Concert Pharmaceuticals, Inc. has Developed In-House the World Leading Expertise in the Use of Deuterium Chemistry and has Applied it in Developing First and Best in Class Compounds for Large Market Areas such as Diabetic Nephropathy and HIV

Healthcare
Biotechnology
(Private)

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Company Profile:
Concert Pharmaceuticals is a clinical stage biotechnology company focused on applying the company’s DCE Platform™ (deuterated chemical entity platform) to create novel and differentiated small molecule drugs. Concert’s approach leverages decades of pharmaceutical and clinical experience to reduce the time, risk and expense needed to create important new medicines. The company has a broad research pipeline encompassing many therapeutic areas including antiviral disease, renal disease, and CNS disorders, among others. Founded in 2006, Concert has raised more than $110 million of venture and institutional capital.

Interview conducted by:
Lynn Fosse, Senior Editor
CEOCFO Magazine

CEOCFO: Dr. Tung, we last spoke early 2009; has there been a change in vision since then or are you still a clinical stage biotech company focused on bringing to bear new medicines using your DCE Platform™ (Deuterated Chemical Entity Platform)?

Dr. Tung: We remain very much on track with that vision. We have progressed several of our programs in the clinic and we have spent a fair amount of resources building up a very experienced clinical team that has the ability to efficiently move compounds into and through the clinic and that has the experience of bringing products to market.

CEOCFO: How is it that Deuterium can help existing best-in-class drug candidates become new chemical entities (NCEs), while reducing R&D time and expense?

Dr. Tung: First of all, let me say that the opportunity for the use of deuterium in new medicines is broader even than what you suggested. For instance, CTP-499, the compound that we are bringing forward in chronic kidney disease, particular in diabetic nephropathy, is a novel agent that had never been independently studied in humans. Therefore, this is a first-in-class molecule, not something that would be potentially an improvement on existing compounds. The use of deuterium is unique in that it does not, in our experience, change the biological activity or selectivity of compounds on a molecular basis, but it can change their metabolism in ways that, we believe, in favorable circumstances can improve their safety and/or efficacy. It affects the metabolism of compounds in ways that can either enhance the exposure in the body to desired species-- the parent drug or desirable metabolites-- or reduce the exposure in the body to toxic or reactive, undesirable metabolites.

CEOCFO: Your most advanced clinical program is CTP-499 for the treatment of diabetic nephropathy; is this an area of unmet need and could it result in death for the patient?

BIO:
Dr. Roger Tung, President and Chief Executive Officer of Concert Pharmaceuticals, Inc., co-founded the Company in April 2006. Before Concert, Dr. Tung worked in venture-backed start-up and major pharmaceutical companies, including Vertex Pharmaceuticals Inc., where he was a founding scientist, and most recently VP of Drug Discovery; Merck, Sharp & Dohme Research Laboratories, and The Squibb Institute for Medicinal Chemistry. At Vertex, Dr. Tung co-invented and headed discovery of Vertex’s two commercial HIV protease inhibitor products, Lexiva® and Agenerase®, and oversaw the Incivek® HCV and Kalydeco® cystic fibrosis programs. Dr. Tung has published widely and has been granted 50 U.S. patents. Dr. Tung received his Ph.D. in Medicinal Chemistry at the University of Wisconsin-Madison from Professor Daniel H. Rich.
Dr. Tung: The answer to that in both cases is yes. Diabetes, of course, results in many metabolic areas of dysfunction. Diabetic nephropathy is the most common cause of patients progressing to what is called end-stage renal failure. End-stage renal disease is defined as patients either going onto dialysis or requiring a kidney transplant. Patients who have advanced kidney disease, such as diabetic nephropathy, are also at very elevated risks for cardiovascular events such as heart attacks and strokes, which of course themselves can be the cause of fatality. So, in a number of regards this is a very unmet medical need. There have been no new classes of drugs approved for diabetic nephropathy since the 1980’s.

CEOCFO: How does CTP-499 relate to the treatment of diabetes and progressive kidney disease?

Dr. Tung: It is not a treatment for diabetes per se, as it has no effect in blood sugar that we are aware of. However, it has an effect in protecting kidney function. That appears to be mediated by anti-inflammatory, anti-fibrotic, and anti-oxidant effects, which we believe stem from selective inhibition of a certain subset of enzymes called phosphodiesterases or PDEs.

CEOCFO: Where are you in your clinical trials for CTP-499?

Dr. Tung: Last year we completed 4 clinical Phase I studies that looked at the tolerability and safety of the drug in both healthy volunteers and patients with chronic kidney disease. These studies also defined the formulation which we will take forward for subsequent studies and examined food effects. We found that the drug appears to be well tolerated at doses which we believe may be required for good clinical efficacy, and we demonstrated that it can be dosed with or without food equally well. We are anticipating in the first half of this year initiating a study in approximately 170 patients with chronic kidney disease and diabetes to look at the efficacy of CTP-499 in reducing protein excretion in the urine, which is a marker for severity of disease.

CEOCFO: Have you looked at potential side effects?

Dr. Tung: We have. The drug, as I indicated, was well tolerated. We did a 28 day study in patients with chronic kidney disease and saw that there were no laboratory abnormalities associated with the drug. We saw that the most common side-effect associated with it was a mild, transient nausea seen in some patients, and that there were no dose reductions and no patients dropped out of the study due to drugs.

CEOCFO: What is the potential market for CTP-499?

Dr. Tung: It is quite large. Unfortunately, the incidence and prevalence of diabetes in the developed world is increasing quite dramatically. Since existing medications are not fully effective in preventing progression of kidney disease, this is a medical area which has a very large current need that is anticipated to increase greatly over the coming years.

CEOCFO: Concert’s HIV program is focused on the development of CTP-298, where are you today with that therapy?

Dr. Tung: We have studied several analogues of atazanavir containing deuterium substitution in different portions of the molecule. CTP-298 was identified as a compound with a particular pattern of deuterium incorporation that enables it to have superior retention in the body, or pharmacokinetics, relative to atazanavir. We studied the drug in what is called a crossover clinical trial where patients are randomized to take either CTP-298 or atazanavir and then after a period of time take the other drug to compare how each drug is retained in the body. We showed in that study that CTP-298 has superior pharmacokinetics relative to atazanavir. We are now carrying on a longer study comparing a repeated dose of CTP-298 to the combination of atazanavir plus another drug called ritonavir, which is used to increase the concentrations in the blood of atazanavir. Based on that, we will conduct several additional studies in healthy volunteers. Pending the successful completion of those studies GlaxoSmithKline has the option of licensing CTP-298.

CEOCFO: How does your approach with CTP-298 differ from the current therapies on the market for HIV?

Dr. Tung: The market in HIV is moving towards single-pill therapies for the disease because of the improved compliance with those medicines and the simplicity of taking them. Currently, all of the HIV protease inhibitors that are dosed once-daily require the addition of ritonavir as a boosting agent. So even within the protease inhibitor class, multiple medicines are required to provide the most effective therapy. We believe CTP-298 has the potential to be the first unboosted HIV protease inhibitor that is delivered once a day and furthermore has the potential to be formulated with other HIV medicines to provide an effective therapy in a single tablet. We believe that, if successful, CTP-298 co-dosed with another HIV medication will be a great advantage to patients and also important for the marketing of the drug.

CEOCFO: Are there any other drugs and diseases that you are working on?

Dr. Tung: Yes, we have a large pipeline that includes potential treatments for epilepsy, spasticity, pain, possibly
depression and hematologic cancers. Our major challenge as a company is balancing our investment across a number of very exciting programs.

CEOCFO: Would you tell us more about your collaboration with the National Institute of Health (NIH)?

Dr. Tung: We recently announced a collaboration with the TRND (Therapeutics for Rare and Neglected Diseases) Group in the NIH. This is in support of advancing a compound for the treatment of Schistosomiasis, which is one of the most prevalent parasitic diseases in the world. The World Health Organization refers to it as the second most devastating parasitic disease behind only malaria. It is very prevalent in Africa and is also prevalent in India and other tropical countries. The compound that we are working on is something that we and the NIH believe will be a significant advancement in therapy for that disease, which has particularly severe effects in children. The NIH has agreed to support the progression of the compound through its preclinical and potentially early clinical stages.

CEOCFO: Would you tell us about your alliance with GlaxoSmithKline (GSK)?

Dr. Tung: We have a collaboration with GSK, which is functionally a joint collaboration with the company Viiv Healthcare. Viiv was spun out of GSK and Pfizer to commercialize HIV products. Our joint hopes are to create a combination drug, with Viiv’s integrase inhibitor dolutegravir, which is in late stage clinical trials and CTP-298 in a single tablet form for the reason that we spoke about earlier.

CEOCFO: What is the goal for Concert Pharmaceuticals; will you remain as a development company or try to bring drugs to the market?

Dr. Tung: The greatest value created in pharmaceutical companies is through commercialization of their own products. In some of our earlier programs, we will partner the programs, such as we did with CTP-298 with GSK. That allows us to bring in funding for the company that is non-dilutive through equity. So that is important for the growth of the company. However, as I indicated, we have a very broad pipeline and we certainly intend to grow the company and to give ourselves every opportunity to be a successful commercial as well as an R&D organization.

CEOCFO: In closing, why should investors and venture capitalists consider Concert Pharmaceuticals?

Dr. Tung: Concert is a big idea. Our technology has very broad applicability to a wide range of novel best-in-class and first-in-class therapeutic agents, some of which we have discussed today. We have the potential to make a real difference in terms of healthcare. There are relatively few companies being funded at present that have that potential. Concert has developed in-house the world leading expertise in the use of deuterium chemistry and we believe that we have the ability and capacity to apply that expertise to the creation of a variety of important new pharmaceutical products.