

A healthcare professional in a white coat is holding a syringe, preparing to administer a vaccine. The patient's arm is visible in the foreground, and the background is a blurred clinical setting.

# Is personalised medicine getting closer?

Excerpted from an article by Johanna Kleine, Senior Editor of IMS Company Profiles.

"The right dose of the right drug to the right patient at the right time." That is the promise of personalised medicine - the use of information about a person's genetic makeup to tailor strategies for the detection, treatment or prevention of disease.

A few decades ago, this would sound like science fiction, but personalised medicine and pharmacogenomics are becoming more and more real. In fact, the model is already operative on a small scale, as some targeted therapies for cancer can confirm. Seen as the future of healthcare, personalised medicine is predicted to bring massive changes to the pharmaceutical industry's 'blockbuster' model. Customising treatments to suit different categories of patients is, perhaps, the biggest challenge, and possibly also the biggest opportunity, facing the industry today.

Some companies are overcoming their resistance to change and are now taking the challenge very seriously. It is easy to see why. Pharmacogenomics may increase chance of cure for the patient, who can be selected to maximise benefit and minimise toxicity. It also has the potential to reduce deaths and unnecessary hospitalisation due to drug adverse reactions, bringing down healthcare costs as a result. Most important from the industry point of view, however, is the fact that pharmacogenomics may bring down drug development costs, ensuring that a higher proportion of drugs actually make it through all the phases of development and onto the market.

#### Focus on use of biomarkers

The science of pharmacogenomics has advanced significantly in research and pharma companies are investing hugely in programmes to identify biomarkers to reduce the attrition rate in drug development, since only one in 15 drugs entering Phase I ever reach the market, with the great majority of compounds failing in Phase II.

Most big pharma companies are actively working on biomarkers programmes, like J & J, Roche GSK, Merck & Co and Pfizer, just to name a few.

GSK, for example, has been collecting DNA samples from all clinical trial patients for biomarker analysis since 2003. Pfizer has been doing the same. Speaking at the FT Global Pharmaceuticals and Biotechnology Conference in London, in September 2006, Dr Jean-Jacques Garaud, Global Head of Exploratory Development at Novartis, highlighted that biomarkers should make R&D less risky and save time in development, in addition to bringing better benefit for the patient and better return in price for the manufacturers.

#### Cancer drugs lead the way

Oncology is at the forefront of pharmacogenomics, given that testing of genetic variation in drug receptors is frequently used to characterize tumours.

Roche/Genentech's breast cancer therapy Herceptin (trastuzumab), linked to the HER2 gene, is by far the best publicised of the target drugs currently on the market, but other well-known names are Novartis' Gleevec (imatinib), for chronic myeloid leukaemia, and Roche/Genentech/OSI's Tarceva (erlotinib), for lung cancer. All are associated with tests that can show if the patient's genetic makeup would respond to the drug.

Roche expects its test for Tarceva to be available in 2007 or 2008.

As pharmacogenomics may reduce costs for payers, regulatory agencies support the new model and have made the progression of personalised medicine a priority.

The FDA considers pharmacogenomics to be a major opportunity on the critical path to new medical products and has begun encouraging submissions of genomic data through its voluntary genomic data submission programme. The agency is also considering developing a standardised labelling format for pharmacogenomic information.

Although big pharma's efforts in pharmacogenomics have been concentrated in oncology, pipelines show that this is slowly changing. Gradually big pharma is expanding pharmacogenomics to therapeutic areas other than oncology. J&J's Invega (paliperidone), approved by the FDA in December 2006 as a treatment for schizophrenia, and Wyeth's Pristiq (desvenlafaxine), submitted for the treatment of depression, for example, are two CNS drugs that could possibly have commercial genetic tests associated with them. In both cases, the action of the drug may be affected by poor or ultrarapid drug metaboliser CYP2D6 gene status, which the patient could be tested for. Novartis' indacaterol, in Phase II trials for asthma and chronic obstructive pulmonary disease, is another example. The respiratory drug could be approved with a genetic test for polymorphism at beta-adrenergic receptors that may affect drug action.

#### Diagnosics being developed in parallel

Since personalised medicine is intrinsically linked to the development of diagnostic tests, the diagnostics side of the healthcare industry is expected to benefit a great deal from this shift, especially companies that have coordinated pharma and diagnostics divisions. Roche, currently the world leader in oncology drugs, believes it is uniquely positioned in this arena. The company plans to take advantage of its knowledge base in both pharma and diagnostics to develop new tailor-made products and services.

Joachim Eberle, Head of R&D at Roche Centralised Diagnostics, told investors in June 2006 that Roche has extensive joint programmes for all drugs throughout their lifecycle. "No drug programme starts at Roche without a diagnostic project," he said during an oncology event promoted by the company. Roche's main five oncology drugs - Herceptin, Tarceva, Xeloda (capecitabine), MabThera/Rituxan (rituximab) and Avastin (bevacizumab) - all have biomarker tests either on the market or in Phase III development. Besides that, the company also develops tests that allow the selection of one or several therapies. The AmpliChip CYP450 Test - launched in the EU in 2004 and in the USA in 2005 - can identify how individuals metabolise many of today's most widely prescribed drugs. By analysing the variations in two genes, the test predicts whether a person is a slow, normal or rapid metaboliser of a particular drug.

Similarly, Enzyme has been involved in diagnostic testing for many years. Specialised in treatments for lysosomal storage disorders (LSDs), genetic diseases caused by enzyme deficiencies, the company has developed genetic tests in LSDs and now is expanding its diagnostics and therapeutics connection in other genetic diseases and in cancer. Genzyme has launched four new cancer tests linked to targeted therapies in the last year and is developing a diagnostic test in Clostridium difficile colitis - it has a Phase III drug for this indication, tolevamer, expected to be launched in 2008.

With the support of government institutions like the FDA, which is stimulating pharmacogenomic dosing information in labelling and the availability of diagnostic tests, the stage is set and personalised medicine may be closer than we think.