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April 09, 2019

Poxel tastes sweet success at last

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The group follows licensing deals with Dainippon and Roivant with a pivotal study win.

After years of trying the French biotech company Poxel seems finally to have scored a clinical success. Imeglimin, which the group claims to be the first of a new class of antidiabetics, has yielded a positive result in the first of three pivotal trials designed to pave its way to a regulatory submission in Japan next year.

Poxel has disclosed little about the data beyond relative biomarker reductions and basic statistics. No doubt more will be forthcoming at a scientific meeting, but the presence of Dainippon Sumitomo and Roivant as recent licensees of the project should give investors comfort.

Interestingly, Poxel struck the Dainippon deal, covering Japan and other key Asian markets, in October 2017 – just five months after insisting to *Vantage* that it wanted to press on alone in Japan (*Interview – Poxel takes high-energy approach to diabetes, May 10, 2017*).

One reason given was that a pivotal programme in Japan seemed manageable, numbering some 1,000 patients, versus an expected 7,000 in the West. The current Japan registrational plan comprises three studies, called Times-1, -2 and -3, which between them will enrol 1,100 type 2 diabetics, Poxel says.

Imeglimin's path to approval in Japan

Study	Subjects	Design	Data	Trial ID
Times-1	213	Double-blind, 24wk, monotherapy, vs placebo	Topline reported	JapicCTI-173769
Times-2	~700	Open-label, 52wk, monotherapy or combo with other antidiabetics	Q4 2019	JapicCTI-173782
Times-3	~200	Double-blind, 16wk (+36wk extension), combo with insulin, vs placebo	Mid-2019	JapicCTI-183846

It is the 24-week Times-1 study, in 213 subjects given 1,000mg of imeglimin twice daily as monotherapy, that read out positively today.

From a baseline HbA1c of 7.99% and 7.93% in the imeglimin and placebo cohorts respectively, the mean placebo-adjusted HbA1c change favouring the Poxel compound was -0.87 percentage points, with a high level of statistical significance, Poxel said.

In Japan imeglimlin's biggest competitor would be Merck & Co's DPP-4 inhibitor Januvia. According to Januvia's US label this drug's 24-week monotherapy study showed a placebo-adjusted HbA1c change of -0.8 points, from a baseline of 8.0% in each cohort.

Poxel also highlighted Times-1's key secondary endpoint, fasting plasma glucose, where imeglimin showed a -19mg/dl placebo-adjusted change, also with high statistical significance. The corresponding number for Januvia is -17mg/dl. Analysis of additional secondaries is ongoing, Poxel said on an analyst call today.

Mitochondria

Imeglimin is a mitochondrial bioenergetics enhancer designed to address mitochondrial dysfunction, which Poxel says is a cause of diabetes.

Development has been tortuous, Poxel having originally been spun out of Merck KGaA in 2009 to develop the compound, which it initially wanted to file in Japan in 2018. Work in Europe stalled for lack of funds, though a 1,500mg twice-daily dose did show promise in phase II.

It is not clear why it was 1,000mg that was taken into phase III in Japan, but it is likely that the added benefit of 1,500mg did not outweigh the risk; Poxel said Times-1 showed a similar safety profile for the active and control groups.

The deal with the Roivant subsidiary Metavant, struck a year ago, should help get the Europe trial under way. Poxel said a US phase III study in chronic kidney disease patients should begin if Metavant's phase II study, due to report mid-2019, was positive.

However, under the tie-up's terms Poxel is on the hook for a disproportionately high share of development costs. The group ended last month with €59m in the bank, and as it is now sitting on a 70% year-to-date share appreciation now could be the time to ask investors for some more.

This story has been updated to add Japan clinical trial registry IDs.