Outsourcing, Technology Transfer & CMO-Client Relationships

CMO Selection Process

Contract Manufacturing / Outsourcing
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BioTherapeutics Pharmaceutical Sciences

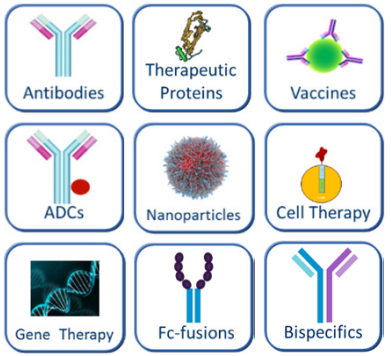
The scope and responsibilities of **PFIZER** BioTherapeutics Pharm Sci

- Discovery Projects
- Bioprocess, Analytical, Formulation And Device Development
- Technology Transfer
- Clinical Supplies Manufacturing
- Regulatory Filings
- Approved Medicines

9 + R&D SITES Innovating to Excel

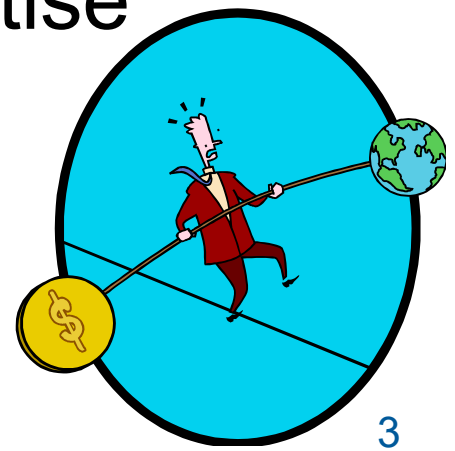
850 + COLLEAGUES Each Having an Impact

50 + DEVELOPMENTAL Medicines under Our Wing

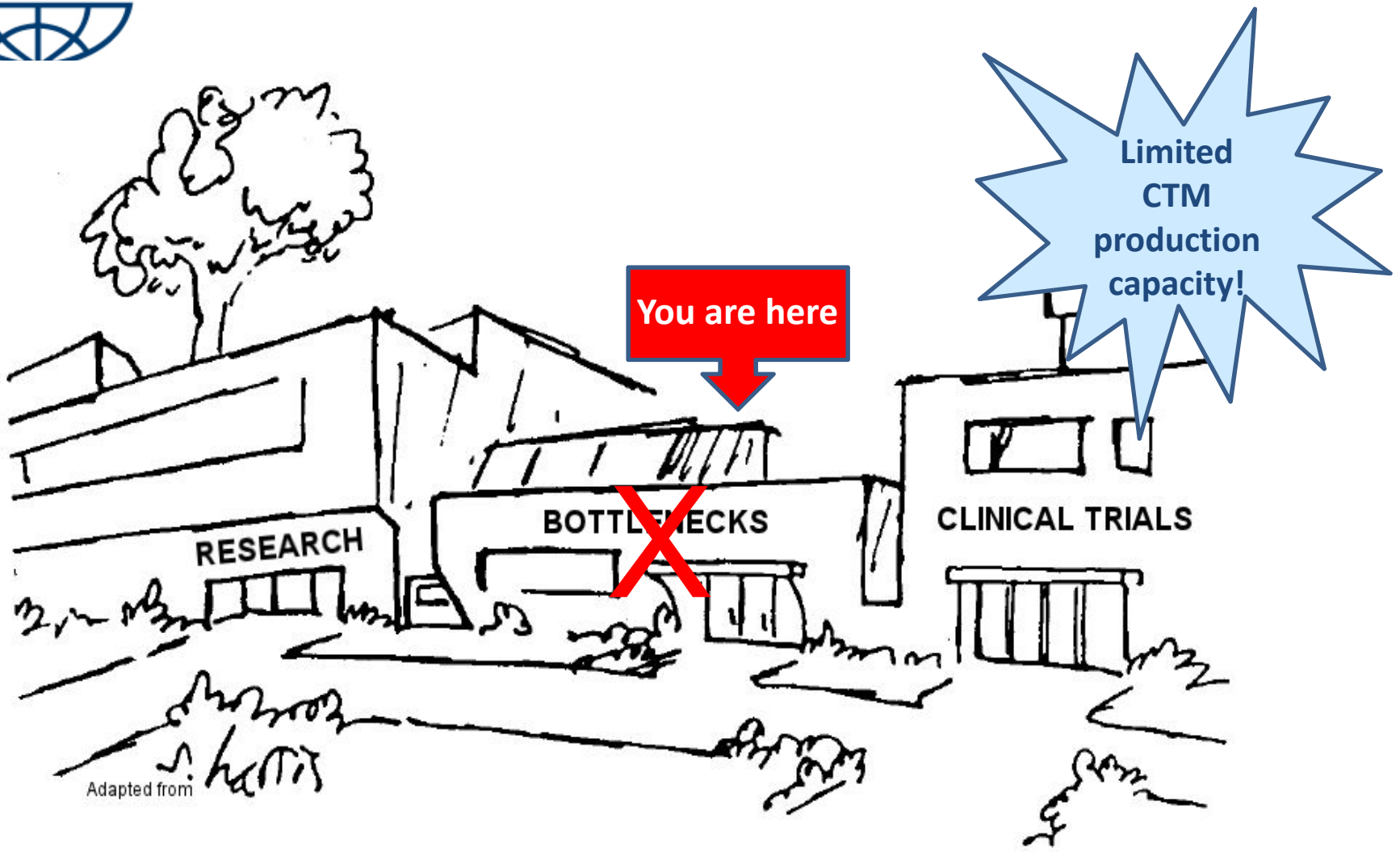


Why outsource?

- No internal capability
- Mitigate risks in upfront capital investment
- Focus internal resources on core competencies
- Rely on CxO's strength and expertise
- Fill gaps in capacity
- Afford greater flexibility



Pre-Commercial Manufacture

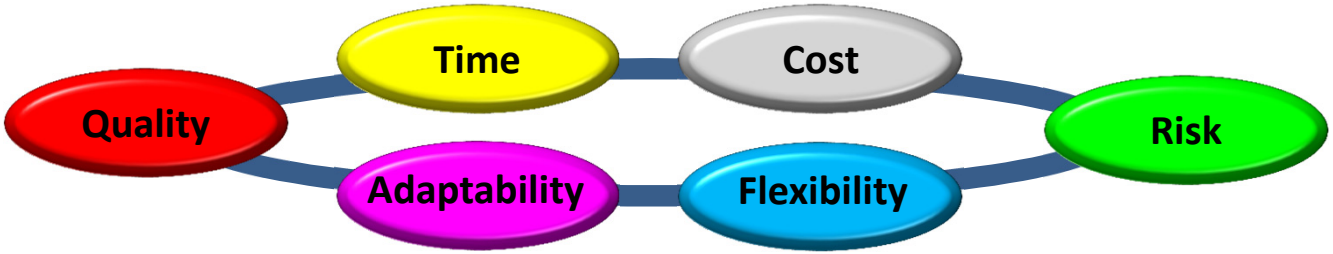


Presentation Outline

- Guiding Principles for Externalization
  - "Make" vs. "Buy" Options
- External Supply Models
  - Integrated vs. Functional Services
  - Strategic vs. Collaborative Vendors
- CMO Screening Process
  - End-to-End mAb: from DNA to Phase 1 CTM
  - **CMO Selection – Interactive Exercise**
- Vendor Management & Metrics
  - Managing Relationships with CMOs
  - Vendor Scorecards

Day 2

Guiding Principles for Externalization



- ✓ **Quality** — Determined by product/process complexity and novelty
  --- Can Quality and Regulatory expectations be met?
- ✓ **Time** — Minimize time to POC & maximize POCs per year
  --- What are the vendor selection and tech transfer time components?
- ✓ **Cost** — COGs / FTEs / licensing & royalty burden concerns
  --- Where is maximum value achieved?
- ✓ **Risk** — Patent state / trade secret / know how / IP
  --- How can we sustain long-term competitive advantage?
- ✓ **Flexibility** — Scheduling, Resources, and Technology platforms to enable facile movement
  --- How do we position Vendor Service models to meet project needs?
- ✓ **Adaptability** — Maintain vendor relations to meet shifting environments & project needs
  --- How do we eliminate peaks and valleys of resource demands?

Make vs. Buy Options

Modality	Core Ability Examples	Non-Core Examples
Drug Substance	• Cell bank manufacture • Purification development • Media development • Process optimization • Conjugation development	• Routine production • Small-scale column lifetime studies • Unique facility concerns (e.g. ADCs, viral vaccines/vectors, cell & gene therapy)
Drug Product	• Formulation development & screening • Lyophilization development & optimization	• Routine production • Unique facility concerns (e.g. ADCs, viral vaccines/vectors, cell & gene therapy)
Analytics	• Methods development • Critical/complex assay testing	• Stability testing • Release testing (e.g. compendial)

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Vendor Management & Metrics

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Functional vs. Integrated Services

Functional Service Model:

Single vendors per modality

Pros:

- Strong relationship & understanding
- Ability to leverage competition in modality space to its advantage

Cons:

- Supply chain more complex

Integrated Service Model:

Offer multiple modalities

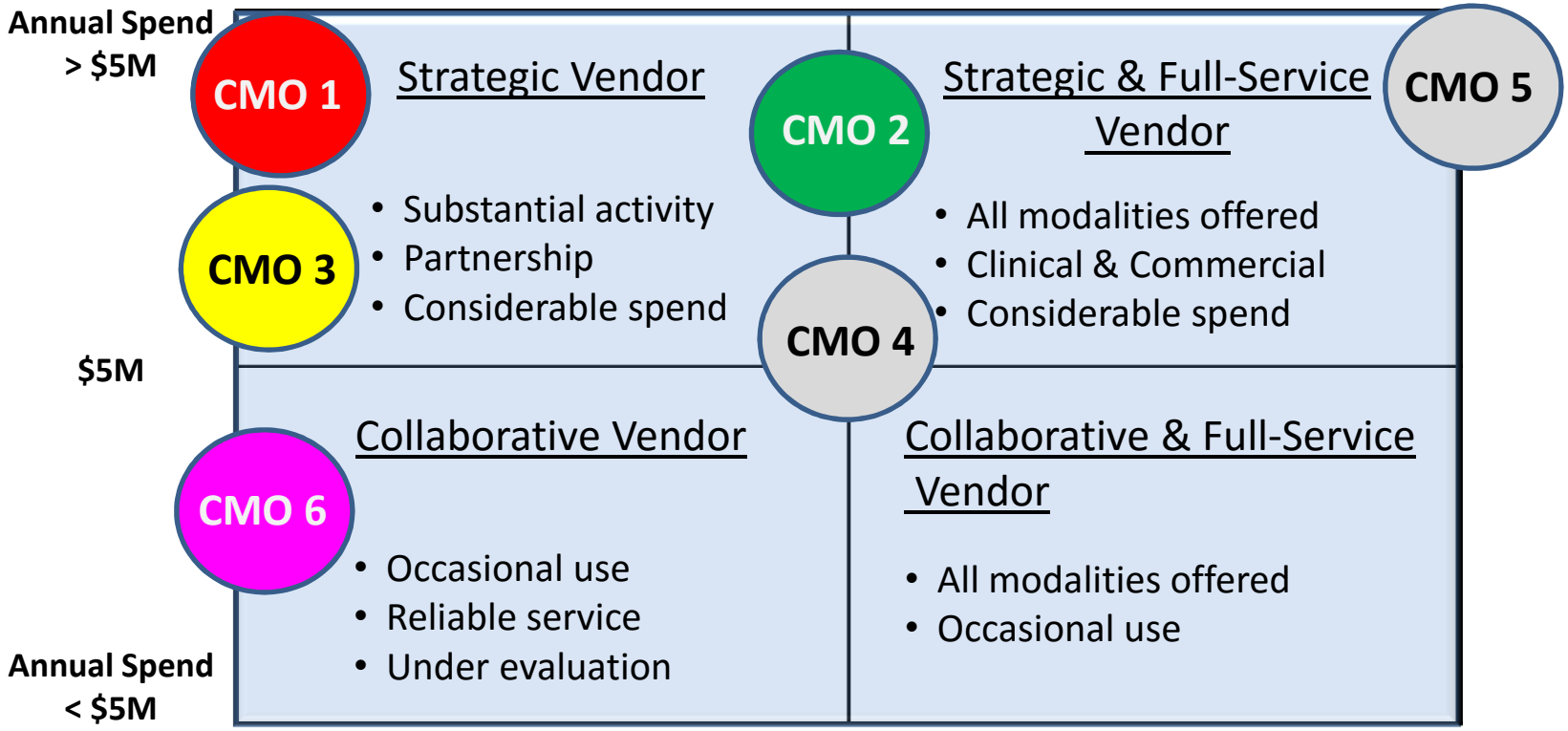
Pros:

- Strategic partnership
- Reduce fixed R&D spend
- Quicker to clinic

Cons:

- Reliance on single provider

Strategic vs. Collaborative



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CMO Screening - Selection

Selection Criteria

Financial Stability	Company Profile	Management	Quality	Capabilities/ Experience	Cost Competitiveness RFP Only
Go / No Go	20%	20%	30%	30%	NA

Criteria Detail

- Treasury Report
- % Revenue from largest customer
- Litigation status

- Geographic reach
- Turnover rate
- Pfizer experience
- Other

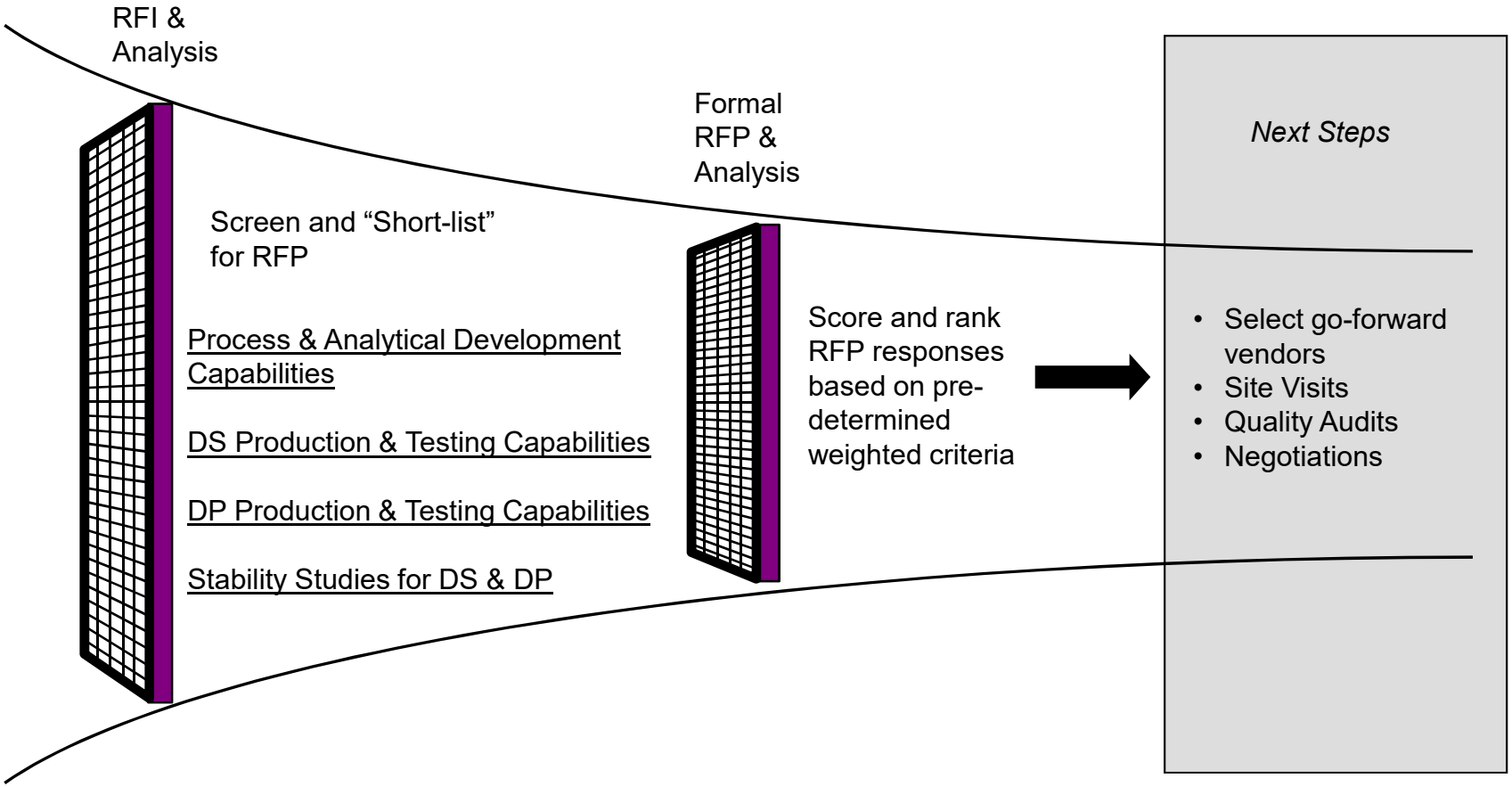
- Unit Management
- Mgt / relationship between focus areas
- Progress reports
- Communication plan

- Science staff to QA staff
- Quality systems
- Investigation / CAPA procedure
- Training records
- Audit history

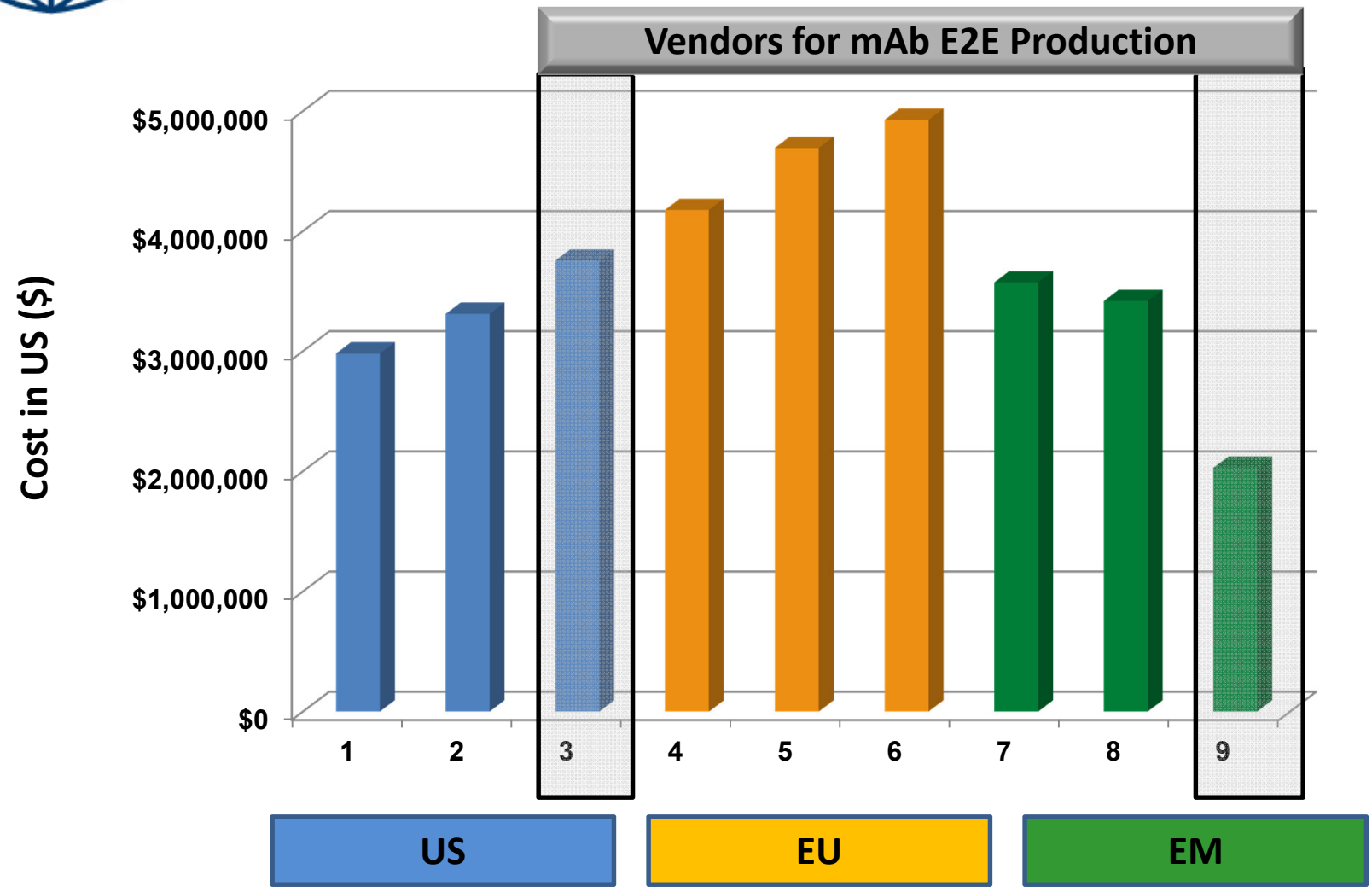
- Technology transfer process
- Project management
- Process & analytical equipment
- Technical staff
- Production & testing staff
- Production & analytical capabilities

- RFP cost results

CMO Screening - Execution



CMO Screening - Results



Onboarding / Qualifying A CMO At Pfizer

CMOs in “short list”:

- Confidentiality Agreement (CDA)
- Request for Proposal (RFP)

Rigorous onboarding process post-RFP:

- Master Services Agreement (MSA)
- Quality Audit by Pfizer MSQA
- Sterility Assurance Assessment by Pfizer MAS (only for aseptic CMOs)
- Environmental Health & Safety Assessment by Pfizer EHS
- Quality Assurance Agreement (QAA)
- Data Integrity Assessment *(new)*
- Multi-Product Facility Assessment *(new)*
- Quality Culture Assessment *(new)*

GROUP BREAKOUT & DISCUSSION I

CMO Selection - Exercise

- You are the External Supply Head for a large US biopharmaceutical company, *Wyzer BioPharma*, and have just been assigned a monoclonal antibody (mAb) project to outsource, due to lack of internal capacity.
- The objective is to deliver clinical supplies for Phase 1 clinical trials of a mAb (*Curemumab*), and submit an Investigational New Drug (IND) application in a 15-month time frame.
- You have a budget of M$8 and 2 Full-Time Equivalents (FTEs), including Process, Analytical, Quality, Regulatory colleagues and yourself, to get this project off the ground. You only need to outsource the production of the Drug Substance since your company has excess Drug Product capacity. Please refer to the ***Request for Proposal*** for more details on deliverables.

CMO Selection - Exercise

- Assume that both upstream and downstream processes are developed and are “platform”, and that all the analytical test methods are developed, and are “platform”, except for Identity and Potency. With these assumptions, there is no need to consider process development and analytical methods development activities at the CMO, except for Identity and Potency.
- You will be provided **6 CMOs to choose from**, with varying profiles, strengths, and weaknesses. Select your CMO and justify your choice. The goal is to enable the correct usage of selection process parameters which were provided to you, so as to expeditiously complete a Contract with a CMO, and mitigate problems before they occur.

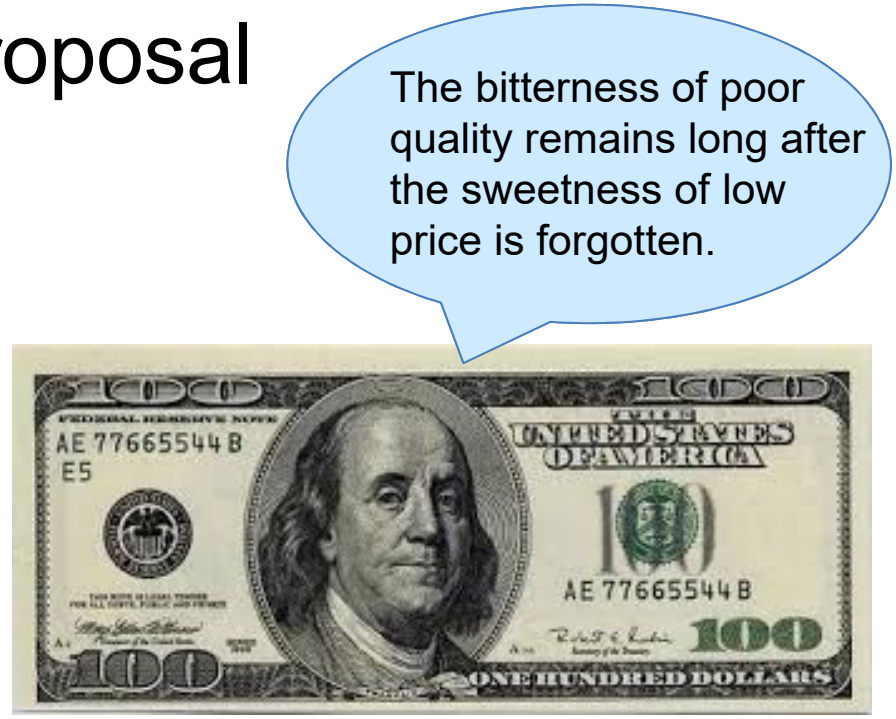
CMO Selection - Scorecard

CMO Selection Scorecard	Diamond Biotechnologies	Garnet Biotherapeutics	Emerald Biologics	Opal Technologies	Ruby BioPharma	Jade Biologicals
Geographic Location	San Francisco CA, USA	Cambridge MA, USA	Dublin, Ireland & San Diego CA, USA	Dusseldorf, Germany	Bangalore, India	Wuhan, China
# of Employees	150	5000	10000	1000	4000	5000
Years in CMO Business	5	15	20	10	15	10
FINANCIAL STABILITY (5%)						
Comments						
QUALITY (20%)						
Comments						
CAPABILITIES/EXPERIENCE (15%)						
Comments						
UPSTREAM PROCESSING (10%)						
Comments						
DOWNSTREAM PROCESSING (10%)						
Comments						
RELATED SERVICES (15%)						
Comments						
REGULATORY EXPERIENCE (10%)						
Comments						
ESTIMATED DURATION (WKS) (15%)						
Comments						
COST COMPETITIVENESS ($)						
Technology Transfer						
Reg/Tox DS Batch						
Number of Reg/Tox Batches						
GMP DS Batch						
Number of GMP Batches						
Total $	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00
Comments						
TOTAL SCORE	0	0	0	0	0	0

1- Lowest Rating
2- Middle Rating
3- Highest Rating

CMO Selection - Exercise

- Profiles of 6 hypothetical CMOs
- Request for Proposal
- Scorecard



Acknowledgement

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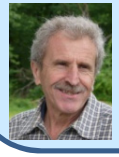
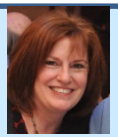
Bernie Huyghe
Ali Javadian



Tom Mueller



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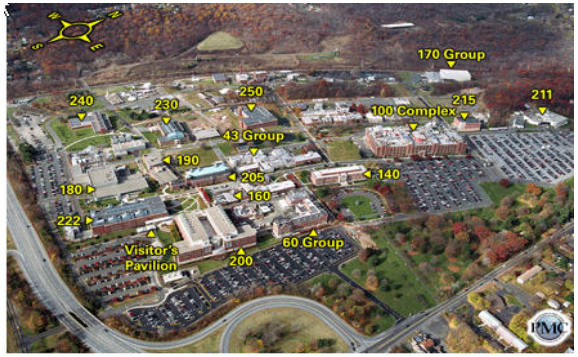

Pearl River, New York