De-Risking and Optimizing First-in-Human Studies

Celerion is a full-service CRO focused on early phase clinical pharmacology drug development, including First-in-Human (FIH) and single (SAD) and multiple (MAD) ascending dose trials. Our three clinical pharmacology units (CPUs) located in Belfast, UK; Lincoln, NE; and Phoenix, AZ were purpose-built to safely and successfully operationalize FIH studies.

Key First-in-Human Study Operational Features Include:

- Pre-Investigational New Drug (IND) and IND regulatory support
- Extensive capacity with over 650 beds across the US and UK
- On-site CAP and CLIA accredited clinical laboratory for rapid screening and safety lab turnaround
- Pharmacy suites for on-site extemporaneous compounding and dose formulation testing
- Fully integrated electrocardiogram (ECG) Core Lab
- Large active database of healthy volunteers for quick recruitment
- State-of-the-art bioanalytical facilities
- Immediate, on-site Peripheral Blood Mononuclear Cell (PBMC) isolation and analyses (e.g. flow cytometry & receptor occupancy)
- Streamlined process includes rapid study start-up and accelerated database lock
- Real-time access to data via Celexus® web portal

Celerion Differentiators:

Experience:

- Over 250 FIH clinical trials successfully completed since 2010
- FIH experience with small molecules, biologics and oligonucleotide drugs

Expertise:

- Knowledgeable Principal Investigators with more than 20 years of FIH study experience
- Highly qualified team of pharmacokinetics scientists, medical writers and subject matter experts provide input on study design, analysis and reporting

Efficiencies:

- In-house regulatory affairs department supports Pre-IND meetings and IND submissions
- Bioanalytical laboratories located in Lincoln, NE and Zurich, CH, able to support rapid pharmacokinetics assessment for dose escalation decisions

Our Promise to Our Participants

Celerion is the only CRO to receive accreditation from the Association for the Accreditation of Human Research Protection Programs (AAHRPP). This recognition highlights our ongoing commitment to ensure human rights protection in clinical research.

De-Risking First-in-Human Studies

The primary objective of a FIH study is to evaluate the safety of an investigational drug. We have robust safety procedures in place to protect participants:

- Our experienced clinical team performs a risk-based assessment to ensure the nonclinical safety data supports the proposed study design and dose
- Apply sentinel dosing approach and close participant monitoring to evaluate drug safety
- Rigorous safety evaluations include multiple vitals, ECGs, safety labs, adverse events (AEs) assessments, as well end-of-study AE follow-up
- Potential to mitigate risks with tailored study drug administration procedures, premedication and rescue medication (if applicable)

Safety Assessments & Risk Mitigation Procedures

Key Safety Evaluations	Risk Mitigation Strategies
✓ Vitals ✓ ECGs ✓ Clinical safety labs ✓ AE monitoring ✓ Immunogenicity ✓ Specialty assessments (as needed) • Injection site reaction • Echocardiography • Telemetry • Safety questionnaire (C-SSRS) • Ophthalmological evaluation • Lung function testing and more	✓ Sentinel dosing ✓ Pharmacokinetic assessment to evaluate for drug accumulation ✓ Premedication and rescue medication (if applicable) ✓ Emergency crash-cart in each clinical ward ✓ All clinics are located within minutes of a hospital ✓ Safety Nurse monitoring

Characteristics of a Standard First-in-Human Study

In general, a typical FIH study includes the following features:

– SAD: 5-7 cohorts

– MAD: 3-5 cohorts

– Sentinel dosing (1 active + 1 placebo), monitored for 24-48h prior to dosing the remaining cohort

– Randomized 2:1 or 3:1 active/placebo

– Healthy volunteers

– Safety & tolerability assessments

– Pharmacokinetic and pharmacodynamic assessments

However, designs can be ***maximized*** to get the most out of a FIH study. Our experienced team of protocol writers can recommend tailored design features to optimize FIH studies.

A Bespoke Approach to Enriching First-in-Human Study Designs

Drug developers can ***customize & optimize*** their FIH trial to get the most out of their study. Consider adding the following design elements:

- Utilize Holter ECG monitoring to gain insight into a drug's cardiac liability and obtain a potential TQT substitute (waiver)
- Insert a food effect cohort into a SAD study to evaluate the impact of a meal on drug absorption
- Conduct specialized assessments and biomarkers for early signals of efficacy
- Incorporate a drug-drug interaction (DDI) arm or patient cohort into a multiple part study
- Insert flexible language in the protocol for adaptive dose escalation decisions

RESOURCES:

Leader in Phase 1 Clinical Research & Pharmacology

Lessons Learned From 50+ Years of First-in-Human Clinical Experience

Leverage our Regulatory Experts for Pre-IND and IND Support