

Biosimilars as Backbone for Successful Product Portfolio Strategies

Project and Portfolio Management for Generics
11th May 2006, Barcelona

Matthias Syska
Head of Business Intelligence
BioGeneriX AG, Germany

■ Definition/ Current Situation

- Main Criteria for Biosimilar Developments
- Portfolio Strategies
- Conclusions

„Biogenerics are Copycats of Biopharmaceuticals, i.e. Pharmaceuticals, whose active agents are achieved by biotechnological Methods using recombinant Cell Cultures.“

Biogenerics are specified as “Biosimilars” or “Follow-On-Biologics”

- **No generic approach**, i.e. proof of bioequivalence in an abbreviated process is not accepted by EMEA/FDA
- The European “comparability guideline” indicates that a complete new filing and **clinical trials** on a case by case basis are required
- Biopharmaceuticals are defined by their **production process**
→ any change can impact safety and efficacy and therefore demands new approval
- Very complex **patent situation**
- **Development time** at least twice as long
- **Development costs 8-100 times higher**

- Approval process distinguishes Biosimilars from generics:
Centralized procedure mandatory, two basic legal bases
 1. **Biosimilar approach:** comparative toxicology; bioequivalence studies, one limited pivotal and a comparative efficacy study
 2. **Stand-alone approach:** non-clinical part without comparator, phase I/II/III, against comparator

CHMP (Committee for Medicinal Products for Human Use)
released „final“ regulatory guidelines for

1. Insulin
2. G-CSF
3. hGH
4. Epoetin,

will come into effect on June, 1st 2006

Despite these guidelines there is no guarantee for a „golden“ development plan

Therefore:

- early Scientific Advise from EMEA is highly recommended
- in the next 3-4 years flexibility on scientific / clinical arguments at CHMP might be possible – and case by case decisions likely

- From the first Steps until Launch it will take approx. 6-9Years



The development timelines are similar to NBE development, only the risk of failure is smaller

- Definition/ Current Situation

- **Main Criteria for Biosimilar Developments**

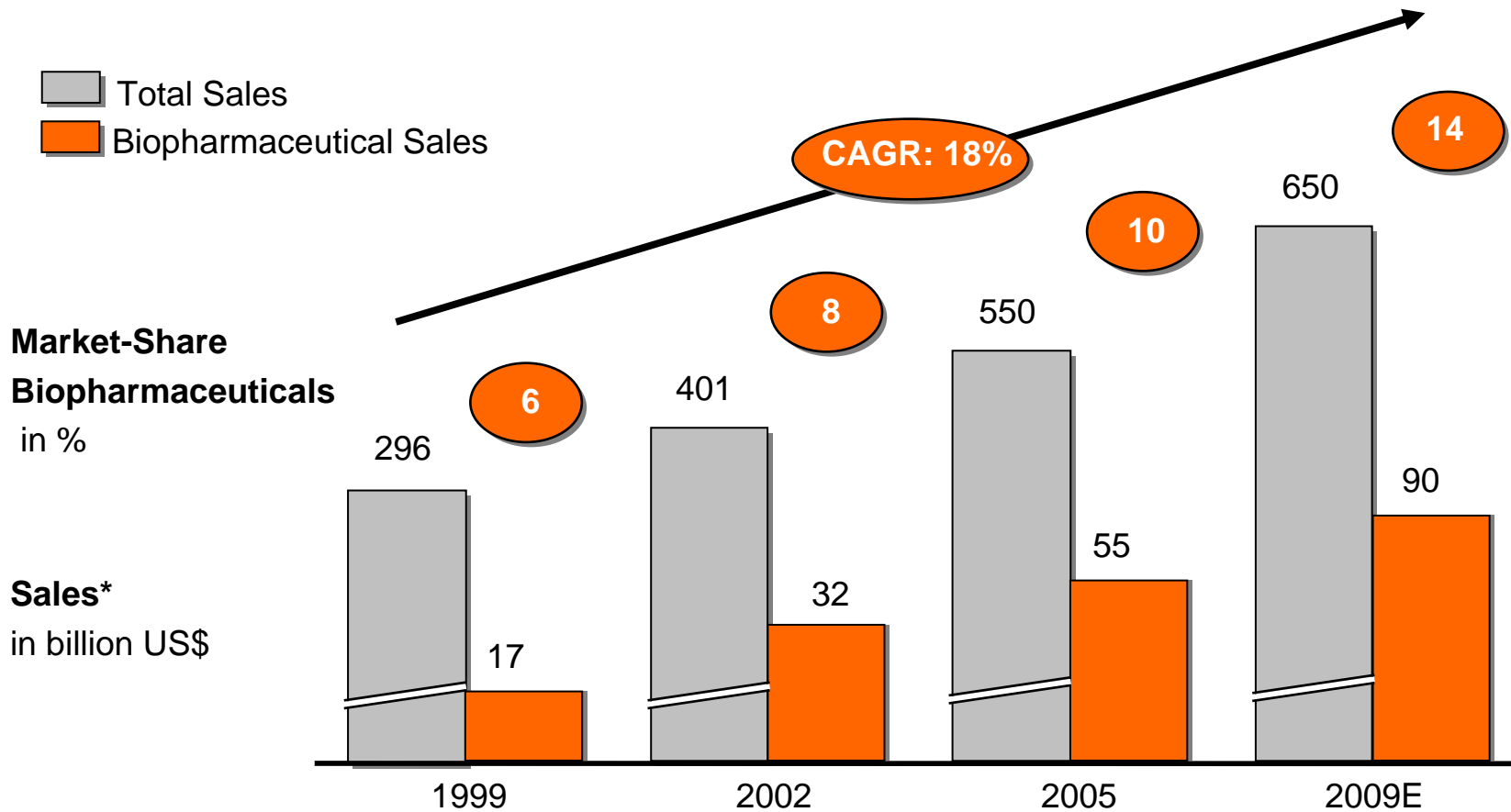
- Portfolio Strategies

- Conclusions

- **Blockbuster Products with high Growth Rates**
- **Most Patents already expired**
- **Limited Number of Competitors due to approval hurdles**
- **Broad international Market Penetration**
- **High Therapy Costs**
- **Importance for future Therapies**
- **Fit to Product Portfolio Strategies**

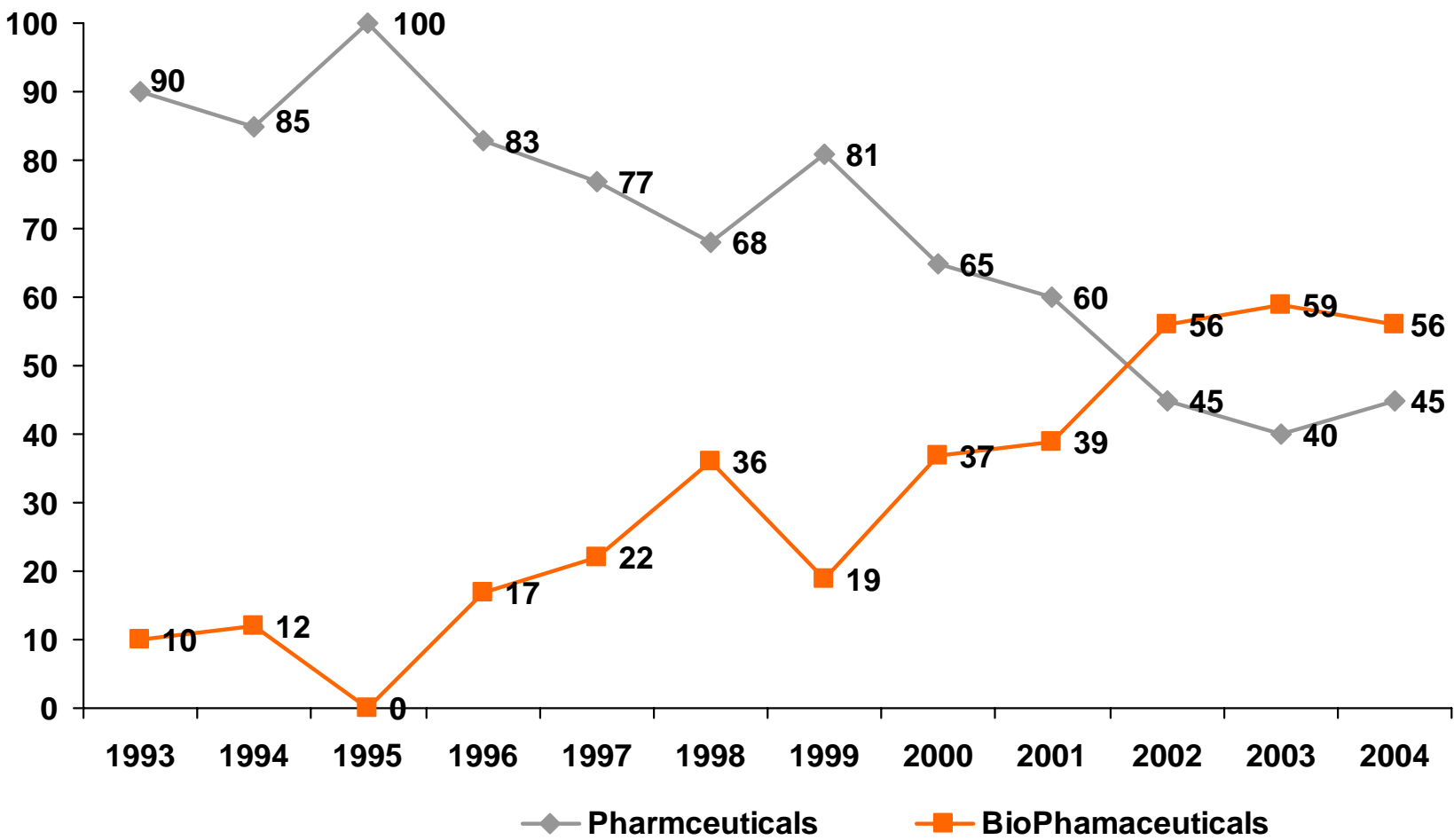
The Global Market

- Biologics are growing at twice the rate of „ Small Molecules“ (Rx Market)



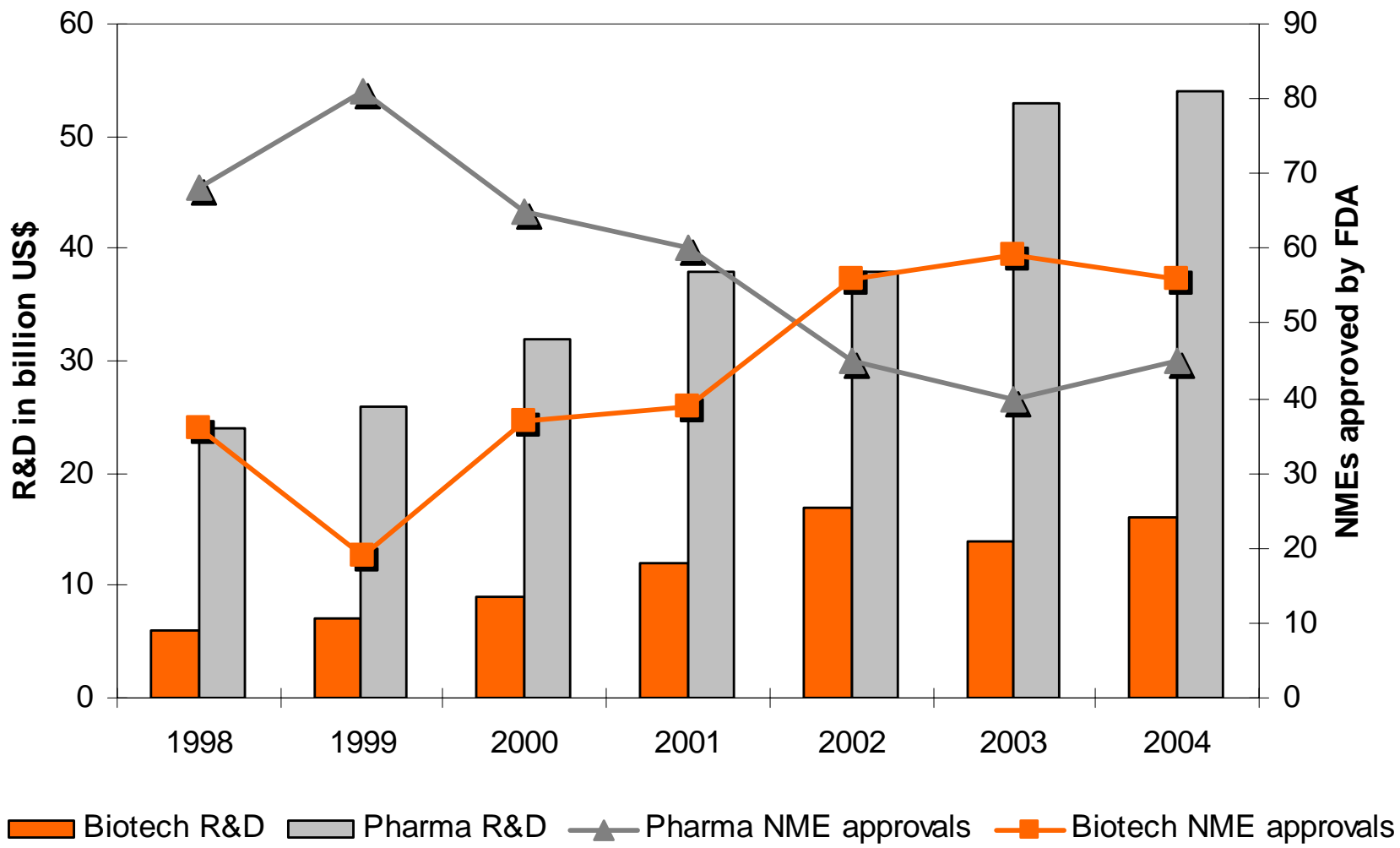
Source: IMS Health, BioGeneriX Projection

Share of New Approvals (US)



Source: FDA

The Innovation Gap (US)

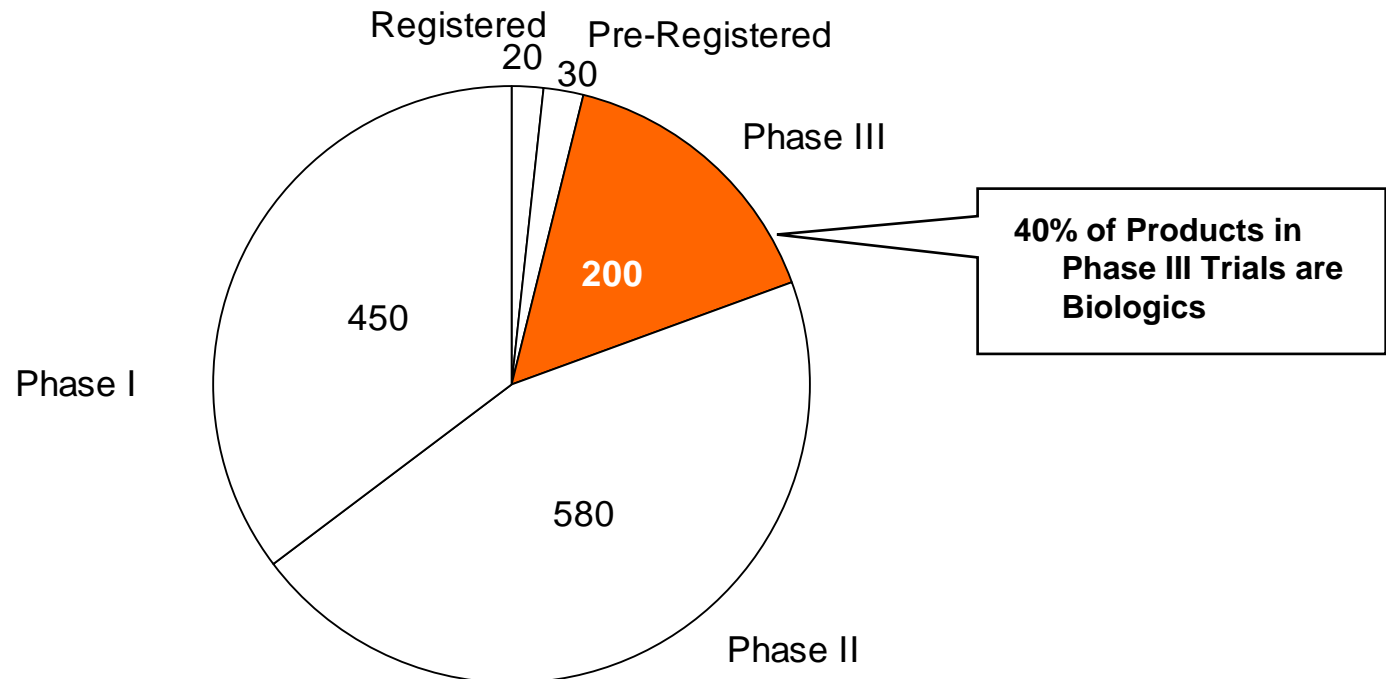


Source: FDA/ Ernst&Young, Global Report 2005

- In 2010 nearly 50% of all new approved Pharmaceuticals will be of biotechnological Origin

Pharmaceuticals in Development

100% = 1.280

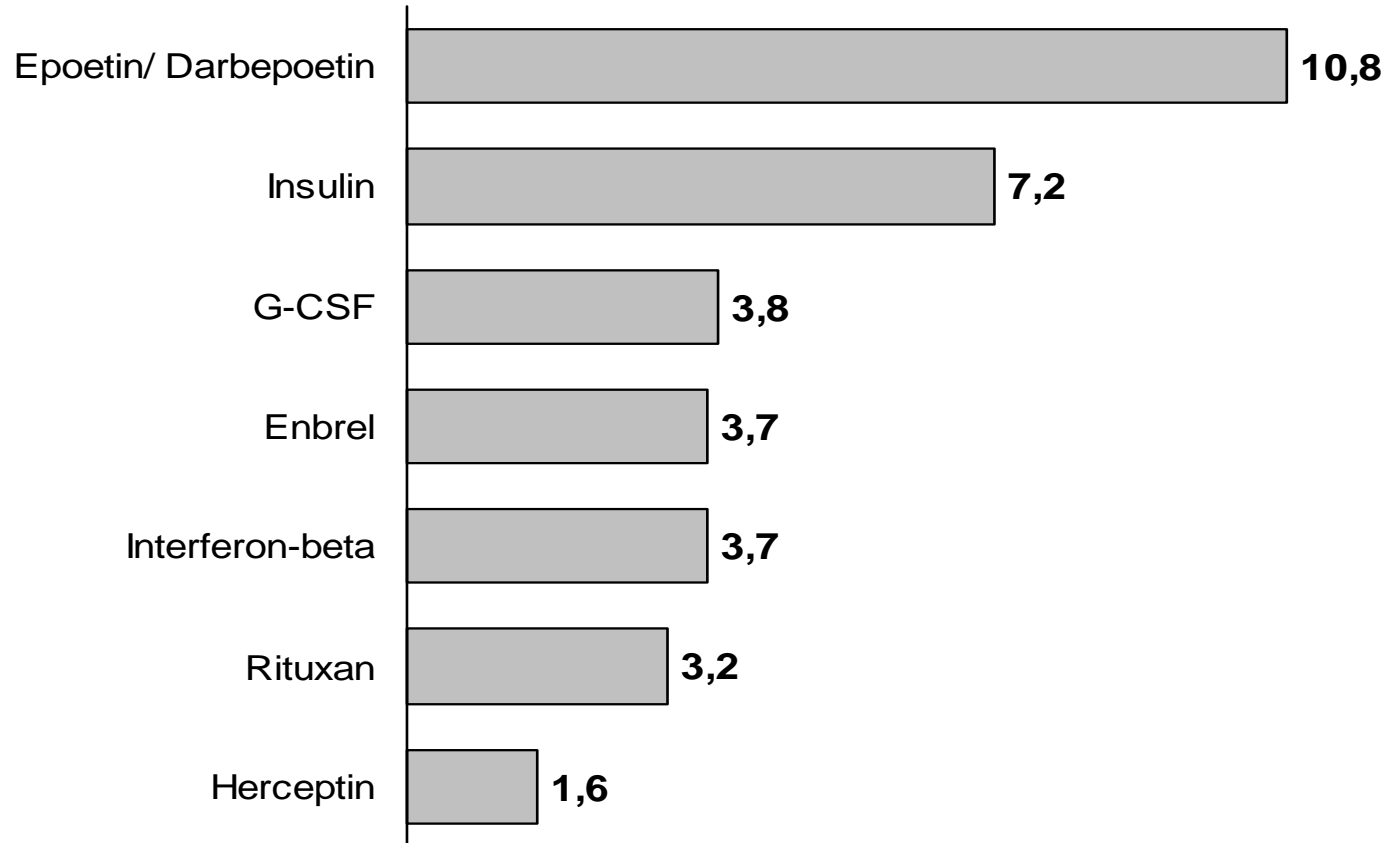


Source: IMS 2003 / Datamonitor

Top Global Biologics

Sales 2005

in b\$



Many Blockbuster Products are Biologics

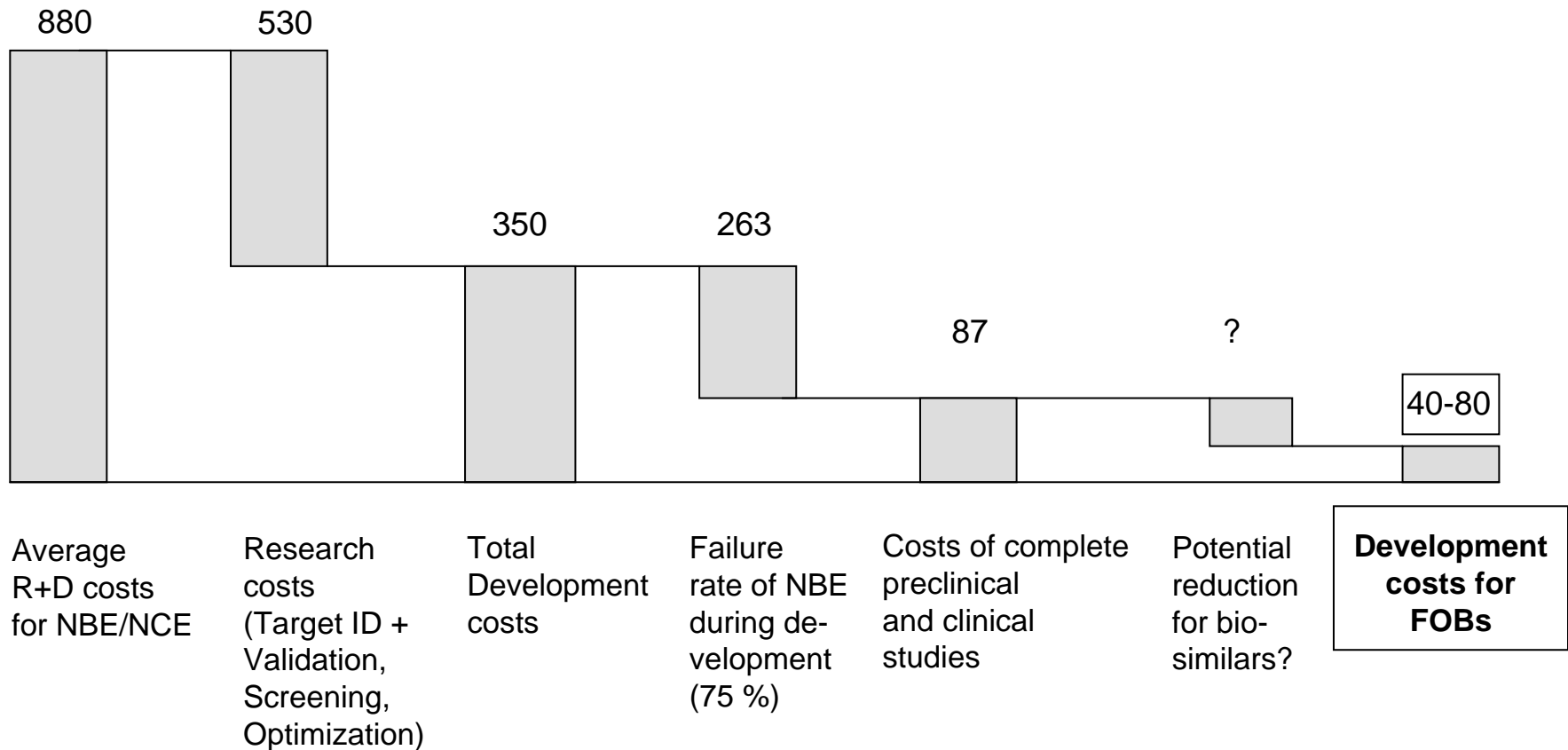
Patent Expiry Dates

Biologic	Indication	Europe Patent Expiry	US Patent Expiry	Annual Sales 2005 in b\$
Erythropoietin	Anemia: Oncology/ Nephrology	2005	2004 (Compound) 2015 (Process)	7,5
Filgrastim (G-CSF)	Neutropenia	2006	2006 (Compound) 2013 (Process)	1,2
Interferon-beta	Multiple Sclerosis	2003	2007	3,7
Human-Insulin	Diabetes	2004	2004	7,2
Human Growth Hormone	Growth Deficiency	2002	2003	2,5

Patents of Blockbuster Products are already expired in Europe

Development Costs

in Mio \$



Due to high development costs, regulatory and GMP-constraints, only a few companies will succeed

- The Therapies based on Biologics are 10 times more expensive than Therapies based on Small Molecules

Substance	Brand	Indication	DDD (Daily Defined Dosage*) Costs in €	Therapy Costs per Year per Patient in €
Erythropoietin	Erypo/ Eprex/ Neorecomon	Anemia (CRF)	16,-	5.800,-
Interferon-beta	Avonex/ Rebif/ Betaferon	Multiple Sclerosis	50,-	18.000,-
Amlodipin (Calcium Antagonist)	Norvasc, Generics	Hypertension	0,32	117,-
Omeprazole	Losec, Antra, Generics	Symptomatic gastroesophageal reflux disease	1,20	440,-

Biologics can be the most expensive part of a Therapy

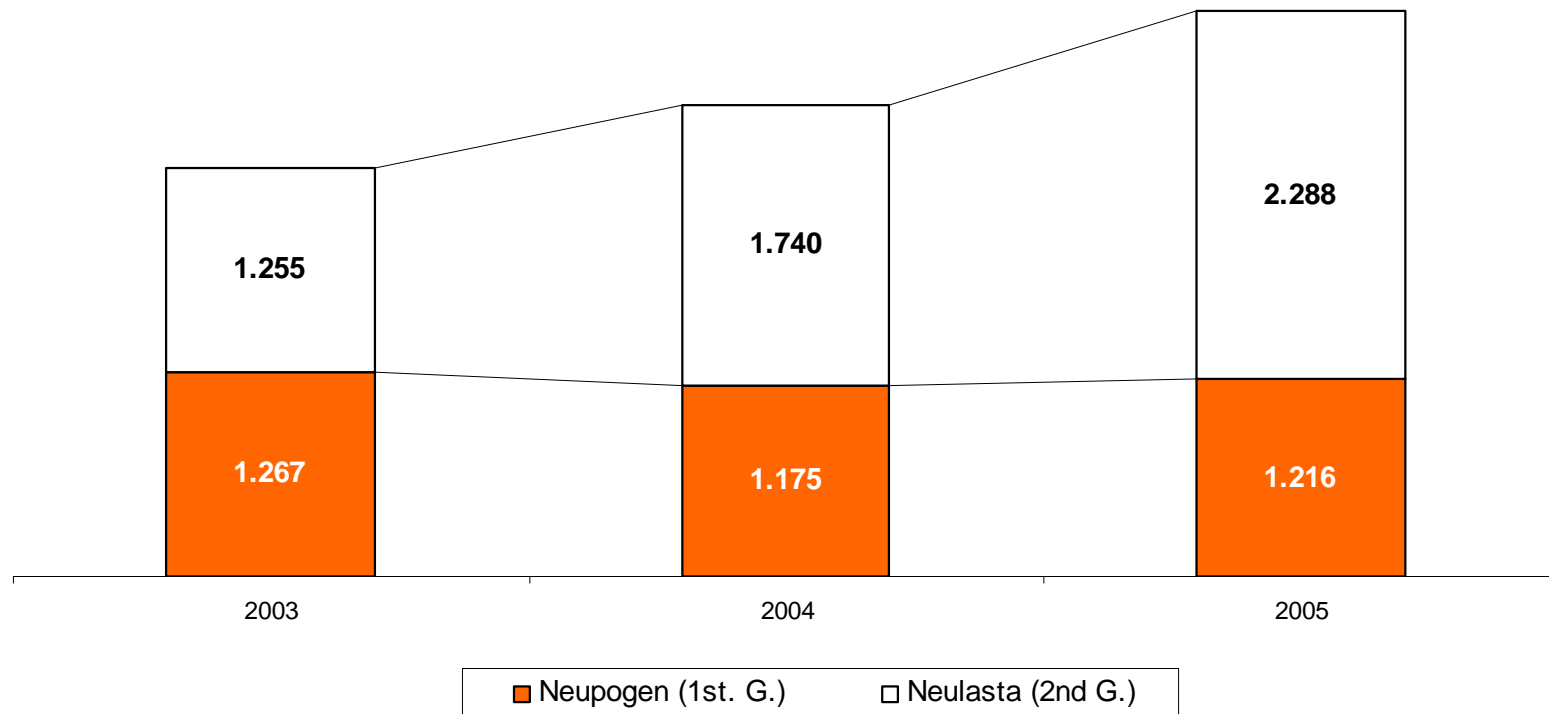
*DDD Definition: The DDD is the assumed average maintenance dose per day for a drug used for its main indication in adults.

Importance for Future Therapies

- Despite the Availability of advanced Molecules the „First Generation“ Biologics is still growing

G-CSF Products – global Sales – 3.504 m\$ in 2005

in m\$

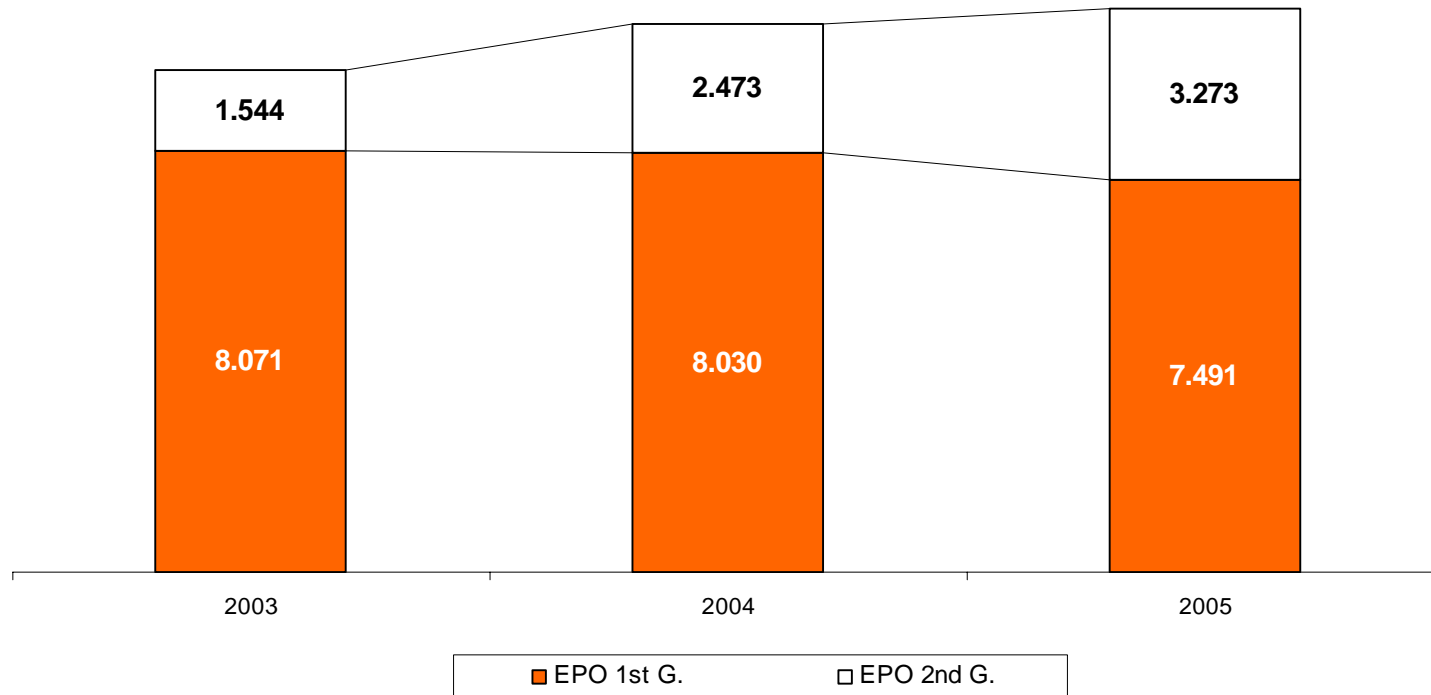


Importance for Future Therapies

-or remain nearly constant

EPO Products – global Sales – 10.764 m\$

in m\$



First Generation Biologics will still play a Role in Future Therapies

Main Criteria for Biosimilar Developments



- **Blockbuster Products with high Growth Rates** **Yes**
- **Most Patents already expired** **Yes**
- **Limited Number of Competitors due to approval hurdles** **Yes**
- **Broad international Market Penetration** **Yes**
- **High Therapy Costs** **Yes**
- **Importance for future Therapies** **Yes**
- **Fit to Product Portfolio Strategies** **Yes**

Biosimilars are a great Challenge but “nothing ventured, nothing gained”

- Definition/ Current Situation
- Main Criteria for Biosimilar Development
- **Portfolio Strategies**
- Conclusions

- **The Relevance of Biosimilars for Product Portfolio Strategies can be defined according to their...:**
 - ...Product Profile and Market Segmentation
 - ...Product Positioning
 - ...Fit to the existing Product Groups/ Portfolios
 - ...Fit to the Company's Core Competencies

- **Product Profile and Market Segmentation:**
 - Does the Product has the required or existing Indications?
 - Is the Product Performance comparable to others?

- **Product Positioning:**
 - Will the Product support the required Therapy?
 - Will the Product be accepted by the appropriate Target Group?

- **Portfolio Fit:**
 - Does the Product fit the existing Product Groups/ Portfolios?

- **Core Competence Fit:**
 - Does the Product fit the Company's Core Competencies?
 - Will the Product expand the Company's Core Competencies?

■ Indications:

- EPO is approved for two Indications: Anemia caused by Chronic Renal Failure and Chemotherapy-induced Anemia (Cancer Treatment)
- Anemia is defined as Hemoglobin (Hb) Level less than 12g/dL and should be treated to avoid the Fatigue Syndrome

■ Market Segments:

- Due to the two Indications the EPO-Market can be split into two Segments: Cancer Treatments and Dialysis
- Both Segments are indicated by different Target Groups, different Therapeutics, Locations, Product and Therapy Positionings

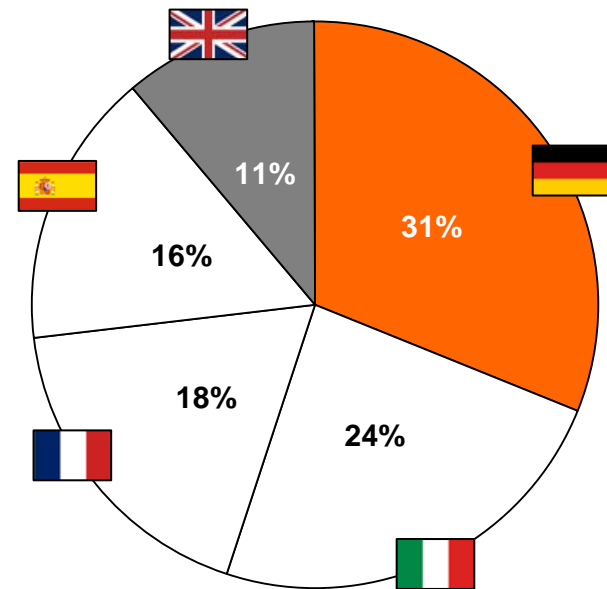
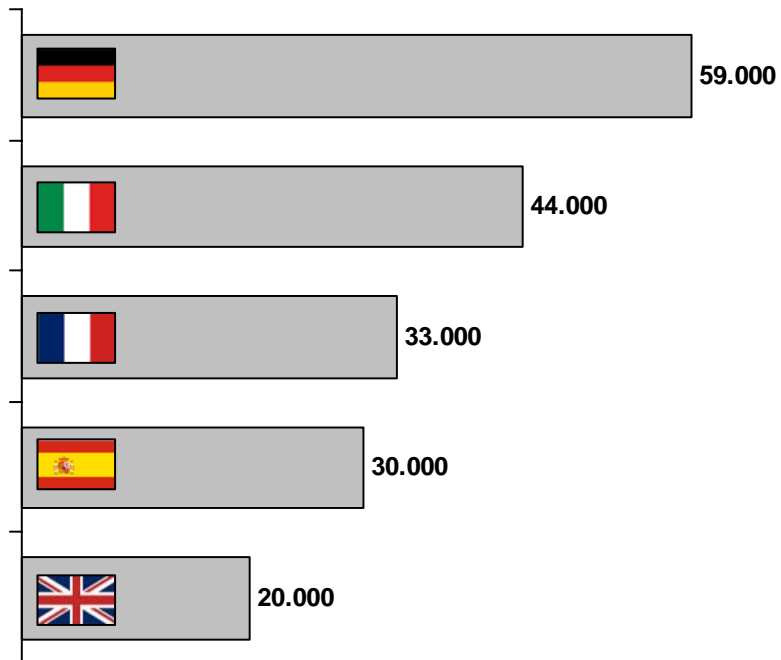
For the following analysis the focus will be set on Dialysis

Example: Epoetin/ EPO

■ Dialysis in EU5 Countries:

Patients

100% = 186.000 patients



Dialysis Patient numbers grow steadily at 3-9% annually

■ Dialysis Therapy Portfolio:

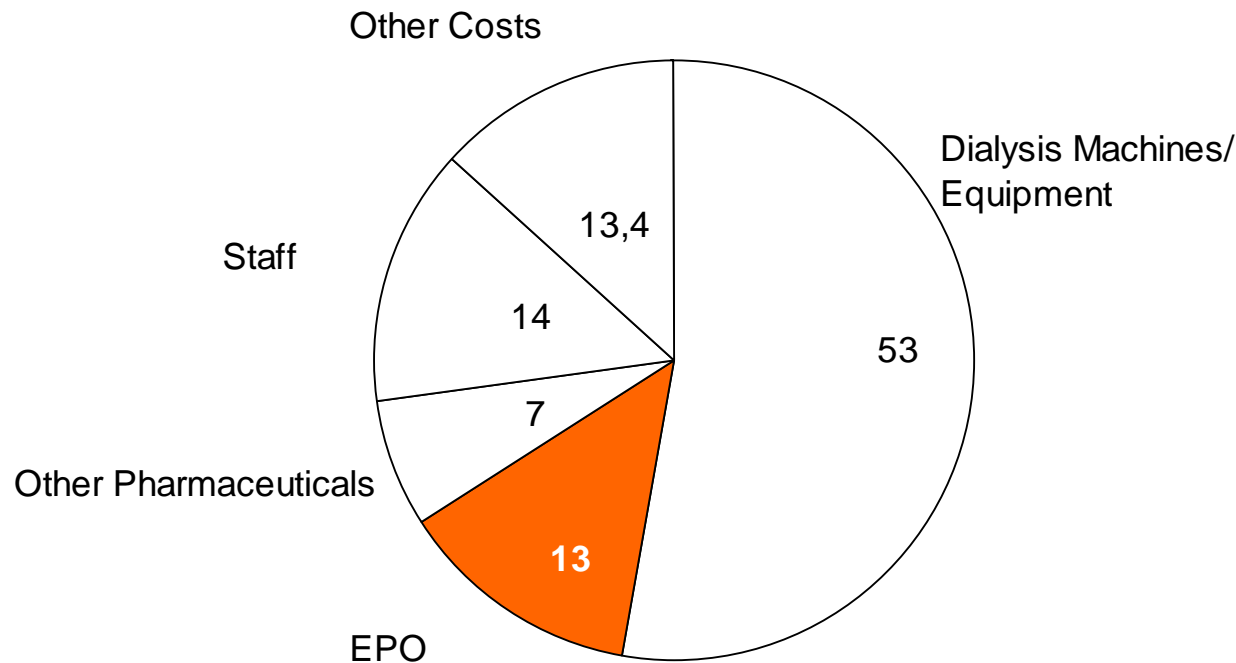
- **Erythropoietin** - to prevent anemia and fatigue due to hormone deficiency (application either sc or iv)
- **Iron Ferrous** - to enhance Epo- effectiveness, regular taking required
- **Heparin** - to inhibit blood coagulation for better blood circulation through the tubes (given during dialysis)
- **Phosphate binder** - to prevent problems with bones, calcification of veins, pain of articulations, itching (taken before or during a meal)
- **Vitamins & Minerals** - to treat deficiencies or to cover increased need
e.g. vitamin D to treat problems with bones and other water soluble vitamins, which were removed by dialysis (given after dialysis)
- **ASS** - to inhibit blood coagulation
- **Laxatives, acidosis products (Sodium hydrogencarbonate, Trometamol), antibiotics**
- **Calcium** - Hyperparathyreoidism
- **Skin creams** - to treat dry skin trough dialysis (Panthenol)

The Dialysis Therapy requires a lot of different Pharmaceuticals

Example: Epoetin/ EPO

■ Costs:

- 13% of all Costs for Dialysis account for EPO
- 65% of all Costs for Dialysis-Pharmaceuticals account for EPO-Treatment



Epo is the main Element of the Pharmaceutical Therapy in Dialysis due to Costs

- Definition/ Current Situation
- Main Criteria for Biosimilar Development
- Portfolio Strategies
- **Conclusions**

- A Biosimilar EPO will have the same Product Performance compared to existing Products, therefore:
 - The Product Positioning will be comparable, i.e. all Indications in all Markets will be covered
 - The Product Profile will be the same, i.e. it will be accepted by the Target Groups
 - And: a cost effective Biosimilar EPO will expand the Ability/ Flexibility to set up „high quality“ Portfolios and competitive Pricings

Biosimilars are able to be the Backbone of a successful Portfoliomanagement

- If the Company does not have a suitable Portfolio or Portfolio Fit, it can be achieved as follows :
 - Find a Partner who is core competent in the required Therapeutic Area
 - Find a Partner who is competent in the required Market Segment (Retail/Hospital)
 - Develop or licence in the required Products by yourself (if possible)

■ Strengths:

- Biosimilars can set the Milestone for the optimized Product and Company Positioning by satisfying the Customer
- Biosimilars can build the Basis for Future Growth by Upgrading the Pipeline and/or the Product Portfolio

■ Weaknesses:

- Biosimilars will cause high Investments
- The Approval of Biosimilars is difficult due to Regulatory Hurdles

■ Opportunities

- With Biosimilars as Part of the Portfolio the Supplier will gain Competence in „new“ Markets
- Good Customer Relationship Management by offering Therapy Portfolios

■ Threats:

- Negative Impact on Price/ Reimbursement by Government and Health Care Systems