IND Enabling Toxicology and Chemistry - General Considerations

INTRODUCTION & BACKGROUND

A virtual pharmaceutical company required chemistry and drug-safety services to file an IND application for an in-licensed, anti-cancer compound. Although some early proof-of-concept work had been done, including extensive human tumor cellular testing, both the timeline and budget were extremely tight. A lab-scale compound synthesis method was available.

CHALLENGE

- Demonstrate oral bioavailability
- Scale up synthesis process to production scale
- Develop CMC section for IND filing
- Conduct concurrent safety, toxicology and DMPK studies for IND filing

APPROACH & EXECUTION

The first priority for our client was the demonstration of oral bioavailability of the drug development candidate. Ricerca performed comparative tests in rodents to determine if an oral dose would provide exposures equivalent to earlier intraperitoneal dosing. An excellent oral dose formulation was identified.

Ricerca's unique capability to provide both nonclinical development and chemical development simultaneously came into play as a safe, scalable synthetic process with improved productivity was constructed. The new process was used to produce 20-kilogram lots of the compound for use in Phase I-II clinical trials. During this time, the chemistry team also provided all other items needed to complete the CMC section of the overall program, including analytical methods development and validation, metabolite and degradant identification and synthesis, and stability studies.

At the same time, on another part of the Ricerca campus, the drug safety team was conducting additional in vivo pharmacology safety profiles, toxicology, and DMPK studies required for IND filing.

Communications were closely managed due to the complexity and time frame of the project and included weekly email reports and bi-weekly teleconferences. Ricerca's integrated project management team worked closely with the client to ensure the right work was done at the right time.

RESULTS

After the compound passed the first milestone of oral bioavailability, Ricerca completed the remaining chemistry and biology work in only six months. The results of our efforts culminated with a successful IND application and Ricerca continued to support this API through Phase II clinical trials.

IMPACT

The client recently licensed this compound to a major pharmaceutical company for commercialization.