CLOSER LOOK

MEMORANDUM

Oramed reports full phase 2b results for oral insulin candidate ORMD-0801 - August 3, 2016

Oramed recently reported full results from the phase 2b trial of its oral insulin candidate ORMD-0801 in adults with type 2 diabetes. The double-blind, 28-day trial (n=180) showed a significant difference in the unconventional primary endpoint of mean change in nighttime glucose from run in (1.66 mg/dl for the ORMD-0801-treated group vs. 13.70 mg/dl for placebo, p=0.0117), as measured by a CGM. We note that this is slightly different from the primary endpoint results presented in the topline data, which highlighted a statistically significant 6.47% reduction in pooled night-time glucose (p=0.0268) with ORMD-0801 compared to placebo. Full results from the trial also demonstrate a significant difference in mean change in (i) 24-hour glucose (-.32 mg/dl for ORMD-0801 vs. 13.26 mg/dl for placebo, p <0.0001); (ii) fasting glucose (-0.41 mg/dl for ORMD-0801 vs. 15.95 mg/dl for placebo, p <0.0001); and (iii) daytime glucose (0.88 for ORMD-0801 vs. 11.88 for placebo, p = 0.0010). The study reports a statistically significant, though small, difference in A1c after 29 days (-0.01% for ORMD-0801 vs. 0.2% for placebo; p = 0.0149). Oramed suggests in its announcement that this relatively inconsequential difference is due to the insufficient amount of time in the study to adequately measure the influence of ORMD-0801 on A1c. There was no difference in morning fasting serum insulin, C-Peptide, or triglycerides with ORMD-0801. Oramed characterized ORMD-0801 as safe and well-tolerated. Overall, we remain skeptical of the candidate's potential as it has not been historically confidence-inspiring. We await further evaluation in the upcoming phase 3 trial. Oral insulin is a very challenging proposition, given the low bioavailability of oral peptide delivery, complex dose titration requirements for insulin, and the narrow therapeutic range. We expect Novo Nordisk's phase 1 oral insulin candidate is more likely to achieve success, given the company's experience with oral peptide delivery through its ongoing development of its phase 3 oral semaglutide - but even for the insulin giant, this is a very big bet.

-- by Emily Fitts, Helen Gao, and Kelly Close