Pre-IND enabling activities: Understanding the Pre-IND Phase through to First-in-Human (FIH) Studies

Before submitting an Investigational New Drug (IND*) [or Investigational Medicinal Product Dossier (IMPD)]* application to the FDA or EMA, a new biotech needs to navigate through what is known as the **Pre-IND phase** - this early stage focuses on gathering the necessary data to demonstrate that a new drug is safe and potentially effective enough to move into human trials.

To take a new drug product into FIH a biotech company will require the following **4 *fundamental* Clinical Development pieces: 1. Drug supply, 2. Pharm/Tox Package, 3. Clinical Plan, 4. Regulatory Strategy**

Core Elements of IND-Enabling

1. Nonclinical Safety Studies

- *Pharmacology*: Establishes how the drug works and confirms its intended biological activity.
- *Pharmacokinetics (PK)*: Examines how the drug is absorbed, distributed, metabolized, and excreted.
- *Toxicology*: Identifies potential safety concerns and helps define a safe starting dose for human trials.

2. Chemistry, Manufacturing, and Controls (CMC)

- Details the drug's composition and stability.
- Describes the manufacturing process, which should comply with Good Manufacturing Practices (GMP).
- Includes documentation of production batches and evidence of meeting required quality.

3. Preclinical Efficacy

- Uses lab-based (in vitro) and animal (in vivo) models *(as applicable)* to demonstrate that the drug works as intended.
- Helps define dose-response relationships to guide clinical dosing strategies.

4. Clinical Development Planning - see next:

What Goes Into an IND Submission ?

To move forward with human trials, the IND application must include:

- **Preclinical Data**: Safety profiles, pharmacokinetics/pharmacodynamics (PK/PD), and toxicology findings.
- **CMC Details**: Information on how the drug is formulated and manufactured.
- **Clinical Protocols**: Plans for trial design, dosing, and safety oversight.

- **Investigator Brochure (IB)**: A comprehensive summary of all relevant data for clinical researchers.

Designing the First Trial

Key considerations when planning an FIH study include:

- **Dose Escalation**: Can follow a fixed rule-based approach or use adaptive, model-based methods.
- **Safety Monitoring**: Includes tracking dose-limiting toxicities (DLTs) and predefined stopping rules.
- **Expansion Cohorts**: May be added to refine the recommended Phase 2 dose (RP2D)
- **Adaptive Designs**: Innovative trial formats like basket, umbrella, or platform designs can be considered.

Planning Ahead: Timeline Tips

- Start preparations at least 18 months before submitting the IND.
- Involve a Contract Research Organization (CRO) and Contract Manufacturing Organization (CMO) early to streamline production.
- Ensure that nonclinical studies are aligned with the goals of the planned clinical trial.

Strategy for success

Product development is not one size that fits all: To get the above right needs deep understanding and an integrated approach. Strong and dovetailed interplay and a well thought out strategy between Non-Clinical, CMC, Clinical and Regulatory is key to success; being able to fully engage this at the stage of pre-IND / pre-IND enabling will best accelerate a product through to FIH

Contact us

For support on IND submissions, please feel free to contact:

Mark Beresford PhD
Global Enterprise Relationship Lead

mark.beresford@thermofisher.com
+44 (0) 7800 569628

www.thermofisher.com