

Maximizing the output of Phase I to streamline clinical development

A KEY QUESTION



How can an efficient clinical development strategy reduce the time and cost of registering an innovative drug delivery platform?

KEYWORDS

Phase I Optimization, Model-Informed Drug Development, Regulatory Strategy, Operational Planning, Drug Delivery



A large company had recently acquired an inhaled delivery platform, and they hoped to reposition an existing drug with this non-invasive delivery route. While the company had some previous experience advancing other clinical programs, it needed the support of a CRO to define the most efficient development strategy and achieve registration in the U.S.

Learn how Fortrea found creative ways to support the dose definition, expedited the incorporation of FDA feedback and helped streamline the clinical development strategy for the sponsor.

Understanding the science

The sponsor wanted to develop an orally inhaled version of an approved drug for systemic effect. Their approach aimed to moderate some of the side effects experienced from injected delivery by reducing the C_{max} , which is the maximum or peak concentration of the drug reached in the target organ following a dose, without significantly impacting the T_{max} of the drug, which is the time it takes for a drug to reach its maximum plasma concentration. With this novel delivery platform, they hoped to make a difference for patients by achieving a comparable therapeutic effect alongside an improved side effect profile.

Recognizing the challenges

Fortrea needed to evaluate how to handle several challenges associated with development:

1. Defining the target dose for local delivery

One significant challenge in delivering a drug locally for systemic effect is determining how to define the target dose for local delivery, which means managing differences in bioavailability. For example, drugs injected directly into the body have 100% bioavailability, whereas for drugs delivered locally, bioavailability is typically lower due to a number of factors, such as delivery efficiency or clearance. For inhaled products, a key factor influencing bioavailability is regional deposition in the lung, which is dependent on the particle size of the aerosolized drug.

2. Determining how to best leverage existing data

Given that the drug was already approved and had a history of use, Fortrea coordinated a multidisciplinary team to define an appropriate regulatory pathway—505(b)(2)—and its corresponding requirements.

The 505(b)(2) application pathway allows the use of published literature from the previously approved (innovator) drug to support the application, which can save considerable time and money if the clinical program can be reduced. However, to define the optimal dose for the new product, Fortrea still needed to determine the extent to which previous data could be used to avoid conducting a full clinical program.

Identifying opportunities to simplify clinical development and align with FDA expectations

The Fortrea team considered the ability to use the totality of data to support dose definition, using IV data for safety and inhaled data for efficacy. They also explored building a physiologically based pharmacokinetic (PBPK) model to support the new product.

To input the model, the team evaluated source data from other products in the published literature. The resulting model was used to define a target dosing window for the new inhaled product. Its justification was used in a Pre-IND briefing package submitted to the FDA to solicit feedback on Phase I design and inform the clinical strategy.

Parallel activities help trim development timelines

While creating the models, Fortrea simultaneously worked closely with the clinical operations team to identify territories and sites.

They located capable sites with experience in orally inhaled products, which enabled the team to rapidly translate regulatory agency feedback into the subsequent clinical study.



Reducing white space and delivering dependable data

Fortrea's holistic efforts showcased their ability to apply creative approaches and use innovative tools to simplify clinical development. The use of a PBPK model demonstrated the ability to:

- Engage the FDA early to align expectations
- Define a target dose for Phase I studies using the new dosage form
- Reduce the need for dose-ranging studies
- Maximize output and bridge from Phase I studies into Phase III
- Save significant time and cost associated with Phase II dose-ranging studies

Throughout the collaboration, Fortrea applied strategic thinking and multidisciplinary support as they embedded new efficiencies into the sponsor's clinical development program. Despite some challenges in developing the PBPK model at the time, the predictions were retrospectively corroborated by recently presented clinical data, supporting the use of model-informed drug development to simplify clinical development and save time and cost.

Learn how Fortrea integrates regulatory, clinical, medical, market access and commercial strategies to streamline clinical development and reduce costs.

READ MORE at: fortrea.com/clinical-solutions/consulting