



biomade innovations

# Unlock the Power of Biomolecules.



At Numaferm we believe in the untapped potential of peptides and proteins as feedstock for better, safer and healthier products in life sciences and beyond.

Don't let cost stand in the way of innovation. Explore and harness the potential of affordable biomolecules with our disruptive bioprocesses for discovery, optimization and production.

Biomade innovations. All you need is less.



# Numascreen

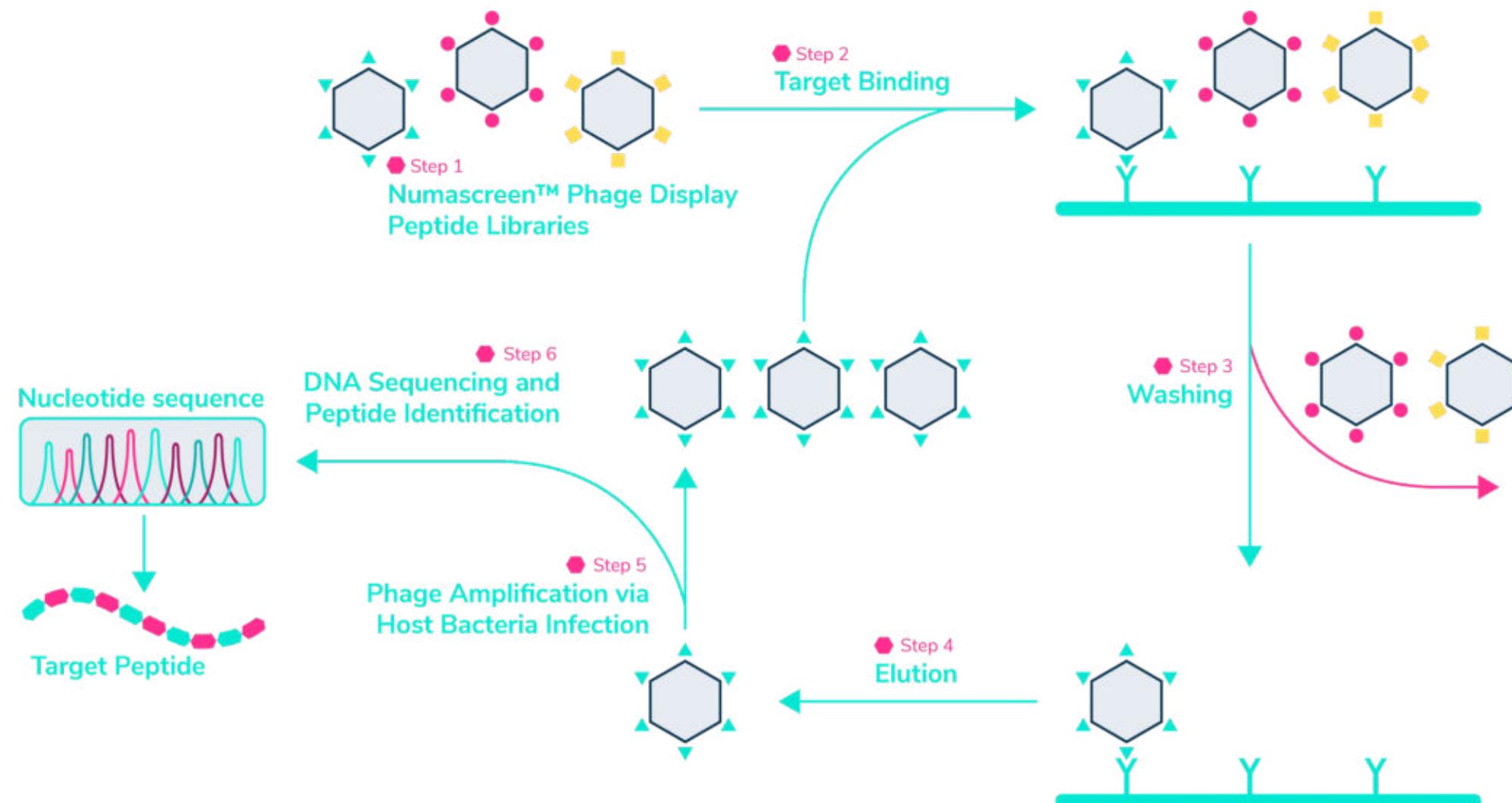
## Discovery of unique leads.

Numascreen phage display libraries are highly efficient screening platforms used to identify binding peptides with unique functionalities. More than 1 billion candidates are analysed within one experiment. Numascreen is based on the nobel prize winning phage display strategy invented by [Professor Smith](#).

Numascreen grants access to true innovation and boosts your development pipelines.



# How It Works



## Numascreen

Numascreen phage display libraries are the first-in-place screening libraries for the identification of long-chained peptides ( $\geq 20$ mer). The libraries contain of more than 1 billion candidates each. Phage display libraries have been used since years very successfully for short peptides ( $< 20$ mer) and for various applications, including the identification of antimicrobial/antiviral, material-specific or cell targeting peptides, molecule binders/antagonists/inhibitors or enzyme substrates and protein-protein interaction sites. Previously, limited access to long-chained peptides stood in the way of releasing their power. With our services, we enable their potential for you. We are offering the identification and optimization of new lead candidates with unique properties (i.e. increased specificities, stabilities). Material supply is ensured by applying our Numatech expression platform.



# Numatech

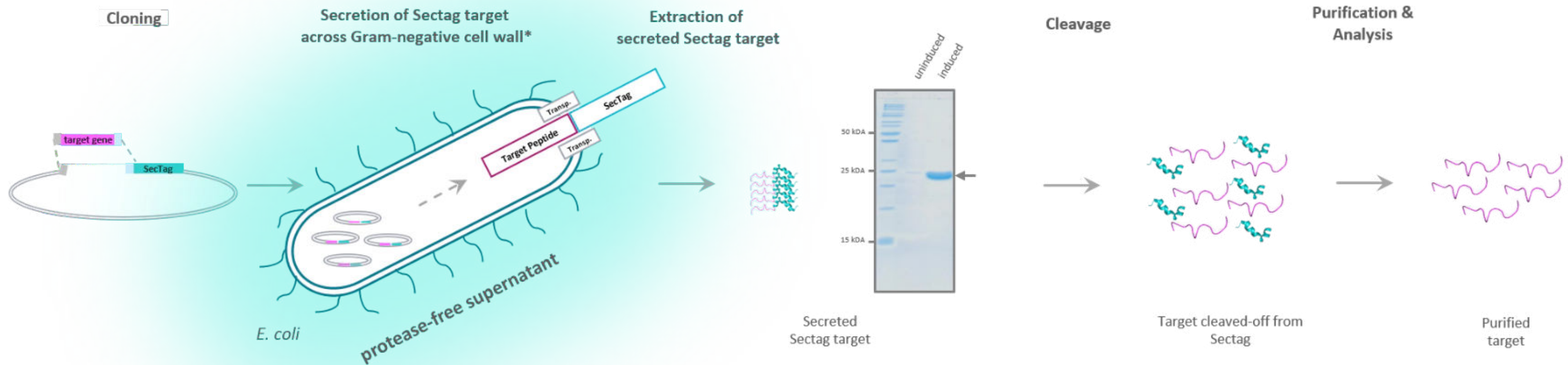
## Transforming Manufacturing.

Numatech is based on a well-designed E. coli microorganism that converts simple nutrients to peptides and proteins. It is the first-in-place bioprocess that serves as a reliable high-expression platform for the production: independent of the sequence, length or functionality.

Numatech stands for sustainability, superior quality and scalability.



# How It Works

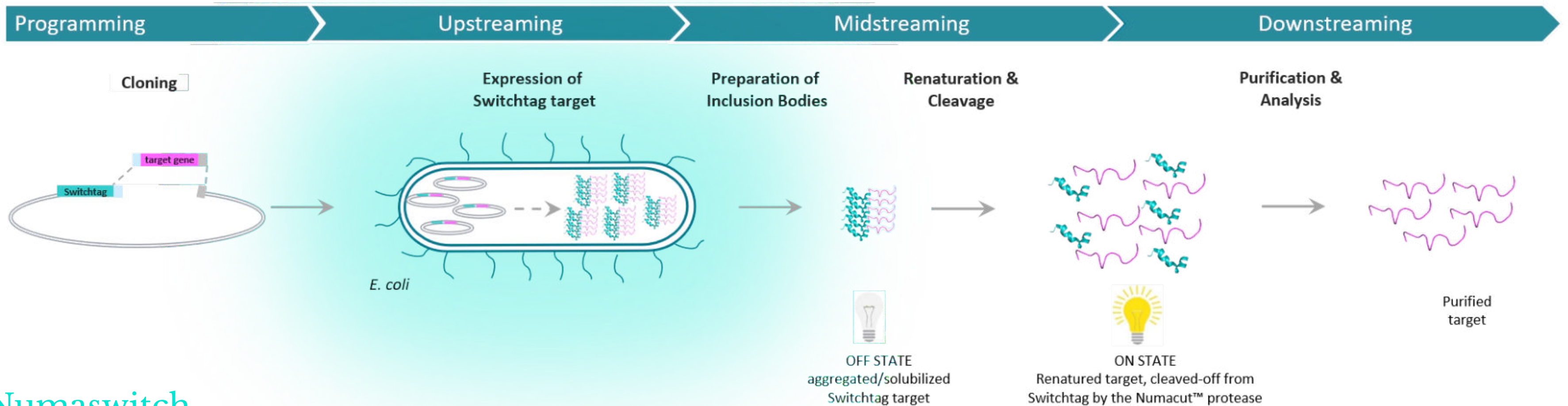


## Numasec

Initiated by the discoveries of Dr. Christian Schwarz during his PhD, the first reliable and efficient secretion technology for Gram-negative bacteria was developed. Numasec™ can achieve titers of more than 30 g per fermentation liter with initial purities of > 95%. This holds true for antimicrobials, highly active compounds and pharmaceuticals without affecting production and growth performance of the *E. coli*. Due to the high secretion levels and outstanding high purities, manufacturing processes with unique productivities and significantly reduced downstreaming efforts are possible. Cost of goods are reduced for the production of biomolecules at the highest qualities. To achieve that, common *E. coli* strains are equipped with a type 1 secretion system (T1SS) and fine-tuned version of a RTX proteins (called Sectag). Sectags are a trifunctional protein tags that provide three essential features: transport, solubility and protection of expressed peptides.



# How It Works



## Numaswitch

Numaswitch™ is designed for the easy, reliable and efficient production of your recombinant peptides and proteins. Here, a proprietary Switchtag library is genetically fused to your target (Figure 3). Switchtags are bifunctional molecular switches. Switchtag fusions are expressed in *E. coli* cells as inclusion bodies (IBs) (the OFF state, 1st functionality: AGGREGATION). This step is important to protect your target from proteolytic degradation inside the *E. coli* cells – nothing special so far compared to common IB-tags. BUT, after extraction and solubilization of the IBs, the Switchtag in combination with a well-defined renaturation buffer catalyzes the efficient folding into water-soluble, functional biomolecules. This folding is called renaturation (ON state, 2nd functionality: RENATURATION) and is essential. Only after renaturation, functional and water-soluble biomolecules are accessible and site-specific proteases are applicable to cleave-off your target from the Switchtag (or other IB-tags). With site-specific proteases your target is released traceless. Numaswitch™ makes use of the advantages of IBs (no proteolytic damage of your target, high expression titers, high initial product purities) and solves the major disadvantage (no/low renaturation efficiencies).





# > 90%

## Reduction of Carbon Footprint

### Cost of Goods

Reduction > 90 %.



### Waterbased Approach

Reduction of harmful chemicals and organic solvents > 90%.



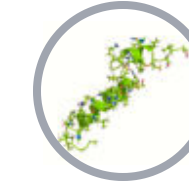
### Scalability

Material supply from mg to > tons.



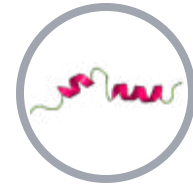


# What to Expect - Selected Examples



	Gomesin	(pre-) Liraglutide	Teriparatide, PTH 1-34	PTH 1-84	anti-SARS-CoV-2 nanobody
Characteristics	18 aa (2.3 kDa) antimicrobial 2 Cys bridges	31 aa (3.3 kDa), API	34 aa (3.7 kDa), API	84 aa (9.0 kDa), API	119 aa (13 kDa), antibody fragment 1 Cys bridge
Upstream	Fermentation, 24 h	Fermentation, 24 h	Fermentation, 24 h	Fermentation, 24 h	Fermentation, 24 h
Midstream	Extraction Hydrolysis (BrCN)	Extraction Renaturation Hydrolysis (Protease)	Extraction Renaturation Hydrolysis (Protease)	Extraction Renaturation Hydrolysis (Protease)	Extraction Renaturation Hydrolysis (Protease)
Downstream	RP-HPLC	RP-FLASH (HPLC-free)	IEX RP-FLASH (HPLC-free)	IEX RP-FLASH (HPLC-free)	IEX (HPLC-free)
Production timeline (to lyophilisation)	5 days	5 days	6 days	6 days	5 days
Production titer (final lyophilisate per fermentation liter)	> 1.0 g/L	> 2.5 g/L	> 2.0 g/L	> 5.0 g/L	> 1.0 g/L
Purity (RP-HPLC)	> 97.5 %	> 98 %	> 99.6 %	> 98 %	> 96 %
API quality	n.d.	yes	yes	yes	yes

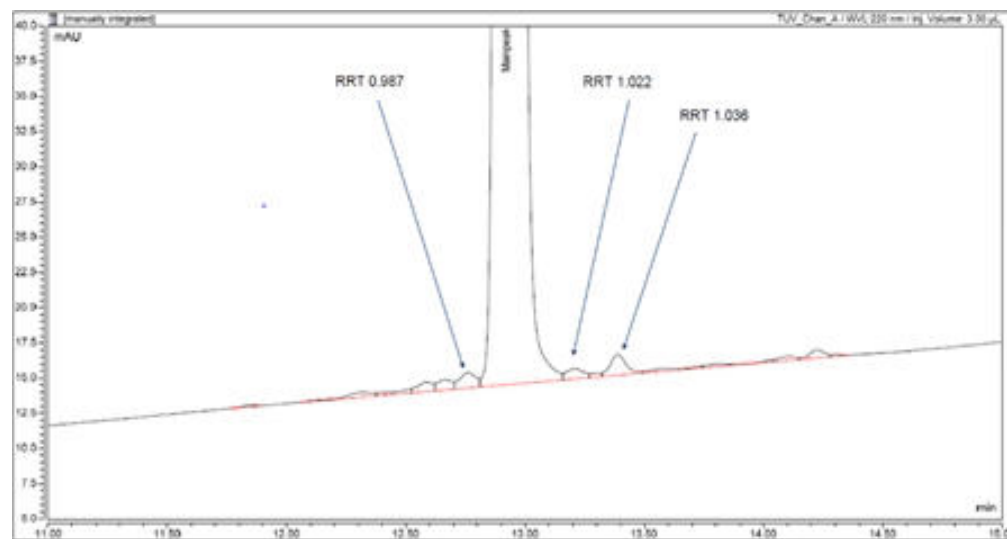
# Liraglutide



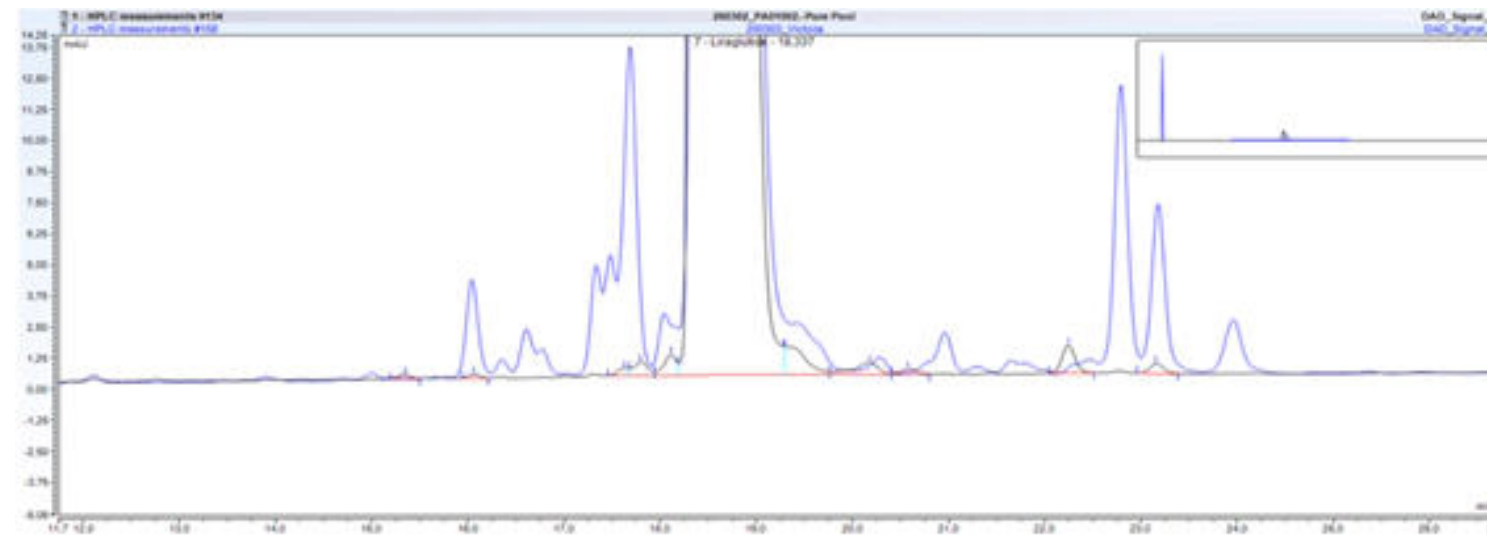
Liraglutide, sold under the brand name Victoza among others, is a medication used to treat diabetes mellitus type 2 and obesity. In 2018, it was the 143rd most commonly prescribed medication in the United States, with more than 4 million prescriptions. Liraglutide is an acylated glucagon-like peptide-1 (GLP-1) agonist, derived from human GLP-1-(7-37).



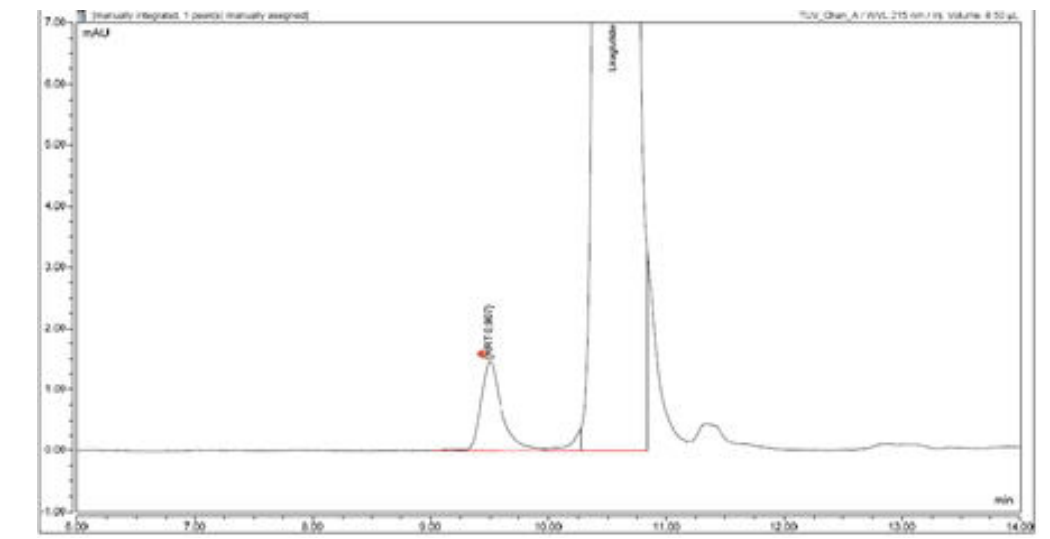
with



QC Release Method (RP-HPLC); Purity and Related Impurities; Purity > 99.3%.



Spiking against an originator per RP-HPLC. Originator chromatogram (blue), PEPdesign/Numaferm Liraglutide (black).



QC Related Substances (SEC-HPLC); Purity > 99.8 %.



# Sample Process: PTH (1-34)

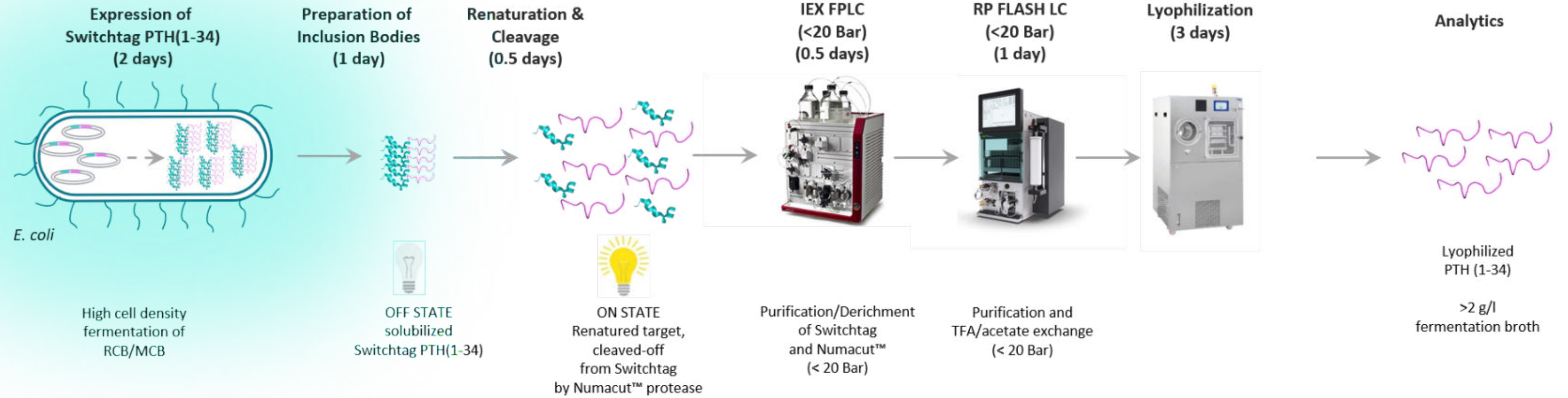


Upstreaming

Midstreaming

Downstreaming & Formulation

Analytics



- Timelines
- Complexity
- Cost-of-goods



- Titers
- Quality
- Performance

# Sample Analytics: PTH (1-34)



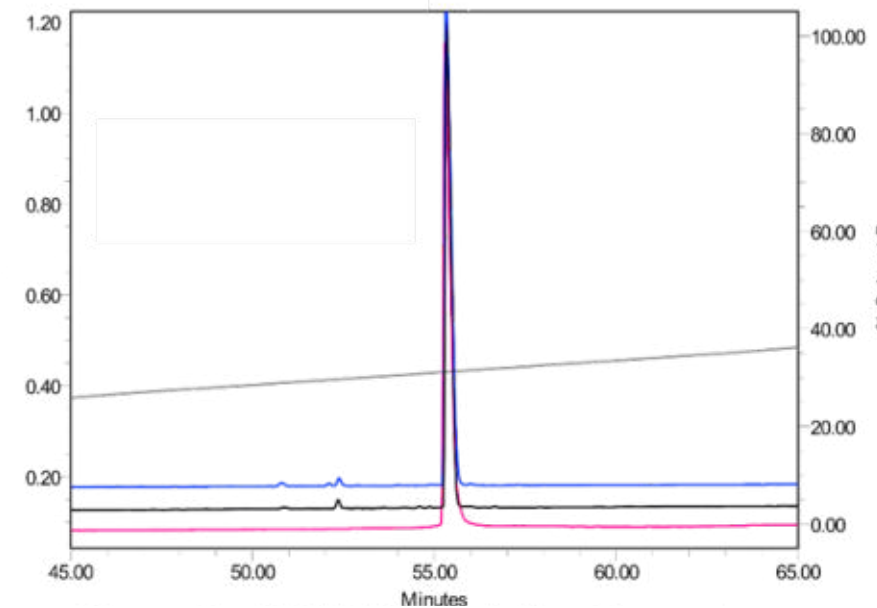
Identity	Analytical method	Limit	Status
a. Molecular weight	Mass Spectrometry	4117.76 Da +/- 1.00 Da	conforms
b. Chromatogram (RP)	RP-HPLC	Conforms with standard(s)	conforms
c. Chromatogram (Ion)	IC-HPLC	Conforms with standard(s)	conforms
d. Peptide Mapping	RP-HPLC, Endopeptidase Glu	Conforms with standard(s)	conforms

Purity	Analytical method	Limit	Status
a. Related Substances/ Impurities <ul style="list-style-type: none"> <li>Product-related sub.</li> <li>Process impurities</li> </ul>	RP-HPLC	standard(s)	conforms
b. Host Cell Proteins	HCP-assay	< 100 ppm	conforms
c. Residual DNA	DNA-specific method	< 200 pg/mg	conforms
d. Bacterial Endotoxins	LAL chomogen method	< 5 EU/mg	conforms

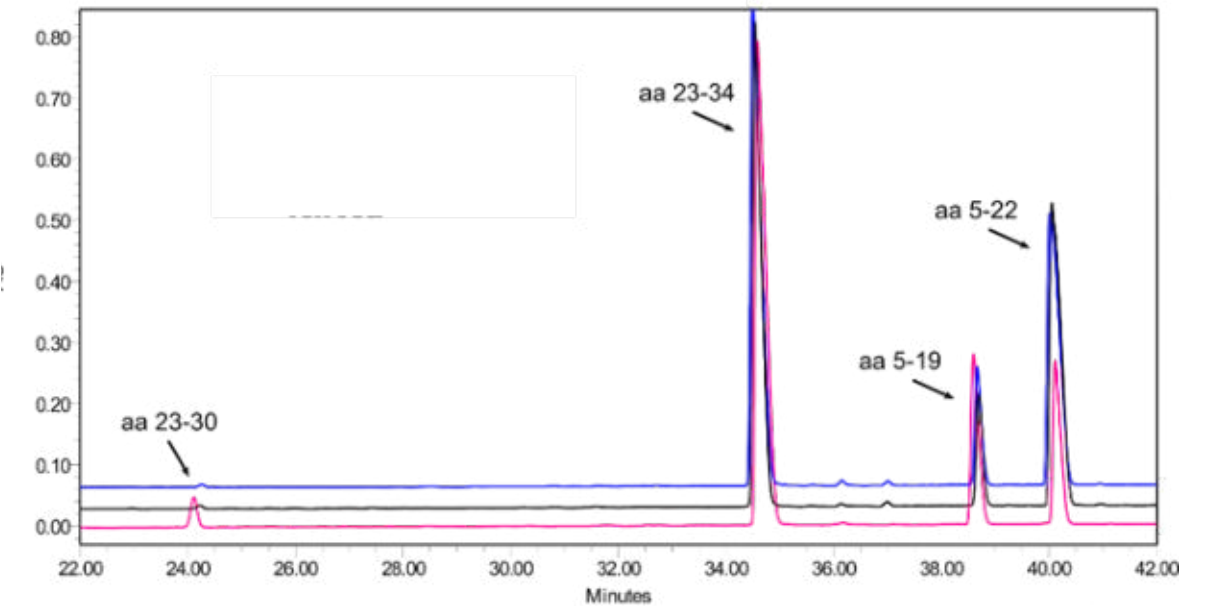
Bioassay	Analytical method	Limit	Status
a. Biological Activity	In vitro PTH-Bioassay (HTRF)	Conforms with WHO International Standard	conforms



Needed in-process-controls and release analytics in-place  
Increased qualities compared to market standards.

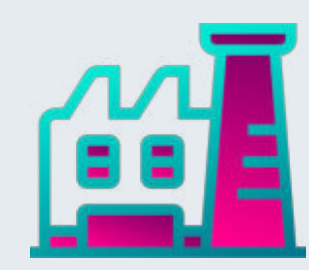
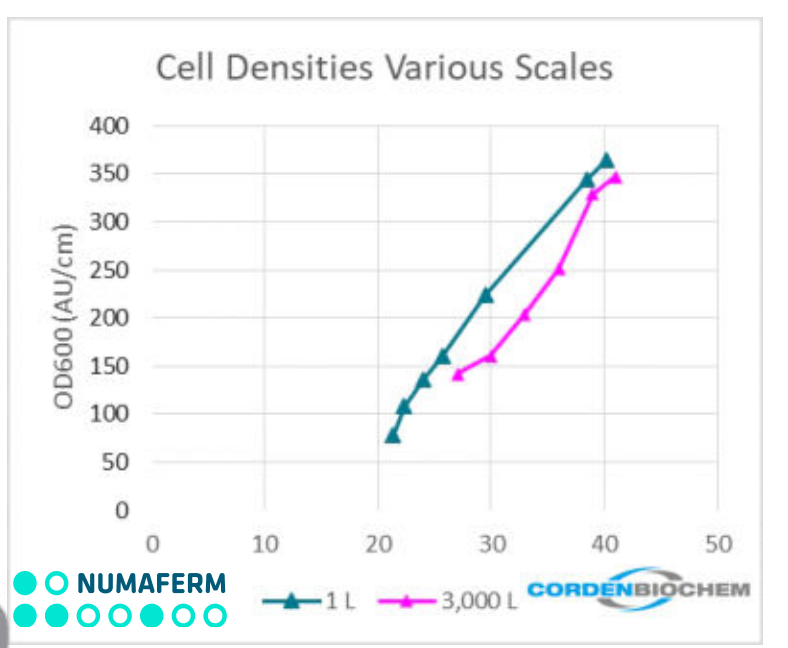
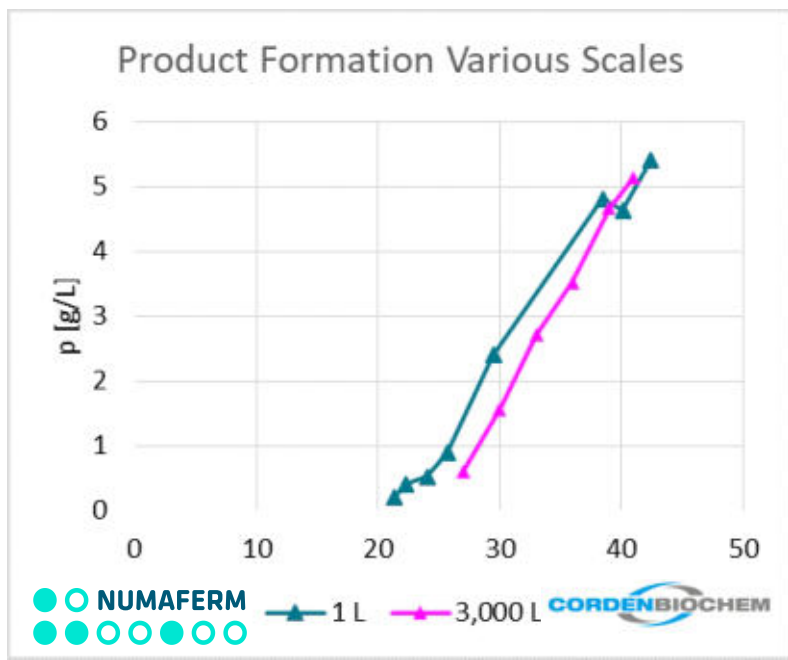
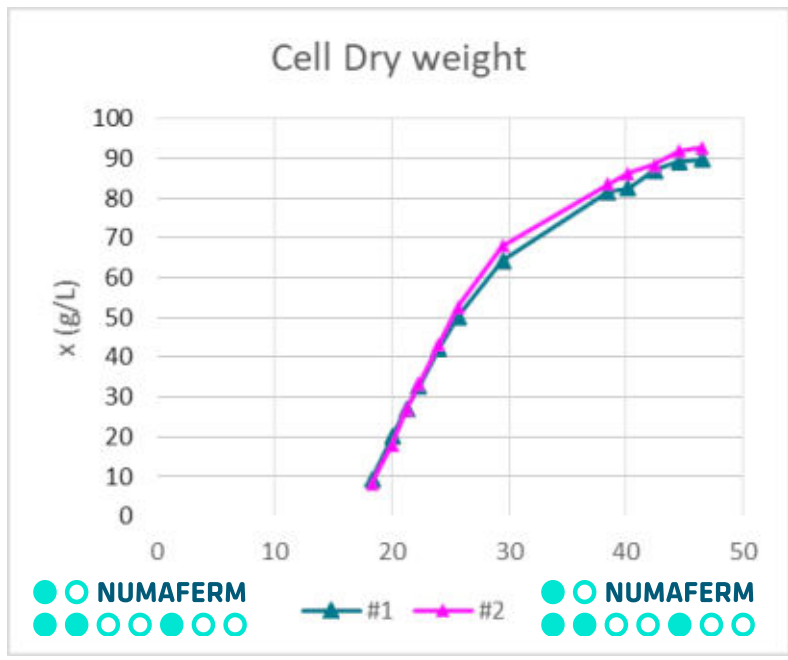


**RP-HPLC analysis.** Chromatograms of the originator (black), an approved biosimilar (blue) and Numaferm's PTH (1-34) peptide (purple).



**Peptide mapping after hydrolases by Endopeptidase Glu.** RP-HPLC analysis of the originator (black), an approved biosimilar (blue) and Numaferm's PTH (1-34) peptide (purple).





Reproducible, Industry-Grade Fermentation Process Independent of Scale and Quality Demands



# Our Services



## Discovery

### Identifying Your Lead.

Our lead discovery service uses our proprietary Numascreen phage display libraries to identify innovative, high-affine, highly-specific binders for your target.

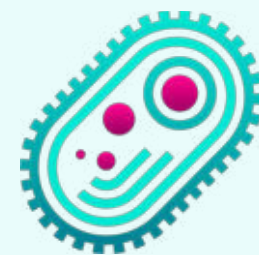


~ 1-3 Months

## Cell Line Development

### Developing Your Cell Line.

A standardized work-flow is established to define the perfect expression cell line for you within weeks. This cell line is used to supply you with initial test material.

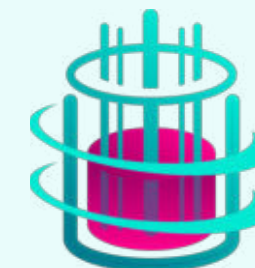


~ 1 Month

## Process Development

### Designing Your Process.

Each project is unique. Despite that, Numatech enables the application of standardized work-flows decreasing time and costs. Each production process meets the highest quality standards.



~ 2 Months

## Production at Scale

### Ensuring Your Material Supply.

The commercial and/or GMP production is realized by our established partner network of experienced CMO companies. Our production processes are industry-grade and ready to be transferred.



~ 1-5 Months





*“The quality of peptides is extraordinary. Working together is real fun and the results continue to exceed my expectations. I appreciate to working with Numaferm.”*

Christian Ewers  
Managing Director  
PEPdesign



*“Numaferm’s technology is highly disruptive. We expect existing markets to change dramatically and new markets to develop.”*

Bernhard Mohr  
Head of Venture CapitalEvonik



*“I became aware of Numaferm's technologies with great interest, as alternative methods failed in the production of a 59mer peptide. It was possible to produce the peptide in high yields and with exceptional purity.”*

Wolfgang Greb  
Managing Director  
FOCUS IP



# Who We Are

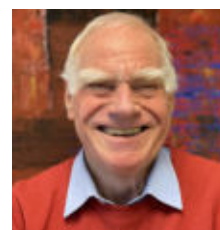
**Numaferm GmbH – Biomade Peptides**  
Duesseldorf, GER

Team: 30 experts  
Facilities: 5,400 sqft  
Established: 2015



Management

Advisory Board







# Thank you!

Get in touch and release the potential of your ideas.

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