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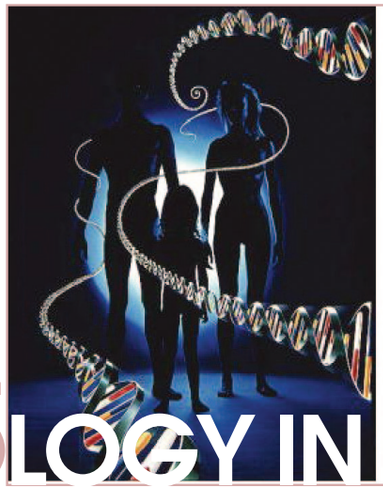

INDUSTRIAL BIOTECHNOLOGY IN PHARMACEUTICAL RESEARCH AND PRODUCTION

With the publication of **the human genome sequence biotechnology** became one of the key drivers of innovation across many industry sectors and virtually all areas of human life. Up to 5,000 disease targets will become available for pharmaceutical research and integrated technology platforms will serve as the basis for efficient drug discovery and further progress towards curative treatment especially in areas where the standard of disease management is poor.

Genomic research is now successfully used to understand the underlying disease mechanisms and explore new medical treatment strategies (Figure 1). In drug discovery new active substances (lead structures) are identified in *highthroughput-screening* and optimized with modern chemical methodology. First products from genomic drug discovery are now reaching the market among which are small chemical entities as well as biopharmaceutical drugs.

Genetic variation among individuals will be an important element of future drug development (Pharmacogenomics). The modern drug discovery process leads to small molecules that can be produced chemically as well as large biomolecules where industrial biotechnology provides the basis for manufacturing. Traditionally, biomolecules were isolated from various natural sources. With the development of sterile fermentation procedures, microorganisms and later also complex mammalian cells could be cultivated under optimized conditions. In recent years modern biotechnological methods including genetic engineering have become widely accepted for the prevention, diagnosis and treatment of disease. Since 1982 a large number of recombinant drugs have been approved for the treatment of chronical and life threatening diseases and there are hundreds of second generation products under clinical investigation (Figure 2). In the foreseeable future transgenic plants and animals will become important tools in drug production and eventually somatic gene therapy will complement the spectrum of available techniques. The worlwide commercialization of biotechnology is gathering momentum. Dramatic infrastructural changes are leading to promising cooperations and strategic development alliances between big pharmaceutical companies and smaller biotechs with synergies in both directions. The biotech industry itself gains critical mass with a growing activity in intra-biotech mergers and acquisitions (Table). The development of a new pharmaceutical drug is both time-con-

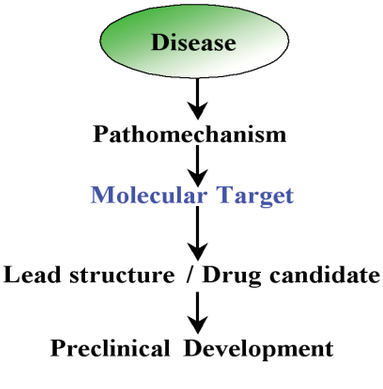

Figure 1 - Development of new drugs in the post genomic era

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suming and expensive. Product development is usually performed in several phases with critical technical issues to be defined very early on (Figure 3).

An integrated, robust, cGMP-compliant manufacturing process is vital for the success of the product. Among other limitations of the industry's growth potential there is a worlwide shortfall of available biomanufacturing space. Access to cGMP production capacity is becoming a critical strategic issue for companies especially in the area of mammalian cell culture and one of the driving forces towards higher efficiency and productivity. Optimized development and manufacturing platforms are now becoming recognized as highly relevant for the ultimate success of the biotech industry. Modern large scale processes for secreted biomolecules derived from fermentation follow the streamlined concept of cell removal, followed by a capturing step, intermediate purification and polishing. Trends in bioprocess engineering and fermentation development challenge the downstream processing towards continuous state of the art operations. Despite the complexity

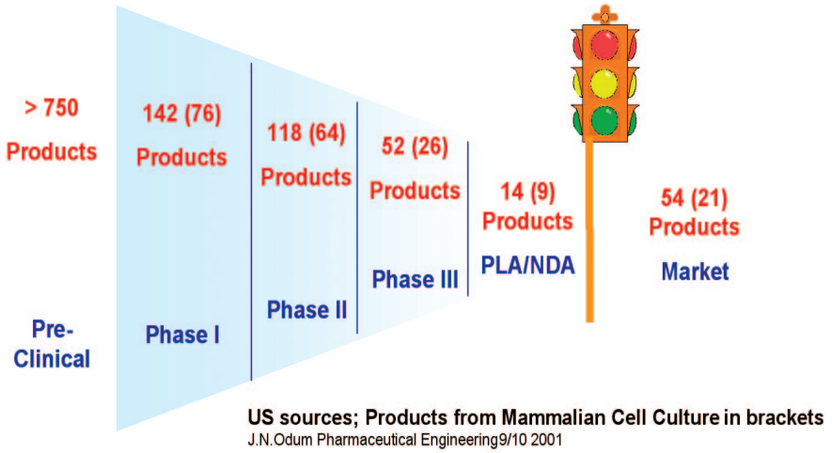

Figure 2 - The biotech product pipeline

The Biotech Industry matures... Core Biotech Industry Usa/Europe 2002

Countries	Total revenues	Companies*	Employees	R&D Expenses	Dev. Products Total	Dev. Products Phase III
Usa	33.6 bill $	1,466 (318)	194,600	20.5 bill $	369*	66**
Europe	12.9 bill €	1,878 (102)	82,100	7.7 bill €	254*	53**

* Start-ups, small companies, mid-size and large companies. Public companies in brackets; ** Public companies
(Source: Ernst & Young, Beyond Borders: The Global Biotechnology Report 2003)

Genetic variations among individuals will be important elements in pharmacogenomics

of biotech processes there is room for improvement with integrated unit operations, automation and rational design of facilities and equipment. One of the most recent enabling technologies for large scale biomanufacturing is the use of disposable bags and plastic tools in upstream (fermentation) as well as downstream (purification) processing. Several comparative analysis have proven the feasibility of disposable systems as there are a number of advantages such as no cleaning and validation requirement, lower investment costs and greater flexibility with regard to handling and space requirement. Altogether there is a clear tendency towards disposable technology in the different areas of biomanufacturing.

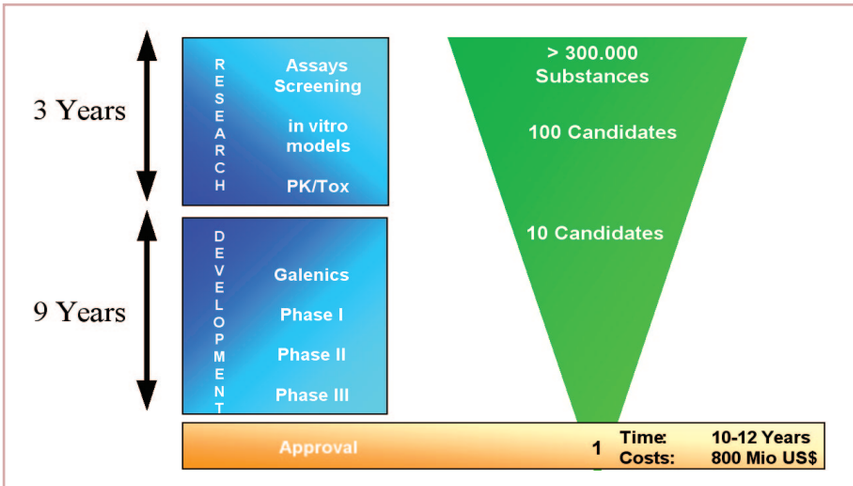

Figure 3 - Drug development from lead to launch