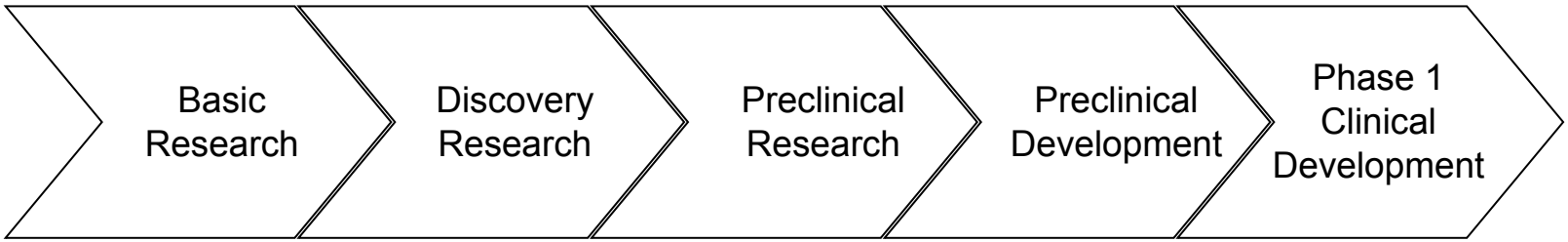
Appendix A

Examples* of Activities Considered in Scope for RFA 10-01: Early Translational II Research Awards

* Applicable to DC or DCF Awards targeting a therapeutic development candidate.

Cell Therapy Development Activities



Development Candidate

File IND

- Target Identification/initial target validation

- Standardize stem cell growth conditions
- Develop reproducible methods to differentiate cells, if needed
- Develop reproducible methods to produce population of sufficient purity
- Assay development to characterize cell populations - identity, purity, activity (potency)
- Develop methods to deliver cells to target tissues
- Pilot MOA studies

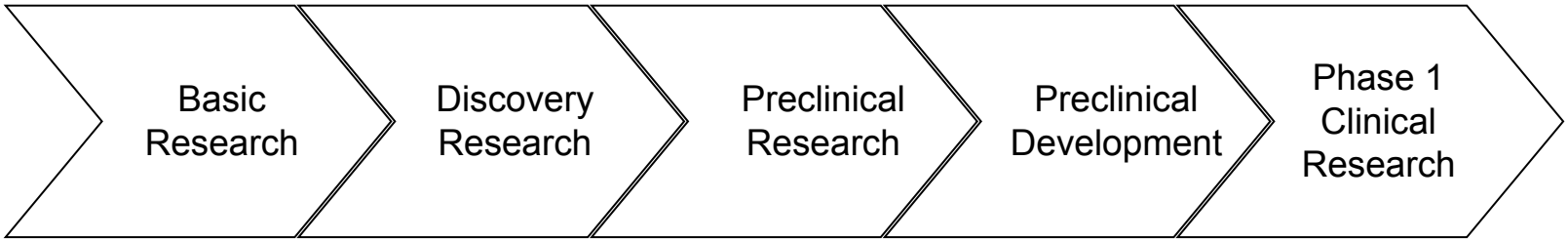
- Select Candidate
- Develop Research Cell Bank
- Demonstrate reproducible evidence of disease-modifying activity (*in vitro* and *in vivo)*
- Pilot studies of dose, formulation, stability, and safety
- Perform early process development
- Develop clinical strategy and prepare development plan

- Develop GMP Master and Working Cell Banks (*)
- Develop formulation and scaled production methods under cGMP
- Analytical Method Development
- Produce GLP and GMP lots
- Perform stability studies
- Perform IND-supporting safety/ toxicology, pharmacology studies
- Develop clinical protocol
- Prepare IND package

Examples of activities considered in-scope of the Early Translational II RFA

(*) These activities can be considered for funding under this RFA.

Small Molecule Development Activities



Development Candidate

File IND

- Target identification/ initial target validation
- Screening feasibility
- Screening strategy

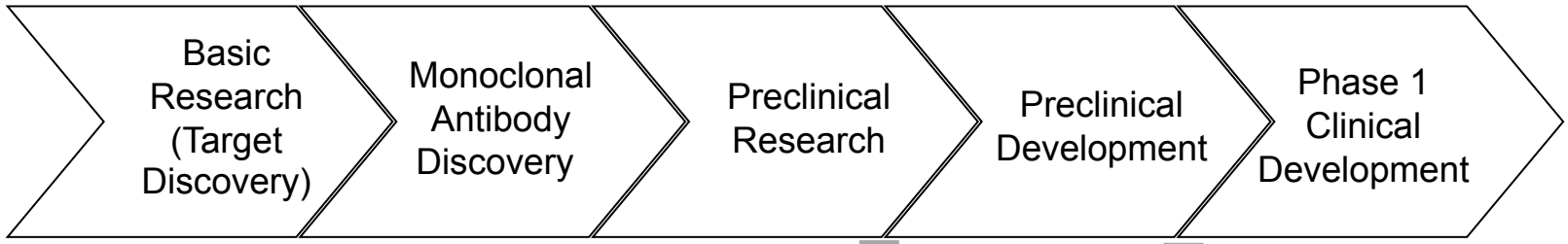
- Perform HTS
- Assay development-identity, purity, potency
- Identify and characterize active compounds
- Evaluate potency, selectivity, reversibility and mechanism of action
- Conduct lead optimization

- Demonstrate reproducible evidence of disease-modifying activity *(in vitro* and *in vivo*) of lead compound(s)
- Pilot studies of dose, formulation, stability and safety
- Create PKDM profile
- Identify potential drug-drug interactions
- Perform early process development
- Develop clinical strategy and prepare development plan

- Develop formulation and scaled production methods under cGMP
- Produce GMP and GLP lots
- Perform IND-supporting safety, pharmacology, PK/PD
- Analytical method development
- Identify clinical toxicity-monitoring parameters
- Develop clinical protocol
- Prepare IND package

Examples of activities considered in-scope of the Early Translational II RFA

Monoclonal Antibody (MAb) Development Activities



▪Target Identification/Initial target validation

Development Candidate

▪Generate/screen Ab panel

▪Assess species cross-reactivity

▪Humanization and Antibody Engineering

▪Select isotype

▪Evaluate HuMab in vitro and in vivo

▪Assay development – identity, purity, potency

▪Develop cell line and research cell bank

▪Demonstrate reproducible evidence of disease modifying activity (*in vitro* and *in vivo*)

▪Pilot MOA studies

▪Pilot studies of dose and safety

▪Perform early process development

▪Develop clinical strategy and prepare development plan

File IND

▪Develop GMP Master and Working Cell Banks

▪Develop formulation and scaled production methods under cGMP

▪Analytical Method Development

▪Perform IND-supporting safety/toxicology studies

▪Perform stability studies

▪Produce GLP and GMP lots

▪Develop clinical protocol

▪Prepare IND package

Examples of activities considered in-scope of the Early Translational II RFA