

„Rising Tendencies in Generic Markets – the new Market Segment of Biosimilars“

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■ Definition/ Current Situation

- Main Criteria for Biosimilar Developments
- Future Outlook for Biosimilars

Biogenerics are:

“Similar versions of originator reference products whose active agents are achieved by biotechnological methods using recombinant cell cultures.”

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

- **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 demands a new approval
- Very complex **patent situation**
- **Development time** at least twice as long as for Small Molecule Generics
- **Development costs** 8-100 times higher than for Small Molecule Generics

CHMP (Committee for Medicinal Products for Human Use)
released regulatory guidelines for:

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

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

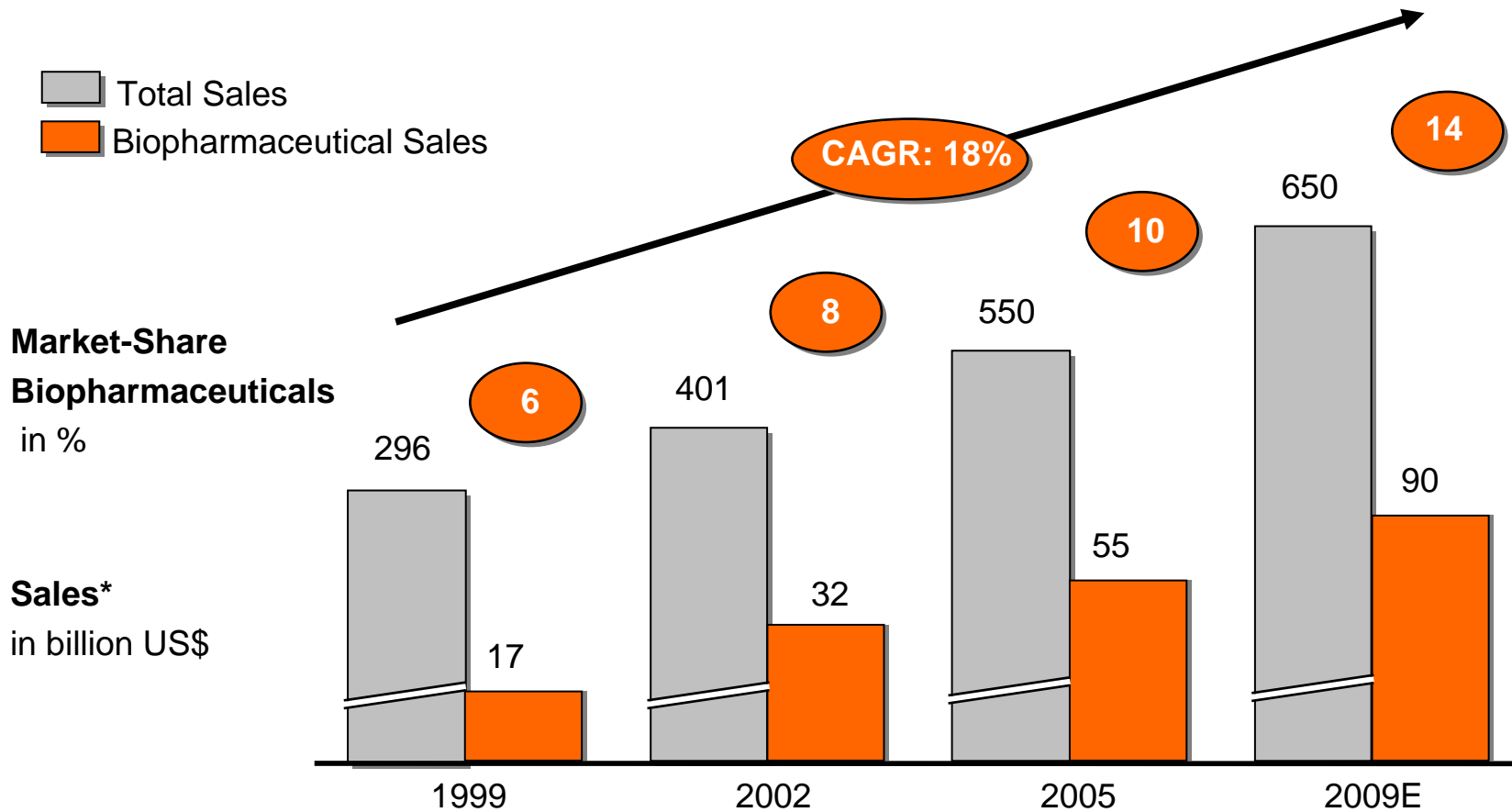
- **Main Criteria for Biosimilar Developments**

- Future Outlook for Biosimilars

- **Blockbuster Products with high Growth Rates**
- **Most Patents already expired**
- **Limited Number of Competitors due to hurdles and costs**
- **High Therapy Costs**
- **Importance for future Therapies**
- **Marketing Capabilities**

The Global Market

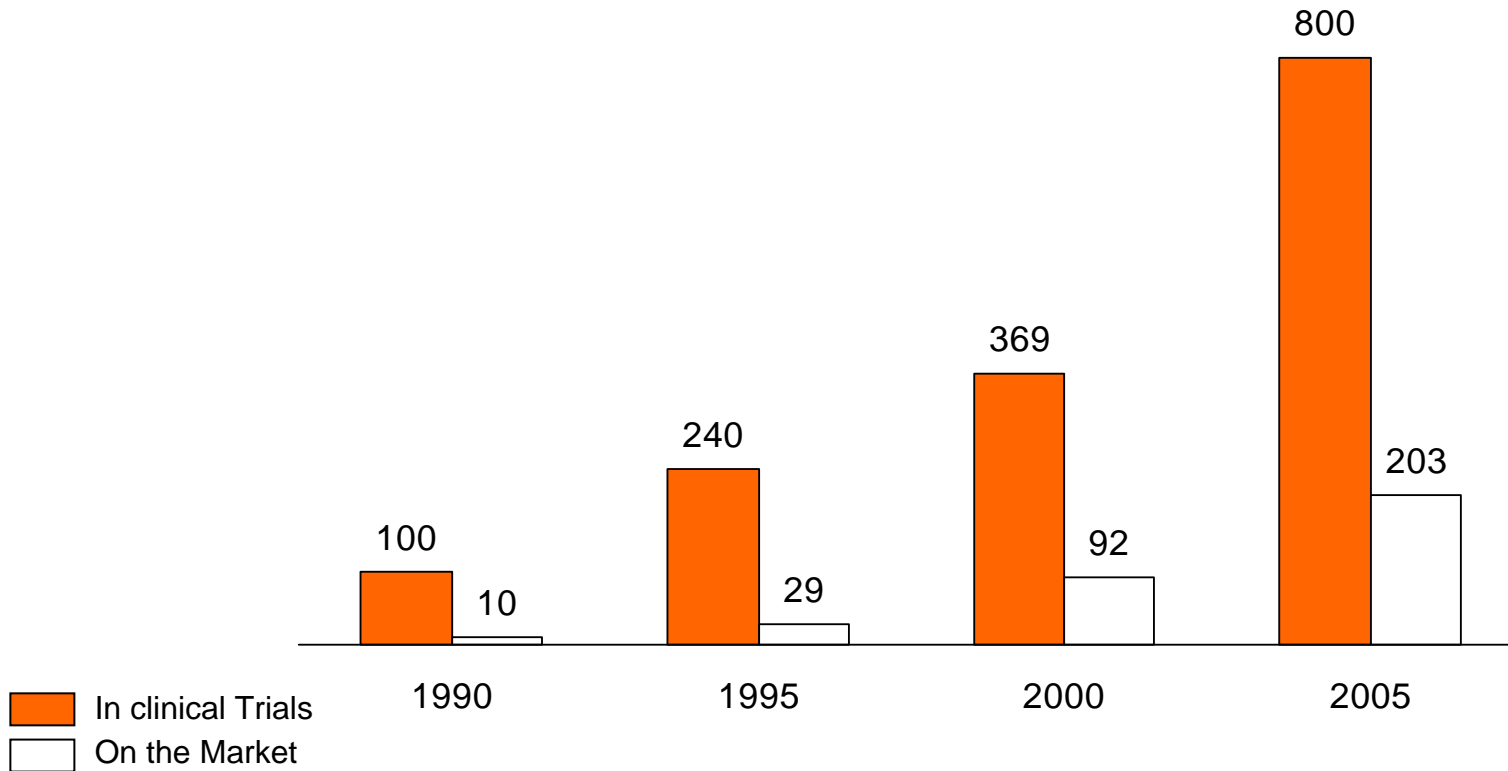
- Biologics are growing at twice the rate of „ Small Molecules“ (Rx Market)



Source: IMS Health, BioGeneriX Projection

Biopharmaceuticals – Global Market

in absolut Numbers

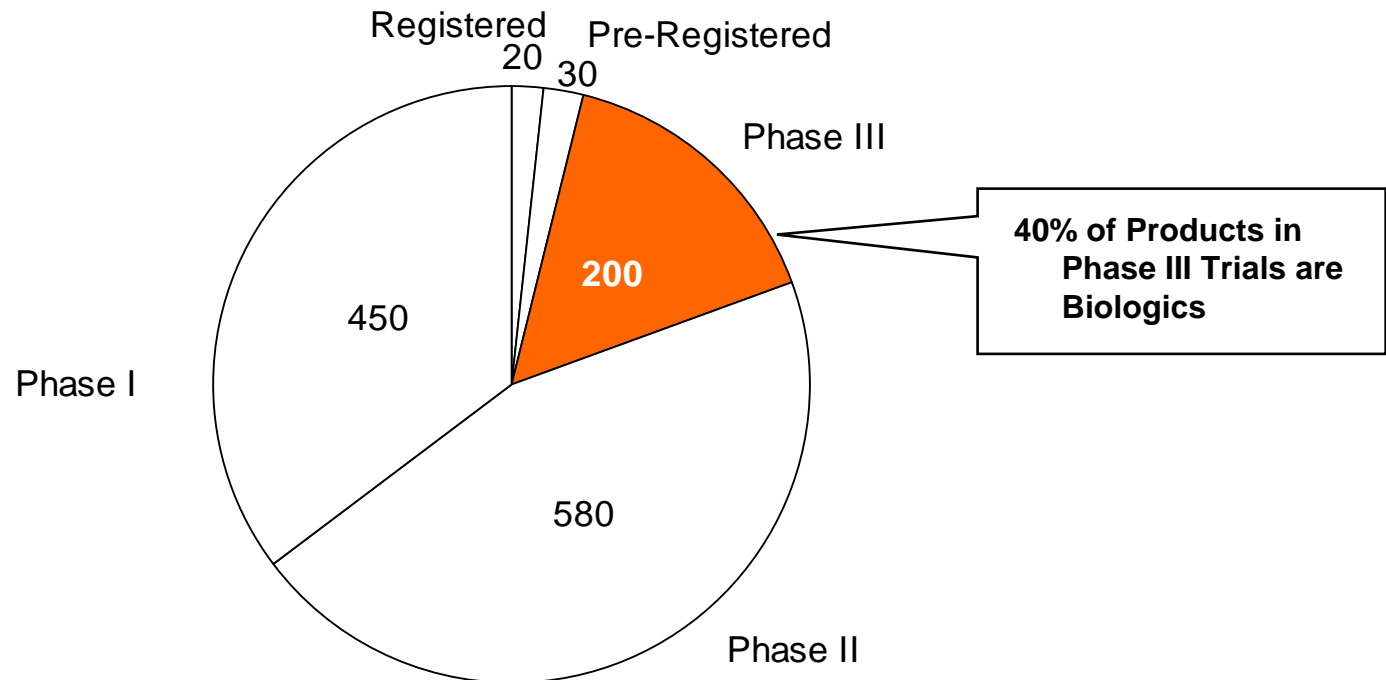


Source: Merrill Lynch

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

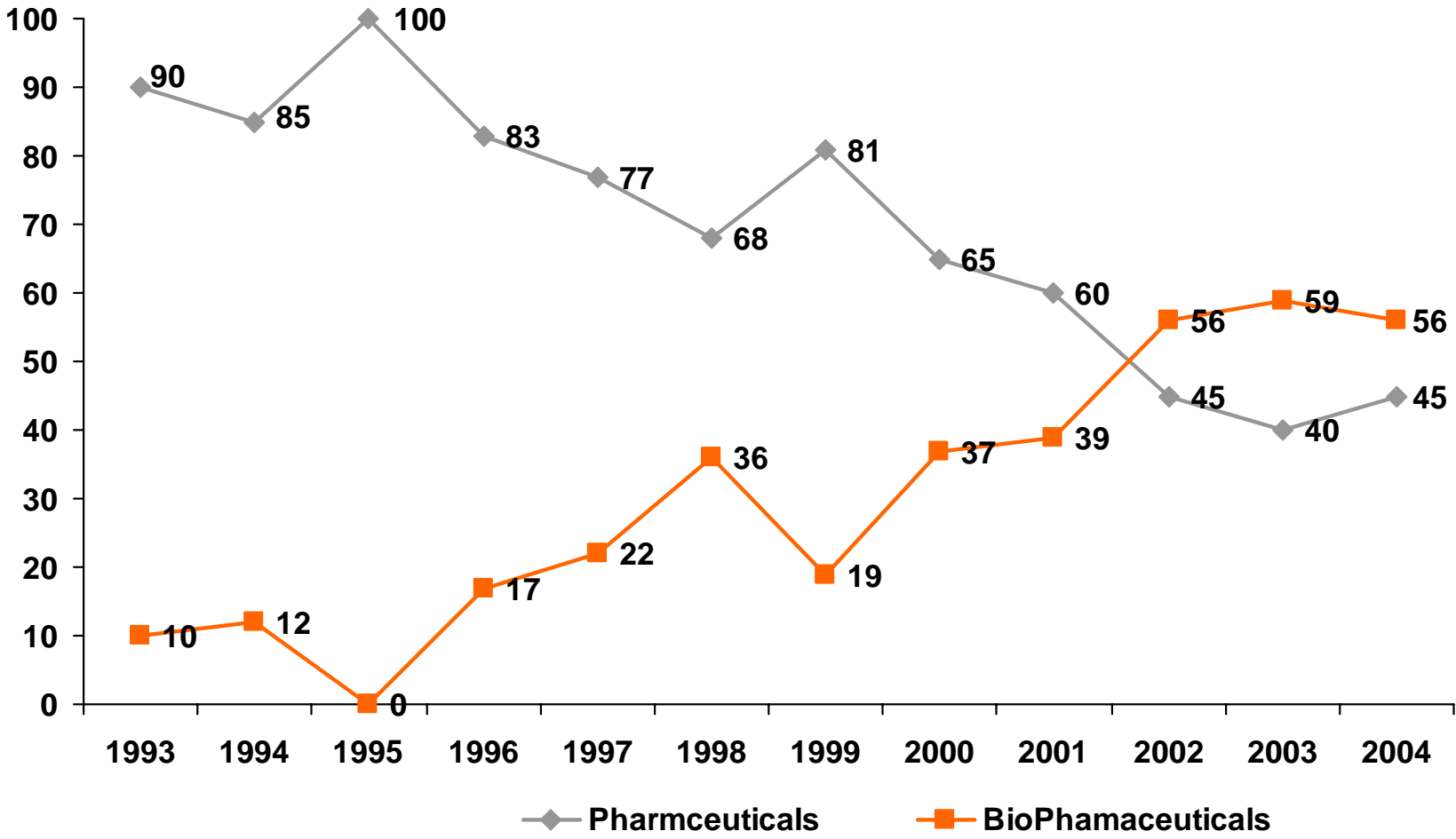
Pharmaceuticals in Development

100% = 1.280

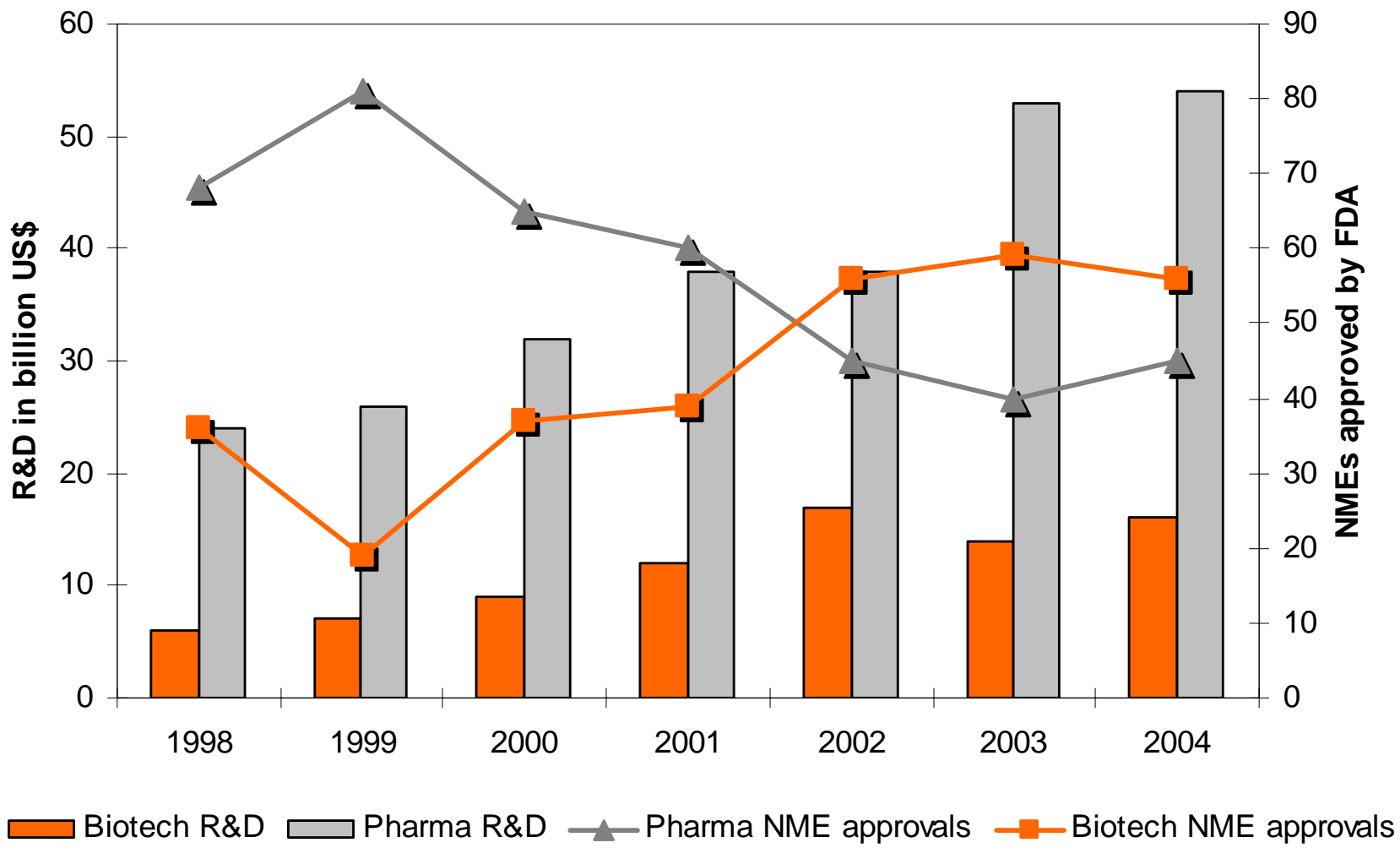


Source: IMS 2003 / Datamonitor

Share of New Approvals (US)



The Innovation Gap (US)



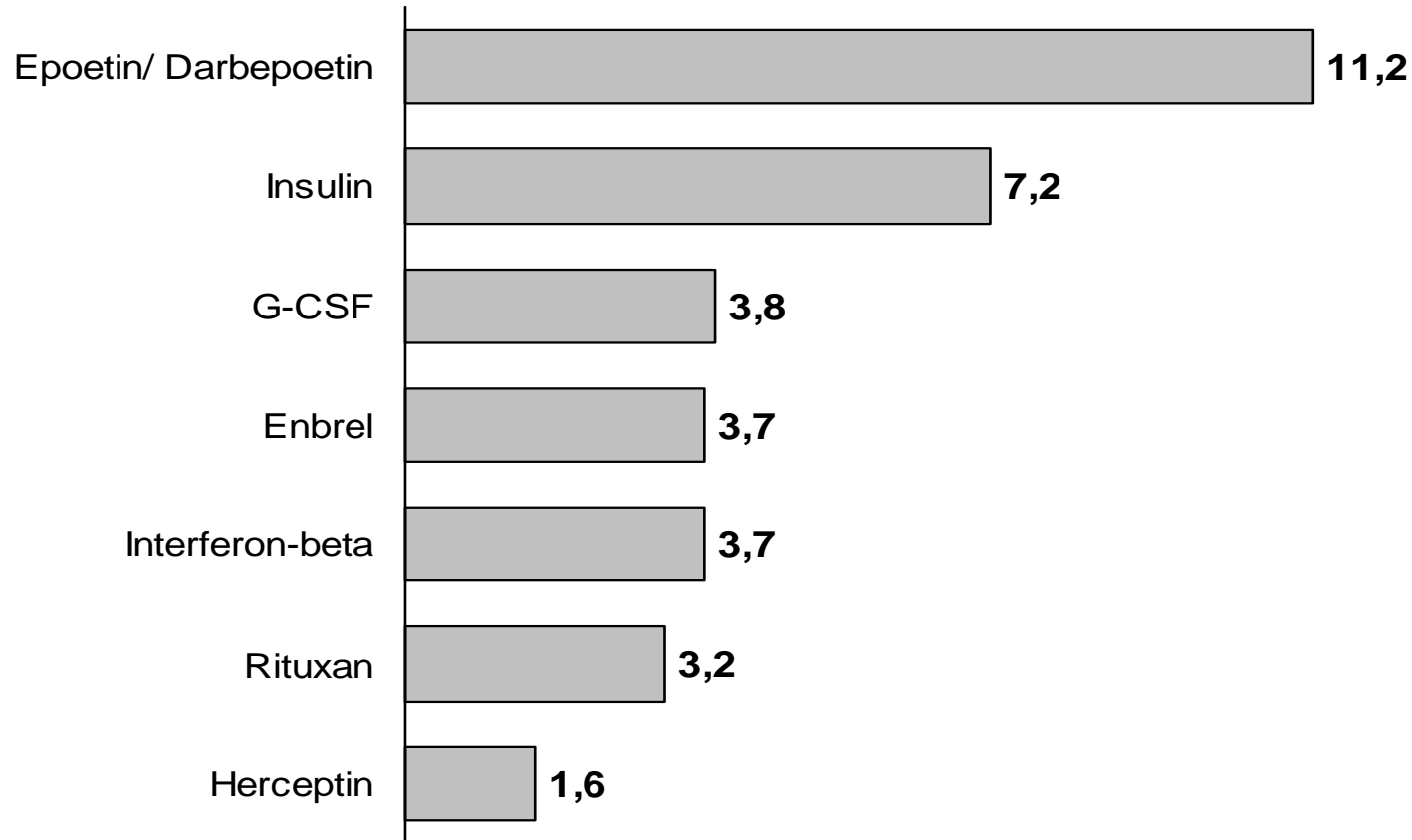
Source: FDA/ Ernst&Young, Global Report 2005

Top Global Biologics 2005



Sales

in b\$



Many Blockbuster Products are Biologics

Source: Company Reports

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Patent Expiry Dates



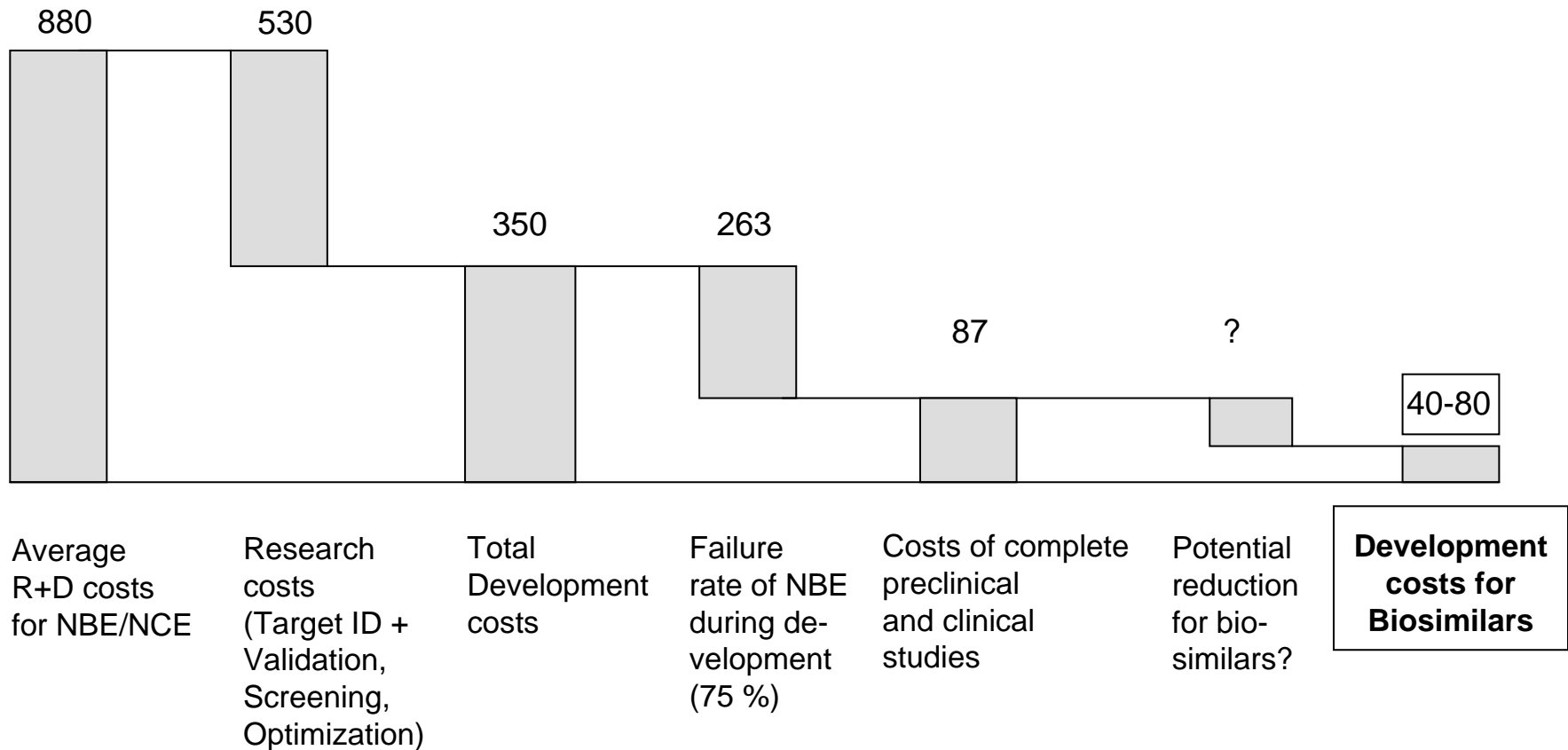
Biologic	Indication	Europe Patent Expiry	US Patent Expiry	Annual Sales 2005 in b\$
Erythropoietin alpha/beta	Anemia: Oncology/ Nephrology	2005	2004 (Compound) 2015 (Process)	7,9
Filgrastim (G-CSF)	Neutropenia	2006	2006 (Compound) 2013 (Process)	1,2
Interferon-beta	Multiple Sclerosis	2003	2007	3,7
Human-Insulin	Diabetes	2004	2004	7,2
Human Growth Hormone	Growth Deficiency	2002	2003	2,5

Patents of Blockbuster Products are already expired in Europe

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Development Costs

in Mio \$



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

Source: Maleck, K., Pollano, F. EBR 2001

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

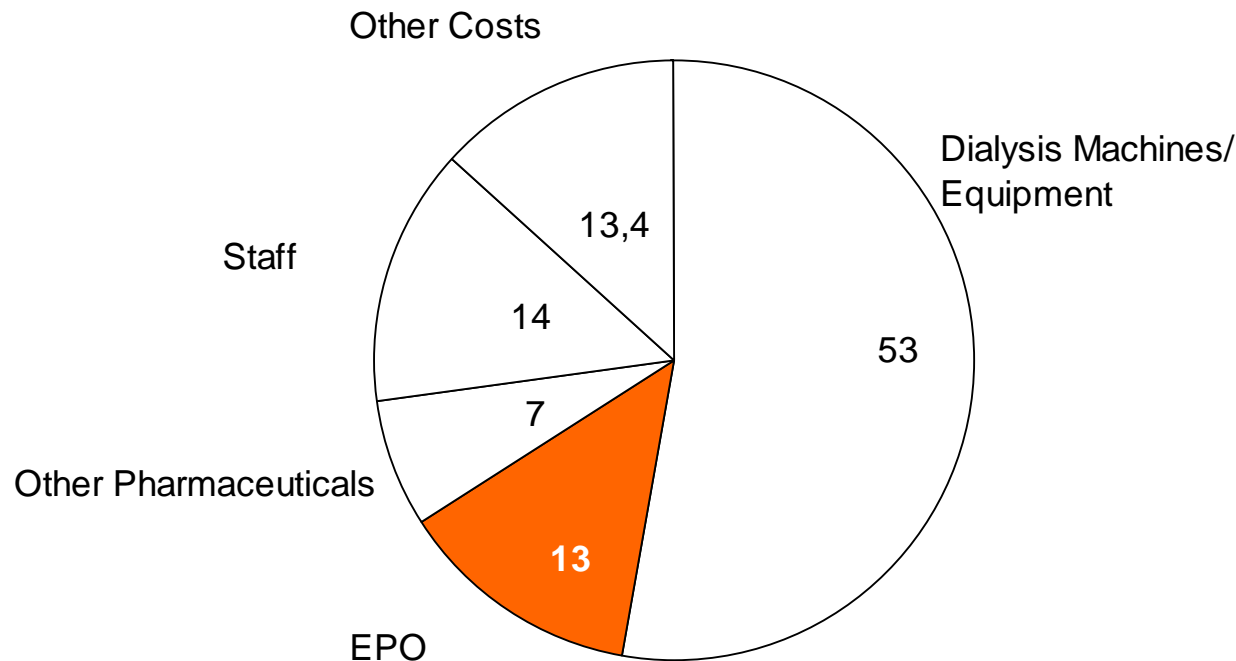
Substance	Brand	Indication	DDD (Daily Defined Dosage*) Costs in €	Therapy Costs per Year per Patient in €
Erythropoietin	Erypo/ Eprex/ Neorecomon	Anemia (CRF)	16,-	5.800,-
Interferon-beta	Avonex/ Rebif/ Betaferon	Multiple Sclerosis	50,-	18.000,-
Amlodipin (Calcium Antagonist)	Norvasc, Generics	Hypertension	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.

■ 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

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Example: EPO Product-Pipeline

- Long-lasting Forms of EPO (2nd Generation):
More Convenience but not a „Therapeutic Innovation“

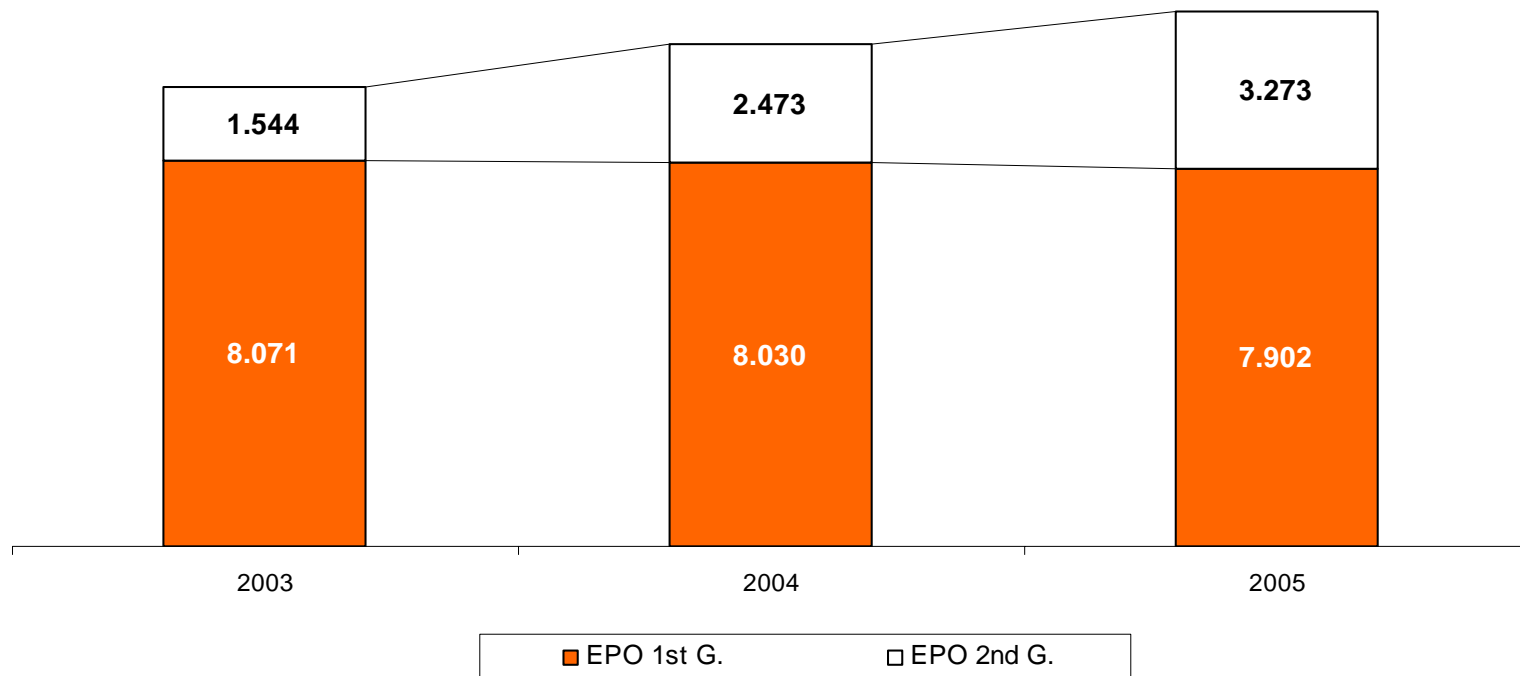
Company	Substance	Phase	Launch EU	Indication
Amgen	Darbepoetin, Aranesp®	Marketed	May 2001	Renal Anemia, Oncology
Roche	C.E.R.A., Mircera®	Filing Apr. 2006	approx. 2007	Renal Anemia
Affymax	Erythropoiesis Stimulating Agent (ESA); Hematide®	Phase II - Dosefinding	approx. 2013	Renal Anemia, Oncology

Example: EPO Generation Split

Market Expansion vs. Cannibalisation

EPO Products – global Sales 2005 – 11.175 m\$ (+6%)

in m\$



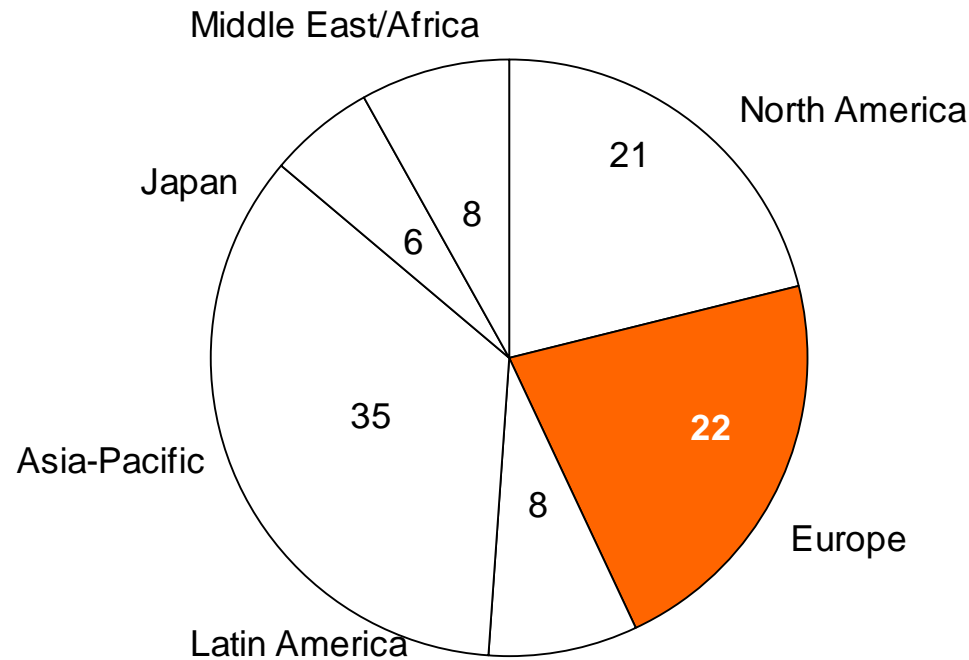
Source: Company Report

Example: EPO Patient-Potential

- The Cancer Patient Population has a double digit growth rate per year

Cancer Patients per Year - Global

100% = 20.500.000 (+35% growth)

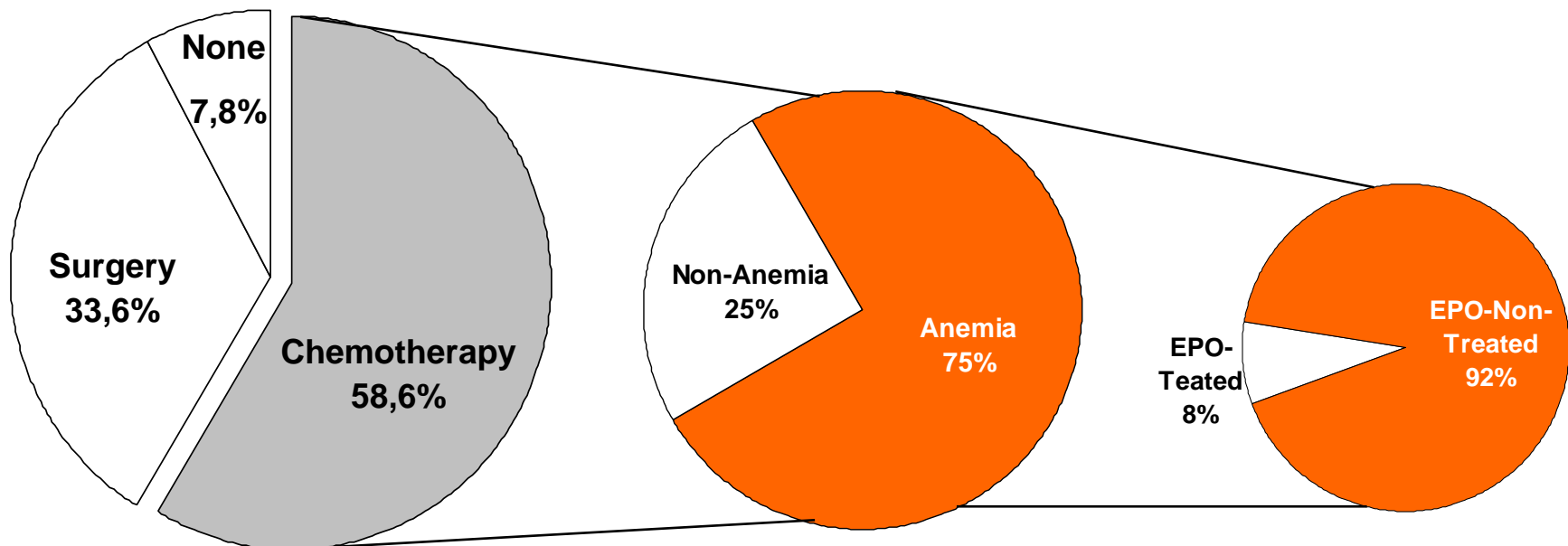


Example: EPO Patient-Potential Europe

- 58,6% of all Cancer Patients are treated by Chemotherapy = 2.6 m Patients
- 75% of all Chemotherapy Patients will become anemic (Hb <11g/d) = 2m Patients
- 8% of all Anemic Patients are treated with EPO = 159.000 Patients
- Potential for EPO-Treatment = 92% untreated - approx. 1.8m Patients

Treated Cancer Patients Europe

100% = 4.510.000



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Product

- Highly scientific products
- Quality & Safety
- Device
- All Dosage Forms/ Strengths
- 2nd Generation-Pipeline

Price

- Try to keep the prices as high as possible
- Offer rebates or services
- Involvement of Payers

**Small
European
team of
highly
qualified
specialists**

Place

- Small group of specialists
- Key account management
- Centralized purchasing decisions
- Different Strategies for Retail and Hospital Segments

Promotion

- No generic positioning
- Value added services and databases
- Co-Promotion or Co-Marketing with competent Partner
- Therapy Portfolio Strategy

Main Criteria for Biosimilar Developments



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- **Importance for future Therapies** **Yes**
- **Marketing Capabilities** **Yes**

- The biogeneric industry initially saw numerous companies, but a lot have failed => limited number of competitors
- Successful Biosimilar companies must have a minimum of profound expertise in **biotechnology, financial strength, patent knowledge** and access to pharmaceutical marketing infrastructure
- Cost leadership might become an issue, depending on the price erosion
- Originators in Europe defend their markets by building up regulatory hurdles, marketing tools, and switches to second generation products
- Generic industry is likely to reduce investments due to margin pressure in their main business

Thank you for your attention

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