

Biosimilars: Fact Or Fiction?

**Are Biogenerics And Biosimilars On The Verge Of
Materialising Or Will The Cost Of Clinical Development
Confine Them To The Theory Books?**

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Geneva, 21st of September 2005

Fall is starting...

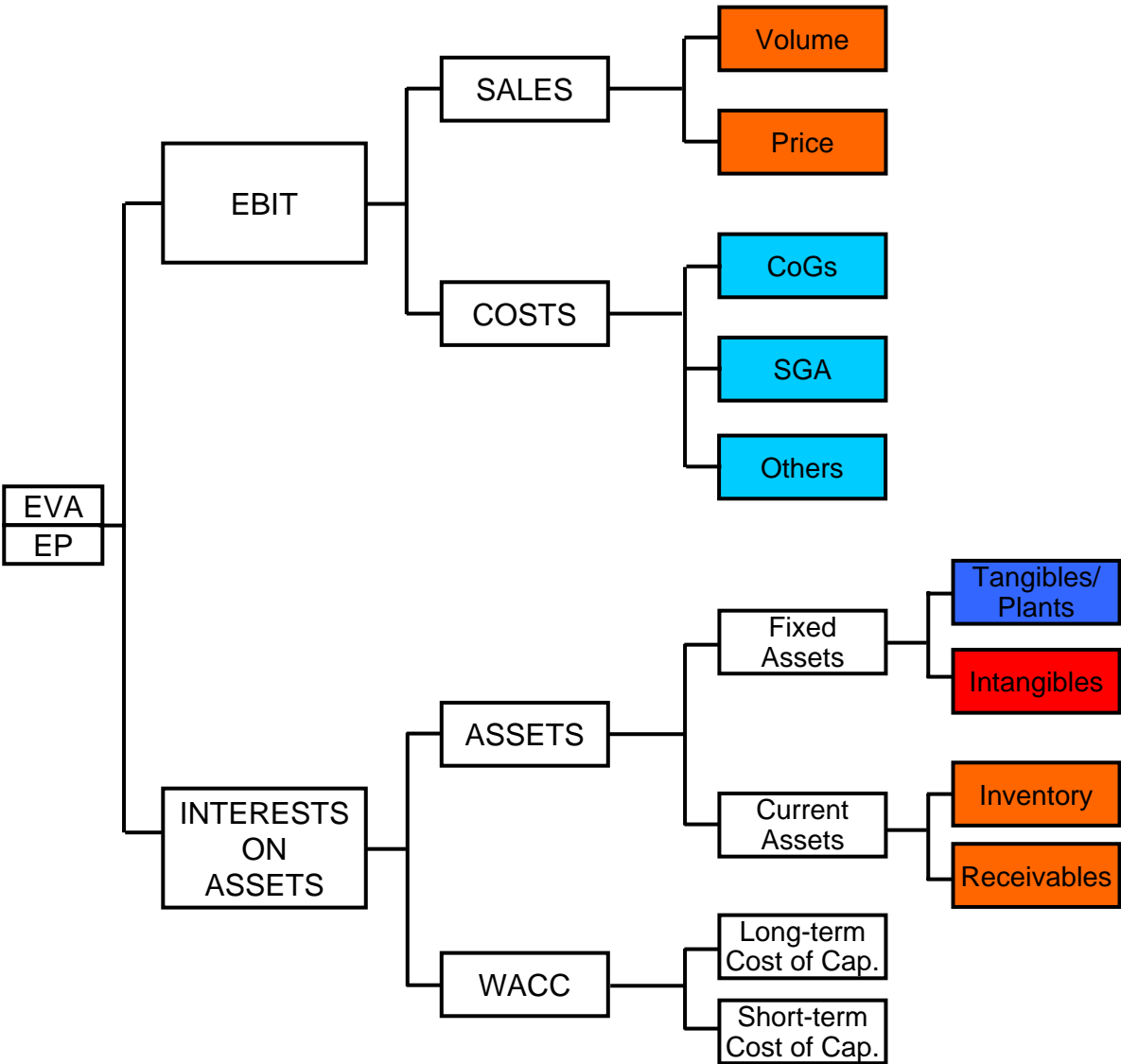


Old biotech drugs:
Is it all falling leaves ...?

...or will we witness an „Indian Summer“?



Measures for Success: EVA & Components

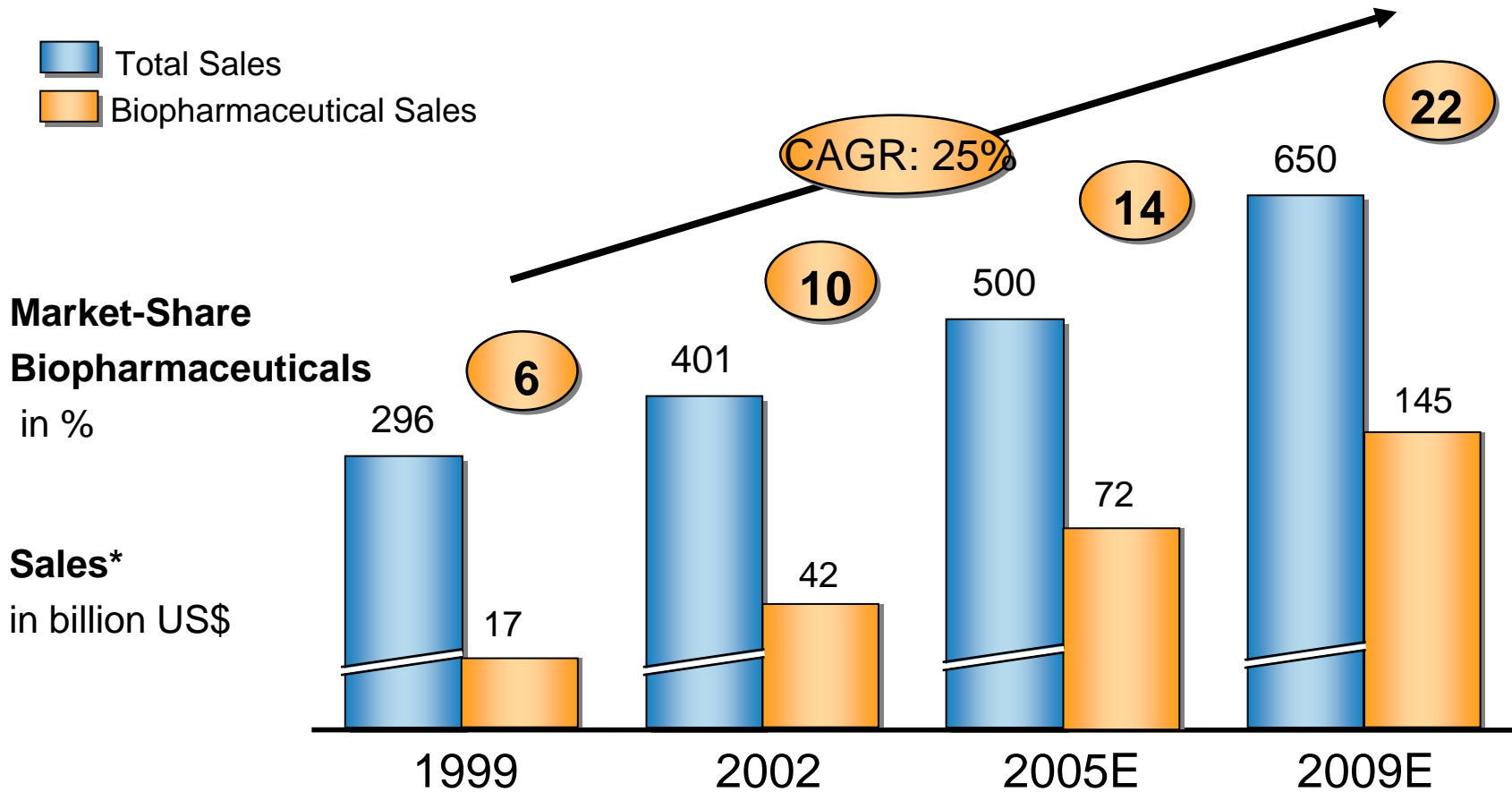


- **Revenues**

- Costs

- Returns

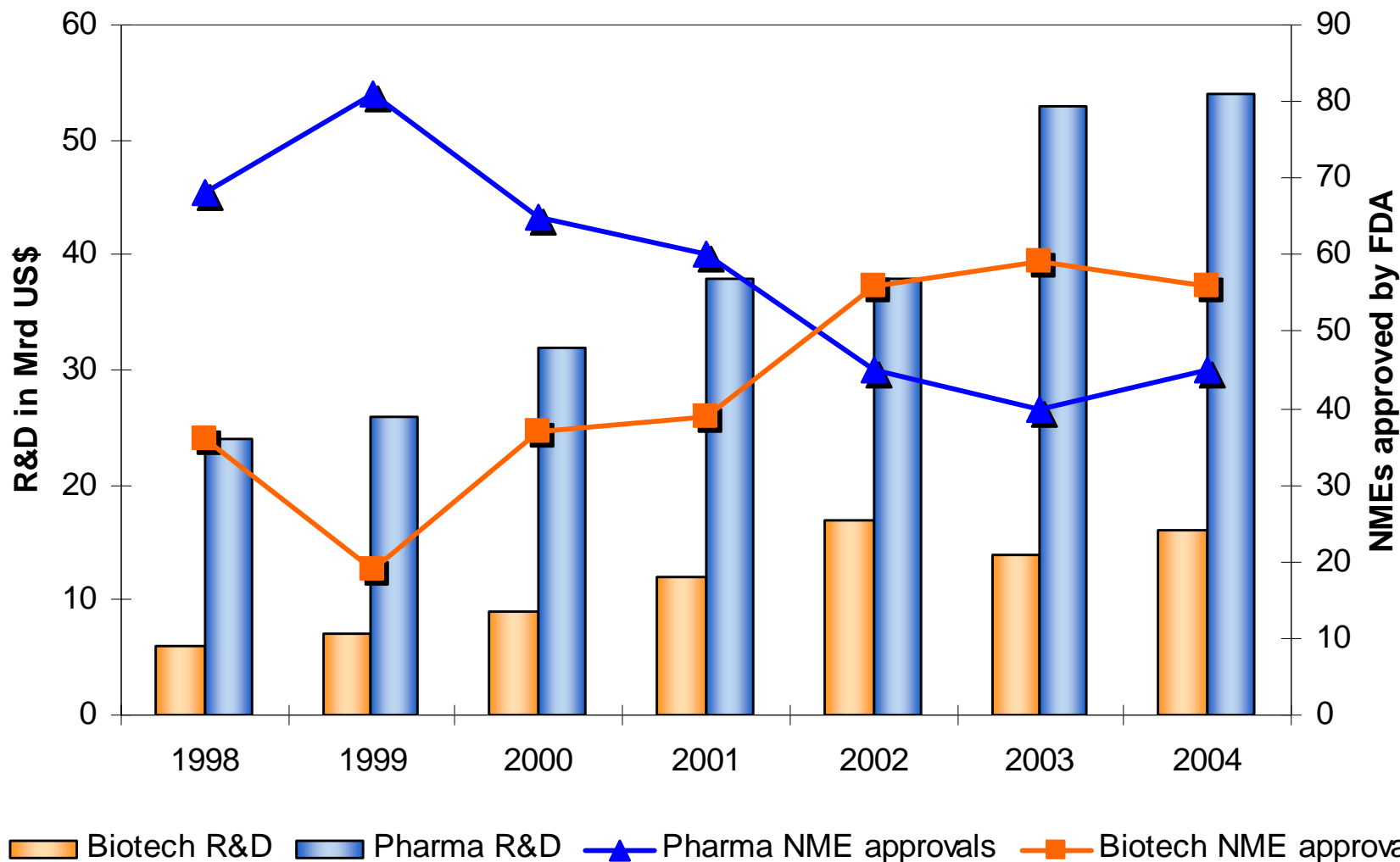
OPPORTUNITY: THE GLOBAL PHARMA MARKET



Biologics are growing at twice the rate of „ Small Molecules“

*Rx
Source: IMS Health, Ernst&Young; BioGeneriX Forecast

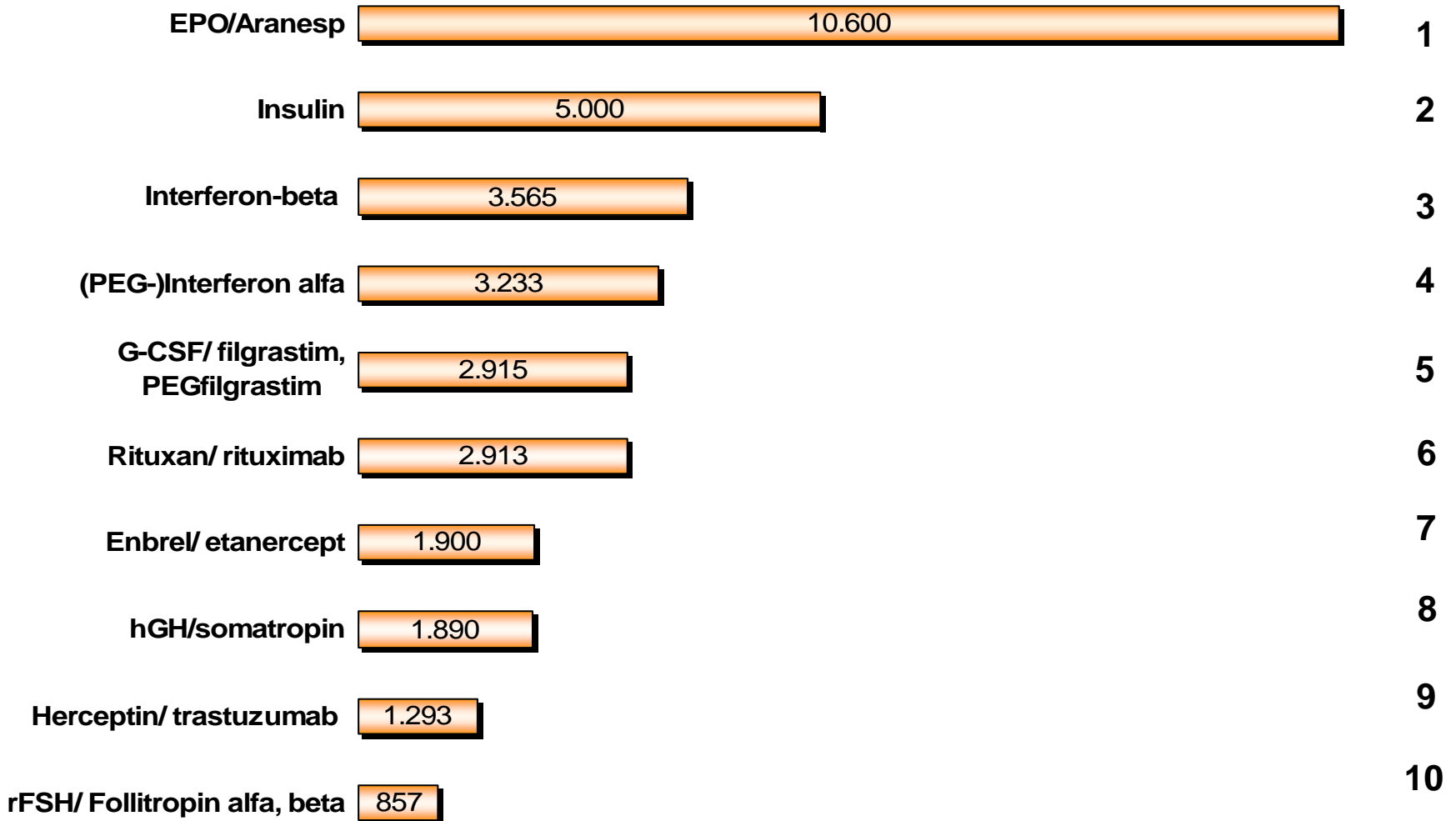
Market Dynamics: The Innovation Gap (US)



Biotech drugs make up more than 50% of new molecular entities

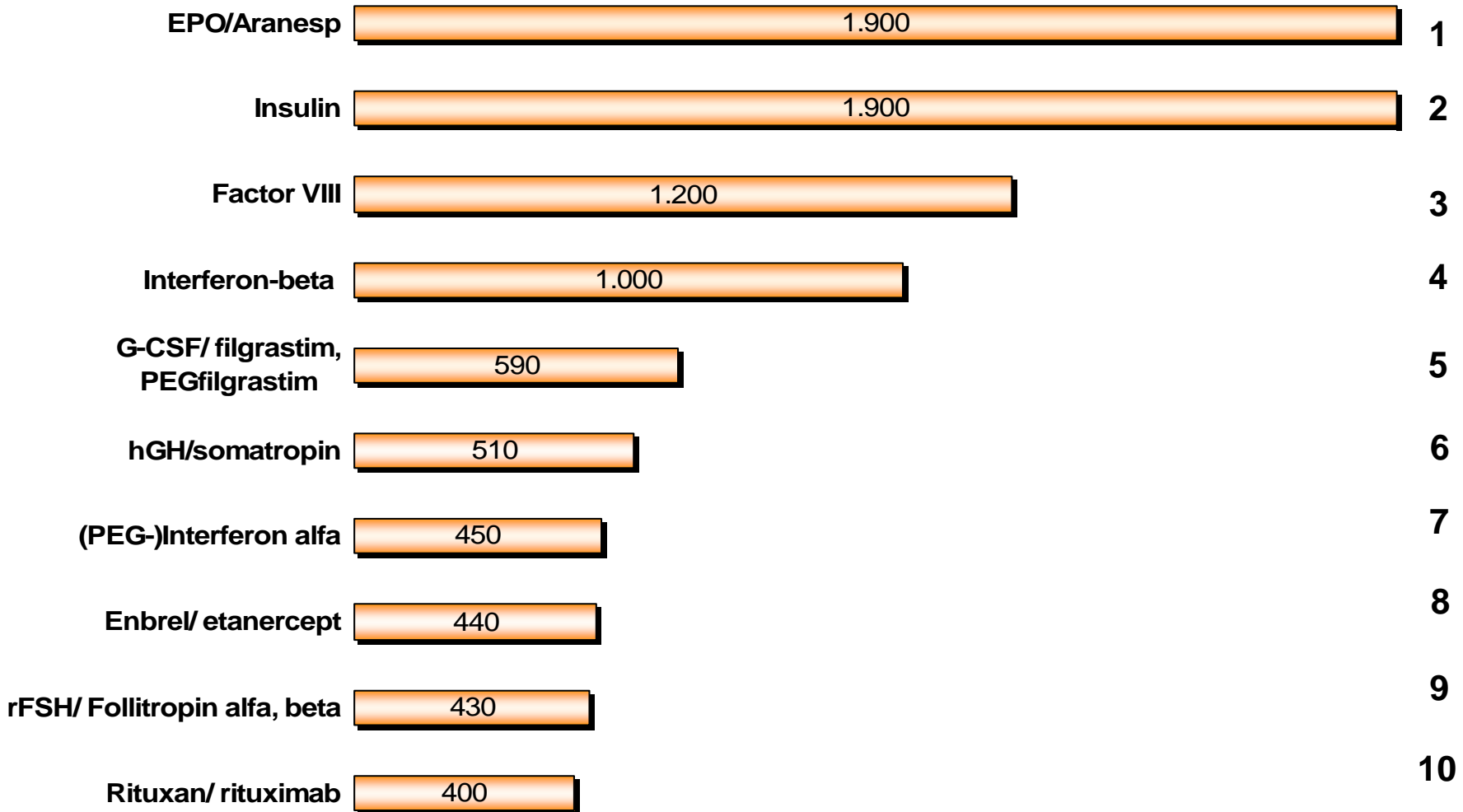
Source: FDA/ Ernst&Young, Global Report 2005

Top 10 Global Biotech-Products 2004 in m\$



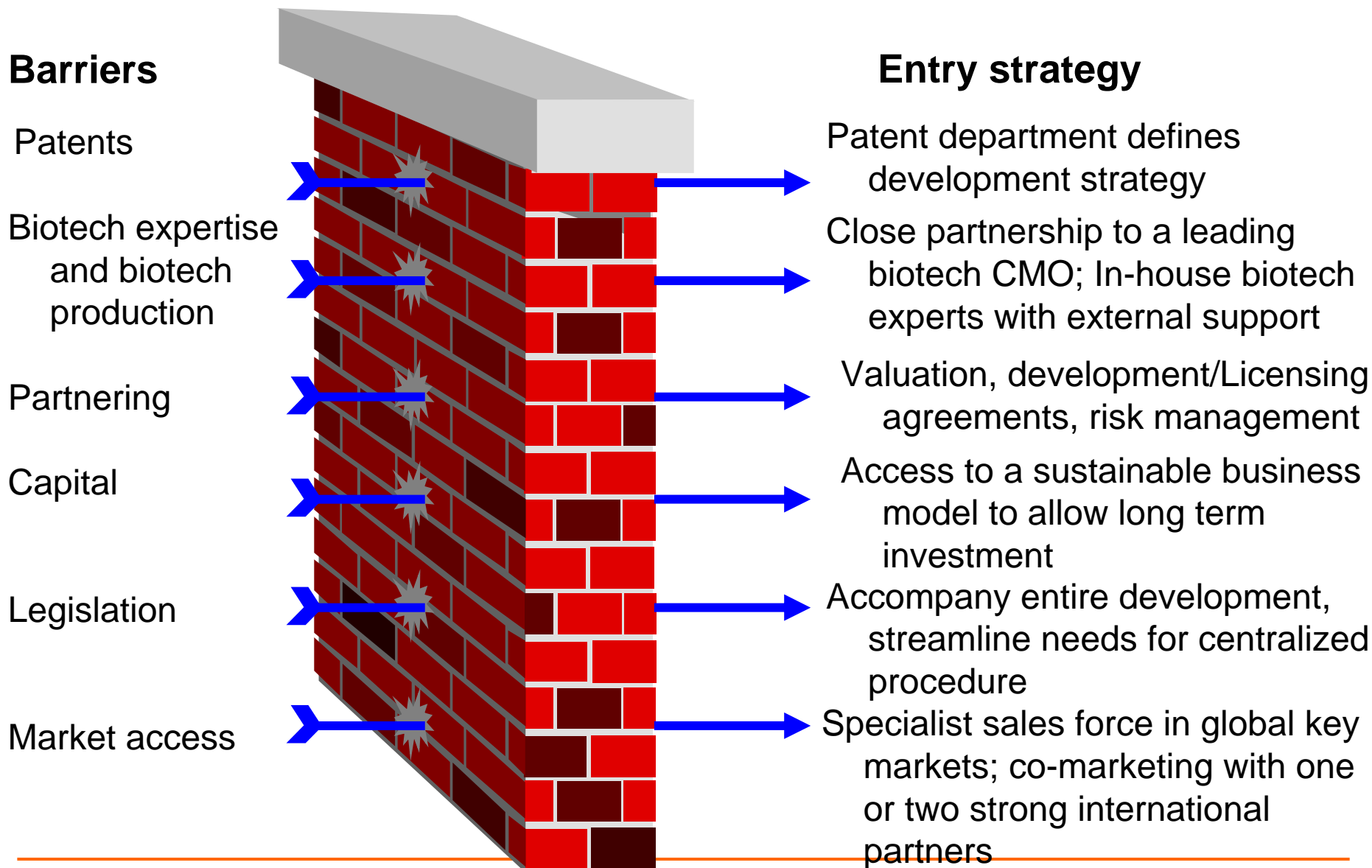
Biotech drugs offer a huge market potential, also after patent expiry

Top 10 European Biotech-Products 2004 in m\$



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

Passing Barriers to Compete in the FoB Market



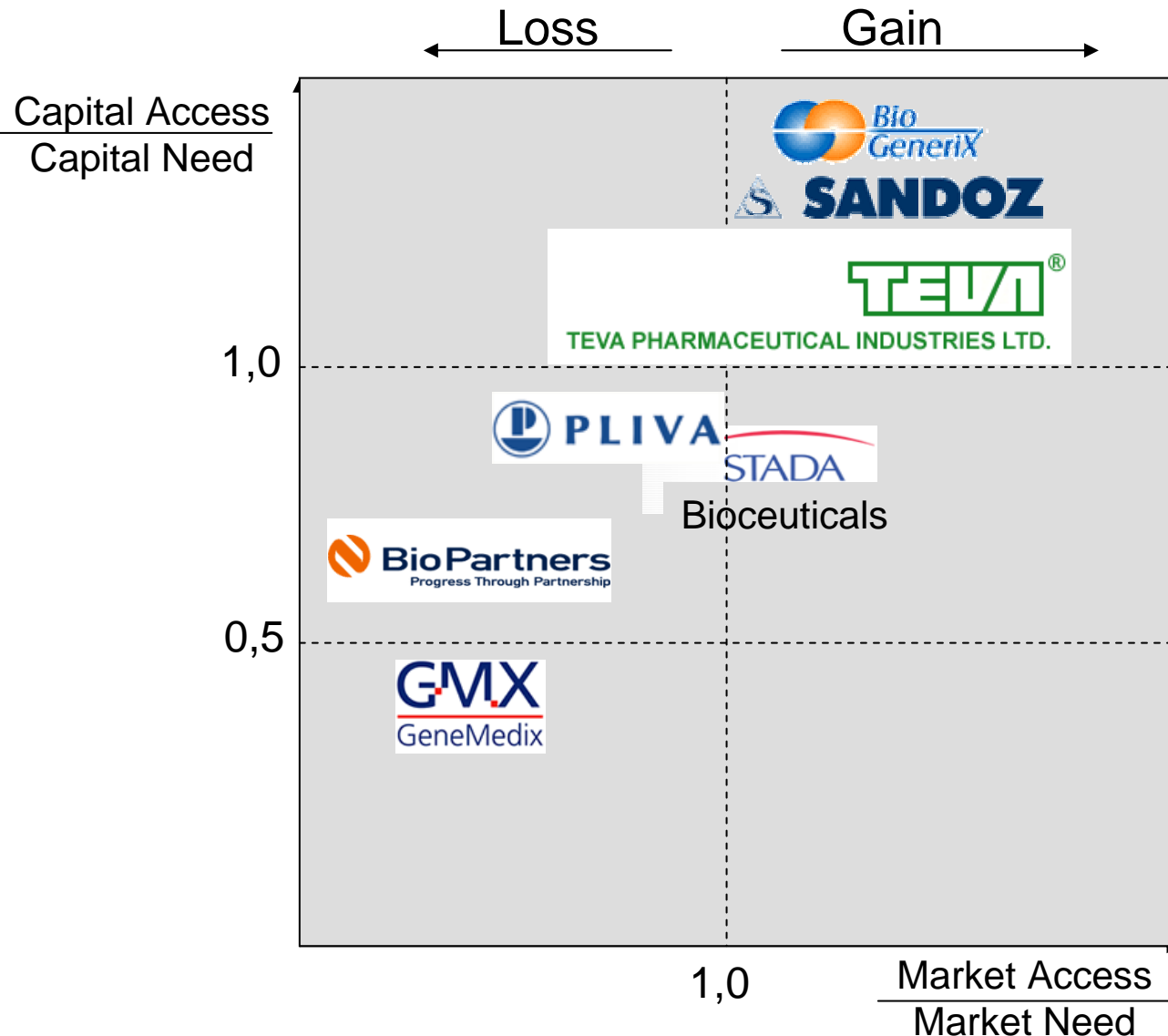
Best Owner Biosimilar Products



Owner	Patent Know-how	Biotech	Partnering	Capital	Legislation	Market access
Pharma	3/4	3/4	100%	1/2	3/4	100%
Biotech	1/4	1/2	1/4	1/2	1/4	1/4
Generics (EMEA/FDA)	100%	0%	1/4	100%	1/2	1/2
Generics (others)	3/4	0%	1/2	1/4	0%	0%
Specialist bio-generic company	1/4	1/4	3/4	1/4	1/4	0%
Biotech-manufacturer	1/4	100%	3/4	1/2	1/2	0%

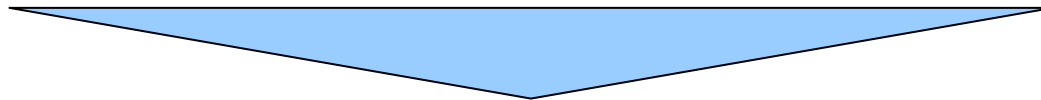
Big Pharma would be able, but is not willing to enter; All others need to complement gaps through partnering
 Capital and market access are/will be strongest selectors

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.

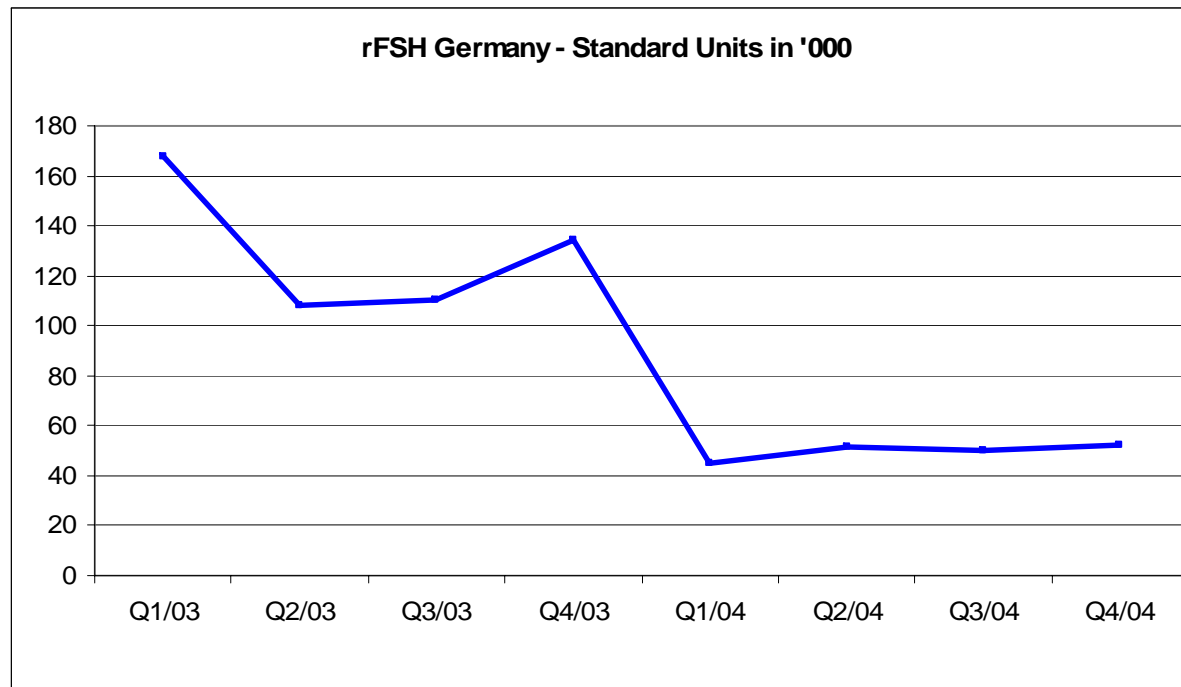
- Limited number of competitors
- From monopolistic to oligopolistic competition
- No marginal costing, no commodity pricing
- interdependent pricing reaction scheme (prisoner's dilemma, signalling)
- Fight for market shares
- Promotion-intense; branding important



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

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.)

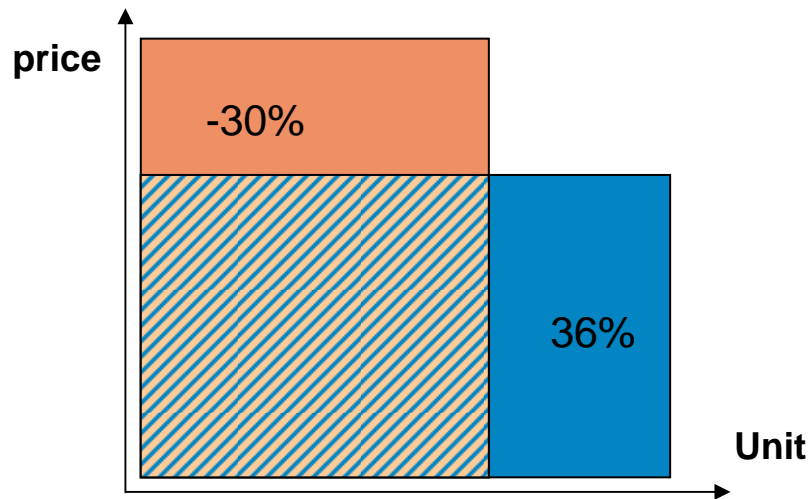
A View on Pricing: Price elasticity

Applying the price elasticity:

A price reduction of 30% would decrease the market by 4,8% (but increase the volumes by roughly 36%).

Change in market sales following price reduction

schematic

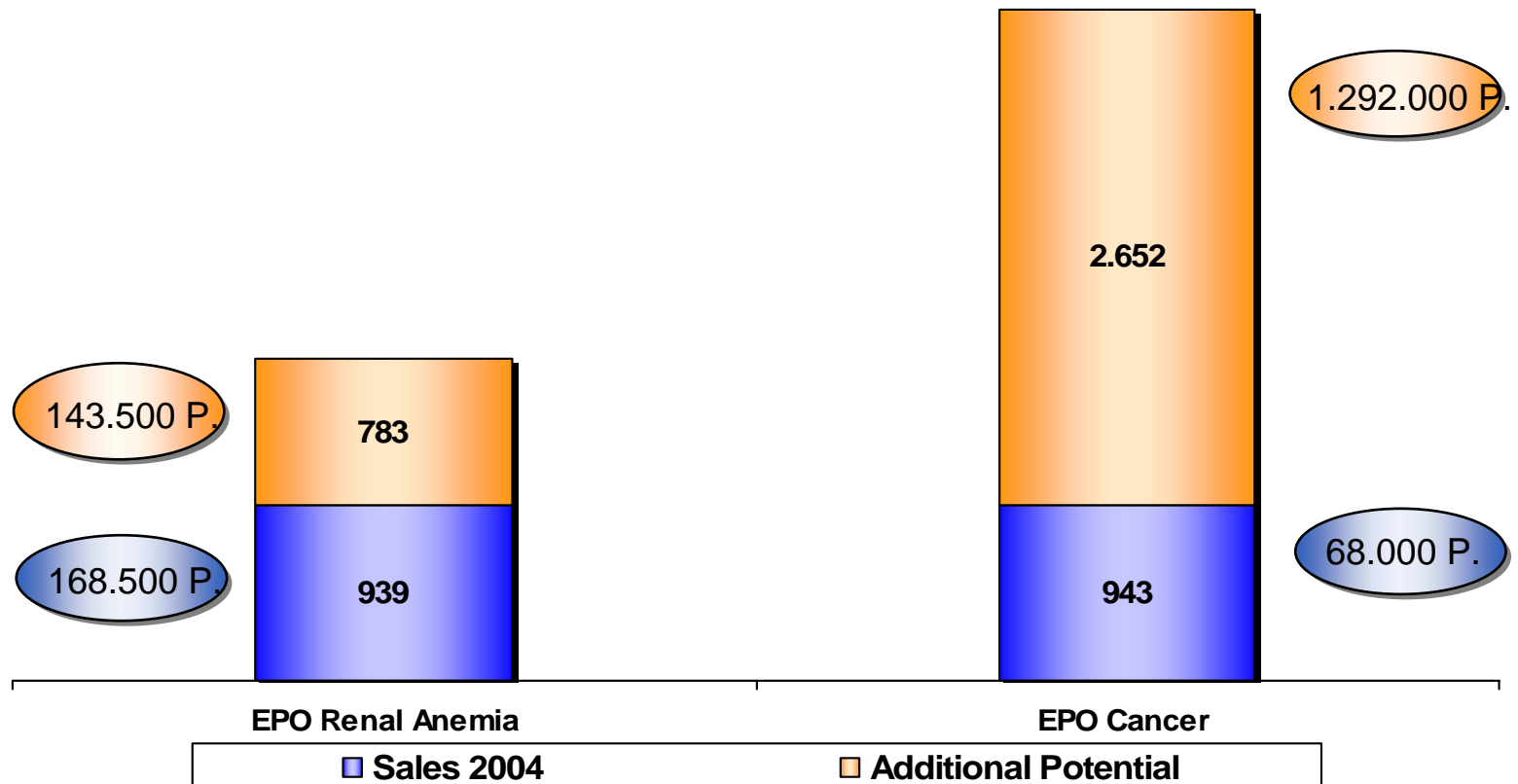


Don't reduce prices, use other marketing tools

A View on Pricing: Price elasticity

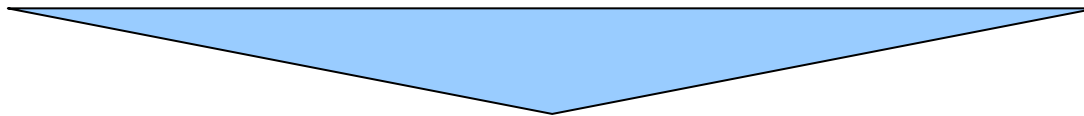
Can the patient pool be expanded as calculated?

European EPO Sales 2004 and additional potential due to Patient Prevalence and Treatment Rate (in Mio €)



Source: IMS/ Patient Population Calculation

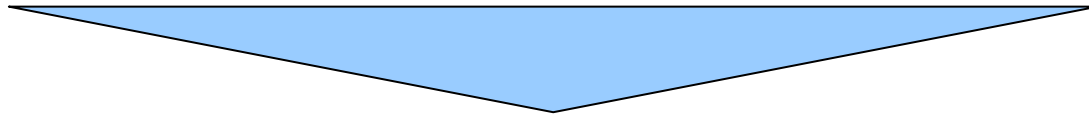
- Primary research (physicians) reveals: Highly price-conscious market in oncology; only 10-20% price reduction would induce a prescription switch by most physicians on new patients.
- Condition is a solid and safe product from a well-known, trustable company
- Originators are unlikely to completely follow price reductions because of weak patient benefits of second-generation molecules (risk of substitution)



„Most of these companies expect to market their product at a 20%-30% discount from Amgen's and Ortho/J&J's prices. This is based on companies' presumption that only a few generic EPO products will have the market to themselves for at least several years, with prices likely falling after more products enter the European market.“

(Biopharmaceutical Products in the U.S. and European Markets; 4th edition; Ronald A. Rader)

- 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...

- Revenues

- **Costs**

- Returns

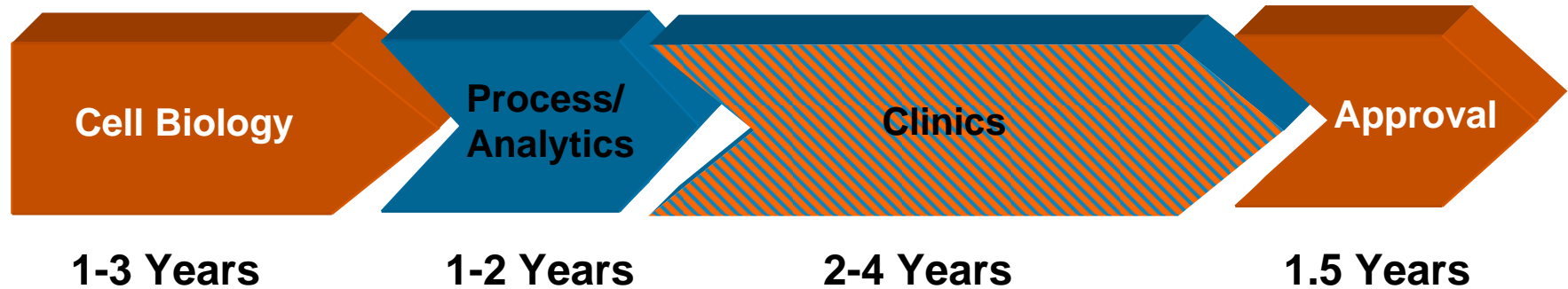
- Definition: „**Biogenerics are Copycats of Biopharmaceuticals, i.e. Pharmaceuticals, whose active agents are achieved by biotechnological Methods using recombinant Cell Cultures.**“

- Approval process distinguishes FoBs from generics:
 - Centralized procedure mandatory, two basic legal bases

 - **Biosimilar approach:** 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)

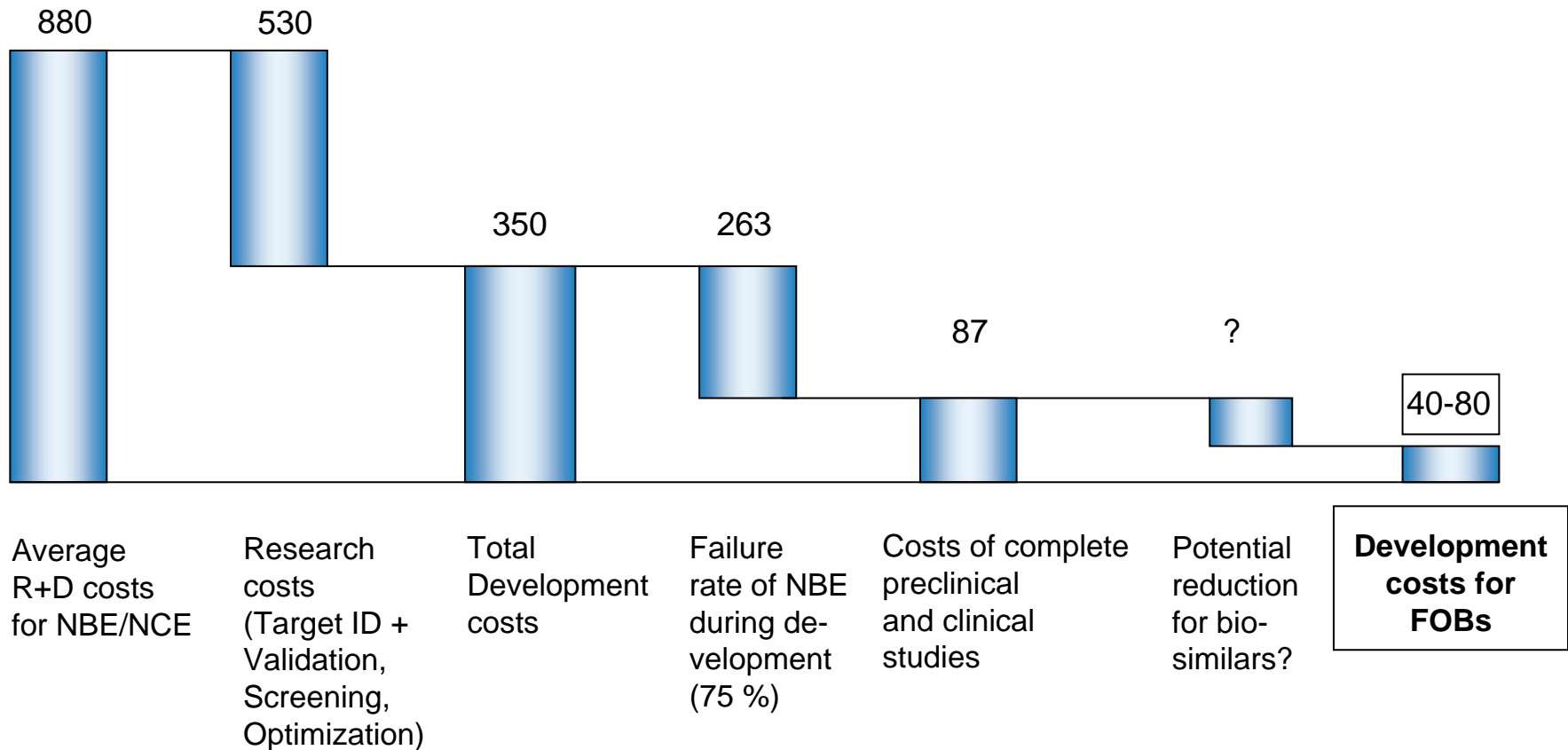
- From the first Steps until Launch it could take approx. 6-9 Years



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

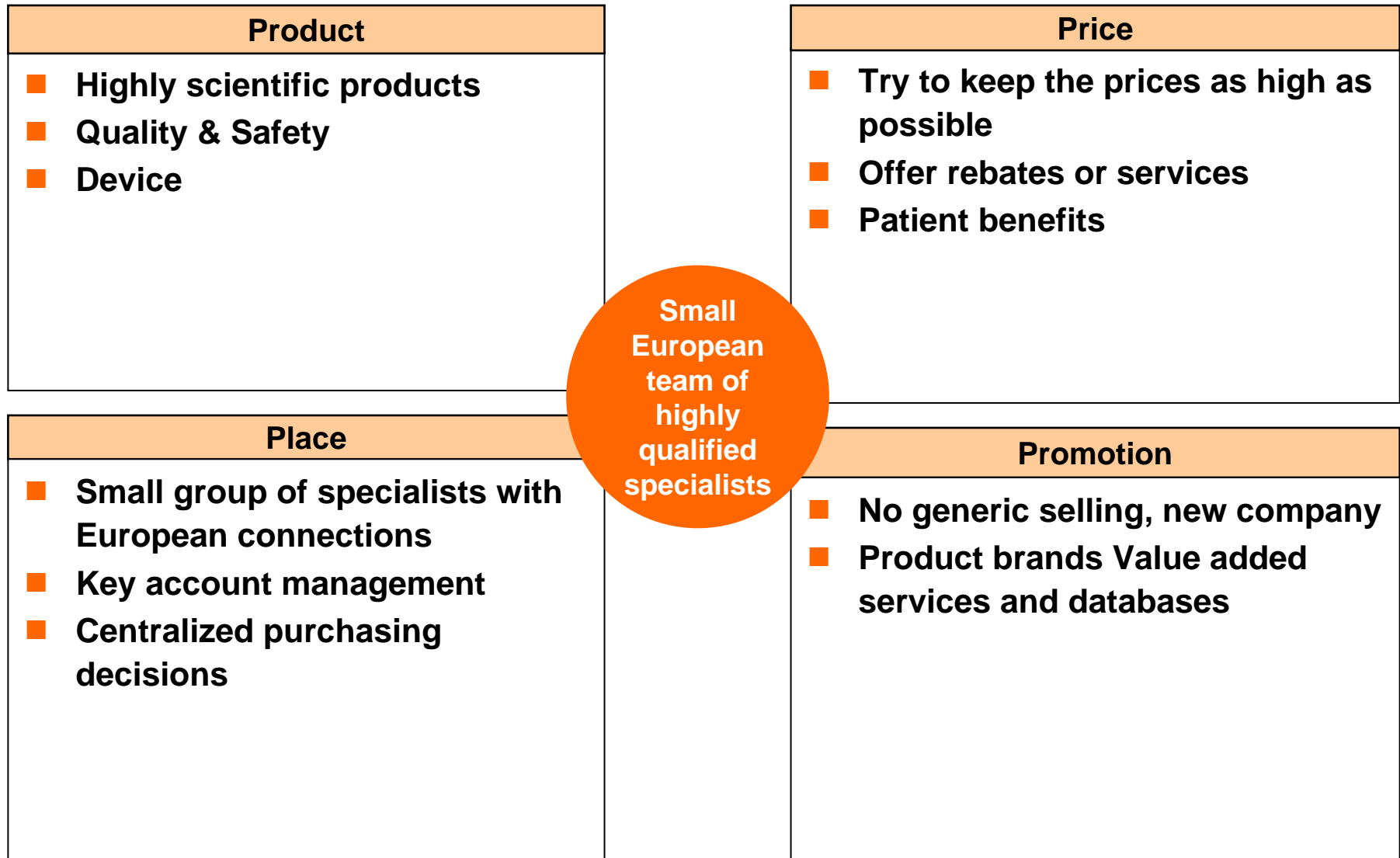
Development Costs

in Mio \$

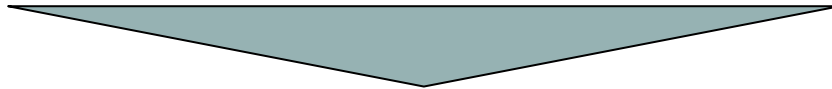


Due to high development costs, regulatory and GMP-constraints, only few companies will succeed

Cost of Selling: 4 P's Summary



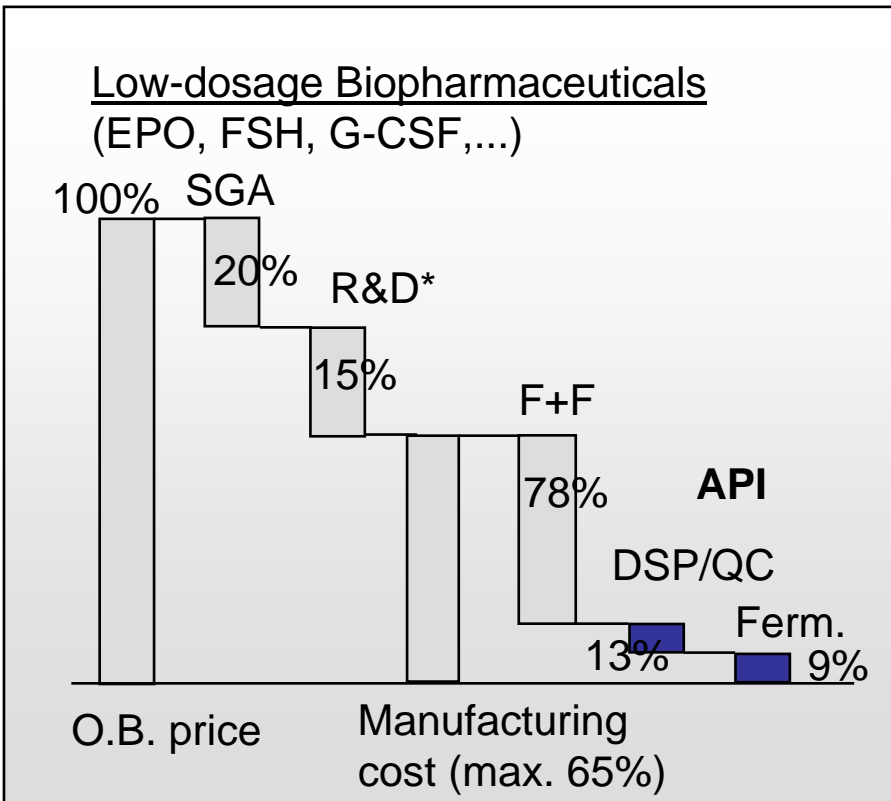
- Most biotech products are sold in restricted markets by scientifically trained key accounters
- Highly competitive direct marketing
- Limited number, well informed patients



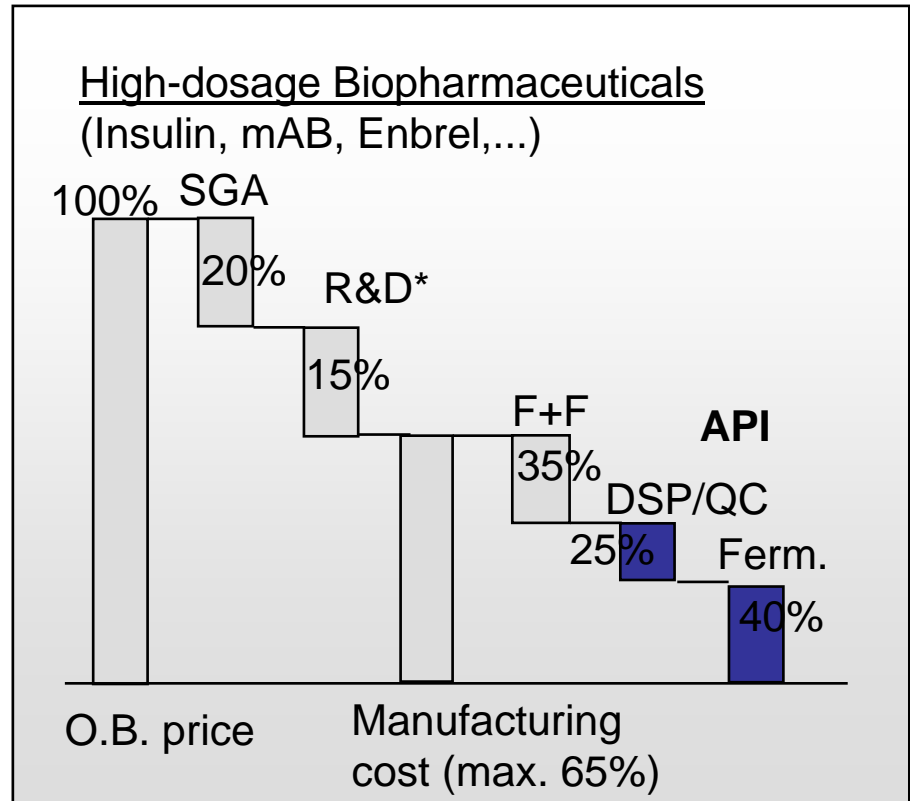
Usual generic sales organization will not do the job,
need for a specialized unit/company



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

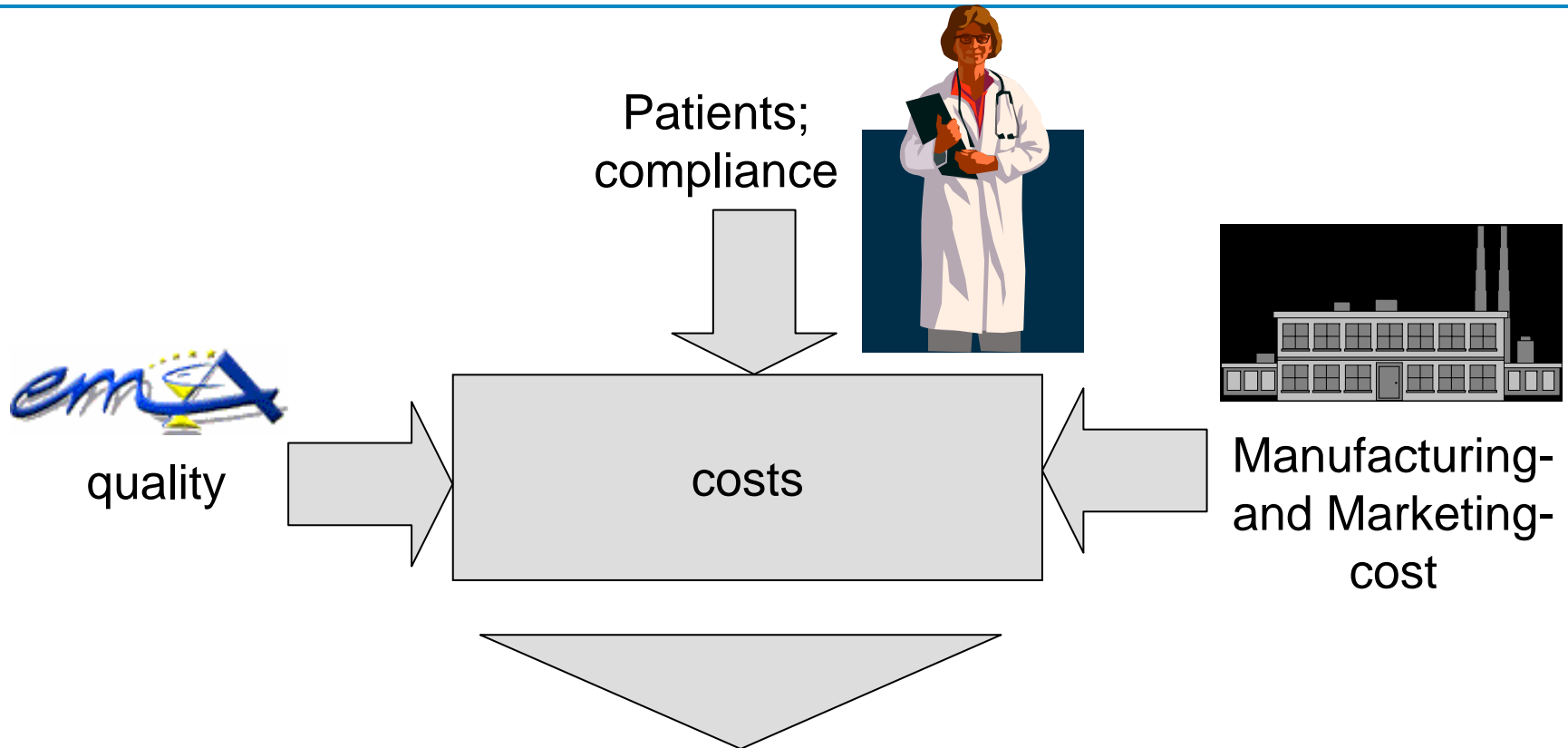


API manufacturing represents max. **14%** of the total costs



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?)



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.

- Costs
- Revenues
- **Returns**

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



in Mio €

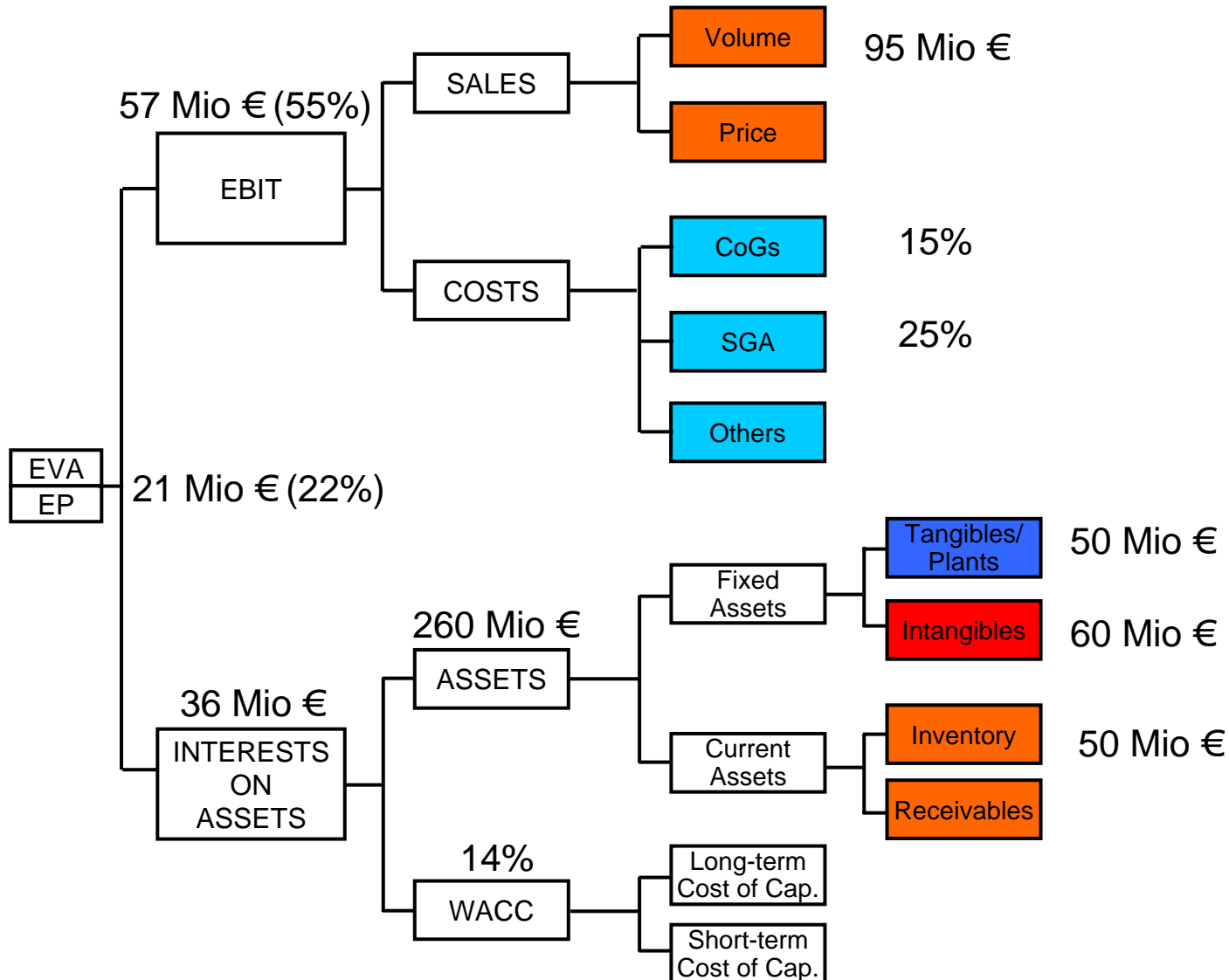
Launch
FoBs

		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**

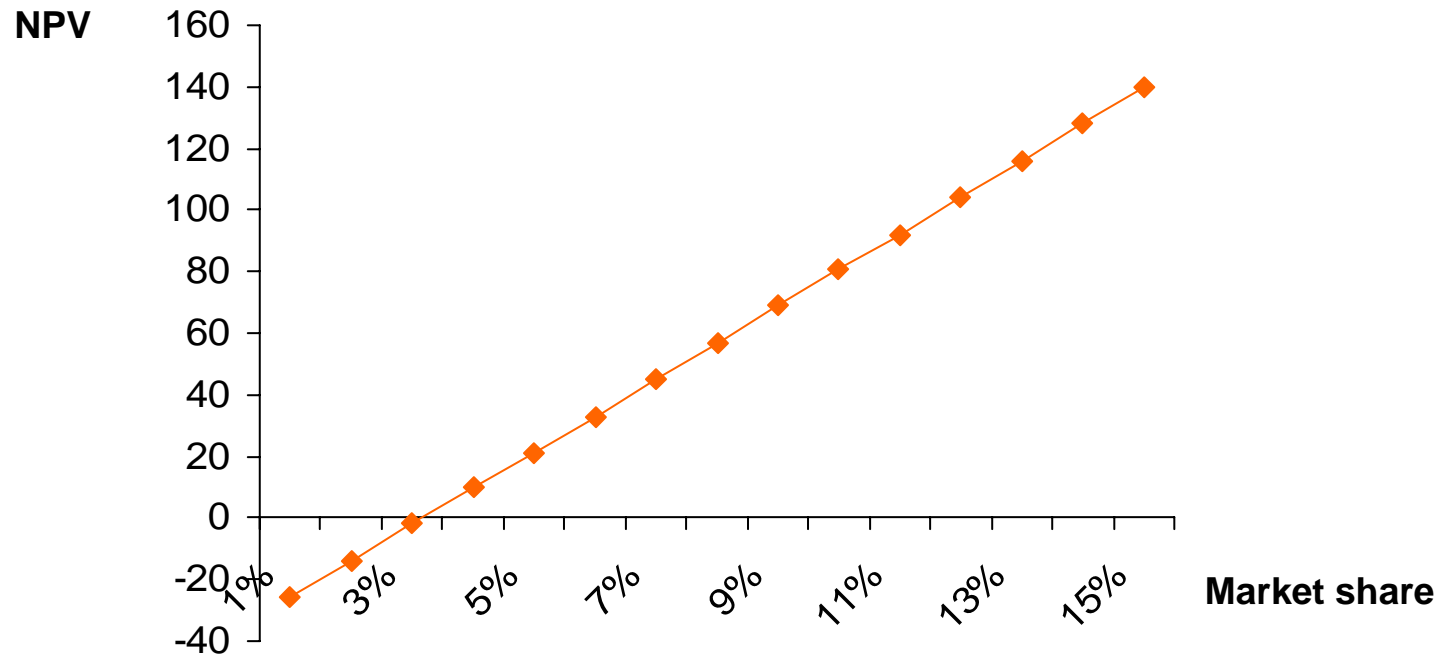
(8 years of sales)

Measures for Success: EVA for FoBs



Sensitivity NPV in function of Market Share

in Unit

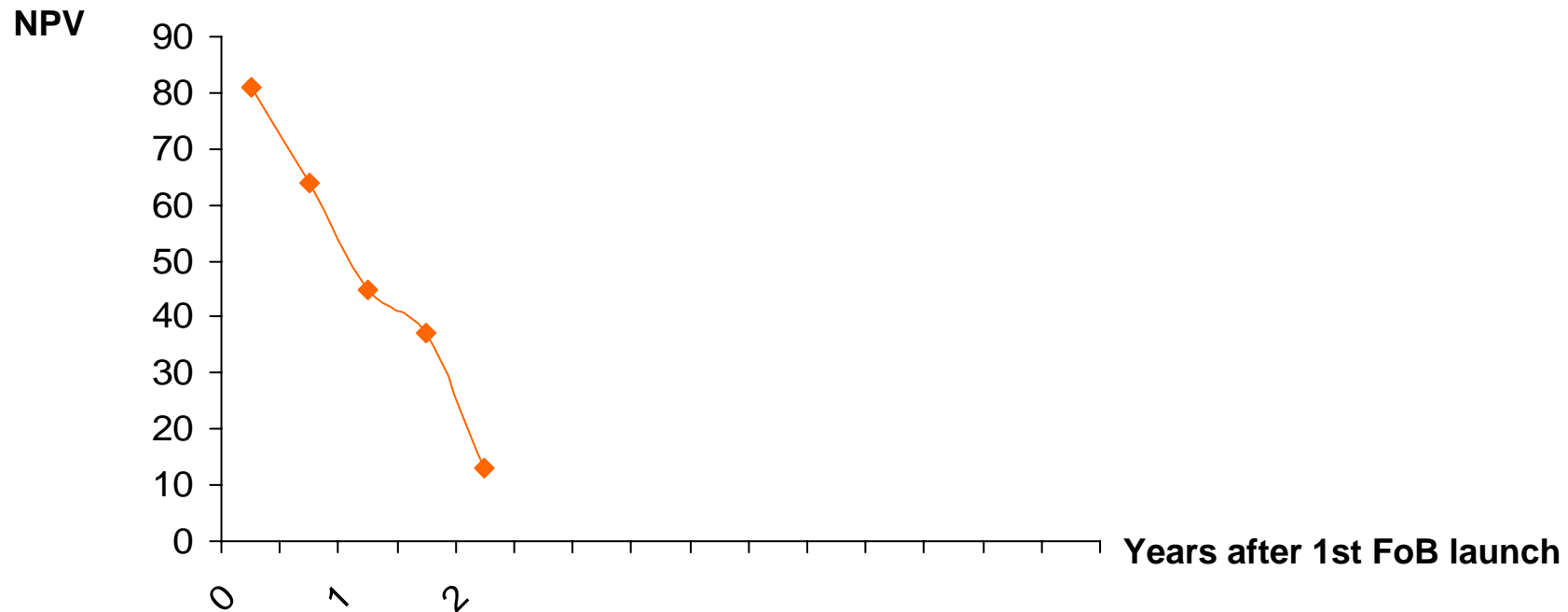


3 - 4% Market share are sufficient to support a 60 Mio € development (30% price erosion); Market share is a key driver for success.

- Similar curves for market size, and price erosion -

Sensitivity NPV in function of delayed market access

in Unit



Under oligopolistic conditions, a delay of 2.5 years brings the RoI to zero, each year of delay destroys (at least) 35 Mio € in value (without counting for idle sales infrastructure). Under more aggressive conditions, a delay is even worse.

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

- The bio-generic industry saw a peak in numbers of companies, but is now starting to sort out
- 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
- 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