Goals / Definition
Clinical safety data and rationale for Phase 2 dose selection.

Clinical Development Plan initiated.
(*Clinical Development Plan is initiated prior to the FIH gate review and is updated & reviewed during development through to the DTF gate review.

<table>
<thead>
<tr>
<th>CRITERIA</th>
<th>SAMPLE CONTENT REQUIREMENT</th>
<th>GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE</th>
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</thead>
</table>
| ▪ Clinical development plan updated | a) Overview of planned clinical activities:  
  • Study phase, objectives / research rationale  
  • Duration of the studies, number of subjects, recruitment criteria (e.g., study arms, patient cohorts, comparators for non-inferiority trials, power calculations etc.)  
  • Dosing & dosing modeling strategies  
  • Detailed rationale for Phase 2 dose range, and target clinical exposures  
  • Toxicology and toxicokinetic results to support doses and dosing duration in Phase 2  
  • Drug combination assessment & plan  
  • Toxicology plan to support Phase 3  
  b) Clinical partners, proposed target countries, and study sites (based on criteria including clinical expertise, sustainability, site capacity, and disease incidence / epidemiology studies, etc.)  
  c) Definition of clinical endpoints (primary & secondary), methodology (clinical endpoint assays, data collection plan, statistical methods, etc.), adverse event reporting, stopping rules, etc.  
  d) Monitoring, data management, and biostatistics strategies  
  e) Post-marketed product surveillance / Phase 4 trial strategy  
  f) Mass product administration considerations (e.g., trial design, safety requirements, etc.)  
  g) Off-label use considerations  
  h) Trial size considerations for diseases with limited incidence rates  
  i) Potential risks and mitigation strategies  
  j) Timelines and budgets for clinical development | ▪ Detailed Phase 2 clinical plan with timeline including supporting CMC and tox plans  
 ▪ High-level / draft plan for Phase 3  
 ▪ Updated risk identification and mitigation needed for all subsequent phases of development  
 ▪ Plans should reflect approaches to accelerate decision making (e.g., adaptive designs, real-time data analysis of clinical trials etc.)  
 ▪ Phase 2 plan is modified during Phase 1 trial as Phase 1 data become available  
 ▪ Clinical development plan extends beyond DTF to accommodate the time needed to report Phase 3 results and also cover additional plans for pediatric studies and post-market surveillance |