**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")

<table>
<thead>
<tr>
<th>CRITERIA</th>
<th>SAMPLE CONTENT REQUIREMENT</th>
<th>GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE</th>
</tr>
</thead>
</table>
| ▪ 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 |