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Case Study

Enabling Formulation Development for Toxicology Studies for a New Chemical Entity

About Our Client

Our client, US-based biotech company involved in the discovery and development of small molecule therapeutics for the treatment of cardiovascular disease.

The Challenges

- The molecule has good solid-state properties but low solubility
- The molecule is neutral in nature and does not have any detectable solubility across the pH range expected in the GIT
- The molecule has less than 10% bioavailability (BA) in preclinical species
- To enable toxicity studies, the molecule required formulation development that could support a high dose delivery while providing a linear dose exposure in preclinical studies
- An enabling formulation would be required for defining the clinical formulation strategy and to achieve the required PK profiles in clinical studies

Our Proposed Approach

- A detailed review of the molecule's properties and initial screening led to the identification of solution and amorphous solid dispersion approaches as possible techniques that could increase solubility and achieve the desired in vivo exposure
- For solution formulation development, a detailed solubility screening was conducted using co-solvents, surfactants, buffering agents and cyclodextrins to select the most suitable vehicle to achieve the desired formulation
- Leveraging our Integrated capabilities in Pharmaceutics and Pharmacokinetics, a stable solution formulation was developed for toxicity studies and successfully tested in in vivo achieving greater than 10x exposure multiples compared to the neat drug
- An amorphous solid dispersion formulation was developed by extensive screening with polymers and surfactants to select the best formulation and drug loading followed by scale-up via a spray dried dispersion process
- A stable, amorphous solid dispersion formulation was developed as a backup strategy for toxicity studies and was successfully tested in vivo achieving greater than 5x exposure multiples compared to the neat drug
- The formulation developed provided an alternate approach for clinical development

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Our Value Proposition

- We started with a bioavailability of less than 10% and achieved greater than 60% BA with the recommended formulation
- A clear formulation strategy was developed for animal toxicology and in-human clinical studies paving the way for clinical development
- Aragen was able to de-risk the poor solubility of the molecule through a thorough, systematic approach
- Aragen Integrated Pharmaceutics plus Pharmacokinetics approach avoids potential delays and helps achieve substantial savings in time and development costs
- Aragen preformulation screening platform supported by actual in vivo PK data, typically requires 4 - 6 weeks to complete and deliver a viable clinical formulation