ALTASCIENCES

CASE STUDY

Nanosuspension Formulation to Maximize Potency for Preclinical Studies

OVERVIEW

A client contracted Altasciences for our Proactive Drug Development approach to rapidly get their new API through the preclinical development phase. Their goal was to develop a robust formulation at the maximum potency. At this point, a formulation needed to be developed from the ground up. This study was proposed to conceptualize and develop a stable drug prototype to be used in clinical trials.

PURPOSE

- Drug Development Phase: preclinical
- Class of Drug: small molecule, BSC Class II/IV
- Dosage form: nanosuspension
- Route of Administration: subcutaneous and intramuscular

METHODS AND RESULTS

Our client presented us with an **API BSC Class II compound**, intended for extended release, with specifications about their requirements for a drug product.

A target product profile was quickly designed, with a clearly defined list of critical characteristics that reflected their specifications. Their goal was to develop a formulation prototype for preclinical work, including efficacy, pharmacokinetics, and toxicology studies.

Various dosage forms were summarized and proposed based on our formulation, manufacturing, and analytical capabilities. The client ultimately settled on a nanosuspension dosage for subcutaneous and intramuscular delivery.

Once critical parameters were identified, a list of potential excipients was provided to the client for experimentation. The excipients provided were expertly selected to provide the best-estimated results based on the appropriate drug delivery systems and manufacturing methods. All excipients provided had well-defined safety profiles and were recognized as safe by the FDA. Once approved, an excipient compatibility study was performed to determine if the API was stable in the presence of each excipient.

We determined feasibility around two critical factors: **particle size distribution** and **concentration**.

The initial experiment screened the approved surfactant excipients to best achieve the target particle size distribution. Our target was a D50<200nm and D90<1µm measure via laser diffraction. Solid API was suspended in an aqueous vehicle at a concentration of 20% w/w containing the different surfactants and 0.4mm YTZ grinding media. These formulations were subsequently milled for up to 48 hours and sampled at various timepoints.

Promising formulations were further investigated by repeating the milling at incrementally higher API concentrations up to 40% w/w. Analytical methods were developed in parallel with the feasibility experiments for particle size, zeta potential, and assay, in compliance with regulatory requirements. Successful formulations were then placed on short-term stability.

Prototype formulations were selected for scale-up and further optimized to meet all remaining parameters. Lead prototype formulations were then tested for appearance, particle size, assay, pH, viscosity, and re-suspendability.

With the data generated by the lead prototype formulations, we moved on to developing a robust and reproducible process necessary for large-scale manufacturing. The manufacturing process was scaled up and moved to our DeltaVita® milling equipment, and the process parameters (pressure, temperature, homogenization cycle, etc.) were optimized to reliably manufacture the nanosuspension. The pilot batch was used to support accelerated and real-time stability studies to assess the long-term stability of the nanosuspension, by evaluating the impact of various storage conditions on particle size and API stability.

HOW ALTASCIENCES PROVIDED VALUE

The above-described approach to preclinical formulation development allowed us to rapidly optimize and produce a stable nanosuspension for preclinical studies.

ALTASCIENCES CAN HELP

Using advanced processes, we have formulated, tested, and/or manufactured nearly every pharmaceutical dosage form currently available on the market, including tablets, liquid- and powder-filled capsules, over-encapsulated capsules, nanomilled suspensions, creams, gels, powders, and terminally sterilized injectables.

Our team offers decades of expertise in drug development, manufacturing, and analytical services, including formulation development, Phase I through large-scale commercial manufacturing, and ICH stability storage and testing, to pharmaceutical and biotech companies worldwide.

We also provide analytical method development, qualification, and validation, and finished product and release testing.

We have a 99% on-time delivery record, and DEA licenses for drug Schedules I to V.

In addition to our CDMO services, our suite of solutions includes preclinical and clinical studies, as well as bioanalytical expertise. With our **Proactive Drug Development** approach, real-time communication and seamless collaboration provide optimal efficiencies for our clients.

ABOUT ALTASCIENCES

Altasciences is an integrated drug development solution company offering pharmaceutical and biotechnology companies a proven, flexible approach to **preclinical** and **clinical pharmacology** studies, including **formulation, manufacturing, and analytical services**. For over 25 years, Altasciences has been partnering with sponsors to help support educated, faster, and more complete early drug development decisions. Altasciences' integrated, full-service solutions include **preclinical safety testing**, **clinical pharmacology and proof of concept**, **bioanalysis**, program management, medical writing, biostatistics, and data management, all customizable to specific sponsor requirements. Altasciences helps sponsors get better drugs to the people who need them, faster.