New technology and the evolving treatments in immuno-oncology

Björn Frendéus, Chief Scientific Officer at BioInvent, sits down with *Pharmafile* to discuss innovative immuno-oncology developments and how combination therapies can support cancer patients across the world

***Pharmafile:* How does your immuno-oncology approach differ from others? And why is this better?**

Björn Frendéus: BioInvent's focus lies in extending the successes of immuno-oncology to settings where known or unknown tumour resistance mechanisms are at play. Some cancers never seem to respond to therapy while, in others, the responses to current therapies may be suboptimal. We are now starting to be able to address the reasons why.

There are three areas of biology that we believe are particularly important to address: the biology of T regs, the biology of tumour-associated myeloid cells, and mechanisms that control resistance to therapeutic antibodies. We have promising clinical data so far, and ultimately validation will come from further strong clinical performance. To this end, our programme is accelerating, with four compounds in the clinic and another expected by the end of 2021.

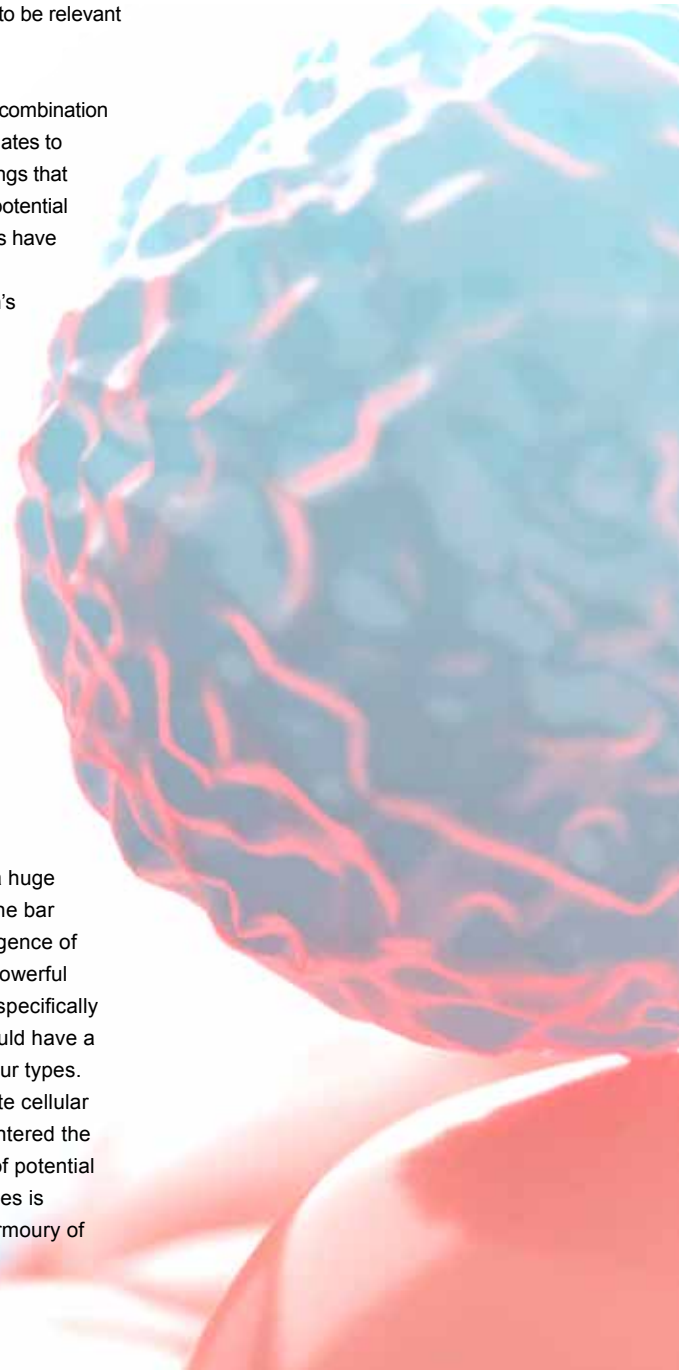
Where has the company's attention been focused most recently when it comes to developing new treatments?

One of the key programmes has been the development of antibodies that selectively block the inhibitory Fcγ receptor, FcγRIIb. In some patients, unless FcγRIIb is blocked, the interaction between the Fc region of 'tumour-targeted' antibodies such as rituximab and FcγRIIb can down-regulate anti-tumoural immune activity. We have published data showing that FcγRIIb controls resistance to rituximab in multiple ways, and we have already seen encouraging signs of clinical efficacy for the combination of our antibody, BI-1206, and rituximab. Thus BI-1206 has the potential to be relevant to several existing approved antibodies and is likely to be relevant to many that are yet to come.

We also have a second antibody combination being tested in the clinic which relates to improving on anti-PD-1. Our findings that the Fcγ receptor is important for potential improvements for PD-1 antibodies have also been corroborated by world-leading labs such as Jeff Ravetch's group at Rockefeller University in New York.

Immunotherapy has been a game changer for oncology, but it is only effective and/or available to a small percentage of patients. How would you suggest this can change over the next decade?

Immunotherapies have completely changed the life prospects of many patients with difficult-to-treat cancers. They have also demonstrated that they are possible to cure by activating the immune system, a huge conceptual change that raised the bar for many in oncology. The emergence of CAR T cell therapy provided a powerful demonstration that directly and specifically boosting the immune system could have a stunning impact on certain tumour types. Since then, many other candidate cellular and molecular therapies have entered the clinic and a continuous stream of potential antibody or antibody-like therapies is under development. This vast armoury of



immune-oncology tools was developed with a somewhat skeletal understanding of their interactions with the immune system. With more flesh on that skeleton, we believe that the performance of these existing tools can be greatly improved.

How big a role do you feel combination therapies will play in cancer treatment going forward, and what are the advantages of these?

Combination therapies will certainly play a huge part in future cancer treatment. The field will probably have to move beyond the current, rather empirical, and opportunistic combinatorial approach to something that is robustly grounded in a mechanistic understanding of cancer resistance.

In other words, effective combinations will require a deeper knowledge of the tumour microenvironment associated with a type of cancer or with a patient's specific cancer. In tumours with a high level of immunosuppressive T regs, for instance, you want an agent that specifically reduces the activity of those cells. On the other hand, it might be effective to add oncolytic viruses to a tumour with no immune cells.

What role do technology platforms such as your own have in cancer research?

In general, biotech is a risky business with high attrition rates for individual drug candidates. The value of a physical platform such as an antibody library in immuno-oncology is that you can continue to query the very fast-moving edge of biology, select agents to test interventional concepts, and, later, screen to identify candidate drugs with a suitable toxicology and efficacy profile. By the end of 2021, BioInvent will have five distinct programmes in the clinic, all based on antibodies from our library, all with novel mechanisms of action. That those candidates from our internal library are now in the clinic provides some validation of our platform and suggests more could enter clinical development in the future. Having said that, I would also stress that the true platform is the network of scientific, clinical, financial, and commercial collaborators who add value to the products that emerge from resources such as our antibody library and our function-first discovery platform.

How has COVID-19 impacted the work you do, and also the wider field of oncology?

The COVID-19 pandemic has had an impact across oncology on the ability to recruit patients for clinical trials. It has restricted access to hospital-based oncology treatments either directly or indirectly. Clinical investigators have continued to see patients, of course. But in terms of running trials, they have had to prioritise and make stringent choices about the programmes in which they involve patients. Many factors play into those choices, and two of them are the strength of clinical networks and the robustness of the preclinical science that underpins innovative programmes.

We have built a long-term relationship with many investigators. More objectively, it helps if a company can offer a compelling preclinical data package to show clinicians the rationale that guides a new treatment. So, we have a strong foundation and beyond that, BioInvent has been very fortunate that recruitment in our programmes has proceeded relatively smoothly and quickly over the last year or so.

What are your expectations for oncology in the coming years, and what do you hope to see?

It is tempting to compare the status of treatment of oncology today with the relatively early treatments for HIV/AIDS. Individual reverse transcriptase inhibitors and viral protease inhibitors were convincingly effective in reducing disease progression, but resistance almost inevitably emerged. The shared problem across the whole of oncology – whether you are developing antibodies or CAR T cells, or bispecific antibodies or some other modality – is the resistance mechanisms inherent in so-called 'cold tumours', where T cell infiltration is low or absent. No modality seems to work well by itself, suggesting that each needs an adjunct to activate immunity better in those cold tumour settings. With that in mind, we are particularly excited about our work with partner Transgene on oncolytic viruses. When the virus is injected into the tumour, it appears to act as a set of multiple innate ligands that summon inflammatory cells. This combination of multiple mechanisms of action and anti-cancer properties is an indication of one way we can seek to address the problem of resistance.

Björn Frendéus, PhD, is the Chief Scientific Officer of **BioInvent**, a Swedish Biotech developing antibody-based treatments for cancer immunotherapy. Björn is a Doctor of Immunology, and a visiting professor at the Cancer Sciences Division in Southampton, UK. Björn chairs the Swedish Foundation for Strategic Research's expert review committee on Infection Biology.