CASE STUDY: ADVANCING THERAPEUTICS FOR MYELOMA

Oncopeptides is a clinical stage company that is developing a molecule for oncology indications. The molecule, which originated at Uppsala University, Sweden and the Karolinska Institute, is focused on multiple myeloma as a first indication.

Myeloma is a very individual cancer. Both in terms of what symptoms and complications patients can have and in the way they respond to treatment. Improvements made to treatment over the last decade have meant that survival rates are increasing. However, there is still no cure and there remains a significant need for more efficacious and tolerable therapies. To this end, Oncopeptides, a small team of 25, based in Sweden and the United States needed an experienced partner to help take its promising molecule from the discovery phase through to clinical trials and finally commercial production.

OVERCOMING HURDLES AT EVERY STAGE

Vendor selection

In the early project stages, Oncopeptides worked with a different partner to manufacture a batch of its molecule. However, the partnership was very prescriptive, lacked innovative thinking and failed to meet the company’s needs at that time. The team at Oncopeptides needed a contract development partner that would take a creative approach to overcome hurdles that can occur during drug development and turned to Recipharm’s analytical chemistry team to reverse engineer the batch.

Commenting on the start of the relationship, Jakob Lindberg, CEO at Oncopeptides explains: “Really good chemists are hard to come by. There are plenty that can follow recipes in a book but a very large part of chemistry is the ability to problem solve. People at Recipharm’s development facility in Uppsala showed every sign of being intellectually curious and we felt confident that they could help us out.”

Formulation development challenges

Having worked on the initial molecule, Recipharm continued to work in collaboration with Oncopeptides as it progressed through the clinical development stages. The poor stability of the drug product in its original organic solvent formulation presented a huge challenge to the team and had the potential to stop the project in its tracks. A new formulation was required and Recipharm was tasked with finding a solution.

Due to the way the drug product interacts in the gut, it was essential for it to be taken intravenously. As the molecule had proven to be unstable in water and in solvent, it couldn’t be formulated as a solution. The only formulation that could be used was a freeze dried powder. Developing this was a huge undertaking and a critical step in the project, taking almost two years and involving serious problem-solving by the technical team at Recipharm.

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Manufacturing the new formulation

The contract development and manufacturing organisation (CDMO) assumed a consultative role to ensure the right vendors were selected for both the API and formulation manufacturing activities. Working in partnership with Oncopeptides, Recipharm acted as chemical consultants, testing batches, analysing results and going through the details of the batch manufacturing records, identifying areas for improvement and proposing solutions to challenges.

Jakob Lindberg explains: “Recipharm acted as our chemistry, manufacturing and controls (CMC) department. They did everything you would expect of your own in-house team. As a small group of 25, this level of partnership and close collaboration was extremely valuable to us.”

Taking the product to trials

In total, 650 patients will be involved in clinical trials for the drug, which are expected to conclude by mid-2019. Recipharm participated in writing the clinical protocols and drug handling instructions to be used by the hospital pharmacies during trials taking place in the US and western Europe. Not only that, the CDMO took care of the regulatory correspondence with regard to CMC with both the FDA and European regulatory agencies.

During the initial stages of the clinical trials, Recipharm has performed most of the preparations and work surrounding the pharmacokinetic (PK) studies, analysing patient samples from all over the world to obtain data on drug absorption, distribution, metabolism and excretion (ADME) under both GMP and non-GMP conditions as required. This was— and is—a substantial project involving four different clinical trials, including a pivotal phase III trial to obtain results for a complete regulatory submission package.

Jakob Lindberg continues: “The team at Recipharm has provided expert analytical support to us throughout the clinical trials. A lot of thinking time has been required to get some of the assays right, so we required a partner with a highly intelligent approach to analysis.

When contract manufacturing for phase I and II trials, it doesn’t necessarily need to be the final formulation of the drug product. It does from a chemical standpoint, but there are a lot of other factors that can vary in the final dosage form. In phase III, which is our current focus, the final product is required.

In order to complete a successful regulatory submission, the clinical data isn’t enough. You have to show you can manufacture the drug to commercial levels in a stable way. This is the next challenge we face, and Recipharm is continuing to help us on this journey as we move from small scale to commercial manufacturing of the API and finished drug product.”

Going commercial

At present, Recipharm is assisting Oncopeptides with the procurement of commercial manufacturing services. All samples from planned future PK studies will be analysed by Recipharm and the team will be instrumental in ensuring all the regulatory documentation is in place for the final submission.

Jakob Lindberg adds: “Over the coming months, scale-up, commercial batches, stability studies and regulatory dossier compilation will be key for us and Recipharm will be working in partnership with us at each step of the journey.”
THE OUTCOME

The true collaboration between Oncopeptides and Recipharm means that a new drug product to treat multiple myeloma is getting closer to a reality every day.

The molecule which continues to progress through the drug pipeline is expected to have a clear advantage in late stage patients where the medical need is huge. Oncopeptides aims to extend and improve life quality for myeloma patients across the world. As such, the tolerability profile of the end product is critical to limit side effects and both Recipharm and Oncopeptides have worked together to devise a novel treatment to overcome the drawbacks of existing therapies.

Lastly, Jakob Lindberg comments "We have been working with the Recipharm team in Uppsala for more than 10 years in what can be best described as a true partnership. Recipharm has been our chemical arm from the early stages of this project and assuming the drug gets approved, they will have been with us all the way from early phase development to commercial supply.

The team’s problem solving abilities and flexible approach to drug development have made this project a success. When developing advanced therapies, you are often working with short timeframes and unexpected hurdles, making a can-do attitude and proactive mentality essential. Recipharm has helped us to manage complexity at every step."

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.

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Recipharm has helped us to manage complexity at every step.
Jakob Lindberg,
CEO, Oncopeptides

Oncopeptides is a research and development stage pharmaceutical company developing drugs for the treatment of cancer. Since the founding of the company, the focus has primarily been on the development of the lead product candidate Ygalo®, an innovative, peptidase-potentiated alkylator intended for effective and focused treatment of hematological cancers, and in particular multiple myeloma. The current clinical study program of Ygalo® is intended to demonstrate better results from treatment with Ygalo® compared to established alternative drugs for patients with late-stage multiple myeloma. Ygalo® could potentially provide physicians with a new treatment option for patients suffering from this serious disease.