LONG ACTING INJECTABLES: CHALLENGES AND POTENTIAL

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Dr Joël Richard is currently Head of Technical & Pharmaceutical Operations at MedinCell (Montpellier, France). He is leading all the pharmaceutical development and non-clinical pharmaco/toxico-kinetic activities of the company, specialized in the development of Long-Acting Injectables. (LAIs), using the proprietary technology BEPO®. Dr Richard has 30 years of experience in chemistry and biopharmaceutical R&D, including several global senior positions in various Biotech and Pharma companies, such as: Ipsen, Merck Serono, Ethypharm and Mainelab (France), a drug delivery company he co-founded, which was specialized in developing solvent-free processes for protein delivery systems. Since 1996, Dr Richard has focused his research activity on new formulation technologies and drug delivery systems (such as microspheres, nanosystems, gelling systems, chemically-modified proteins, supercritical fluid technology), especially for injectable peptide and protein formulations. Dr Richard has graduated from Ecole Normale Supérieure (Cachan, France). He has got a PhD in Materials Science from University of Paris, France, and the "Habilitation à Diriger les Recherches" degree in Chemistry from University of Bordeaux I. He has published 68 peer-reviewed scientific papers, 8 book chapters and 2 review editorials in various fields (colloids and interfaces, drug delivery systems, supercritical fluids, protein formulations, nanoparticles). He is the author of more than 140 international communications and 55 patent families.

What are you working on currently?

I am currently working on the development of Long Acting Injectables (LAIs), using the proprietary BEPO technology of MedinCell. I am leading all the product development, non-clinical, regulatory and clinical activities for the whole portfolio of projects of the company. This is a very versatile technology based on the association of biodegradable, amphiphilic, block copolymers, where the formulation scientist can play with many different parameters to adjust the drug release profile and get duration of action between a few days to up to 6 months, with a limited burst release. In addition, the BEPO technology makes it possible to produce ready-to-use liquid formulations in pre-filled syringes, easy to administer through small Gauge needles without any preliminary constitution step, and able to form a subcutaneous polymer implant after injection, due to a solvent exchange mechanism.

What are the major challenges with Long Acting Injectables?

One of the major challenges with LAIs is related to the control of the burst release which may lead to high circulating concentration of drugs and potential associated safety concerns. BEPO technology actually allows for a very good control of the burst effect, based on specific diblock and triblock copolymer compositions. Another key challenge is related to the delivery of fragile, hydrophilic molecules like peptides and proteins. As regards peptides, long acting injectable formulations based on biodegradable microspheres have been available on the market since more than 20 years ago, but most of the time these are not ready-to-use (RTU) formulations, and they need extemporaneous reconstitution before administration. Preformed solid implants made of biodegradable polymers are also available, but need the use of large Gauge needles (16-18 Gauge) which results in very invasive, painful and stressful injections for patients. The in situ implant forming BEPO technology would bring the unique combination of a RTU liquid product (solution or suspension) associated with a patient-friendly injection procedure with the possibility to control the burst and the release duration between days and months.

What do you see as the most interesting developments in the field?

There is likely a strong interest from the market to deliver fragile biotechnology products, like engineered antibodies or antibody fragments, since these very promising drug candidates show short plasma half life. In this context, a recent work has shown that BEPO technology makes it possible to deliver small bispecific antibody for immunotherapy in prostate cancer, binding both Prostate Specific Membrane Antigen (PSMA) and the T-cell receptor CD3 over several weeks after injection, improving half life and subcutaneous bioavailability of the bispecific antibody, while keeping bioactivity and high anti-tumor efficacy in animal models. This is a very promising result that shows the great potential of BEPO technology for long acting (LA) delivery of engineered antibodies.

What do you see as the major therapeutic areas for development with novel formulations?

Novel LA formulations will likely show a very favorable benefit/risk balance in patients with chronic, highly life-impacting conditions, in particular in the field of treatment of central nervous system, cancers, auto-immune diseases, and diabetes. A greater interest may even be found when the depot formed by the injected solution of block copolymers make it possible to keep the drug released in a specific local area of the body (like e.g. a joint, or a solid tumor, etc...), limiting potential systemic toxicity of the drug and improving its efficacy locally.

What do you look to achieve at the Formulation & Drug Delivery Congress?

As for me, attending the Formulation & Drug Delivery Congress means meeting the best experts in the field, confronting ideas and having high level scientific inputs from experienced leaders. I feel really excited to have the opportunity to learn from my peers, I am convinced that these conversations will generate new ideas to design the next innovative drug delivery systems that patients are expecting.