

## Development Stages in Scope Vaccines

What CARB-X considers a “Hit” when identifying your project/program in “Hit-to-Lead”?

- Vaccine antigen(s) has been identified and supportive immunogenicity data in appropriate animal models have been generated.

### **Hit-to-Lead (Lead Generation)**

- Characterization of the immune response to the antigen(s) *in vivo*, with mechanism for protection defined
- Determination of the optimal antigen expression (or vaccine production) system
- Preliminary characterization for product quality attributes (lab scale) such as purity, protein conformation, stability, yield, etc., as appropriate
- Adjuvant/formulation screening studies
- Standardization of methods to assess immunogenicity in relevant animal models

### **Lead Optimization**

- Determination of final drug product composition (e.g., adjuvant, delivery platform, etc.)
- Qualification of assays to assess immunogenicity and functional antibody and/or cellular response
- Determination of Immunogenicity/efficacy in animal models with route of immunization, regimen, and endpoints to reflect clinical plans
- Assay development to quantitate potency
- Cell bank generation (research)
- Reproducibility runs performed at lab scale and appropriate analytical characterization
- Assessment of stability profile
- Tech transfer and scale-up of vaccine production
- Development of analytical assays for vaccine product release
- Elaboration of a clinical development plan
- Pre-IND consultation (or guidance sought from another relevant regulatory body)

### **Pre-Clinical (IND Enabling)**

- Production and release of Master (and Working, if appropriate) Cell banks
- Qualification and validation of the analytical release assays
- Upstream and downstream process development for GMP scale
- Engineering run
- Toxicology studies
- GMP manufacture of vaccine material for clinical study
- Product characterization at production scale to demonstrate purity, stability, and potency, and product released as per regulatory guidelines
- Submission of IND to US FDA (or clinical trial application to another relevant regulatory body)

### **Phase 1**

- Dose-escalation study in healthy volunteers to determine safety, to include endpoints for assessing immunogenicity and potential vaccine efficacy
- Activities related to Phase 2 readiness, (e.g., vaccine manufacture, assay validation, plans for onward clinical development, etc.)

## Development Stages in Scope Antibodies

What CARB-X considers a “Hit” when identifying your project/program in “Hit-to-Lead”?

- An antibody has been identified that has the specific binding activity needed for preventative or therapeutic activity

### **Hit-to-Lead (Lead Generation)**

- Optimization of antibody product to improve suitability for use in humans (eg, humanization, isotype switching, Fc sequence modifications for manufacturability and /or stability)
- Mechanism of action defined and characterized
- Demonstration of *in vitro* binding activity and preliminary *in vivo* efficacy data

### **Lead Optimization**

- Qualification of assays to measure antibody binding activity
- Characterization of the antibody binding activity (e.g., avidity)
- Non-GLP tissue cross-reactivity screening
- Initiate PK/PD studies in appropriate animal model(s) to establish exposure-response relationship
- Qualification and validation of the analytical method(s) to measure the drug antibody in animal serum for PK/PD studies (titer and function)
- Tech transfer to CMO
- Pre-IND consultation (or guidance sought from another relevant regulatory body)

### **Pre-Clinical (IND Enabling)**

- Production and release of Master (and Working, if appropriate) Cell banks
- Qualification and validation of the analytical release assays
- Upstream and downstream process development for GMP scale
- Engineering run
- Tissue cross-reactivity testing (GLP)
- GLP PK/PD and toxicity studies performed in relevant animal model(s); human dose selected
- GMP manufacture of vaccine for clinical study
- Product characterization performed at production scale demonstrating purity, stability, and potency, and product released as per regulatory guidelines
- Qualification and validation of the analytical method(s) to measure the drug antibody in human serum (titer and function)
- Development and qualification of anti-drug antibody (ADA) assays
- Submission of IND to US FDA (or clinical trial application to another relevant regulatory body)

### **Phase 1**

- Phase 1 single ascending dose (SAD) and multiple ascending dose (MAD) clinical trial(s) to determine the safety and pharmacokinetics of the clinical test article in healthy volunteers (in certain circumstances, patients)
- Activities related to Phase 2 readiness, (e.g., product manufacture, assay validation, plans for onward clinical development, etc.)