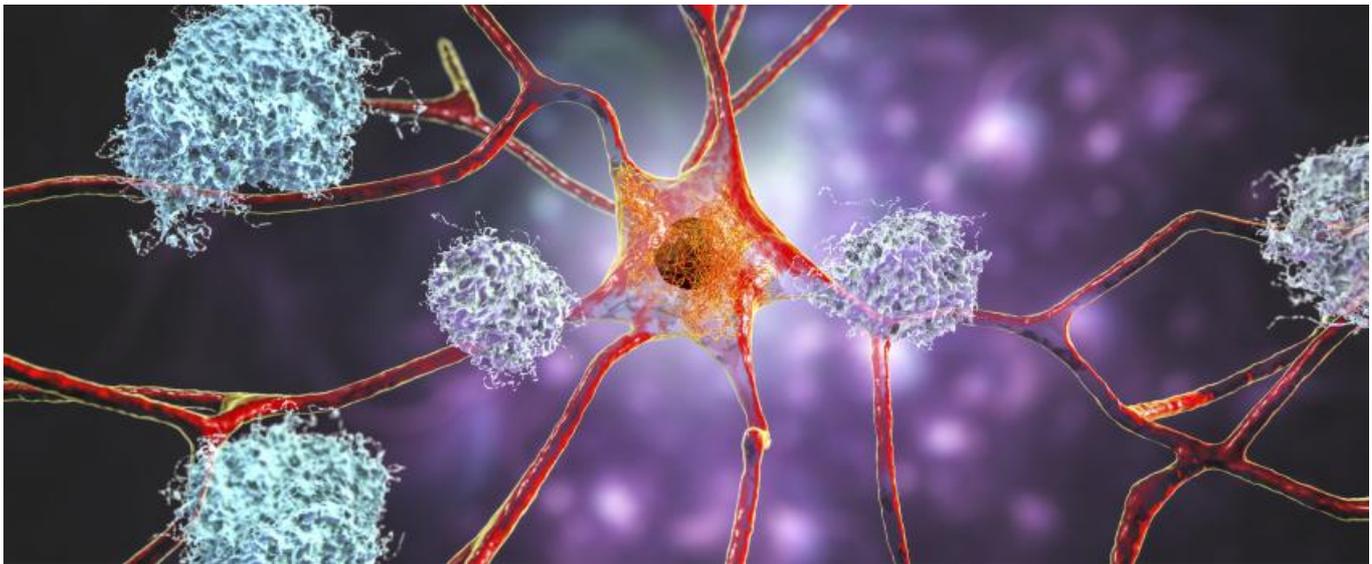


The next wave of amyloid-targeting projects approaches



Madeleine Armstrong



Acumen is the latest player to take aim at amyloid, but competition is fierce.

Monday's approval of Biogen's Alzheimer's drug Aduhelm raised the possibility [that old amyloid-targeting agents might be resurrected](#). But there are plenty of young companies also trying to get into this space – and one, Acumen Pharmaceuticals, disclosed plans for a \$100m flotation yesterday.

Acumen's supposed unique selling point is that its lead project, ACU193, targets amyloid-beta oligomers, rather than monomers or plaques, something the company believes could lead to improved efficacy and safety over other candidates. But a look at the pipeline shows that there are several more advanced projects that also hit oligomers.

ARIA avoiding?

[As the clearance of plaques is associated with brain oedema](#), Acumen hopes that ACU193 can avoid the side effect of ARIA-E that has hit other anti-amyloid antibodies. This will be put to the test in the group's phase I study, which began this quarter, with data due by the fourth quarter of 2022.

Still, a greater affinity for oligomers over plaques did not allow Biogen/Eisai's lecanemab, previously known as BAN2401, to avoid this issue. The groups pushed lecanemab into phase 3 despite disappointing mid-stage results, [with the best responders at the highest dose being at greatest risk of brain swelling](#).

Lecanemab does have some impact on plaques, however, while [Acumen claims that ACU193, which was originally developed in collaboration with Merck & Co, has "limited or no binding"](#).

In this respect ACU193 is similar to Alzheon's ALZ-801, a small molecule designed to inhibit oligomer formation [by enveloping amyloid-beta monomers and preventing their aggregation](#). Alzheon's asset, which does not hit plaques, recently started its phase 3 trial in early Alzheimer's patients with two copies of the $\epsilon 4$ allele of the apolipoprotein E gene.

Selected amyloid-targeting projects in development for Alzheimer's

| Project | Company | Description | Disease setting | Note, clinical trial |
|---------------------------------------|------------------------|---|---|--|
| Phase III | | | | |
| Gantenerumab | Roche | Anti-amyloid-beta antibody, preferentially targets plaques | Prodromal/mild | Graduate 1 , ends Sep 2022 Graduate 2 , ends May 2022 |
| BAN2401 (lecanemab) | Biogen/Eisai | Anti-amyloid-beta antibody, preferentially targets oligomers | Early | Clarity AD , ends Jun 2022 |
| Solanezumab | Lilly | Anti-amyloid-beta antibody, targets monomers | At-risk asymptomatic | A4 , ends Dec 2022 |
| Donanemab (LY3002813) | Lilly | Anti-amyloid-beta antibody, targets plaques | Early symptomatic | Trailblazer-Alz 2 , ends Feb 2023 |
| ALZ-801 | Alzheon | Small molecule targeting amyloid-beta oligomers | Early disease with APOE4/4 genotype | ApolloE4 , ends Apr 2024 |
| Phase II | | | | |
| ACI-24 | AC Immune | Vaccine targeting amyloid-beta | Mild | EudraCT: 2018-000445-39 , 18mth interim recently reported |
| Elayta (CT1812) | Cognition Therapeutics | Sigma-2 inhibitor, targets amyloid-beta oligomers | Mild to moderate | NCT04735536 , ends Jul 2021 |
| ABvac40 | Araclon/Grifols | Vaccine targeting amyloid-beta40 | Mild | NCT03461276 , ends Dec 2021 |
| Crenezumab | Roche/AC Immune | Anti-amyloid-beta antibody, targets various forms of amyloid, inc oligomers | Preclinical PSEN1 E280A mutation carriers | NCT01998841 , ends Feb 2022 |
| RG6102 ("brain shuttle" gantenerumab) | Roche | Brain-penetrating antibody fragment, targets amyloid plaques | Prodromal or mild to moderate | Ph1/2, NCT04639050 , ends Oct 2024 |
| Phase I | | | | |
| LY3372993 (N3pG-Aβ mAb) | Lilly | Anti-amyloid-beta antibody | Mild | NCT04451408 , ends Apr 2022 |
| ACU193 | Acumen Pharmaceuticals | Anti-amyloid-beta antibody, targets oligomers | Mild | Ph1 began Q2'21, data due Q4'22 |

Source: Evaluate Pharma, company releases, clinicaltrials.gov.

Cognition Therapeutics also has a small molecule in phase 2, Elayta, targeting oligomers in a different way. The asset binds to sigma-2, a receptor on neurons that regulates the cellular damage response; the theory is that Elayta displaces amyloid-beta oligomers from these receptors and allows the cell's damage response to return to normal.

Other oligomer-targeting projects are at the preclinical stage, and Acumen lists the likes of Alzinova, Promis Neurosciences, Kalgene Pharmaceuticals and Wren Therapeutics among its potential rivals. The last two groups are privately held – maybe a resurgence of interest in amyloid-beta could prompt them to follow Acumen onto the public markets.

Perhaps the most remarkable thing about the table above is that so many companies have kept faith with

amyloid-targeting agents despite repeated failures in the space. Following Aduhelm's approval, more are sure to join the fray.

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