

Accelerating drug product development from early phase to scale up and commercialization



Gábor Heltovics
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Druggability Technologies (DRGT) is developing DRGT-46 as a novel therapy for pain. Gabor Heltovics, CEO of DRGT, explains how Quotient Sciences enabled the rapid development, clinical assessment and commercial readiness of its DRGT-46 product using integrated services across Quotient's network of harmonized development and manufacturing sites in the UK and US.

DRGT is a specialty pharma company developing an array of drugs in diverse indications with the objective of achieving measurable and meaningful improvement in their clinical utility. The company uses its proprietary platform to screen and select Super-API compositions and its portfolio contains over 30 preclinical and clinical stage compounds.

DRGT-46 is a novel composition of Celecoxib (Celebrex®), a COX-2 inhibitor prescribed for pain. Celecoxib is the only COX-2 inhibitor on the market and, although the drug is off patent, it still commands a large share of the market. Gabor explains *“Celebrex’s use is limited in acute pain management due to its relatively long “kick in” time of 50 mins to 1.5 hrs or, if taken with food, this can be as long as 3 hrs. This is particularly important with the current opiate crisis. There is a significant need for molecules which provide rapid pain relief to remove the need for opiates.”*

Fast-track and de-risk programs

Dog pharmacokinetics (PK) data showed that DRGT-46 reached the required blood concentration to give onset of pain relief in under 5 mins, providing preclinical proof of concept for the molecule.

DRGT wanted to rapidly develop a clinical formulation and, if successful, a commercial product. *“This is where our collaboration with Quotient became very important for us. Our objective was to transition rapidly from a preclinical formulation to a commercial drug product. We needed to develop our product as fast as possible and reduce the complexity of drug development to de-risk the whole program”.*

“We had worked with Quotient successfully on other programs. Our first objective for this program was to demonstrate formulation proof of concept in a Phase I clinical PK study.” The Phase I drug product was manufactured and dosed in Quotient’s UK facility using their unique Translational Pharmaceuticals® platform which integrates formulation development, real-time adaptive manufacturing and clinical testing to rapidly select formulations to progress to scale up. As the molecule is poorly soluble,

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a number of solubilization technologies were applied with a spray dried powder in a bottle format selected for the study. *“Quotient has become an extension of our project team and have knowledge of our product. They are highly interactive and committed to helping us achieve our goals”*

“The healthy volunteer PK showed that DRGT-46 achieved the effective concentration claimed to be needed for pain relief within 12 minutes at



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100 mg or 200 mg in comparison to 45 mins for 400 mg of Celebrex. Having demonstrated clinical proof of concept, we decided it was important to transition from a Powder in Bottle to a sachet format as that would be a more suitable commercial product for the patient group. To ensure patient acceptability, the sachet product would need the inclusion of taste masking agents.”

The successful drug product formulation was transferred to Quotient's development and clinical manufacturing site in Philadelphia and optimized using flavor/sweetener combinations to provide the required taste enhanced sachet format for commercial manufacture. The Translational Pharmaceutics® platform was again used in the program to rapidly manufacture these new formulations and to

evaluate and optimize the taste properties and determine the PK profile at Quotient's clinical pharmacology facility in Miami. Again, clinical data were used in real-time to drive the manufacture of the selected drug product formulation composition for this pivotal PK study.

Unique therapy for acute pain

“The optimized product developed by Quotient showed an even better PK profile in the pivotal study than in the Phase I study. The expected time to onset of action was reduced even further to 8 mins rather than 12 mins. This final drug formulation gives us a unique COX-2 therapeutic for the management of acute pain. This hasn't been possible before now.”

“The final stage of the program was to scale the process to meet late stage clinical and commercial needs, and develop process robustness and stability data to support product registration.”

Following the identification of the commercial formulation, the spray-drying process was scaled up alongside the establishment of suitable blending and granulation process trains. Manufacturing design spaces for the critical process steps were then identified to support the late stage clinical and registration batch production. In parallel, later stage product development activities such as packaging development, longer term stability studies and method validation were performed to efficiently transition the product to being commercial ready.

DRGT used the Translational Pharmaceutics® platform twice; to clinically validate early formulations in the UK; and to optimize a commercial formulation in the US. *“We are now moving rapidly to a Phase III multi-site clinical trial. While the Phase I pivotal study was ongoing, we continued to work with Quotient on the CMC and process scale up to get us ready for the late clinical stages*



Quotient has reduced our time-to-clinic and time-to-market. They understand the issues in drug development and have taken us from early stage to commercial in the most efficient way.”

and commercialization. As a result, Quotient will manufacture the drug product for the Phase III study.”

Working with a development and manufacturing partner with integrated capabilities across countries and continents was so important for DRGT. Gabor explains *“Quotient has become an extension of our project team and has built up considerable knowledge of our product. Their internal capabilities and knowledge extend well beyond traditional CDMO services, with expertise that includes regulatory affairs, biopharmaceutics and medical research. This means we can access skills and resource as required, rather than investing in setting up those functions internally. For small companies like DRGT, Quotient's project management team means we can rely on them to maintain timelines and work within an agreed budget.”*

Through its partnership with Quotient Sciences, DRGT has clinically demonstrated that its novel drug product, DRGT-46, may have a significantly faster onset of action than Celebrex® and at a lower dose. *“In working with Quotient, we have been able to bridge from Phase I product to commercial ready in 18 months which really is remarkable!”*

