INITIAL DS/DP CHARACTERIZATION COMPLETE

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

To evaluate the drug substance (DS) and drug product (DP) that is well-characterized (stable with known impurity profile) and practical to administer in the clinic to ensure ready supply of drug of sufficient quality in Phase 1 clinical trials.

Clinical study start-up plan initiated with consideration of feasibility and identification of risks.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
• Initial drug product characterization completed	a) Delivery & formulation strategy to support animal and human studies (e.g., IV, injection, tablet, capsule, oral strip, inhalant, prodrug etc.; assess IP space if special delivery system) b) (For injectables) Consideration for hemolysis studies, adhesion of drug to delivery syringes, tubing, equipment, assess precipitation of drug at injection site (in vitro testing) c) (For prodrug) Characterization in vitro and in vivo conversion to active form d) Particle size considerations and formulation dependency (e.g. milling, micronization, etc.) e) Excipient selection and characterization f) Form-specific physicochemical properties (e.g., bulk & tap densities, flowability, compressibility, pXRD, IR, dissolution, disintegration, etc.) g) Form- and formulation-specific in-use stability studies h) Assess formulation bioavailability / PK for clinical dosing regimen, determine whether "blinding" of clinical formulation needed	▪ Summary of key data to substantiate conclusions ▪ Illustrative data tables or figures may be reported in an appendix
• Initial cGMP manufacturing process defined	a) Drug substance manufacturing process overview (e.g., synthetic pathways, intermediate selection, high-level description of unit operations and equipment) b) Drug product manufacturing process overview c) Documentation of external manufacturing plan via Partner Selection Milestone d) Reference standards, analytical GMP methods for drug substance and drug product release and stability, impurities specs for drug substance and drug product	▪ Initial cGMP manufacturing process defined
• GMP manufacturing	a) GMP DS and Ph1 DP released	▪ Summary of key data e.g. Certificate of Analysis

*Candidate progression is discussed at standing grantee update meetings with the investment team