# Cell and Gene Therapy Product Development – Key Tasks

| | Optimization<br>(Research to Pre-IND) | Development<br>(Pre-IND to IND) | Early Clinical Development<br>(Phase I, Phase I/II) |
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| **General** | • Target Product Profile (TPP), version 1 | • Revise TPP, incorporating information from preclinical and CMC development. | • Further TPP revisions as needed |
| **Preclinical Pharm/Tox** | • Initial animal studies<br>o Identify animal model(s)<br>o Plan and conduct studies<br>o Proof of Concept (POC), dose determination, toxicology, cell fate/survival/engraftment, tumorigenicity studies<br>• Limited, targeted histological examination<br>• Plan IND-enabling GLP preclinical studies | • Modify plans for animal studies based on FDA comments from Pre-IND meeting<br>• Perform IND-enabling GLP animal studies, include results and interpretation in IND | • Additional pharm/tox animal studies as needed |
| **CMC** | • Define research version of manufacturing process.<br>• Process development to establish manufacturing process, version 1<br>o Improve consistency and cell yield, introduce automated processing devices and closed-system processing<br>• Select/establish analytical methods for in-process and release testing – safety, purity, identity, and candidate potency assays<br>• Initial versions of Critical Quality Attributes and Critical Process Parameters | • Modify manufacturing, testing, and other aspects of CMC based on FDA comments from Pre-IND meeting<br>• Further manufacturing process development<br>• Qualify manufacturing process version 1<br>• Qualify raw materials/reagents and suppliers<br>• Qualify assays<br>• Qualify shipping | • Manufacturing for clinical trial using manufacturing process version 1<br>• Process development to establish manufacturing process version 2<br>• Refine specifications, further development of analytical methods and standards. Continue potency testing development; select potency assay(s) and establish potency testing prior to pivotal trial.<br>• Continue stability studies |

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| | | • Initiate stability studies | |
| **Clinical** | • Prepare draft version of clinical trial design, clinical development plan<br>• Prepare draft version of statistical analysis plan | • Finalize clinical trial design and study protocol<br>• Finalize statistical analysis plan | • Conduct clinical trial<br>• Prepare clinical study reports, prepare and submit reports of any adverse events |
| **Regulatory** | • File Request for Designation if developing combination product<br>• Pre-Pre-IND meeting (optional)<br>o Prepare Pre-Pre-IND briefing document<br>o Schedule and conduct meeting<br>• Modify development plan based on Pre-Pre-IND comments<br>• Pre-IND meeting<br>o Identify questions to address, prepare Pre-IND briefing document<br>o Schedule and conduct meeting | • Response to FDA Pre-IND comments – Modify development plan, follow-up with individual reviewer(s) as needed<br>• Plan and task list for IND preparation<br>• Draft and revise IND application, submit | • Study reports, adverse event reporting as listed in Clinical, above. |