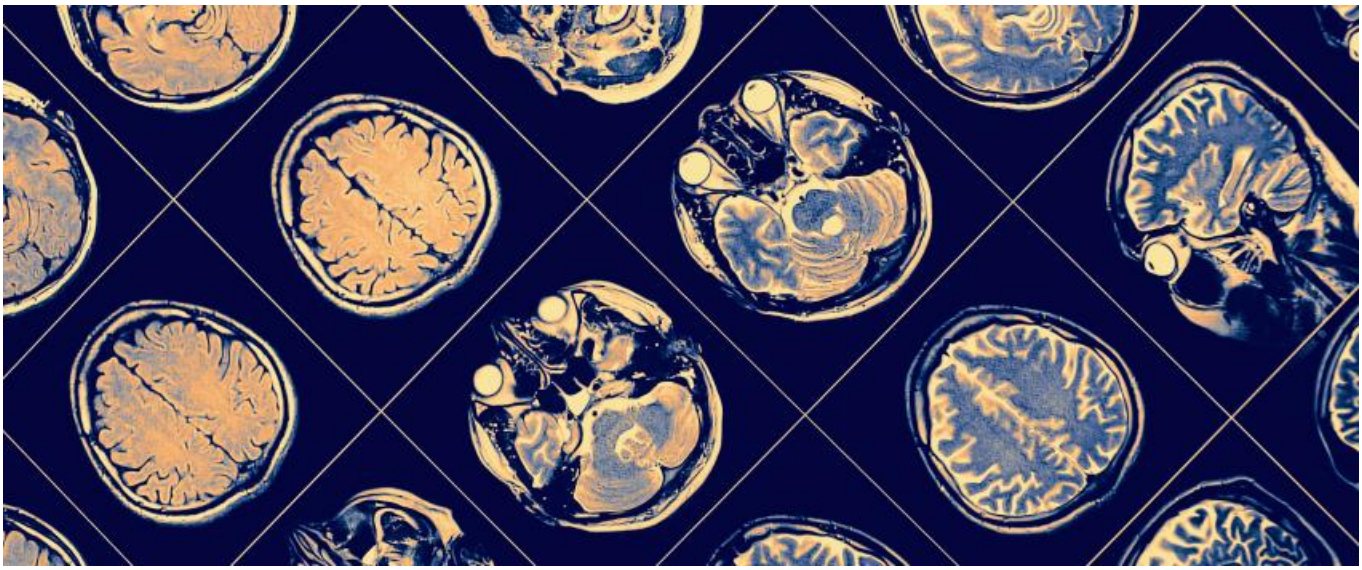
Evaluate Vantage

October 21, 2020

Roche buys into Prothena... kind of

Jacob Plieth



The Swiss group moves to start a further trial of prasinezumab, but this will not be phase III.

Perhaps the fact that Roche has not scrapped development of its Prothena-partnered Parkinson's disease project prasinezumab is good news in itself. This and the Swiss group committing to pay Prothena $60m on the initiation of the asset's next study has sent up the smaller company's shares 7% this morning.

Some might herald this as a vote of confidence in Prothena, while others will criticise Roche for ploughing on in the face of some decidedly mixed earlier data. The truth lies somewhere in the middle: Roche is not taking prasinezumab into pivotal development, instead hedging its bets with another confirmatory phase II study.

The design of this trial has yet to be revealed, but it will involve patients with early Parkinson's, and will include those who are stable on levodopa therapy. The $60m clinical milestone will only be triggered once dosing starts, and this will not happen until next year, at which point more details of the study will emerge.

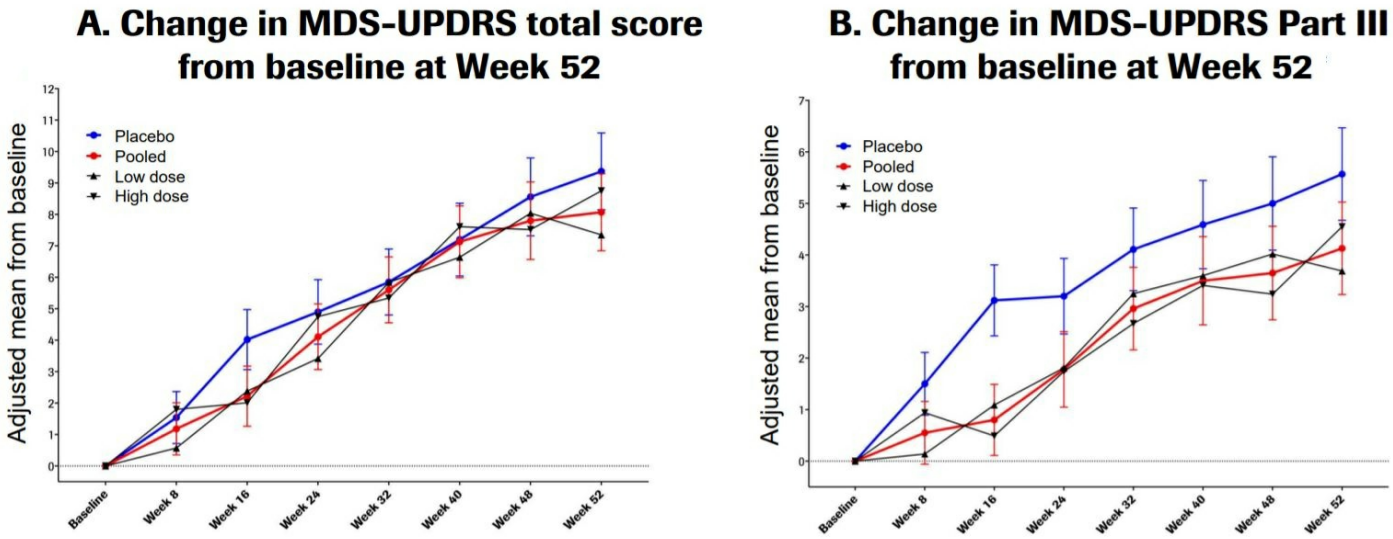
Alpha-synuclein

The project, an anti-alpha synuclein MAb, is Prothena's lead asset after the AL amyloidosis project NEOD001 failed in the phase IIb Pronto trial in 2018.

Abnormal alpha-synuclein is a major component of Lewy bodies, which are deposits sometimes found in Parkinson's patients. Mechanistically prasinezumab had potential: Roche had highlighted the near elimination of alpha-synuclein serum levels after a single high dose, shown in phase I.

But a bigger test came up short. In April Roche quietly revealed that the 316-patient phase II Pasadena study failed its primary objective, which was for prasinezumab to beat placebo in terms of MDS-UPDRS total score from baseline to 52 weeks. Roche claimed to have seen "signals of efficacy", however.

Then last month a presentation at the MDS Congress put more flesh on the bones. There was indeed absolutely no difference between placebo and prasinezumab on MDS-UPDRS total score, but what did show a numerical separation was MDS-UPDRS's part III, which relates to motor symptoms like bradykinesia, tremor, rigidity and gait.



Summary of prasinezumab's Pasadena study; change in MDS-UPDRS total score (A) was the primary endpoint. Source: MDS Congress.

A further 52-week blinded extension of Pasadena was to have yielded results this year, but has been derailed by the Covid-19 pandemic, which has caused some patients to miss assessments. Roche says it is monitoring the situation.

Prasinezumab is an important asset not only for Prothena investors, but for those in Biogen too. According to *EvaluatePharma* the latter group is developing the next most advanced alpha-synuclein MAb in the industry pipeline, BIIB054 (cinpanemab).

While the immediate focus for Biogen is the upcoming aducanumab adcom, given the company's thin pipeline the results of BIIB054's phase II Spark trial are keenly awaited too. The data are expected in the first half of 2021, having earlier been delayed from the late 2020 timeframe.

Prasinezumab's slow progress will provide some comfort but at best the project has shown glimmers of activity in an otherwise unsuccessful dataset. Roche's caution is warranted.