Q&A SESSION WITH ANTONIN DE FOUGEROLLES

ANTONIN DE FOUGEROLLES, Chief Executive Officer, **Evox Therapeutics**

Dr. Antonin (Tony) de Fougerolles joined Evox Therapeutics as CEO in late 2017 and oversees the management of the company. Evox is engineering exosomes, the body's natural delivery system, to enable a wide variety of drugs to reach previously inaccessible tissues and compartments, such as crossing the blood brain barrier to deliver drugs to the CNS, intracellular delivery of biologics, and extra-hepatic delivery of RNA therapeutics. Evox was founded in 2016 and expects to enter the clinic in 2020. Tony has over 20 years of biotech R&D experience in building out drug pipelines, and he has played a key role in developing and advancing 3 new drug modalities towards the market (RNAi, modified mRNA, single domain antibodies). Prior to joining Evox, Tony was CSO of Ablynx, where he led the company's non-clinical R&D operations, including Discovery, Pharmacology, CMC, and Clinical Trial Supply.

What are you working on at Evox Therapeutics?

Evox Therapeutics is a privately held, Oxford-based biotechnology company focused on harnessing and engineering the natural delivery capabilities of extracellular vesicles, known as exosomes, to develop an entirely new class of therapeutics. Exosomes are conserved across all multi-cellular organisms and represent the way cells naturally and effectively transfer and deliver nucleic acids and proteins from cell to cell. Evox has created substantial proprietary technology to modify exosomes using various molecular engineering, drug loading, and targeting strategies to facilitate targeted drug delivery to organs of interest, including the brain and the central nervous system. We can load practically any type of drug cargo into or onto our exosomes and deliver them to tissues that are currently inaccessible using other technologies. Our internal therapeutic pipeline is focused on delivering protein or RNA-based drugs to treat rare genetic lysosomal or metabolic diseases. We also work with some our pharmaceutical partners on other exosome therapeutic applications, including treatments for cancer.

What is the function and potential of exosome-based therapeutics in particular?

Exosome-based drugs have the potential to address some of the limitations of protein, antibody and nucleic acid-based therapies by enabling delivery to cells and tissues that are currently out of reach using other drug delivery technologies. Among the type of things we have been able to do with our exosome therapeutic platform is: 1) express hundreds of antibodies or proteins on the surface of a single exosome and thereby making highly multivalent and multi-specific drugs with improved activity, 2) enable functional delivery of antibodies into the cell cytoplasm and thereby opening up the possibility of using antibodies to address intracellular targets, 3) expand the utility of RNA therapeutics such as RNAi and mRNA and thereby enabling delivery to organs outside of the liver, and 4) allow different drugs modalities (antibodies, proteins, RNAi, mRNA, or small molecules) to be easily combined into a single drug product thereby rendering possible a multi-specific therapeutic approach that uses the optimal combination of the most relevant drugs.

What potential do you think the Bispecific Antibodies industry has for healthcare as a whole?

The bi-specific antibody industry has significant potential for the healthcare industry as a whole. Firstly, it has already given us approvals of drugs, like blinatumomab (anti-CD3+CD19 BiTE) to treat leukemias and emicizumab (anti-F9+F10 mAb) to treat haemophilia, that would not have been possible using conventional mono-specific antibody approaches. Advances in bi-specific engineering over the past 5-10 years has now been translated into over 50 different bi-specific antibodies in clinical development, including many other T cell engagers as well as a number of bi-specific antibodies to treat oncologic and autoimmune/inflammatory diseases. The ultimate utility for any bi-specific antibody product will rest on its efficacy/safety profile and its ability to differentiate from other competitive and combinatorial approaches.

How and to what extent is multi-specificity important for biotherapeutics?

Multi-specificity is an increasingly important area of biotherapeutics. As we understand biological mechanisms better and see what pathways are clinically beneficial to interfere with, it is not surprising that we are seeing that blocking multiple pathways at once result in improved efficacy. The decision as to which combinations to use is often first done clinically by co-administering 2 different drugs or antibodies and thereby interfere with multiple pathways at once. Many of these combinations are now being advanced as engineered bi-specific antibodies – most notably when treating inflammatory diseases (e.g., blocking TNF/IL17) and cancer (e.g., blocking CTLA4/PD1, VEGF/Ang2, or Her2/Her3). In certain cases, combining these specificities into one drug can not only give you additive efficacy but also potentially result in synergistic activity. Bi-specific antibodies can also be designed to induce a specific biologic effect which is not possible through simple combinatory use of the individual antibodies (such as bi-specific CD19-CD3 mAbs that recruit T cells to kill leukemias or anti-Factor IX/X bi-specific antibodies that act as a Factor VIII mimetic to treat haemophilia). Lastly, the field is also exploring biologics that have more than 2 specificities, with examples including blocking 3 different immune-oncology checkpoint pathways at once or developing tri-specific killer cell engagers.