

**BENOÎT VAN DEN EYNDE and ITEOS THERAPEUTICS**

# BOOSTERS OF ANTITUMOR IMMUNITY

WHEN BENOÎT VAN DEN EYNDE ASKED Michel Detheux in 2010 if he would like to start a new biotechnology company, Detheux did not hesitate. “It took me three seconds to decide,” he recalls.

Van den Eynde, director of Ludwig Brussels, was eager to develop drugs against two immunotherapy targets he had identified, indoleamine 2,3-dioxygenase (IDO) and tryptophan 2,3-dioxygenase (TDO). Compounds that blocked these enzymes could fend off cancer in mice, but Van den Eynde was a long way from turning them into testable drugs. The new company would provide the framework for that effort and help him secure the funding to make it happen.

“The proposal involved a partner I could trust, excellent scientists, and people who shared my vision for a drug discovery company,” recalls Detheux, a biochemist with extensive experience working in biotechnology companies.

Neither partner has been disappointed. In August 2011, the researchers cofounded Brussels-based iTeos Therapeutics, and by April 2012 they had won major backing from Ludwig and other investors. In December 2014, with Detheux as its chief executive officer, the biotechnology company forged a multiyear, multimillion-Euro partnership with the pharmaceutical giant Pfizer. Detheux and Van den Eynde’s path to this agreement showcases Ludwig’s dedication to moving basic findings to the clinic through partnerships—a process buoyed by the extensive scientific and technological know-how of its network of scientists.

Pfizer will soon initiate clinical trials of drugs targeting IDO and TDO. As part of the deal, iTeos received an upfront payment of €24 million, some of which will go toward the discovery of new drug targets. It’s not a bad outcome for a project that began as a hunch.

## **Embryonic idea**

“I sometimes have ideas that are a bit



*Jonathan Skipper*

crazy,” admits Van den Eynde. One of them popped up in 1998, when he read a study on how the placenta protects the fetus from immune attack. The researchers reported that the organ produces an enzyme named IDO, which participates in the degradation of tryptophan, an amino acid especially important to immune cells.

A tumor looks like a foreign body to the immune system, mused Van den Eynde. Perhaps tumors also use the same defense mechanism. It was a shot in the dark, but he asked a research technician in his lab to begin looking into that possibility in his down time. “I didn’t believe it would be the case,” says Van den Eynde.

Much to his surprise, however, the technician found that IDO was present in a large variety of human tumors. IDO-blocking compounds, it turned out, could dissolve the immune shield around tumors and expose them to devastating attack.

Van den Eynde’s journey had just begun with this discovery. “Between fundamental research and a drug candidate there is a huge amount of applied research,” says Dethoux.

## **Sustained support**

Van den Eynde had a few false starts, including unsuccessful attempts to identify a competitive anti-IDO drug. But along the way he identified a second drug target, TDO, which has the same function as IDO and is similarly exploited by tumors. And in the summer of 2011, iTeos got its big break—a €6 million award to fund IDO and TDO drug discovery programs from the Walloon Regional Government in Belgium. But the award came with a stipulation: iTeos had to raise €3 million from other sources by the end of the year.

iTeos approached Jonathan Skipper, executive director of technology development at Ludwig, starting an intense series of discussions. The scientific solidity and clinical potential of Van den Eynde’s discovery were immediately apparent to Skipper, but he also knew the tough and costly business of drug development. “It was clear they needed substantial investment if they were going to be successful,” recalled Skipper, who started a discussion within Ludwig that culminated in an investment of €1.5 million in the project. Ludwig’s vote of confidence convinced other private and angel investors in Belgium to provide another €1.5 million to the fledgling company.

iTeos was ready to roll.

Researchers across Ludwig supported the project over the next two years. Chemists in San Diego, for instance, advised iTeos on where to outsource tasks such as drug synthesis. Colleagues like Gerd Ritter of Ludwig New York provided invaluable advice on the preclinical development of the compounds.

After about two years, the company emerged with a pair of promising drug candidates. In mice, the compounds synergized with other immunotherapies such as cancer vaccines and immune checkpoint



*Benoît Van den Eynde*

drugs like ipilimumab, shrinking tumors more powerfully than either treatment could alone. Van den Eynde and Detheux were finally ready to find a partner who could take them into clinical development.

### **Partnering up**

“We spoke with more than 40 venture capital groups and 28 pharmaceutical companies,” recalls Detheux. In December 2014, they sealed the deal with Pfizer. “The company has access to our programs, but in a setting where it will be collaborative,” says Van den Eynde, who now regularly meets with Pfizer to help chart the project’s course.

Pfizer also brings to the table a pipeline of immunotherapy drugs, opening a world of possibility. “The scope of different combinations of IDO and TDO with immunotherapies that can be tested before going into clinical trials is very large,” says Detheux, who anticipates that clinical trials will begin soon. iTeos will also collaborate with Pfizer on a program to identify new

immunotherapy drug targets, which will then be developed by the two companies either together or alone.

Though he continues to work with iTeos as head of its scientific advisory committee and as a board member, Van den Eynde is back to focusing primarily on his own research into how tumors evade the immune system. “I like being back in my lab, exploring new ideas,” he says.

So 2014 was a very eventful year for iTeos and its founders. But one moment in particular stands out for Van den Eynde. After signing off on their agreement, iTeos and Pfizer organized a kickoff meeting in San Diego last December. “There was Michel, and me, and several other scientists, and more than 30 people from Pfizer involved in our programs,” recalls Van den Eynde. “It hit me then—the research I did ten years ago in Brussels had given rise to a major worldwide pharmaceutical program. That was very gratifying.” 📌