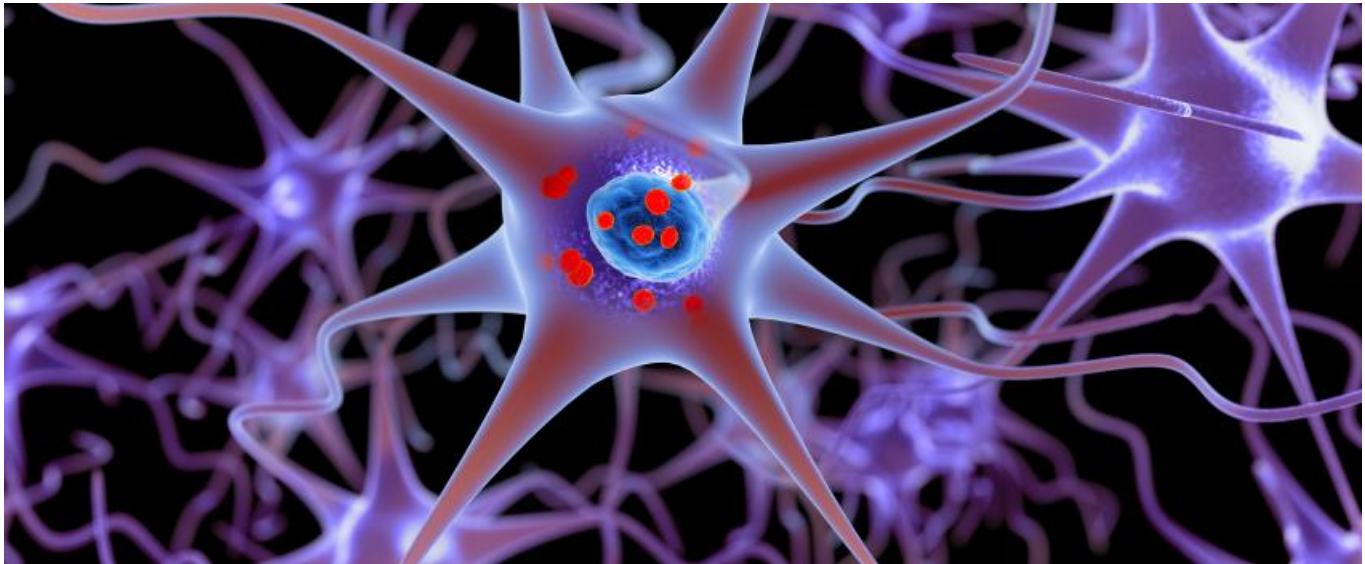


AC Immune backs alpha-synuclein despite recent setbacks



Madeleine Armstrong



The group's purchase of Affiris's Parkinson's portfolio comes after stumbles from Roche/Prothena and Biogen.

AC Immune is going all in on targeting alpha-synuclein for Parkinson's disease. The group's tie-up yesterday with Affiris gives it a phase 2-ready anti-alpha-synuclein vaccine to add to the preclinical antibody and small molecule it was already developing against this protein.

Still, recent setbacks in this space might not bode well. The most advanced alpha-synuclein-targeting project, Roche and Prothena's antibody prasinezumab, produced mixed phase 2 data last year, although the companies are pressing on. Biogen, meanwhile, discontinued its contender BIIB054 after the failure of the Spark study.

AC Immune is clearly not deterred by these developments, swooping for Affiris's alpha-synuclein-targeting portfolio in an all-stock deal valuing the assets at \$53.7m. Chief among these projects is the vaccine ACI-7104, which AC Immune plans "immediately" to take into a phase 2 adaptive trial.

As part of this study the company eventually hopes to measure alpha-synuclein levels via PET imaging, Leerink analysts noted; the group is also developing a PET tracer for the protein, according to its website.

Disease-modifying?

Despite the recent setbacks, AC Immune is not the only group looking to decrease alpha-synuclein levels as a potentially disease-modifying approach in Parkinson's. The protein is a major component of Lewy bodies, the brain deposits that are one of the hallmarks of Alzheimer's disease and some other forms of dementia.

The jury is still out on this target. The Pasadena study of Roche/Prothena's prasinezumab failed to meet its primary endpoint, although the companies saw enough to commit to another phase 2 trial, Padova, which started in May.

The two studies both focus on early Parkinson's patients, but have slightly different primary endpoints: Pasadena evaluated the MDS-UPDRS total score, while Padova will measure MDS-UPDRS part III, which focuses on motor symptoms. Notably, [Pasadena did uncover a signal on the latter score](#).

Biogen did not even see these glimmers of hope. The group slipped out during its fourth-quarter 2020 earnings [that it was ditching BIIB054](#) (cinpanemab) after the [Spark](#) trial failed its primary or secondary endpoints.

Both prasinezumab and BIIB054 are anti-alpha-synuclein antibodies, and there are several other similar contenders in development, the table below shows.

Alpha-synuclein-targeting projects in development for Parkinson's			
Project	Company	Description	Trial details
Phase 2			
ENT-01	Enterin	Small-molecule α -synuclein aggregation inhibitor	Karmet in PD-related constipation, data due H2 2021; ph2 planned in PD + psychosis & PD + dementia
Prasinezumab (PRX002/RO7046015)	Prothena/Roche	Anti- α -synuclein Mab	Pasadena failed, Padova completes Nov 2023
UCB0599	UCB/Neuropore Therapies	Small-molecule α -synuclein misfolding inhibitor	Ph2 completes Nov 2023
ANVS401	Annovis Bio	Small-molecule amyloid precursor protein, α -synuclein & Tau inhibitor	Ph1/2 in PD & AD, data on 14 pts reported May 2021
Phase 1			
ACI-7104/PD01	AC Immune (via Affiris)	Anti- α -synuclein vaccine	Ph1 completed, ph2 to start "shortly"
Lu AF82422	Lundbeck/Genmab	Anti- α -synuclein Mab	Healthy volunteer trial completes Aug 2021
TAK-341/MEDI341	Takeda/Astrazeneca	Anti- α -synuclein Mab	MAD trial (NCT04449484) completes May 2022
UB-312	Vaxxinity	Anti- α -synuclein vaccine	Healthy volunteers & PD pt trial completes Jun 2022
NPT088	Proclara Biosciences	Fusion protein inhibiting amyloid-beta, tau and α -synuclein	Ph1 completed in AD only, plans in PD
ABBV-0805	Abbvie/Bioarctic	Anti- α -synuclein Mab	Ph1 withdrawn for "strategic considerations"

Source: Evaluate Pharma & clinicaltrials.gov.

However, the status of one of these, Abbvie and Bioarctic's ABBV-0805, is unclear. A phase 1 trial was withdrawn last year for strategic reasons, but the asset is still listed in Abbvie's pipeline.

There are other signs that Abbvie is cooling on this mechanism: nearly a year ago it [pulled out of a collaboration with Voyager](#) on anti-alpha-synuclein vectorised antibodies.

The big pharma has also recently signalled an interest in other Parkinson's targets, this year [gaining rights to acquire Mitokinin](#) for its Pink1 activators, [and collaborating with Caraway Therapeutics](#) over small molecules hitting TMEM175; so far neither company has projects in the clinic.

Even if Abbvie is out of alpha-synuclein, there remains plenty of competition for AC Immune. Given the size of the Parkinson's market, this might not be a problem – if this target does turn out to be valid.

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