siRNA THERAPEUTICS

ADDRESSING NONCLINICAL & MANUFACTURING COMPLEXITIES

#DYK
Did you know?

siRNA therapeutics are **advancing precision medicine** by safely and efficiently **targeting previously undruggable genes**

- A **hybrid and risk based regulatory approach** is most appropriate for siRNA therapeutics
- **Key CMC considerations:** specifications, starting materials, and sameness challenge
- **Key nonclinical considerations:** on- and off-target safety assessments, and immunogenicity risks
- Alignment with **ICH M3(R2) guideline** with case-by-case modifications for product specific needs
- New FDA guidance for **oligonucleotide therapeutics** provides recommendations for nonclinical safety evaluations

Several **delivery technologies and strategies** are under development for **extrahepatic targets**

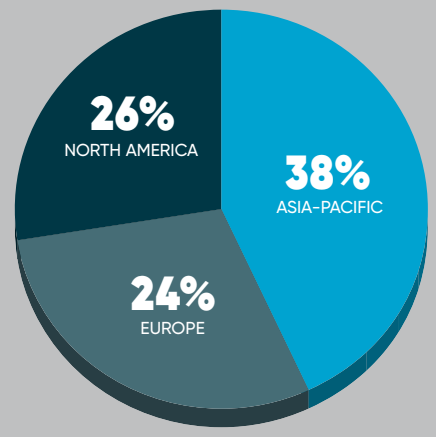
Well designed and predictive **nonclinical studies** are critical for clinical translation

Early engagement with **Regulatory agencies** is crucial

siRNA THERAPEUTICS CLINICAL TRIALS

Trials are growing at **79.5% CAGR**, with 80% in the early phases, and 20% in Phase III

China and the **United States lead globally**, with significant contributions from Europe and Asia-Pacific



Oncology leads siRNA drug development, followed by CNS, cardiovascular, and metabolic disorders