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INDIANA'S ROLE IN THE ALZHEIMER'S BATTLE:

Meaningful Research, Clinical Interventions,
and Public Health Policy

INDIANA LIFE SCIENCES
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More than [6 million Americans live with Alzheimer's disease](#), and the number is projected to swell to nearly 13 million by 2050. The disease not only affects a person's memory and cognition, but also claims more seniors' lives than prostate and breast cancer combined.

Alzheimer's disease has disrupted the quality of life in seniors for decades, but also devastates families. Today, over 11 million Americans serve as caregivers for loved ones with Alzheimer's or other dementias.

Despite Indiana's small but growing footprint on the global stage, the Hoosier state plays a leading role in developing Alzheimer's research, diagnostics and therapeutics that are improving lives and providing tangible hope for people struggling with one of our most vexing medical conditions. Leading pharmaceutical companies, top research university scientists, new biotech startups, and organizations focused on caregiving in Indiana all are playing a role.

[The annual Indiana Life Sciences Summit, hosted by BioCrossroads](#) in November 2023, spotlighted Indiana's leadership

role in research and medical advances related to Alzheimer's disease. The day-long summit at the Mavris Arts & Event Center in Indianapolis brought together a world-renowned panel of researchers, educators and clinicians, as well as caregivers and people currently living with the disease.

"It's so personal and, for so long, there seems to have been virtually non-existent hope. It's exciting to see not only that there's hope that's developing and expanding, but that Indiana is right in the middle of it," said Dan Peterson, Board Chairman of BioCrossroads. "It's just amazing the outsized impact and the point-of-the-spear impact that Indiana and our partners have in the diagnosis and treatment – in particular going forward – for Alzheimer's."

The speakers and panel discussions focused on personal experiences with the disease, challenges faced by caregivers and the importance of early detection and accurate diagnosis. The summit also highlighted the progress being made in research and the need for collaboration between healthcare systems, researchers and advocacy organizations.



THE BURDEN OF ALZHEIMER'S

The medical community has struggled for decades to find solutions to identify and treat Alzheimer's disease. Just 10 years ago, the only way to diagnose Alzheimer's was through a brain biopsy after a person passed away from the disease and donated their brain to research.

Yet, with recent advancements in diagnostics, imaging and the rapidly changing field of fluid biomarkers, researchers can now see the amyloid pathology in the brain appear 10 to 20 years before symptoms occur.

"If I get a cancer diagnosis, I don't want it at stage four. I want it at stage one because it leaves so many more degrees of opportunity," said Phyllis Ferrell, a consultant and advocate for Alzheimer's disease research and brain health. "With the advent of the new disease-modifying therapies being approved by the FDA right now, we actually know that by treating this disease as early as possible, we make the biggest impact."

The future of Alzheimer's care requires a shift from extremely late-stage treatment to early-stage detection and individualized intervention. It requires a collective strategy that begins with the science and translates to clinical practice,



while considering the people who live with Alzheimer's and their caretakers.

"I'll challenge you to think about what you could do in your position of influence to make a change because we know none of us alone are going to be able to do it," Ferrell said. "It's going to take science, advocacy, academia, private sector, public sector and communities to work together."

Despite these game-changing advancements, Alzheimer's continues to present complex challenges for people living with the disease and their caretakers, including financial, physical, social, disease progression, and – historically – a lack of diagnostic and treatment options.

Overcoming Myriad Challenges

Logistical barriers make it difficult for people to connect with services, especially those in rural and underserved communities, as many treatments and testing facilities are only available in wealthy countries or major population centers.

"We have to continue to find answers for everyone, not just the few that can afford it or that have that technology near to their home," said Maria Carrillo,

PhD, Chief Science Officer at the Alzheimer's Association.

Even in a state rich with Alzheimer's support like Indiana, services not only become much harder to access outside of the Indianapolis metro area, but many people are unaware of available support.

"One of our biggest challenges is raising awareness of the programs and services that we offer," said Natalie Sutton, Chapter Executive of the Alzheimer's Association Greater Indiana. "We have these incredible services, but last year we reached a little over 7,000 people. To put that in context, 110,000 Hoosiers are living with Alzheimer's disease and 216,000 are providing unpaid care for someone with the disease."

Those services, Sutton said, include a 24/7 helpline, a catalog of educational programs for patients and a network of 50 support groups that bring caregivers together to process through their journey as a group. Sutton said the Alzheimer's Association and other groups successfully lobbied for the passage of [House Bill 1422](#) to fund a dementia care specialist program in the state.

"This program is going to put a full-time staff person in every one of Indiana's 16 area agencies on aging," Sutton said. "That person's role is going to be to raise awareness in the community, provide education and help connect people with the resources that exist but aren't utilized early or often enough."

Identifying Early-Stage Alzheimer's

Another key challenge involves identifying individuals early who need to undergo treatment, yet the

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Maria Carrillo
Chief Science
Officer, Alzheimer's
Association®



current healthcare system lacks a means for identifying warning signs in primary care settings or other patient interventions. Research shows [1 in 3 seniors](#) dies with Alzheimer's or another dementia, yet current interventions rarely screen for the disease.

In 2021, Indiana University School of Medicine was chosen as one of only seven sites in the world to join the [Davos Alzheimer's Collaborative](#), whose mission is to accelerate innovation and deliver solutions for Alzheimer's care. The team at IU developed a pilot plan to test for cognitive impairment during primary care visits.

"At Indiana University, we went to our primary care clinics where we saw quite a few individuals over the age of 65, and we said, 'What if we gave you a digital tool? What if we were able to hand your patients an iPad where they would spend three minutes before you walked into the room and we would get some cognitive score for them?'" said Jared Brosch, MD,

“Maybe we get our first test for amyloid when you’re 45 as a part of a panel with your PSA and your colonoscopy.”

Jared R. Brosch, MD
Associate Professor of Clinical Neurology



Associate Professor of Clinical Neurology at Indiana University School of Medicine.

If the scoring method reveals signs of impairment, the primary care physician can refer someone living with the disease to further resources and connect them with a brain health navigator, which is a nurse specifically trained to help patients navigate Alzheimer’s care.

“This nurse would meet with them, do more testing, go over their medications and try to figure out if they’re having cognitive problems because of the medicines they’re on,” Dr. Brosch said. “They could order a brain scan or referral to a neurology clinic.”

Even with these pilot programs and the ability to detect Alzheimer’s via PET scan or biomarkers sooner than originally thought, early-stage testing is uncommon and currently difficult to deploy.

“On my wish list would be a blood panel where you go in at age 45, when you’re due for your first colonoscopy—because that’s the new 50,” Dr. Brosch said. “Maybe we get our first test for amyloid when you’re 45 as a part of a panel with your PSA and your colonoscopy.”

If testing becomes more widespread and applicable for people with early-stage

Alzheimer’s, they can be connected with services, either private or public sector, to help them learn more about the disease and improve their quality of life.

“Invite them to learn about research, but also frankly give them more practical lifestyle tips and opportunities to invest in themselves and their family to deal with dementia. Perhaps until we can get them into clinical trials that can help them,” said John Dwyer, President of the Global Alzheimer’s Platform Foundation.

Despite these complex challenges, there’s renewed hope of finding a cure.

“I’m incredibly hopeful that we’re at a turning point where Alzheimer’s, dementia—and more broadly, aging—is no longer going to be ignored,” Carrillo said. “That’s going to provide a wave for all of us to ride on because, for a long time, I do feel this disease and other diseases connected to dementia and aging have been discriminated against. We are now changing that tide, and this community is leading that.”



HOPE ON THE HORIZON

Alzheimer's research has made tremendous strides since neuropathologist Alois Alzheimer first discovered the presence of beta amyloid and the buildup of tau protein in a deceased patient's brain in 1906.

"What he observed were two different hallmark pathologies, which has really defined the disease for the coming decades or coming century," said Bruce Lamb, PhD, Executive Director of the Stark Neurosciences Research Institute at Indiana University School of Medicine. "And that is the presence of what are called senile plaques. And these are deposits, extracellular deposits that have a little peptide called beta amyloid. Up until very recently, we required a postmortem diagnosis to really diagnose the disease. And that obviously is a real problem."

Researchers achieved a major breakthrough in Alzheimer's detection in 2012 when the FDA approved Eli Lilly and Company's [Amyvid](#), a radioactive diagnostic agent for PET imaging of the brain to estimate beta-amyloid neuritic plaque density in adults with cognitive impairment. For the first time in the disease's history, people could be diagnosed with Alzheimer's disease while still alive.

"Lilly was really central in some of those efforts. And that was only in 2012. Again,



just to give you an idea of how fast we have come. And then a few years later being able to [image tau](#) in people was also developed," Dr. Lamb said.

Another breakthrough occurred in 2021 when [aducanumab](#), developed by Biogen, was approved by the FDA's Accelerated Approval Program, followed by [lecanemab](#) in early 2023. These monoclonal antibodies target and reduce amyloid beta found in the brains of people with Alzheimer's disease.

Over the summer of 2023 while at the Alzheimer's Association International Conference, Lilly announced successful Phase 3 results of [donanemab](#), another monoclonal antibody which significantly slows the progression of cognitive decline in people with early stage Alzheimer's disease. The drug has been submitted for approval with the FDA with a decision expected in 2024.

At the conference, Cristian Lasagna-Reeves, PhD, Associate Professor of Anatomy, Cell Biology and Physiology, at IU School of Medicine and Investigator at Stark Neurosciences Research Institute, presented research on tau protein that was named the "most impactful study published in Alzheimer's research over the preceding two years" and received the prestigious [Inge Grundke-Iqbal Award for Alzheimer's Research](#).

Also in 2023, Acumen Pharmaceuticals, with a presence in Carmel, Ind., and with plans to move to 16 Tech in downtown Indianapolis, announced positive results from trials of the [monoclonal antibody drug ACU193](#), further strengthening the Hoosier state's role in Alzheimer's research and development.

"Those trials that remove amyloid, and remove it fairly quickly, are the ones where we're beginning to see a cognitive benefit. And I think that's really the take-home message thus far with a lot of these trials," Dr. Lamb said.

The results from the recent trials are significant. With donanemab, Dr. Lamb said trials showed an almost 30% reduction in amyloid at 24 weeks, a 66% reduction at 55 weeks and 76% reduction at 76 weeks.

"We still don't know a lot of what's going to happen to those people as they now have amyloid removed and continue to go on. But importantly, there's a cognitive benefit," Dr. Lamb said. "And basically, what you see in the population as a whole is, either at 22% or 29%, slowing of cognitive decline in the total Phase 3 results."

While new drugs slow cognitive decline, they don't stop it altogether. But Dr. Lamb said they can dull the spread of the disease and expand quality of life for people in the early stages of Alzheimer's.

"That's a really important take home that, again, we need to think about as we're moving forward with these trials as well as others. We need to start as early as we possibly can.



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As researchers continue to make breakthroughs and further understand how different medications affect different amyloids, the future will include using multiple interventions to attack the disease, similar to treating cancer.

"I think that's where the field is moving. We're immediately entering an age of combination therapies," Dr. Lamb said. "So, how do we move together with these anti-amyloid therapies plus other new therapeutics moving forward?"

Indiana's Spotlight Shines Bright
Advocacy by clinicians, researchers and the Alzheimer's Association has led to an explosion of federal funding for Alzheimer's disease research in the United States. In the last decade alone, funding from the National Institutes of Health (NIH) increased by over 700%, fueling research and development like never before.

In 2021, [Indiana ranked fourth](#) in the U.S. in Alzheimer's research funding from the National Institute on Aging (NIA),

the NIH branch that primarily funds Alzheimer's research.

Indiana's growing reputation as an Alzheimer's research powerhouse is a result of several organizations, research centers, universities and biotech companies collaborating together seamlessly, from Lilly and Roche Diagnostics to IU School of Medicine and the [Stark Neurosciences Research Institute](#), Purdue University, [Indiana Biosciences Research Institute](#) and the [Regenstrief Institute](#).

"IU School of Medicine has really been at the center of a number of these very large programs, and we're leading a number of them," Dr. Lamb said.

These programs include the [National Centralized Repository for Alzheimer's Disease and Related Dementias](#) (NCRAD), which collects and analyzes samples from all of the state-based Alzheimer's Centers; the [Longitudinal Early-onset Alzheimer's Disease Study](#) (LEADS), an international study on early stages of the disease; and [CLEAR-AD](#), which is a program in partnership with the Mayo Clinic to identify new biomarkers for Alzheimer's disease.

"Indiana is really playing a central role and critical role in finding solutions for Alzheimer's disease patients, caregivers and communities," Dr. Lamb said.

Biomarkers Give Hope for the Future

One of the newest solutions involves studying biomarkers, short for biological markers, which is a measurable substance or characteristic that indicates the presence and/or progression of the disease. Biomarkers can include proteins, genes, antibodies, imaging and digital biomarkers.

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Bruce Lamb, PhD
*Executive Director
of the Stark
Neurosciences
Research Institute,
Indiana University
School of Medicine*

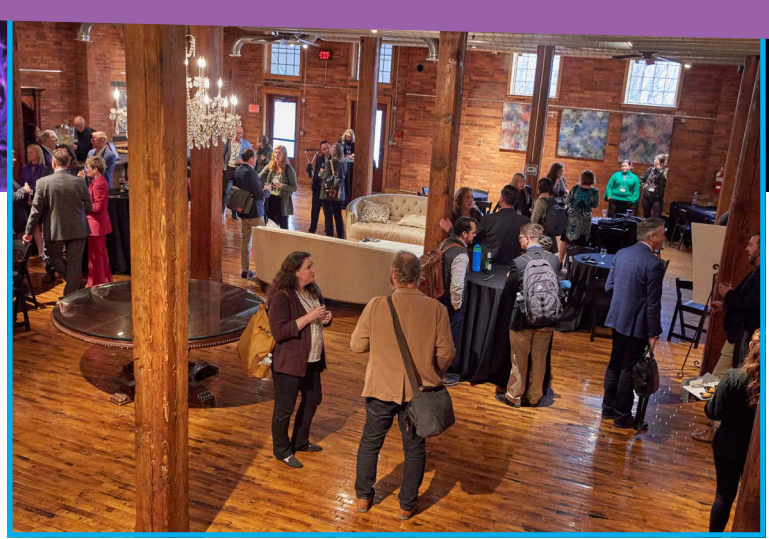


Biomarkers can be used to identify the risk for disease, to measure disease and to assess efficacy of treatments. By taking a lumbar puncture of spinal fluid, researchers can identify biomarkers in both amyloid and tau.

"Biomarkers are going to provide novel and accessible diagnostic (prognostic and agnostic) tools and will likely lead to [precision medicine](#), which will deliver the right treatments to the right patients," Dr. Lamb said.

More recent studies give hope for the detection of beta amyloid and tau in plasma biomarkers, an approach that could prove more equitable and accessible for patients, especially those in underserved areas or far from research sites.

"This has the potential to really transform the field because plasma biomarkers are a lot cheaper than doing PET imaging on every individual and can be brought out into the community and ultimately even into primary care."



THE VOICE OF PEOPLE WITH ALZHEIMER'S DISEASE

Receiving an Alzheimer's diagnosis can be devastating, both for the individual with the disease as well as for the family members who often take on caregiver roles for their loved one.

"Alzheimer's disease is really a two-person condition," said Dustin Ziegler, Program Director, Caregiver Advocacy at Anthem of Indiana. "There's the person with the actual disease pathology, but then they usually have at least one other caregiver. Evidence has demonstrated that the caregiver's health usually goes down. They suffer from their own conditions and ailments specific to their caregiving role and the stress and complexity it entails."

Living with Alzheimer's

As a high-performing employee, Darlene Bradley suspected something was off when she started struggling at work. Having watched her mother and father suffer from the effects of Alzheimer's, she knew the signs and symptoms. But that also complicated matters.

"So many of my friends and even a lot of my family kept saying, 'You just think you have it because your parents had it.' But I knew in my heart," she said.

Within a couple months after retiring at 56 years old, Bradley underwent a

PET scan and MRI, which showed both amyloid plaque and tau tangles. Since her diagnosis, Bradley maintains an independent lifestyle.

"Every day is a little bit different, but I feel so blessed that I'm doing so well," she said.

Still, Bradley knows challenges lie ahead.

"The reality is still there," she said. "I watched my dad pass from it, and all the stages that he went through to where he didn't really know us. My mother didn't get quite as far down that path, but she was pretty confused. I know that's a strong possibility, but I have a strong faith. I'm not afraid to die. I know where I'm going, and I know that my family will be very helpful to me."

In the meantime, Bradley looks forward to time spent with her husband, four children and 12 grandchildren. She continues to advocate for Alzheimer's funding and research through speaking engagements, as well as hosting fundraising events at her church.

"This is such an important fight," Bradley said. "I'm so blessed and appreciative for all the things that I've been able to continue to do and will be able to continue to do because of the

treatment that's becoming available and the drug studies."

Supporting Caregivers in their Journeys

Karen Campbell, a news anchor and reporter for WTHR in Indianapolis, serves in a long-distance caregiving role for her mother, who lives in Maryland.

"I moved to Indianapolis about four years ago. The hardest part of leaving was understanding what it would take to care for her long distance," Campbell said. "Who was going to get her to her doctors' appointments? Who was going to make sure she's taking her medications every day? What I've learned over the past four years is that there's help out there."

A resource Campbell relies on is the [Alzheimer's Association 24/7 Helpline](#). You can call for free and receive confidential support and information from specialists and master's-level clinicians.

"There have been times when I've gone into the closet and bawled my eyes out, because I didn't know where to go until I found the Alzheimer's hotline," Campbell said.

Now, she calls and receives comfort and support, which she can share with her three older siblings as they all work together to support her mother.

Those emotions a caregiver experiences and the support they need is so varied and individualized, according to Kimberly Roop, MD, President of Indiana Medicaid at Anthem. Even as a medical professional, she wasn't fully prepared for the reality of caring for

her mother-in-law, whose Alzheimer's disease progressed rapidly.

"A lot of assumptions are made, particularly about clinicians. We understand the biology and the biochemistry, and we prescribe drugs and perform surgeries. We should know this," Dr. Roop said. "Until you're really in it every day, you cannot make assumptions that you know what it's like and what people need. You need to hear from people who have lived experience with it to really understand what kind of support is needed."

Roop's father-in-law served as the primary caregiver, and Roop said they missed the signs of burnout, which led to her mother-in-law moving into a facility.

While Ziegler noted there's been more focus recently on caregiver support, he said there's still progress to be made.

"We're putting a tremendous focus on caregiving at the [Anthem Indiana Pathways](#) program, along with the state



A Discussion: Helping People with Alzheimer's and Their Families - Panelists: Karen Campbell, Dustin Ziegler, Kimberly Roop, Tina McIntosh

of Indiana,” Ziegler said. “We’re really looking forward to building that out and seeing how that cascades through the health outcomes of those who we serve.”

One accomplishment he’s particularly proud of is getting a [Dementia Friends Indiana seminar](#) included in the curriculum for first-year students at Indiana University School of Medicine.

“That was a big win to get these future practicing physicians to think differently about the condition and be aware of how much the caregiver influences the health outcomes,” Ziegler said.

In addition, the Centers for Medicare and Medicaid Services recently announced the [Guiding an Improved Dementia Experience \(GUIDE\) Model](#) – co-developed by teams from Indiana University School of Medicine, Eskenazi Health, and Regenstrief Institute – which aims to support people living with dementia and their unpaid caregivers. Through a comprehensive package of care coordination and care

management, caregiver education and support and respite services, the model aims to improve quality of life for people living with dementia and reduce strain on their unpaid caregivers.

“It’s still very, very new,” Ziegler said. “But I think just the fact that we’re going in this direction is huge. That’s what is going to move health outcomes.”

Joy’s House, a provider of adult day services and caregiver resources, will soon launch [Caregiver Way](#), an online community for family caregivers to access peer support, education and resources.

“We’re going to be helping to humanize caregiving in the state of Indiana and meeting people where they are, because nobody’s caregiving journey is exactly the same,” said Joy’s House Founder Tina McIntosh. “We want to join forces with our friends at the Alzheimer’s Association and at Anthem to say, ‘There’s not going to be one solution for caregivers, but we are ready.’”

“... we know none of us alone are going to be able to do it. It’s going to take science, advocacy, academia, private sector, public sector and communities to work together.”

Phyllis Ferrell

Consultant and Advocate for Alzheimer’s Disease Research and Brain Health





TRANSLATING RESEARCH TO PRACTICE

Recent progress in detecting and treating Alzheimer's has renewed hope for people living with the disease, caregivers and the medical community alike. In just the last decade, researchers discovered new ways to detect Alzheimer's long before symptoms appear and new treatments to slow cognitive decline. There's a sense of optimism that a cure for the disease could be on the horizon.

"In the blood biomarker world five years ago, everyone thought it was impossible. We quickly discovered that we could measure some proteins in your blood that would correlate with pathology going on in the brain," said Jeff Dage, PhD, Senior Research Professor of Neurology at Indiana University School of Medicine and Primary Member at Stark Neurosciences Research Institute. "But now we've really stepped beyond just the amyloid and tau, and we can measure other things like the markers of osteophytosis or general neurodegeneration, and all of these things together can really help us put a picture together of what's going on."

Yet, many of the latest developments are still in clinical research, and the challenge becomes not only continuing the research, but interpreting the results and translating them to patient care.

"I want to make these blood tests available to everybody around the



world," Dr. Dage said. "We're now working in a space where you can do a finger prick and put it on a blood card and mail it in. You don't have to go to the lab. In the future, you're going to be able to do it at home, just like testing your blood sugar."

Producing new diagnostic tests in the lab is one thing but getting them approved for everyday use by the FDA involves a rigorous approval process.

"There's some flexibility in the clinical lab industry where they have the ability to introduce a test that's deemed for research use only, and they're able to do the studies themselves," said Laura Parnas, Disease Area Network Lead, Neurology and Cardiometabolism, Medical and Scientific Affairs, Roche Diagnostics U.S. "They're not as extensive as what we do as a manufacturer, because they're going to use it only in the laboratory and then they are able to offer it clinically as a laboratory development test."

Roche is currently developing the Elecsys Amyloid Plasma Panel (EAPP), a blood biomarker test that received the FDA's breakthrough-device designation in 2022, essentially fast-tracking the review process for hopeful [approval in 2025](#). While the test is not intended to replace other diagnostics, widespread

application in primary care offices or testing centers will help physicians identify the disease much sooner and connect people with treatment.

Beyond receiving approval, Laurie Gutmann, MD, Chair of the Department of Neurology, Indiana University School of Medicine, said it takes both an educational and operational approach to ensure new tests become widely used in clinical practice.

“With any new available tests, part of what you have to do is educate the people who are seeing those with the disease so they know it’s available, what to look for and who to test,” Dr. Gutmann said. “On the operations side, you have to get it into the electronic health record in a way that people can easily find it, order it and know what to do when the results come back.”

Despite the operational barriers, Gutmann said new developments in Alzheimer’s research are already being implemented, such as the nurse who serves as the brain health navigator in IU Health primary care offices.

“They talk to the brain health navigator, they figure out what tests do they need, and in what order to move them on to. (They help determine) ‘You can get this disease-modifying therapy or this isn’t the right thing for you. You need this other test. Here’s how we can support you,’” Gutmann said.

These immediate interventions can also connect patients with therapies or services much faster.

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“Rather than having people wait six months to get an appointment with a neurologist, you get plugged right in and then prioritized based on where you are with the disease or where you are with testing the next step.”

Laurie Gutmann, MD
Chair of the
Department of
Neurology, Indiana
University School of
Medicine



and then prioritized based on where you are with the disease or where you are with testing the next step. And I think those are the kind of really incredibly thoughtful operational approaches that we need,” Gutmann said.

Ultimately, implementing a sea change in Alzheimer’s diagnosis and care requires seamless collaboration between primary care clinicians, neurologists, radiologists, specialists, drug makers and people who are being treated and their caregivers.

“This collaboration across stakeholders could really move the needle and move us toward getting the appropriate patient on the appropriate therapy,” said Brandy Matthews, MD, Vice President of Global and US Medical Affairs at Lilly. “I also think we need a kind of seismic shift in the culture as it relates to prioritizing brain health and destigmatizing brain disease.”

CELEBRATING A LEGACY OF ALZHEIMER'S RESEARCH

To culminate the Indiana Life Sciences Summit, Peterson and Tatiana Foroud, PhD, Executive Associate Dean for Research Affairs at IU School of Medicine, presented Dr. Lamb with the 2023 [August M. Watanabe Life Sciences Champion of the Year Award](#).

The award is named after BioCrossroads' late Chairman August Watanabe and was presented to Dr. Lamb to recognize his globally significant research into the causes of and potential treatments for Alzheimer's disease, as well as his many years of advocacy to increase research funding and raise awareness for challenges the disease brings to families and caregivers.





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