CASE STUDY

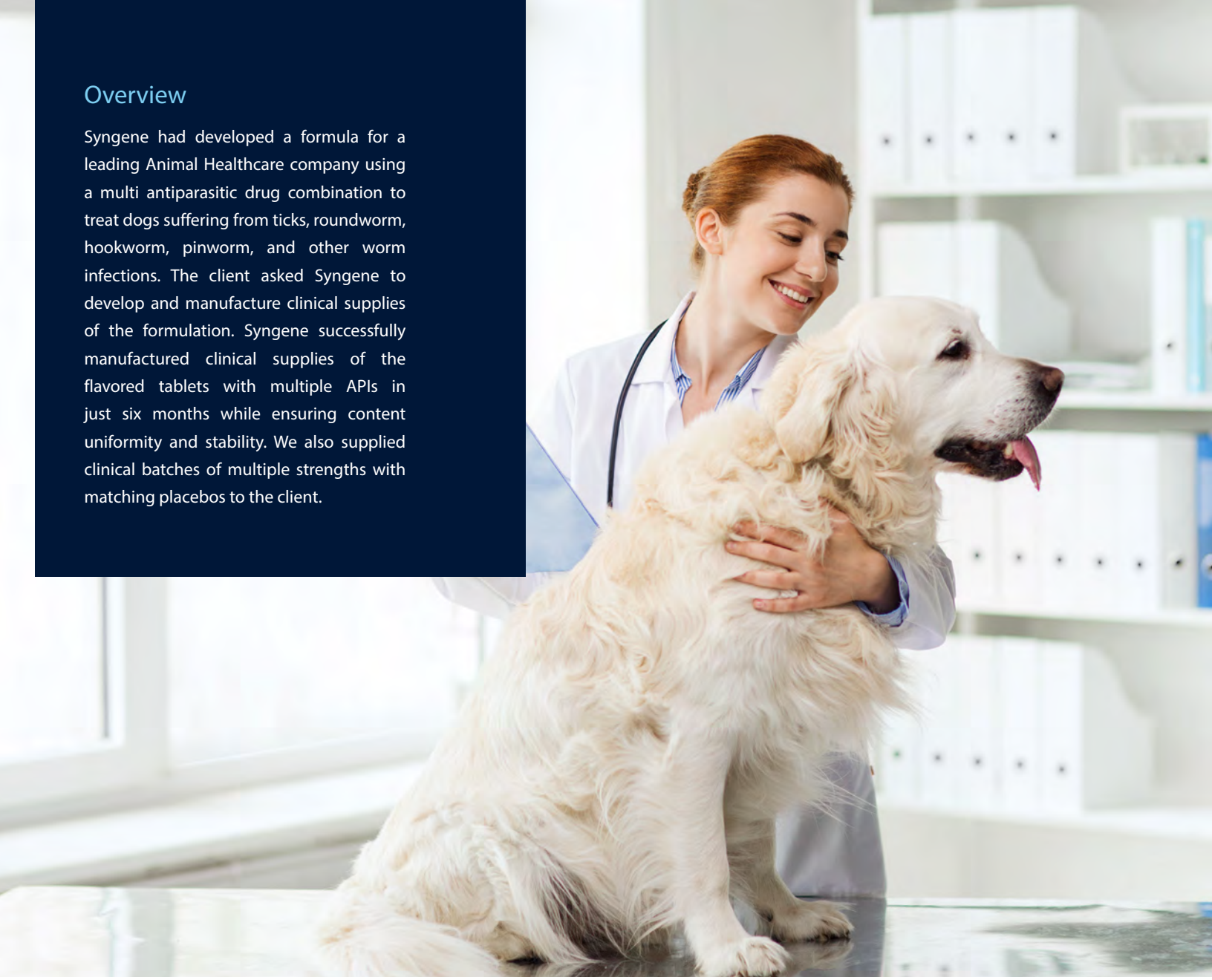
How Syngene developed **a multi-drug combination, antiparasitic drug for dogs** for a leading Animal Health company

Syngene

Putting Science to Work

Overview

Syngene had developed a formula for a leading Animal Healthcare company using a multi antiparasitic drug combination to treat dogs suffering from ticks, roundworm, hookworm, pinworm, and other worm infections. The client asked Syngene to develop and manufacture clinical supplies of the formulation. Syngene successfully manufactured clinical supplies of the flavored tablets with multiple APIs in just six months while ensuring content uniformity and stability. We also supplied clinical batches of multiple strengths with matching placebos to the client.



The challenge

The client is a leading, global Animal Healthcare company dedicated to innovating and delivering products and services to prevent and treat diseases in farm animals and pets.

The client approached Syngene to help them develop and manufacture clinical supplies of a formulation comprising a multi antiparasitic drug combination. The drug was for treating dogs suffering from ticks, roundworm, hookworm, pinworm, and other worm infections.

The challenges were as follows:

- Incorporating multiple molecules into one formulation
- Developing and manufacturing multiple active strengths of the drug with higher drug load while ensuring minimum tablet weight for higher active strengths (~5.5g)
- Ensuring the formulation has good palatability
- Incorporating animal flavor in the formulation even though it had every possibility of triggering degradation of one of the drugs since the drug is highly prone to acidic degradation
- Maintaining content uniformity of the actives within each tablet
- Ensuring solubilization of water-insoluble drug substance with the help of solubilizer (concentrated aqueous solution of solubilizer)
- Developing the formulation without using any organic solvent

The Solution

Syngene came up with different strategies to develop and stabilize the drug substance, which is sensitive to degradation during the stability period. Syngene undertook the following studies to arrive at the end product:

Drug-drug and drug-excipient compatibility studies for the following:

- Preparation of slurry in water, including overnight staging at high temperature,
- Selection of functional ingredients and screening based on compatibility results
- Studying the impact of the pH of slurry on the stability of drug substances

Stressed stability studies for quick selection of prototypes

- Evaluating prototypes with different types and levels of pH modifiers to stabilize the drug substance
- Manufacturing different prototypes using different processes and studying them for drug substance stability
- Assessing different types of flavors for the formulation

Prototype evaluation for PK and palatability studies

- Developing and evaluating prototypes with different levels of flavors
- Developing and evaluating prototypes with different types of flavors
- Manufacturing prototypes using different processes

Informal Stability studies using different prototypes

- Studying prototypes with different flavors, processes, and levels of pH modifiers
- Finalizing control strategy based on accelerated Stability study data of one month
- Conducting accelerated Stability studies for six months, after which the product was found to be stable

Development of simple, robust, and one-step process to include all multi-drug substances in one formulation, including scale-up

- Developing single granulation for all drug substances
- Dissolving a low dose drug in an aqueous binder solution and achieving granulation
- Adjusting the level of pH to maintain the required alkaline microenvironment in the tablet throughout the stability
- Optimizing process parameters to achieve content uniformity and the desired drug release profile
- Scaling up batches manufactured at 50kg scale including achieving reproducibility

Manufacturing of clinical batches

- cGMP manufacturing of multiple active strengths along with matching placebos
- Manufacturing blister packaged tablets staged on stability as per VICH guidelines (bracketing samples strategy)
- Analysis and validation of analytical methods

Conclusion

We successfully manufactured the drug substance containing multiple APIs (one of which is a very low dose), while ensuring content uniformity and stability in just six months. The client confirmed that the formulation had good palatability and that the in vitro drug release profile was appropriate based on PK study data. Subsequently, we supplied clinical batches of multiple active strengths with matching placebos to the client.

The case brings to the fore, Syngene's expertise in formulation services for animal health products for global clients. By outsourcing critical R&D processes to contract development and manufacturing organizations (CDMOs) like Syngene, animal health companies can accelerate their drug development programs from preclinical to commercial at optimum costs.

To know more about our Animal Health Drug Development services or to contact our experts, click here

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About Syngene

Syngene International Ltd. (BSE: 539268, NSE: SYNGENE, ISIN: INE398R01022) is an integrated research, development and manufacturing services company serving the global pharmaceutical, biotechnology, nutrition, animal health, consumer goods and specialty chemical sectors. Syngene's more than 4700 scientists offer both skills and the capacity to deliver great science, robust data management and IP security and quality manufacturing at speed to improve time-to-market and lower the cost of innovation. With a combination of dedicated research facilities for Amgen, Baxter and Bristol-Myers Squibb as well as 2 Mn sq. ft of specialist discovery, development and manufacturing facilities, Syngene works with biotech companies pursuing leading-edge science as well as multinationals, including GSK and Merck KGaA.

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