NEUWAY Pharma GmbH
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NEUWAY PHARMA

Crossing the barrier to treating brain diseases

Building on an evolutionary ruse to cross the physiological blood–brain barrier, NEUWAY Pharma's engineered protein capsules (EnPC) are poised to usher in a new era of effective CNS therapies.

Brain diseases pose a double challenge for drug developers: first developing an efficacious therapeutic for a given disease or condition; and second, getting the therapeutic to the brain where it needs to act. The delivery challenge is posed by the blood–brain barrier (BBB), which prevents around 95% of small molecules, and almost all therapeutic biologics, from leaving the bloodstream and entering the brain, rendering standard administration routes such as intravenous and subcutaneous delivery ineffective.

Nature, however, has provided a solution to this problem. A human polyomavirus, known as John Cunningham virus (JCV), has evolved the natural ability to penetrate and cross the BBB and enter the brain, where it causes progressive multifocal leukoencephalopathy in immunodeficient patients. The BBB-penetrating capacity of JCV lies in the proteins that make up its capsid, which comprises the major protein VP1 and the minor proteins VP2 and VP3.

> NEUWAY is using EnPCs to deliver mRNA encoding functional versions of defective genes causing certain diseases to the brain

A neu way to cross the BBB

NEUWAY Pharma, based in Bonn, Germany, has created a technology platform for delivering therapeutic agents across the BBB by mimicking the capsid shell of JCV. This is achieved by recombinant expression and purification of VP1 proteins, which self-assemble into particles NEUWAY calls engineered protein capsules (EnPC). Each EnPC is about 40 nm in diameter, with a hollow lumen that can be loaded with a wide variety of therapeutic cargo, from small molecules to antibodies and nucleic acids.

Crucially, these EnPCs are completely free of virus material and retain the ability to traverse the BBB (Fig. 1). Published in vitro and in vivo studies by NEUWAY have validated the transport of EnPCs across the BBB, and demonstrated uptake by brain cells. NEUWAY has used EnPCs to deliver an mRNA encoding the firefly luciferase gene into mice via intravenous injection, which was subsequently expressed in the mouse brain.

EnPC crosses the BBB, enters the cell and opens up to release the drug

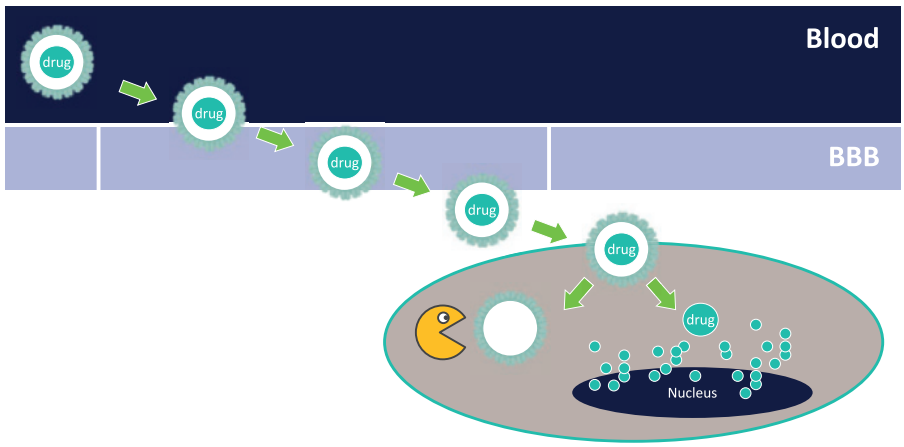

Fig. 1 | EnPC crossing the blood–brain barrier (BBB).

NEUWAY has expanded the production of EnPC in pure batches and at large scale and is now prepared for GMP qualification. In addition to creating a strong base for this platform technology, NEUWAY has also established a pipeline of therapeutic candidates focused on orphan diseases, specifically the lysosomal storage diseases such as metachromatic leukodystrophy, and Canavan disease, both of which result from mutations in enzymes in the sulphatide pathway. There are no cures for these diseases, which are typically treated with enzyme-replacement therapy that imposes a heavy burden on patients and at best slows disease progression.

Delivering corrective mRNA

NEUWAY is using EnPCs to deliver mRNA encoding a functional version of the defective gene causing these diseases to the brain. NEUWAY's studies have shown that the EnPCs are delivered to the brain, and preclinical proof of concept studies are ongoing to assess the level of gene expression and of functional enzyme achieved. The company is interested in forging partnerships to take these pipeline candidates through clinical development and to market, which would serve the desperate need of patients and also demonstrate clinical proof of concept.

When developing a potential central nervous system (CNS) drug, delivery should be a key focus from the beginning of the process. NEUWAY is keen to partner with pharma companies working in the CNS space and who would like to explore the ability of EnPCs to deliver candidate therapies of any kind to the brain by having NEUWAY carry out feasibility studies on their behalf. EnPCs also offer the potential to rescue drugs that have demonstrated a valuable mechanism of action and shown early promise, but which eventually failed because they could not be successfully delivered to the brain. Similarly, EnPCs can support the lifecycle management of existing drugs, by providing a new patent-protected formulation, and may also have a role in repositioning drugs that may offer benefits in brain disease, if only they can be delivered there.

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CONTACT
Oliver Ernst, Managing Director
Business Development
NEUWAY Pharma GmbH
Bonn, Germany
Tel: +49 228 522798 0
Email: ernst@neuway-pharma.com