

Goals/ Definition

To develop the drug substance (DS) and drug product (DP) to provide larger amounts (kilo scale) of clinical trial materials that will be required for Phase 2 studies.

cGMP DS manufactured at kilo-scale and scale-up processes defined.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
<ul style="list-style-type: none"> Drug substance characterization & analytical method development completed/finalized 	<ol style="list-style-type: none"> Salt & form selection (e.g., amorphous vs. crystalline, polymorph ID, etc.) Structural characterization (e.g., enantiomers, diastereomers, etc.) Chemical purity, impurity characterization, and associated analytical methods Stability & shelf life studies (e.g., T, pH, humidity, light, etc.) Cold chain requirements 	<ul style="list-style-type: none"> Summary of key data to substantiate conclusions Illustrative data tables or figures may be reported in an appendix
<ul style="list-style-type: none"> Drug substance manufactured at kilo-scale 	<ol style="list-style-type: none"> DS process developed to kilo scale with acceptable yield Confirmation of reproducibility of stoichiometry, stable DS physical form and required particle size Confirmation of acceptable impurity profile 	<ul style="list-style-type: none"> As above
<ul style="list-style-type: none"> Drug product characterization & analytical method development completed 	<ol style="list-style-type: none"> Delivery & formulation strategy (“light touch” quality-by-design [QbD] approach) to support animal and human studies (e.g., IV, injection, tablet, capsule, pediatric dosage form etc.) Particle size considerations and formulation dependency Excipient selection and characterization Chemical purity, impurity characterization, and associated analytical methods Form-specific physicochemical properties (e.g., bulk & tap densities, flowability, compressibility, pXRD, IR, dissolution, disintegration, etc.) Form- and formulation-specific stability studies 	<ul style="list-style-type: none"> As above
<ul style="list-style-type: none"> GMP Manufacturing 	<ol style="list-style-type: none"> Kilo lab GMP DS, Ph 2 DPs Released 	<ul style="list-style-type: none"> Summary of key data, e.g. CoA

Prior to EP1, CMC will ensure that the DS manufacturing process is developed to produce the required salt, form, and purity profile in larger amounts. DP formulation components, manufacturing processes and packaging should be final and scalable so that larger amounts of Phase II clinical study materials can be supplied in a timely manner.

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