VERMILION THERAPEUTICS INC.

Introducing a new treatment modality for amyloidosis related diseases such as Alzheimer's with photoactivatable oxygenation catalysts.

3-11-8 Sendagaya
Shibuya-ku, Tokyo 151-0051
Japan

https://www.vermilion-tx.com

Founded in 2019
Founder & CEO: TORII Shin-ichi, Ph.D.
No. of employees: 5
Type of Ownership: Private

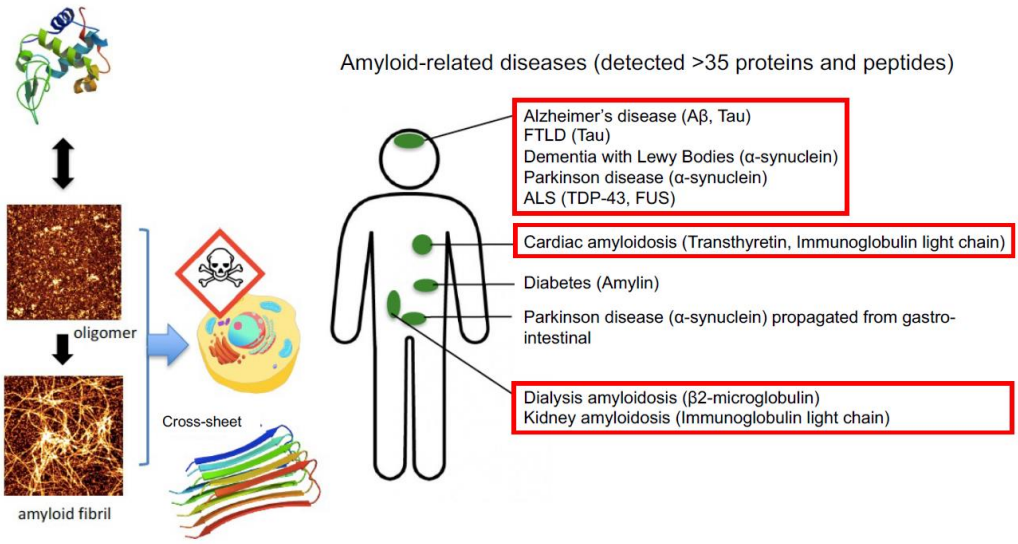
March 2022: Developing a promising therapeutic technology which may contribute to treat various amyloidosis related diseases, incl. Alzheimer's Disease.

Vermilion Therapeutics
バーミリオン・セラピューティックス

Venture Valuation (VV) interviewed TORII Shin-ichi, Ph.D., founder and CEO.

VV: **Among amyloidosis related diseases, your photocatalyst technology has proven preclinical efficacy on several abnormal proteins that cause diseases such as amyloid beta, tau, alpha-synuclein, amylin, insulin, transthyretin, and beta2 macroglobulin.**

Torii Amyloidosis is a group of disorders in which amyloid fibrils (abnormal proteins) are built up in various organs: brain, heart, kidneys, liver, spleen, soft tissue, central/peripheral nervous system, and other parts (see below). There are over 35 peptides and proteins causing amyloidosis.

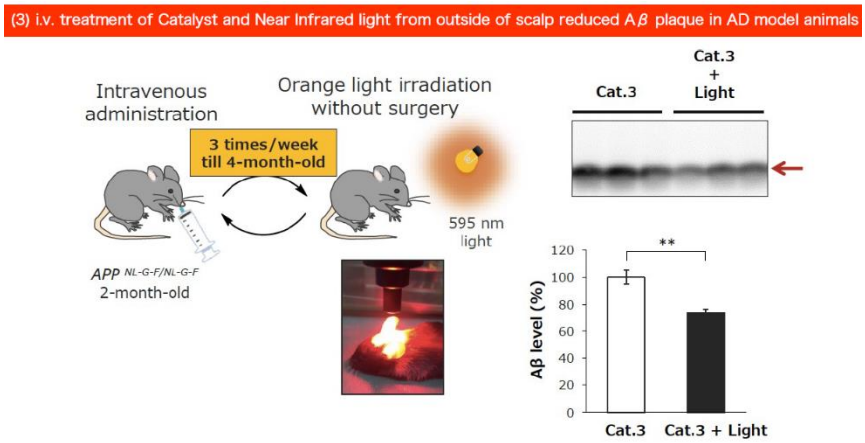


The different types of amyloidosis are categorized as systemic or localized. Alzheimer's and related diseases (e.g. Tau and synuclein) are localized amyloidosis in CNS (Central Nervous System). Systemic types are AL (Primary) amyloidosis, AA (Secondary) amyloidosis, hereditary ATTR amyloidosis, and wild type ATTR amyloidosis. Our photocatalyst technology is effective with all types of amyloidosis, so it is new treatment modality and technology in these hard-to-treat diseases.

VV: **Experiments with your photocatalyst technology on living Alzheimer's disease model mice demonstrated the reduction of amyloid beta plaque.**

Torii: The results were published in 2021 in *Science Advances*[1] as well as *Brain*[2].

The photocatalyst specifically combines oxgen atom with aggregated-amyloids upon irradiation with light, and reduces the neurotoxicity of aggregated amyloid beta peptide via inhibition of amyloid formation. This effects are generated by aggregation inhibition and phagocytosis with mictoglia or macrophase cells.



Nagashima, Ozawa, Furuta, Oi, Hori, Tomita, Sohma, Kanai, *Sci. Adv.* **2021**, *7*,

The above image displays the results of an irradiation experiement exhibiting the reduction of amyloid beta. We have also recognized that photo-oxygenation enhances microglia, the first and main form of active immune defense in CNS, so degrading amyloid-beta aggregates.

While immunotherapy deliverying antibodies into the brains, as limited BBB (Blood Brain Barrier) penetration, is limited to its efficiency, our photocatalyst technology by means of small molecule, which is a low molecular weight catalytic compound, is expected to produce a higher beneficial effect with stable penetration into CNS and systemic organs. With this catalytic compound, we are going to develop small molecule drugs which could be administered intravenously and preferably orally and pass efficiently through G.I. (GastroIntenstinal) cell membranes and BBB. For patients small molecule drugs are simpler to take than receiving a frequent infusion given by medical proffesionals for immunotherapy treatment. Moreover, medical costs are far more affordable than immunotherapy towards huge number of potential early stage of Alzheimer's diseases such as "Preclinical or MCI (Mild Cognitive Impairment)" stage Alzheimer's diesease patients in the world. As to our advantage over photo-immunotherapy in oncology fields, our photocatalyst does not generate cytotoxic radicals (ROS) to the cells, so it is much safer treatmet confirmed in in vivo animals by repeated dose studies with light irradiation.

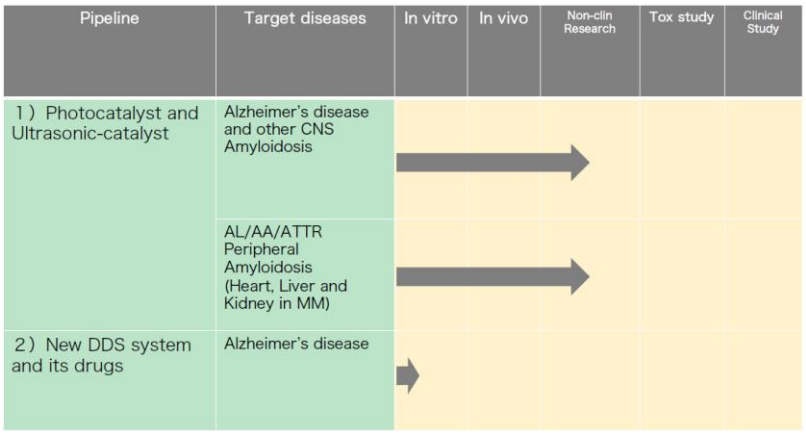
VV: **Your business strategy is to get approval first as an orphan drug and then move to drug development for Alzheimer's disease.**

Torii: It is risky for us as a small startup with limited financial resources to engage in drug development for Alzheimer's Disease first. Big pharma companies are intensely investing there and competing with each other.

[1] Nagashima et al,. Sci. Adv. 2021; 7: eabc9750 24 March 2021
[2] Doi:10.1093/brain/awab058

Being specialized in treatment for amyloidosis related diseases, we will prove our technological competence. As shown in the chart below, we are moving towards toxicology studies on rare disease types of systemic amyloidosis, for example cardiac, renal and hepatic amyloidosis (ATTR, AL, AA) in parallel with brain localized amyloidosis (Alzheimer's and other CNS amyloidosis).

Also, we recognize that our strength is that our photocatalyst compound can remove already existing amyloid aggregates and promote excretion of amyloid from body, which differentiates with other aggregates inhibition approach or peptide knock-down approach such as siRNA or RNAi or oligonucleotide therapies.



VV Comments after the interview:

Grand View Research reports that the global amyloidosis treatment market was valued at 3.6 billion USD in 2017 and is projected to rise at a CAGR (compound annual growth rate) of 7.2% thru 2025[3]. As most people diagnosed are between aged 60 and 70[4], the increasing population of those ages is one of the reasons driving market growth.

Regarding Alzheimer's disease treatment, the global market was estimated at 4.8 billion USD in 2020 and should grow to 6.3 billion USD by 2025[5] with a CAGR of 5.5% thru 2025. Alzheimer's mostly occurs in people aged over 60 but can affect younger people as well[6].

Small molecule weight drugs, such as Vermilion Therapeutics Inc. is developing, have the advantage over immunotherapy in terms of oral administration and affordable medical costs to Alzheimer's disease. For instance, in the case of aducanumab, the first FDA-approved but scientifically controversial immunotherapy drug for Alzheimer's, its wholesale acquisition cost was said to be 56,000 USD a year, although recently reduced to half that amount.

A main cause of Alzheimer's disease is thought to be a result of a complex interplay among amyloid beta and tau. One hopes that Vermilion's photocatalyst technology will offer a new therapeutic solution for over 44 million patients suffering from Alzheimer's worldwide[7].

[3] https://www.grandviewresearch.com/industry-analysis/amyloidosis-treatment-market
[4] https://www.mayoclinic.org/diseases-conditions/amyloidosis/symptoms-causes/
[5] https://www.bccresearch.com/market-research/pharmaceuticals/alzheimers-disease-therapeutics-diagnostics-markets-report.html
[6] https://www.hopkinsmedicine.org/health/conditions-and-diseases/alzheimers-disease/earlyonset-alzheimer-disease
[7] https://alzheimersnewstoday.com/alzheimers-disease-statistics/#:~:text=It%20is%20estimated%20that%20there,all%20ages%20have%20Alzheimer's%20disease

Contact **Mariko Hirano,** m.hirano (at) venturevaluation.com

Venture Valuation specializes in independent assessment and valuation of technology-driven companies in growth industries, such as the Life Sciences (Biotech, Pharma, and Medtech), ICT, Femtech, Nanotech, Cleantech and Renewable Energy. In addition to valuation products, Venture Valuation offers high-quality, focused information services like the Global Life Sciences Database, Biotechgate.com and this "*Let's Interview Series*" with companies with interesting technologies and services. We select and interview thriving companies and organizations especially in Switzerland and Japan.