HM*i* meets... Ivo Timmermans

Pleco targets partnerships to fund toxic metal treatment

Pleco Therapeutics, a specialty biopharmaceutical company developing treatments to detoxify the cancer micro-environment, wants to demonstrate the market value and therapeutic potential of its proprietary Plecoid products through an initial focus on treatments for orphan cancers.

Pleco's novel Plecoid therapies have the potential to positively change the balance of protein expression within the cancer microenvironment, removing the burden of toxic metals within the cell, thereby improving the effectiveness of existing chemotherapy.

Its current pre-clinical development programmes focus on the development of treatments for Acute Myeloid Leukaemia (AML), a relatively rare blood cancer, and Small-Cell Lung Cancer (SCLC), an aggressive subtype of lung cancer. Both diseases carry a poor prognosis.

It plans to expand its scalable product platform to the treatment of other cancers as well as neurodegenerative disorders where aberrant metal patterns have been shown to play a role.

To fund development and expansion – it recently incorporated a subsidiary, Pleco Therapeutics USA – it pursues co-development and licensing deals with medium sized pharmaceutical companies and commercial partnerships for late-stage clinical trials and marketing, and for combination studies.

In November 2021, Pleco entered a strategic partnership with Belgium-based and listed Hyloris Pharmaceuticals, a biopharma company reinventing existing medications. The agreement, of up to €8.7m (US$8.6m), sees Hyloris providing €1m in tranches over time, automatically convertible into Pleco equity, together with potential funding of up to an additional €7.7m in pre-defined R&D activities against an agreed development plan.

In September 2022, it announced the final close of its Series A financing at €17.3m, exceeding the company's €15m target and providing sufficient funds to complete the development of PTX-061's (the company's lead Plecoid Product) regulatory dossier in AML and to be ready for submission to the FDA and EMA as early as 2024.

The investments include €3.6m in new equity from Oost NL and a select number of private investors, €5m in government funding from the Netherlands Enterprise Agency, as well as the €8.7m equity and R&D project financing from Hyloris.

HM*i* caught up with CEO Ivo Timmermans to discuss his journey in Life Sciences, the company's aspirations and its chosen route of financing development.

Timmermans has worked for pharmaceutical and biotech companies for 30 years, during which time he has been involved in the strategic development of medicines and various product launches.

He held senior positions such as global medical director of Rhein Biotech, and chief medical officer of Clinigen Group. He was CEO of four start-up companies in the Netherlands and non-executive director of Phico Therapeutics in Cambridge, UK. His specialties include oncology, immunology, viral diseases, and vaccines.

HM*i* **How did you arrive at Pleco?**

Ivo Timmermans It all has to do with what I did in the past in pharmaceutical and biotech.

When I graduated from medical school, I got involved in working for a specialist in tropical medicines and special infections. The specialist treated AIDS patients at a time when nobody knew what the agent was, and nobody knew what treatment would be effective. I was involved in some of the first clinical studies that Wellcome organised; Wellcome had the first effective anti-HIV compound called Retrovir.

I saw the effects of these drugs. Patients recovered remarkably – just after one week they walked out of the hospital. That encouraged me to investigate the possibility of working in drug development.

> THE ACCUMULATION OF METALS IN THE BODY OVER TIME CAN CAUSE DISEASE AND PROLONG THE IMPACT OF CANCERS

I worked for several pharmaceutical companies before deciding to work for myself because I thought it would be more interesting to offer my services as a consultant.

Six years ago, I joined Clinigen as chief medical officer. While there I was approached by an investigator from the MD Anderson Cancer Centre in Texas, one of the powerhouses in oncology and one of the leading leukaemia centres. She wanted to speak to me because Clinigen had two compounds in which she was interested.

Her research was based on the role of metals in the contamination of people throughout their lifetime – the accumulation of metals in the body over time can cause disease and prolong the impact of

HM*i* meets...

Ivo Timmermans

Chief executive officer, Pleco Therapeutics

Career

Chief executive officer
Pleco Therapeutics BV
(Jul 2018–)
Interim Head of Clinical Development
Mundipharma Research
(Dec 2017–Jun 2018)
Chief medical officer
Clinigen Group
(Feb 2016–Nov 2017)
Medical director – Germany, Austria, Switzerland, the Netherlands
The Medicines Company
(Sep 2015–Feb 2016)
Medical Marketing Advisor, Business Developer
(2003–2015)
Global medical director
Rhein Biotech NVR
(Jan 2001–Oct 2002)

Education

MD, Medicine
Radboud University
1981 - 19901981 - 1990
MBAMBA
Henley Business School
2000 - 2003

www.linkedin.com/in/ivo-timmermans-5b33701/

cancers. She'd noticed that her leukemic patients had an elevated level of several toxic metals in their blood. Elevated levels of toxic metals are also evident in other diseases and in some neurological diseases.

Two weeks after I left Clinigen as part of a reorganisation, I was on a plane to Houston because I wanted to explore the concept further. The Centre needed an external partner to develop it commercially and we decided to work together. That led to the establishment of Pleco Therapeutics.

We started with four founders, and we are developing a series of agents that have the potential to work in cancer and some other diseases where we suspect that metals are involved.

How do you go about financing the operation?

IT The first years are challenging, particularly to get appropriate financing. Every company finds its own way but, to start with, the founders put in some money of their own.

We found our first private investor, who invested €100,000, and then we received interest from a regional development company in the Netherlands that wanted us to settle in its area.

After one year we had attracted €500,000.

Those first couple of years were challenging. You must suffer a bit at the start and it's a big gamble for the founding team. The founders essentially worked as volunteers for the first one and a half years.

For the next step, we convinced a few angel investors to get involved and that brought in another few €100,000s. We later moved from our first location to Nijmegen, receiving €600,000 from Oost NL.

What about VCs?

IT We've probably made between 100 and 120 presentations to VCs and there were a few that expressed an interest for the next rounds.

But the problem with VCs is that they have too much choice and they'd rather invest in something where there's a known mechanism or a certain receptor that can be targeted and where they can most-easily justify an investment. But if there is something a bit outlandish, some cutting-edge science like ours, then they like to see more results before deciding to participate.

THE FIRST COUPLE OF YEARS WERE CHALLENGING. YOU MUST SUFFER A BIT AT THE START AND IT'S A BIG GAMBLE FOR THE FOUNDING TEAM

In my experience, the ones that advertise on their website, 'we like to support breakthrough concepts and cutting-edge science', are the worst.

Where do you go for financing in that situation?

IT We began contacting pharma companies because we thought they would better understand what we were doing.

We contacted Hyloris Pharmaceuticals in Belgium, which repurposes medicines, and they expressed an interest in Pleco if part of the research goes to reformulating already existing molecules.

After four or five months of negotiation, we struck a deal and that led to the €8.7m agreement last November.

On top of that we found more support from the regional investment company Oost NL in the Netherlands, a few angel investors willing to help, and the Dutch Ministry of Economic Affairs.

THE PROBLEM WITH VCs IS THAT THEY HAVE TOO MUCH CHOICE... IF THERE IS SOMETHING A BIT OUTLANDISH, SOME CUTTING EDGE SCIENCE LIKE OURS, THEN THEY LIKE TO SEE MORE RESULTS BEFORE DECIDING TO PARTICIPATE

What do they take in exchange?

IT We have a profit share agreement with Hyloris for our first product. So, for our first product to the market, we have agreed to divide profits and they take €1m equity.

The angels and the regional development company take equity and the Dutch innovation credit is, in essence, a business loan.

The business loan runs as long as the project runs, and the agency adds 25% on top as interest.

It is still much more advantageous to us than having to dilute our equity.

We have investment of €17.3m. No venture capital involvement, only pharma companies, angel investors and investment companies.

And the founders still have more than 60% of the equity, so we are able to control the strategic direction the programme.

We are well funded for the next two and a half years, and we are funded to complete the clinical programme and the first indication on acute myeloid leukaemia, an aggressive blood cancer.

And how will you finance future growth?

IT Not with VCs at the moment because it gives us more freedom to manoeuvre. We're talking to pharma companies that have an interest in certain indications.

We're also exploring the possibility of research grants. So, we're looking at non-dilutive funding to explore a few additional indications.

For the next six months at least, we won't be looking at traditional finance by talking to VCs or equity investors.

In the long run, however, Pleco will likely remain a research vehicle and look for larger partners to market and sell the compounds.