Alessandro Riva – CEO, Ichnos Sciences

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Alessandro Riva, MD joined biotech Ichnos Sciences as its founding CEO in 2019, leaving behind a storied career in oncology R&D at Novartis and Gilead. In an exclusive interview, Riva outlines his motivations behind taking on this new challenge, how the company's approach to oncology treatment differs from - and complements - those of its competitors, and his ambitions for the future of Ichnos.

Having come from quite an illustrious background in Big Pharma, could you begin by talking us through your rationale for leaving this behind to join a new company, Ichnos, as CEO?

I am an oncologist by training and have spent my entire professional life trying to move the needle for cancer patients. I started out at the University Hospital of Milan, in Italy, as an oncologist/haematologist at a time when bone marrow transplantations for patients with haematological malignancies, were just beginning. I was very lucky to be there as the University Hospital of Milan is one of the most important bone marrow transplantation units in Italy.

In this role, I was close to the science, close to patients, and gained a sense of the strong need for new therapies among the oncology community and their real-life consequences. While I was doing that job in the hospital, I was also – on behalf of a pharmaceutical company, Farmitalia Carlo Erba –

testing a compound for acute myeloid leukaemia in patients. Farmitalia, later acquired by Pharmacia that was in turn acquired by Pfizer, offered me a position in the company, which was a turning point in my life.

I decided to take this opportunity based on my belief that by joining the pharmaceutical industry I would be able to contribute more broadly to the oncology community and touch more patients indirectly through the work of my teams and I.

After this, I worked for several different pharmaceutical companies and was again lucky to be in the right company with the right team at the right moment. We were able to contribute significantly to moving the needle for cancer patients through the development of compounds in chemotherapy, small molecules, biologics, and cell therapies. We are extremely proud to have brought key innovations to patients that are still being used to fight against their disease.

Two years ago, by chance I was contacted by a recruiter looking to fill a board position at a new company being spun off from Glenmark's business innovation division. I asked the recruiter who the new CEO was, and he told me that they did not have one. I put myself forward, was interviewed for the position, and the rest is history! Joining Ichnos as CEO represented a once-in-a-lifetime opportunity to connect all the dots in my career from both a scientific and business perspective. This role has given me the chance to design a new, modern company that follows the pace of innovation, has a culture of inclusiveness and diversity, and is driven by science.

Having been used to working in Big Pharma, with all its associated resources, what have been some of the challenges, and perhaps opportunities, you have found in your first two years at a smaller organisation?

The challenges here are in fact closely related to the opportunities. The big opportunity was to transform the business innovation unit that Glenmark put together many years ago into a functional global oncology-focused biotechnology company. Although we have also a couple of innovative compounds in autoimmunity, oncology is our main focus area.

This process has involved transforming the organisation itself, our people, and – most importantly – our mindset. As essentially a spinoff from Glenmark, the organisation had the pace of a generic company and was largely opportunistic, reacting to what was happening in the innovation world. Changing this to a long-term, innovation-focused biotech mindset has been challenging and has taken time but has been achieved. We have made this journey step by step, in full alignment with

our parent company, but by operating independently.

Another challenge was setting up the right priorities from a scientific, strategic, operational, process, and people perspective. That also took time, especially given the fact that almost all our employees were new.

Ichnos is currently still a subsidiary of, and fully funded by, Glenmark. How far along are you in this journey to becoming an independent innovative biotech company?

We are rapidly advancing along this journey and have created an organisation that operates independently of Glenmark and has everything that you would want to see in a biotech company. Everything is ring-fenced to Ichnos in terms of technology, processes, people, infrastructure, and IP so legally and financially we are independent. Ichnos, therefore, considers Glenmark to be an investor – so far our only one – and we need to defend our strategy to them to convince them to continue to invest in Ichnos. We have an independent management team with varying experiences, a board which has both Glenmark and non-Glenmark people sitting on it.

There are several steps to pass through as we gradually build up the organisation’s value through our pipeline, our platform, and the compounds that we choose to develop. Our priority is to prepare Ichnos legally, financially, and operationally, for the final stage of the journey: when new investors come on board and we become a public company.

Ichnos has chosen to focus on probably the most competitive and talked about therapeutic area in existence – oncology – where there is a huge amount of noise, many competitors, and a litany of different approaches. Why oncology and how does Ichnos’ approach differ from that of its competitors?

The unmet medical need that exists in oncology is enormous despite the innovations of the last three decades in chemotherapy, small molecules, biologics, and cell therapy. The survival curves of many different cancers are not yet where we would like them to be and, for most cancer patients, once their cancer becomes metastatic, there is no plateau in the survival rate. Additionally, and this is correlated, there are very few long-lasting complete responses in cancer, which for us is the first step to curing the disease. Although we have prolonged the survival of many cancer patients, shrunk tumours, and been able to keep the disease under control, we are not able to offer a cure in the majority of cases. That is the bigger mission and challenge that today’s oncologists are facing.

Ichnos is therefore operating in a field that is evolving very rapidly and where, despite the innovation, medical need is significant. Essentially, we have taken on that challenge in oncology and, within that, we are focusing on what is emerging as one of the most transformational approaches for haematological malignancy patients today and potentially in the future for solid tumours.

This ‘transformational approach’ involves what we call immuno-cell engagers and immuno-cell modulators which may enhance the patient immune system to ultimately kill cancer cells. In the clinical setting, this approach is already showing itself to be transformational in terms of long-lasting complete response rate and is a strong candidate to move the needle on haematological malignancies. Additionally, we have a proprietary platform which, from an antibody engineering perspective, allows us to build up different molecules around immuno-cell engagers and immuno-cell modulators.

How does Ichnos’ approach work in relation to cell and gene therapies like CAR-T? Do you see these other approaches as competitors or complementary?

These two approaches have the same potential to be transformative for patients with haematological malignancies and potentially also solid tumours. Ultimately, these two approaches are going to be complementary, for many reasons.

The first reason is because we know that it is impossible for all patients to access cell therapy. The autologous approach is very cumbersome and takes up a lot of time and hospital infrastructure etc. We know that although autologous cell therapy is transformative, it is unrealistic to expect to serve the community and all patients’ needs with this approach.

Looking at the data on the bispecific approach, including that presented at the American Society of Hematology in December 2020, bispecific immuno-cell engagers may provide the patient with as much benefit as a cell therapy in indications like multiple myeloma, for example. It is still early days, but this is the emerging trend. Therefore, these two approaches may be complementary for the patient community in need of innovative treatments for haematological malignancies.

The second reason is that both approaches could be used for the same patient. Once both approaches are approved, we can envisage a sandwich like scenario where immuno-cell engagers or modulators are administered both as induction to reduce the tumour burden before cell therapy and as maintenance after cell therapy. This approach has the potential to be transformative for

haematological malignancies patients.

We are not competing with cell therapy – that is not what this is about – but rather we are creating additional value for patients. This is because we want to make sure that all patients that need therapy can access it. We are convinced that both approaches can move the needle for patients, both as a mono-approach as well as a sequential approach.

Bispecific antibodies also offer the opportunity to work at a different velocity; they can be quicker than cell therapies as they offer more flexibility to design new medicines.

The flexible antibody engineering platform that we have offers a lot of opportunities to design new compounds. As we learn more from cell therapy and from immuno-cell engagers, we also will learn how to categorise the patient populations that may benefit more from one approach. Always, we aim to be complementary to other approaches; we are not here to compete against other pharmaceutical companies but to fight cancer.

One of the pain points of cell and gene therapy has been manufacturing. Although these are still early days for Ichnos, how do you envision the challenges of manufacturing your therapies? Are they de-risked in comparison to cell therapies?

We need to think about immuno-cell engagers as having the same journey as an antibody. Once the challenge of mimicking a natural antibody in a bispecific or trispecific format has been overcome, as we have done, then the door is open from a manufacturing perspective. It is the same, well-defined process. The challenge is to get to the format closest to the natural antibody and then to develop the cell lines that give sufficient yield of the antibody. Nothing is simple in medicine, but this is a relatively straightforward process that has been validated for decades.

Another interesting field to follow is the allogeneic approach to cell therapies. The first generation of cell therapies were autologous, taking cells from patients, re-engineering the cell, and injecting the modified cell into the same patients. That is what takes time and what the new approach is trying to counter. In the allogeneic approach, cells are taken from a donor, re-engineered, and given to patients. This can be more ‘off the shelf’ and can be scaled up much more quickly. However, we are still a long way from understanding whether, from a gene-editing perspective, re-engineering T cells from a donor is going to impact the persistence of those T cells in the blood of patients.

Until which phase of the R&D process do you want to bring these therapies forward?

Our vision for Ichnos is to be able to commercialize or co-commercialize with a partner a compound or a few compounds in haematological malignancies in the USA. We would also like to partner with a pharmaceutical company as our ex-US partner, taking on everything else. Because we are a very small organisation, we have to go step by step and develop in a staggered manner. However, anything can happen and as we continue to create value and interact with potential partners, different permutations of this model may emerge.

COVID-19 has been a great example of how R&D and regulatory timelines can be compressed. Where do you feel you can increase the speed at which your medicines can be developed, trialled, approved, and ultimately brought to market?

For a small biotechnology company like Ichnos there can be improvements to our drug development through working with partners who have a good network as well as experience and understanding of drug development. The experience of those companies will significantly accelerate everything we do and put us on a different trajectory.

Of course, we can do all this without a partner, but the timelines will be longer. While we are doing our proof-of-concept trials, we do not need a large network, but as we advance to the next phase and we explore additional indications, it would be nice to have a partner.

From an R&D perspective, at what point do you start discussing the issues of pricing, access, and affordability for these therapies that have so far tended to be eye-wateringly expensive?

At small biotech companies like Ichnos, we do not talk a lot about pricing at the beginning of the journey, because what drives us is trying to find a cure for a disease focusing on something potentially transformative. At that stage, we do not want to be distracted by pricing and market share discussions. We are guided by the conviction that what we do, ultimately, is going to represent a significantly better treatment option for patients than what they have today.

I have of course been involved in pricing discussion when I was at Novartis and Gilead. However, for a small biotech company like ours that has a mission to advance science, if the pressure of pricing is there from the beginning then innovation is stifled. It is counterproductive to restrict the

science at this stage because a potential treatment reaching the market might be very expensive.

If a therapy is truly transformative, I believe that the community, along with the pharmaceutical company bringing it to market, has an obligation to find a way to make it available to the patient.

The pricing debate around autologous CAR-T is a unique case, because it requires a lot of infrastructure and preparation. However, it has opened the way to advance science. The reason we are now working on bispecific and tri-specific immuno cell engagers is because of cell therapy and what it has taught us from a scientific perspective. Pricing is important but pricing arguments should not be put in the lab.

What is the significance of Switzerland for Ichnos, a company with strong historic ties to India and now a focus on the US market?

Having worked for a Swiss company, I am well aware of Switzerland's importance as a global biotechnology and innovation hub. It is very easy to attract talent in Switzerland due to the big companies as well as smaller biotechs that are present there. Historically, Glenmark started its innovation division in Switzerland for exactly this reason. As an Indian company they had to choose between the US and Switzerland and found the latter more approachable, just as stacked with talent, as well as closer to India geographically.

When we created Ichnos we validated what the market has been thinking for many years. We have invested significantly during the past two years in our antibody engineering discovery footprint in Switzerland. As just one example, when I joined, we had 28 scientists at the Biopôle in Lausanne working on antibody engineering and discovery whereas now we have 90 coming not only from Switzerland, but also from elsewhere in Europe and the US.

At Lausanne Biopôle we have a very solid antibody engineering and discovery organisation in an environment close to the University Hospital and to other biotechnology companies with whom we can collaborate. It is really a scientific campus where you can perceive the dynamics of science and get inspired.

Switzerland is a good opportunity for us to be part of a biotech hub, close to other companies working in our field, with the ability to attract people, and in a modern environment at the heart of Europe.

Of course, we are also thinking about the potential of having an arm in the US. So far, we have not felt the need as we have been able to attract strong people, expand, and do the necessary work in Switzerland, even during the pandemic in 2020. We are going to continue to invest in Switzerland.

What would you like our global executive audience to take away about Ichnos?

The name Ichnos comes from the Greek word for footprint and our philosophy and vision is well represented in our logo, which contains three dots before and after the company name. The three dots before represent the fact that we are built upon everything that has been done in the past; science has advanced tremendously and we have learned many lessons. The word Ichnos itself represents us in the community today, working together towards better compounds and better innovation. There are three dots after because we want to make sure that we leave a marker, or a footprint, for those to come, whether patients that will continue to benefit from what we contribute or scientists themselves. Every time you generate new data, that data – whether negative or positive – will help others to move forward.

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