TechEx.in is a Regional Tech Transfer Office supported by:

Insulin Detemir, Certolizumab PEGOL & Others

Technology from the group of **Natasa Skoko**
at **International Centre for Genetic Engineering and Biotechnology, Trieste, Italy**

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About Certolizumab PEGOL

Certolizumab Pegol is a pegylated Fab fragment of a humanized anti-TNF IgG molecule

- **Originator / reference product:** The originator product, UCB's Cimzia (certolizumab pegol), was approved by the US Food and Drug Administration (FDA) in April 2008 and by the European Medicines Agency (EMA) in October 2009. The patents on Certolizumab PEGOL will **expire in Europe in 2021** and in the **US in 2024**. (Source: GaBI Online)

- **Indications:** Treatment of adult patients with moderate to severe **Rheumatoid Arthritis**, **Crohn's disease**, psoriatic arthritis and ankylosing spondylitis.

Market and Industry Overview

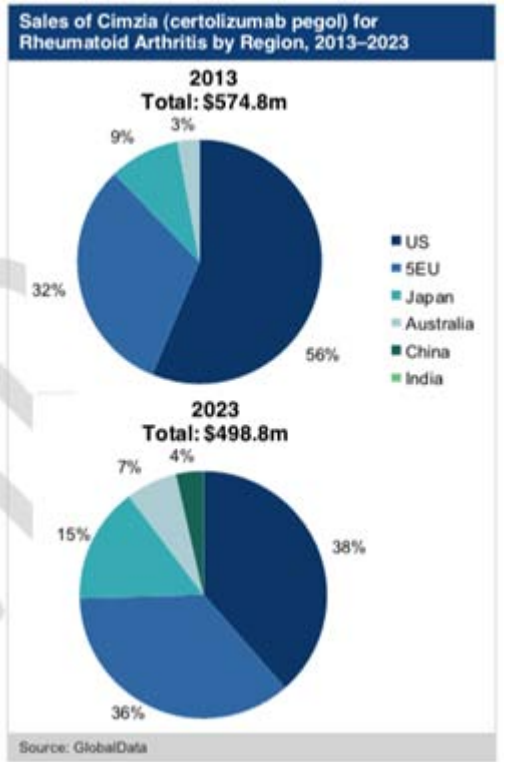
Market:

Estimated global market for Certolizumab **by 2023 is $0.5 billion** (Source: Market Research)

Industry players:

- **Global:** UCB, Pfenex (in the pipeline)

- **India :** None

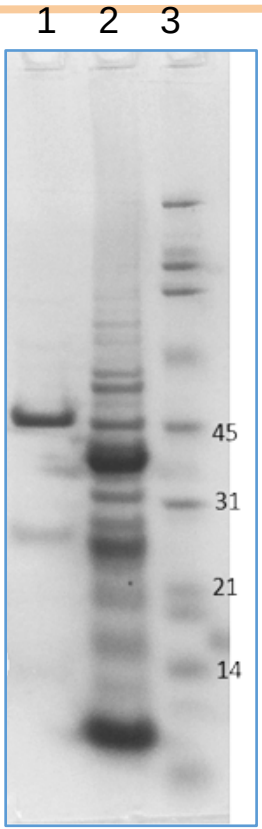


The Opportunity: Why you should be interested?

- **Market interesting:** a) The patents on Cimzia (Certolizumab PEGOL) will expire in the US in 2024. **Next generation Biosimilar** b) Certolizumab pegol is currently the **only PEGylated anti-TNFα biologic approved** for the treatment of **Rheumatoid Arthritis and Crohn's disease.**

- **Industry not yet crowded: Sole manufacturer** of Cimzia in UCB. Opportunity for other companies.

The Technology Offering

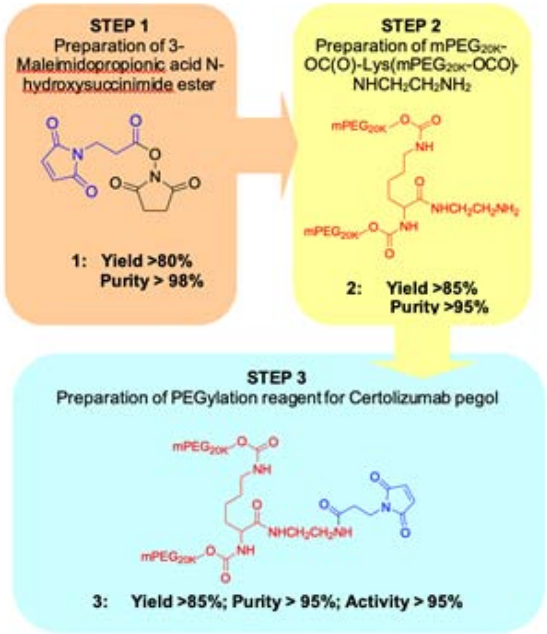


- We produce Certolizumab by fermentation in the periplasm of E.coli in a native state with approx. **yield of 250 mg/L (post-capturing purification step)**

SDS-PAGE analysis of Certolizumab pools:

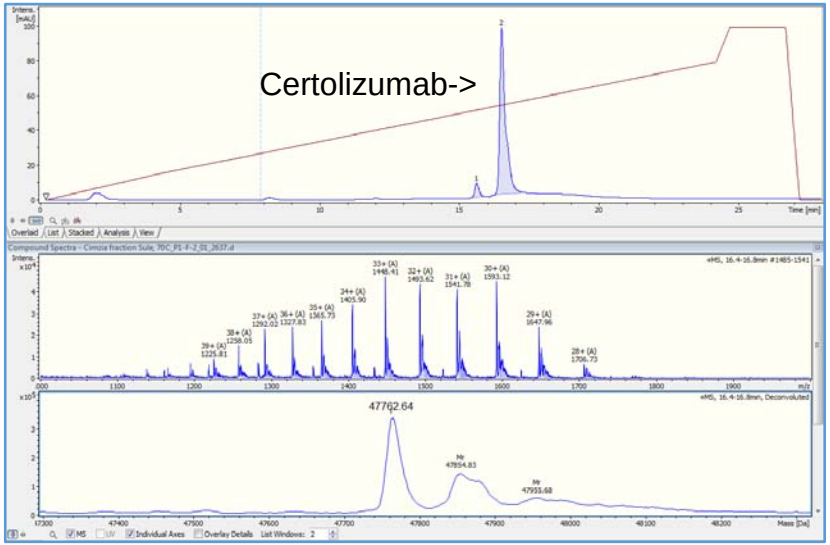
Lane 1: Certolizumab after first chromatography capture step
Lane 2: Flow through from first chromatography capture step
Lane 3: Molecular weight marker

The Technology Offering



- We developed the process for the synthesis of the branched PEG reagent for PEGylation of Certolizumab to obtain Certolizumab pegol, at gram scale with **activity and purity > 95%**
- Preparation of PEGylation reagent in around 10 g scale with **yield of over 85%, purity of over 95% and activity of over 95%.**

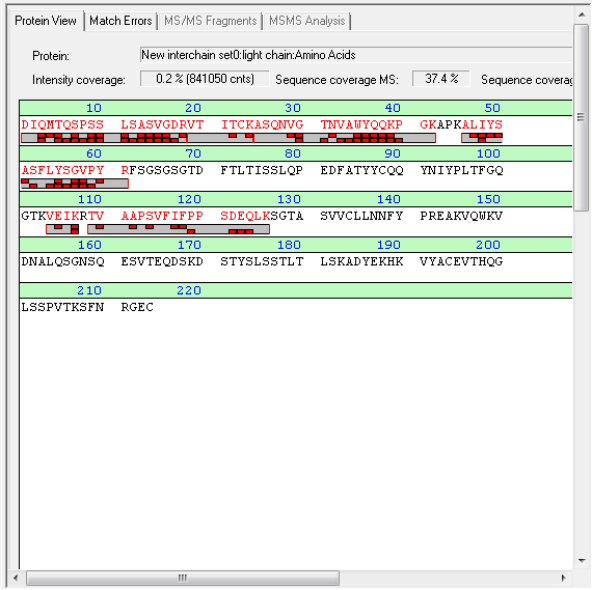
Selected Data: Biosimilarity- Intact mass analysis

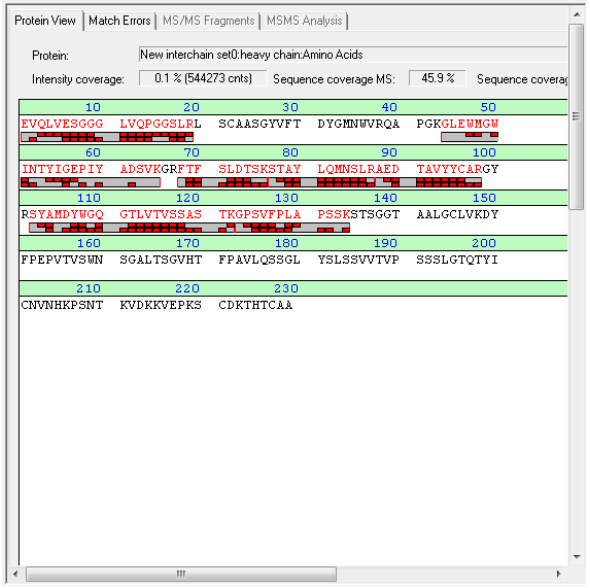


LC-MS (RP-HPLC) of Certolizumab after first chromatography capture step **shows purity >80%.**

Intact Protein mass analysis of Certolizumab is also performed after chromatography capture step:
ESI-MS determined molecular mass is 47762.64 in **agreement with the calculated average molecular mass** of 47759.98.

Selected Data: Biosimilarity- Peptide mapping

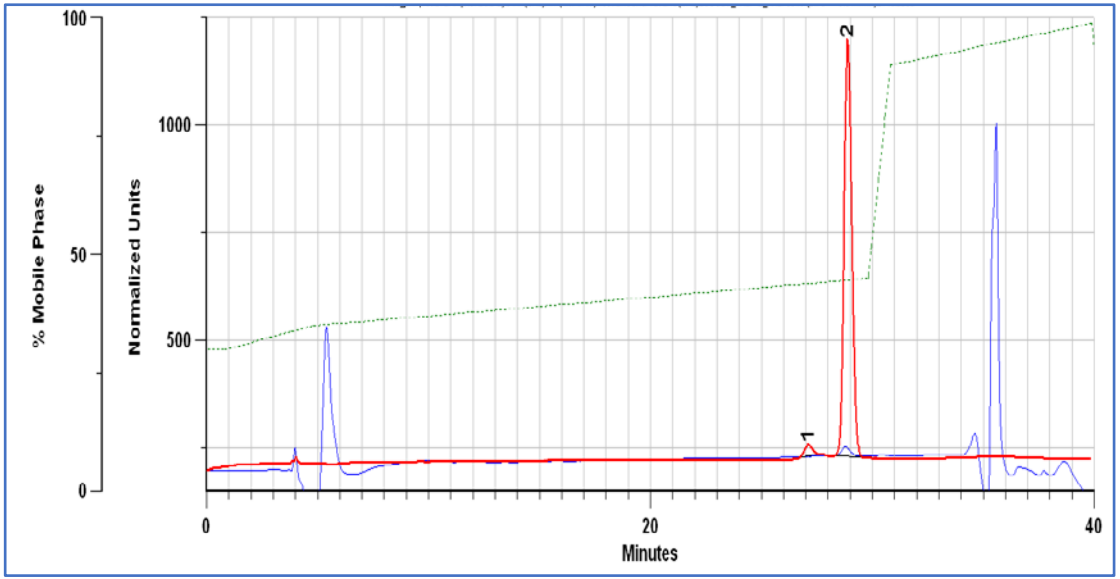




Peptide mapping and MS/MS analysis of protein band from SDS-PAGE:

MS/MS sequencing showing partial coverage in both heavy and light chains of the protein, especially in the N-termini portions.

Selected Data: Purity and activity

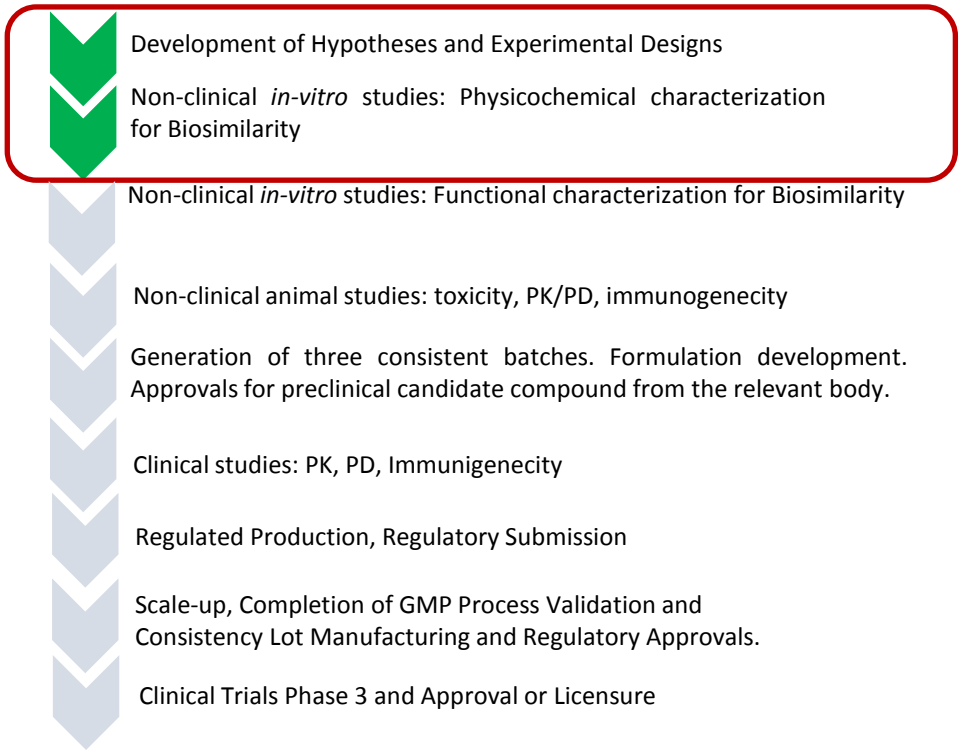


RP-HPLC-UV-ELSD analysis of the PEGylation reagent for Certolizumab: the PEG reagent maleimide activated is reacted with a thiol containing tracer **demonstrating > 97% purity and activity** (peak n.2, red trace is ELSD)

Current Status of Technology and Path Ahead

Stage of Development

- Protein expressed in shake flask and 10L bioreactor.
- Achieved yield of **250 mg/L (post-capturing purification step)**



What are we seeking?

Seeking Industrial partners interested in:

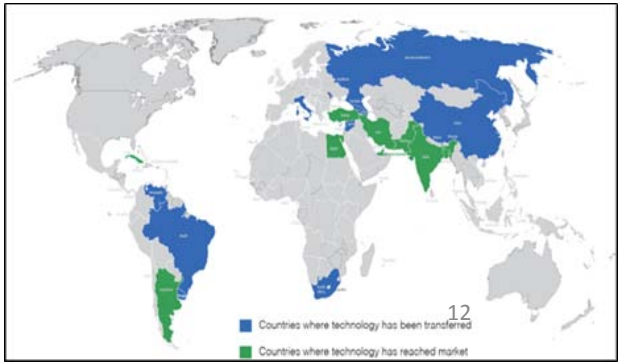
- **R& D Collaboration** : To increase the production yield, optimize purification steps and develop conjugation step
- **Technology co-development**: To carry out further development/validation work
- **Technology licensing**: For commercializing Certolizumab PEGOL

Dr Natasa Skoko's Group: Biotechnology Development Unit

Lead Scientist: Dr Natasa Skoko

Group Leader, Biotechnology Development Unit, ICGEB, Italy
Member and reviewer, Women in Science in the Developing World
Expertise: Production of biologics in bacteria, yeast and mammalian cells, bioprocessing operations such as upstream, downstream and quality control analysis following European Pharmacopoeia monographs

- **Key assets and strengths of Dr Skoko's Lab:**
  - **Authored more than 20 publications** in her areas of expertise
  - Team strength: 8
  - Well equipped labs and analytical facilities
    - Microbial and mammalian cell line facility
    - Downstream processing, chemical lab and **QC lab**
    - **Clean rooms in Class C and D**
  - Industry Project /Tech transfer
    - More that 25 years of experience in the field of biologics/biosimilars, **more than 70 technology transfer agreements with companies**
    - Companies from 22 countries, more than 100 scientists trained in our lab



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