

Braizon Therapeutics, Inc.

Advancing brain drug delivery with its inventive nanoparticle technology based on glucose-conjugated polymeric micelles

www.braizon.com

Braizon Therapeutics, Inc.
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Founded in: 2015
CEO: Mariko Tosu, PhD
No. of employees: 13
Type of Ownership: private
Primary stock exchange: N/A

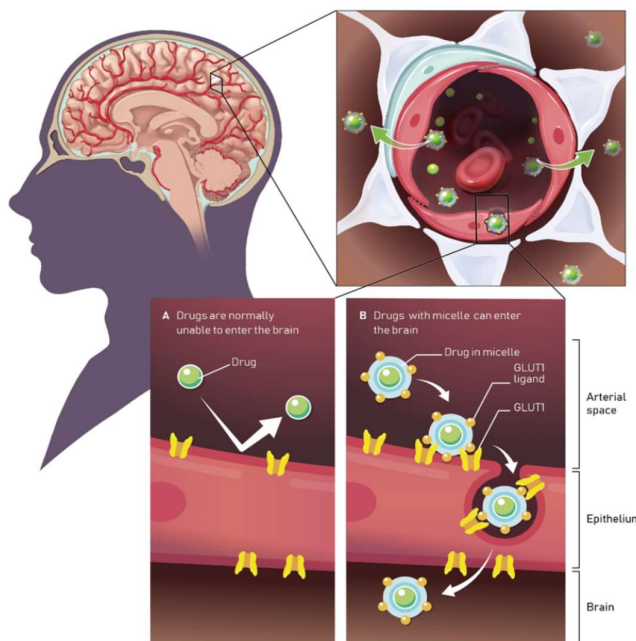
June 2019: Applying intelligently glyceemic control and a systematic route through the BBB (blood-brain barrier) to effectively reach neurons

Venture Valuation (VV) interviewed the CEO, Mariko Tosu, PhD.



VV: **The BBB is vital to protecting the brain. That makes it the major impediment to efficient drug delivery for treatment of CNS (central nervous system) diseases. Your nanoparticle technology targets GLUT1 (glucose transporter 1) to reach neurons.**

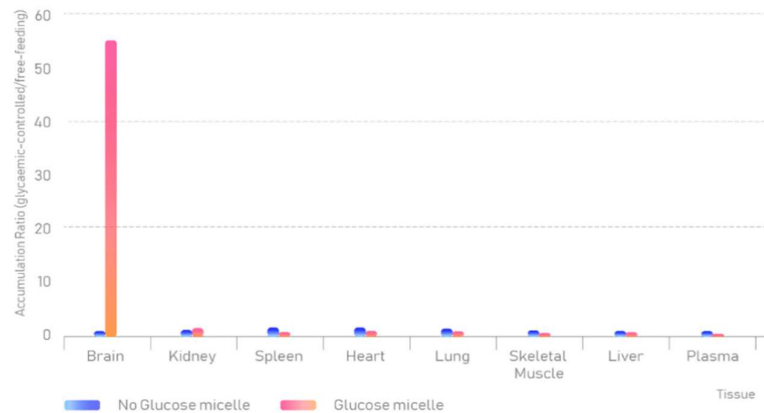
Tosu: Glucose is the primary energy source for the brain. GLUT1 is highly expressed on the surface of brain capillary endothelial cells which are major constituents of the BBB. Under fasting conditions, its expression is known to dominate on the plasma membrane of the endothelial cells.



As shown in the image's right bottom corner, glucose-conjugated polymeric micelles (30nm in diameter), in which a drug is encapsulated, interact with GLUT1; they are taken into cerebrovascular endothelial cells; the micelles move away from GLUT1 on the brain parenchyma side; they are designed to deliver encapsulated drugs to the specific brain sites, and, being biodegradable, the micelles decay naturally.

VV: What are major advantages of your technology?

Tosu: First, our technology excels in the dose accumulation reaching the brain. We have proved an accumulation rate of 6% dose/gram-brain. The chart below demonstrates the accumulation ratio in mice (glycemic-controlled/free-feeding) in different organs. The accumulation in only the brain was observed.



A recent example for comparison is a BBB crossing nanocarrier with peptides recognizing the transferrin receptor on brain capillary endothelial cells. Its accumulation rate in the brain didn't exceed 1.0% dose/gram-brain, very much lower than our technology.

Scientific evidence proves that our technology is significantly better than those reported to date for other brain drug delivery systems using glucose or peptide ligands¹.

For reference, the accumulation rate in the brain of Aricept, a low molecular weight drug for treating dementia related to Alzheimer's disease, is reported to be 0.13%. Solanezumab (Eli Lilly) and Bapinezumab (J&J Pfizer), both antibody drugs which failed in phase 3 to treat Alzheimer's disease, have an accumulation rate less than 0.1%.

Second, our nanoparticle technology has an advantage of delivering various modalities such as small molecular, anti-sense oligonucleotide, and antibody drugs across the BBB directly into the brain. This means that our technology supports not only new drug development but also repositioning existing and/or failed drugs for new therapeutic indications.

¹ "Glycaemic control boosts glucosylated nanocarrier crossing the BBB into the brain" Nature Communications <https://www.nature.com/articles/s41467-017-00952-3>



VV: Braizon's technology was patented in 2017 in Japan and the U.S.² This spring your U.S. research lab opened in Boston, MA. Now you are ready to develop the business by offering various applications for different targets.

Tosu: Braizon was founded in 2015 to develop practical applications of the technology to use nanoparticle for drug delivery to the brain that was invented by Prof. Kazunori Kataoka³ and Prof. Takanori Yokota⁴.

To accelerate collaboration with our existing and potential alliance partners, we are starting research operations in Boston, one of the global hubs of the multinational pharmaceutical industry.

This year we are actively raising funds for Series C for transition of our drug delivery platform from pre-clinical to clinical studies.

VV Comments after the interview:

Degenerative brain disorders such as Alzheimer's, Parkinson's, Multiple Sclerosis, brain cancer, and other more rare CNS diseases are serious medical and social challenges in the aging society we are facing.

According to The Grand View Research⁵, the global CNS therapeutic market is expected to reach 128.9 billion USD in 2025 from 77.2 billion USD in 2016. Meanwhile due to the complexity of brain disorders, over 95% of attempts to develop new drugs for CNS diseases are reported to end in failure.

Small molecules that are lipid soluble and also have a molecular weight <400~500 Da are only proven to cross the BBB. And most macromolecules can't penetrate the brain endothelium.

The absence of competent technologies to deliver drugs across the BBB delays CNS drug development. One hopes that promising brain drug delivery technology such as Braizon's will expand horizons for drug discovery and development in the near future.

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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,

² JP 6086566 B2, WO2015/075942

³ Policy Alternative Research Institute, The University of Tokyo

⁴ Center for Brain Integration, Tokyo Medical and Dental University

⁵ <https://www.grandviewresearch.com/press-release/global-central-nervous-system-cns-therapeutic-market>

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