RUN CLINICL PROGRAM PHASE 3 (1/7)

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

Track clinical trial start date.

Track the dosing of the first subject enrolled thereby indicating the beginning of the clinical trial.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Track first dosing event for a patient recruited to the Phase 3 clinical trial	a) Conduct recruitment analysis and compare study starts to the clinical plan b) Inform impact on other planned downstream activities in the case of study start delays	▪ Notification of date first subject dosed and any delay, if incurred

RUN CLINICL PROGRAM PHASE 3 (2/7)

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

Track that enrolment in the clinical trial is proceeding according to plan.

Track the progress and feasibility of Phase 3 clinical trials.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
• Track recruitment and budget by comparing actual patient enrollment to previously established benchmarks at 25% of the projected recruitment period	a) Conduct recruitment analysis and report number of patients recruited and budget within 25% of the projected recruitment period b) If suboptimal recruitment is identified, submit an analysis of recruitment barriers and a corrective recruitment plan with revised budget and timeline c) If recruitment levels are below minimum acceptable levels: evaluate feasibility to complete study within acceptable budget or timeframe and submit corrective recruitment plan	▪ Notification of milestone achievement, any delay, mitigations and revised timeline

RUN CLINICL PROGRAM PHASE 3 (3/7)

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

Check that data quality is on track to meet target clinical study report date.

Monitor data cleaning process to expedite database lock, data analysis, and data submission.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Initiate data cleaning process as data becomes available to allow access to high integrity and quality data and expedite data analysis and submission *NOTE: Data cleaning process and plan should be clearly defined at the beginning of the study. Readiness for database lock should be considered at patient level and entire data base level.*	a) Streamlined data cleaning process to expedite clinical data analysis and submission b) Provide estimated time to database lock, data analysis, and data submission c) Report SAEs and any other issues	▪ Notification of milestone achievement, any delay, mitigations and revised timeline

RUN CLINICL PROGRAM PHASE 3 (4/7)

GLOBAL DRUG DEVELOPMENT

Goals / Definition

Obtain an early read-out on the Phase 3 (if applicable) that may enable acceleration of regulatory submission.

Phase 3 interim analysis completed (preferably by independent committees).

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Safety assessment completed	a) Rate of severe adverse events (SAEs)	▪ Interim clinical study report
▪ Efficacy assessment completed	a) Statistically significant efficacy	▪ As above
▪ Futility assessment (inability of trial to meet its objectives) completed	a) Futility of trial effects (unlikely to achieve statistical significant efficacy) b) Operational futility (i.e., poor execution, lack of adequate resources, low adherence, poor quality of data)	▪ As above
▪ Clinical trial strategy adjustment (if needed)	a) Sample size re-adjustment b) Additional testing requirements	▪ Updated IPDP
▪ TPP achievement assessed	a) Probability assessment of whether candidate will meet target product profile	▪ Use cTPP template

RUN CLINICL PROGRAM PHASE 3 (5/7)

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

Track Clinical Trial end date.

Track the date for the last subject to complete the trial thereby indicating the end of the clinical trial.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Track last patient to complete the Phase 3 clinical trial	a) Conduct recruitment analysis and compare study duration to the clinical plan b) Inform impact on other planned downstream activities in the case of study completion delays	▪ Notification of date last subject last visit and any delay, if incurred

RUN CLINICL PROGRAM PHASE 3 (6/7)

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

Leading indicator of availability of study analyses.

Track the time of database lock that informs the lag between the last subject dosed and the availability of study analyses.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Action taken to prevent further changes to the clinical trial database	a) Database review and query resolution completed b) All pharmacokinetic, laboratory safety data and CRF data transferred to Data Management c) Database review and quality checks complete, data queries identified d) Query resolution completed	▪ Notification of milestone achievement, any delay, mitigations and revised timeline

RUN CLINICL PROGRAM PHASE 3 (7/7)

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

Track availability of clinical trial data for decision making.

Track the availability of top line results that enable real-time discussions of clinical trial data analysis and earlier investment decisions.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Statistical analyses using preliminary or final data are completed	a) Pharmacokinetic and pharmacodynamics (PK/PD) analyses of data completed b) Comparison of the observed results to the minimum criteria in the candidate TPP c) Working data sets delivered d) Tables, listings, figures produced to support topline report writing	▪ Notification of milestone achievement, any delay, mitigations and revised timeline