies	▪ Summary of data and rationale
▪ TPP achievement assessed	a) Probability assessment of whether candidatewill meet target product profile	▪ Use cTPPtemplate