MEMORANDUM

Tolerx and GSK announce disappointing news on DEFEND - March 11, 2011

Executive Highlights

- Tolerx and GSK announced disappointing news today that the phase 3 study DEFEND-1 for otelixizumab, an anti-CD3 therapy, failed to meet the primary efficacy endpoint of change in C-peptide at 12 months post treatment in those with recent onset type 1 diabetes.

This morning, Tolerx and GSK announced the disappointing news that the phase 3 study DEFEND-1 for otelixizumab, an anti-CD3 therapy, failed to meet its primary efficacy endpoint of change in C-peptide at 12 months post treatment in individuals with recent onset type 1 diabetes. While a preliminary analysis did not reveal any unexpected safety concerns, as we understand it, a subgroup analysis was also unable to discover potential benefits with treatment. We await further word on dosing as we believe different dosing may well have yielded significantly different results. In response to these results, recruiting and dosing in the confirmatory phase 3 study DEFEND-2 was suspended. GSK has stated that it will explore alternative dosing regimens as it weighs its decision about the future development of otelixizumab.

Anti-CD3 therapies have shown promise in animal and initial human studies for preserving beta cell function in the type 1 diabetes setting. At least in animal models, these therapies are thought to work by not only by preventing the activation of T-cells involved in the attack of beta cells, but by also inducing natural regulatory systems that restore the ability of the immune system to properly recognize beta cells as self-cells. This news follows a similar announcement in January by Macrogenics/Eli Lilly that their late stage anti-CD3 compound teplizumab also failed to meet its phase 3 study's primary efficacy endpoint of A1c reduction and insulin usage in October.

In our view, these recent setbacks on the cure-based front (not to mention Roche's recent decision to drop Bayhill's insulin vaccine BHT-3021 from its pipeline - although Roche emphasized this was related to resource constraints) highlight the still incomplete understanding of the immune system processes and pathways involved in the development of type 1 diabetes. Furthermore, the results may also suggest that a combination of immune modulating therapies that target different aspects of the immune system involved in beta cell destruction may be more effective than any one therapy alone. We also wonder whether progress on the artificial pancreas front (especially if it's use can be initiated early in the course of disease) can do more to preserve beta cell function by significantly improving glucose control and lowering beta cell stress. Still, in the case of Tolerx, we are hopeful that the question of dosing will be an important factor to explore and that additional data from DEFEND-1 will provide greater insight into the efficacy, safety, and future of otelixizumab.

-- by Ben Kozak and Kelly Close