„Bio-Generika“

Dr. Klaus Maleck
Chief Financial Officer & VP Business Development
BioGeneriX AG

Nürnberg, 28. Juni 2006

Agenda

- **The Opportunity: Market Size and Potential**
- Entrance Barriers to the FoB Market
- Marketing FoBs
- Rentability in the FoB Market
- Conclusion

Guidelines on Follow-on biologics

- Definition: **„Biogenerics (Follow-on biologics) are Copycats of Biopharmaceuticals, i.e. Pharmaceuticals, whose active agents are achieved by biotechnological Methods using recombinant Cell Cultures.“**

- Approval process distinguishes FoBs from generics:

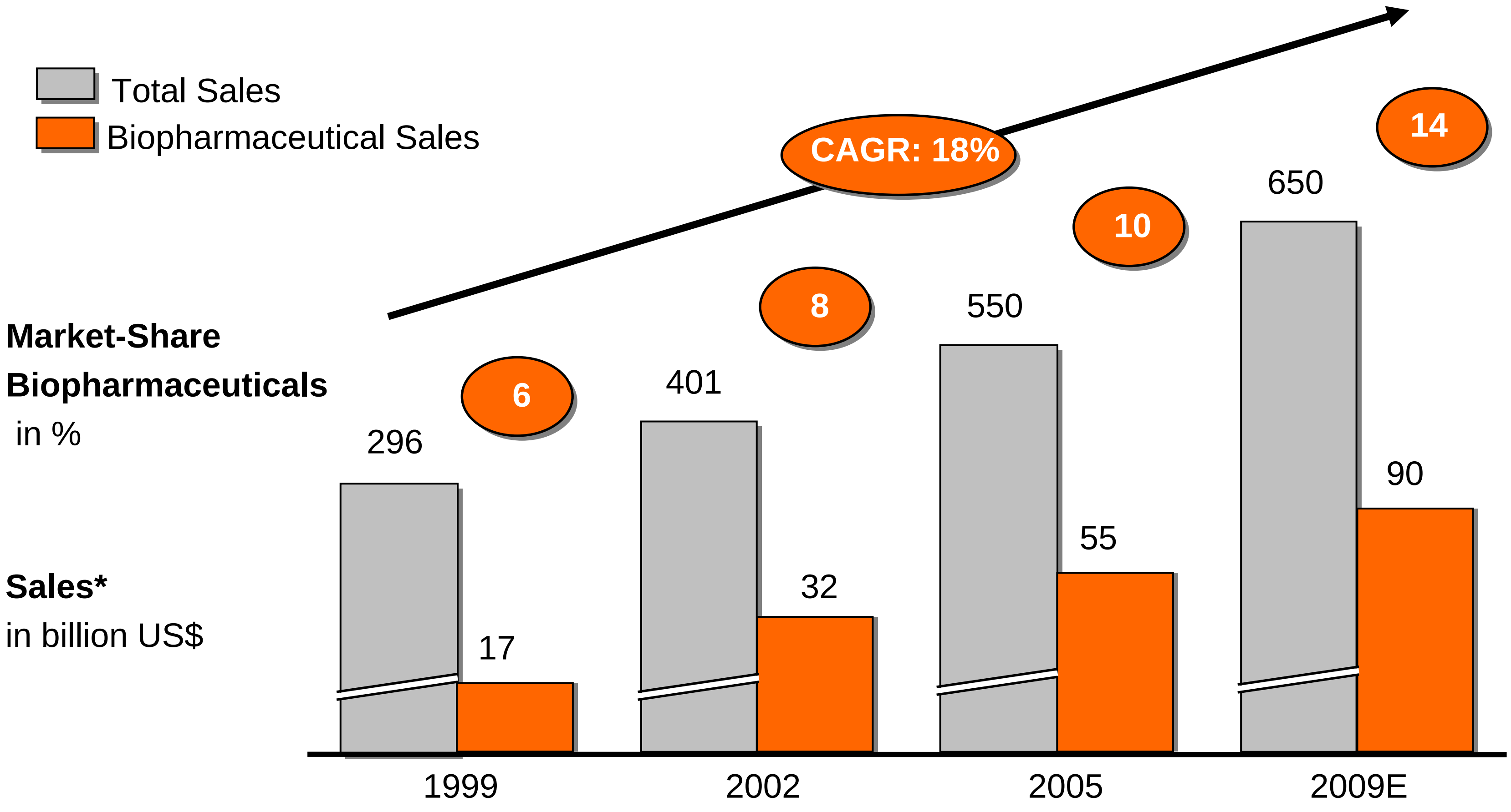
  Centralized procedure mandatory, two basic legal bases

  – **Biosimilar approach** (EC2001/83): comparative toxicology; bioequivalence studies, one limited pivotal, comparative efficacy study (caveat: statistical power and assay sensitivity)

  – **Stand-alone approach:** non-clinical part without comparator, phase I/II/III, against comparator (no reference citation)

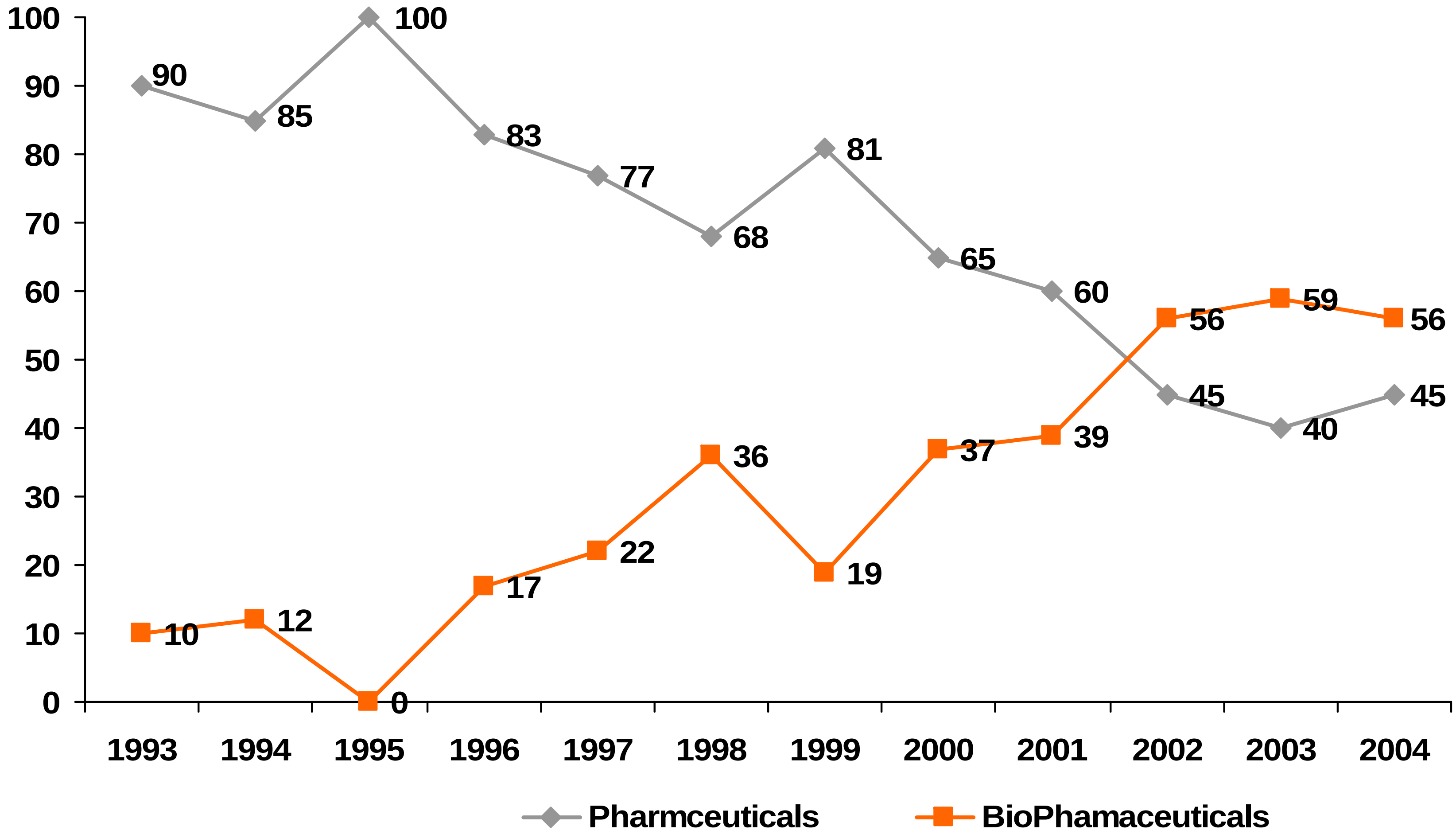
Opportunity: The Global Pharma Market

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



Source: IMS Health, BioGeneriX Projection

Share of New Approvals (US)

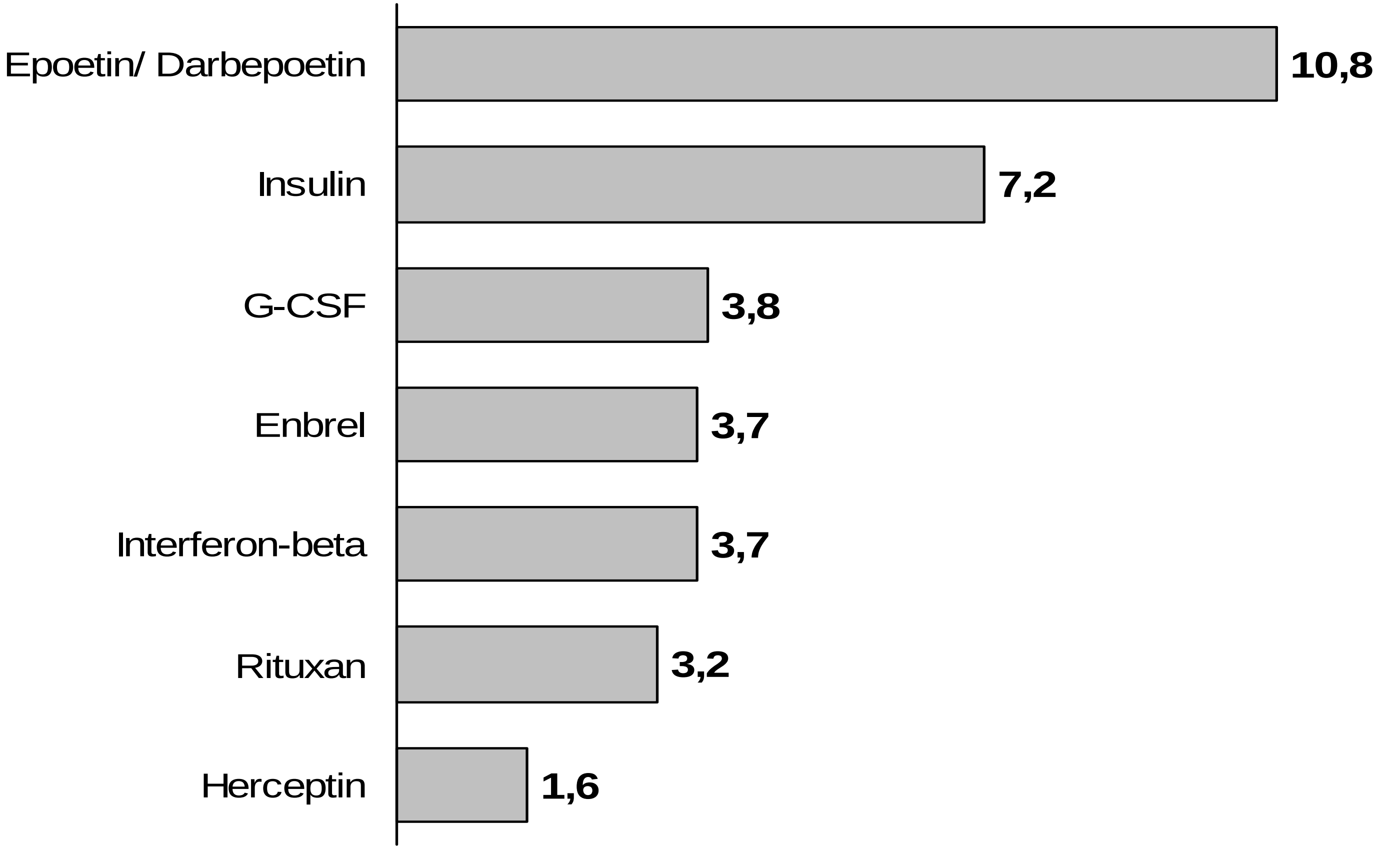


Source: FDA

Top Global Biologics

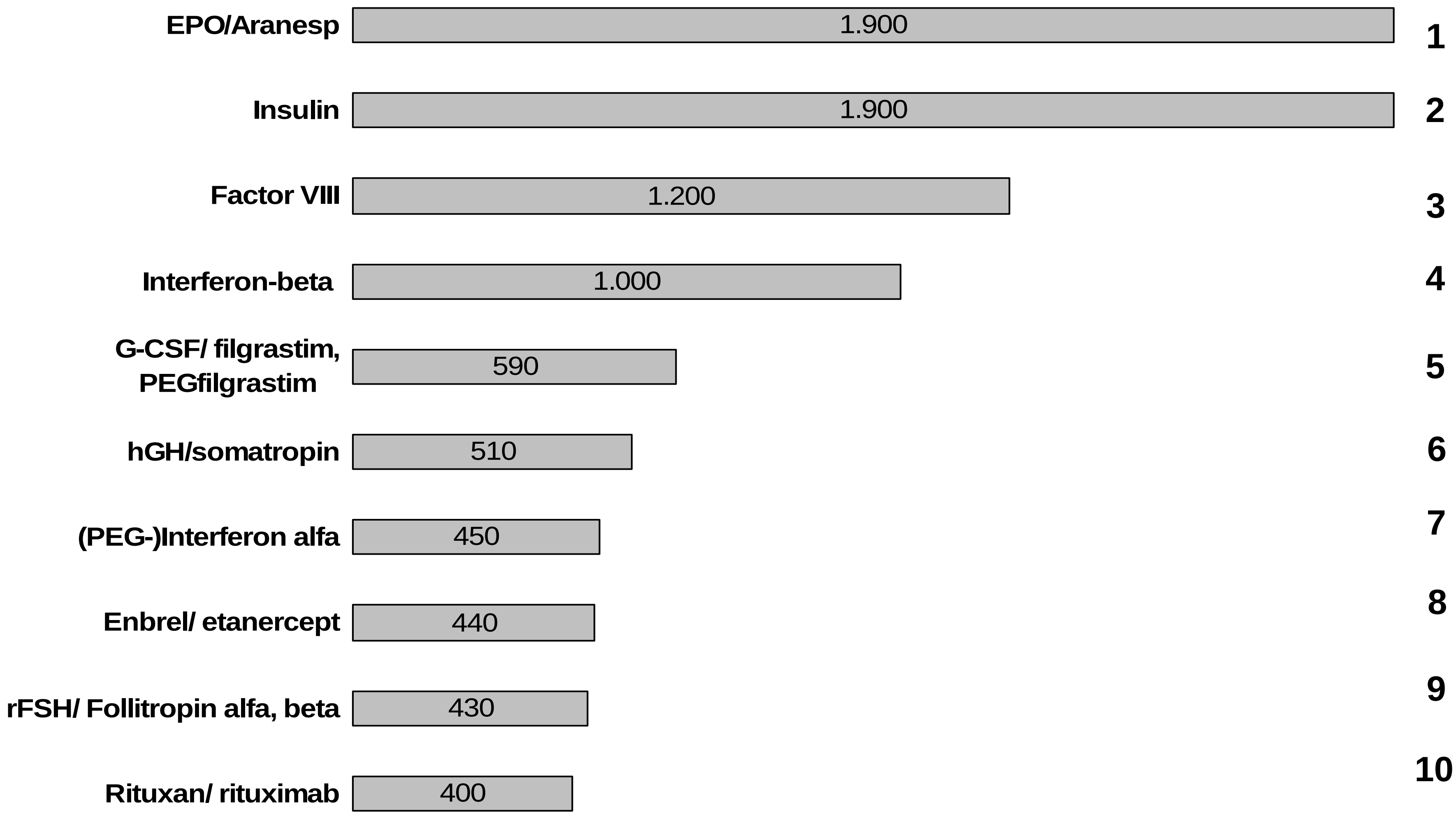
Sales 2005

in b$



Biotech drugs offer a huge market potential, also after patent expiry

Top 10 European Biotech-Products 2004 in m$



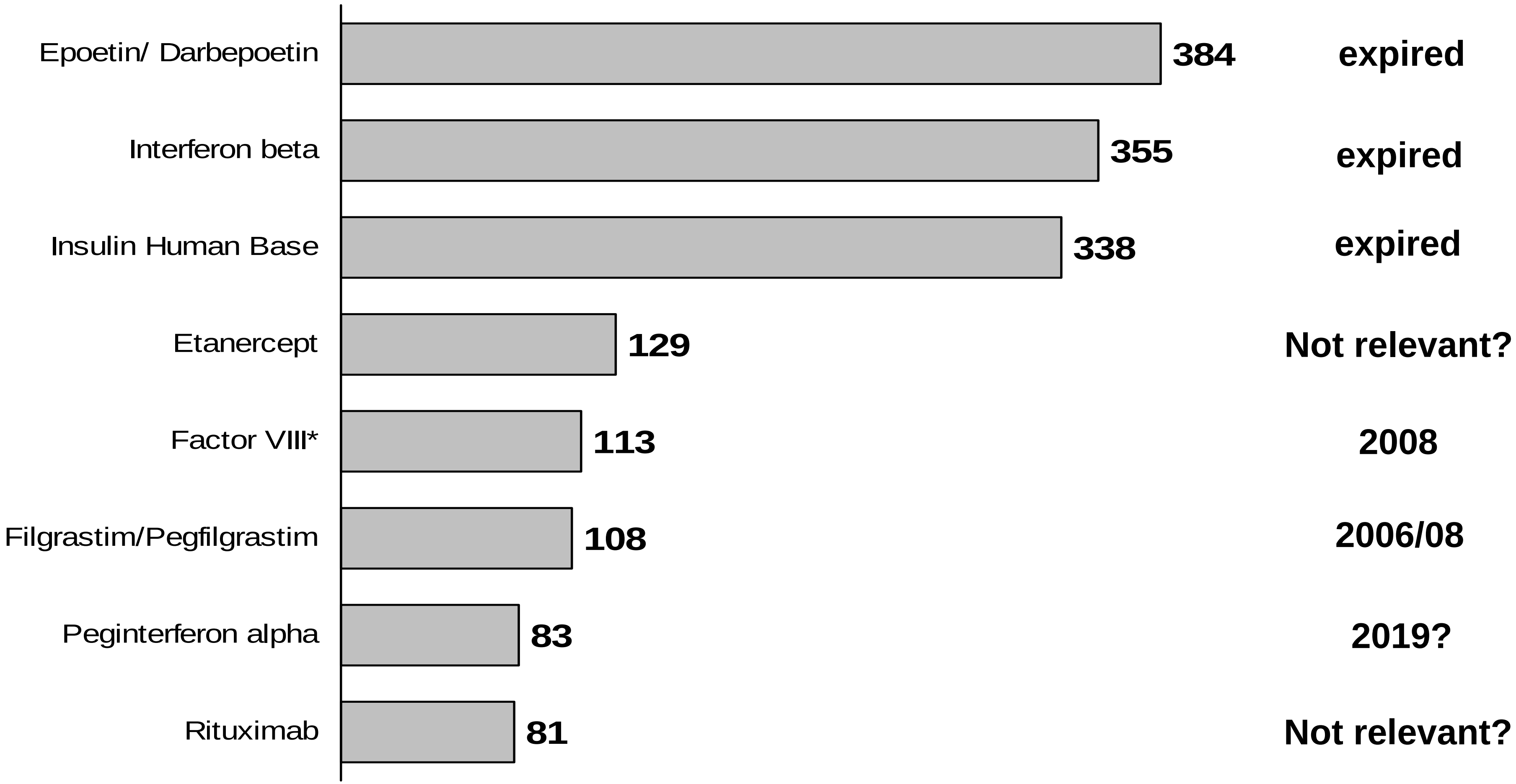
The average sales figure of a top10 Biotech product in Europe is ~ 900 Mio €

Source: IMS Health/ Company Reports/BGX estimates

Top 10 Biopharmaceuticals in the German Market

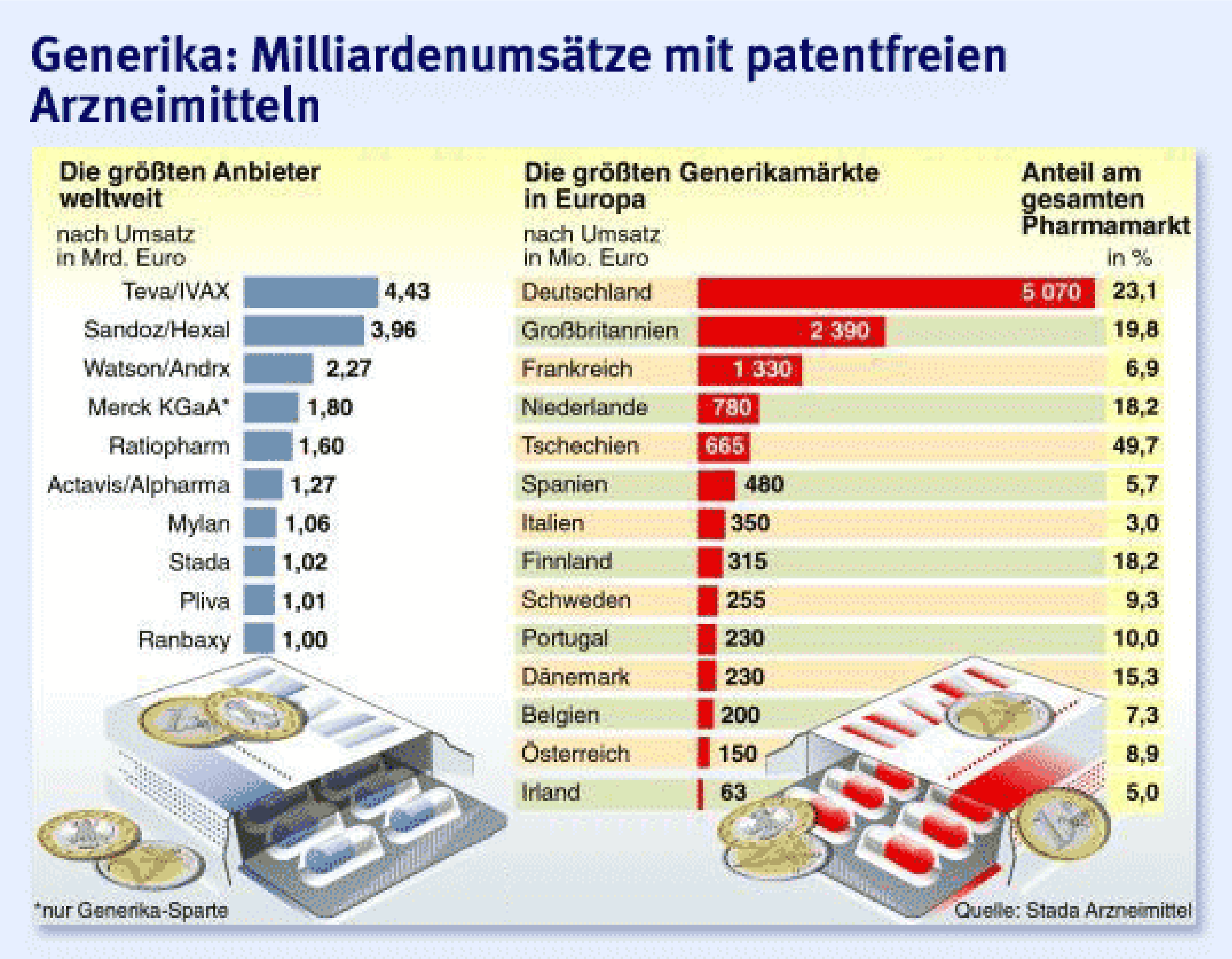
Combined Sales Retail +Hospital 2005 **Patent expiry**

in m€



Source: IMS/ BGX - *No Direct Sales

Share of Generics in Europe



Agenda

- The Opportunity: Market Size and Potential
- **Entrance Barriers to the FoB Market**
- Marketing FoBs
- Rentability in the FoB Market
- Conclusion

Guidelines: Current Situation EU

CHMP released „final“ regulatory guidelines for

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

will come into effect on June, 1st 2006

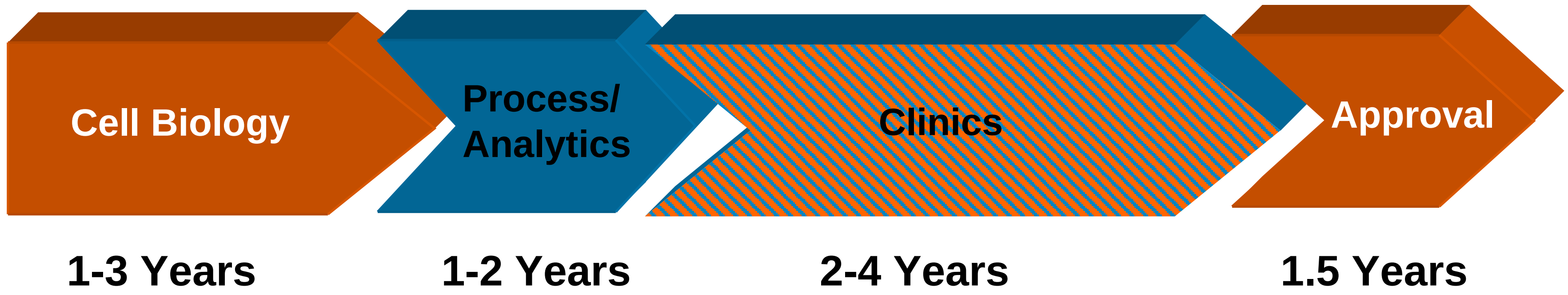
Despite these guidelines no guarantee for a „golden“ development plan

- Therefore:

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

Development Timelines EMEA

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

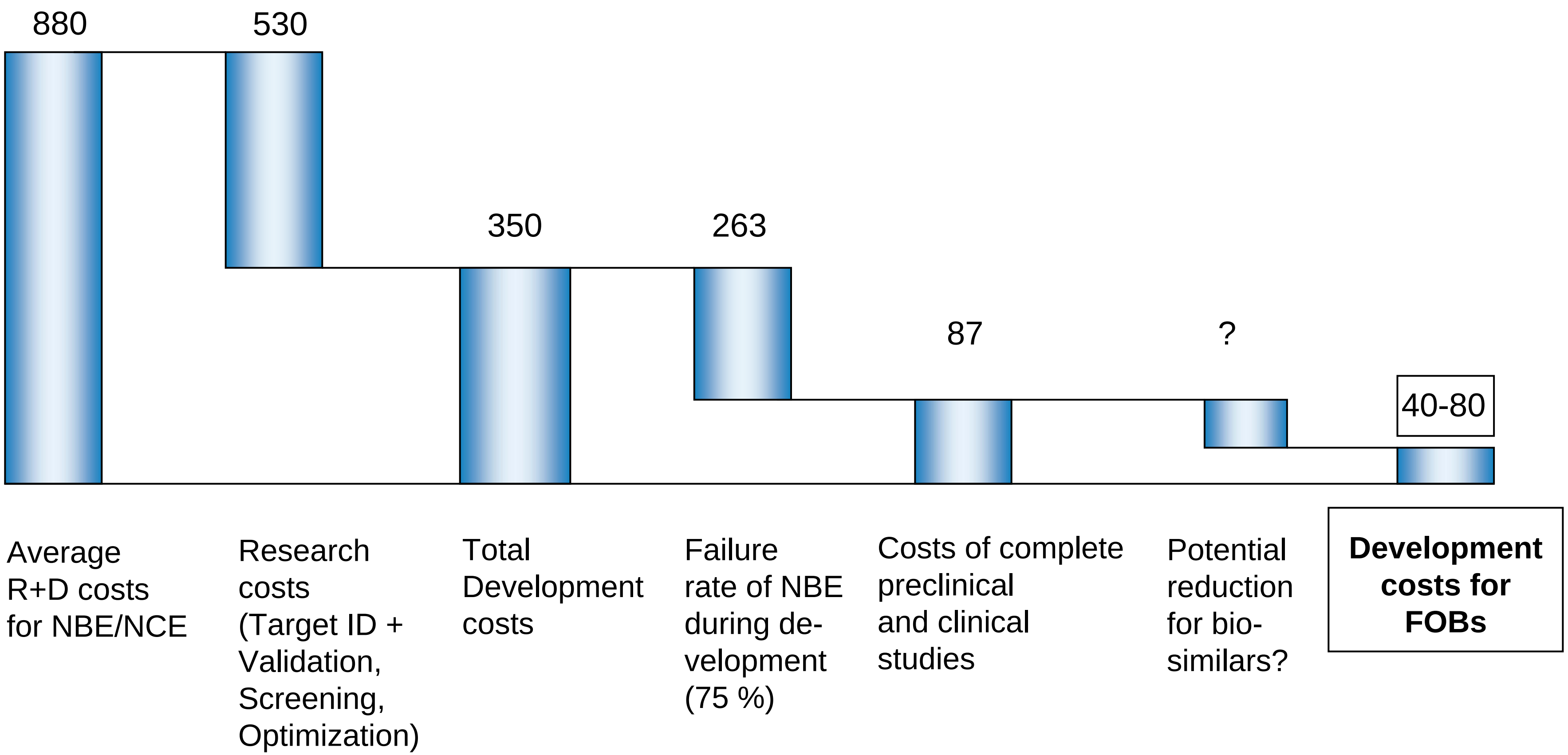


The development timelines are similar to NBE development, only the risk of failure is smaller

Source: BioGeneriX AG

Development Costs

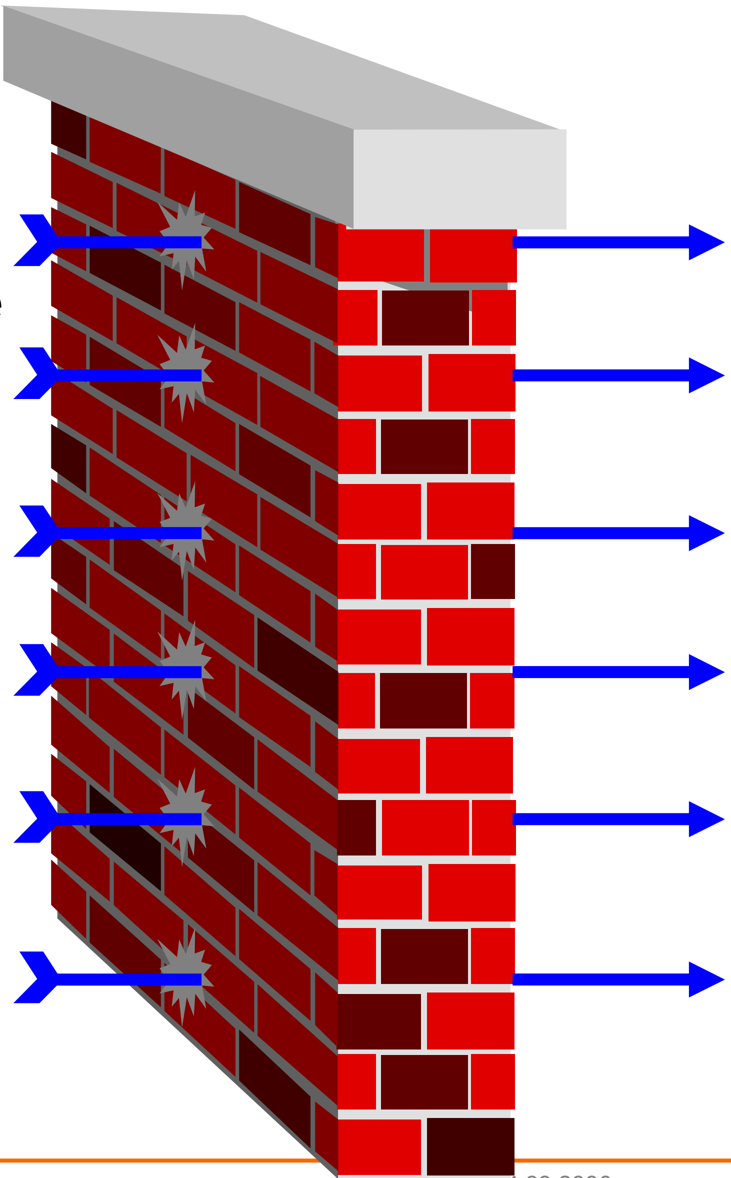
in Mio $



Due to high regulatory and GMP-constraints, development costs for FoBs are a multiple of those usually found in the chemical generics business

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

Passing Barriers to Compete in the FoB Market



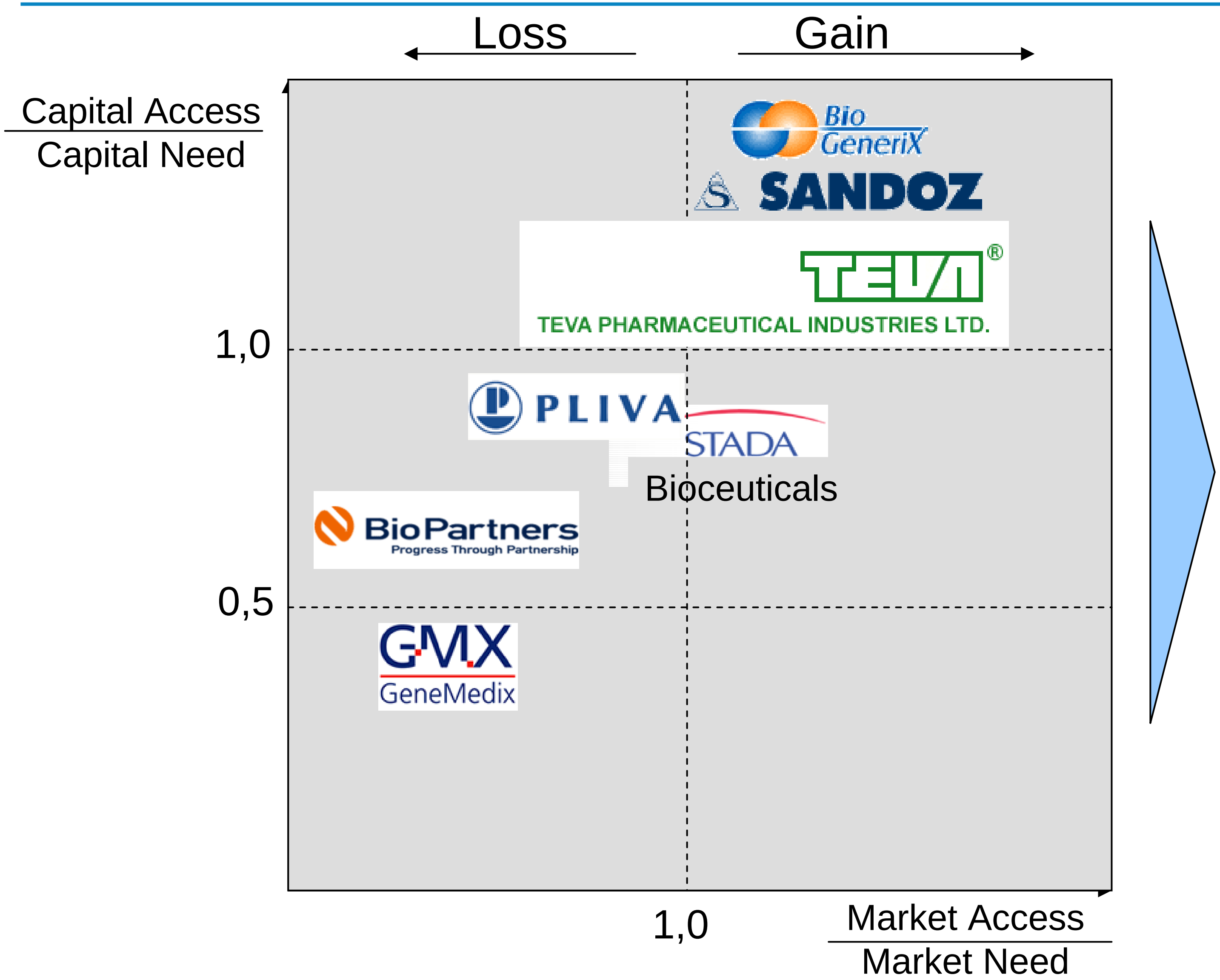
Barriers	Entry strategy
Patents	Patent department defines development strategy
Biotech expertise and biotech production	Close partnership to a leading biotech CMO; In-house biotech experts with external support
Partnering	Valuation, development/Licensing agreements, risk management
Capital	Access to a sustainable business model to allow long-term investment
Regulatory	Accompany entire development, streamline needs for centralized procedure
Market access	Specialist sales force in global key markets; co-marketing with one or two strong international partners

Best Owner Biosimilar Products

Owner	Patent Know-how	Biotech	Partnering	Capital	Legislation	Market access
Pharma	◕	◕	●	◑	◕	●
Biotech	◔	◑	◔	◑	◔	◔
Generics (EMEA/FDA)	●	○	◔	●	◑	◑
Generics (others)	◕	○	◑	◔	○	○
Specialist bio-generic company	◔	◔	◕	◔	◔	○
Biotech-manufacturer	◔	●	◕	◑	◑	○

Big Pharma would be able, but is not willing to enter; All others need to complement gaps through partnering
Capital and market access are/will be strongest selectors

Competitors in the Field



In Europe, depending on the products, up to four FoB developments will compete on market shares. Rather than „perfect competition“, an **oligopol** with limited price erosion will prevail for some time.

Five-Forces eines „biosimilar“ Markts

Substitutionen
-“second generation“ Entwicklungen
-low-molecular Agonists
-nicht-toxische Chemotherapien

Hersteller, Technologieentwickler
-Knappes Angebot cGMP-qualifizierter Anlagen
-Monopolisierte Technologien

Konkurrenz
-Preise/Rabatte
-Patentstrategien
-Regulatorische Hürden
-Patientenbindungen

Kunden
-Ärzte: Sicherheit, Preis, Ruf, Handling
-Patienten: Compliance, Service, Vertrauen

Neue Einführungen
Generische Konkurrenz

Agenda

- The Opportunity: Market Size and Potential
- Entrance Barriers to the FoB Market
- **Marketing FoBs**
- Rentability in the FoB Market
- Conclusion

Marketing FoBs: Between generics and ethicals

- FoBs are primarily special care products, sold to key accounts in specialized therapeutic areas
- Scientific selling required
- High price rebates not possible
- But: No new messages/innovations

A new Marketing concept is needed

- Description along the 4 „P“s:

Product	**P**romotions
Price	**P**lace

P

„Product“: SWOT-Analyse eines typischen „biosimilar“

Stärken	Schwächen
-Gleiche Qualität wie Originator -Preisgünstiger -Produktbündeln -Starkes Branding	-Schwache Stellung im Spezialvertrieb -Evtl. keine unabhängige Produktion und reduzierte Preisflexibilität -Kein signifikanter „value add“
Chancen	**Bedrohungen**
-Vertriebspartnerschaften -Marktausweitung -Evtl. geringere Nebenwirkungen als Originator -Patentgeschützte 2nd gen. Produkt	-Folgemedikationen/neue Dosierungen mit kompletter Marktumstellung -Therapieveränderungen -Schwierige Akzeptanz im Markt -Starke Konkurrenz und Preiserosion/Zwangsrabatt -Patentverletzungen

„Pricing“: Microeconomics

- Limited number of competitors
- From monopolistic to oligopolistic competition (not perfect competition)
- No marginal costing, no commodity pricing
- interdependent pricing reaction scheme (prisoner's dilemma, signalling)
- Fight for market shares
- Promotion-intense; branding important

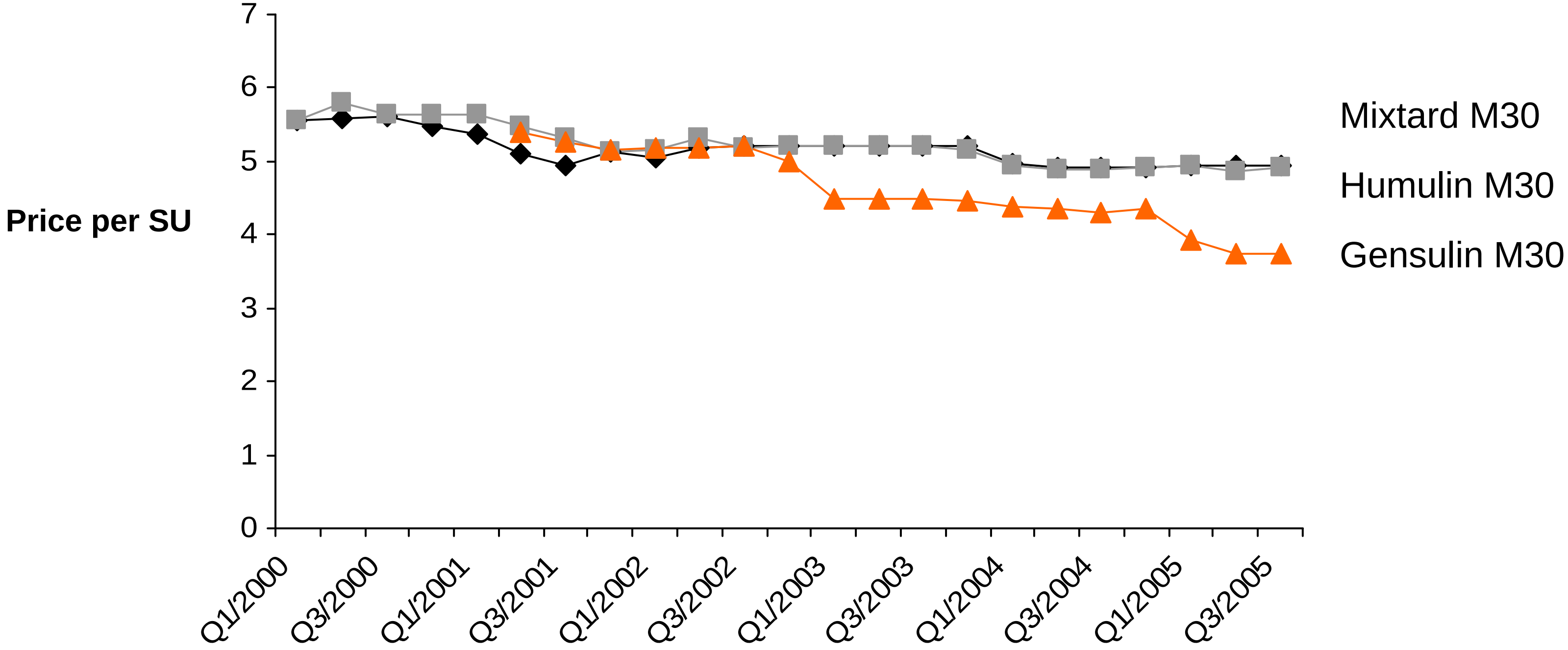
The market for patent-free biologics will likely be an attractive, but expensive niche market; Spending does not end with obtaining the market authorization

“Pricing”: Historic example Gensulin

- Compared to Originator Products the max. Price Difference is 24%; Over three years, Price erosion is 30%.

Retail Market Poland

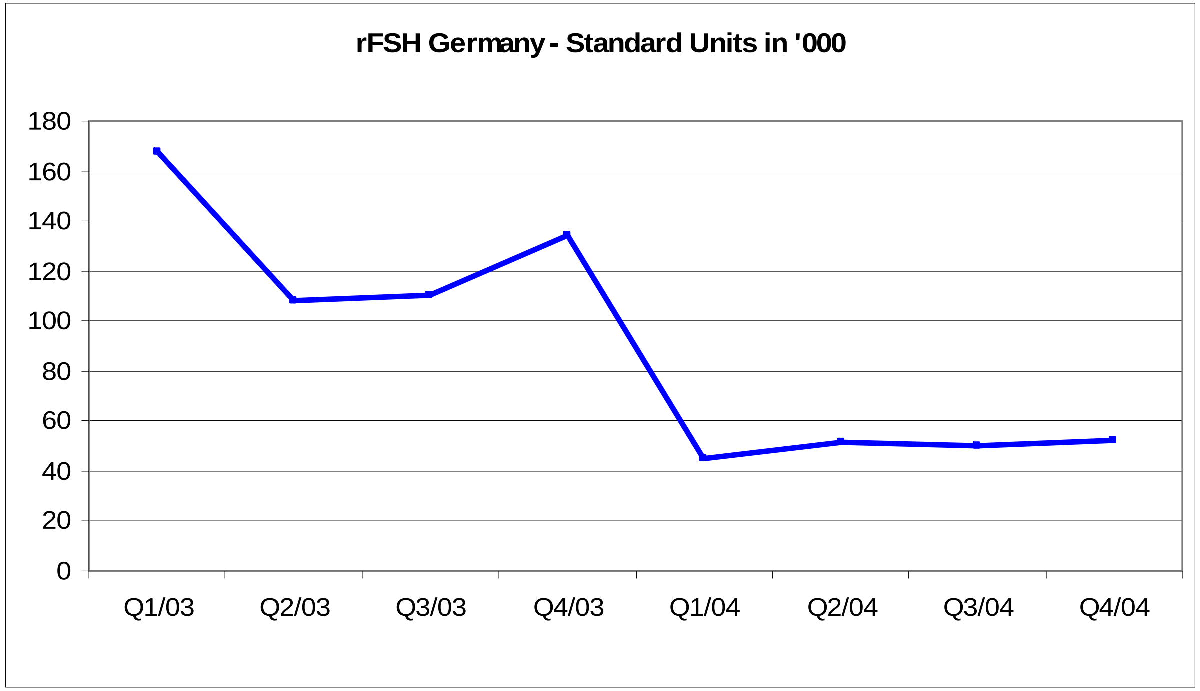
in €



„Pricing“: Price elasticity

Optimum of volume expansion vs. price reduction?

- Example: FSH sales after change in reimbursement in Germany



Price elasticity: -16% (inelastic demand), corresponding to literature values for pharmaceutical drugs (-22%*)

* Nicholson (1995); Microeconomic Theory, 6th ed.)

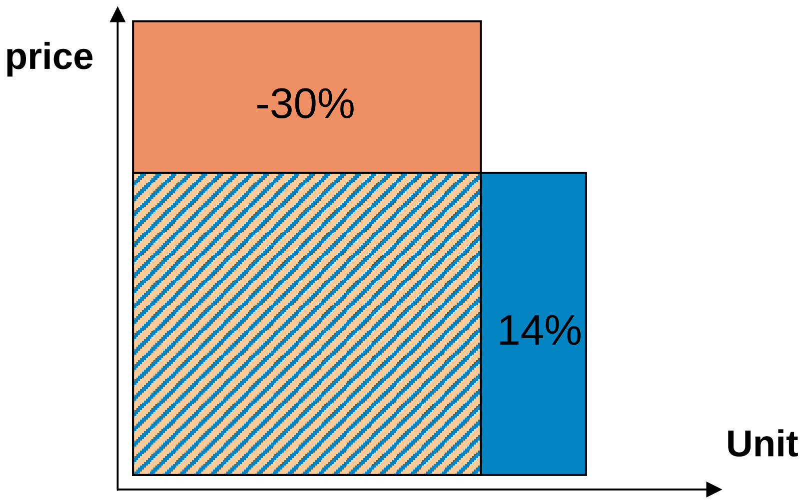
„Pricing“: Price elasticity

Applying the price elasticity:

A price reduction of 30% would decrease the market by 20% (but increase the volumes by roughly 14%).

Change in market sales following price reduction

schematic



Don´t reduce prices, use other marketing tools

„Place“: Europäisches Vertriebsnetz

Kunden:
Key account/Tender

Absatz:
Direktgeschäft

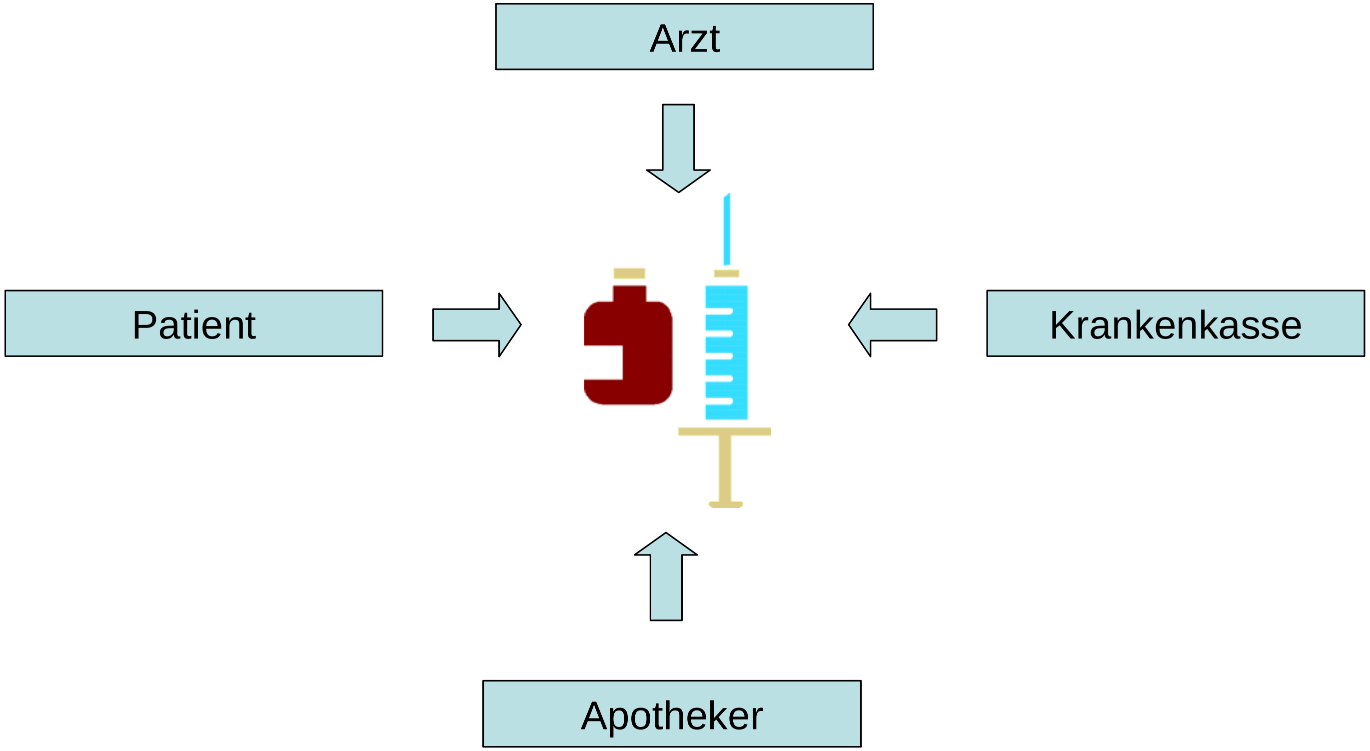
Logistik:
Geschlossene Kühlkette

Eigener Vertrieb,
Getrennt vom generischen Geschäft

Beispiel: Gate Pharmaceuticals für den Vertrieb des Tevtropins in den USA

„Promotion“: Key decision makers

Zielgruppen im Rahmen der Kaufentscheidung



Für jede Zielgruppe müssen spezifische Verkaufsargumente identifiziert werden

P

„Promotion“: Selected Vehicles

Potential promotional vehicles

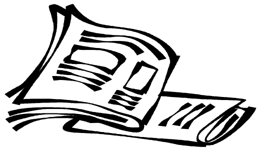
Detailing

- Targeted detailing
- Dedicated Losec salesforce
- Part-time salesforce
- Rep support (detail aids etc.)
- Local rep budgets
- Special rep bonuses

Education/ support

- Congresses
- Targeted meetings
- Overseas symposium
- GP support services
- Patient call back

Mail/ advertising

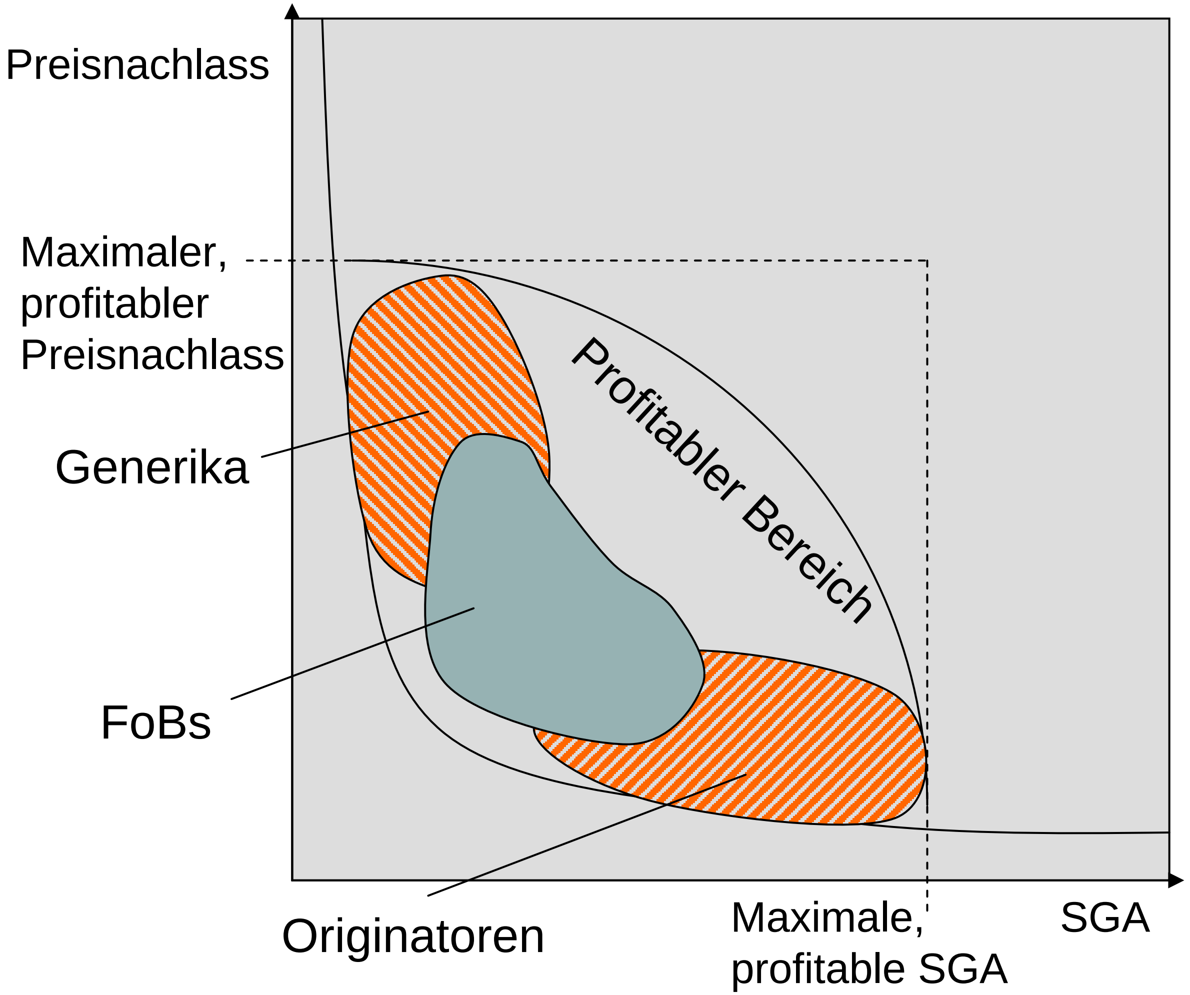


- Personalized mailing
- Journal advertising
- Use of video tapes

Scientific work

- End point studies phase IIIb and IV
- Disease management, outcomes analysis

Marktpositionierung von FoBs: Preisnachlass vs. Marketingkosten



Quelle: nach Tremml (2004)

Marketing FoBs: 4 P´s Summary

Product
- Highly scientific products
- Quality & Safety
- Device

Price
- Try to keep the prices as high as possible
- Offer rebates or services
- Patient benefits

Small European team of highly qualified specialists

Place
- Small group of specialists with European connections
- Key account management
- Centralized purchasing decisions

Promotion
- No generic selling, new company
- Product brands Value added services and databases

Agenda

- The Opportunity: Market Size and Potential
- Entrance Barriers to the FoB Market
- Marketing FoBs
- **Rentability in the FoB Market**
- Conclusion

Conclusion on the revenue side

- Price erosion likely to be modest
- Sales volume increase as seen with classical generics, resulting in a small total turnover reduction; patient pools
- Market share of all FoB-Products likely to be smaller than for classical generics, but still significant
- Market share divided among only a few players

This market can be an attractive niche for generics companies; for some originators, the margins will likely be too small

It depends on the cost...

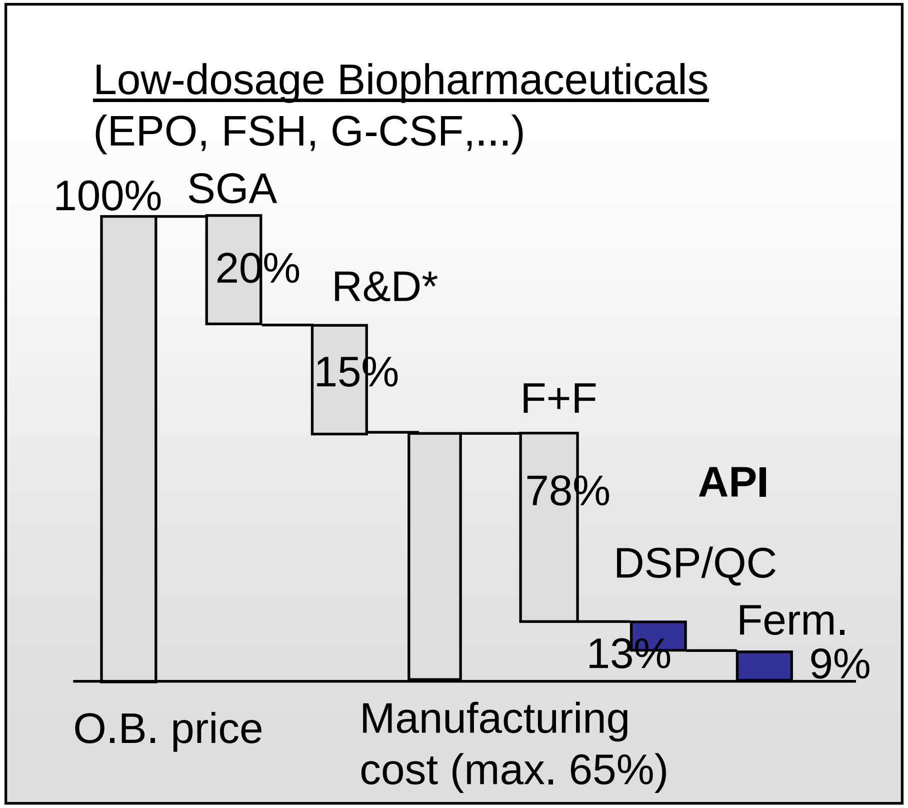
Selling, General and Administrative Expenses (SGA)

- Most biotech products are sold in restricted markets by scientifically trained key accounters
- Highly competitive direct marketing
- Limited number, well informed patients

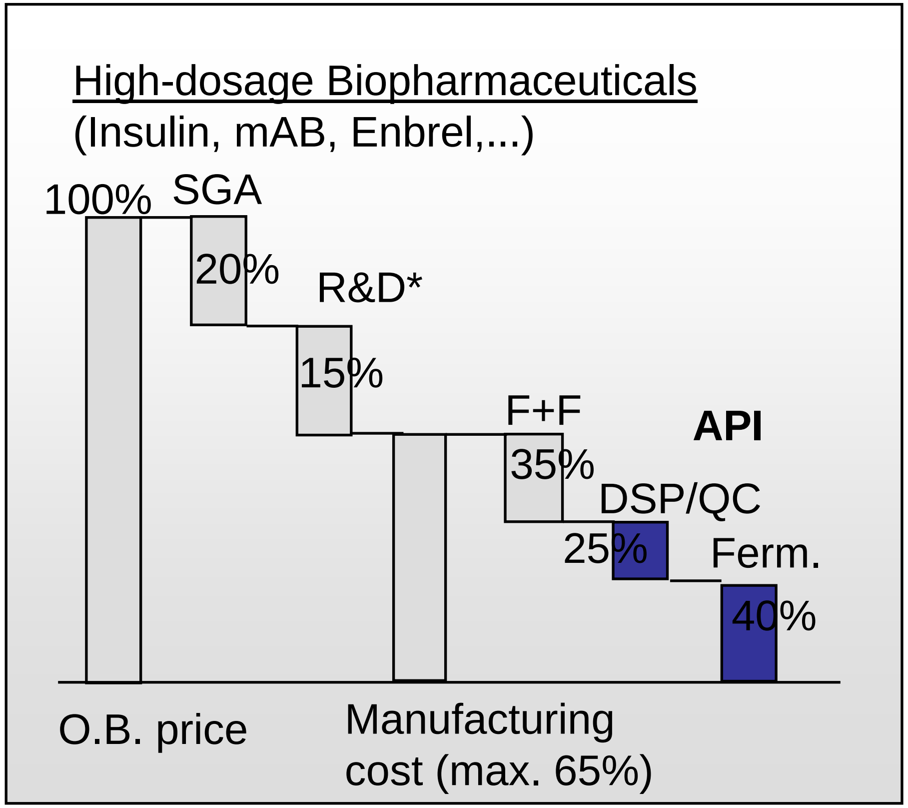
Usual generic sales organization will not do the job,
need for a specialized unit/company

High costs for set-up and operations (25% of net sales; or bottom-up)

Cost of Manufacturing: CoGS



API manufacturing represents max. **14%** of the total costs



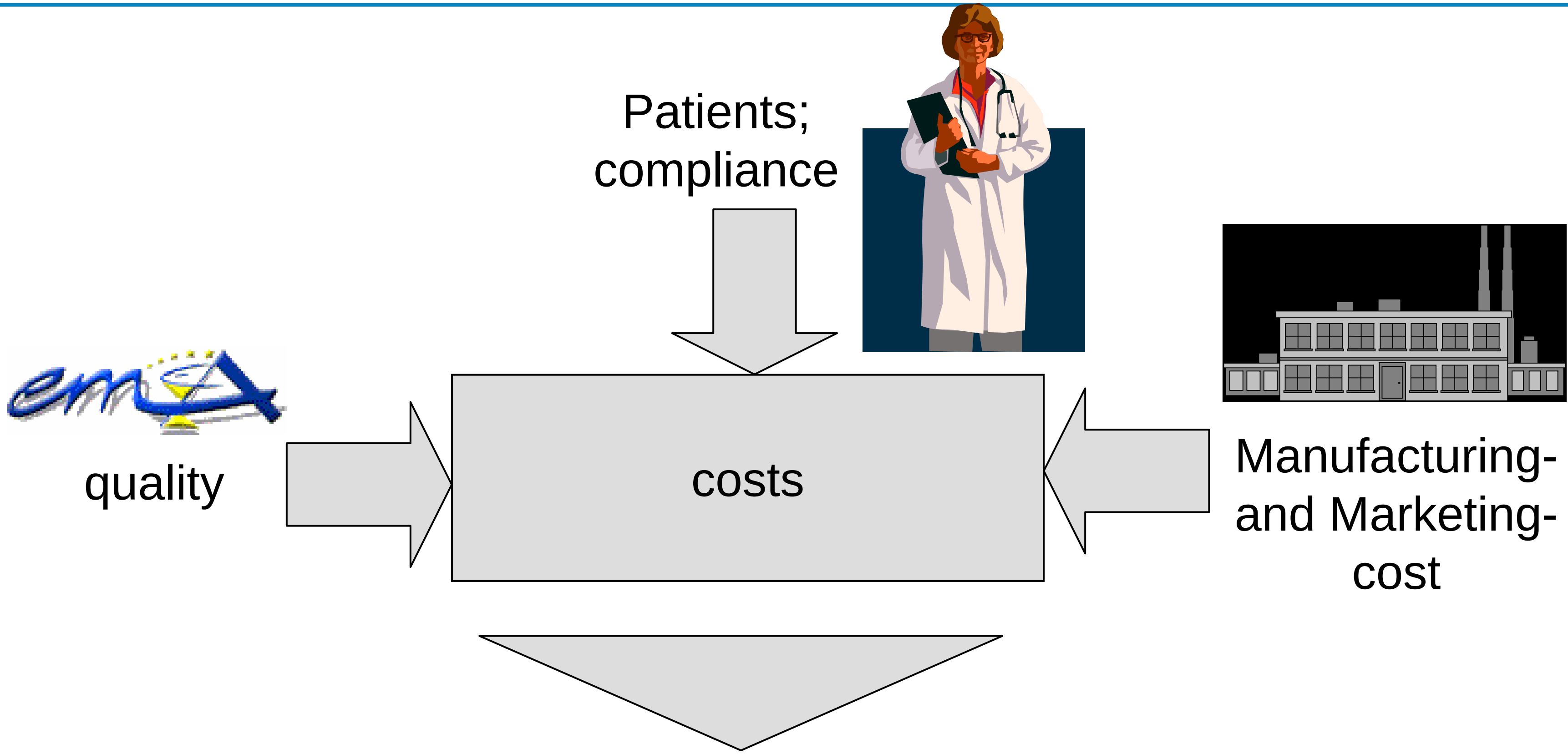
API manufacturing represents max. **42%** of the total costs

Manufacturing becomes a key business driver only in high-volume, mature markets (e.g.commodity goods, or bio-generics?)

* R&D costs distributed over seven years of sales

Source: BioGeneriX; RG Werner, Arzneimittelforschung 1998

Conclusion on the cost side



In order to fulfill the EMEA-/ICH- and GMP-requirements during development, and to meet the marketing needs, total costs of successfully bringing FoBs into the market are high and cannot be significantly reduced.

A Simple Model for Return on Investment in the FoB-Market

in Mio €

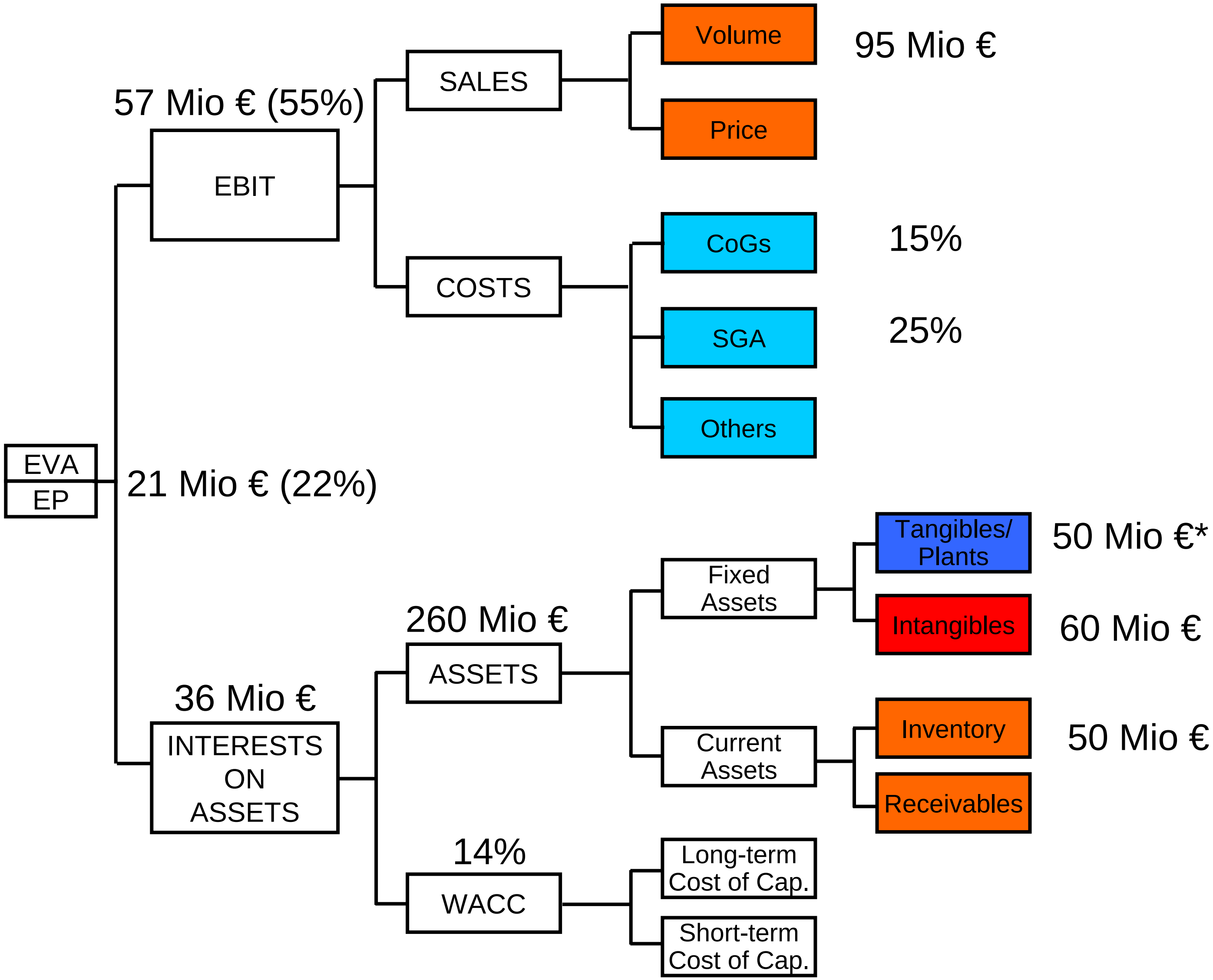
Launch FoBs

		Development							Commercialization						
Year		**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**
Market	1000	1.020	1.040	1.061	1.082	1.104	1.126	1.149	1.172	1.195	1.219	1.243	1.268	1.294	1.319
Price erosion	30%	1.020	1.040	1.061	1.082	1.104	1.126	1.149	879	896	853	870	888	906	924
Market expansion	40%	1.020	1.040	1.061	1.082	1.104	1.126	1.149	1.142	1.165	1.195	1.219	1.243	1.268	1.293
Market share	10%	0	0	0	0	0	0	0	3%	6%	9%	10%	10%	10%	10%
Sales		**0**	**0**	**0**	**0**	**0**	**0**	**0**	**34**	**70**	**108**	**122**	**124**	**127**	**129**
Development cost	60	2	4	7	8	18	20	1							
COGS	15%	0	0	0	0	0	0	5	10	16	18	19	19	19	20
SGA	25%	0	0	0	0	0	0	0	9	17	27	30	31	32	32
Cash Flow		**-2**	**-4**	**-7**	**-8**	**-18**	**-20**	**-6**	**15**	**36**	**62**	**73**	**74**	**76**	**77**
DCF	14%	-2	-4	-5	-5	-11	-10	-3	6	13	19	20	18	16	14

NPV	**81**

(8 years of sales)

Measures for Success: EVA for FoBs



* In case, own manufacturing facility is used

Sensitivity Analysis: Results

Critical Market Share (of a 1000 Mio € Market):	3.3%
Critical Market Size:	350 Mio €
Critical Price Erosion:	80%
Latest Launch Date:	2.5 Y after 1st FoB
Critical Development costs:	180 Mio €

Under the presented assumptions, the business case is very robust.

- Several **levers** can be used to make it even more valuable:
- Global partnering (to originators)
- Additional patient benefit (multi-dose, pen, sustained release, new combinations, new indications,...)
- Bundling
- Scientific key accounting rather than price-driven generic distribution

To enter the FoB market remains, however, a risky and expensive undertaking

Agenda

- The Opportunity: Market Size and Potential
- Entrance Barriers to the FoB Market
- Marketing FoBs
- Rentability in the FoB Market
- **Conclusion**

Conclusion

- Successful FoB companies have as a minimum a profound expertise in biotechnology, the financial strength, patent knowledge and access to pharmaceutical marketing including a trusted brand and product portfolio
- The current entrance barriers limit the number of FoB companies to 3 – 4 per molecule
- The price erosion will at first not be dramatical, but the return remains small due to high development and marketing costs
- The macroeconomy is likely to profit less compared to chemical generics
- In the long-run, the investments might be wise to create a mid-rage margin niche business, compared to a low-margin generic busienss

FUTURE OUTLOOK

- The bio-generic industry saw a peak in numbers of companies, but is now starting to sort out
- Cost leadership might become an issue, depending on the price erosion witnessed (number of competitors), but this is unlikely to occur in the beginning
- Originators in Europe seem not to defend their markets by patent disputes, but rather by building up regulatory hurdles, marketing tools, and switches to second generation developments. No early entry deals were done up to now.
- Generic industry is likely to reduce investments due to margin pressure in their main business, although the RoI is most likely positive