Takeda licenses small molecule developed by Krembil Brain Institute researchers, targeting tau protein implicated in Alzheimer's disease

TORONTO—As announced today in a press release by biotechnology company Treventis, global pharmaceutical company Takeda has agreed to exclusively license a group of small molecules that target tau – a protein in which misfolding and aggregation are believed to be a cause of Alzheimer's disease.

The molecules were developed by the team at Treventis, building upon the Alzheimer's & neurodegenerative research expertise of Dr. Donald Weaver's lab at UHN.

"There are currently no effective drugs out there that target tau in the brain," says Dr. Donald Weaver, Senior Scientist at Krembil Brain Institute, Professor at the University of Toronto and Chief Medical Officer at Treventis. "This has the potential to be such an agent."

Current medications for Alzheimer's are biologics, which means they have to be injected or delivered by infusion, invasively. A small molecule could more effectively be developed into a pill or capsule, to be taken orally.

"Small molecules are the Holy Grail," says Dr. Marcia Taylor, Vice President of Research at Treventis.

"Much research and funding has gone toward amyloid beta (Aβ) as a therapeutic target. We've shown that Aβ misfolding and aggregation may be happening for 20 years, but it's only when tau starts to misfold and bunch up that the first symptoms of Alzheimer's appear."

"It's now appreciated that tau misfolding and clumping is the trigger that brings forward the symptoms. That's when the person says, 'Something's wrong. My memory is not what it should be. My cognition is not what it should be," says Dr. Weaver.

"Now that this sort of information is in hand, we can actually use that insightfully in the design of therapies."

Researchers at Treventis developed a proprietary platform technology called Common Conformational Morphology (CCM) which uses computer-aided modeling to design molecules that can prevent the pathogenic misfolding of a number of different proteins at the earliest stages. One of the group's lead projects is targeting tau.

"We use this model to design molecules and then we optimize them for safety and target engagement, demonstrating that we can reduce the portion of tau that causes pathogenicity, at the earliest stages of disease," says Dr. Taylor.

The researchers have also been able to incorporate features into this molecule to ensure that it crosses the blood brain barrier, a complex cell-based system made up of blood vessels and tissue that helps to prevent toxic substances from reaching the brain.

“We used new computational models developed by Dr Weaver’s group to design compounds that not only penetrate the brain but have the required safety profile to become a drug," says Dr Mark Reed, Chief Scientific Officer at Treventis, and Staff Scientist at UHN. “This has proven a painstaking, but highly effective strategy.”

Coming up with innovative approaches and new therapeutic targets for Alzheimer’s disease has proven incredible elusive and challenging for many research teams worldwide.

“It has taken us 15 years and a lot of failures to come up with this class of small molecules,” says Dr. Weaver. “Most drug discovery programs don’t have that kind of patience. Most small biotech companies don’t have the survivability. It’s thanks to the flexibility and ingenuity of all the people involved that Treventis has had the time, and the runway, to make this possible.”

“We have actually been on the right track the whole time but the technology to be able to test our hypothesis has only just caught up,” adds Dr. Taylor.

Alzheimer’s is just one example of a disease that involves misfolding proteins. Researchers hope the CCM platform technology could lead to a better understanding of how proteins misfold in other diseases, such as Parkinson’s, Amyotrophic lateral sclerosis (ALS) and cancer.

“I always say that global diseases such as Alzheimer’s deserve a global solution,” says Dr. Weaver. “Well, only small molecules that can be developed into therapeutics are a global solution.”

About the Krembil Brain Institute
The Krembil Brain Institute at Toronto Western Hospital, part of University Health Network, is home to one of the world’s largest and most comprehensive teams of physicians and scientists uniquely working hand-in-hand to prevent and confront problems of the brain and spine. One in three Canadians will experience a brain-related condition such as Parkinson’s, Alzheimer’s or epilepsy in their lifetime. Through state-of-the-art patient care and advanced research, we are working relentlessly to find new treatments and cures. For more information: https://www.uhn.ca/krembil

About University Health Network
University Health Network consists of Toronto General and Toronto Western Hospitals, the Princess Margaret Cancer Centre, Toronto Rehabilitation Institute, and The Michener Institute of Education at UHN. The scope of research and complexity of cases at University Health Network has made it a national and international source for discovery, education and patient care. It has the largest hospital-based research program in Canada, with major research in cardiology, transplantation, neurosciences, oncology, surgical innovation, infectious diseases, genomic medicine and rehabilitation medicine. University Health Network is a research hospital affiliated with the University of Toronto. For more information: https://www.uhn.ca/

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