Evaluate Vantage

May 09, 2017

Interview – Poxel takes high-energy approach to diabetes

Madeleine Armstrong

In the highly competitive space of diabetes, players will look for any edge they can get. One way companies can set themselves apart is by targeting a new mechanism of action – and this is the approach that the French group Poxel has taken with imeglimin, a mitochondrial bioenergetics enhancer.

Mitochondrial dysfunction has been linked with diabetes for some time but Poxel is alone in this niche, its chief executive, Thomas Kuhn, believes. “We don’t think there are any other products in the clinic targeting mitochondria for the treatment of type 2 diabetes,” he tells *EP Vantage*.

This could make Poxel attractive to the bigger fish in the diabetes sector, which have been contending with US pricing pressure and slowing sales growth. And positive data from a Japanese phase IIb study of imeglimin, reported last week, cannot have hurt its cause (*Novo needs new blood despite earnings relief, May 4, 2017*).

More energy

By targeting mitochondria Poxel hopes to address an underlying issue in type 2 diabetes. Patients have dysfunctional mitochondria because “they usually eat too much, until they have an excess of nutrients coming into the mitochondria. On the other hand, they don’t exercise as much as they should,” Mr Kuhn says.

Overall, this leads to an excess of nutrients and a low demand on energy, which creates oxidative stress that impairs mitochondrial function, according to the chief exec.

“Imeglimin restores normal functioning by increasing the capacity of the different proteins of the mitochondria to transform nutrients into energy – even in the diabetic pathological process.”

Mr Kuhn is adamant that Poxel will press on alone in Japan, where it should only need a relatively small phase III programme – three trials of roughly 1,000 patients each, he estimates – to get approval. “The path to market is reasonable compared with other countries,” he says. “This is something we have the experience for – we have a team in Japan that’s looking after the clinical and regulatory processes.”

The company plans to start phase III in the fourth quarter and hopes to submit imeglimin for Japan approval by the end of 2018. It will need more cash for this – Poxel only had €38.8m ($42.2m) in the bank as of the end of March 2017.

This lack of funds helps explain why development in the US and Europe has stalled in spite of promising data from a phase IIb dose-ranging trial in December 2014, which supported taking a 1,500mg dose of imeglimin monotherapy into phase III.

Mr Kuhn admits that Poxel will need a partner to support a pivotal programme here, which he believes will need to total seven trials in around 7,000 patients overall. He says the company is already in talks with potential collaborators, in parallel with discussions with the FDA and EMA about study design.

With the onerous requirement of huge trials to tease out cardiovascular risk in Europe or the US, it will take a bold partner to jump in on such a novel diabetes approach.

AMP it up

Meanwhile, Poxel has an earlier-stage diabetes asset with another novel mechanism, the direct AMP kinase activator PXL770.

According to *EvaluatePharma*, no AMPK activators are approved in diabetes, though Betagenon’s O304 is already in phase II, putting it ahead of PXL770. There are also various projects in preclinical development.

Like imeglimin, PXL770 is designed to regulate energy – the AMPK enzyme’s role is to maintain cellular energy homeostasis. “Put simply, our product will mimic the benefit of doing sport – that’s the concept,” says Mr Kuhn.

However, Poxel has had a hiccup in development. It had to go back to the preclinical stage after a phase I trial

found differences in the way the product was metabolised in humans versus animals. The chief executive insists that no safety worries were uncovered in the clinic, and the company hopes to start the second phase of the phase I trial in the second half of this year.

PXL770 acts directly on the liver, Mr Kuhn says, so could also have utility in diseases such as Nash. The Nash space has garnered a lot of attention – and investment – potentially providing another avenue for Poxel to attract a partner.

But with limited resources Poxel will not want to stretch itself too thinly. For now the focus has to be on progressing imeglimin in diabetes.

Poxel's pipeline

Project	Status	Indication	Mechanism of action
Imeglimin	Phase II	Type 2 diabetes	Mitochondrial bioenergetics enhancer
PXL770	Phase I	Type 2 diabetes	AMPK activator
PXL007*	Phase I	Hepatitis B	FxR agonist

**Partnered with Enyo Pharma.*