

A Development Company

The Development of a Company



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How could we sustain a startup
whose key expertise is R&D in the
Argentine (Latam?) Context?

pharmADN
20 years of experience in
Biopharmaceutical Innovation



1990	Research Scientists start a garage company. <i>Genargen</i>
1991	First agreement with local pharma company.
1993	Launching of recombinat Interferon Alfa 2b.
1995	50% share deal with local pharma company. <i>PC-Gen</i>
1995	Joint-Venture with Rhein Biotech GmbH (Dusseldorf) to produce the first Hep B vaccine in Argentina. <i>Rhein Americana</i>
1999	Joint Venture adquisition by Aventis Pasteur (actually Sanofi).

2001

Rhein acquires a majority stake in the company.
PC-Gen

2002

Rhein is acquired by Berna Biotech (Switzerland)

2005

Berna Biotech is acquired by Crucell (Netherlands)

2005

The company is acquired by Amega (Argentina)
PC-Gen

2006

The group successfully transfers technology for Interferon Alfa production to a cGMP plant in Germany. (Inverted Paradigm)

2008

The group starts a new company.
pharmADN

2010

Chemo acquires a majority stake in the company
pharmADN

- In a period of 4 years, the joint-venture was created, the production facility designed and constructed, the antigen produced, the vaccine developed, clinical trials staged and the vaccine approved.
- The whole project, including cell lines, facility , file and clinical trials, was acquired by Sanofi Aventis.



pharmADN scientists have developed

- IFN alfa 2b
- IFN alfa 2a*
- IL-2
- GM-CSF
- Teriparatide
- G-CSF
- Erythropoietin
- IFN Beta 1a
- Pegfilgrastim**

* Transferred to a German Company

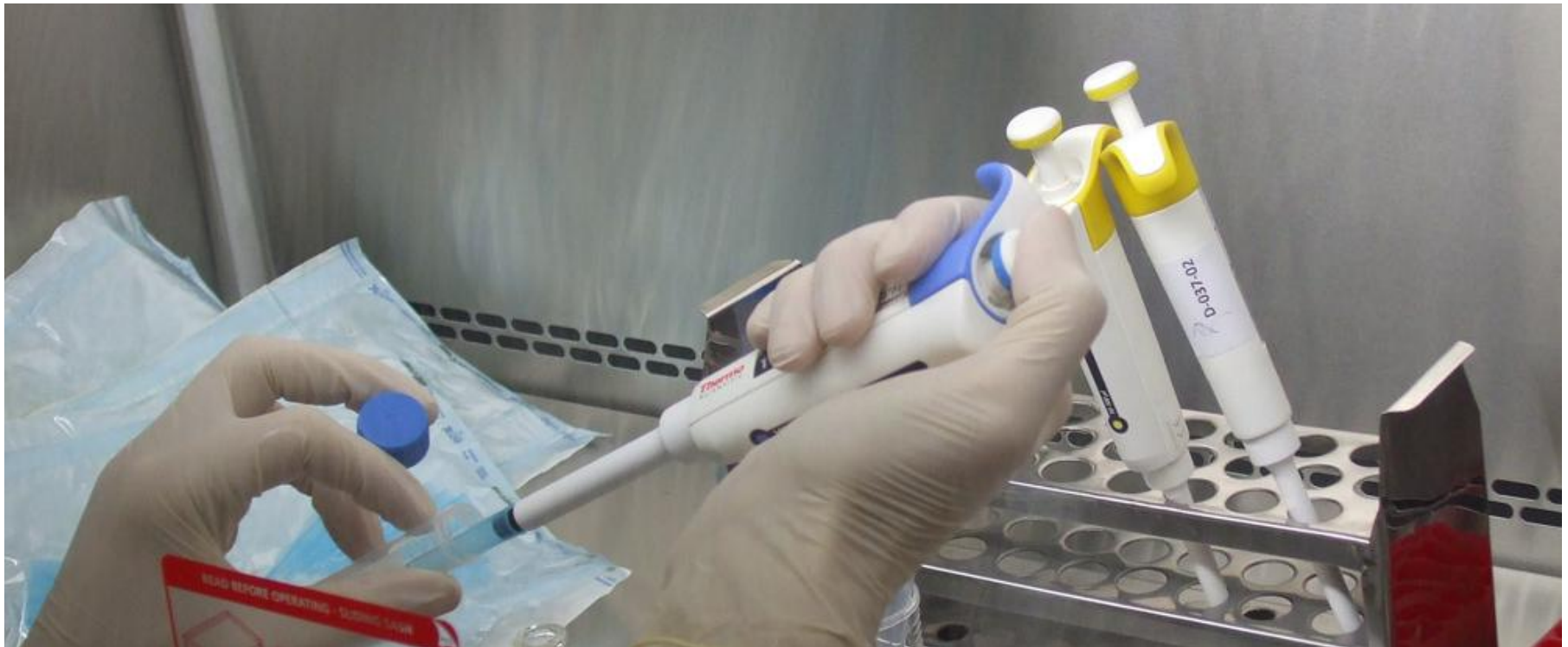
** Transferred to a Brazilian Company

The group has cultivated relationships with academia and has actively utilized the financial instruments offered by the Science and Technology agencies. In addition participates of the National pharmacopeia, CILFA's Bio group ,and Biotecsur.

The group has worked on many co-development projects and has supplied services to companies in Europe, Asia, USA and Latam.

pharmADN has consolidated 20 years of experience integrating development into production, quality control, tech transfer(in-out), filing and business development in the area of Biosimilar biopharmaceuticals, while establishing a strong local and international network.

Biosimilarity by design Development of Biosimilar Monoclonal Antibodies



Example: Rituximab

Strategic Decisions: Partners, funding

- Development
- Manufacturing for Drug Substance
- Manufacturing Finished Product
- Marketing

Biosimilars should be developed in comparison with the reference product from the start of the project.

- Determination of “Key Product Quality Attributes” (KPQA)
 - Extensive Literature Search.
 - Extensive Characterization of various reference lots.
 - *The protein sequence must be determined experimentally and checked against literature*

Understanding the reference product to establish biosimilar expectations

- Cell Line development
 - Clon selection considering replication rate, antibody expression level and biosimilarity.
- Upstream y Downstream process development.

Choosing the best clone and develop the process ensuring biosimilarity and competitive costs.

- Non-clinical testing
- Clinical Testing

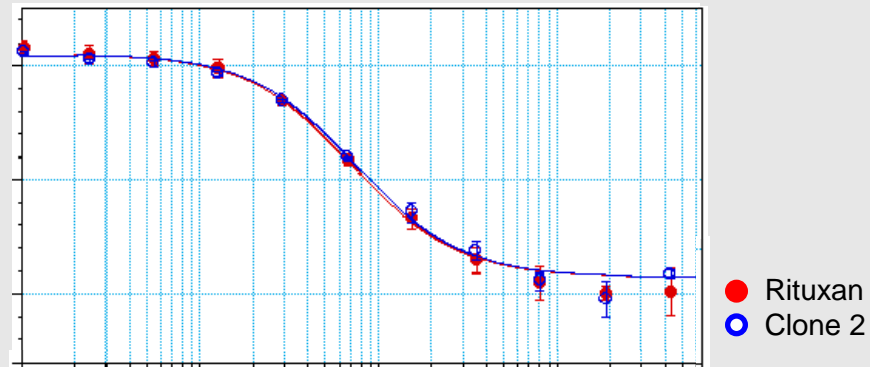
Confirming Efficacy and Safety

- Creation of CHEF1™ DG44 CHO cell lines and clone selection. Reverse Engineering based sequence.

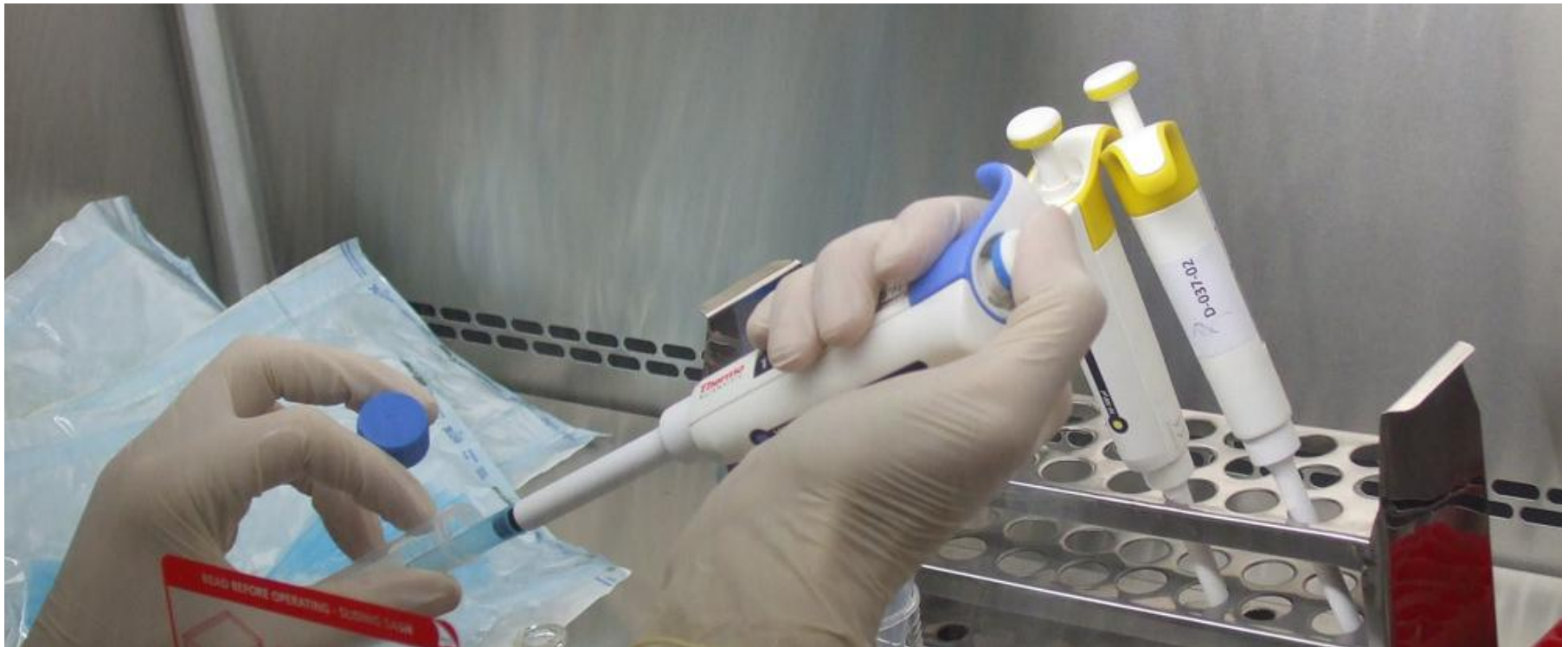
4 clones were selected according to growth, level of expression and product similarity.

- Example of 2 clones selected : Potency Determination: Cell Dependent Cytotoxicity Assay
 - Clone # 2 is similar to reference product.

Clone #	Potency
2	95,20%
7	48,80%
21	40,50%
36	67,60%



Manufacturing Strategy



Sinergium Biotech

- 7415 square meters.
- 40.500.000 USD.



Sinergium Biotech

- Pharma Facility for Formulation and Fill & Finish of injectable biotech products.
- Designed together with Liconsa from Spain.
- Under construction

- 1390 square meters.

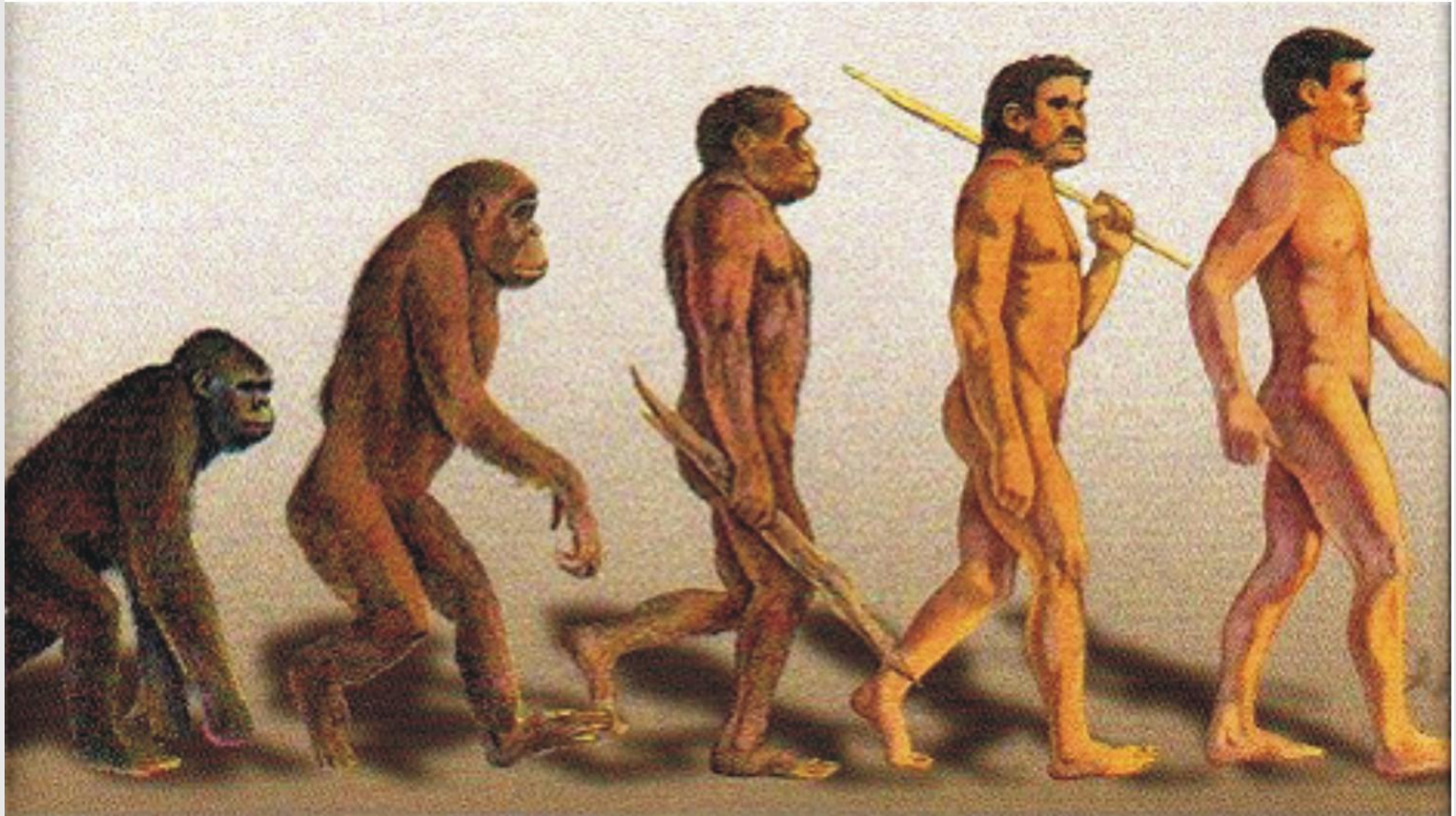
- USD 6.500.000



pharmADN

- Partially financed through “Fondos Sectoriales”
- Pharma Facility for Drug Substance Manufacture.
- Designed together with Liconsa from Spain.
- Single Use Bioreactor.
- Under construction (December 2011)

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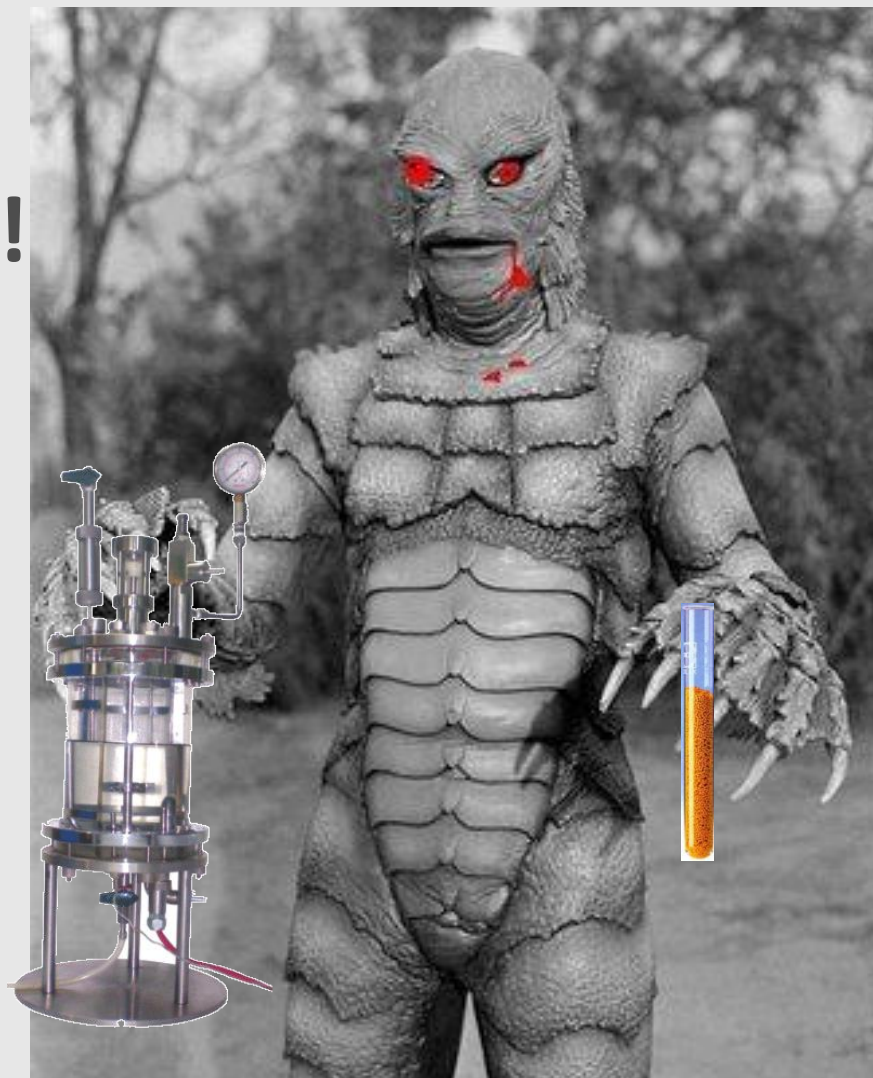


A Biologist!!!





A Biotechnologist!!



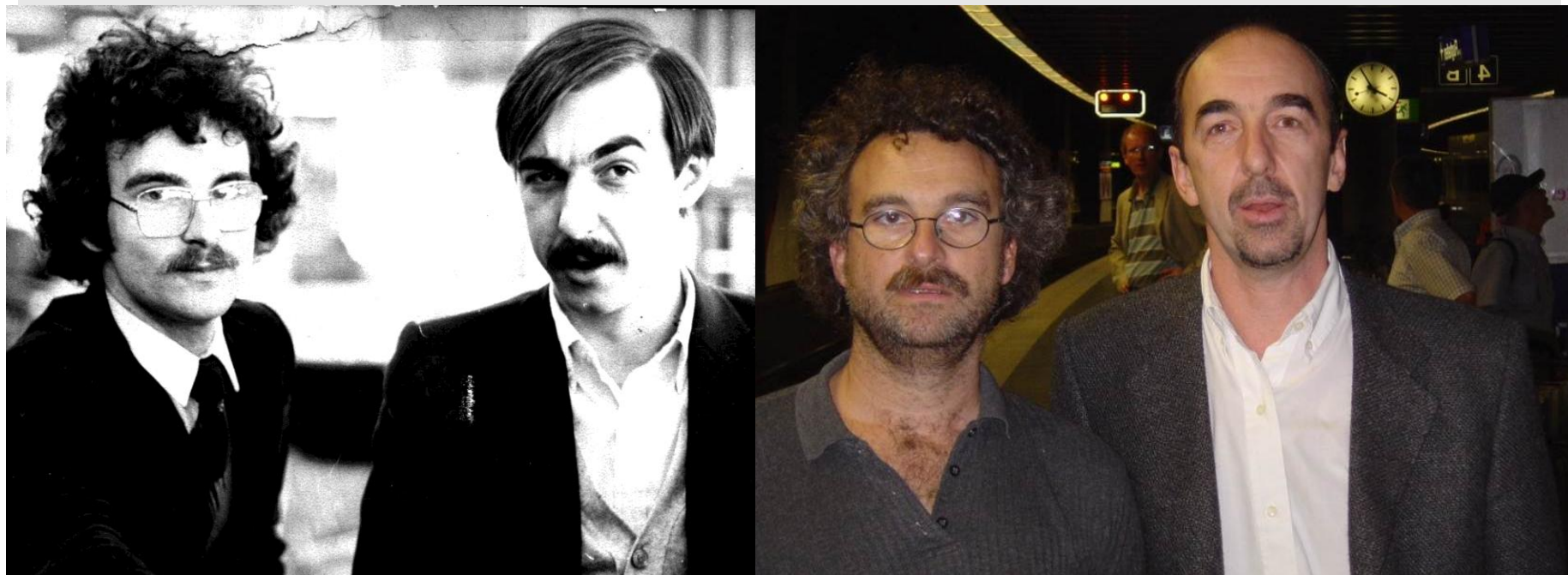
Flexibility ! In our case,
incorporating the R&D into
concrete products as a proof of
concept

i.e. Forward Integration

Finally evolving to a *manufacturer*
of Biopharmaceutical Drug
Substances.



However there are some consequences!



THANK YOU!!!!!!