Jean-Paul Clozel – CEO, Idorsia (October 2017)



"We want to integrate all the modern technology at Idorsia, which includes discovery, development, and future marketing."

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In an exclusive interview, Jean-Paul Clozel, former head of Actelion and now CEO of exciting biotech newcomer Idorsia, discusses his new company's unique drug discovery methodology, the pressure of past success, and how he hopes to usher in a new era of collaboration to tackle disease.

In August 2016, when we interviewed you as CEO of Actelion, you made quite a clear statement that you were not interested in selling the company! A few months later, Johnson and Johnson (J&J) acquired Actelion for USD 30bn. This deal is somewhat unique in that no-one was laid off, J&J acquired Actelion's sales arm, there was no disruption to the project pipeline, and the development part was spun off. Please tell us about the deal and whether you think this is a sign of things to come.

I think this was a very interesting deal for both J&J and Actelion, and I would like to extend my sincere gratitude to J&J, because they realised the mutually-beneficial nature of this deal for both sides. Sometimes in these situations, everyone is interested in making the best deal for themselves without considering whether it is a good one for the other party involved and for society in general – as yes, the ultimate concern should always be the patient. There was no value destruction. It is true that I have always claimed I would never sell, but in fine, we didn't sell the company, we were bought. J&J made a fair offer that Actelion could not refuse, and I hope there will be more deals like this in the future.

With Idorsia, you have a single-centre approach, multiple therapeutic areas, and a focus on small molecules. Could you please tell us about your drug discovery methodology and the rationale behind this strategy?

From day one it has been a continuation of Actelion's research. Nothing has changed since the creation of Idorsia, other than the fact that we might start to limit the scope of our discovery efforts to be able to focus on the most important projects. We have not changed our strategy of having one centre here in Basel, a focus on small molecules, and we will continue striving to go where science and innovation bring us. Once we discover a drug that addresses a rare medical need or is a breakthrough, we will follow the lead and develop it for commercialisation.

Joint development is inherently risky and J&J were happy to not take on this part of the business. What makes you so confident you can repeat the success story of Actelion?

I am confident, but I am not certain. There is some risk, and it is not a done deal. There is a lot I am unsure of, but I am sure of one thing: we will have problems! It will go up and down, it will not be linear and there will be some obstacles along the way. However, I think we are in a much better situation now than we were when we started Actelion. We were successful with Actelion despite not having money, projects, and human resources; now, we have all of those. We were able to succeed with nearly nothing at Actelion, so with all these assets I am more confident.

You have described Idorsia as "the perfect constellation": initial funding of CHF 1bn, existing facilities, research experience, the same HR… Is there not a risk then that you might rest on your laurels by not having as much pressure?

You are right, and this is a risk. But as everyone who has worked in this biotech environment can tell you, three years of cash goes very fast. Idorsia's management knows that this is not such a comfortable situation. If we do not move quickly, we will have problems. It is a less comfortable position than it looks like, as it is very different not to post revenues or a profit every year. We are not there yet, but we have the possibility to get there one day.

I don't believe in putting financial pressure per se on our researchers and R&D department. Their pressure is to find a new drug. Perhaps there is some pressure at the management level, but I

generally do not think that adding too much pressure is really a good thing. It does not add anything to be honest.

Past success is the biggest enemy of future success. Just because you have succeeded in the past does not mean you will succeed in the future. This has been true with the creation of Idorsia, as well as it was true with Actelion. You need to be constantly reinventing yourself. Nokia is an example of a really successful company that has just collapsed. Idorsia's story could be seen as a reinvention.

Idorsia is embracing digitalisation, innovation and integrating that with the drug discovery process; is this part of the company's reinvention?

We do not want to change the way we discover drugs. We want to integrate all the modern technology at Idorsia, which includes discovery, development, and future marketing. We need to think of what role modern, i.e. digital media channels will play in future drug launches and partner with people who represent this digital aspect. I do not want Idorsia to be an Actelion clone. If anything, it is an improved Actelion, an 'Actelion plus'.

Take us through your pipeline. You have ten different compounds with four of those candidates that are moving towards phase III.

Our number one compound is called aprocitentan (ACT-132577) and is a dual acting endothelin receptor antagonist, which is used for a resistant form of hypertension. It is a big market, and represents not only patients with hypertension, but those with diabetes and obesity too, which are very difficult to treat. I think these patients' conditions are very badly controlled with existing drugs, and I think the addition of aprocitentan will be a new very important way of treating these patients. J&J has the possibility of licensing this product. Our number two compound is a sleep drug called DORA (ACT-541468) which is a follow-up of a drug that failed and which we stopped in 2010 due to unwanted side effects. Since then, we have synthesised 25,000 new products in order to get the perfect drug, trying to avoid the problems we had with the previous drug. We therefore found this new drug, and are very happy to see it reach phase II, which showed and confirmed fantastic efficacy. Then we have a compound called Lucerastat used in Fabry disease which is starting phase III. We have agreed with the FDA on the clinical endpoint. The last one is Clazosentan which is used for a certain form of stroke. This is also going to start phase III next year. Japan will be the first

country where the drug will be launched.

Then, we have six other drugs, some in phase I, some in phase II. We will not go through all of them, but there are some very innovative products. The focus is, as with Actelion, on unmet needs where a real difference can be made.

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In terms of financial sustainability, when are you looking at achieving profitability?

In 5-6 years. There might be partnerships or the opportunity to raise money. We have CHF 1bn in cash, and we have received CHF 243m in loans. There are other sources of income, for example some financial milestones if aprocitentan is licensed by J&J.

What difference does it now make to have collaboration agreements with Janssen and to operate with the might of J&J behind you?

It makes a significant difference, but we remain an independent company. We are not a spinoff of J&J. We know that if we fail and do not offer good drugs, J&J will not be there to give us money. They reap all the benefits without the risk. It is quite a good situation for them.

Are you saying that J&J puts less of an emphasis on R&D risk then?

It is not that J&J were not interested in the R&D side. They just thought that the current situation was a better solution for everyone involved. The projects need the people as well. There is no project without people behind it. Very often people are not interested in moving to a large company, so when you try to integrate these projects into large companies, you are losing a lot of your talent, and you are losing your ability to do these projects. With the agreement, the people interested in the project are staying, and I think it is a win-win situation.

When we started doing our Reviews 12 years ago, everyone wanted to work for Big Pharma, but today we are seeing R&D teams wanting to go to mid-sized players and even CEOs leaving Big Pharma so as not to have the constant pressure for quarterly

results. How do you view this shift?

When I started Actelion, people asked me, “what is the difference between a biotech and a pharma company?” I remember replying that a biotech company was a pharma company that loses money. This was the definition 15 years ago. This has changed completely…

It seems that Big Pharma is increasingly an investment and sales vehicle, while the other functions are being outsourced. Would you agree with that?

I do not agree with that. I think Big Pharma has made a lot of progress in research. They are launching many more drugs than they used to. Some of this is due to acquisitions or partnering. Whatever your strategy is, it is important to develop good drugs. Pharma has made a lot of progress, I think the research is very good. At Actelion, we knew that 99.5 percent of big discoveries would not be done at Actelion. 99.5 percent will also not be discovered at Roche or Novartis, so they should be open and not only try to discover new drugs themselves, but to look outside when possible.

So you see a new collaborative spirit going forward?

A lot of people say that the competitor is a company that is right next door, but I do not think so. I think the real competitors are the terrible diseases we are fighting against. The real enemy is a cancer that is killing people or a disease making children’s lives terrible. I wish that all pharma companies would work together against this common enemy. I think there is a lot of progress to be made to find the right deal. It is for example incredible to see that J&J considers the deal we made to be unique. Yes it is unique, but it was such an obvious deal. In the future, I think this is a much better way to collaborate. Collaborations can however be improved at every level. There are many opportunities for deals and partnerships. We have not been very imaginative in how to collaborate, so there is still some improvement to be done.

When you were negotiating the deal with J&J it was not easy. What were the concerns you had or what resistance did you face?

It was a very difficult deal to execute. For example, there were 40,000 contracts to go over. Who is paying the electricity here? Is there one electrical counter? One building belongs to J&J, one

belongs to Idorsia. Same with the water, the internet, etc. There were 40,000 contracts to be split. Lawyers were working extensively to figure out how to share the intellectual property. Although it was the right idea, the deal was very challenging to complete. Also, there needs to be mutual trust, so that there are no accusations that one party is being unfair in the way they behave. Importantly, even if there is a change in ownership, there needs to be a strong focus on the future development of the company.

Tell us about the execution. From the outside looking in, it seems everything has progressed very seamlessly.

This is thanks to J&J. They are made to make acquisitions. I do not think there are many companies other than J&J that could have made such a deal.

How would you define Idorsia's corporate identity today?

It is the only start-up with 650 people! That pretty much sums it up. I think it is a unique situation. It is a model that has never been done. Usually you start from zero, or you are a company which is split or spun off. This is not really our case as we were there before. This project is 15 years old, and is a sort of hybrid of everything. The identity will be created along the way. I do not want our main concern to be "to put this product on the market as soon as possible." We are a drug-hunting company.

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For a long time entrepreneurs have looked up to Actelion, even more so after the acquisition and now with Idorsia. What advice would you give to entrepreneurs trying to achieve similar success?

Do not try to replicate Actelion! Do what you think is right for you. Copying never works. Think of building real value with your hard work and infrastructure.

Build your company and do not think of how you are going to sell it. How can you sell a company that does not have a value?

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