

- SAL CAUSI AND DR. TERRI COOPER -

## Pharma Sector Finds New Reward By Redefining Disease Treatments

Sal Causi is a Business Development Executive with IBM Life Sciences;  
Dr. Terri Cooper is a Partner with IBM Business Consulting Services



**B**y 2010, the pharmaceutical industry will extend its reach beyond the white powders it has used to fight disease. In many cases, the development of a broad new range of sophisticated products, including diagnostic tests, drugs, monitoring mechanisms and patient support, will not only redefine the view of some diseases, but pave the way for more targeted treatment.

In a recent report on the future of pharmaceutical sector, IBM analysed the trends shaping the industry over the next seven years and found this new approach to “targeted treatment solutions” will not only change the traditional approach to many diseases but will also create significant opportunities for bigger shareholder returns.

### The real promise of the molecular sciences - a new view of disease

Genomics, proteomics, metabonomics and the like have already provided pharma with plenty of new biological targets, but scientists currently know very little about which targets are relevant or which diseases they are associated with. The immediate promise of the molecular sciences is not that they will generate a stream of new drugs. It is, rather, that they are changing the way in which scientists look at disease.

Pharma is gradually acquiring a much better grasp of the factors involved in a specific disease state, including its severity, how it progresses and why some individuals are susceptible in the first place. Thanks to these insights, it will soon be able to separate diseases that currently get lumped together as if they were the same disease, and treat them as different diseases within a particular disease family (or collection of related diseases).

One instance where this is already happening is asthma. Early treatments for asthma, such as steroids, worked on the basis of general immune suppression. But with more sophisticated molecular techniques, pharma has begun to redefine asthma as a series of distinct disease states, such as atopy and airway inflammation. Scientists are now working on the development of different drugs for different forms of asthma and diagnostics based on molecular biomarkers for distinguishing between conditions that superficially seem the same.

In terms of cancer, at least one project is already underway to develop a system that segments breast, prostate, lung and other kinds of cancer into subtypes - and experts predict that the 200-odd forms of the disease which are recognised today could eventually be sub-divided into as many as 2,000 forms.

### Targeted treatment solutions

This redefinition of disease will culminate in the creation of healthcare packages for specific disease pathologies. Many of them will consist of biologics rather than chemical entities. These health care packages will measurably modify the disease states for which they are prescribed, with outcomes data and disease progression markers providing proof of efficacy; and they will include a network of services for diagnosing, treating, monitoring and supporting patients.

For example, earlier this year Vancouver-based iCAPTURE initiated a program that will investigate the linkages between genetic and environmental influences on heart, lung and blood vessel diseases. iCAPTURE has partnered with IBM to build an information system that will help relate genetic susceptibility of patients with cardiovascular and respiratory diseases to environmental influences such as culture and socio-economic status, educational backgrounds, inhaled cigarette smoke, pollutants, viruses, allergens, diet, and obesity.

As researchers begin to understand how different influences change the structure of cells, tissues and organs, iCAPTURE researchers will transform patient care. They'll be able to create targeted treatment therapies and early intervention for chronic illnesses like asthma, emphysema, bronchitis, arteriosclerosis, and heart failure. They also hope to perform pre-symptomatic screening, wellness and preventive care programs.

Targeted treatment solutions will improve the quality of healthcare and simultaneously provide the industry with new sources of revenue. Patients will get comprehensive therapies that work for them - diagnostics for evaluating their susceptibility to a particular disease; molecular markers for defining, and tracking the course of the disease states from which they suffer; and monitoring mechanisms to help them comply with their regimens. Doctors will get the tools with which to provide better medical care and healthcare payers will get better value for money.

Similarly, pharma companies will be able to charge premium prices for treatments that demonstrably work for particular disease states, even though the target market may be smaller; to add value with the provision of related products and services; and to increase drug utilisation with better compliance and persistence. But substantial though the potential rewards for making such healthcare packages are, any company that wants to take this route will have to alter its entire scientific and commercial model - and here massive advances in computing will play a major role.

## New techniques for drug discovery

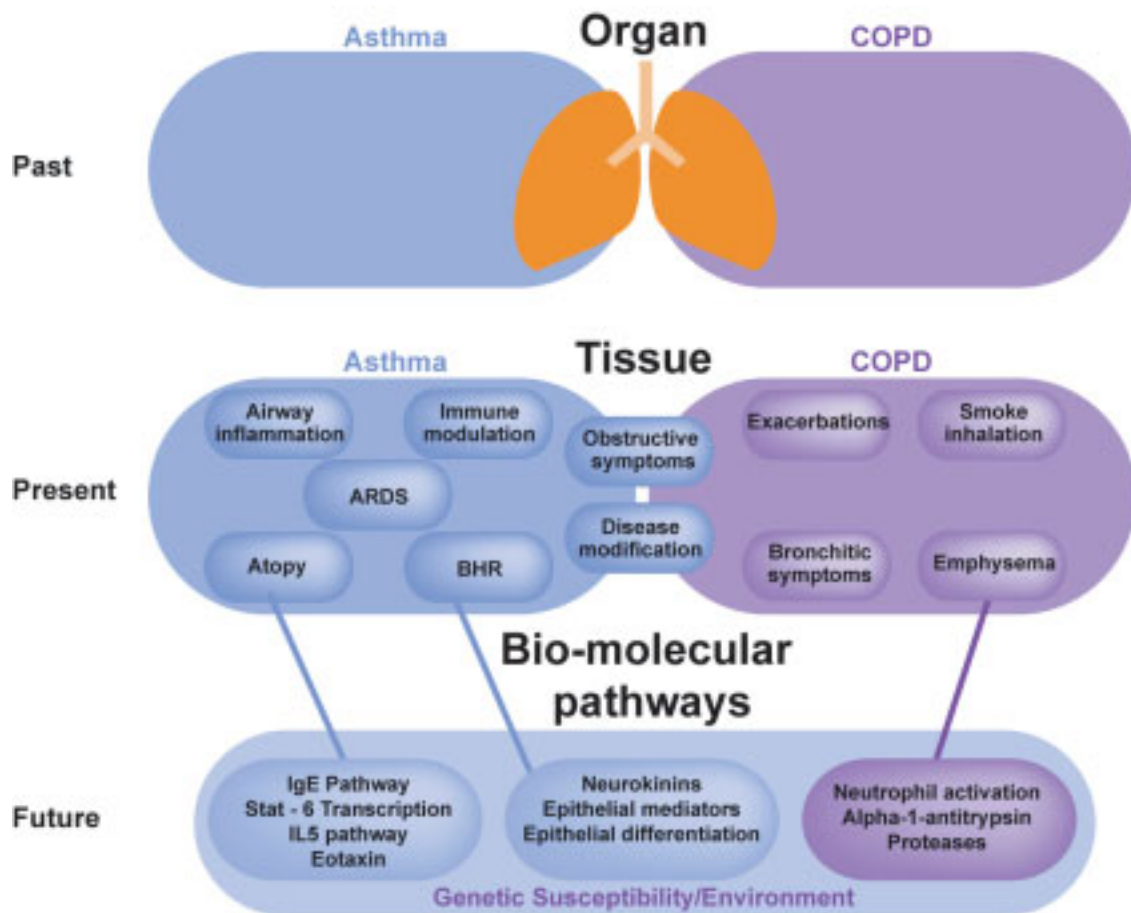
Several companies - including Amgen, Celltech and Cambridge Antibody Technology - are already using a disease-centric, biological approach to discover drugs for life-threatening conditions like cancer, with dramatic results. They are defining different disease states very precisely and using genomics-based techniques to identify novel targets. They are then validating those targets, using biological molecules, and thus cutting validation cycles to about two years.

While most chemical drugs are small, relatively simple molecules that are fairly simple to produce on a consistent basis, biologics are typically much larger, much more complex molecules that can be

way in which the discovery process will evolve for all drugs, regardless of the seriousness of the diseases they treat. By 2010, a pharma company will decide which disease family it wants to concentrate on, and begin defining the different disease pathologies and molecular mechanisms in that family. It will use the molecular sciences to identify targets and test them against various biological molecules that have been designed to interact with them - and simultaneously start developing diagnostics based on molecular markers.

Defining diseases much more narrowly makes it much easier both to validate a target and to find molecules that will interact with the target. Moreover, since biologics are usually less toxic than chemical entities, using biological molecules reduces the risk of

**Figure 1: Redefining Asthma at a Molecular Level shows that it is a Cluster of Diseases rather than a Single Disease**



far more costly to produce. But while they can be more costly, research shows that biologic drugs can be far more effective than their chemical counterparts, with fewer side effects

When taken, chemical drugs can also affect various other aspects of the immune system and can even damage non-immune cells. On the other hand, biologics are able to target very specific disease cells and can be much safer for the user than standard drugs. And because biologics are created from living sources like viruses, animals and people, they also enter the body and begin working more quickly than a chemical drug. The body's immune system often identifies chemical drugs as 'foreign' and inadvertently lessens the drug's effect.

The techniques used by companies pioneering biologics point to the

producing a drug that fails because it has undesirable side effects. Indeed, the latest analysis of industry success rates by CMR International shows that biologics have a four-fold greater chance than chemical entities of making it to market from the point at which they first get tested in man.

## A new development process

The development process will likewise need to be transformed in several key respects. Modelling and simulation will enable the industry to model how drugs act in whole body systems, organs and at a sub-cellular level; and to design much more accurate trials. Meanwhile, electronic data capture and other such technologies will accelerate drug testing by providing access to data in near real time.

For example, researchers at the University of Alberta's Institute of Biomolecular Design are creating a virtual Ecoli cell. The researchers will be able to manipulate the cell and study how it responds to, exploits and reacts in its virtual environment. As scientists do not have to actually physically manipulate cells in a lab, research can be done much more quickly and at far less cost. Scientists do not require extensive laboratories and no longer have to produce thousands of actual Ecoli cells to do the testing.

Similar technology can be used to study everything from cancer to psoriasis, and since the data from these virtual tests is created and collected in near real time, companies will be able to research and produce drugs much more quickly.

Collecting research data in near real time will also expand the scope of the research process as a typical pharma portfolio will change from a collection of disparate medicines into a set of disease-specific packages. It will become much more iterative as work on product A for one disease state gets fed into work on products B, C and so forth for other disease states in the same disease family.

Lastly, the way in which trials are conducted will change. The traditional distinction between the various phases will collapse, with greater use of "adaptive" trials - where information acquired during a trial is used to alter the course of that trial without compromising its statistical validity. Eli Lilly has used adaptive principles in Phase I cancer trials for some years. Pfizer also used adaptive dose-ranging trials to test neutrophil inhibitory factor in stroke patients - and to terminate the drug rapidly when it proved disappointing.

## New sales and marketing strategies

The move to targeted treatment solutions will have an impact on sales and marketing, too. Pharma companies typically put most of their effort into marketing primary-care products to general practitioners, but some of the targeted treatment solutions they make will cover secondary care. So they will have to create smaller, smarter sales teams capable of conversing with consultants - as Novartis has done with Gleevec, its new treatment for chronic myeloid leukaemia.

Moreover, most companies price and market their drugs relative to competing products, an approach that no longer works when the distinguishing feature is the specific disease state a drug is designed to treat. So the very basis on which targeted treatment solutions are promoted will be different. They will be priced according to the medical results they deliver, and a substantial part of their value will lie in the services that come with them. They will also have to be supported by objective evidence of efficacy - including outcomes data and even, perhaps, persistence and compliance algorithms.

## Forces of change

But though the industry is facing an enormous upheaval, the rewards will more than justify the effort required. We estimate that, even if the market for targeted treatment solutions is slow to get started, companies that learn how to make such medicines could triple their shareholder value by 2010. If the market for such medicines takes off more rapidly, they could enjoy almost double the growth the industry enjoyed in the early and mid-1990s, when investors were clamouring for pharma stocks.



**Figure 2: Simulation modeling of metabolism of e-coli depicted to scale at the University of Alberta's Institute of Biomolecular Design.**

