RECIPHARM PATHWAY TO CLINIC®

A RAPID PATHWAY TO CLINIC

How Recipharm and CTC supported Swedish biotech Betagenon with its important phase I milestone.

INTRODUCTION

A Swedish biotechnology company called Betagenon was ready to take its new drug candidate O304 to clinical trials. The molecule is an AMP-activated protein kinase (AMPK) activator for the treatment of chronic energy balance disorders in metabolically challenged elderly and/or obese individuals.

Clinical Trial Consultants (CTC) and Recipharm were selected to perform the work needed to reach the customer's important phase I milestone. Although phase I was the priority the subsequent progress to phase II after a successful phase I was an important goal from the start.

Services delivered:

- GMP manufacture of active pharmaceutical ingredient (API)
- Drug product manufacture
- Design and clinical conduct of a first in human study - SAD and MAD in healthy volunteers and patients
- Bioanalysis

Project highlights:

- First study performed and report delivered approximately eight months from project initiation
- Recudes study timelines by approximately six months using a combined adaptive design

DEVELOPING THE DRUG

The scope of the project was to develop a manufacturing process and a suitable placebo formulation for a phase I study. A suspension formulation for preclinical studies had already been developed. In order to develop a placebo suspension as identical as possible to the active suspension, a number of excipient characteristics were of importance, including colour, particle size and sedimentation properties.

MANUFACTURING PRODUCT FOR CLINIC

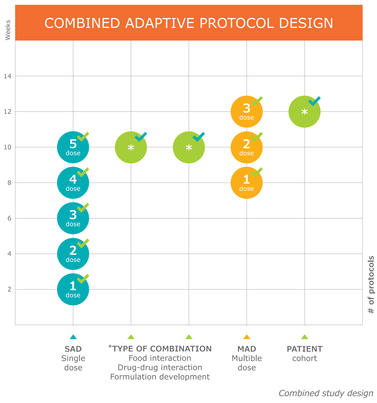
The manufacturing scale for the first study was late increased in size in order to provide the desired amount of clinical trial material to cover the phase IB and phase II requirements. Recipharm simplified the clinical supply service by providing a complete package, including labelling, randomisation and packaging of patient kits to supply the different studies.

THE CLINICAL TRIAL

Preparations for the clinical trial started early and involved close collaboration between the sponsor, Recipharm and CTC. The first in human protocol had a combined adaptive design with both a single (six cohorts) and multiple ascending dose part (three cohorts). By performing the two in parallel, CTC could reduce study timelines by approximately 6 months*. This was followed by two exploratory cohorts, one with patients and one healthy volunteers to determine drug-drug interaction. The protocol was submitted to the regulatory authorities and approved after 41 days.

Conventional study design

***Reduced study timelines by 6 months**



Combined study design

BIOANALYSIS

A bioanalytical method was developed and validated according to both European Medicines Agency (EMA) and Food and Drug Administration (FDA) guidelines. What was unusual for the project were the very high expected plasma concentrations of the analyte of interest. As a result, the bioanalytical method had to be designed to ensure proper solubility of the analyte in all steps of the method. Another important aspect of the method was to ensure that no study samples could have reported concentrations outside the established calibration interval and, for example, saturate the analytical detectors.

COORDINATION

In order to adapt to developments and hurdles during phase I, coordination between the project team at the clinical research unit, manufacturing teams and bioanalysis experts is crucial. This project involved close partnership working between the two Recipharm sites and CTC. Due to the close contact between all three sites, the coordination could be handled very efficiently due to pre-defined processes. By communicating and working together from the start of the project, both partners had the opportunity to discuss, foresee and handle challenges that may arise in the clinic at an early stage.

In addition, the bioanalytical and clinical facilities had close and direct communication, which included the overall project manager. This allowed for precise coordination of study sample shipment and receipt, as well as for a smooth transfer of the obtained bioanalytical data.

> *Working with CTC and Recipharm has allowed us to streamline our phase I project, speeding up timelines and reducing risk. Close coordination between the clinical research, development, manufacturing and bioanalysis experts helped us to overcome hurdles along the journey to clinic.*
>
> Thomas Edlund,
> CEO, Betagenon

CHALLENGES

1 Challenge one: Dose homogeneity of the IMP

Achieving good dose homogeneity with suspensions in early clinical studies can be challenging due to sedimentation and reconstitution problems. This was ensured through a rigorous protocol for dispensing which was developed with close collaboration between the clinical research unit and the manufacturing team. Formulation scientists were also in direct contact with the dispensing pharmacists to ensure adequate dosing.

2 Challenge two: Bioanalysis

The high expected study sample concentrations posed some initial challenges during method development, but could quickly be overcome by screening and selecting suitable solvent mixtures that ensured minimal adsorption of the analyte, as well as maximum solubility. As the API had not previously been analysed at the bioanalytical laboratory, a full method development and EMA/FDA validation had to be performed.

3 Challenge three: Timelines and coordination

The clinical timelines had deliberately not been specified in detail in order to allow for a maximum flexibility in the performance of the individual study cohorts. This subsequently also called for the bioanalytical support to have flexible time slots for the analysis of the received study cohorts, which could only be achieved by having close communications between the clinic and the laboratory.

SUMMARY

By applying an adaptive design and delivering well-coordinated activities during the manufacturing, clinical trial management and bioanalysis stages, a fast and flexible path to phase I clinical results could be achieved. Testament to the success of the phase I project, the sponsor continued with the phase 2a study with the same team. This significantly shortened the start-up time for the next stage of the molecule's journey to commercial success.

ABOUT RECIPHARM

Recipharm is a leading contract development and manufacturing organisation (CDMO) headquartered in Stockholm, Sweden. We operate development and manufacturing facilities in France, Germany, India, Israel, Italy, Portugal, Spain, Sweden, the UK and the US and are continuing to grow and expand our offering for our customers.

Employing around 5,000 people, we are focused on supporting pharmaceutical companies with our full service offering, taking products from early development through to commercial production. For over 20 years we have been there for our clients throughout the entire product lifecycle, providing pharmaceutical expertise and managing complexity, time and time again. Despite our growing global footprint, we conduct our business as we always have and continue to deliver value for money with each customer's needs firmly at the heart of all that we do. That's the Recipharm way.

ABOUT CTC

CTC is a Swedish full-service CRO with clinical conduct in focus. Our mission is to facilitate clinical and translational research by providingour customers with cost-effective advice and implementation of early clinical trials (Phase 0/I/IIa). CTC has three dedicated research clinics in in Sweden, which of one is located at the Akademiska University Hospital in Uppsala, specialised for first time in human studies.

CTC
CLINICAL TRIAL CONSULTANTS AB
TRANSLATING SCIENCE INTO TREATMENT

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