ESTEVE CDMO

Delivering GMP Certainty for Orphan Drug API Programs

Case Study

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Program Background

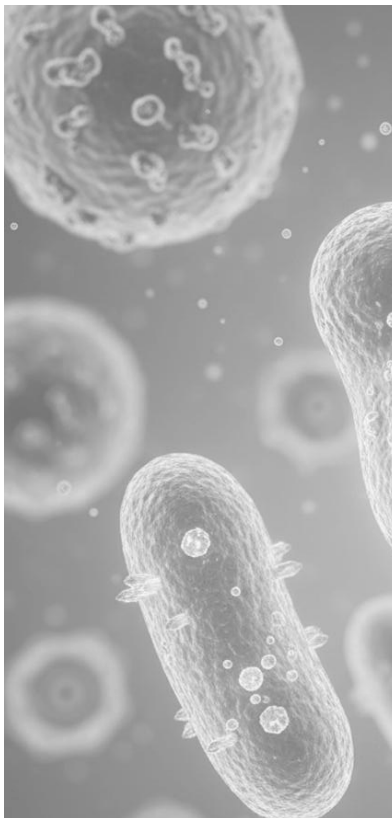
A biotech company developing an orphan drug therapy partnered with ESTEVE CDMO to **transform an inefficient, non-GMP synthesis into a robust**, **CGMP-ready process.** The original route showed clear limitations: poor scalability, inconsistent yields, and an amorphous API unsuitable for clinical and registration manufacturing. The goal was clear: redesign the process to achieve a scalable, crystalline API capable of reliable multi-kilogram CGMP production and future commercial validation.

Rather than optimizing a constrained route, ESTEVE CDMO **re-engineered the process from the ground up**. By simplifying the chemistry, eliminating unscalable operations, and controlling solid form, the program progressed from lab proof-of-concept to multiple registration batches within three years.

Challenges and Key Factors

The process presented multiple development challenges:

- **Highly inefficient**: Excessive unit operations with multiple extractions and solvents.
- **Unscalable operations**: Concentration to dryness and oil isolation.
- **Variable performance**: Steps involving aqueous concentration caused yield inconsistency.
- **Uncontrolled solid form**: Resulted in amorphous API and poor reproducibility.



Solution Overview and Execution

ESTEVE CDMO executed a **comprehensive process of re-engineering program** to address scalability and reproducibility issues.

Process Development

- Redesigned the synthesis into a **four-step route.**
- **Telescoped one step** to streamline operations
- **Eliminated aqueous concentration steps** and minimized extractions.
- **Increased yield** for a key step from **50% to 75%,** improving overall throughput.
- Established a **controlled crystalline API form**

Scale-Up and Validation

- Produce **multiple 3–5 kg CGMP batches** to support clinical supply.
- Successfully delivered **three 6 kg registration batches**,
- Process validated, with completion **of three PPQ batches planned for early 2026.**

The program achieved a **robust, reproducible, and scalable crystalline process**, suitable for registration and commercial readiness. Over approximately **three years**, ESTEVE CDMO transformed a complex, low-yielding route into a reliable CGMP process—demonstrating its ability to **convert inefficient early-stage chemistry into industrially viable, commercial-ready manufacturing solutions**.

Summary

ESTEVE CDMO transformed an inefficient, non-scalable synthesis into a robust, crystalline, and validation-ready API process. By re-engineering the route, eliminating unscalable operations, and introducing solid-state control, a key step yield was increased from 50% to 75%.

The optimized process enabled the successful production of multiple 3–5 kg CGMP batches and three 6 kg registration batches, with validation and PPQ planned for early 2026. This case demonstrates ESTEVE CDMO's ability to turn early-stage chemistry into scalable, high-quality, and regulatory-compliant API manufacturing solutions.

ESTEVE CDMO, *The Science of Collaboration*

ESTEVE CDMO is a global pure-play partner in small-molecule APIs and advanced pharmaceutical intermediates, collaborating closely with our customers to turn complex science into scalable solutions.

Powered by 1,500+ experts worldwide and recognized as the 2025 CDMO Leadership Award Global Champion in Small-Molecule API, we support programs from early development through large-scale commercial manufacturing.

Our end-to-end capabilities include process R&D, analytical and stability services, CMC, and commercial intermediates, with proven expertise in Spray Drying and HPAPI (up to OEB5) across six sites in the U.S., Spain, Mexico, and China.

THANK YOU

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