The impact of biotechnology on modern healthcare and drug development

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Peter Reinish, partner at Global Life Science Ventures, argues that biotechnology will play a decisive role in the development of the healthcare sector.

Health is the most fundamental of human needs, and the priority accorded to healthcare reflects the overriding importance of health to people's lives and general well-being. In this article we will argue that, in the 21st century, biotechnology is set to play a decisive role in the development of the healthcare sector, meeting unmet medical needs and bringing to market powerful, innovative new drugs.

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Biotechnology has already yielded safer, affordable therapeutics, and the most successful drugs issued from biotechnology have already included several blockbusters with sales in excess of $1 billion (€784 million). The sector is proving to be one of the most important drivers of the healthcare industry and a source of innovation for pharmaceutical companies. Extending well beyond the techniques of "gene cloning" or "gene transfer", biotechnology today encompasses breakthrough developments in many medical research areas, including pharmacogenomics, RNA interference applications, stem cell research and protein therapeutics.

There are huge unmet medical needs

The extent of currently unmet medical needs is apparent if one considers that of about 30,000 known diseases, only a third can be treated and most lack cures [1]. There are only limited or, in many cases, no effective treatments available for AIDS, Alzheimer's disease, multiple sclerosis, the many different forms of cancer and cardiovascular disease, as well as inherited diseases such as muscular dystrophy and cystic fibrosis. Where treatments exist they often have significant side effects, and many individuals do not benefit from treatment. Chronic, noncommunicable diseases (NCDs) alone now account for 59 percent of the 57 million annual deaths occurring worldwide. The burden of chronic diseases is set to have a major impact on healthcare systems and economies across the world, with an expected cost in 2007 of over $200 billion.

New infectious diseases also regularly arise, and AIDS and avian flu are just two major examples of the challenges these represent. Today, there are still no marketed vaccines for AIDS, malaria, and tuberculosis, the "big three" in the infectious disease panorama.

With the steady increase in lifespans in the developed world comes also an increase in degenerative diseases and morbidity, leading to rising healthcare costs and greater demands on increasingly fragile healthcare systems. There will therefore be a growing need for cost-effective new drugs and solutions to decrease the amount of time spent by patients in hospitals.

Modern science can make a difference
Although these challenges are considerable, history has repeatedly shown that research into the causes of diseases leads to more effective treatments. Insulin has saved many diabetics from an early death, and penicillin has saved countless lives. Vaccines have been developed against childhood diseases such as measles, mumps, diphtheria, tetanus and rubella, as well as the debilitating disease polio, and smallpox has been eradicated.

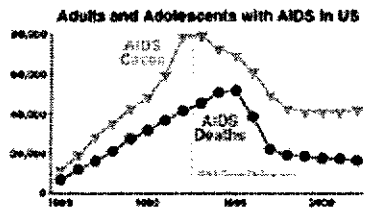

Figure 1: Gladstone Institutes, UCSF [2]

A more recent example is AIDS, which shows the tremendous progress medical science can make in transforming an invariably fatal disease into a manageable one (Figure 1). Biotechnology has had a major impact on several fronts in the fight against AIDS, including the following breakthroughs:

-Identification and sequencing of the HIV virus.
-Development of diagnostic tools to prevent infection through blood products and identify infected individuals.
-Introduction of reverse transcriptase and protease inhibitors, which have greatly reduced the annual number of deaths from AIDS in developed countries and allowed infected people to lead relatively normal lives.

Recombinant technology will also certainly be instrumental in developing a future vaccine against AIDS.

For other acute and chronic diseases, like the different forms of cancer, biotechnology offers equally strong hopes for new therapeutics that may turn them into manageable diseases like AIDS or, to use a classic example, diabetes.

A milestone in the progress of biotechnology was the completion of the Human Genome Project in 2003. Genomics is providing a new set of approaches and tools as well as considerable insight into a wide range of human diseases and conditions, the benefits of which will only become evident in the coming years. This progress represents a quantum leap in our ability to understand physiological processes and diseased states, and will help scientists to identify new potential drug targets.

The biotechnology industry can rejuvenate big pharma
The promise of biotechnology can be further understood by looking at the problems faced by the pharmaceutical industry, the traditional source of new medications. Until about ten years ago, the pharma industry had an enviable track record in terms of research productivity and commercial success: new medicines were discovered, developed and marketed at a rate that supported double-digit sales growth across the industry. But today, big pharma is struggling to transform basic scientific innovation into commercial products. Many of today's pharmaceuticals are not living up to expectations regarding innovation and direct benefits to the patient compared with their cost, and pharma's label as the "innovator industry" is being called into question [3]. The number of new active pharmaceutical substances reaching the market in 2004 was close to 20-year lows.

The cost of bringing a new medicine to the market, generally in the range of $0.8billion to $1.7 billion, is one major barrier to the investment in innovative

drugs. Although there have been more products entering the pipeline recently, fewer are advancing through development, with the biggest bottleneck at phase II clinical testing (Figure 2) [4]. But another, more fundamental issue is big pharma's relative difficulty to quickly exploit the latest academic know-how and turn it into new treatments.

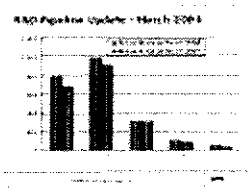

Figure 2: R&D pipeline update - March 2004

Innovation is not the pharma industry's only challenge. By 2008, patents on more than 58 products are expected to expire worldwide, putting potential revenues of about $50 billion at risk [5] while spurring growth in the generics market.

Finally, there is the issue of safety. Following several recent high-profile product withdrawals and questions about drug safety, the pharma industry has increasingly come under the spotlight of regulatory authorities and the public at large. The industry and the regulatory agencies will have to work harder to convince the general public that they can bring safe drugs to the market. Some observers predict a tightening of legislation to prevent similar events from happening in the future. The overall effect could be even slower times to market for drugs in development.

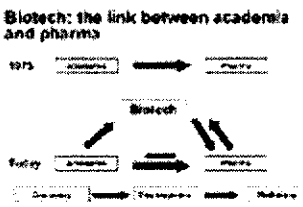

Figure 3: Biotech - the link between academia and pharma

The biotechnology industry, with a flexibility and culture of innovation that have often been lacking in the pharmaceutical industry, and with an acute ability to tap into the latest discoveries on the academic front (Figure 3), harbours many of the newest life science technologies and is in a strong position to provide solutions to the issues mentioned above. These technologies are already driving growth in the biotechnology sector, with sales now growing at around 20 to 30 percent per year, compared to the pharma industry's single-digit growth. They also bode well for the sector's future. As biotechnology companies increasingly retain ownership of their developmental compounds and create more blockbuster drugs, they are poised to continue to grow faster than their pharmaceutical counterparts.

Biotechnology offers more specific medicines addressing multiple targets at different stages of a disease, tools to empower life science research and development, as well as routes to new biopharmaceuticals offering improved benefits to patients. It is also well positioned to help fill the compromised drug pipelines of many pharma companies, as can be seen by the numerous in-license agreements. The pharma-biotech partnering opportunities that have developed over the years, with an order of magnitude increase in partnerships since 1993, have been instrumental in shaping the healthcare sector, and are a healthy sign for both industries.

Healthcare challenges, biotechnology solutions

As mentioned at the outset, unmet medical needs are the main driver of growth for the biotech and pharma industries. Biotechnology can provide better targeted biopharmaceuticals addressing different stages of a disease. Genomic and proteomic approaches offer new information on the mode of action of drugs that will lead to better, safer treatments. Biotechnology also allows the development of tools that can advance research and development in different therapeutic areas.

Recent examples of how biotechnology can provide solutions stem from the field of cancer therapy. In February 2004, two new drugs were approved by the U.S.

Food and Drug Administration (FDA) for cancer treatment. Avastin, from Roche, is a monoclonal antibody (MAb) that attacks the blood vessels feeding a tumour, thereby preventing growth - an entirely new mode of action for a cancer drug. The benefits of this new targeted approach are reflected in the record speed with which Avastin was adopted by prescribers. Erbitux, a drug from Bristol-Myers Squibb/Merck KGaA/ImClone Systems used for the treatment of colorectal cancer, is a genetically engineered version of a mouse antibody that also contains human components. Erbitux targets a specific protein present in larger than usual amounts on the surface of rapidly proliferating cancer cells, thereby inhibiting their growth. These two recent success stories were preceded by products like Herceptin and Rituxan, MAbs which are widely used today for the treatment of breast cancer and lymphoma, respectively. MAbs are now one of the fastest growing product classes in the biopharmaceutical industry, with the European market alone set to grow at a compounded annual growth rate of 34.1 percent, reaching $11.4 billion (€8.7 billion) by 2011 [6].

Other innovations in biotechnology are leading to a substantial transformation of the healthcare sector by providing new tools that can lead to greater efficiencies and improved safety. An example is pharmacogenomics, a tool with great potential for physicians for assessing patients' genetically-linked risk factors for certain diseases. In time, genetic testing via rapid genome-wide sequencing methods will become routine, and drugs will increasingly be given in connection with patients' individual genetic profile. For example, for metastatic breast cancer, diagnostic tests can already identify whether individuals are overexpressing particular proteins linked to the disease. Pharmacogenomics will also have a large impact on drug development and on the way clinical trials are designed and executed by allowing the selection of the most appropriate target groups.

Toxicology issues can also now be addressed earlier in the drug development process, and new biotechnologies are now allowing for the identification and use of improved biomarkers for diagnostic purposes as well as the use of new "humanized" laboratory model systems [7].

Biotechnology: an industry with momentum

Over the past quarter of a century, more than 150 biotechnology drugs and vaccines have been introduced, and more than 370 are currently in clinical trials [8].

Biotechnology products accounted for 10 percent of the global pharmaceutical market in 2004, and seven biotechnology products were among the top 50 drugs worldwide in 2003, representing combined sales of $15.1 billion [9]. In 2003, licensed products from biotechnology companies amounted to more than $70 billion in revenues for the top 20 global pharmaceutical companies [10]. Twenty brands of biotechnology products, including Erythropoietin (EPO), several interferons, granulocyte-colony-stimulating factor and insulin, each had sales of over $1 billion in 2004 [11].

There are now over 5,000 biotechnology companies worldwide, with some of the leading ones, such as Amgen and Genentech, rivalling their pharmaceutical peers in terms of market capitalisation (in the range of $50 to $80 billion). Amgen is now ranked among the top 20 global pharma companies in the world and is expected to break into the top 10 by 2008 [10].

Blockbuster drugs

Despite claims that the blockbuster model is compromised, the number of drugs with sales of over $1 billion continues to increase annually, and other candidates are in the pipeline [12]. Biotechnology has already demonstrated its clear potential to generate blockbusters. Erythropoietin (EPO) is a good example. Initially introduced in 1989 as a niche drug for treating kidney disease-related anaemia, it has since found applications for the treatment of cancer and AIDS

patients. This shows that the successful introduction of a therapeutic for one indication can open up new market opportunities with other indications. EPO is without doubt the top selling biotechnology therapeutic; in fact, in 2004, EPO (adding together the sales figures for all brands) was the best selling human medicine, with sales of over $11 billion [11].

As an ever-increasing percentage of marketed healthcare products are derived from biotechnology, success stories of this kind will become more widespread. Erbitux is predicted to achieve sales of over $1 billion by 2008 [10], and Avastin's sales already exceeded this figure in 2005, with predictions that they could reach over $8 billion by 2010 as the range of indications for which the drug is prescribed grows.

Biotechnology-based products are potentially less vulnerable

As mentioned, two distinct but major threats that can affect pharmaceuticals at different times during their life cycle are safety issues and the eventual expiration of patents. Products issued from biotechnology appear to have key advantages in these respects. Traditionally, pharmaceuticals have often been discovered through the random screening of chemical libraries for a desired activity, followed by clinical testing for an acceptable safety profile. Side effects with a low incidence may not be discovered until a drug has been on the market. Products based on biotechnology, on the other hand, are often designed from the beginning with specificity for their desired targets – as is the case with MAb-based drugs. While unwanted side effects can never be ruled out, the tendency towards more specific drug-target interactions is clearly an advantage and offers the possibility of lower toxicity and greater acceptance [13].

Because they tend to be much more complex molecules than traditional drugs, biotech products are also more difficult and more expensive to copy and have approved by the regulatory authorities. This fact makes them potentially less vulnerable to competition from generics once their patents expire [14].

Investing in the healthcare era

The Russian economist Nikolai Kondratieff identified regular innovative cycles lasting 40 to 60 years that were based on technological and economic developments and appeared to drive world economies [15]. Following four cycles driven by heavy industry [16], the current Kondratieff cycle is based on the sweeping influence of information technology. The foundation of the sixth Kondratieff cycle will be healthcare, a motor of growth and employment in the 21st century, and biotechnology will be its primary driver.

To allow the healthcare era to reach its full potential and for biotechnology to play a decisive role in shaping the future, we must take every opportunity to invest in the best early-stage life science companies. In a recent article published in the *European Venture Capital Journal* [17], we have looked at how venture capital funding of early-stage companies has progressed in Europe and at its impact on the biotechnology industry. Investing in true innovation is a necessity if we are to create new jobs, develop new drugs and technologies for unmet medical needs, and benefit from the exciting developments taking place in the life science sector. This ultimately will lead to healthy capital gains for investors, for whom the current market environment represents an unprecedented opportunity.

Global Life Science Ventures will soon be conducting its 2nd annual Biotech Investment Barometer, to be presented at the Sachs Biotech Investment in Europe Forum in Zurich, 4-5 October 2006. To participate, or to receive the results of this survey, please send a short e-mail to mailmaster@glsv-vc.com.

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