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CANCER DRUG DEVELOPMENT: THE ADVANTAGE OF COLLABORATIVE NETWORKS

A conversation with **JOANNA LISZTWAN**, Head of Global In Vitro Biology

Cancer treatment is one of the fastest-changing areas of drug development, as doctors now have access to immunotherapies, cell therapies, targeted biologics and tailored chemotherapeutic combinations. Traditionally focused on CNS-related diseases, metabolic disorders, immunology and inflammation, Evotec expanded its work in the busy world of oncology in 2015 when it acquired Sanofi's drug discovery facility at the Oncopole in Toulouse. The deal included over 200 employees, open innovation access to Sanofi's drug discovery libraries, and co-development of specific oncology assets.

What difference did the move to the Oncopole make?
When we acquired Sanofi's site at the Oncopole, our oncology R&D took a huge leap forward. Not only did we integrate a team of oncology specialists and a portfolio of existing drug discovery projects, but we also became part of a collaborative network at the Oncopole.

This network is centred around the Toulouse University Hospital and the Institut Claudius Regaud, which provide cancer care, research and teaching, and together make up the third largest Phase I clinical trial centre in France. The Oncopole is also home to a blood bank, to biopharma and to biotech companies and start-ups. The move to the Oncopole therefore meant that we could build mutually beneficial collaborative relationships within the hospital, with academia and with industry to accelerate and enhance our drug discovery efforts.

Are there any other benefits to moving to the Oncopole?
Our location and the 2015 strategic alliance with Sanofi has also given us access to French 'academic bridge' projects. We are working with Sanofi to scout and incubate projects in France and bring them into our pipeline, to support the translation of academic science from bench to bedside.

In addition, we have had the possibility to benefit the Oncopole and the region. For example, we can provide access to services and technologies for researchers within our network, or explore new approaches with clinicians and histopathologists. We have also begun to work with smaller companies and academics in drug discovery. We are recognised as a scientific partner with both proven experience and state-of-the-art technologies who can help to find faster and more cost-effective routes to the clinic.

What are your key areas of focus in oncology?
We are targeting the mechanisms of immune regulation, metabolic adaptation and tumour survival in cancer, including exploring ways to address so-called 'immune desert' tumours – those without pre-existing immunity. Our internal projects include work on DNA damage agents and on immunomodulatory agents.

We take a rational approach to drug discovery, which begins with target validation, a key pre-requisite to any successful programme. Then by leveraging our experience, expertise and technology platforms, we aim to identify effective combinations with standard-of-care treatments and with immunotherapies, including checkpoint inhibitors. I believe the combination approach is, and will continue to be, very important to see durable responses in the clinic.

Why is clinical translation an important step?
Over recent years there have been many publications highlighting the increasing cost of drug development, and the falling numbers of candidates making it through clinical development and onto the market. This clearly indicates that we have to get better at drug discovery, and I believe that clinical translation is an important part of that puzzle.

How does Evotec improve its translatability?
To improve translatability to the clinic, we need a deeper understanding of the biology, and more confidence that the preclinical results will translate into clinical efficacy and safety. At Evotec, we continue to invest in technologies that can help us do both and thereby improve the success rate as drugs move from preclinical to clinical development. Examples are application of targeted metabolomics and proteomics, single cell RNA sequencing, CRISPR knockout, and immuno-phenotyping.

The quality of our science, our early hypothesis testing for targets, biomarkers and chemical series, and our ability to integrate biomarker discovery into the drug discovery process plays an important role. We also rely on feedback from clinicians and pathologists to help to guide translation to the clinic during biomarker evaluation.

How can patient samples support this process?
Access to patient material is very important for optimising clinical translation, and our collaborations within the Oncopole mean that we have access to annotated patient material, either sourced from the cancer biobank of the Oncopole, or directly from patients. In this way we can even carry out ex vivo experimentation on fresh tumour or blood samples, which is often essential to having a better understanding of the biology.

A better understanding of the biology then feeds back into translatability, helping us to identify and validate target engagement, stratification, and maybe even toxicity biomarkers which help with the design and running of successful, cost-effective clinical trials.

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