



# *Global Pharmaceutical & Biotechnology R&D*

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## *Challenges – Opportunities - Pathways*

*Thomas J Schulze, PhD, PMP®*  
August 24, 2010

# Welcome to “Global Pharmaceutical & Biotechnology R&D: Challenges – Opportunities - Pathways”

## Presenter

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## *Before We Begin....*

- **Submit Questions as we go along**
  - Click the “?” icon at the lower right corner of your screen to bring up Q&A panel where you can type and submit questions.
  - There will be time for questions at the end of the presentation.
  - We may not be able to answer every question but will focus on the most representative.
- **PMI / PDUs**
  - 1 PDU
  - PMI reference number will be sent to attendees in a follow-up email along with a link to download this presentation.
- **Boston BioPharmaPM September Conference**

# ***Boston BioPharmaPM Conference***

***September 21, 2010 Reggie Lewis Center, Boston, MA***

***“Delivering Value Through Projects”***

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- Leaders from top Life Science companies will discuss why project management is one of the most important capabilities for competitive advantage, how it's defined differently from other industries, and how it will evolve as a result of the industry trends.
- Conference speakers include:
  - Mike Bonney, CEO, *Cubist Pharmaceuticals Inc.*
  - Maryann Ciampa, Director, Office of Program Management and Services, *Becton Dickinson Diagnostics*
  - Rosemarie Day, former COO, *Commonwealth Health Insurance Connector Authority*
  - Rich Maltzman and David Shirley, authors, *Green Project Management*
  - Ron Rammage, Engineering Manager Software, *Abbott Medical Optics*
  - Dee Suberla, Senior Program Manager, *Baxter Pharmaceuticals & Technologies*

# *“Delivering Value Through Projects”*

- Learn how to redefine project success criteria by understanding the difference between delivering a product and delivering long-term sustainable value to the business and customers.
- Gain insight into practical and proactive techniques for building and executing effective program and project plans, including how to overcome some of the toughest challenges in building and maintaining a realistic schedule under pressure, and delivering a quality product to market.
- **Early Bird Special Extended Through August 31<sup>st</sup>!**
  - *BPPM Members: ~~\$299~~ \$249*
  - *Event & BPPM Membership: ~~\$339~~ \$289*
  - *Non-Members: ~~\$359~~ \$309*
  - *Groups of 3 or more: 20% Off*

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# *Agenda for Today*

- Current Biopharmaceutical Industry Model
- Science and the Science-based Business: A Brief Overview
- R&D Productivity: Definition and Dimensions
- Biopharmaceutical Value Chain: Discovery Research, Drug Development, and Commercialization
- Discovery Research
  - Stages – Objectives – Key Outcomes
  - Challenges – Opportunities – Pathways
- Future Outlook
- References



## *Credo of an Industry in Transformation?*

**“Reason is the understanding of necessity.”**

*Immanuel Kant*

# Threats to Current Business Model

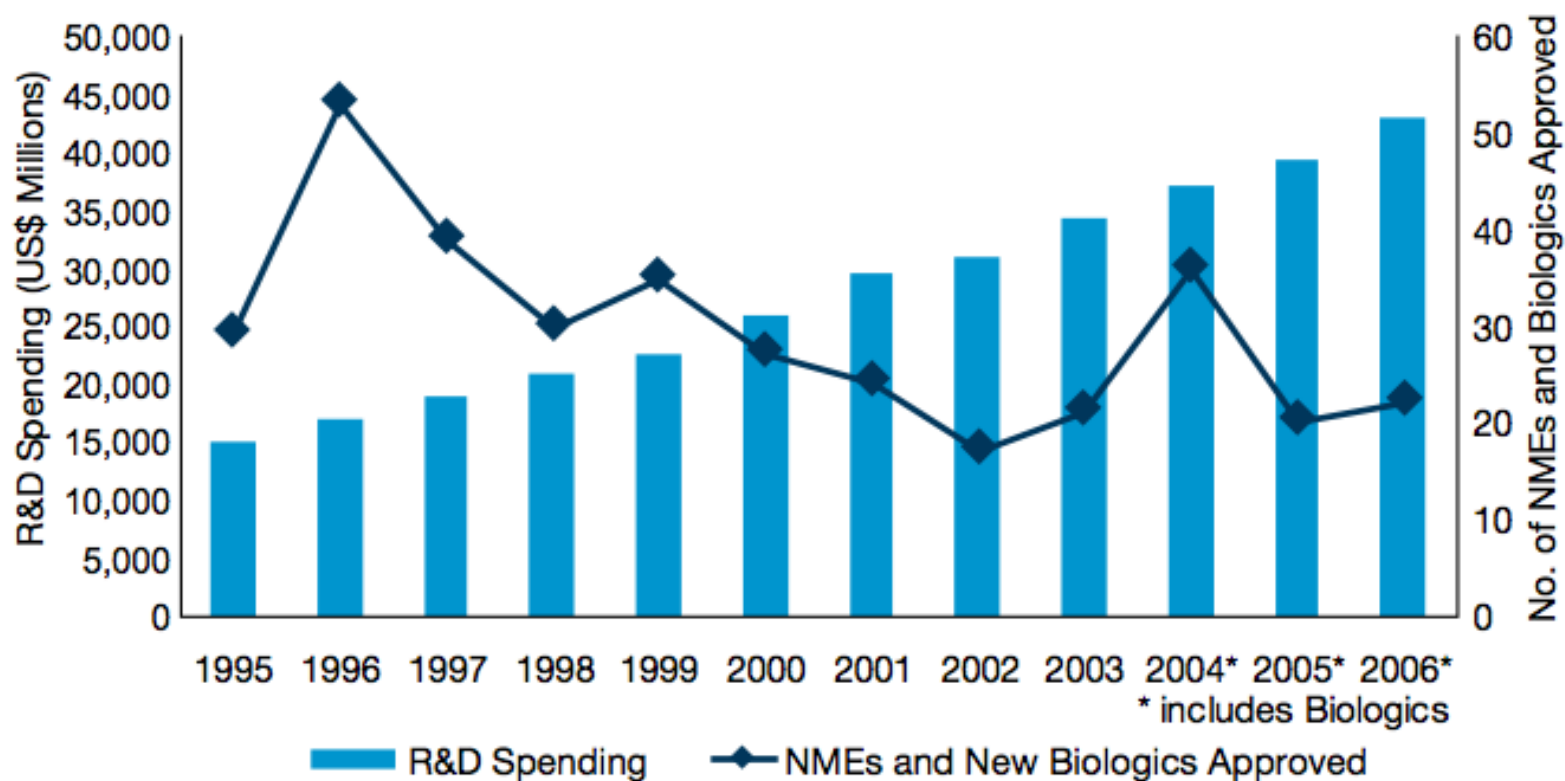
- \$850B loss in shareholder value (2000-2008)\*
- Pricing pressures\*
- Inroads by generics\*
- Industry P/E ratio decreased below S&P 500 index
- Declining profitability
- Decreasing growth prospects
- Increasing R&D investments for less NME approvals
- Revenue losses due to key patent expirations
- Increasingly cost-constrained healthcare systems
- More demanding global regulatory requirements

\* Source: Re-Building the R&D Engine in Big Pharma; Jean-Pierre Garnier, *Harvard Business Review* (May 2008).



# More Investments for Less Approvals

Figure 2: R&D spending has soared but the number of NMEs and biologics approved by the FDA is down

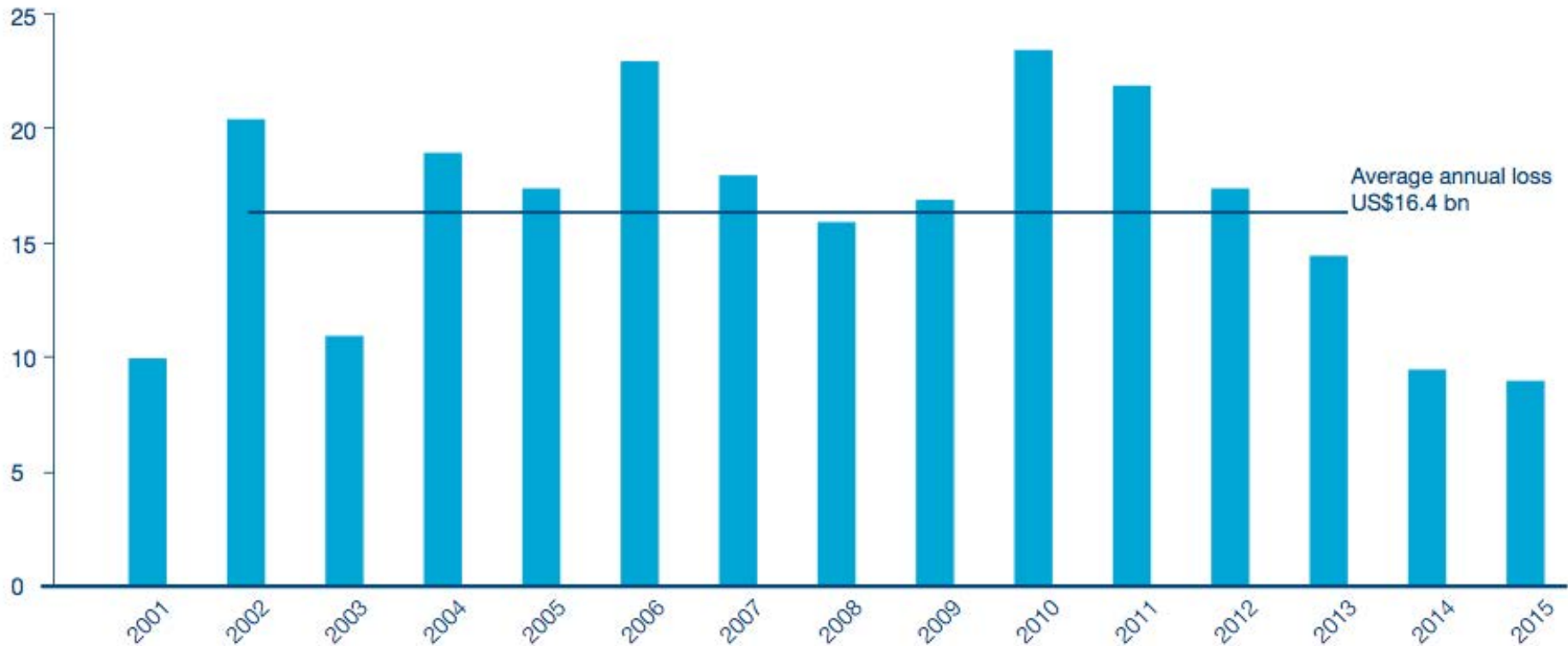


Sources: FDA/CDER Data, PhRMA data, PricewaterhouseCoopers analysis

Note: Data on R&D spending for non-PhRMA companies are not included here, because they are not available for all 11 years

# 2010-2015 Projected Sales Losses

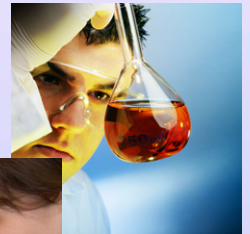
Figure 2. Impending losses stack up due to “patent cliff”



\$157 billion sales exposed to generic competition by 2011  
Source: IMS Health Midas

# *Science is the Heart of This Industry*

- “Science is about predictive power.” (Gary Pisano)
  - Predictive power is based on sufficient accumulation of underlying principles, cause-effect theories and supporting empirical evidence
- **Biopharmaceutical sciences are lacking predictive power**
  - Levels of biological complexity e.g. systems of molecular networks
  - Incompleteness of biological scientific knowledge
- **Implications on biopharmaceutical R&D are profound**
  - Highly iterative
  - High failure-to-success ratio



# *Science-based Business is Unique*

- The Science-based business model faces 3 fundamental challenges:
  - Risk Management
  - Integration
  - Learning
- These challenges are relevant to Discovery Research, Drug Development and Commercialization
- Specifically reviewed for Drug Discovery Research
  - Organization
  - Research Project Teams

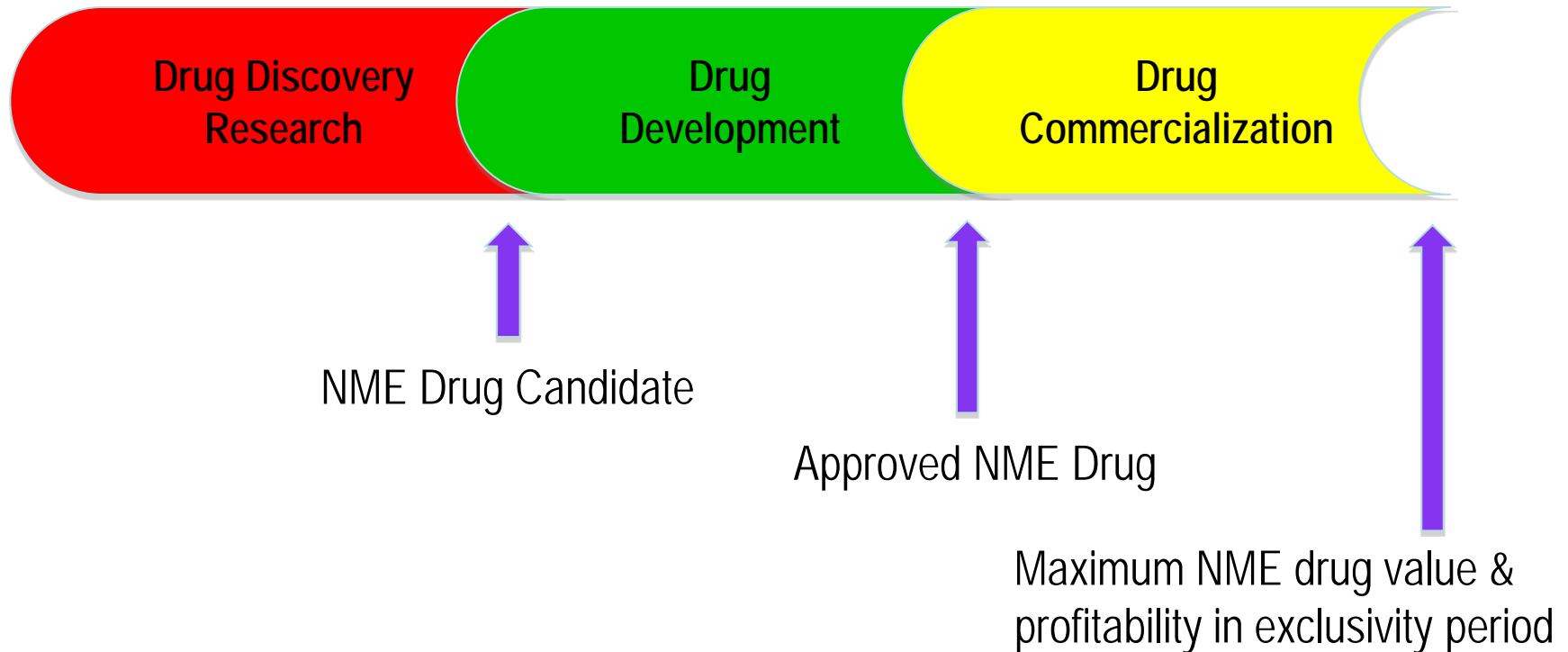
Source: The Evolution of Science-Based Business: Innovating How We Innovate Gary P. Pisano;  
Harvard Business School (Working Paper 10-062, 2010)

## *R&D Productivity is Considered Key*

“But I believe that declining R&D productivity is at the center of its (the biopharmaceutical industry) malaise.”

Source: Re-Building the R&D Engine in Big Pharma;  
Jean-Pierre Garnier, *Harvard Business Review* (May 2008).

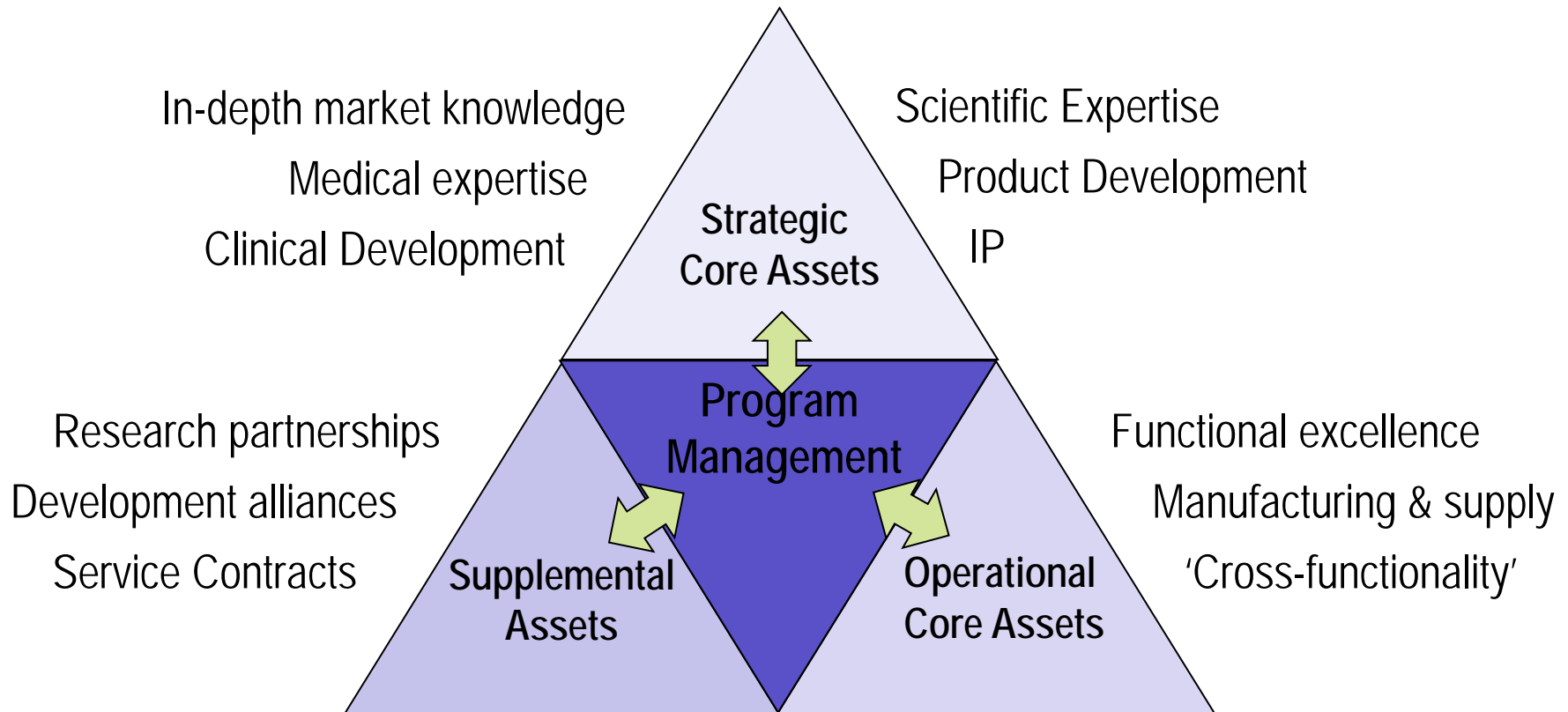
# *What are the Strategic Core Competencies of Your Organization?*



# *What Does Your Organization Need to Do to Address Productivity in R&D?*

- Determine your strategic core areas and your level of capabilities and competencies.
  - In-depth market knowledge
  - Medical & clinical development expertise
  - Scientific and product development expertise
- Determine your ability to execute efficiently and your level of capabilities and competencies.
  - Functional area excellence and 'cross-functionality'
- Determine your capabilities and competencies in managing your network of partnerships, alliances and service providers.

# *Program Management is Key to Integrating These Assets Productively and Creating Value*



# *Program Teams Directly Impact R&D Productivity*

$$P \propto \frac{WIP \times p(\text{TS}) \times V}{CT \times C}$$

numerator

denominator

**P = R&D Productivity**

**WIP = Work in Process** (total amount of scientific research conducted simultaneously; single NME or drug candidate equals WIP = 1, per project basis)

**P(TS) = Probability of Technical (& Regulatory) Success**

**V = Value (intrinsic valued outcomes)**

**CT = Cycle Time**

**C = Cost**

Source: How to improve R&D productivity: the pharmaceutical industry's grand challenge; *Nature Reviews Drug Discovery*, 9, 203-214 (March 2010).

# *Drug Discovery Research: Objective*



NME Drug Candidate

Efficiency: Quantity of NME drug candidates per year

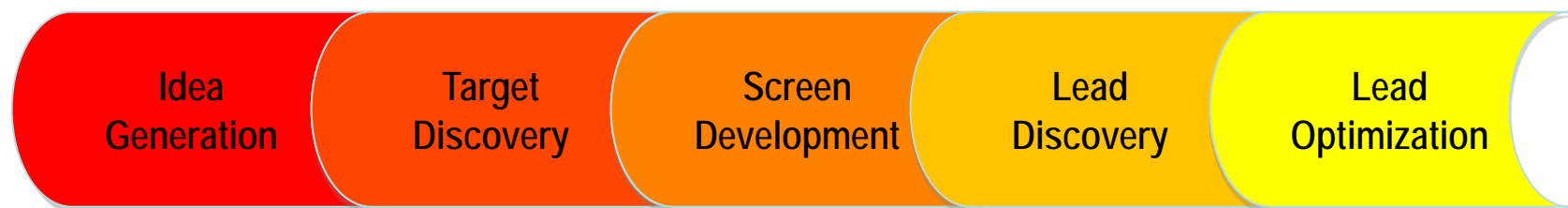
Effectiveness: 'Quality' of NME drug candidates by value attributes

*Generate a sustainable pipeline of validated targets, robust HT screens, NME hits, leads and drug development candidates.*

# ***Drug Discovery Research: Fundamentals***

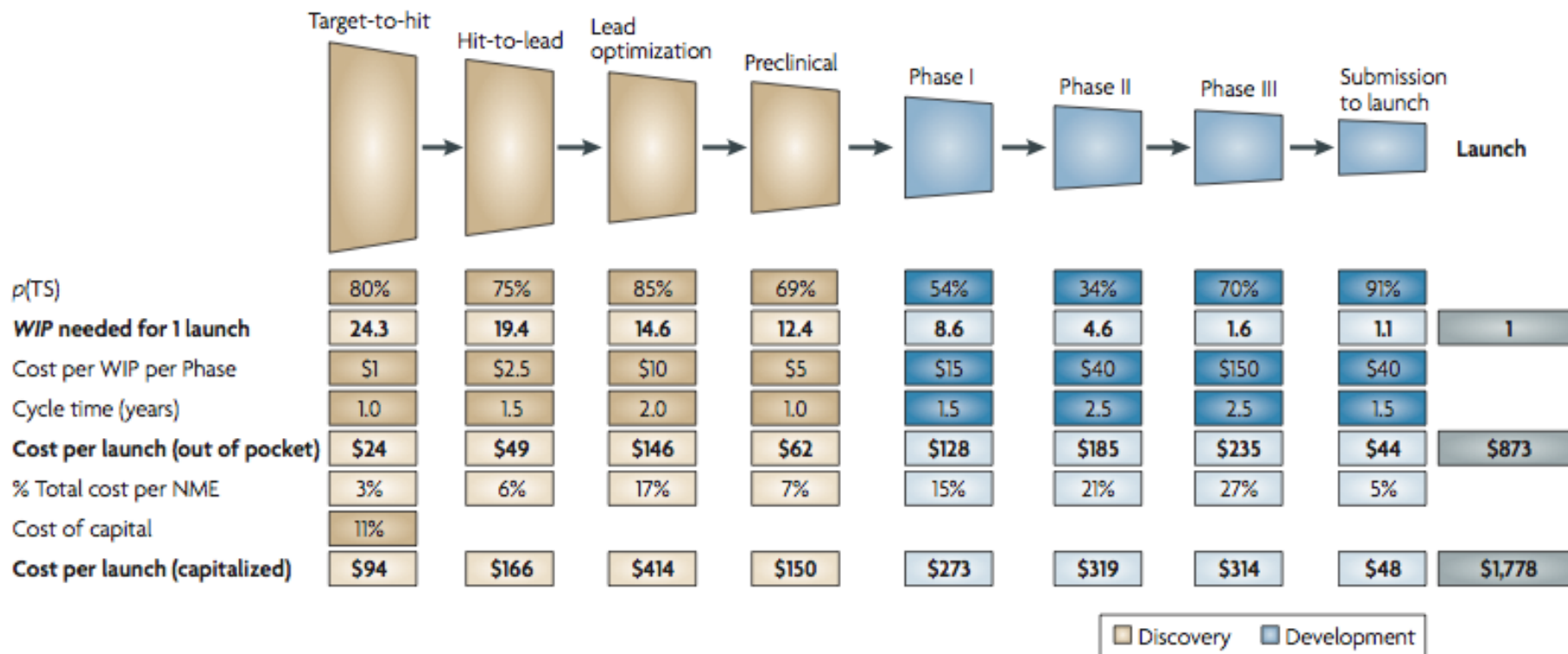
- Level of scientific/technical uncertainties & risks: ***Highest***
  - First-in-Class (vs. Best-in-Class) approach
  - Protein signaling pathways: normal vs. disease?
  - Criticality of target for overall disease pathogenesis?
  - Is target susceptible to therapeutic intervention?
- Need for integration (and systems thinking): ***Highest***
  - Novel disciplines e.g. functional genomics, proteomics
  - 'Computer-assisted' disease-area research; bioinformatics
  - Across organizations
- Need for Learning: ***Highest***
  - Highly iterative
  - Fail quickly, but productively to improve iteration cycles
  - Investment into key experiments to fail early

# *Drug Discovery Research: Stages & Key Outcome*



- **Idea Generation:** Research Plan Proposal
- **Target Discovery:** Validated Target for HTS
- **Screen Development:** 1<sup>st</sup> bioactive NME hits
- **Lead Discovery:** Bioactive 'drug-able' lead NME
- **Lead Optimization:** commercially viable NME drug candidate

# R&D Productivity Measures in Discovery Research



**Program Management focus: risks (attrition), costs, cycle time, WIP and value**

Source: How to improve R&D productivity: the pharmaceutical industry's grand challenge; *Nature Reviews Drug Discovery*, 9, 203-214 (March 2010).

# ***Drug Discovery Research: Challenges***

- **R&D Organization: A sustainable pipeline of programs/projects**
  - Identify strategic core strengths & capabilities in all stages
  - Balance novelty, complexity and diversity of programs/projects
  - Identify critical constraints e.g. Screening Development, Target Discovery
  - Is there critical mass in Lead Discovery & Optimization?
- **For Research Project Teams: Deliver sufficient 'quality' (e.g. value-added) programs in all stages**
  - Program/Project Team structure, size, and composition to ensure productivity in all stages
  - What is a productive level of science (risk, learning) vs. program management (integration)?

# ***Drug Discovery Research: Opportunities***

- **R&D organizations: Alliances & partnerships with academia, non-profit organizations and Discovery Research companies**
  - Stage-specific strategic alliances e.g. Bayer Schering/DKFZ in oncology (Target Discovery)
  - Share risk/return for first-in-class programs/projects (vs. potentially retaining best-in-class programs in-house)
  - Broad partnering and/or complete outsourcing of programs/projects e.g. EvoTec AG as fully-integrated discovery research organization
- **Research Project Teams: Ability to operate with critical mass for in-house programs/projects**
  - Team structure, size, and composition adapted to partnerships
  - Increased level of program management (integration)

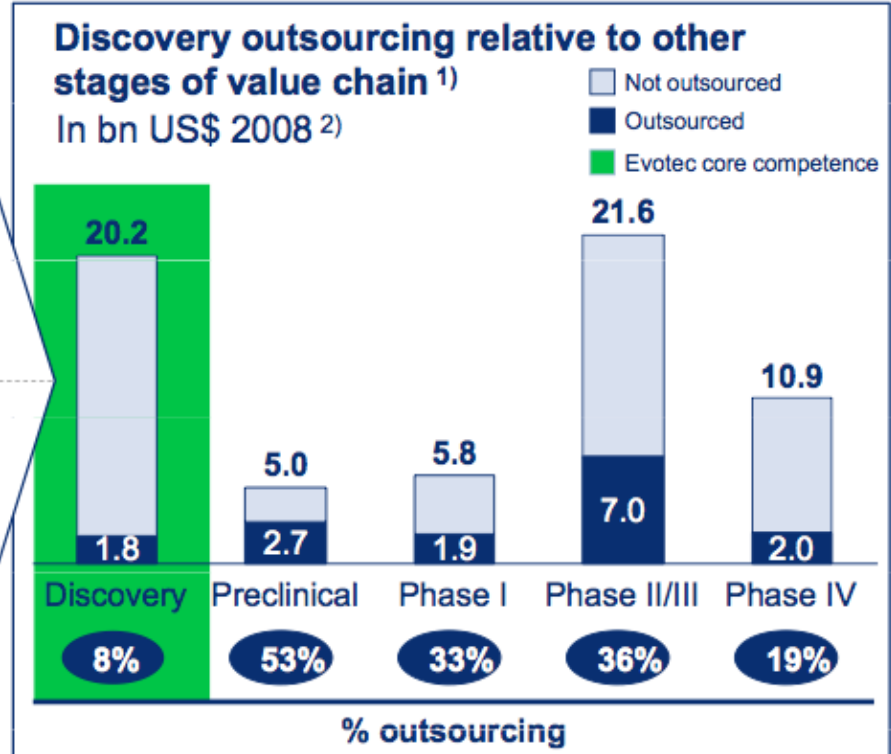
# Discovery Research: Future Pathways (Example)



## The opportunity of the drug discovery industry

### Key reasons for growth

- 1 Pipeline needs will keep R&D expenditures at least at current levels, but with a strong demand for increased productivity
- 2 Outsourcing and joint innovation teams lead to higher efficiency in the drug discovery process
- 3 Top-class scientific offerings will become high growth businesses as fixed costs become variable
- 4 Only a few players have built up scientific quality for sustainable innovation alliances



Source: Evotec AG, Company Presentation July/August 2010

# Discovery Research: Future Pathways (Example)



## Fully integrated R&D platform from target to clinic

### Technology overview

Screening	Hit-to-lead	Lead optimisation	Preclinical development	Clinical development
<ul style="list-style-type: none"> <li>Assay development &amp; screening</li> <li>(u)HTS</li> <li>High content screening</li> <li>Electrophysiology</li> <li><i>In silico</i> screening technologies</li> <li>Fragment-based drug discovery</li> </ul>	<ul style="list-style-type: none"> <li>Medicinal chemistry</li> <li>Hit expansion</li> <li>Library design</li> <li>High throughput chemistry</li> <li>Protein-ligand crystallography</li> <li><i>In vitro</i> biology</li> <li>Early ADMET</li> </ul>	<ul style="list-style-type: none"> <li>Medicinal chemistry</li> <li><i>In vitro</i> biology</li> <li>Target class expertise</li> <li>Computational chemistry and structure-based drug design</li> <li><i>In silico</i> ADMET</li> <li><i>In vivo</i> pharmacology</li> </ul>	<ul style="list-style-type: none"> <li>Custom synthesis</li> <li>Analytical development</li> <li>Process R&amp;D</li> <li>Large scale synthesis</li> <li><i>In vivo</i> pharmacology</li> </ul>	<ul style="list-style-type: none"> <li>Clinical alliances</li> <li>Clinical project management</li> </ul>

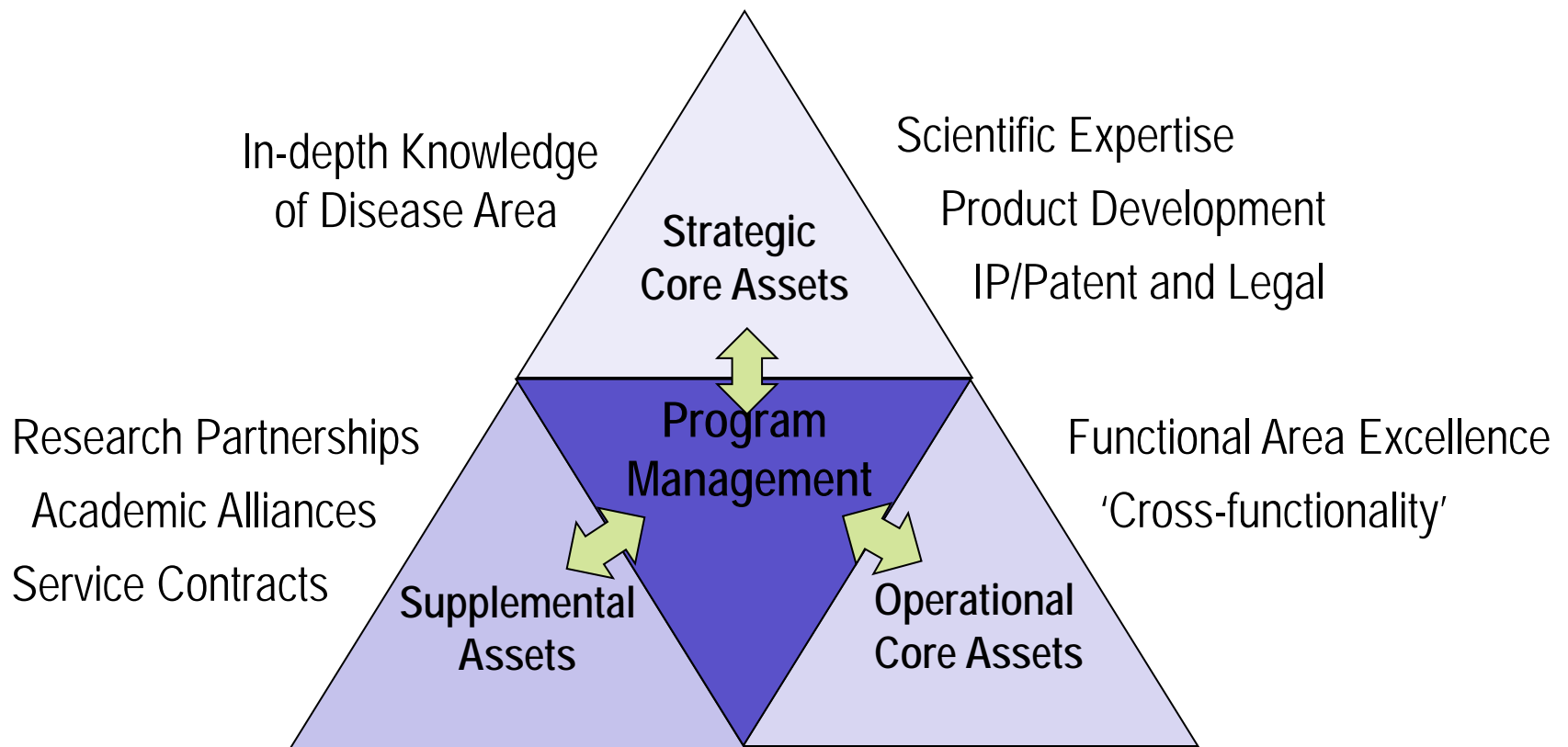
Disease biology expertise

Proven programme management

Flexible deal structures

Source: Evotec AG, Company Presentation July/August 2010

# *Research Project Teams are the Key Units to Contribute to Overall R&D Productivity*



# *Discovery Research: Proposed Team Structure*

- **Highly Flexible, Evolving and Adaptive Program Teams**
  - *Target Discovery*: Strongly biology; disease area or platform-driven
  - *Screen Development*: Biology, chemistry, computer sciences
  - *Lead Discovery*: Chemistry, biology, pharmacology, ADMET
  - *Lead Optimization*: Above + selected drug development core disciplines
- **Team Leaders from a Scientific Discipline**
  - Strong scientific focus (risk, learning)
  - Strong productivity, outcome and value orientation
  - Program management competencies based on integration level e.g. partnerships, alliances

## *Outlook into the Future*

- Biopharmaceutical organizations need to assess their spectrum of core assets (strategic, operational, supplemental) to understand their position in the value chain.
- R&D productivity is a key measure to build a sustainable pipeline of 'quality', value-added NME drug development candidates.
- Program management is a strategic discipline to ensure R&D productivity.
  - Key to integrating all core assets productively on organizational, functional and team level.
- The Program Team will be the most important smallest operating unit.
  - With capabilities and competencies needed to be effective and efficient
  - Specifically organized per research stage, highly integrated

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## Upcoming Events/Courses

Sept 21, Boston BPPM Conference  
**Delivering Value Through Projects**  
Reggie Lewis Center, Boston, MA

Sept 14-16 and Oct 6  
**mScholar PMP Exam Prep 3+1** (Deerfield, IL)

Sept 28 (Kick-off), Tuesdays@12pm Eastern  
**mScholar PMP Exam Prep Virtual Study**  
Group (10 sessions)

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# *Backup Slides*



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