Early Translational IV: In-Scope Activities

Cell Therapy

- Develop reproducible methods for research grade production (cell expansion, differentiation, purification)
- Develop assays and assess identity, purity and activity
- Develop cell delivery method(s)
- MOA studies
- Select a candidate
- Develop a Research grade cell bank
- Demonstrate efficacy in preclinical models
- Pilot studies to determine formulation, dose and safety
- Process scale up feasibility
- Develop clinical plan
- Develop GMP compatible cell bank

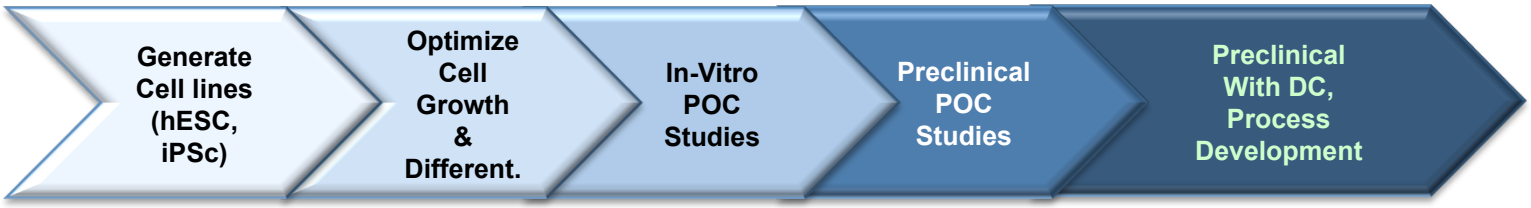
Monoclonal Ab

- Generate mAbs against validated antigen
- Develop screen(s), assays to select potent and selective mAb
- Chimerize and/or humanize mAb, perform in vitro maturation
- Identify lead mAb
- Develop cell line to produce lead mAb
- Develop assays and assess identity, purity and activity
- Develop reproducible methods for research grade production
- Demonstrate efficacy in preclinical models
- Pilot studies to determine formulation, dose and safety
- Process scale up feasibility
- Develop clinical plan

Small Molecule

- Develop assays (screening, potency, selectivity)
- Perform HTS and secondary assays to identify lead compound(s)
- Select a lead and back-up candidates
- Lead optimization (medicinal chemistry, SAR)
- Determine potency, MOA, selectivity
- Demonstrate efficacy in preclinical models
- Create PKDM profile
- Pilot studies to determine formulation, dose and safety
- Process scale up feasibility
- Develop clinical plan

Sample milestones and success criteria



1. Select Pluripotent (PSC) line – Derive and characterize therapeutic cells:

- Define cell source, optimize culture conditions and establish robust differentiation protocol
- Develop assays (e.g. identity, purity) and characterize cell population
- Elect pluripotent parental cell line for POC testing based on defined selection criteria (e.g. genetic stability, differentiation efficiency, and scalability)
- Generate research bank

Success criteria: *Select GMP compatible cell line(s) that is reproducibly differentiated to the x % of the desired linage and can be expanded in a scale sufficient to support preclinical POC studies while maintaining a normal karyotype*

2. Demonstrate preclinical POC with elected cell line(s):

- Demonstrate therapeutic activity in at least one disease model with at least one cell line
- DC awards: select a single lead DC for reproducible disease modifying activity studies

Success Criteria: *Therapeutic activity should be defined as a quantifiable, therapeutically relevant improvement in an established disease read out compared to and appropriate control/sham treatment*

3. Demonstrate reproducible disease modifying activity with GMP compatible lead cell line in a relevant disease model:

- Cell banking, process development and generation of GTP/GMP compatible cells at scale and differentiation efficiency sufficient to support reproducible disease modifying activity studies
- Define therapeutic cell dose and delivery route. Demonstrate reproducible statistically significant disease modifying activity in a relevant disease model using GTP/GMP compatible cells
- Conduct preliminary safety and histological assessment of treated animals (e.g. survival, cell related toxicity, tumor and/or off target tissue formation, and engraftment of desired cells), perform MOA studies
- Develop methods to scale up production adequate to support IND enabling studies

Success Criteria: 1) *Produce GMP compatible small-medium research scale lots to support reproducible disease modifying studies (e.g. y number of cells in x% purity* ***2)*** *Therapeutic activity should be defined as quantifiable, therapeutically relevant improvement in a disease read out compared to appropriate control/sham treatment*