Scaling-up Active Pharmaceutical Ingredient (API) Chemistry for Phase 3 Clinical Trials and Bulk Manufacturing for a Potentially Novel Treatment for Schizophrenia

Case Study

About the client

Karuna Therapeutics is a leading US biopharmaceutical company developing drugs for psychiatric and neurological conditions. Their focus was on scaling up an NCE API for a combination CNS drug, meeting clinical trial and commercial manufacturing needs. The program began when the molecule was in Phase 2 stage and eventually Neuland successfully scaled up manufacturing to meet the client's requirements for Phase 3 trials. Leveraging its decades of experience, Neuland maintained the timelines throughout the project tenure, increased the yield in all stages significantly and reduced the overall project cost by 60%. In a short span of time, Neuland became the preferred CMO for the client's development programs.

The challenges

The client's priority was to develop a timebound, safe, scalable and cost-effective process right from the lab scale to cGMP manufacturing. With stringent deadlines for their Phase 3 clinical trials, ensuring regulatory compliance and managing supply chain risks were critical challenges. The compound had a low yield at each stage and involved the usage of hazardous reagents and conditions during route development.

Neuland's approach

An experienced group of scientists, engineers and cross functional team evaluated the process and identified the potential gaps to be focused on. Neuland established the process on commercial scale with the stage-specific achievements as listed below.

STAGE-1

Yield improved by **52%**

Replaced hazardous Cyanating reagent with milder one

STAGE-2

Reaction timeline minimized to **3hrs against 48hrs**

Yield improved by **10%**

Replaced hazardous base with an ecofriendly base

STAGE-3

Minimized work-up timelines

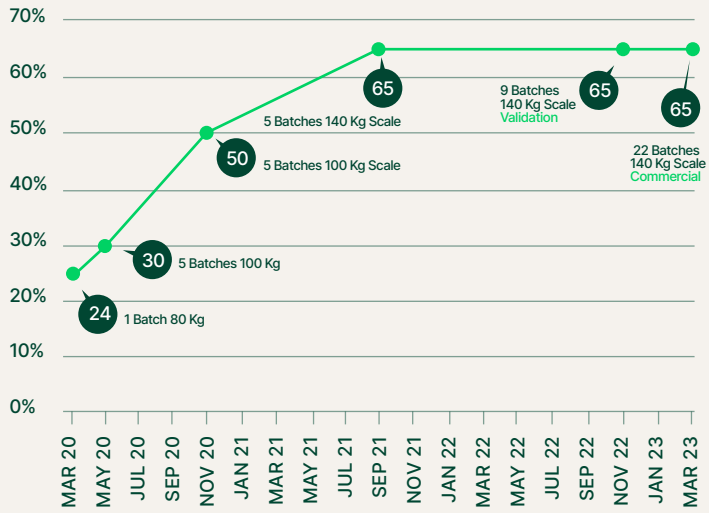
Yield improved by **25%**

Avoided multiple filtrations

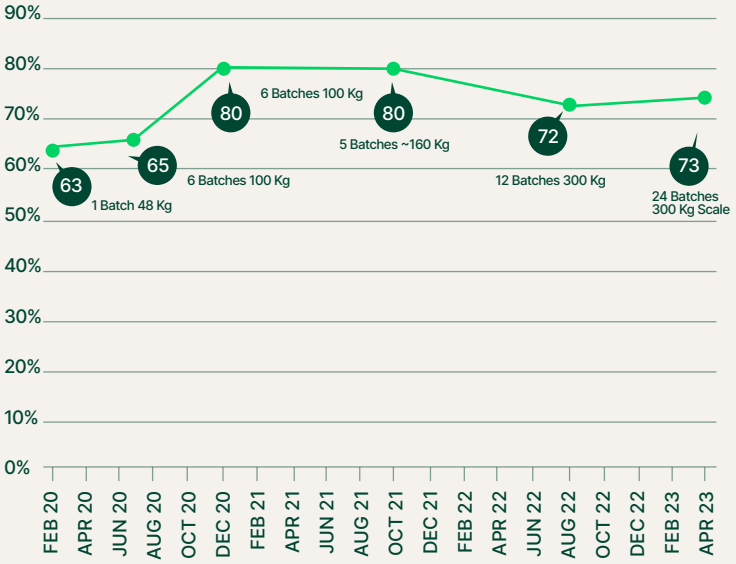
STAGE-4

Developed a single solvent purification process to achieve a higher quality output material

Stage 1 Yield Improvement



Stage 3 Yield Improvement



Project Objectives

- Develop a quick, robust, safe and scalable process to support commercial scale
- 2 X 200g lab representative sample as an outcome of lab development
- Sequential scale-up from 25kg to ~100s of Kgs output batch size
- Analytical method development and validation
- Undertake Stability studies and provide CMC documentation and regulatory filing support

Value Adds to the Project

Considering the growth projections in the market, Neuland also performed the following activities to add further value to the project & ensure the right outcome:

- In-house synthesis of starting material to reduce the cost, lead time and dependency
- Impurity profiling (including genotoxic impurities absence of Nitrosamines)
- Polymorph screening & particle size distribution
- Design of Experiments (DoE), Failure Modes and Effects Analysis (FMEA)
- Analytical method development and validation
- Sequential scale-up of target API (pilot batch, scale-up batches, registration batches & validation batches)

Outcome:

Neuland successfully designed, developed and demonstrated the process for the target drug substance resulting in:

- Overall yield improved by 3 folds
- Project cost eventually reduced by 60%
- High conversion and yield in each stage
- Avoided hazardous reagents and reaction conditions
- Reduced the number of processes in each stage through Process Optimization
- Easy isolation and crystallization methods
- Successfully upscaled the process from 25kg to 100s of Kgs output per batch

Conclusion

Neuland's collaboration with Karuna Therapeutics resulted in successful API development, process scaling, and manufacturing efficiency improvements. The project met clinical and commercial milestones, also significantly enhanced Karuna's supply chain security, reducing costs and improving process yields threefold.

About Neuland

Neuland Labs is a leading global Contract Development and Manufacturing Organization (CDMO) providing an end-to-end continuum of customised chemistry services. Our services include process development, process optimization, analytical testing, and regulatory support. Right from early-stage drug development through to commercial manufacturing of Complex APIs, we offer both small- scale clinical trial quantities and full commercial- scale supply with minimal tech transfer timelines. We are a project-oriented company that fosters collaborative customer relationships with a culture of agility, transparency, and quality at its core. We work with over 500 pharma and biotech organizations, advancing healthcare solutions, to help create a healthier world

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