Innovative Synthesis of a 25AA Peptide: Tackling Insolubility and Impurities with SPPS

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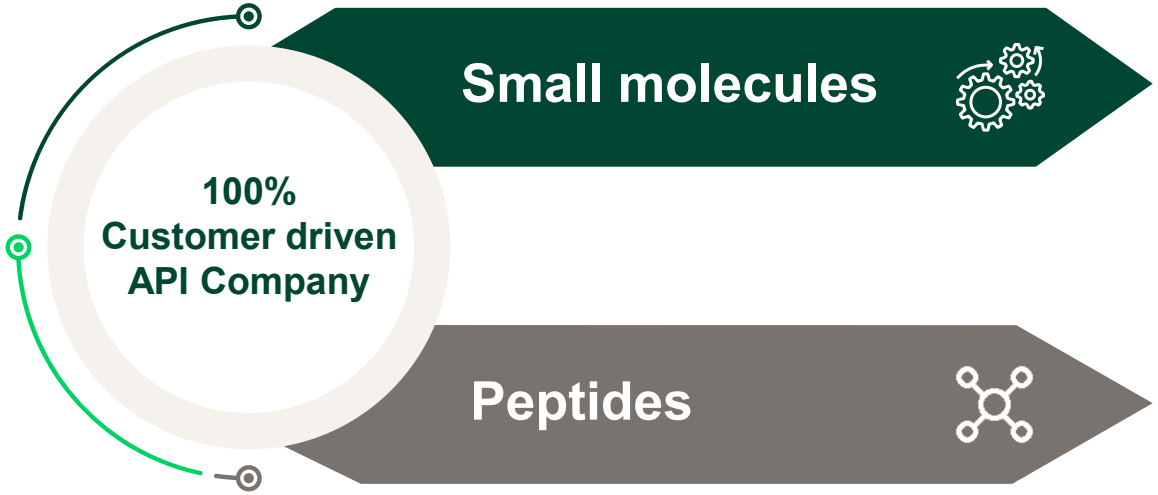
Company Overview – Neuland Laboratories Ltd.



KRMs, cGMP Intermediate and API

Solution phase synthesis, Solid phase synthesis, and Hybrid technology

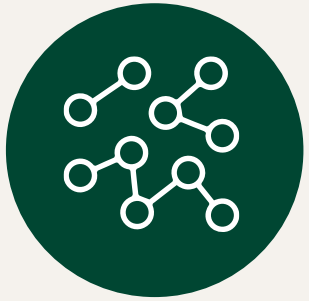
25 IND Filings
4 NDA Filings

3 Manufacturing Units
1,174 KL capacity

Neuland Expands Global Peptide Production Capabilities Investment of $30 Mn

A dedicated new peptide facility at its manufacturing Unit-I, Hyderabad, India

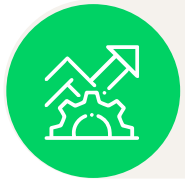
- ✓ Multi-product & multi-modular facility automated through DCS
- ✓ Peptide synthesizer capacity (SPPS & LPPS) of 6.37 KL
- ✓ Ability to handle up-to OEB level 5



Peptide R&D capabilities

- ✓ Automated peptide synthesizers
- ✓ Circular dichroism and fluorescence spectroscopy
- ✓ Tangential flow filtration

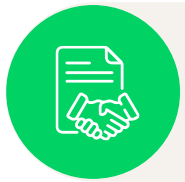
Why Peptide Capacity Expansion?



To meet the growing demand for peptides and the rising number of novel peptides under clinical investigation

15+ years of expertise in developing & delivering various peptides for innovator, using Solid Phase, Liquid Phase, & Hybrid synthesis methods at existing facility in Unit-I, since 2009

Module 1 completion by H2 2026, achieving annual capacity of multi kgs, ramping up to 100+ kgs across four modules



Support early clinical stage development through commercial-scale production and regulatory filings

Our current cGMP Peptide Pilot Plant

Equipment list

- 1 × 250 L glass-lined reactors
- 1 × 100 L solid-phase reactor
- SS316 vacuum tray drier
- 3 fume hoods
- Tray lyophilizer (Virtis G35EL5) 2 × 35 L capacity
- Isolator to handle OEB5 non-cytotoxic peptide
- compounds (OEL > 0.1 µg/m3)
- Nutsche filter SS316, 50 L capacity
- 20 L and 50 L Rotary Evaporators
- Preparatory HPLCs - 2 (DAC X HPLC system; 15 cm and 30 cm DAC columns to increase the efficiency of purification)
- Class 100,000 clean room area

Neuland’s Upcoming Peptide Facility

Our new peptide facility is a greenfield expansion planned across four modules, designed and equipped with:

cGMP-compliant manufacturing spaces	Automated systems (DCS) for process control
250 L & 500 L SPPS capacity	100 L and 200 L lyophilizer capacity with isolator (0.1 µg/m³)
1 X 45 cm DAC column 2 X 60 cm DAC columns	

With precipitation, crystallization and spray drying techniques, Neuland is trying to eliminate the bottleneck of lyophilisation

Peptide R&D infrastructure

Automated peptide synthesizer	Quadrupole time-of-flight high resolution mass spectrometer (QTOF-HRMS)
Tangential flow filtration (TFF)	
2 X 15 cm dynamic axial compression (DAC) columns	Circular dichroism and fluorescence spectroscopy
20 L rotary evaporators	Ion exchange columns

Automated Peptide Synthesizer

Circular Dichroism and Fluorescence Spectrometry

QTOF-HRMS

CASE STUDY

SPPS for a 25AA Peptide NCE

The Client

European biotech developing a 25AA peptide for Osteoporosis

The Task

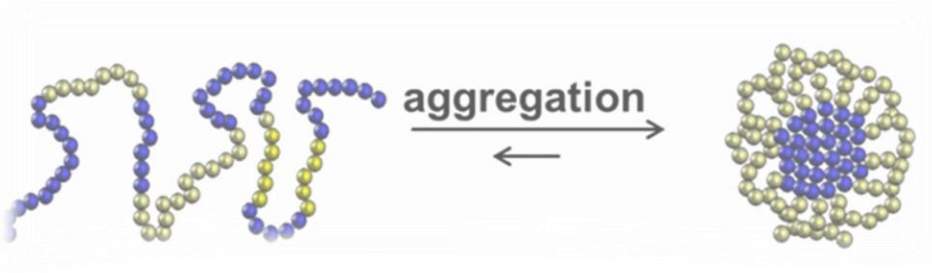
Develop a scalable, impurity-controlled synthesis for a 25 AA peptide API, including lab validation and GMP batches for Phase 1 clinical trials within 6 months

Key Challenges

- The client was unable to share the existing process, and only the final peptide sequence was provided
- After cleavage from the resin and global deprotection the peptide was highly insoluble
- 9 major impurities required removal
- Expedited timelines

SPPS for a 25AA Peptide NCE

Neuland's solution



- Rapidly develop a scalable SPPS synthesis
- Aggregation of the crude peptide was resolved by the addition of acetic acid during the prep-HPLC
- Orthogonal preparative HPLC and lyophilization to purify and isolate the peptide API

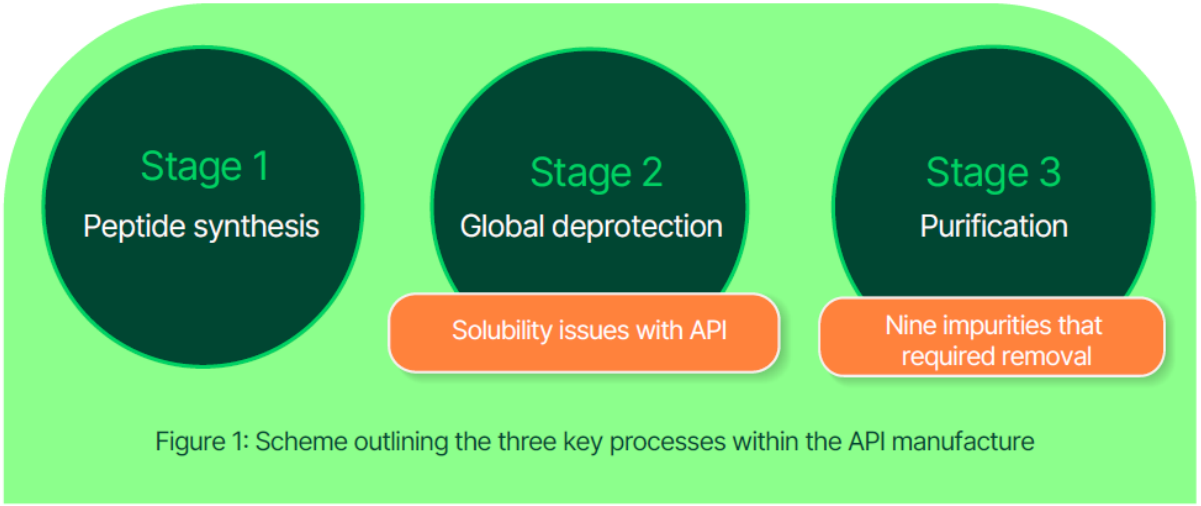


Figure 1: Scheme outlining the three key processes within the API manufacture

SPPS for a 25AA Peptide NCE

Outcomes

30% Overall yield

Orthogonal preparative HPLC enabled purification and removal of 9 major impurities

Timely delivery of 120 g of the final 25 AA peptide API with >96% purity

Thank you

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