Clinical and Bioanalytical Oligonucleotide Experience and Expertise

Oligonucleotide therapeutics are an exciting and emerging modality of drug development that alter RNA and/or protein expression by targeting specific RNA sequences. Oligonucleotide products share certain features with peptide and protein biologics; for instance, they do not undergo CYP metabolism and can accumulate in target tissues or cells leading to prolonged pharmacodynamic responses, requiring less frequent dosing.

At Celerion, we bring over a decade of expertise in supporting the clinical development of oligonucleotide-based therapeutics. Our dedicated teams integrate bioanalytical innovation with clinical insight to provide comprehensive support across all phases of drug development. From preclinical through clinical stages, we deliver reliable and timely results tailored to meet your study requirements.

Oligonucleotide Modalities

Our extensive experience includes working with a wide range of oligonucleotide modalities, such as:

- ASOs (Antisense Oligonucleotides)
- siRNAs (small interfering RNAs)
- mRNA Therapeutics
- CRISPR/Cas9 Components

We excel in overcoming the unique challenges associated with oligonucleotides, including their complex pharmacokinetics (PK), delivery mechanisms, and the need for highly sensitive, specific, and robust analytical methods.

Oligonucleotide Drug Safety Profile

In general, oligonucleotide therapies tend to have a favorable safety profile. Key safety considerations include:

- **Low Immunogenicity:** Oligonucleotides typically have a low immunogenicity risks and immune toxicity adverse events tend to be rare.
- **Potential Adverse Reactions:** Administration can be accompanied by injection site reactions as well as hepatotoxicity and nephrotoxicity. To mitigate these risks, routine monitoring of liver and kidney function, along with a comprehensive immunogenicity risk assessment, is strongly recommended.
- **Common Adverse Effects:** Oligonucleotide administration can be associated with flu-like symptoms including chills, fever, headache and body aches. These symptoms typically resolve within 48 hr of dosing and if needed can be managed with acetaminophen and ibuprofen prior to and after dosing

Celerion Differentiators:

Experience:

- Successfully conducted several clinical studies in the past decade across a range of therapeutic areas including respiratory, cardiology and gastroenterology diseases
- Experience with multiple routes of administration (e.g. oral, inhalation, intramuscular, subcutaneous and intravenous)

Expertise:

- In-house bioanalytical experts specializing in oligonucleotide PK analysis
- Clinical expert team, including Principal Investigators (PIs) and Protocol Writers, with oligonucleotide experience

Efficiencies:

- Fast recruitment of oligonucleotide-naïve healthy subjects for efficient PK/PD assessments

Recommended Clinical Pharmacology Studies for Oligonucleotide Drug Development:

Healthy volunteers (HV) studies can expedite oligonucleotide drug development. Particularly, clinical pharmacology studies in HV provide robust pharmacokinetic (PK) data compared to patient trials. Here is a list of recommended clinical pharmacology studies for oligonucleotide drug development, including when HV can be considered.

Study Type	Recommendation
First-in-Human (FIH)	Single ascending dose (SAD) studies can be done in healthy volunteers, while multiple ascending dose (MAD) studies often enroll patients
Thorough QT (TQT)	A dedicated study is recommended if a TQT substitution is not sought
Renal Impairment (RI)	Recommended if oligonucleotide drug is eliminated by kidneys
Hepatic Impairment (HI)	Only recommended if therapy targets liver
Drug-Drug Interaction (DDI)	To consider if drug targets CYPs or drug transporters, or if a pharmacodynamic interaction is anticipated with a concomitant drug

CYP, cytochrome P450 enzyme

Celerion's Oligonucleotide Bioanalysis Capabilities & Platforms:

Capabilities	Platforms
✓ Real Time PCR (qPCR) ✓ Hybridization ELISA/ECLIA ✓ High resolution Mass Spectrometry ✓ LC-MS/MS	✓ Quant Studio qPCR ✓ Sciex TripleTOF 6600 ✓ Sciex 7500+ Triple Quad ✓ MSD ECLIA reader ✓ Multifunctional plate readers

RESOURCES:

Key Clinical Pharmacology Studies to Support Biologic Drug Regulatory Submission