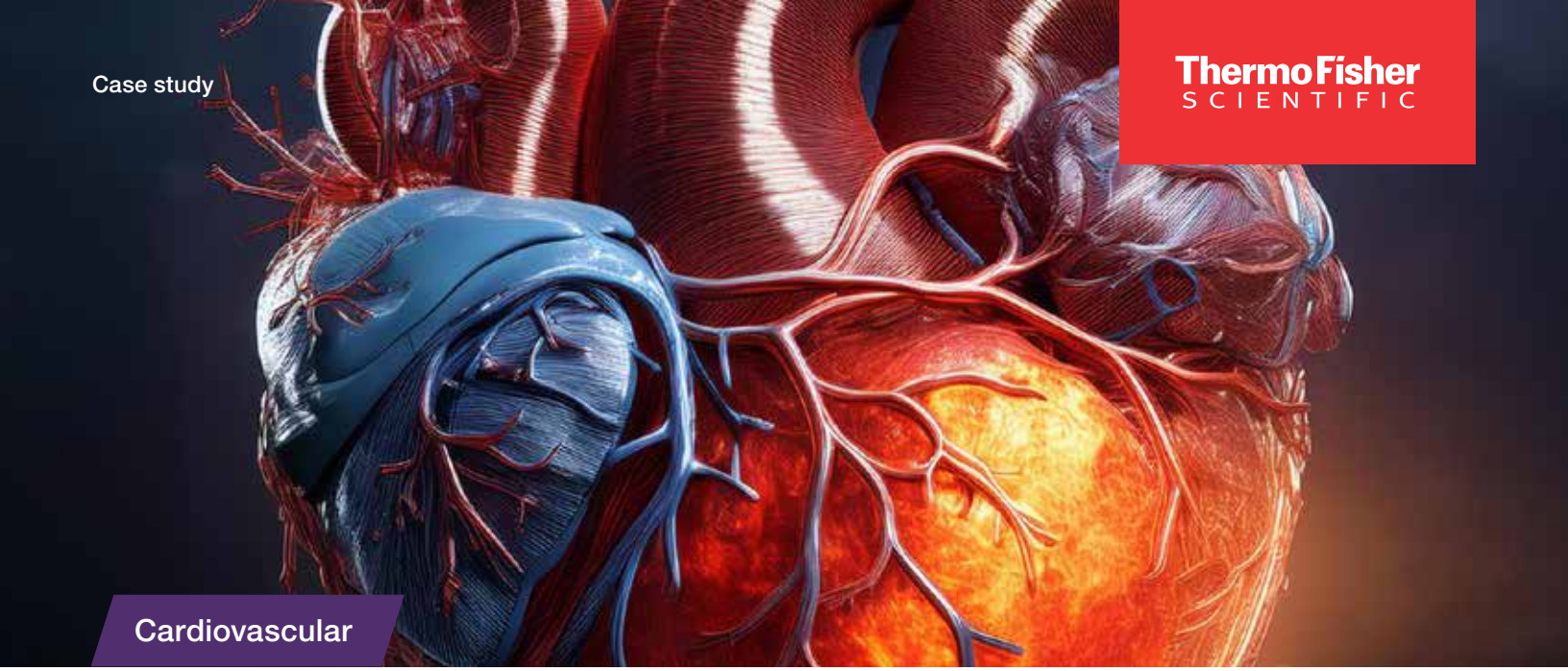

Case study

Cardiovascular

Challenging first-in-human cardiovascular study with mRNA IP

Background

Our client is conducting the first-in-human Phase I study of a cardiovascular gene modifier (GMO) mRNA therapy. The ongoing study features a single ascending dose (SAD) and multiple ascending dose (MAD) design. Patient identification has been challenging due to stringent inclusion/exclusion criteria. Participants receive the investigational product (IP) via infusion and those in the SAD group are required to remain in-patient for 24-hour observation. Continuous patient enrollment and dosing are facilitated through dose cohort escalation meetings.

Challenges

- **Regulatory landscape:** Considered gene product in some countries
- Navigating country-specific regulatory pathways
- **Site selection:** Ability to support IP handling per protocol requirements.
- **Specialized equipment for IP preparation:** Laminar flow hoods, centrifuges and –80°C freezers
- Acquisition of specialized and costly diagnostic equipment (renal doppler and ECHO)
- **Urine PK collection:** Supplying BSA buffers for patient collection — import and distribution challenges
- First in human and requirement for in-patient 24-hour observation

Strategy

- Robust onsite PSV supported by **IP flow document and site protocol requirements, in-patient capabilities**
- Strong site relationships supporting in-depth **mapping of approval pathway**; including multiple institutional reviews and IBCs
- Obtained import and distribution license for BSA
- **Reduced burden:** Provided specialized coolers for at home urine collection
- **Pre-randomization site validation monitoring visit:** Upfront on-site visit prior to randomization by two CRAs to ensure patient eligibility and site training ahead of complex randomization visit
- **Pharmacy support:** Created IP preparation videos to support complex IP preparation and provided **pharmacy concierge support**
- **Weekly screening calls** to coordinate across multiple sites/countries/functional teams to individual patient green light for screening

Results

The study successfully completed five SAD (plus extension) and three MAD cohorts on time. Transparency and trust from the client allowed our team to successfully manage the complex study.

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