Interview: Manfred RÃ¼diger â?? CEO, Robbert Van Heekeren â?? CFO, Jeroen Rovers â?? CMO, Kiadis Pharma, The Netherlands

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Manfred RÃ¼diger (MR), Robbert Van Heekeren (RVH) and Jeroen Rovers (JR), respectively CEO, CFO and CMO of Kiadis Pharma, a Dutch biopharmaceutical company focused on cell-based

immunotherapy products for the treatment of blood cancers and inherited blood disorders, discuss how the companyâ??s recent IPO will allow them to move forward on the development of their lead compound, which aims to transform stem cell transplantation for blood cancers and inherited disorders and to dramatically enlarge the current donor pool.

You became CEO of Kiadis Pharma in 2011, a difficult time for the company following Hospira backing out from your partnership deal to develop your lead compound. What were the main priorities you set yourself upon taking on this role, and how did you succeed in turning this situation around?

MR: Hospira backed out from our research partnership in 2011, given the strategy of their new CEO to refocus on the companyâ??s core competencies in generics, whereas our partnership was clearly at the other side of the innovation chain. Hospira was also at this time under a class action lawsuit by its shareholders given manufacturing issues in their US facilities, while cell therapies are notoriously reputed to be extremely challenging on the manufacturing side. They made the decision to leave the partnership, which was not positive at all for us at this moment given that they had been covering 50% of the development costs of our joint project. When I was appointed, I had to deal with additional other issues related to clinical studies but my key task was to ensure that the financial gap following Hospiraâ??s withdrawal would be filled and that a way forward for ATIR would be established.

As a first step, we went back to the original manufacturing process and redesigned it almost from the beginning. Within only six months, we had successfully redesigned the entire manufacturing process, and we managed to raise 10 million euros from our shareholders to move into phase II trials for our lead compound, as they were particularly impressed by the excellent profile of the compound.

Looking back, it was essential to rebuild trust among our partners and shareholders. When such an important partnership is suddenly cancelled, it is usually not perceived as a positive sign, even if, in hindsight, the end of the partnership deal was after all a highly positive milestone for Kiadis! We now fully control our compounds and our fate. Today, we are a public and well-financed company that can freely and fully benefit from the upsides of the companyâ??s recent developments.

Kiadis Pharma successfully went public on Euronext in July 2015, raising 34.7 million euros gross. What were the main rationales behind this move, and what are your main strategic priorities for the money that has been raised?

MR: In mid-September 2014, we received very promising interim results of phase II clinical trials for our lead compound and began considering three distinct options to raise money â?? out-licensing with big pharma, listing in the US, or listing in Europe. At that time, we entered into discussions with pharma MNCs, but ultimately decided that it was too early for such a deal and that we wanted to remain independent. We finally decided to list on Euronext rather on Nasdaq, as it seemed a more natural fit as it is our â??home marketâ?• and given the amount of time and money we wanted to invest in raising funds.

RVH: The market was also particularly open to life science IPOs this summer, while our cash flow would not have allowed us to move forward on clinical trials without new funding. Choosing Euronext instead of Nasdaq was also related to the amount of money we wanted to raise, as we were looking as for a limited amount of funding and our historical shareholders did not want to totally dilute their shares.

MR: The key objective for the money that has been raised is to further develop our key compound ATIR101. We estimate that we will be able to get through at least half of phase III clinical trials with

the funds raised. In the meantime, we will report the phase II data during the second quarter of 2016, and, depending on the course of our clinical results, we will decide whether we want to raise more money. The money raised will also help us to launch a new project focusing on hematological inherited diseases and genetic disorders, as well as scaling up our manufacturing process.

Your lead compound ATIR101 indeed showed promising interim phase II results for acute myeloid leukemia and acute lymphoblastic leukemia. Could you please elaborate on how this treatment can benefit patients suffering from blood cancers?

MR: To summarize, our technology allows family members to become donors for allogeneic hematopoietic stem cell transplantations (HSCT) to patients suffering from blood cancer. HSCT has over thirty years of history and is generally regarded as the most effective curative approach to blood cancers and certain inherited blood disorders. However, the treatment is currently not the first choice for patients suffering from these cancers, given its current disadvantages â?? namely the limited availability of donors that display a good match and the risks associated with the procedure such as Graft-versus-Host-Disease and infection.

The time is now for cellular-based approaches, such as ATIR1010, which increases the donor pool and almost completely hedges the life-threatening risk associated with donor immune cells attacking the patient. In our trials so far, we have not seen any such symptoms at a severe level in our patients, although we are only using family members as donors, which according to the current standards of care should not be possible. We estimate that approximately 35% of patients who are eligible for HSCT will not find a matched donor in time, while a partially matched family donor will be available to over 95% of patients. ATIR101 will allow transplantations for many of these patients and also has the potential to decrease the waiting lists for transplantations, given the extended donor pool.

There is obviously no other approved treatment already on the market addressing the same unmet medical need, and there are only one or two similar medical developments underway all over the world.

What is your timeline for bringing ATIR101 to the market?

MR: The baseline scenario would be to initiate phase III clinical studies in the second half of 2016, via a randomized-controlled study conducted both in Europe and North America. We hope to be able to end up enrolling patients into the phase III study at the end of 2017 followed by a one-year period to assess mortality, which would provide the requested results at the end of 2018. If the public authorities follow the usual regulatory framework and timelines, we would expect to bring our product on the market in 2020.

In a more optimistic scenario there is a reasonable likelihood that the product could be brought to the European market earlier thanks to conditional approval procedure. This specific process targets diseases with a very high unmet medical need for which there is not currently an approved treatment as well as for orphan indications, which are two conditions that our treatment already meets. Relevant authorities will also have to assess whether our treatment displays robust and consequent efficacy, while the risk/benefits ratio of the treatment is also particularly scrutinized. If we meet all these conditions, authorities may grant us a conditional approval to market our drug all over Europe. In this scenario, we would receive the requested data to submit a conditional approval form at the beginning of the second quarter of 2016, while EMA usually reviews this kind of applications in less than a year, meaning that a conditional approval could allow us to bring the product to the European market as early as 2017.

Kiadis Pharma undertakes clinical trials and manufacturing in several countries in Europe such as Belgium, Germany and the UK as well as in Canada. Why was the Netherlands not chosen for these activities?

JR: There were few centers only in the Netherlands a few years ago that would already have been experimenting with alternative donor sources and the need for that may not have been as high in the Netherlands as like in Belgium or Canada. This has changed more recently and we see a strong potential that we can pursue our phase III clinical trials in the Netherlands, even if it is not yet a common practice to work on these kind of transplantations here..

MR: We anticipate enlarging the number of partners for future clinical trials, and we of course hope that the Netherlands will be included, as well as the United States.

Kiadis Pharma is also simultaneously developing a second compound, ATIR201, for thalassemia. At what stage is this research?

MR: This compound stands at an earlier stage than ATIR101, as we needed to raise funding to fully kick-off the project. We expect this project to be clinically active as from the first half of 2016. This compound will directly start in phase II clinical trials, as it almost shares the same base as the ATIR101 compound and there is thus no scientific interest to test its effects on healthy patients.

Kiadis Pharmaâ??s compounds are based on the Theralux product platform, developed in partnership with the University of Montreal. How does this cutting-edge technology work?

MR: Theralux technology basically allows us to identify the transplanted immune cells that will attack a patientâ??s tissues instead of the disease and to kill these cells off in a laboratory setting, in an elegant and effective fashion. We are then able to re-administer the remaining cells (which will only attack pathogens or cancer cells but not the patientâ??s healthy tissues) in the immune system of the patient suffering of blood cancer. All this, thanks to a molecule that will attract all the targeted cells and, once activated, destroy the immune cells that cause the rejection of the transplant. As this procedure is conducted in a laboratory setting and not within the patientâ??s body, there is no risk of harming the patient, and this procedure allows us to make use donor material that would otherwise not be usable in patients, as it would attack the patient.

The resulting immune cells allows the patient to fight infections more quickly and to be immune competent earlier than with a regular transplantation. Patients usually have to wait from three months to a year for the immune system to become fully functioning, and during this period the are very vulnerable to any kind of infection, a major cause of death.

What is the nature of your collaboration with the Technische Universitat Munchen?

MR: Thanks to this partnership, we have been able to develop an assay to confirm that our product ATIR101 contains immune cells that can attack structures that are specific mutations on cancer cells at about the same frequency and density as in the donor. We expect that transplant patients will benefit from those immune cells to help protect from further infections and cancer relapse.

In addition to this partnership, we are particularly open to international cooperations or partnerships. We cannot obviously conduct all our researches in our in-house facilities, while the current state of sophistication of scientific research encourages us to work closely with the best experts in our diverse fields of interest to build expertise more quickly. We are particularly interested in partnerships with immunology, oncology and inherited blood disorders specialists to move forward on our productsâ?? development.

How do you stimulate a company culture that bolsters true innovation to create game-changing therapies?

MR: Basically, I tell my people to not take anything for granted and to always ensure that they could not find a differently or better way to continue their work. We are also not afraid to admit that in some areas we do not have all the needed competencies in-house, and we always have to remain open to new partnerships. I finally think that our mix of young graduates, experienced pharma managers and fundamental scientists is the best way to foster creativity. As a small team with 30 employees, we remain particularly flexible.

What achievement are you the most proud of since becoming CEO of Kiadis Pharma?

MR: So far, we have undoubtedly been able to demonstrate that the manufacturing of our products can be set up in a very robust way and highlight the clinical efficacy of our compounds. We want to change patientsâ?? lives, and luckily we seem very close to being able to do so!

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