

How to succeed in the biogeneric sector



Dr. Klaus Maleck
CFO BioGeneriX AG

How to succeed in the biogeneric sector??

We don't know....

We will see...

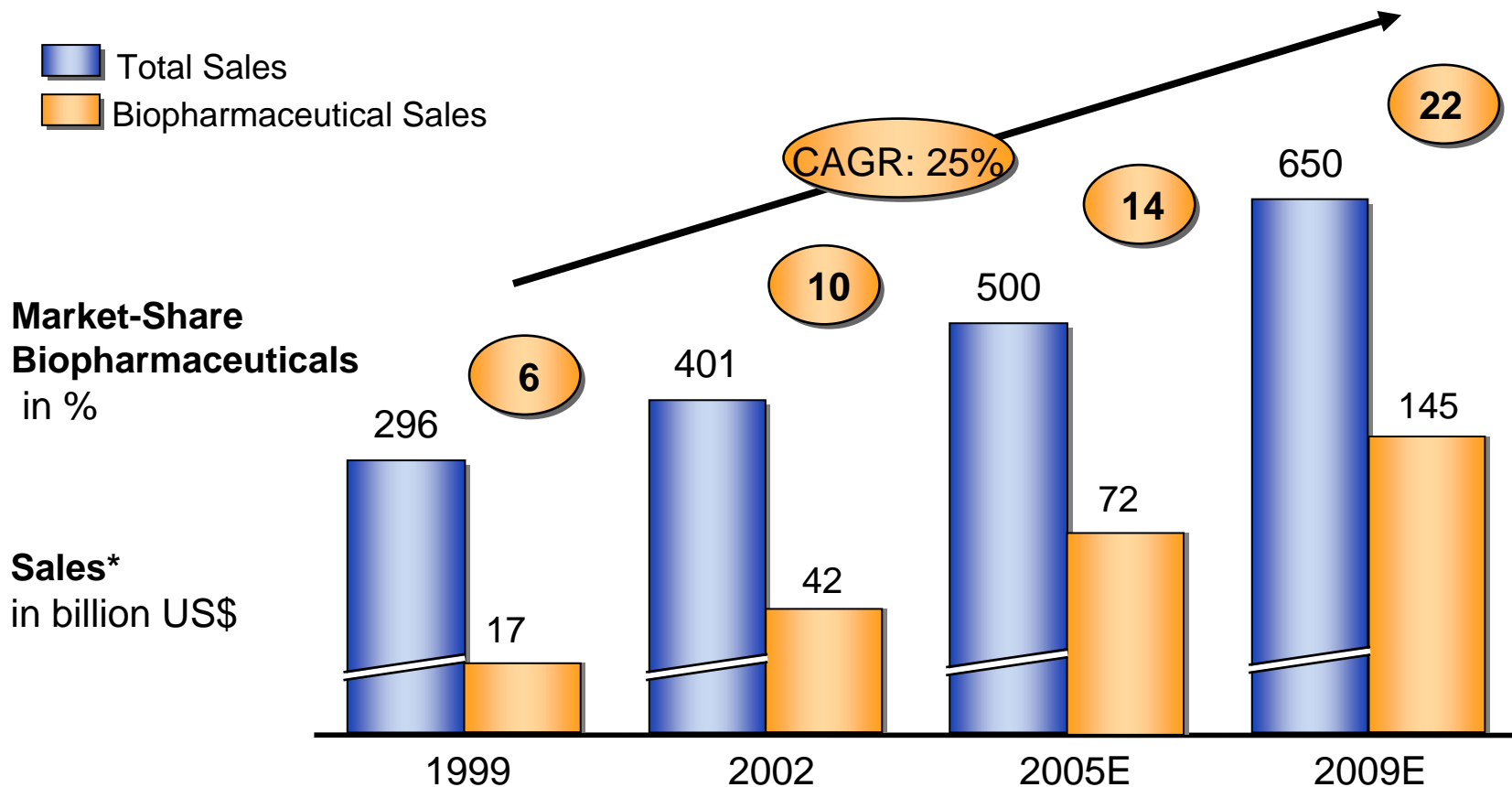
Well, good question, we believe...

SUCCESSFUL BIOGENERICS

- **Battlefields**

- Key factors of success
 - Strategic initiatives
 - Future outlook
-

OPPORTUNITY: THE GLOBAL PHARMA MARKET



In 2010 more than 50% of all newly approved pharmaceuticals will be of biotechnological origin

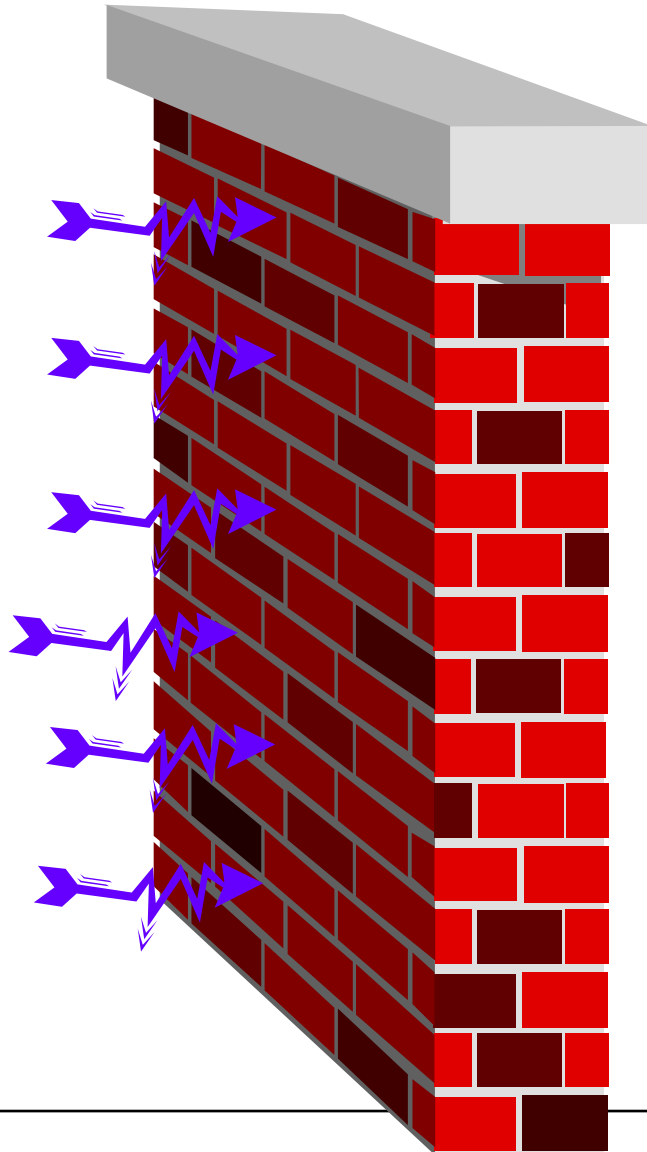
*Rx

Source: IMS Health, Ernst&Young; BioGeneriX Forecast

ENTRANCE BARRIERS OF BIOTECH “GENERIC” PRODUCTS

Barriers

- Patents
- Biotech expertise and biotech production
- Partnering
- Capital
- Legislation
- Market access



LEGISLATION

There are no *biogeneric* products!
Follow-on biologics, biosimilar products,...



Original and biotech „generics“ are **not** identical from a **regulatory** perspective

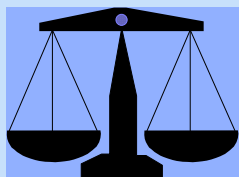


The approval of a biotech „generic“ requires a complete new filing, including clinical trials

Good knowledge of centralized procedures, regulatory requirements (GMP), lobbying (case-by-case), and legal proceedings (cf. Omnitrop) required throughout the development process

The development is likely to take 7-8 years, due to process development and clinical studies

PATENTS: COMPLEX AND DANGEROUS



Original and biotech generics are identical from a **legal** perspective



Before patent expiry, the marketing of biotech generics causes patent infringement

By numbers: 10.000 patents on Insulin, 5.000 patents on INFalpha

By duration: Are biotech patents prolongeable??

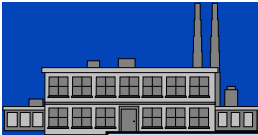
EPO in US: Amgen profits from 30 years market exclusivity (large span between first and last patent expiry)

By clarity: Uncertain claims, multiple references, SPCs,...

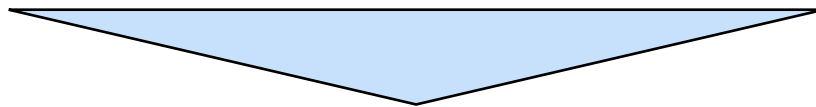


Design your own development path, using novel technologies

BIOTECH KNOW-HOW

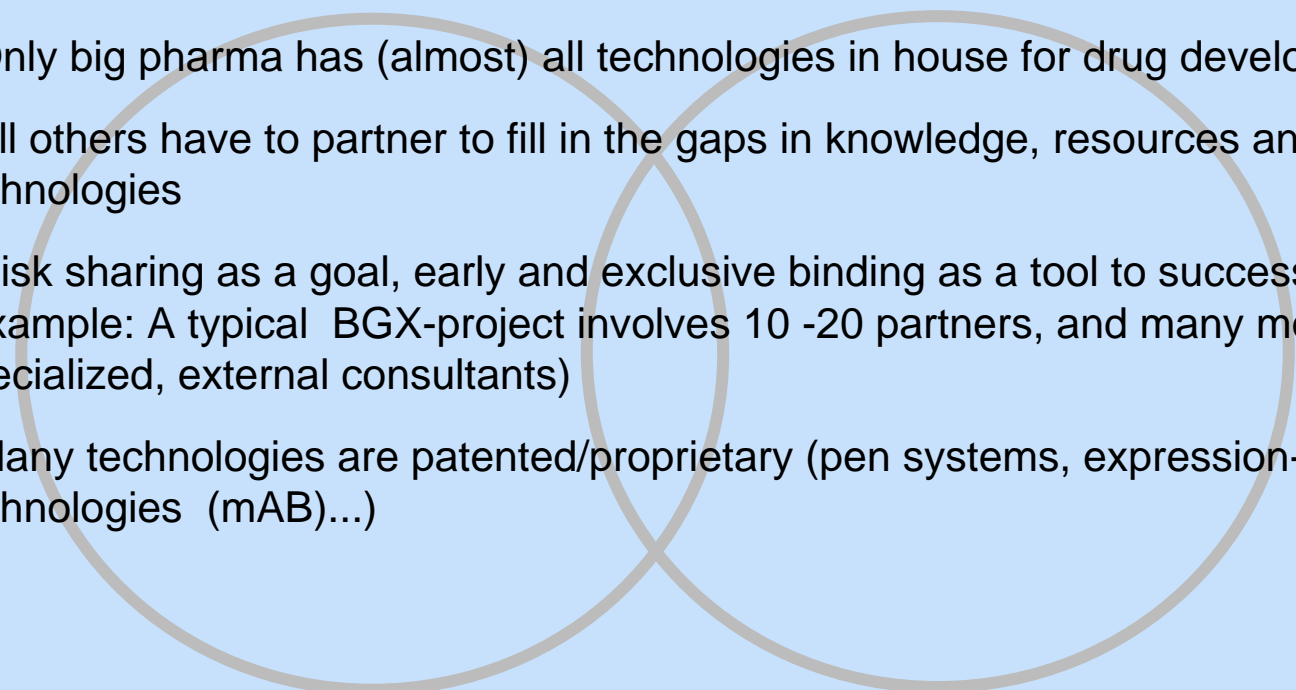


- Copying is not an option (example process patents; cell banking, mAB)
- Biotech manufacturing needs narrow supervision
- Production capacity is a scarce (?) resource and expensive
- Innovation must be foreseen (2nd gen.)



Partnering is required, but not sufficient; in-house knowledge is needed

PARTNERING

- 
- Only big pharma has (almost) all technologies in house for drug development
 - All others have to partner to fill in the gaps in knowledge, resources and technologies
 - Risk sharing as a goal, early and exclusive binding as a tool to success (Example: A typical BGX-project involves 10 -20 partners, and many more specialized, external consultants)
 - Many technologies are patented/proprietary (pen systems, expression-technologies (mAB)...))

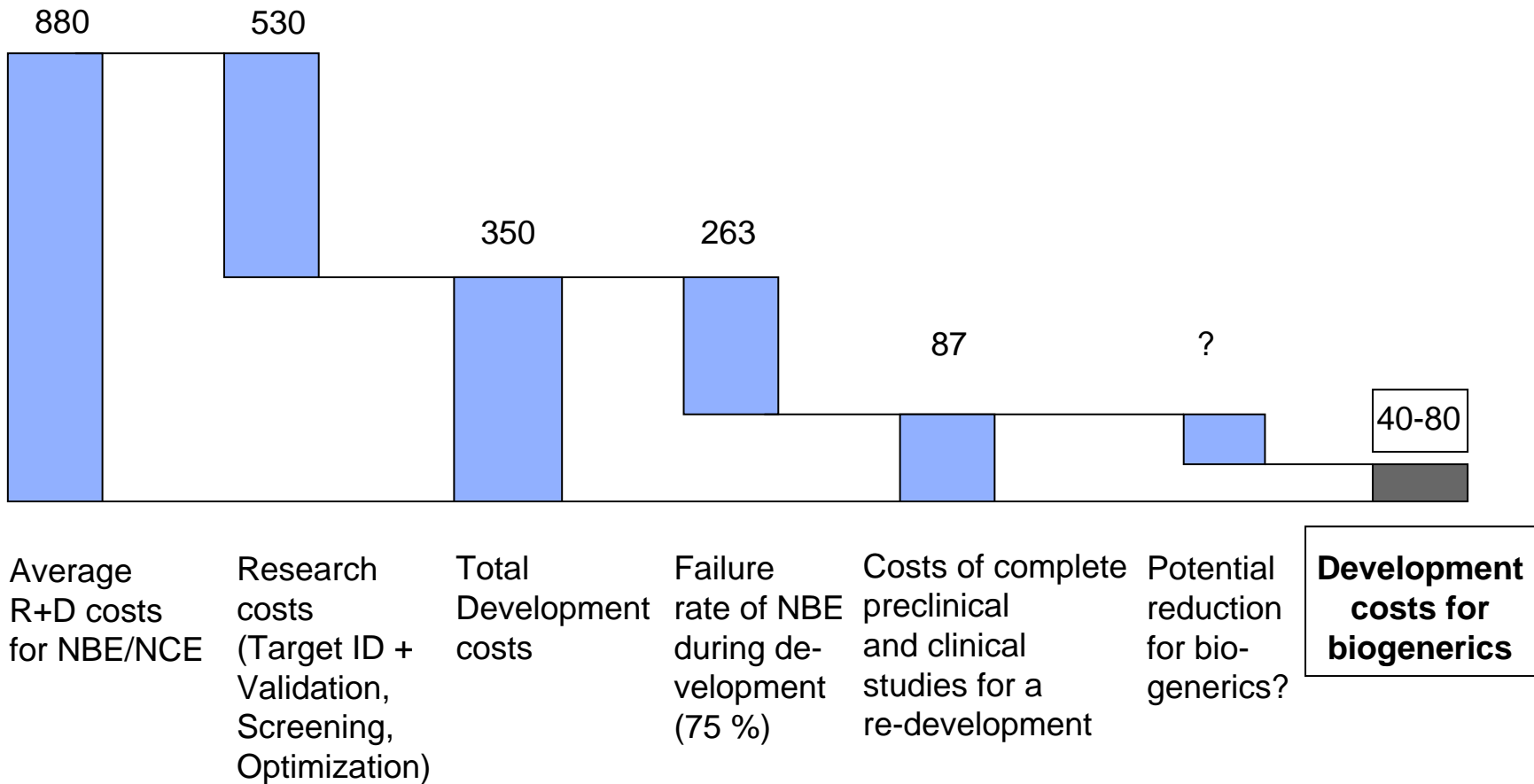


Partnering is for most companies in the biogeneric industry a must, some partners might represent a bottleneck

CAPITAL (1/2)



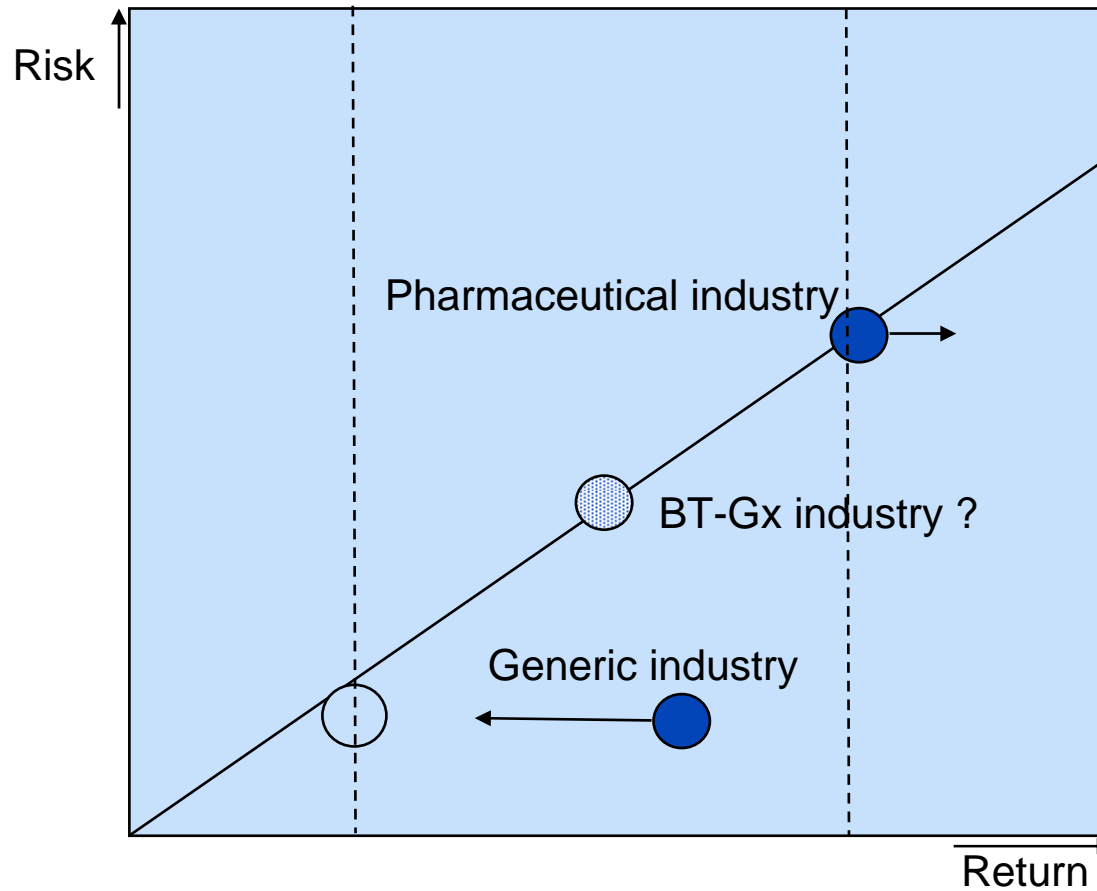
Development costs in Mio USD



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



CAPITAL (2/2)



Although risk is lower than for NCEs, the expected return will be less attractive for big pharma

MARKET ACCESS

- Brand/reputation to create trust at prescriber (clinical data as a requirement, but not sufficient)
- Pricing/price elasticity vs. quality suggestion
- Payor's pressure (pricing) vs. life style drugs (limited reimbursement)
- Sales structures (generic sales force vs. scientific key accounting)
- Bundling with broad and deep portfolio

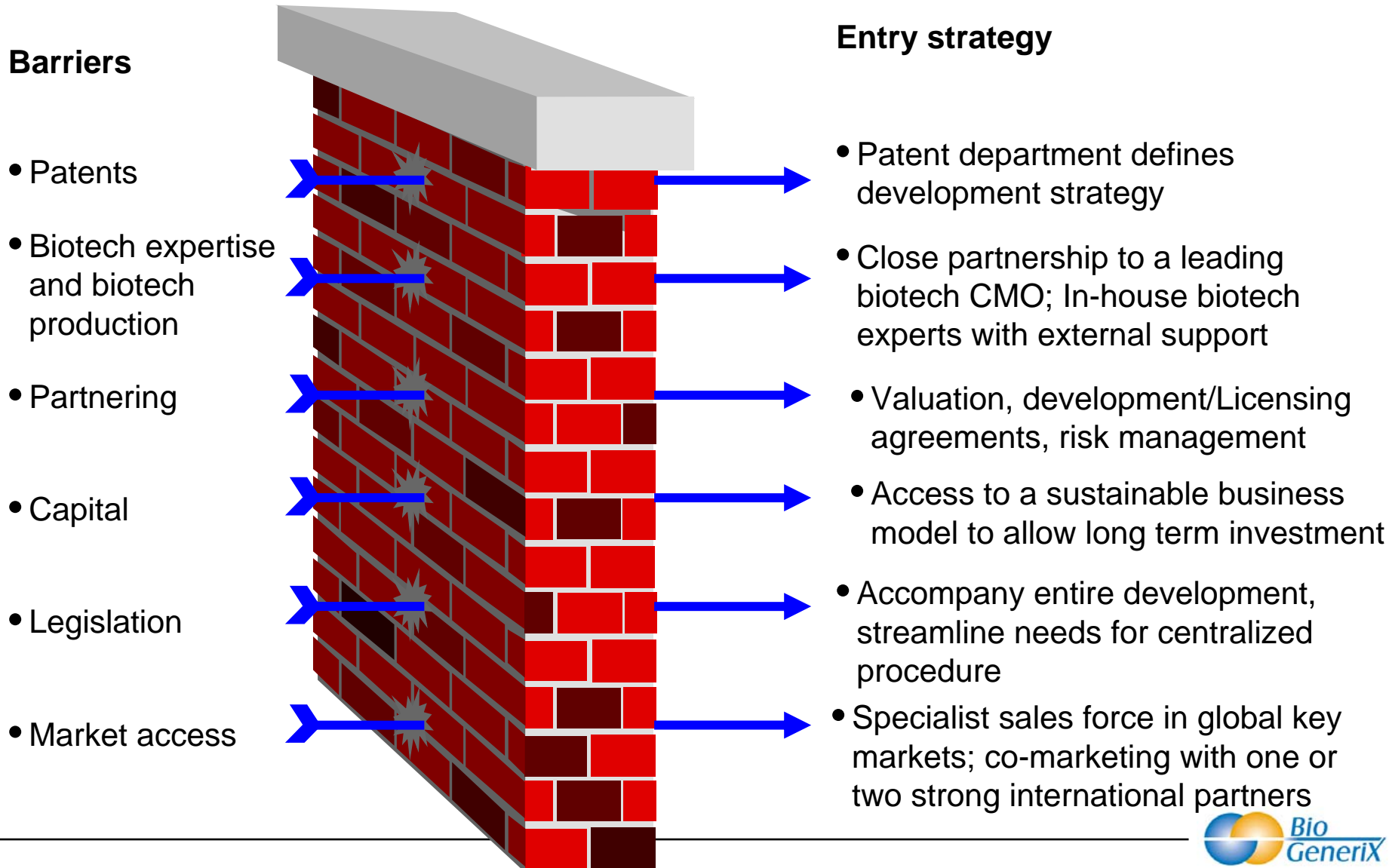


In order to leverage the high investment, a good market access need to be secured (specialist sales force with global reach)

SUCCESSFUL BIOGENERICS

- Battlefields
 - **Key factors of success**
 - Strategic initiatives
 - Future outlook
-

PASSING BARRIERS TO COMPETE SUCCESSFULLY IN BIOTECH GENERICIS MARKET



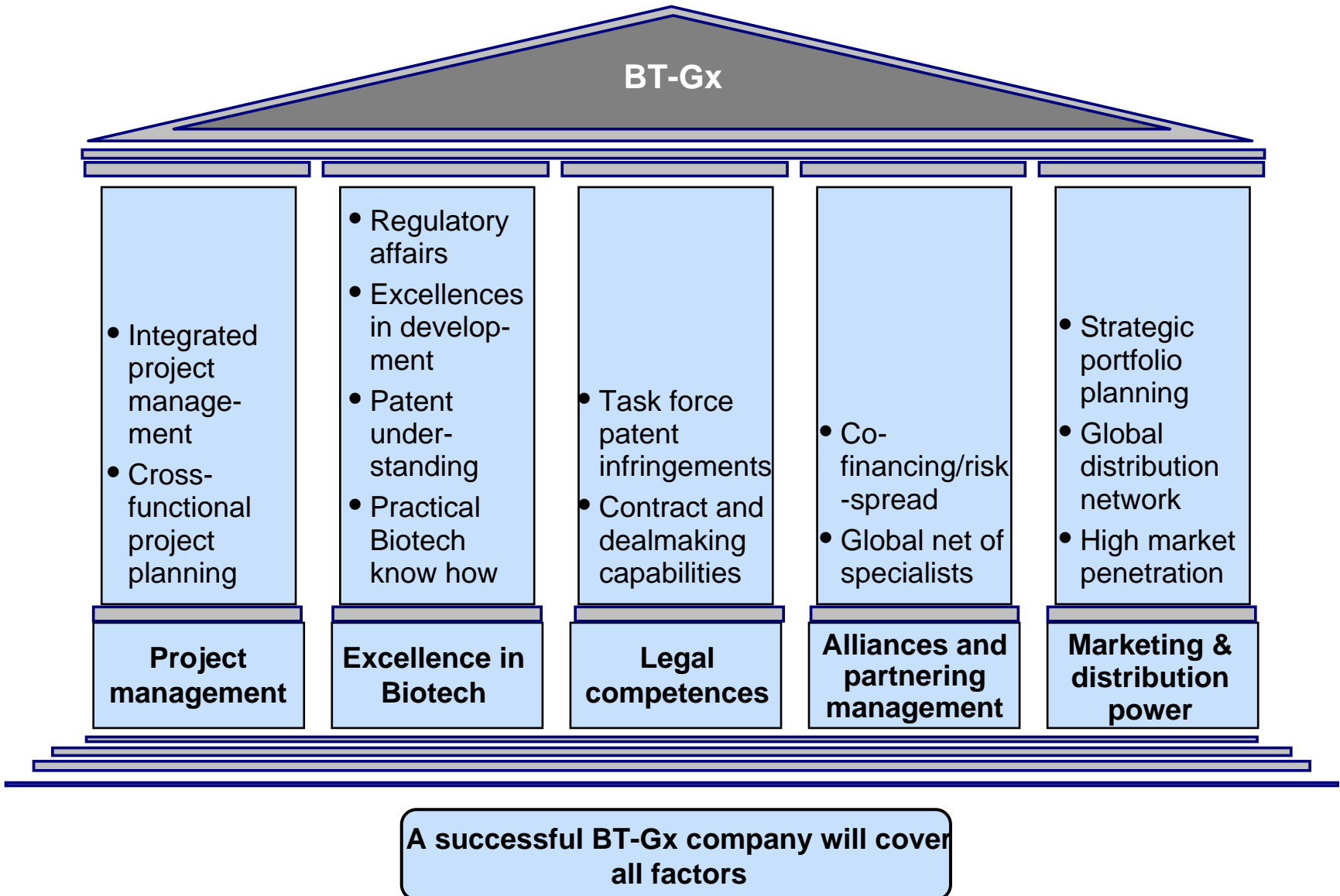
BEST OWNER BIOGENERICS

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

KEY FACTORS OF SUCCESS IN THE BT-GX-BUSINESS

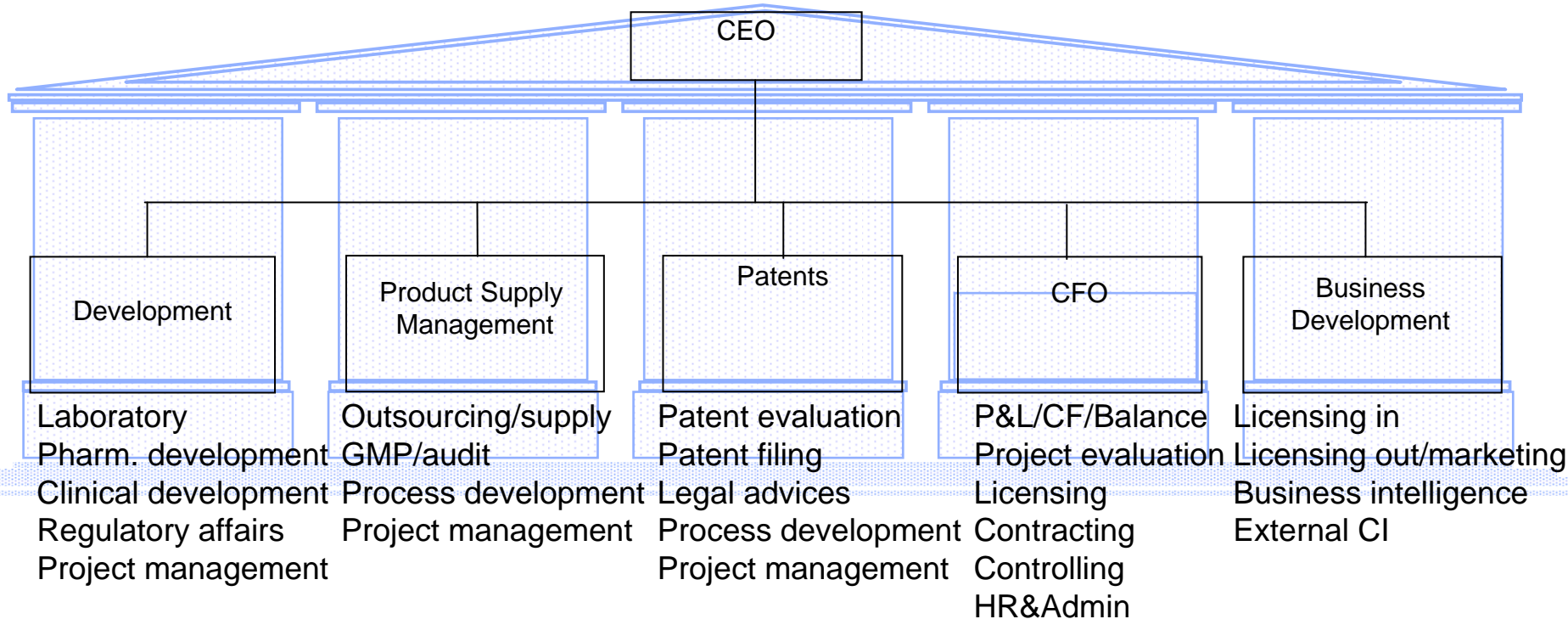


BIOGENERIX KEY PERSONNEL

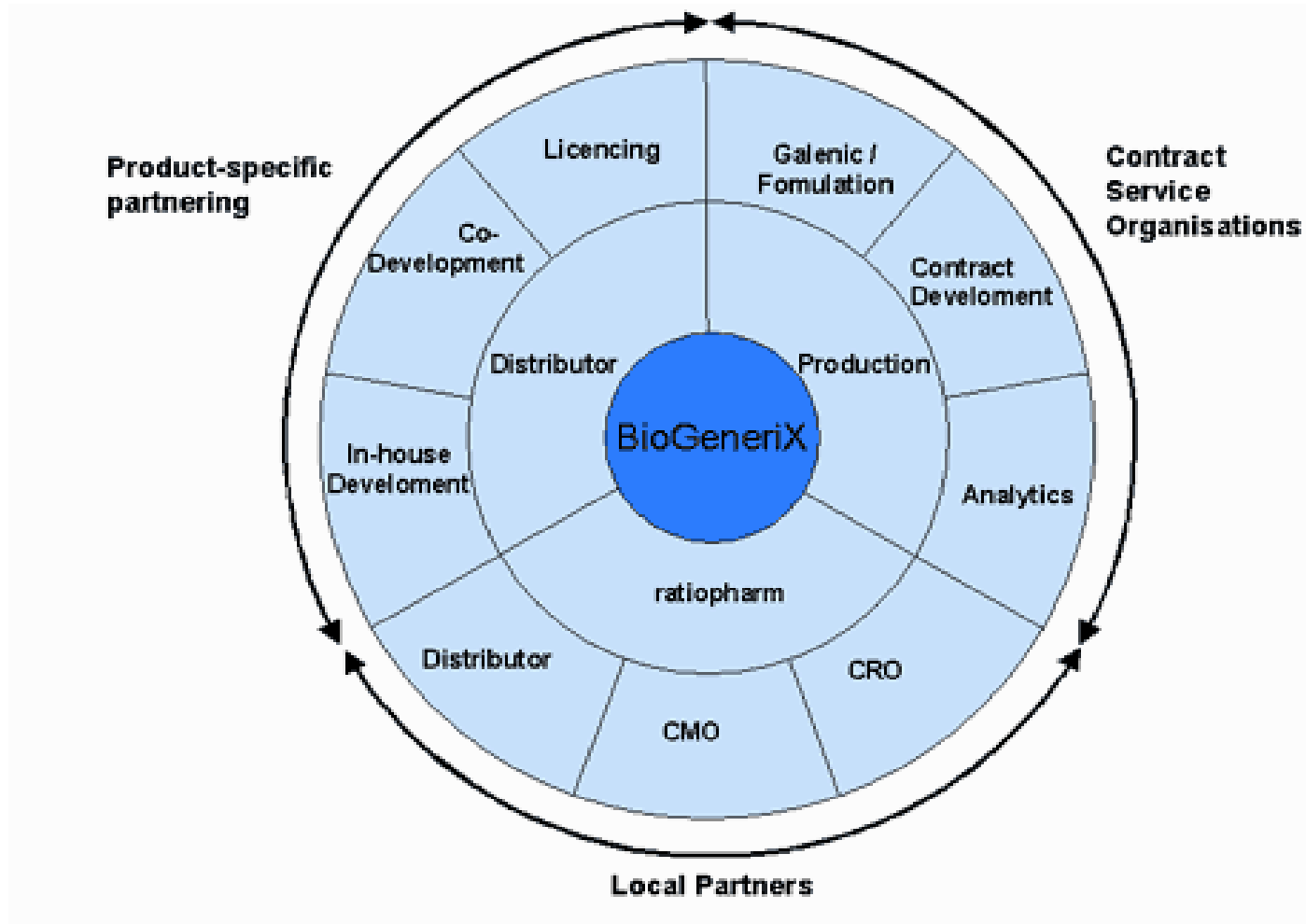
Idea of the semi-virtual company: cover all KFSs with own employees, to communicate at high level with your partners

35 highly skilled employees (not included: HR, bookkeeping, legal services)

- 17 PhDs; 8 higher university level/Engineer
- Almost all with long-time, high-level industry experience

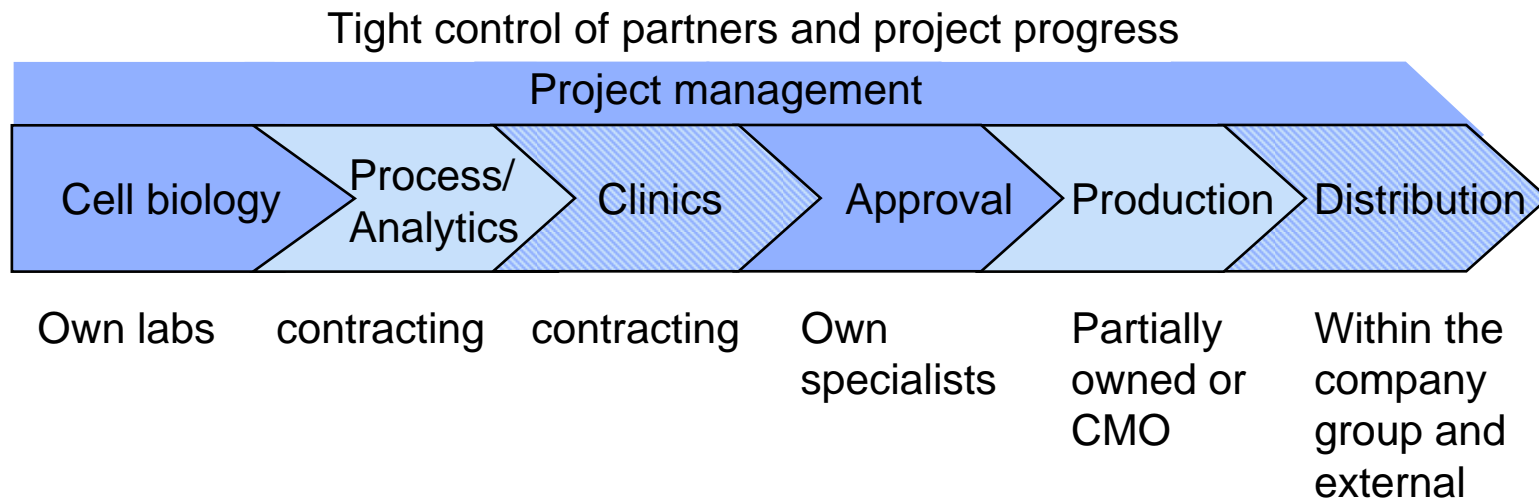
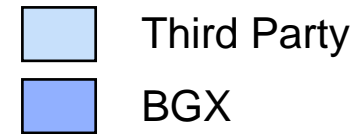


THE BGX BUSINESS CONCEPT



Partnering in combination with own knowledge and experience

SUPPLY CHAIN IN BGX BUSINESS

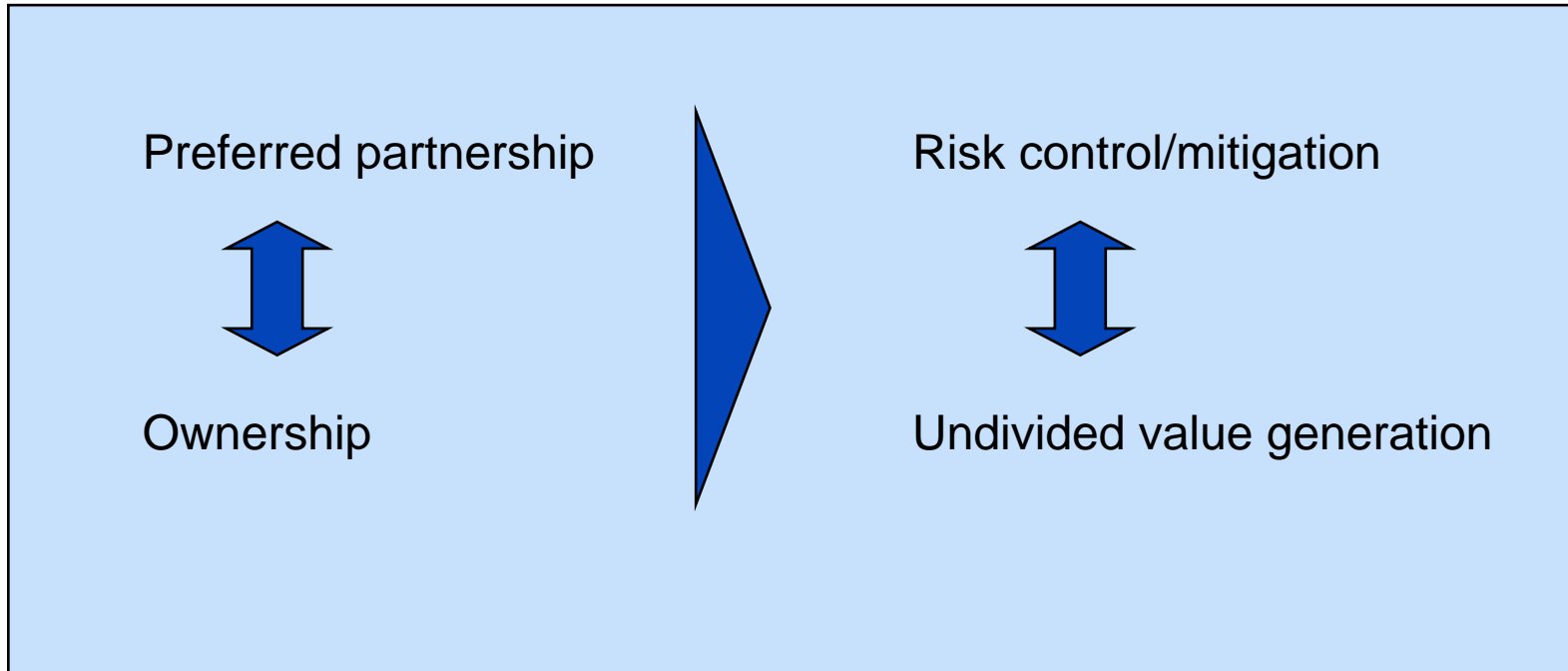


With only a hand full strategic functions, BGX can control a complex project flow and participate in the entire value chain.

Successful Biogenerics

- Battlefields
 - Key factors of success
 - **Strategic initiatives**
 - Future outlook
-

BUILDING A NETWORK COMPANY



For crucial partners (production, distribution) ownership becomes an option at later stages of development, when risk is reduced.

EXAMPLE MANUFACTURING: MAKE OR BUY?

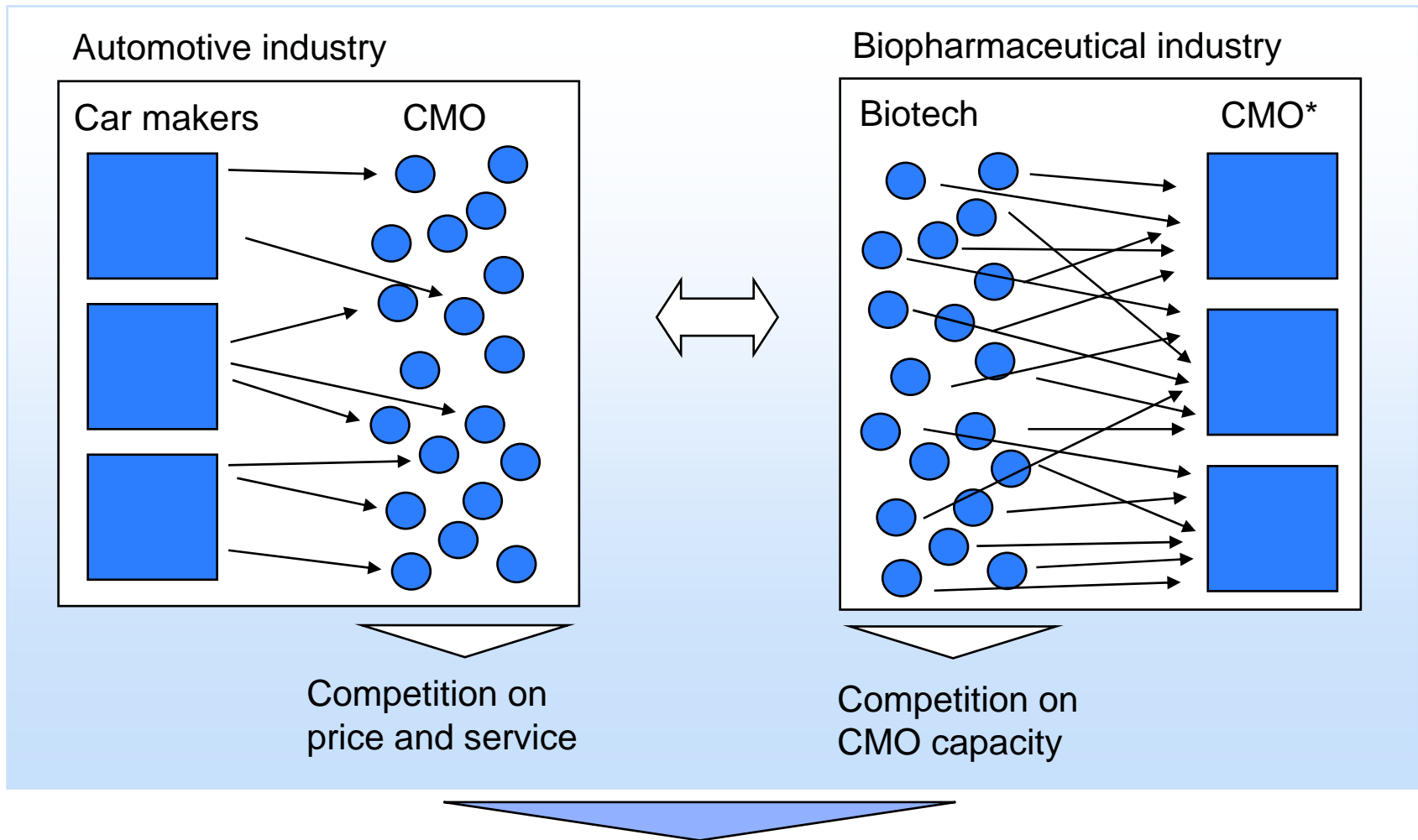
A SWOT-analysis of do-it-yourself

<p style="text-align: center;">Strengths</p> <ul style="list-style-type: none"> • Best location choice • Optimal supply chain construction • In-house knowledge building • Long-term cost controlling 	<p style="text-align: center;">Weaknesses</p> <ul style="list-style-type: none"> • No established skills • High labour/procurement costs • Diversion from business focus • High time requirements (construction, validation, learning)
<p style="text-align: center;">Opportunities</p> <ul style="list-style-type: none"> • Retention of greater profit share • Strategic value creation (fast product ramp-up; technology development) 	<p style="text-align: center;">Threats</p> <ul style="list-style-type: none"> • High „fixed assets“ • High risk bearer (developmental and financial) • Difficult technology change response • Waste of time

Avoid threats and weaknesses, profit from strengths and opportunities!

Establish a long-term, strategic partnership (including partial ownership) during development

EXTERNAL OPPORTUNITIES: MANUFACTURING



Goal: Outsourcing shall help improving a company's performance and maximizing value

BIOPHARMACEUTICAL CMOs: AN OLIGOPOLY?

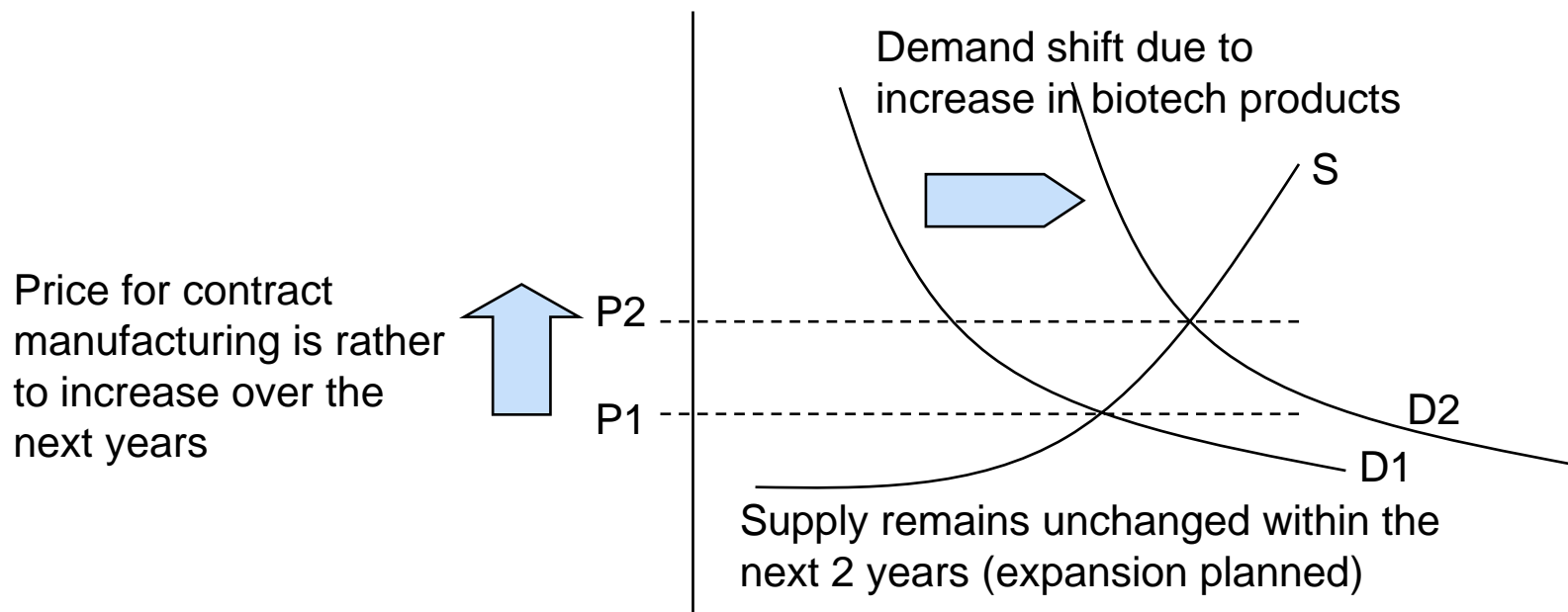
- 30 Bill. USD market for pharmaceutical CMOs, with **growth rates of 17 - 20%**
- 32,7% total return to shareholders** (average 1996 -2001)
- High economies of scale foster **oligopolistic** industry structure (which tend to encourage collusion, and may lead to *monopolistic pricing*)

Pricing requests (provided by a general consulting service): How much does the cell culture fermentation of 24.000 l p.a. incl. DSP cost (in Mio €)?

CMO B	CMO C	CMO D	CMO L
10-15	11-17	~11	~13

It might be as expensive to develop your own expertise (but: time, capital expenditures)

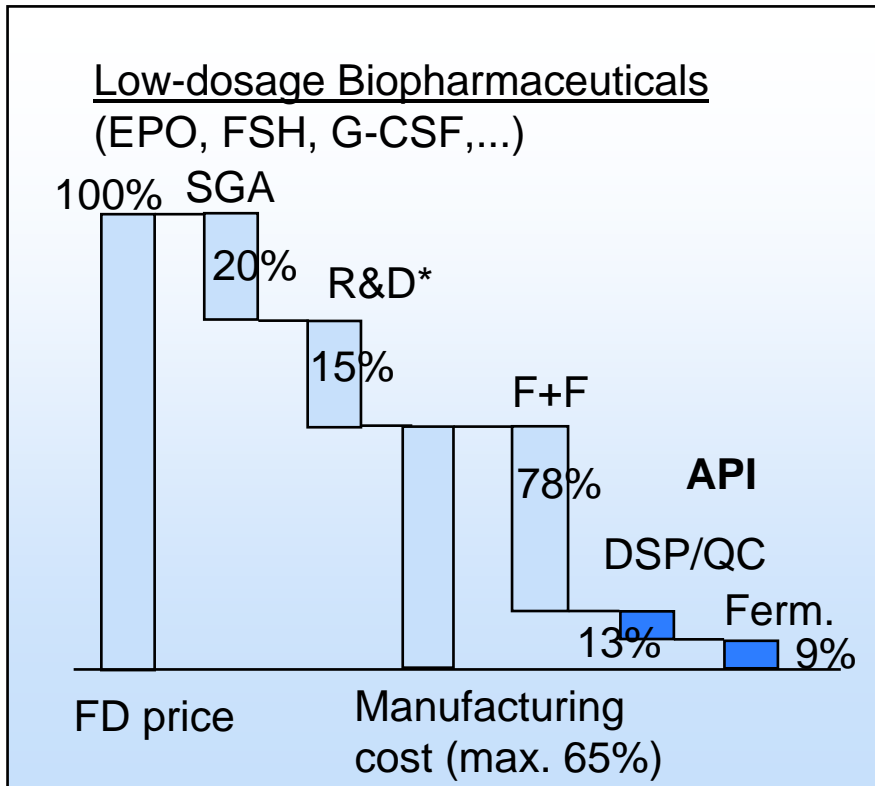
THE DEMAND CURVE SHIFTS FASTER THAN THE SUPPLY CURVE



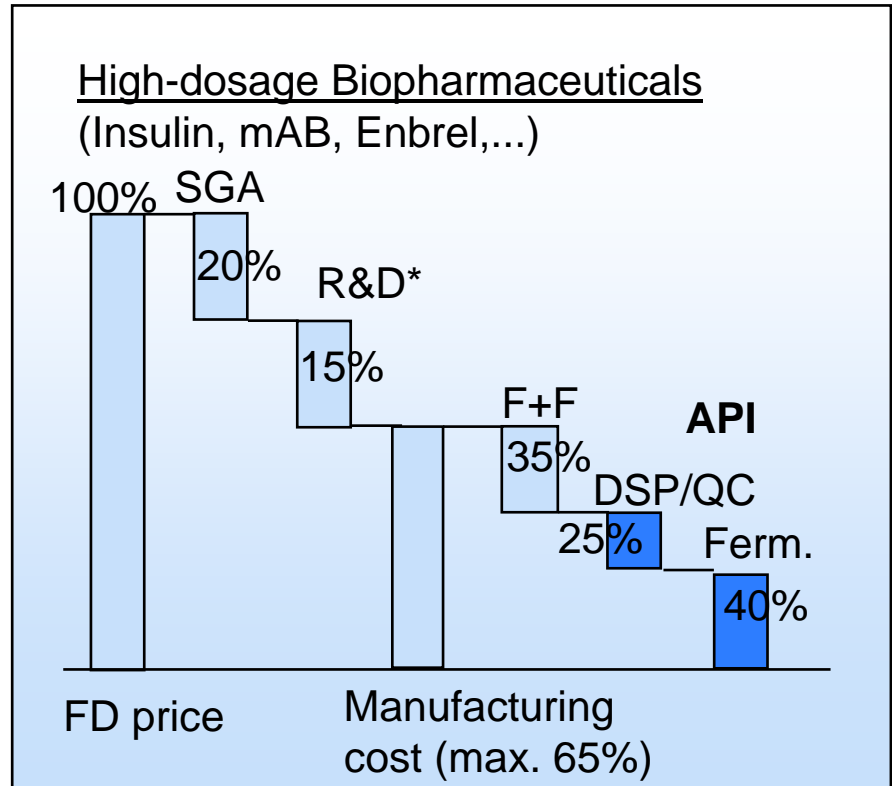
CAGR of 30 - 50% increase in biotech products over the next 5 years will not be matched by the increase in production capacities.

COST STRUCTURE IN THE VALUE CHAIN

- DO WE FINANCIALLY NEED TO MANUFACTURE?



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

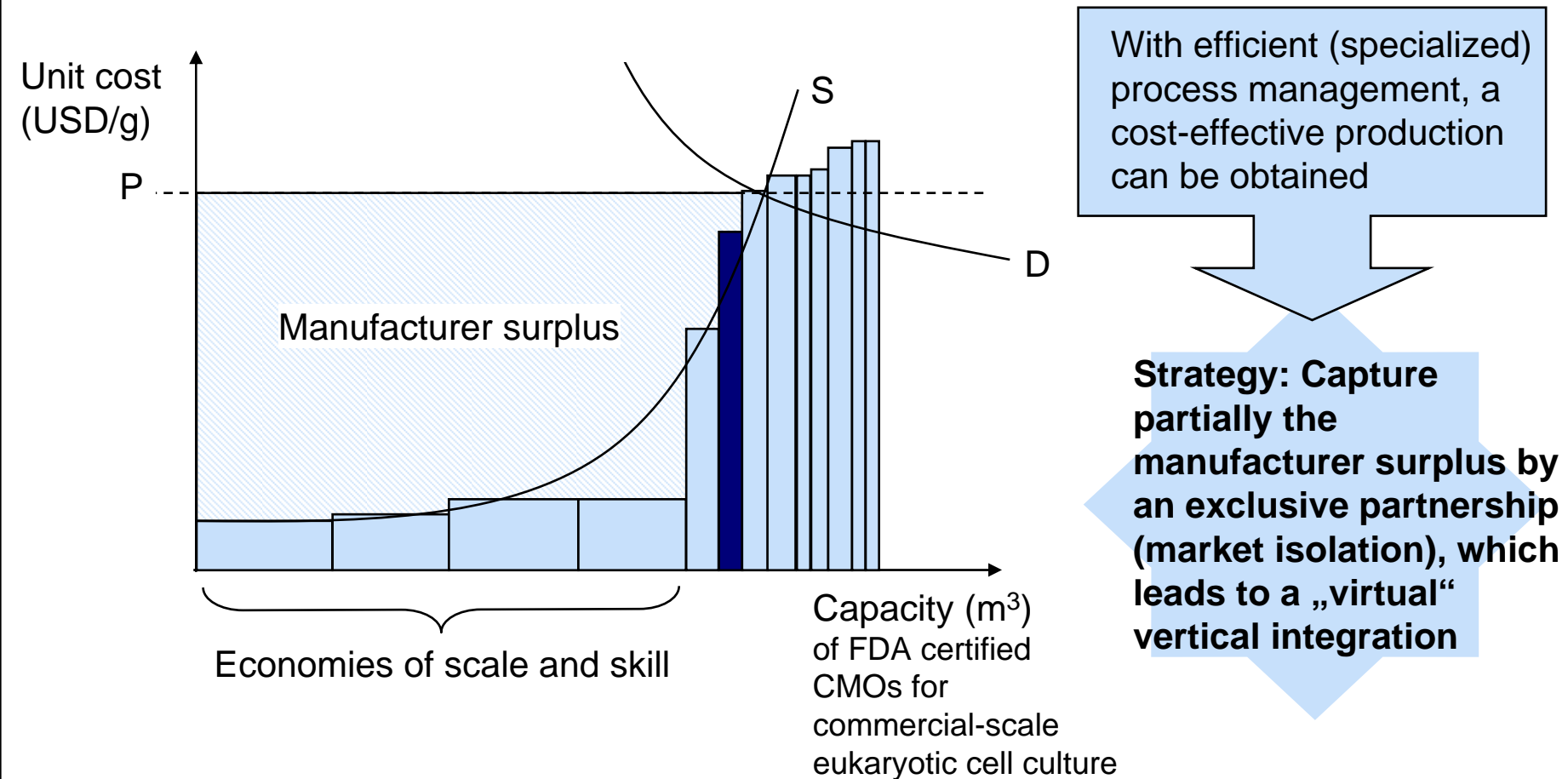
STRATEGIC VALUE OF OWNING A PRODUCTION PROCESS

-DO WE STRATEGICALLY NEED TO MANUFACTURE?

- Biologics are defined by their manufacturing process
- Process validation and batch consistency are as important as product characterization and release testing

Change in manufacturing process, site or partner might require costly clinical testing of safety (and efficacy): high switching costs and probably supply shortage

A CLOSER LOOK AT THE SUPPLY CURVE: COST CURVE ANALYSIS



THERE IS A LONG LIST OF SMALL, YET CERTIFIED CMOs... -WITH WHOM TO CO-OPERATE?

The *high entrance barriers* do not allow the niche players to become a first-tier CMO; they specialized mainly in technology development, upscaling and production of clinical trial batches

Small CMO

- 🔔 FDA/EMEA certified
- 🔔 clean room technology
- 🔔 skilled personnel
- 🔔 some GMP experience
- 🔔 basic equipment in place

Need investment help or
guaranteed production utilization

Bio-generic Company

- 🔔 prefers to stay „asset light“
- 🔔 needs to focus human resources
- 🔔 no practical in-house knowledge
(learning curve)

Needs production facility

**Strategic partnership
followed by (partial) ownership**

SUCCESSFUL BIOGENERICS

- Battlefields
 - Key factors of success
 - Strategic initiatives
 - **Future outlook**
-

FUTURE OUTLOOK

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