Taking drug development into the virtual world

In her series of profiles of bioinformatics companies, Sophia Ktori looks at the work of biosimulation specialist, Certara

Everyone is familiar with the notion of harnessing informatics tools to achieve the truly paperless office, but what about being able to exploit biosimulation and modelling systems to reduce testing in patients during drug development? It may seem a distant prospect, but biosimulation specialist, Certara, is spearheading the drive both to virtualise much of drug development, and to facilitate the optimisation and personalisation of precision medicine at the point of care.

Virtualising drug R&D

While computer-aided modelling and simulation technologies are now mainstream in many areas of industry, including the design of aeroplanes, trains, and automobiles, the use of mathematically based simulation technologies to model, explain, compare, contrast, and analyse biological processes and interventions is far more complex, says Dr Edmundo Muniz, Certara’s CEO. ‘Nevertheless, the virtualisation of multiple aspects of research and development through the application of in silico methodologies and computational and analytical capabilities is a key and significant trend in drug development. It’s a tall order considering that, as Muniz suggests, today, less than 10 per cent of drug R&D, is carried out in silico. Yet we are talking about a $150 billion global R&D market, which virtual technologies can feasibly have a huge impact on, significantly reducing drug development timelines, costs, and attrition rates.’

End-to-end in silico platforms

Certara offers what it claims is the most comprehensive portfolio of biosimulation software and consultancy services worldwide, spanning discovery, preclinical, clinical, and post-marketing phases of synthetic and biologics drug development. ‘Certara software informs key safety and efficacy decisions, identifies, optimises, and validates drug targets, determines optimal dosing, designs clinical trials, triages compounds, makes comparisons with competitor compounds, and assesses mechanistic drug performance,’ comments Ellen Leinfuss, chief marketing officer.

Modelling clinical trials design

Using in silico approaches to aid the design and optimisation of clinical trials is a major area for Certara’s platforms. The firm’s model-based meta-analysis (MBMA) platform analyses existing data from in-house and public sources, to help characterise drug class, dose, and response, and so facilitate the design of clinical trials to maximise efficacy, tolerability, and safety. The MBMA platform also allows the comparison of trials, and combination treatments that may not previously have been dosed in parallel in the same trial. ‘Using our software, drug developers can model different clinical trial designs to reduce complexity, increase reliability, and optimise outcomes, inform which drugs are likely to fail and, in some instances, replace the need to carry out some human trials – for example, when recruiting subsets of patients will be problematic,’ Muniz states. ‘Our tools can identify the optimal drug dose to achieve the best therapeutic and safety profiles for patient subpopulations, based on genetic profiles, or for subpopulations with co-morbidities, for example. This is really important when you consider that almost 40 per cent of doses selected during drug development are either too high or too low, and can result in unnecessary drug toxicity, reduced efficacy, or drug interactions. Further, the use of biosimulation fulfils an ethical imperative,
Certara’s simulation and modelling solutions are also being used at the point of care

another significant trend that we believe will influence patient care globally over coming years,’ Muniz stresses. ‘Biosimulation and modelling could have huge benefits for the global patient care market, especially when you consider the capacity for such technologies to take the guesswork out of prescribing. Yet today, just about zero patient care is currently carried out in silico.’

Certara has partnerships with some 1,200 commercial clients, including all the top-tier pharmaceutical companies, the majority of second-tier, 250 academic institutions, and the world’s leading regulatory agencies, including the US FDA, the European Medicines Agency, and the Japanese and Chinese regulators. Global regulatory agencies represent major users of Certara’s software, Muniz notes. ‘They use our software to confirm simulations that companies have already carried out on their drug candidates, or to apply modelling techniques to investigate additional attributes of a drug, and to enhance the level of understanding about drug behaviour in the human body. Regulators also use Certara’s modelling and simulation platforms to explore the potential effects of drugs in patient populations for which real world trials may not be feasible, such as neonates or groups of patients with multiple diseases. And they also use our mathematical and computational capabilities to analyse huge datasets.’

Biosimulation informs drug labelling

Drug labelling is a key area that the regulatory agencies are intimately involved with, and in which biosimulation is now increasingly starting to inform drug claims, Muniz says. ‘The drug label is effectively the manual for that therapy, and each claim on that label will directly impact on drug utility at the front end, and thus on profitability. The label is the ultimate result of possibly 10 to 15 years of R&D and billions of dollars of investment. The ability of modern simulation to shape and optimise the final drug label is hugely important.’

Certara has been working with companies and with the regulatory agencies to demonstrate the utility of modelling and simulation, using mechanistic modelling and pharmacokinetic-pharmacodynamic modelling, in the derivation of labelling claims. ‘It is over the last couple of years that biosimulation has started to have a major impact on label claims,’ Muniz suggests. ‘FDA’s acceptance of physiologically-based pharmacokinetic modelling and simulation has to date led to Certara’s software playing a key role in the final wording of some 20 new drug labels. To date, our modelling software has directly informed 80 to100 statements on drug labels related to safety and dosing.’

Certara works in close collaboration with its clients, to ensure optimum utilisation of its software, backed by its consultancy services. ‘Every transaction implies the utilisation of our software and an ongoing partnership around our consultancy expertise. We do not see ourselves as selling software and services. We act as a strategic partner for our clients, and our products help to inform, optimise and verify the most crucial decisions in drug discovery, development and, ultimately, utilisation in the patient. As we believe we are the only company that can provide end-to-end modelling and simulation services, it is important that we collaborate with our partners very early on in the discovery process, and then work closely with them right through to post marketing all the way to the point of care.’

Small molecules and biologics

In the rapidly growing discipline of physiologically-based pharmacokinetics (PBPK), Certara’s Simcyp simulator for both small molecules and biologics is supported by a unique consortium, which the firm claims includes the majority of leading pharmaceutical companies, key academic institutions and regulatory bodies. Through its XenologiQ purchase, Certara now also provides quantitative systems pharmacology technology, which is used for lead optimisation. The firm’s portfolio also includes the Sybyl and Muse Invent software for molecular modelling, and its informatics platform, D360, which facilitates scientific data access, analysis and collaboration across and between departments and researchers within an organisation, and development partners.

‘We have transformed a set of complementary, yet fragmented technologies and expertise offered by disparate companies, into an integrated, consolidated and synergistic set of modelling and simulation disciplines. This can model biological processes to facilitate decision making at every stage of drug discovery and development, from target validation, drug discovery and lead optimisation, to preclinical and clinical development,’ Muniz concludes.