Cyril Konto, President & CEO – Ichnos Sciences

... the Ichnos team has further accelerated our clinical stage pipeline in haematological malignancies to better position the firm and prepare it to host new investors aside from parent company Glenmark Pharmaceuticals.

05.05.2022

Tags: Ichnos, Biotech, Oncology, Autoimmune Disease, Glenmark Pharmaceuticals

Cyril Konto, President & CEO of Ichnos Sciences comments on the company's unique approach to finding new cancer treatments, the possibility of becoming fully independent from parent company Glenmark Pharmaceuticals and the licensing agreement Ichos has with Almirall for the IL-1RAP antagonist, ISB 880.

Around one year ago, you left behind a career in big pharma and big pharma sponsored biotech to join Ichnos. What was the value proposition that led you to make this leap?

Joining Ichnos represented an exciting opportunity to create and develop novel immuno-oncology (IO) therapies for cancer patients alongside a team of accomplished biotechnology executives. I advocate for the potential of multispecific antibodies as the next wave of innovation in IO, as they stand between standard biotechnology and engineered cell therapies. Additionally, the Ichnos BEAT® (Bispecific Engagement by Antibodies based on the TCR) Platform has the potential to position the company as a leader in the field.

What have been some of the major developments with Ichnos' pipeline in your first year in the position?

Taking on the work done by my predecessor, under my tenure the Ichnos team has further accelerated our clinical stage pipeline in haematological malignancies to better position the firm, broaden its portfolio into solid tumours, and prepare it to host new investors aside from parent

company Glenmark Pharmaceuticals.

More specifically, our lead asset ISB 1342, a CD38 x CD3 BEAT first generation bispecific antibody, is in Phase I development and being tested in the US and now in France since Q3 2021. The trial protocol was amended to further leverage translational sciences for Proof-of Mechanism, accelerate the dose escalation schema, and test subcutaneous administration. We implemented all the modern IO clinical development tools within the trial, firmly positioning Ichnos as a clinical stage biotechnology company.

Secondly, we moved forward with ISB 1442, our CD38 x CD47 BEAT second generation bispecific antibody, which was featured in an oral presentation at the American Society of Hematology (ASH) in December 2021. The investigational new drug application (IND) was filed at the end of March 2022 and the first in-human study is on track to start in mid-2022.

Thirdly, Ichnos is preparing for the future. ISB 2001, our first trispecific antibody, is now being tested in IND enabling studies which will continue during 2022 after Ichnos selected the candidate in March.

Another big milestone was the decision to divest our autoimmune disease candidate – ISB 880, an IL-1RAP antagonist monoclonal antibody – to Almirall in order to focus on oncology, the area that Ichnos management team knows best. We now have a strong alliance with the Almirall team and they have announced that IND filing is planned for the first half of 2022.

Ichnos continues to meet with potential partners to out license ISB 830, an OX40 antagonist monoclonal antibody, which successfully completed a Phase IIb study in moderate to severe atopic dermatitis. Two products acting on the OX40 pathway were recently out-licensed, and we feel that our asset is well positioned to compete as a third market entrant.

What has changed on a company/structural level over the past 12 months?

Beyond the pipeline, Ichnos' success is highly dependent on its people and culture. We continue to foster a biotech culture following the spin out from Glenmark and are being driven forward by our exceptional leadership team and talent pool.

In the past year, we have been able to attract top talents, including Eric Feldman, M.D. who joined as chief medical officer in November 2021. Dr Feldman is a well-known researcher and clinician in the treatment of haematological malignancies and has a strong track record of developing

oncology drugs. Additionally, Eugene Zhukovsky, Ph.D., a renowned expert in the field of biotechnology with over 25 years of international experience in the R&D of novel IO therapies, joined as chief scientific officer. Moreover, we have a new chief technology officer in the name of Stephen Hearty, Ph.D., someone with a successful history in designing, engineering, and executing antibody discovery programs for novel immune cell engagers. Finally, in November 2021, we also added Sonia Quaratino, M.D., Ph.D., former CMO of Kymab, as a new director on Ichnos' board.

Ichnos also established a Scientific Advisory Board to help us advance our pipeline and develop innovative IO therapies. This group is comprised of seven distinguished leaders in cancer immunology, tumour microenvironment, and protein engineering, and adds to the expertise of the two scientific directors we already have on the board.

Aside from the successes achieved with Ichnos' technology platform thus far, has the company experienced any significant setbacks in the past 12 months? What are the pitfalls that you are keen to avoid?

Ichnos is not the only player in the multispecifics field and we want to lead from the front. Multispecifics are large molecules with great potential but which, due to their size, can be challenging to work with. We are constantly conducting analyses to ensure that the tumour indications we are targeting are conducive to our technologies.

Additionally, Ichnos is taking a broad approach to innovation in multispecifics. For example, we want to make sure that our technology can be administered subcutaneously for patients' convenience; increase the half-life of the molecule so that the administration interval can be widened; as well as ensure stability of the platform, and make it more 'plug and play', and more adaptable. This will allow us to create new assets internally more quickly as well as attract more research partners interested in using the BEAT platform.

There are also other immune cell subsets that we are focusing upon. We started in the field of haematological malignancies, even more specifically in multiple myeloma, which is a crowded space where development is difficult. It is also a disease that becomes chronic and, as the benefit of new approved technologies, has lower unmet medical needs than other haematological malignancies. Because of this, we are shifting from multiple myeloma to all other haematological malignancies with our CD38-targeting assets. Haematological malignancies are a low hanging fruit for immune cell engagers. We know that patients, physicians, and investors are expecting progress from the company on solid tumours, and we feel that the new features to the BEAT 2.0 platform

will increase our chances of success in this space.

What are your hopes for the near future in terms of pipeline development?

Ichnos' focus is on finding new treatments for cancer patients. I have a lot of hopes, and I am at Ichnos to transform them into reality. Ichnos' success will be measured by bringing innovative medicines to patients.

Our approach has been to start with a T cell engager in relapsed/refractory multiple myeloma before using the same target to create a myeloid cell engager for hematologic malignancies more broadly, before finally expanding to solid tumours. We hope to see clinical proof of concept with ISB 1342 in mid-2022 and present preliminary clinical data at ASH in December. The entire corporation is focused on this critical goal. We will also be moving the first in class myeloid cell engager ISB 1442 into clinical studies over the summer. This bispecific antibody targets CD 47 specifically on tumour cells and is gaining significant interest from the scientific community and the industry.

At the same time, we will continue to advance our discovery portfolio to create a steady stream of novel immunotherapies. All our future oncology assets are built using BEAT 2.0, Ichnos' proprietary protein engineering platform, which allows maximal flexibility and manufacturability of full length multispecific antibodies. BEAT 2.0 follows a plug and play approach to creating multispecific antibodies, responding best to tumor biology and known mechanisms of resistance. Ichnos' discovery and protein engineering teams have designed this platform to expand our pipeline and we are also open to working with external partners that are interested in using it to advance their own portfolios.

How is the company's financing situation evolving?

On the investment side, our parent company Glenmark has mentioned publicly that Ichnos is continuing the process of becoming fully independent following the spinout. We have been assessing multiple ways of accessing financing besides Glenmark, but the market has been quite stormy recently, for multiple reasons, and we therefore decided to postpone those plans.

In order to succeed in this strategy of independent fundraising for Ichnos, we need three key elements. The first is a preclinical story, i.e. the BEAT platform, which potential external partners are currently reviewing. The second key element will be demonstrating anti-tumour activity

clinically with our lead assets. The third element will be an external validation of our technology and expertise by joint development or joint research collaborations.

What types of partnerships are you looking to foster; should we expect more link ups with European mid-caps like Almirall moving forward?

Almirall is a great partner for ISB 880 because of their expertise in dermatology and autoimmune diseases. When it comes to oncology partnerships, we are open to a range of partnership and licensing models that can help us advance our portfolio. We are currently in discussions about our assets with leading companies in oncology. Ideally, we will secure global co-development partnerships with key IO pharma players.

Ichnos is also open to setting up research collaborations to let other companies use the BEAT platform with their own ideas.

Finally, I recently hired Ichnos' first head of business development, licensing and alliance management, who will support the company in validating Ichnos' technology and expertise externally.

How challenging is it to strike a balance between external collaborations and ensuring the development of internal projects?

We must be careful not to stretch resources to the point where bandwidth for our own internal objectives is compromised. On one hand, we want to promote the BEAT platform and are open to working with others to develop their own ideas, but we must also protect the work of our own teams. By biotech standards, Ichnos is a large company with its own discovery, protein engineering, process development, manufacturing and development groups; therefore, there should be the capacity both to support internal objectives as well as work with external partners.

Given your personal history in successfully developing and achieving regulatory approvals for immuno-oncology therapies, how have you seen the clinical trial process develop? Are we any closer to seeing the price and complexity of clinical trials go down as remote trials and machine learning start to become more effective?

Firstly, the R&D process is inherently risky. However, I am hopeful that with the emergence of new technologies spanning this entire process, we are entering a new era for discovery and development, and I am committed to employing them in Ichnos.

Ichnos has a rigorous multi step process including R&D governance milestones to review research program advancement through candidate selection and IND enabling studies, with the aim of ensuring preclinical safety and anti-tumour activity of our assets.

We are fortunate to have a team of experts skilled in the implementation of clinical development tools to support efficiency in the selection process of the right dose, dosing schedules, mode of administration, and the early discontinuation of investigational products that are not useful for the patient. With its medicines, Ichnos is striving to achieve incremental benefit for patients..

That being said, the amount of clinical and translational data points produced in our clinical trials today surpasses our brain capacity. Moving forward, I would like to see greater interaction and interoperability between these vast amounts of data and the various data systems employed, a mission for which AI and machine learning can be leveraged. These tools have proven efficient in recognising correlative patterns for safety and/or efficacy early and transforming them into future scientific hypotheses.

AI and machine learning can also accelerate the successful identification of targets in the preclinical space and I am convinced that AI will revolutionise medicine by making diagnosis and treatment more accessible and more effective. At Ichnos we are evolving with technology and adopting new tools that can simplify and speed candidates to market.

Clinical trial population diversity has become a hot topic among Big Pharma, especially in the USA, but how much can biotechs really integrate issues like these into their planning, given their earlier stage of development?

It is essential that our trials are representative of real patient populations and are conducted in a manner that both helps the regulator and those in communities who may be disproportionately impacted by a disease. We need to reassure regulators that the populations we enrol in our clinical trials are representative of the population that they have to protect. This focus needs to be part of the development process from the start; we must consider the needs of these communities in both the design and execution of our clinical programs.

Diversity is in Ichnos' DNA and a strong component of the environmental, social and corporate governance (ESG) that inspires our executive leadership team and will be formalized soon. We strongly believe that clinical trials must be representative of the targeted population; otherwise, the lack of diversity becomes the first risk of data misinterpretation.

One example comes from our anti-OX40 program, ISB 830, currently developed in atopic dermatitis, which has enrolled patients mainly from the US, while our competitors have predominantly enlisted patients from Asia and Europe. We are asking the question how much the difference in demographics could interfere with cross-trial comparison.

In addition, we as we have learned, a treatment can only help patients if new innovative drugs are accessible. Therefore, while it is early for us to discuss efficacy and pricing, we do aim to develop multispecifics that bring substantial benefits for patients, improving quality of life and extending survival while being more affordable than, for instance, engineered cell therapies in terms of cost of goods and achieving a lower price for innovation.

Your predecessor mentioned that pricing discussions were a bar on innovation for early- and early-clinical-stage biotechs; has there been a change of tack at Ichnos in terms of pricing considerations?

I stick with my predecessor's views. Nonetheless, I am sensing a shift in the drivers for investors with a new generation focused on ESG, which we ourselves are implementing in all our actions. Topics like accessibility, diversity, and the environment are at the top of the political agenda today, which we are sensitive to.

Some engineered cell therapies are currently expensive in part due to the cost of raw materials used to make them (eg. retroviral vectors). If multispecifics could achieve clinical efficacy close to cell therapies, price would be less of an issue with a technology like Ichnos' BEAT; something worth noting, even for a company at an early clinical stage of development.

How has the way in which companies like Ichnos interact with regulatory bodies evolved? Is there still work to be done to adequately explain cutting-edge technologies to bodies like the FDA?

COVID-19 demonstrated that the regulatory process could be faster and more flexible than ever imagined, as well as the transformational impact of ongoing dialogue between sponsors and regulatory authorities. One good example is the work done between the FDA and Pfizer, achieving very impressive timelines.

The urgency of creating a vaccine for COVID 19 crisis was clear and regulators took extraordinary steps to streamline the process. We need to look for ways to pull these practices through to other therapeutic areas with high unmet medical needs, like oncology. I am hopeful that the pace of development that occurred during the COVID 19 pandemic will provide regulatory agencies around the globe with inspiration on ways they can further streamline their processes and launch new programs that can benefit patients.

Ichnos also closely monitors the ongoing discussions led by the FDA on how to improve the system for accelerated approvals; running fast confirmatory trials for the determination of clinical benefits/risks after approval seems to be at the heart of the current debates. Additionally, some companies have used unvalidated surrogates for efficacy leading to low-quality studies for accelerated approvals, and I believe that our experienced leadership team is a way to protect Ichnos from wrong strategic choices onwards.

In terms of dialogue between the FDA and Ichnos, I have always been a strong advocate of early interaction with the FDA. Pre-IND meetings are a great opportunity to prepare regulatory authorities on our development, explain our intent, and receive meaningful comments. Additionally, closely monitoring our safety and proactively taking safety measures rather than waiting for regulators to impose them is at the heart of what we do. We have, thankfully, not encountered any such situations so far, but we are prepared in case any such instances arise.

During my career, I have even been in situations where new technologies – such as allogeneic CAR-T cell therapy – were pioneered with the help of the regulators, fostering mutual learnings. We see the regulators as partners with a broader view, since they are able to do meta-analyses of multiple technologies in the same class.

Do you have a final message for our global executive audience on behalf of Ichnos?

It is time to make Ichnos better known and recognised in the field of multispecifics and advocate even more widely for the BEAT platform. This platform has a fantastic potential that people deserve to hear more about. I invite all interested parties to consider BEAT in comparison to other

competitive platforms and the key attributes of their technologies.

Naturally, as a biotech company we have limited means and human resources and so cannot do everything. We are actively looking for partners in research and/or development to help us succeed.

Lastly, we also need to make sure that Ichnos is recognised by the investor community. All fundraising options are on the table: whether crossover IPO, SPAC, or reverse merger. If companies are willing to entertain discussions with us, the management team will be happy to reach out to them.

This company is sure to grow as soon as clinical proof of concept is reached with the first asset, and we are preparing for the future today.

See more interviews