Evaluate Vantage

May 28, 2021

Provention’s diabetes project takes a tentative step forward

Amy Brown

A 10-7 advisory committee vote in favour of approving teplizumab to delay the onset of type 1 diabetes is a step in the right direction for Provention’s project. But it is far from the end of the road. For a start there are FDA concerns about pharmacokinetic inconsistencies between the MAb used in the clinic and the one Provention plans to take to market; regardless of the agency's opinion on approvability, the issue is thought likely to result in the July 2 Pdufa date being missed. Other concerns raised by the panel included the small sample size, with only 44 patients receiving teplizumab, and lack of long-term safety data. The panellists and the FDA seem to agree that a 32.5-month delay in median time to clinical diagnosis is meaningful, but it is easy to see why the agency might choose to tread cautiously here. Another aspect troubling investors is the commercial potential of this opportunity, which in the short term would be hampered by the lack of effective ways to identify at-risk people, outside of having close relatives with the disease. The harsh realities facing Provention won out this morning, with the stock opening off 14%.

Teplizumab in type 1 diabetes: a long development history		
Year	**Event**	**Note**
2002	Ph1 data on teplizumab in new-onset type 1 diabetes reported in NEJM	Trial finds improvement in metabolic control and mitigation of deterioration of insulin production
2005	Macrogenics buys teplizumab from Tolerance Therapeutics	Terms undisclosed
2005	NIAID starts the Abate trial of teplizumb to halt the progression of newly diagnosed type 1 diabetes	Study finds that teplizumab significantly reduced the loss of C-peptide after two years (p=0.002) but responses vary widely
2007	Macrogenics starts the Protégé Study in newly diagnosed type 1 diabetics	-
2007	Lilly buys global rights to teplizumab	Terms include $41m up-front fee and up to $450m in milestones, plus royalties
2010	NIDDK starts the "At risk" trial, or TN-10	-
2010	Protégé fails to meet primary endpoint of lowering insulin use and HbA1c	Macrogenics and Lilly ultimately abandon the project
2018	Provention buys teplizumab from Macrogenics	Terms include a warrant to buy 2.2 million shares at $2.50 (exercised in 2019); plus $170m on regulatory milestones, incl $60m on FDA approval, plus $250m sales milestones and single-digit royalties
2019	Provention starts the Protect trial in recently diagnosed type 1 diabetics	Topline data data due in H1 2023
2019	TN-10 succeeds, extending diabetes diagnosis by two years.	Provention announces plans to file teplizumab for approval
2021	Provention files teplizumab for US approval	-
2021	FDA adcom votes 10-7 in favour of approving teplizumab to delay type 1 diabetes.	-
July 2, 2021	Pdufa date	-
Source: Evaluate Pharma, company statements & SEC filings.		