Mark Roithmayr â?? CEO, Alzheimerâ??s Drug Discovery Foundation

There has never been a more exciting time to be in Alzheimerâ??s research

27.03.2025

Tags:

USA, Global, Alzheimerâ??s, ADDF, Foundation, R&D, Clinical Trials, Neuroscience, Diagnostics

The Alzheimerâ??s Drug Discovery Foundation (ADDF) operates in the critical niche of translational research, attempting to bridge the â??Valley of Deathâ?• between discovery and commercialisation using a venture philanthropy model that reinvests returns into new science. CEO Mark Roithmayr explains how the ADDF has helped launch major diagnostic tools for Alzheimerâ??s and shifted focus to underfunded areas like ageing biology, inflammation, and mitochondrial function. Roithmayr is hopeful that a more holistic, multifactorial view of Alzheimerâ??s is emerging, but warns that progress depends on capital moving faster to the most promising science.

Can you explain the niche in which the Alzheimerâ??s Drug Discovery Foundation (ADDF) operates and what makes it unique?

The ADDF was founded 27 years ago by the Lauder family. EstÃ©e Lauder had Alzheimerâ??s, as did her sister. When she passed, she left a trust to her two sons with the mission of making a difference in Alzheimerâ??s research. The Lauder family still covers all ADDFâ??s overhead costs, meaning that every dollar donated to the organisation goes directly to the science.

At the outset of the ADDF, the Lauder family sought advice from experts and were told that, if they wanted to fund science, they should focus on translational research. The US National Institutes of Health (NIH) was already channelling a great deal of funding into basic science, but there was a clear gap in getting discoveries into the clinic.

From the beginning, the organisation saw its role as simply funding translational science â?? bringing money in to bridge the â??Valley of Deathâ?• [the critical gap between drug discovery and commercialisation, where many promising compounds fail due to lack of funding, regulatory hurdles, or technical challenges â?? ed.].

That became our niche. From the start, ADDF took a venture philanthropy approach, meaning we do not give grants, we make investments. Every dollar we invest, whether in an academic institution or a biotech, comes with a contract. If the research leads to a successful deal, we receive a small return on that investment, which goes straight back into funding more science. This structure keeps us nonprofit while ensuring that every dollar is reinvested in the fight against Alzheimerâ??s.

Today, our work is focused on three pillars: biomarkers, prevention, and treatments. Another core principle from the Lauder family is that we partner with anyone who shares our goals. This field requires enormous resources, and collaboration is essential.

What have been some of the biggest success stories for the ADDF over these 27 years?

One of our biggest successes has been the Amyvid PET scan, which is now the most widely used PET scan for Alzheimerâ??s in the US, holding 75 percent of the market. It started as an idea from a researcher at the University of Pennsylvania who pitched it to our co-founder and chief science officer, Dr. Howard Fillit. The ADDF funded that initial idea and helped spin it out into Avid Radiopharmaceuticals, which Lilly later acquired. To this day, we still receive quarterly returns from its use; another example of how our model sustains itself.

Before Amyvid, the only way to confirm Alzheimerâ??s was through an autopsy or spinal tap. This scan changed everything by allowing researchers to see plaques and tangles in living patients.

Another milestone was C2Nâ??s blood test, the first Alzheimerâ??s blood test to hit the market. That idea started at Washington University in St Louis and eventually spun out a biotech, C2N Diagnostics, where ADDF funded early research.

How has the ADDFâ??s investment strategy evolved?

We have always funded projects at risk of falling into the Valley of Death. Initially, this meant helping ideas move from the bench to the clinic. However, about ten years ago, we stopped funding research targeting the plaques and tangles research, not because we donâ??t believe in it, but because pharma had already stepped in to take those ideas forward. Our job is to de-risk early-stage science so that pharma or other funders will take it across the finish line.

Instead, we shifted our focus to underfunded areas, particularly the biology of ageing and how it contributes to Alzheimerâ??s. We now invest in novel pathways like inflammation, vascular health, genetics, and mitochondrial function

This shift was based on the realisation that Alzheimerâ??s is multifactorial. Ageing is the single biggest risk factor, yet very few organisations were funding ageing-related research in the context of Alzheimerâ??s.

We also realised that there is a second Valley of Death: not just getting into the clinic, but getting from Phase Ib to Phase IIb. Many Phase II trials are underpowered due to funding limitations. Today,

85 percent of our portfolio is funding clinical trials and 15 percent is pre-clinical. We have over 30 active clinical trials, investing around USD 55 million in ongoing projects. Many of these are focused on primary or secondary prevention and are stuck in this second Valley of Death.

Thatâ??s the big picture of ADDFâ??s work: funding translational science, moving promising ideas out of the Valley of Death, and ensuring that the best research reaches patients.

And how different is the picture for Alzheimerâ??s clinical trials today compared to five or ten years ago?

We now know that, in some past trials, up to 30 percent of participants did not even have Alzheimerâ??s. The monoclonal antibody trials that have now broken through, whether for Aduhelm, Leqembi, or Kisunla, all have one thing in common: every participant received a PET scan. That changed everything. For the first time, we knew exactly who had Alzheimerâ??s going into a trial, and we used PET scans alongside other diagnostics to track their progress.

When I first interviewed for this job with Howard over eight years ago, he told me, â??Youâ??re going to hear a lot about failures, but there is one trial I am really keeping my eye on.â?• That trial ended up being the Aduhelm trial. It was the first time we had the right patients, the right biomarkers, and the ability to truly measure whether removing plaques and tangles made a difference. By this measure, Alzheimerâ??s trials have only been done properly in the last five years.

At the same time, we have seen the advent of blood-based biomarkers. Most every pharma company running trials today is using blood tests alongside PET scans to determine whether these tests are showing the same results. Some of these blood tests are found to be up to 90 percent accurate in detecting Alzheimerâ??s pathology.

Why does this matter? Because without factoring in blood tests, youâ??re missing a critical part of the story. They will do two things: First, they will speed up clinical trials. Second, they will democratise early detection. Right now, the only way to get a PET scan covered is if a patient is looking to get on a drug. But a blood test in a primary care setting could change everything. My young grandkids will, one day, get a routine blood test at 40 years old, and it will tell them about their risk for Alzheimerâ??s.

Given the limited effectiveness of the newly approved Alzheimerâ??s treatments, how significant a breakthrough do they truly represent?

I must credit Biogen, Eisai, and Lilly, who did not abandon the Alzheimerâ??s field along with many of their peers. They stayed, despite repeated failures, because they saw the science progressing. They saw that people had plaques and tangles, that removing plaques and tangles was possible, and they measured how it delayed cognitive decline in people with mild cognitive impairment.

To be clear, Leqembi and Kisunla are only modestly effective. They are given intravenously, either once or twice a month. Once the plaques and tangles are cleared, some people might stay on them, some might not.

Right now, the conversation is all about improving delivery: can we make it once a month? Can we make it subcutaneous? Can it become a pill someday? The real story is that this is a multifactorial disease. The future is not only the monoclonal antibodies, it is combination therapy, precision

medicine, and prevention. Thatâ??s where the real action is going to be over the next decade.

Anyone who understands this field will tell you that. But it is not what gets covered in the press. It is not what gets highlighted at big scientific meetings, because the focus is still mainly on monoclonal antibodies, how effective they are, how safe, whether we can deliver them earlier, and if we can make them easier to administer? Without downplaying these phenomenal breakthroughs, they are just the first crack in the wall.

Is there a danger that Alzheimerâ??s R&D focuses too much on disease-modifying treatments rather than symptom management?

The answer here is this is not the right question to be asking. There is this idea that you either believe in the amyloid theory or you do not, and that binary thinking has hurt the field. At ADDF, we believe in the science. Yes, symptomatic treatments are important too, but it is not an either/or choice.

The real danger is not focusing too much on disease-modifying drugs; it is not focusing enough on what comes next. The real scientific progress will come when we combine therapies. Some people might need a monoclonal antibody plus an inflammation drug. Others might need a vascular drug. Someone else might need a mitochondrial-targeting drug.

This is a multifactorial disease. Ageing is the number one risk factor for Alzheimerâ??s, so now we must look at all the other ageing-related pathways. Just look at the shift in clinical trials. Five years ago, 75 percent of Alzheimerâ??s trials focused on amyloid and tau, with only 25 percent exploring other pathways. Today, those numbers have flipped; only 25 percent of trials are focused on amyloid and tau, and nearly 75 percent are targeting the biology of ageing.

If you really want to follow the science, you need to look at what is next. The field is moving beyond amyloid, beyond tau, and toward precision medicine, combination therapies, and prevention.

What do you see as ADDFâ??s role in promoting this more holistic approach?

Pharma, biotech, and academia all have their own perspectives and preconceived views based on where they sit in the ecosystem. Our job is to take the broadest possible view because the future of Alzheimerâ??s treatment is not in a single drug, but in understanding the full landscape of the disease.

If there is one thing I know about pharma, it is that if one company has something that shows promise, the rest will jump on board; just look at what is happening with GLP-1 obesity drugs right now. Pharma understands that Alzheimerâ??s is multifactorial and that ageing pathways play a role. Each company has its own focus areas, with some being more willing to take risks than others. But they all agree with the underlying theory.

What we are going to see in the next few years is a shift toward mitochondrial and inflammation pathways. There is a ton of science in Phase II right now, and even some in Phase 3 thatâ??s moving forward. Just like with monoclonal antibodies, there will be breakthroughs, and when they happen, companies will follow. I believe we are three to five years away from Alzheimerâ??s becoming a bull market; just like what happened with immunotherapy in cancer.

We are expecting a first readout on a major study of GLP-1 drugs in Alzheimerâ??s at the Clinical Trials on Alzheimerâ??s Disease (CTAD) conference later this year. What do you see as the potential in this space?

Part of the mitochondrial pathway involves GLP-1 drugs, which are tied to metabolism. Howard saw this coming years ago. The ADDF invested USD two million into a Phase II study at Imperial College London with Paul Edison, looking at whether liraglutide (a GLP-1 drug) could have an effect on Alzheimerâ??s. Following the ADDFâ??s investment, Novo Nordisk also decided to fund the liraglutide trial.

The data generated from that early trial laid the ground work for the semaglutide trial in Alzheimerâ??s run by Novoand the results will read out this fall.

I was at JPMorgan HealthCare earlier this year, listening to pharma leaders talk about Alzheimerâ??s. One of the moderators said, â??If this GLP-1 trial shows any effect, can you imagine what is going to happen to the Alzheimerâ??s market?â?• Because guess what? Every major pharma company already has a GLP-1 drug. So, of course, we hope the study reads out positive. But even if it doesnâ??t, there will be valuable insights in the data.

This reminds me of what happened with Aduhelm. Initially, Biogen discontinued the phase 3 trial because it was not hitting its primary endpoints. At the time, the ADDF was one of the only organizations talking about the fascinating science. That trial was the first real evidence that removing plaques and tangles could make a difference. Biogen abandoned it but then did a deeper analysis and brought it back. That became Aduhelm.

Why do I bring this up? Because we are going to look at Novoâ??s GLP-1 study the same way. Alzheimerâ??s was never going to have a single solution. It is too complex. It is a multifactorial disease with multiple biological pathways. The idea that there would be one drug to solve it was always a flawed way of thinking, and it held the field back for too long.

The real challenge now is figuring out which combinations work best. And I promise you, ten years from now, weâ??ll look back at this moment and see that all the key pieces were already in motion.

The popular narrative around the Aduhelm launch is that Biogen overestimated the market demand for a drug which lacked the expected efficacy and safety. What lessons has the Alzheimerâ??s R&D community learned from that experience and how different will the successful Alzheimerâ??s drug launches of the future look?

The only bad study is one you donâ??t learn from. I spent the first 20 years of my career at March of Dimes [a US nonprofit that works to improve the health of mothers and babies â?? ed.] and saw firsthand that you learn more from failed science than from science that doesnâ??t fail.

There was a lot of blame to go around in the Aduhelm rollout. Biogen was given a broad label by the FDA and pursued it aggressively. But buried in all that controversy was something critical: for some patients in the earlier phases of Alzheimerâ??s, that drug actually helped.

And despite all the drama, Biogen, Eisai, and Lilly all stayed on the monoclonal antibody track. Why? Because the PET scans and blood tests told them the science was real. Follow the science, follow the balance sheetâ??it is all there. Monoclonal antibodies are modestly effective by slowing cognitive

decline by around 30%, and thatâ??s phenomenal. But what about the other 70 percent? Thatâ??s the real story. And thatâ??s where the next breakthroughs will come from.

The US led the way through the dark past two decades of Alzheimerâ??s research failures, with the NIH allocating almost USD four billion to the cause annually, and the FDA showing regulatory flexibility for candidates that may not meet traditional endpoints. With NIH and FDA funding and staffing now being radically cut by the Trump administration, do you see this as a threat to the future of Alzheimerâ??s research, as well as Americaâ??s prominence in it?

The ADDF is only about the science. We donâ??t have an advocacy arm. We are a small organizationâ??30 people, half of whom are PhD neuroscientists. The other half are the business team, such as myself. We rely on great organisations like the Alzheimerâ??s Association and Us Against Alzheimerâ??s to lead the advocacy efforts. Our mission is simple: get drugs to market. Bridge the Valley of Death, fund translational science, and get promising ideas to pharma or other funders can take them across the finish line. Thatâ??s the only reason we exist.

And in that regard, the political uncertainty in Washington does not affect our model. We do not take government funding and are fully supported by private donors. What we do expect, however, is more demand for our funding from academics and even some biotechs due to the uncertainty with public funding.

More broadly, the way we think about this is simple: Science leads and regulation follows. Then comes reimbursement. Science must prove itself first. If it works, regulators will approve it. Once it is approved, insurers and governments will decide how to reimburse it. Thatâ??s the order in which things happen.

From a geopolitical standpoint, we see how different countries handle this process. We work with regulators in the US, Europe, the UK, Japan, China, and Australia, and see how each region approaches approval and reimbursement. Right now, there are more roadblocks in Europe and Australia when it comes to monoclonal antibody reimbursement compared to the US, Japan, or China.

Another major uncertainty right now is academic funding. Weâ??ve supported research thatâ??s also been backed by the NIH, particularly around repurposed drugs and early-stage novel ideas. Many of these projects are in Phase I or Phase II and are still in the second Valley of Death. Government funding has been critical in this space. But with all the uncertainty around NIH funding, where will that money come from? This is where private capital may have to step in.

There are also critical research areas such as studies on vascular dementia in black populations that rely on government funding. If that funding becomes uncertain, does private capital need to fill the gap? That is something we are actively watching.

What are your main causes for optimism and concern in your work at ADDF today?

There has never been a more exciting time to be in Alzheimerâ??s research. We have entered a new era of clinical trials thanks to PET scans and, soon, blood tests. For the first time ever, we have approved treatments and if you look at the clinical pipeline, nearly 75 percent of current trials are focused on what comes next. The glass is not just half full, it is getting shorter, which means we are

making real progress.

My biggest concern? That this scientific optimism is not being discussed widely enough. Two years ago, a financier told me, â??It is not that there is not enough money to solve Alzheimerâ??s. The problem is that the money is not going to the right places.â?•

If you look at the three-quarters of Alzheimerâ??s trials that arenâ??t focused on amyloid and tau, the majority are underfunded Phase IIa trials working on repurposed drugs and novel therapeutics. To get one drug to market, pharma spends USD 3 to USD 4 billion. Imagine if that kind of capital was directed toward combination therapies, precision medicine, and prevention; not just monoclonal antibodies, but the next wave of breakthroughs.

So, what is the answer? Move capital faster toward these ideas. That is how we will take the next step in solving Alzheimerâ??s.

See more interviews