

## Key Facts

### Indication:

monogenetic diseases of the CNS:

- MLD (metachromatic leucodystrophy)
- Huntington's disease

**Foundation:** 2014

**Employees:** 20

**Revenue:** n/a

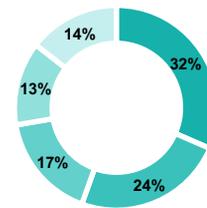
**# of Financing Rounds:** Series A

**Capital Raised:** ~EUR 12m

### Intellectual Property Portfolio:

- 5 patent families
- 3 trademarks

### Shareholder Structure:



- Wellington Partners
- LSI Pre-Seed-Fonds
- KfW
- Founder
- Others

## Summary

- NEUWAY Pharma GmbH, Bonn, Germany is focusing on the preclinical and clinical development of innovative therapeutics for the treatment of brain diseases using its proprietary CNS Drug Delivery Technology. This technology is based on a protein that naturally forms capsules, named Engineered Protein Capsules (EnPC®). EnPCs may be used as a carrier to transport highly active drug substances - ranging from small molecules to large nucleic acid strands – across the blood-brain barrier (BBB) after intravenous (i.v.) injection.
- NEUWAY uses this technology to encapsulate active drug substances that do not cross the BBB to successfully treat severe orphan brain diseases with a very high medical need. Besides these in-house projects, NEUWAY plans to partner its CNS Drug Delivery Technology with pharmaceutical or biotech companies, preferably if large indications, like Alzheimer's disease, are addressed.
- The Company is backed by venture capital from renowned investors as well as from private investors and supported by a strong Advisory Board.

## Problem

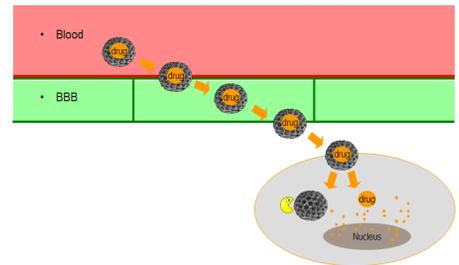
- The blood-brain barrier (BBB) is an epithelium layer surrounding cranial blood vessels. This layer controls the transport to and from the central nervous system (CNS) and protects the human brain from substances that are not needed for its function, especially toxins and pathogens. Unfortunately, many drugs are regarded as not useful by the BBB and are prevented from passing it and exerting their activity in the brain. This is why many potential drug candidates may not be suitable for treatment of CNS diseases.

## Solution

- NEUWAY uses the unique properties of a naturally occurring protein that forms capsules which are able to pass the BBB without affecting its physiological function. These capsules can be filled with highly active drug substances - ranging from small molecules to large nucleic acid strands. Filled capsules can be administered intravenously and distributed to the brain while remaining intact. In addition, they have the unique property enabling them to cross the cell membrane releasing their cargo within the cell.

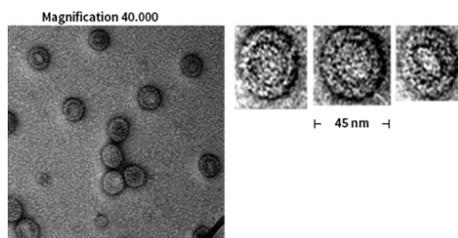
### Brain cell delivery using Engineered Protein Capsules (EPCs)

EPCs cross the Blood Brain Barrier, enter the cell and open up to release the drug



## Technology

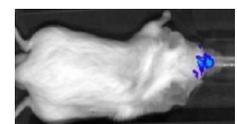
- NEUWAY developed a biotechnological process to produce such capsules in an appropriate quality - named Engineered Protein Capsules (EnPCs) - and to fill them with active pharmaceutical ingredients (APIs), which may be used for, e.g. gene therapy of rare CNS diseases.
- Preclinical Proof-of-Concept (PoC) was demonstrated using a plasmid encoding for FireflyLuciferase that was successfully transported across the BBB into cells of the mouse CNS. The plasmid was packed into EnPCs which were injected i.v. into the tail vein of mice. The expression of the Luciferase protein in brain cells was proven by the detection of bioluminescence of the brain (right mouse). The i.v. injection of the plasmid alone did not show any luciferase expression (left mouse).
  - This result was supported by the detection of luciferase in brain slices using immune histochemistry.



Picture shows purified EnPCs under electron microscopy



Plasmid i.v.



Plasmid-EnPC i.v.

## Business Model

- NEUWAY positions itself as the company for the treatment of brain diseases using its proprietary CNS Drug Delivery platform. A dual business model secures a solid venture:
  - development of own compounds to treat rare severe brain diseases with a high unmet medical need, with the ultimate goal to commercialize these compounds by itself, and
  - partnering with pharmaceutical companies to apply its CNS Drug Delivery technology to their proprietary compounds, with the goal to generate a steady stream of income via milestone payments and royalties.

## Pipeline

- NEUWAY Pharma (NWP) uses its CNS Drug Delivery Technology for treating Metachromatic Leukodystrophy and Huntington's disease. Additional genetic diseases of the CNS are currently under evaluation.

### – Metachromatic Leukodystrophy (MLD)

MLD is a rare autosomal recessive inherited genetic disease caused by alterations in the ARSA gene leading to a loss of function of the encoded protein Arylsulfatase A (ASA). ASA is a key enzyme in the breakdown of sulfatides. ASA deficiency leads to the accumulation of sulfatides causing severe malfunctions of the CNS.

### – Huntington's disease (HD)

HD is a rare inherited, progressive neurological and neuropsychiatric disease caused by an autosomal dominant mutation of the gene Huntingtin. This leads to the accumulation of a mutated Huntingtin protein which is toxic to certain cell types, particularly in the brain and leading to impaired nerve cell function. Small interfering RNAs (siRNAs) may successfully reduce the amount of mutated protein, that leads to reduced toxicity, but the development of these compounds is hampered by the poor delivery over the blood brain barrier.

## Past >>> Future Milestones

- Development of the upstream process and required analytics to manufacture primary EnPCs >>> Establishment of GMP process
- Development of downstream process to manufacture EnPCs loaded with a specific API >>> GMP implementation.
- Development and packaging of specific APIs relating to NEUWAY's lead indications.
- Preclinical PoC studies in healthy mice to demonstrate delivery of packed APIs in the brain >>> PoC studies in a genetic animal disease model to measure the extent of the pharmacodynamic effect.
- Expand the in-house research pipeline to additional genetic diseases of the CNS that might benefit from the CNS Drug Delivery Technology.
- Launch of collaborations with pharmaceutical and biotech companies to apply NEUWAY's CNS Drug Delivery Technology to their proprietary compounds and APIs.

## Market

- **1. Exploitation of the CNS Drug Delivery Technology** to design, develop and commercialize own compounds for the treatment of rare severe brain diseases with high a medical need - metachromatic leukodystrophy (MLD) & Huntington's disease as well as additional genetic diseases, such as Krabbe disease, etc. The goal would be to evolve into a fully integrated pharmaceutical company for the treatment of severe brain diseases.

MLD is reported to occur in 1 of 40,000 to 160,000 individuals translating into 3,125 to 12,500 patients in the EU. The average incidence of Huntington's disease is 0.38 per 100,000, i.e. 1,900 patients in the EU. Krabbe disease has an incidence in the EU of ~1 in 100,000, i.e. 5,000 patients.

Current treatment costs for lysosomal storage diseases are in the order of magnitude of +250,000€ per treatment / year (enzyme replacement therapy). For instance, for each of the a.m. lysosomal storage diseases minimum peak sales in the order of magnitude of high three digit hundred million range may be achievable.

Income from this branch of NEUWAY is scalable depending on the number of projects NEUWAY may afford to design and run in parallel.

- **2. Licensing agreements with pharmaceutical companies** to apply NEUWAY's proprietary CNS Drug Delivery Technology to partners' proprietary compounds with the goal to generate early income from upfront and milestone payments as well as a steady royalty stream after MAA.

Income from this branch of NEUWAY is scalable depending on the number and scope of license agreements. Milestone payments for such "Technology Deals" may be in the order of magnitude of low to medium double digit EURm amounts and royalties in a low single digit range.

## Competition (selection)

- **2-BBB Medicines BV, Leiden, The Netherlands (private):** Uses pegylated liposomes with a brain-targeting ligand glutathione to transport cargo through the BBB and delivery behind the BBB (NOT within cells) – called G-Technology. Completed Phase II for Doxorubicine in different forms of brain cancer (partnered 2017 to Oncology Venture) and completed PI with methylprednisolone in acute and chronic neuro-inflammation of different origins.
- **Spark Therapeutics, Philadelphia, USA (public):** Uses adeno-associated viral (AAV) vectors to encapsulate genetic material for the potential treatment of genetic diseases. Batten disease, Huntington's disease: Preclinical stage (but clinical stage and commercial stage in non-CNS diseases)
- **Armagen, Calabasas, USA (private):** Targets natural receptors that shuttle, e.g., transferrin over the BBB. Hurler Syndrom: Phase II, Hunter Syndrom: Phase I, MLD & SanFilippo: pre-IND.
- **AngioChem, Montreal, Canada, (private):** Develops peptide drug conjugates to leverage the LRP-1 mediated pathway to cross the BBB for treatment of neurological diseases. Paclitaxel conjugate Phase II in glioma. Research stage for other conjugates used for the treatment of lysosomal storage diseases.
- **Bioasis technologies Inc., Richmond, Canada (public):** Uses metallothionein to shuttle drugs over the BBB. All projects preclinical or discovery stage. Compounds are a lysosomal enzyme (Hunter), Herceptin and an oligonucleotide (siRNA targeting NOX4 gene).

## Management

- **Dr. Heiko Manninga**  
CEO/CSO
  - Life Science Inkubator (Bonn):  
Project Director of Virus-Like Particles (VLP) Technology
  - Max Planck Institute: Post-Doc
- **Dr. Oliver Ernst**  
COO
  - Brainlab AG:  
Director Intellectual Property Management
  - BASF AG:  
Patent Counsel