CERTARA

Model Development and Trial Simulation Accelerates Clinical Development

Modeling strategy enabled sponsor to provide rational basis for Phase III dose selection and avoid additional dose-ranging study, saving 12 months and $6 million

Background

A global pharmaceutical company was seeking to advance its drug candidate, indicated for the treatment of osteoporosis, into pivotal Phase III trials. Data from Phase I and II studies were available on the drug candidate, including a Phase IIB dose-ranging trial currently underway.

Challenge

As the sponsor prepared for a rigorous internal and external review of its clinical data and requirements for its confirmatory studies, it became critical to establish a comprehensive picture of the drug candidate's efficacy profile. Specifically, the sponsor sought to establish a quantitative basis for the minimally effective dose to take into Phase III studies.

Solution

Certara extended the use of existing models of drug action, and created new predictive models of drug response based on the Phase I/II data, to support a clinically meaningful Phase III dose. First, Certara incorporated additional data from the sponsor's existing population pharmacokinetic (PK) models to include other data and relevant information on factors that influence the compound's behavior. Certara then built and tested additional new models of drug activity, including bone formation biomarkers and clinical endpoints of bone mineral density, as functions of time and treatment. The development team then used the linked models to perform simulations of expected response to different doses.

The models accounted for differences in response due to different clinical measures and patient characteristics. Finally, the models were simulated to help evaluate potential outcomes from the Phase IIB clinical trial. Simulations were conducted and analyzed using Certara Trial Simulator and Drug Model Explorer software.

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Solution

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Benefit

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The sponsor's model-based analysis offered compelling evidence to demonstrate the dose-response relationship for the compound, and to support an appropriate dose range for Phase III. In particular, based on the weight of the clinical data and accompanying model-based approach, the sponsor was confident that it could proceed to Phase III without conducting an additional dose-ranging trial.

Impact

The sponsor commenced with its Phase III program, avoiding further direct investment of $6-8 million and 12 months required to conduct an additional Phase II dose-ranging trial.[1,2] In addition to the direct cost savings of an avoided Phase II study, the sponsor was able to proceed with a smaller and more informative Phase III trial design. Finally, the expected time-to-market savings from a more efficient pivotal trial and earlier approval offered the promise of providing a beneficial treatment to patients much sooner, which could be worth tens of millions of dollars to the commercial value of the drug over its patent life. The modeling and simulation strategy helped the sponsor establish a comprehensive picture of the drug's efficacy profile to justify dose selection and accelerate clinical development.

References

1. Sponsor data on Phase II trial design and investigational program.

2. Mean out-of-pocket clinical period costs for Phase II investigational compounds. DiMasi, Hansen, Grabowski. The Price of Innovation: New Estimates of Drug Development Costs. Estimates of Phase II trial length for selected therapeutic categories from Pharmaprojects, January 2008. Published in PAREXEL's R&D Statistical Sourcebook, 2008/2009.

About Certara

Certara is a leading provider of decision support technology and consulting services for optimizing drug development and improving health outcomes. Certara's solutions, which span the drug development and patient care lifecycle, help increase the probability of regulatory and commercial success by using the most scientifically advanced modeling and simulation technologies and regulatory strategies. Its clients include hundreds of global biopharmaceutical companies, leading academic institutions and key regulatory agencies.

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