

to-BBB

to-BBB® is a private biotechnology company focusing on enhanced drug delivery across the blood-brain barrier.

Vision

The treatment of currently unserved brain diseases will be best achieved by safely enhancing the blood-to-brain delivery of drugs.

Mission

The company is developing novel treatments for devastating brain disorders by combining existing drugs with the G-Technology®, to-BBB's proprietary brain drug delivery platform.

"No other technology is able to enhance the brain delivery of drugs with the favorable pharmacokinetic and safety profile of the G-Technology®"

Contact

Willem van Weperen, CEO

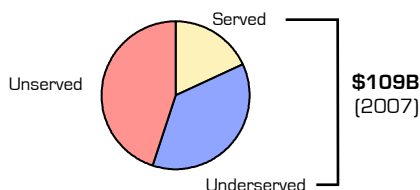
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The global CNS market

The human brain is the single most common origin of illness with 2 billion people worldwide suffering from brain-related disease causing an economic burden of \$2 trillion a year. For the majority of patients no treatment exists. Responding to this unmet medical need and scenting the vast revenue potential, the CNS disorders market became one of the largest and fastest growing markets in the pharmaceutical industry. In 2007, neuro-pharmaceutical companies alone generated \$109 billion in revenues, looking forward to 8% annual growth.



Source: Neuroinsights' Neurotechnology Industry 2008 Report

Opportunities in CNS drug development

In attempts to cure brain diseases many promising active compounds have shown potential therapeutic effect, however, over 95% never reach the brain in therapeutically relevant concentrations. Pharmaceutical compounds are denied access to the brain by the neuroprotective blood-brain barrier (BBB). This sophisticated physiological system regulates the selective uptake of essential nutrients and metabolites and keeps out foreign and potentially harmful substances. While this is life-supporting protection for the brain, it caused resignation in past drug development, as many promising therapeutic compounds were doomed to failure due to dose-limiting toxicity.

The future of getting drugs into the brain is to hijack the uptake-machinery of the blood-brain barrier by associating the drug with compounds that are naturally transported into the brain.

to-BBB platform technologies

to-BBB developed state-of-the-art proprietary technologies that create safe drug delivery opportunities to the brain. to-BBB's platform technologies utilize endogenous receptor-targeted mechanisms in combination with nanosized drug-loaded liposomes. This approach is unique in that it does not require drug modification and at the same time gives rise to metabolic protection during transport and increased bioavailability at the target site.

G-Technology®

The G-Technology is the company's core platform and enables superior transport of drugs across the blood-brain barrier and a better safety- and pharmacokinetic profile compared to competing technologies. The technology is based on the proprietary use of glutathione as a targeting moiety and its matching receptor on the blood-brain barrier.

A second patented platform technology of to-BBB is the HB-EGF Technology™ which has unique potential in site-specific drug targeting, bio-imaging, and as a non-toxic adjuvant.

Science Collaborations

NKI, the Netherlands; Industrial Technology Research Institute (ITRI), Taiwan; VUmc, the Netherlands; University of Uppsala, Sweden; University of Padua, Italy; Joanneum Research, Austria; Leiden University, the Netherlands

Industry Collaborations

MedImmune (AstraZeneca); Shire; Genzyme; Lundbeck; two undisclosed Top 10 pharma companies; GSK R&D China; Janssen; Abbott; Ablynx; NeuroVive; Synageva

Investors

Aescap Venture
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Entrepreneur & Partner at Aescap

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Senior Pharma & Biotech Executive

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2B3-101 for Brain Cancer

to-BBB's lead compound is glutathione pegylated liposomal doxorubicin hydrochloride (2B3-101), which is based on the already marketed pegylated liposomal doxorubicin (Caelyx) that does not effectively cross the blood-brain barrier. Studies in an experimental brain cancer model have shown that 2B3-101 reduces brain tumor growth more efficacious than Caelyx, and, prolongs survival up to 60% when given at the maximum tolerated dose. Extended GLP toxicity, safety and toxicokinetic evaluations have shown equal or less severe findings for 2B3-101 as compared to Caelyx, possibly driven by the PK profile; the half-life of 2B3-101 in plasma was about 25 hr vs. 28 hr for Caelyx. to-BBB obtained clinical scale batches of 2B3-101, produced according to cGMP by TTY Biopharm (Taiwan). to-BBB has received approval to start treating patients with brain metastases in a Phase I/II clinical trial in June 2011.

- ✓ The blood-brain barrier blocks most modern medicines
- ✓ to-BBB provides the safest proprietary brain delivery platform
- ✓ to-BBB aims to become the leading brain drug delivery company by enabling successful development of novel treatments for patients with devastating brain diseases

Pipeline

to-BBB is currently in the preclinical development of their second product 2B3-201 for neuroinflammation. Based on available proof-of-concept animal data, to-BBB is considering the development of other product candidates in the disease areas of Alzheimer's disease, MS, lysosomal storage diseases, Parkinson's disease and ALS.

	Indication	Discov.	Optim.	Preclin.	I/II	IIb
2B3-101	Brain Cancer	[Progress bar showing stages from Discov. to I/II]				
2B3-201	Neuroinflammation	[Progress bar showing stages from Discov. to Preclin.]				
2B3-XXX	Other candidates	[Progress bar showing stages from Discov. to Preclin.]				

■ Situation in 12 months from now

Partnering Opportunities

Since its inception, to-BBB has closed partnering agreements with several top tier and small focused biotech companies. In these partnerships, to-BBB offers access to its proprietary platform technologies to jointly determine pre-clinical proof of concept with the CNS drug and model of interest of (future) partners. In addition to current ongoing collaborations, to-BBB wants to enable multiple value adding industrial collaborations for specific product-indication combinations using its unique brain drug delivery capabilities.

