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FROM THE ALZHEIMER'S ASSOCIATION INTERNATIONAL CONFERENCE 2022

ALZHEIMER'S ASSOCIATION STATEMENT ON NEW CLINICAL TRIAL RESULTS REPORTED AT AAIC 2022

The [Alzheimer's Association](#)® is pleased to highlight results from a variety of clinical trials, which address multiple aspects of the disease, at the [Alzheimer's Association International Conference](#)® (AAIC®) 2022. We know that Alzheimer's and other dementia are complex diseases, and we envision a future of effective treatment by powerful combinations of therapies that address the diseases in multiple ways.

Encouraging and supporting a diverse treatment pipeline, including both drug and non-drug strategies, is essential to achieving the Association's vision of a world without Alzheimer's and all other dementia. As the world's largest nonprofit funder of Alzheimer's research, the Association funds independent researchers worldwide through our [International Research Grant Program](#). Currently, the Alzheimer's Association is investing over \$310 million in more than 950 projects in 48 countries across six continents, including some of the most instrumental [research in Alzheimer's and dementia science](#).

The Association's boldest and most successful effort in this space is the [Part the Cloud](#) initiative. Part the Cloud is committed to funding novel research ideas to determine if they will be effective treatments for the millions of people affected by Alzheimer's. With Part the Cloud, the Alzheimer's Association has funded 65 innovative clinical trials spanning a variety of treatment targets and engaged a variety of the field's most prestigious scientists, universities and companies.

The **EXERT Study** was the longest-ever Phase 3 study of exercise in older adults with mild cognitive impairment (MCI). The results, first reported at AAIC 2022, are especially noteworthy since the trial was conducted during the COVID-19 pandemic. Even with the lockdowns, isolation and constantly shifting social guidelines, 80% of study participants complied with their exercise regimen and completed the study. This is a tribute to the commitment and flexibility of the study participants and personnel.

After 12 months, study participants with MCI in both the aerobic exercise intervention arm and stretching arm showed no cognitive decline. A comparison group of other older adults with MCI from the Alzheimer's Disease Neuroimaging Initiative who experienced neither of the EXERT interventions showed significant cognitive decline over 12 months. This is remarkable and encouraging.

The findings from EXERT are important because they suggest that regular physical activity, even modest or low exertion activity such as stretching, may protect brain cells against damage. It is well known that exercise increases both anti-inflammatory activity and release of nerve growth factors.

The Alzheimer's Association is working toward a future of effective combination therapies, including behavioral interventions, for dementia treatment and risk reduction, as we do now with heart disease. For example, the Association is leading the [U.S. POINTER Study](#), which is looking at comprehensive risk factor interventions, including regular physical activity, but also diet, heart health management, social activities and cognitive stimulation. Laura Baker, Ph.D., associate director of the Wake Forest Alzheimer's Disease Center and principal investigator (PI) of the EXERT Study, is also PI of U.S. POINTER.

At AAIC 2022, **T3D Therapeutics** reported positive interim results from their **Phase 2 trial of T3D-959**, which seeks to overcome insulin resistance in the brain and restore the brain's metabolic health. These encouraging preliminary results are a positive sign and we look forward to hearing final results in 2023.

Alzheimer's is a complex and devastating disease. As our understanding of the biological underpinnings of Alzheimer's expands, the opportunity to advance novel approaches such as T3D-959 will also expand. We will most likely need to combine multiple treatments that address the disease in different ways for effective treatment and prevention.

T3D-959 is one of four innovative Phase 2 studies featured in an AAIC 2022 session on Thursday, August 4 that spotlight new approaches to treating Alzheimer's — none of which are strictly amyloid focused. All are working to keep brain cells healthy, alive and functional longer. Three of the trials, including T3Ds, are funded by the Alzheimer's Association's Part The Cloud grant program.

In June, the **Alzheimer's Prevention Initiative (API) ADAD Columbia prevention study** reported topline results that their trial overall was negative. It is, however, well known that the anti-amyloid compound being studied, crenezumab (Roche), is an older technology and not as effective at clearing amyloid from the brain compared to the "second generation" anti-amyloid treatments now approved (Aduhelm) and being tested (lecanemab, donanemab, gantenerumab).

However, the population being studied — a family cohort of roughly 6,000 people in Colombia with a very high incidence of a younger onset, genetic version of Alzheimer's — was thought to be uniquely well suited to a prevention trial because the age of onset of dementia symptoms is highly predictable in this group. As a result, there was significant anticipation about the researchers' deeper dive into the data at AAIC 2022.

Unfortunately, the scientists found no significant beneficial effects of the intervention on any of the clinical, brain imaging or biomarker measurements. Annual changes in clinical and biomarker measurements consistently numerically favored treatment over placebo, but none of the differences were statistically significant.

We will learn much from this landmark study. The researchers created a highly functional clinical trial network in an under-studied and under-represented population. They showed that treatment and prevention trials can be effectively conducted in people living with, and at risk for, Alzheimer's, and in low and middle income countries. The [Dominantly Inherited Alzheimer's Network](#) (DIAN) study also is

doing important work in this area. The Alzheimer's Association recently funded an [extension of DIAN into Latin America](#).

The API ADAD Colombia study did not confirm or refute the amyloid hypothesis, nor the value of amyloid as a treatment target.

Phase 3 clinical trial results are expected from two other anti-amyloid compounds (lecanemab and gantenerumab) before the end of 2022. FDA decisions are anticipated on applications for both accelerated and full approval (lecanemab and donanemab) in the first half of 2023. Notably, these three drugs target different species of amyloid and different aspects of amyloid buildup and clearance. Treatments that address the full scope of Alzheimer's biology are also advancing. Future treatments will need to address amyloid, tau, neurodegeneration and other brain changes that play a role in Alzheimer's.

At AAIC 2022, the Alzheimer's Association announced the launch of the [Alzheimer's Network for Treatment and Diagnostics \(ALZ-NET\)](#) — a new platform that will collect long-term clinical and safety data from patients treated with FDA-approved Alzheimer's therapies in real world clinical settings.

ALZ-NET is the first network developed specifically for new FDA-approved Alzheimer's treatments, collecting evidence on effectiveness and side effects over a long period of time, in all communities. Similar successful networks for heart disease, cancer, HIV/AIDS and multiple sclerosis have enabled tracking of long-term performance of therapies. The Alzheimer's Association, with its partners and collaborators, is developing the future of Alzheimer's and dementia treatment and diagnostics, and has created an infrastructure to build the future of clinical readiness for all new treatments and care.

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Other treatment-related reports at AAIC 2022 include:

- Advances in amyloid lowering therapeutics, what questions remain?
 - Tuesday, Aug. 2, 11:15 a.m. PT
- Efficacy, Safety and Tolerability of Brexpiprazole for Agitation in Alzheimer's Dementia: A 12-Week, Randomized, Double-Blind, Placebo-Controlled Trial.
 - Thursday, Aug. 4, 9:45 a.m. PT
- Phase 2 clinical trials from Athira Pharma, INmune Bio, Annovis Bio, and T3D Therapeutics.
 - Thursday, Aug. 4, 8:00 a.m. PT