



Where will the future source of Innovation and wealth creation in Pharmaceutical research come from?

A personal perspective: Opportunities for innovation and entrepreneurialism from academia and small companies

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To create a successful spin out company

Identify the business sector.

Identify a key need in the sector.

Create a product or provide a service that meets the business need.

Be consistent in quality

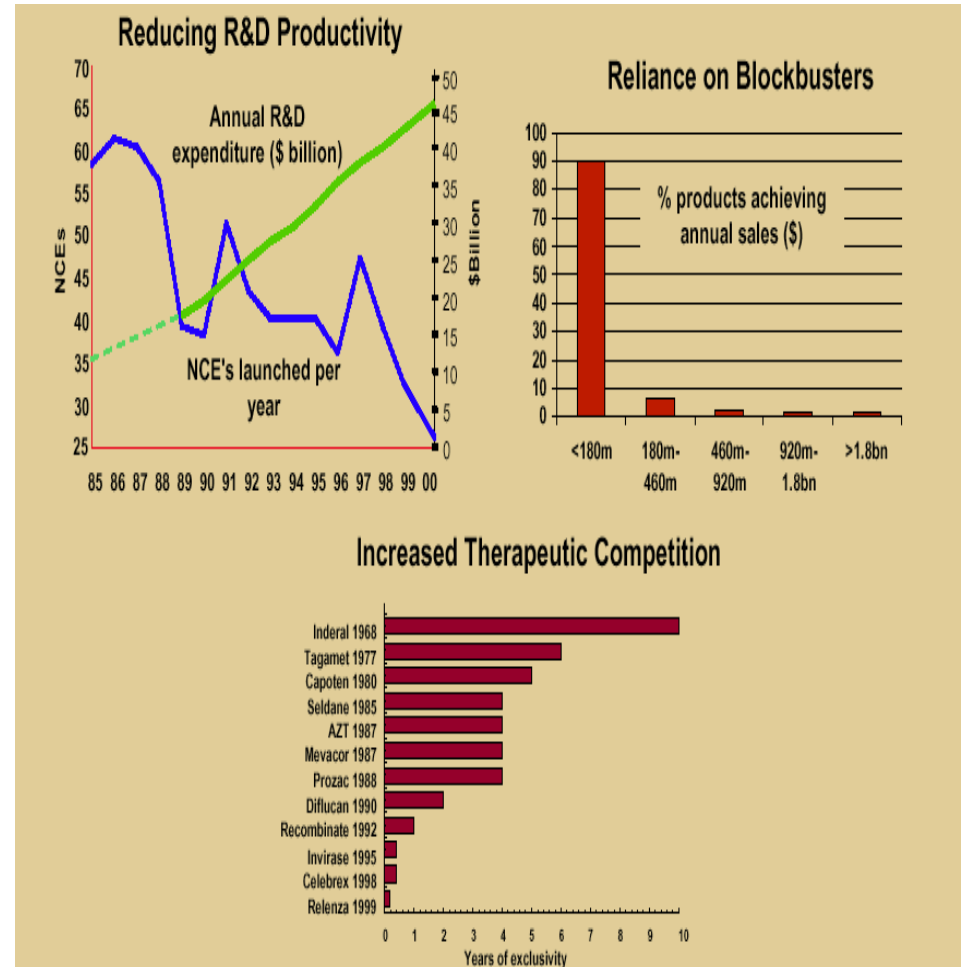
Evolve !

Agenda

- The pressures associated with productivity and return on investment in major pharmaceutical company R and D
- How relationships between academic groups and Entrepreneurial small companies will help sustain innovation and growth in the pharmaceutical sector
- The importance of networks
- Opportunities for new science disciplines, in particular nanotechnology
- The ability to respond to changing environments

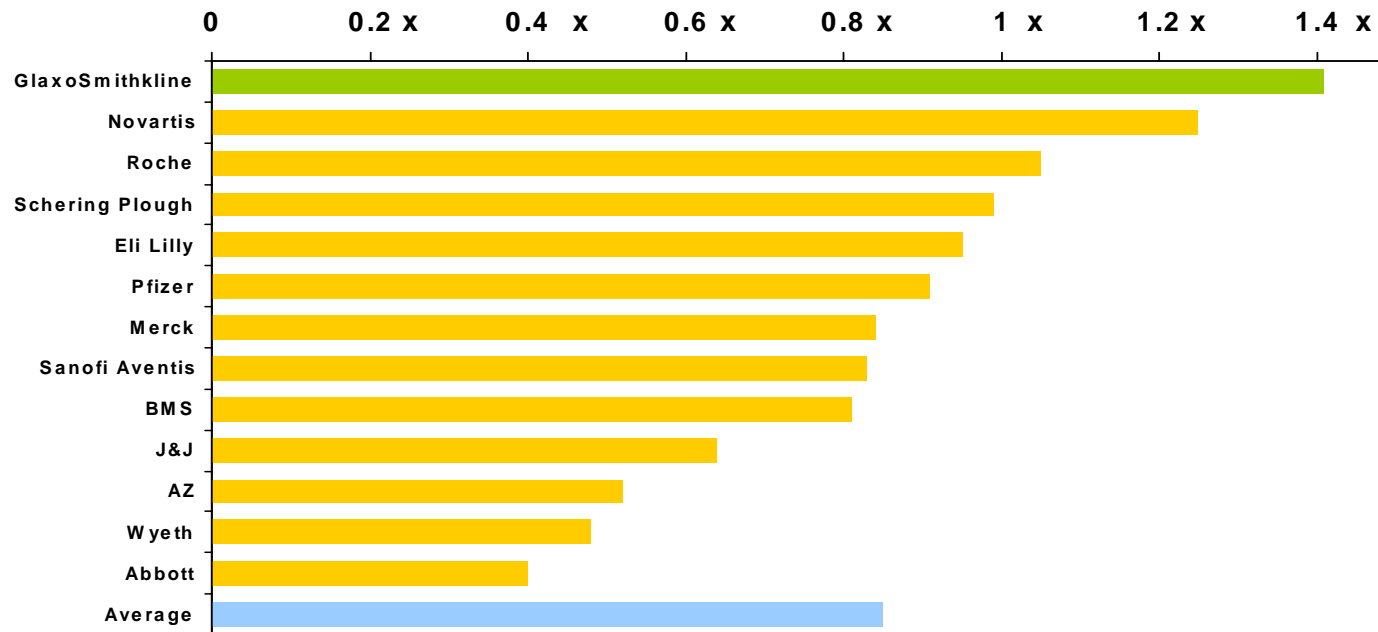
The pressures associated with productivity and return on investment in major pharmaceutical company R and D

- The industry is spending more on launching fewer drugs
- There is decreased exclusivity for new product indications
- Major Pharma needs large drugs to cover its costs or large numbers of multi indication smaller products



The pressures associated with productivity and return on investment in major pharmaceutical company R and D

Pipeline Replacement Power - Sales



Peak sales of expected Product launches (risk adjusted) divided by 2005 sales



The Challenge

To maintain 10% annual growth and justify their R & D spend the top tier companies will need to launch at least 4 £500 million per annum drugs every Year

So where can spin out companies provide the solutions?

Increased productivity:

Decreased time to discover new entities

Decreased time to bring them to clinic

Decreased Costs

Increased product lifetime

Access to new products- Inlicensing

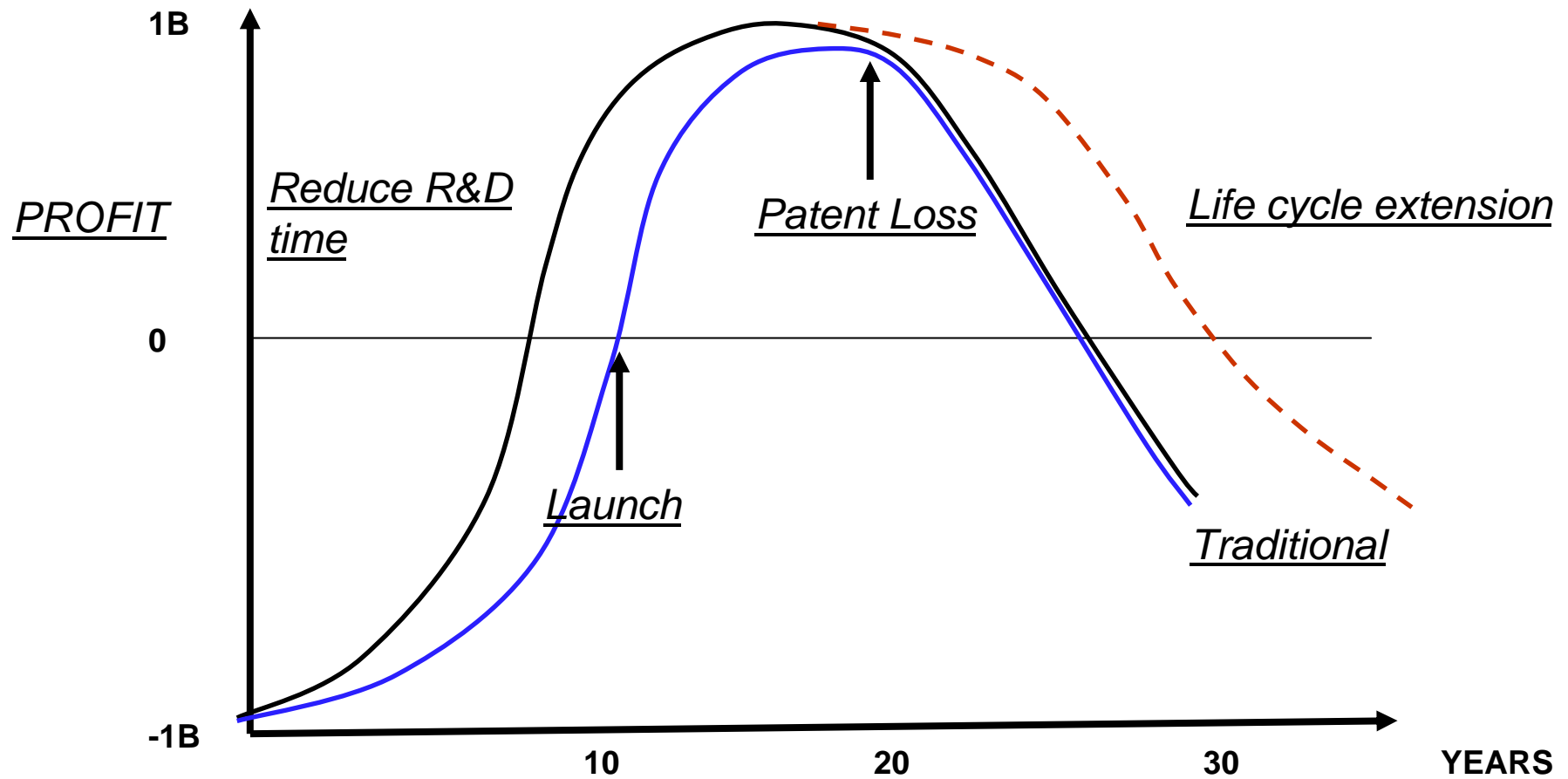
Opportunities for small companies and academics

Access to new technologies

Staying at the cutting edge of technology

- Nanotechnology

Life Cycle Management



Opportunities for academics and small companies to help sustain innovation

- Small companies are continually spinning out of universities in the UK and the US to capitalise on commercial needs within the pharmaceutical sector
- All companies are looking to licence in technologies that meet their needs from academia and spin outs
- University departments are increasingly carrying out their own drug discovery programmes

Opportunities for academics and small companies to help sustain innovation

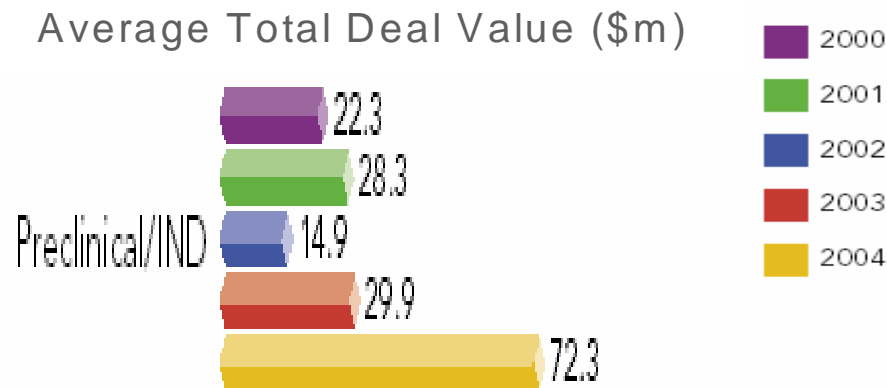
- In Licensing products
 - The internal productivity of the large Pharma and Biotech companies is not sufficient to meet the financial targets of these large companies
 - For major Pharma companies 40-60% of their pipeline comes from external In Licensed products
 - This trend is set to grow

Opportunities for academics and small companies to help sustain innovation

- In Licensing Products
 - The initial trend was to in license Phase 3 compounds
 - As competition grew amongst the big companies earlier phase products were in licensed
 - Phase 1 and pre-clinical compounds are now actively being sought
 - The value of all assets has increased as a consequence of this competition

Opportunities for academics and small companies to help sustain innovation

Preclinical / IND Deal Valuations



Source: Data from Windhover's Strategic Intelligence Systems database, Analysis by Burrill & Company

Opportunities for academics and small companies to help sustain innovation

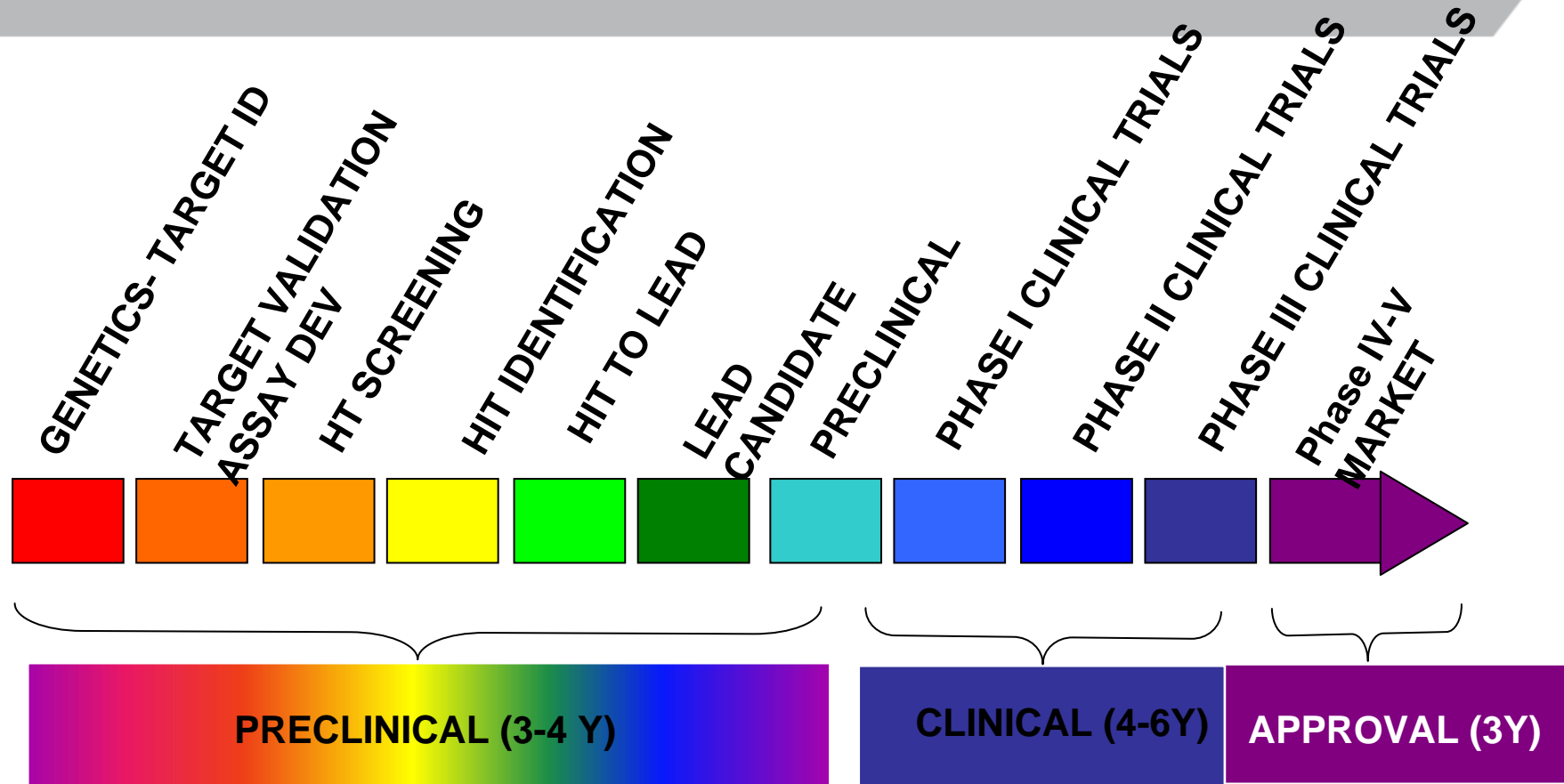
- In 2006 more patents and more IND's were filed by the biotech, small company and academic sector than by big Pharma companies

The Importance of Networks

- Novartis have a total of 450 collaborations
- 150 are with Biotech
- The Novartis forecast for 2010 is that only 34% of their NME's will come from internal research
- Merck evaluates 5000 in licensing opportunities per annum
- Big pharma winners of the future will need a very big network for the identification of external leads.

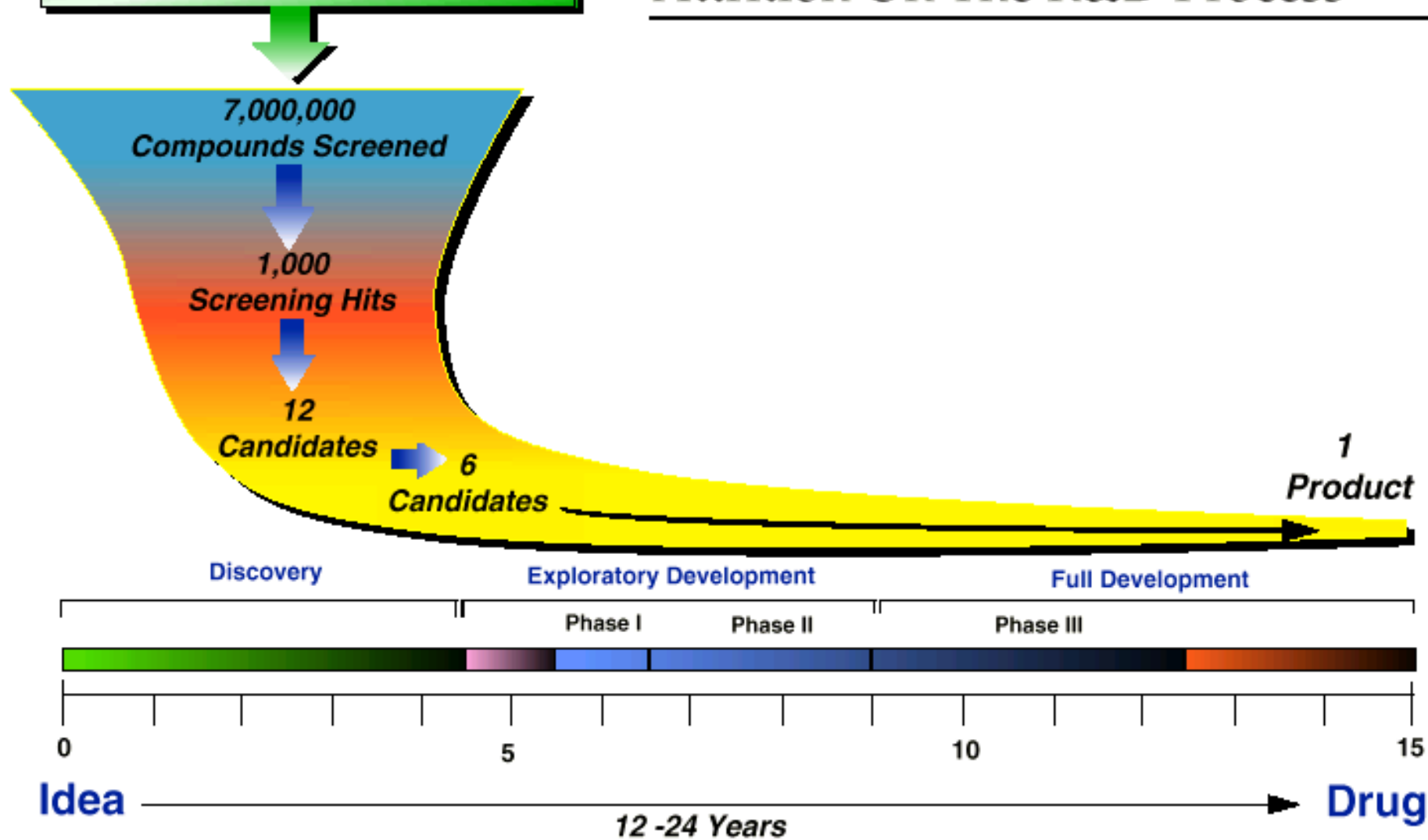
Opportunities for new technology spin outs e.g.. nanotechnology

The Spectrum of Drug Discovery and Development Activities

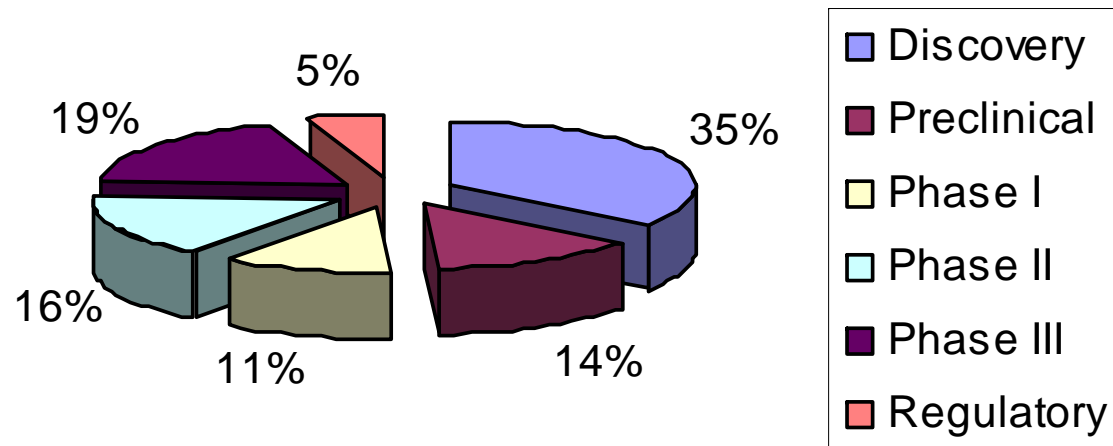


~100 Discovery Approaches

Attrition On The R&D Process



% Expenditure at different phases of drug development



Total expenditure approx US\$ 1Bn

Analysis by stage of the Nanotechnology Opportunities in Pharmaceutical R and D

- **D. Lead Candidate**
- Selection of the candidate for development - if wrong potential loss of \$800m
- Nanotechnology - human diversity
- More accurate prediction of efficacy
- More accurate prediction of toxicology
- More accurate prediction of metabolism
- Lower attrition rate in development

Analysis by stage of the Nanotechnology Opportunities in Pharmaceutical R and D

- **Pre-Clin**
- Establish the safety of the drug candidate in animal studies and identify the dose. Identify the initial formulation for administration to animals and man. Study pharmacokinetic & pharmacodynamic properties of the candidate drug. Begin assessment of stability. Identify potential route to manufacture and produce phase 1 supply.
- Nanotechnology
- Imaging studies - use of nano-materials in imaging, nano-synthesis in PET (Positron Emission Topography)
- Rapid Screening & optimisation of route and process of synthesis - can be much faster with reduced lead times and reduced use of expensive materials
- Rapid identification of the optimal formulation
- Toxicology studies - remote sensing of concentration of key parameters i.e. heart rate, blood pressure, levels of specific hormones.
- Identification and measurement of key Biomarkers - minimal disruption of system observed
- Potential for elimination of animal studies

Analysis by stage of the Nanotechnology Opportunities in Pharmaceutical R and D

- Clinical
 - **Phase I**
 - First administration (safety study) in Man! Dose ranges administered to a small group (10) of healthy human beings. Acute life threatening diseases i.e. cancer, aids may use patients
 - Nanotechnology
 - Imaging - in all aspects providing effective data mining but creating issues around data storage
 - Remote Sensing of key parameters - potential for patients being monitored at home
 - Measurement of key biomarkers
 - Dosing Machines - measure concentration and automatically administer drug to maintain optimum levels

The conclusion

- Having a robust strategy for the appropriate application of nanotechnology in the drug discovery and development process will
 - Reduce lead times in discovery
 - Increase knowledge as to the best candidates to take forwards
 - Reduce pre-clinical and clinical failures
 - Reduce the potential for unwanted side effects
 - Reduce product withdrawals**Leading to Increase in share price!**

Beyond Pharmaceuticals?

“Medicine is one area where nanotechnologies are likely to make an especially profound impact. Because artificial nanostructures, such as nanoparticles and nanodevices, are of comparable size to biological entities, they can readily interact with biomolecules inside cells and on their surfaces – and are therefore likely to create a revolution in diagnostic and therapeutic methods. They could do much to meet the need for improved, more efficient and affordable healthcare to address the challenge of Europe’s ageing population and meet increasing expectations for a better quality of life.”

European Commission for Research in Industrial Technologies
ec.europa.eu/research/industrial_technologies/articles/article_2971_en.html

Beyond Pharmaceuticals?

- “What if doctors could search out and destroy the very first cancer cells that would otherwise have caused a tumor to develop in the body? What if a broken part of a cell could be removed and replaced with a miniature biological machine? What if pumps the size of molecules could be implanted to deliver life-saving medicines precisely when and where they are needed? These scenarios may sound unbelievable, but they are the long-term goals of the NIH Roadmap's Nanomedicine initiative that we anticipate will yield medical benefits as early as 10 years from now.”
 - NIH Roadmap for Medical Research

www.zyvex.com/nanotech/feynman

The key to success! :The ability to respond to changing environments

It is all about evolution!

“It is not the strongest of the species that survives, nor the most intelligent that survives. It is the one that is the most adaptable to change!”

Charles Darwin



Thankyou for your
attention

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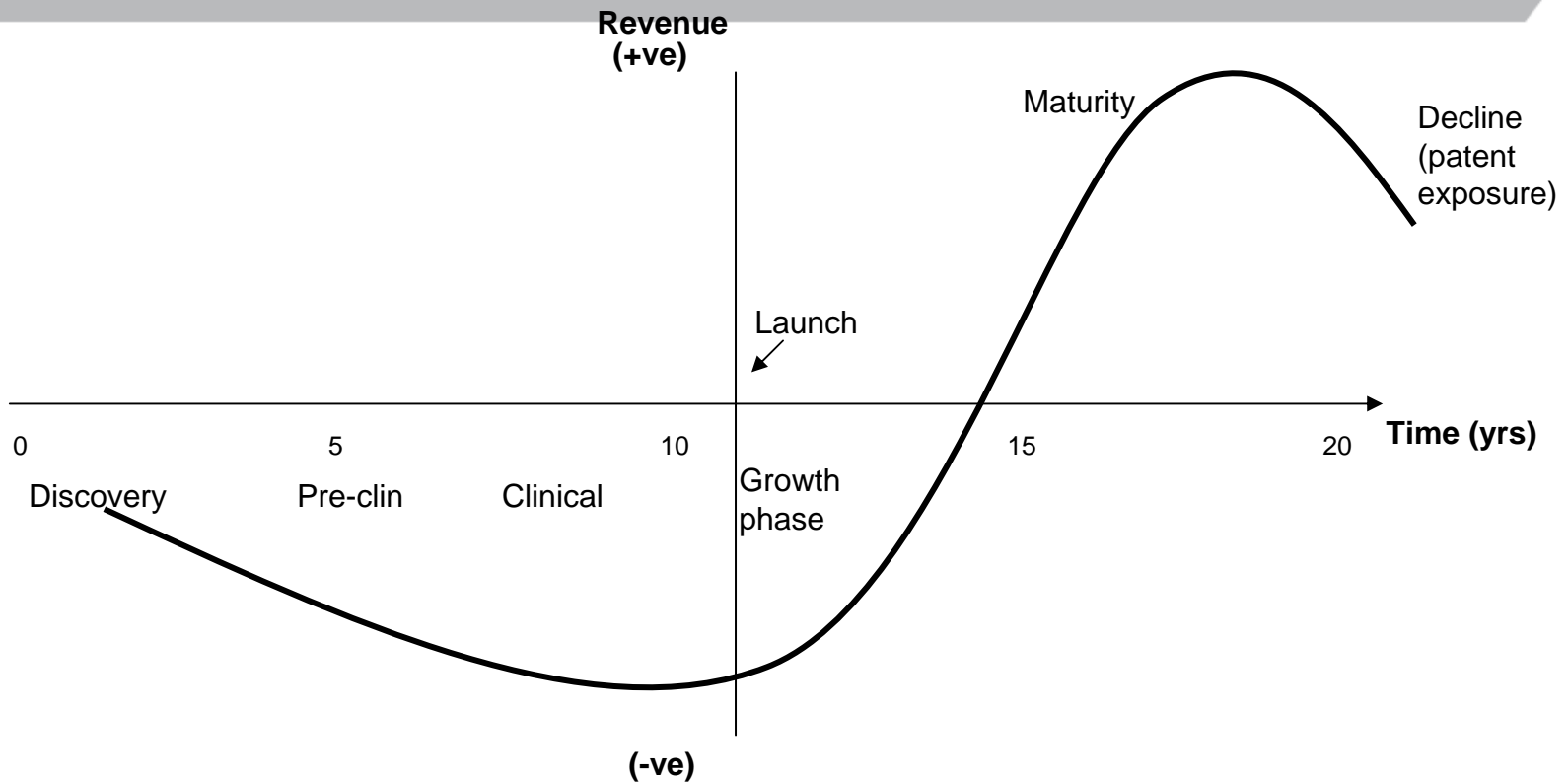
Additional slides for information

The pressures associated with productivity and return on investment in major pharmaceutical company R and D

“Unless drugs firms continually bring enough new products to market to replace lost revenues they will shrivel and die. “Yes, this is a 'cyclical' downturn,” says AstraZeneca's Mr Brennan. “But a lot of the top 20 drugs firms [of a few years ago] aren't around any more because they couldn't get out of the last cyclical downturn by coming up with key new drugs.””

Jan 25th 2007 | NEW YORK
From *The Economist* print edition

THE TRADITIONAL PHARMA MODEL



Productivity gains must be sought during discovery, development and commercialisation phases

The Importance of Networks

- “Mr Kindler (CEO Pfizer Inc) also wants his secretive researchers to open up and work more closely with outsiders. He has put the company's drugs pipeline on the internet for all to scrutinise and declared his intention to pursue outside collaborations and acquisitions keenly.”

Jan 25th 2007 | NEW YORK From *The Economist*
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Analysis by stage of the Nanotechnology Opportunities in Pharmaceutical R and D

- **Target Validation**
- Establishing a robust connection between the gene or protein and the disease
- Nanotechnology
- Speed up process

- **Assay Development**
- Development of robust biological techniques (assays) for measuring quantifiably the effect of compound, protein, gene or even virus on a biological system
- Nanotechnology
- Speed up process
- Reduced quantities of biological and chemical materials required
- Massive reduction in costs

Analysis by stage of the Nanotechnology Opportunities in Pharmaceutical R and D

- **Genetics**
- Proteomics - identify proteins/genes and protein/genes function
- Understanding which proteins/genes have which function Nanotechnology
- Studying structure
- Means of detecting & quantifying
- Analysis
- Synthesis
- **Target Identification**
- Identification of a specific protein or gene and associating its function with a disease state
- Nanotechnology
- Rapid screening
- Data storage and information mining

Analysis by stage of the Nanotechnology Opportunities in Pharmaceutical R and D

- **Screening**
- Running the assay, gathering data, storing and mining. This stage currently requires storage of masses of information, large quantities of re-agents and compounds
- Nanotechnology
- Speed up the process
- Reduction in volume/scale of activity
- Increased accuracy of results
- Reduced costs
- **HIT Identification**
- Take the screen data, re-qualify hits and generate knowledge
- Nanotechnology
- Speed up data mining
- Provide better cross referencing and more accurate information
- Assist in more effective decision making
- Nanotech facilitated artificial intelligence

Analysis by stage of the Nanotechnology Opportunities in Pharmaceutical R and D

- **Phase II**
- Second administration in Man! Dose ranges administered in a larger group (40 +) to check for efficacy.
- Nanotechnology
- The same points apply as in Phase I with the addition of the following:-
- Imaging - focussed on changes in disease state
- Patients can potentially be monitored at home.

Analysis by stage of the Nanotechnology Opportunities in Pharmaceutical R and D

- **Phase III**
- Wider ranging studies in patients. Key pivotal registration study which will allow regulators to approve the drug.
- Nanotechnology
- Data collection via remote sensing
- Enhanced data storage and mining
- Greater focussed imaging studies
- **D. Phase IV**
- Usually conducted retrospectively when the product is on sale, studies have market penetration and scope is increased. Currently there are no remote imaging applications with difficulties experienced tracking and maintaining data collection.

Analysis by stage of the Nanotechnology Opportunities in Pharmaceutical R and D

- **Phase V**
- Currently poorly done and retrospective with the cumulative effects identified in an untimely fashion.
- Current and future technology will make this stage more effective providing results in real time. This area has the potential to pick up an early VIOX before the catastrophic damage occurs!
- Nanotechnology
- Monitoring in real-time and cumulative effects picked up early