

## PRESS RELEASE

### to-BBB starts clinical trial in patients with brain metastases

Leiden, 27 June 2011

**to-BBB, the Dutch brain drug delivery company, is pleased to announce that it has received approval to start treating patients with brain metastases with its lead product 2B3-101 in a Phase I/II clinical trial.**

Based on its proprietary G-Technology<sup>®</sup>, to-BBB is developing its lead compound 2B3-101, brain-targeted doxorubicin liposomes. These liposomes are coated with the endogenous antioxidant glutathione at the tips of polyethylene glycol (PEG) to safely enhance the delivery of free drug to the brain. 2B3-101 has shown reduction of brain tumor growth in preclinical proof-of-concept studies at the Netherlands Cancer Institute. Clinical batches of 2B3-101 have been produced by to-BBB's manufacturing partner TTY Biopharm and pivotal preclinical safety studies were completed in 2010.

to-BBB is now ready to start recruitment of a Phase I/IIa trial involving approximately 40 patients. The trial will be conducted at the NKI-AVL (Dr. Brandsma, Amsterdam), VUmc (Prof. Verheul, Amsterdam) and LUMC (Dr. Gelderblom, Leiden), all located in the Netherlands. The trial will be managed by the clinical research organization, SMS-oncology.

The primary endpoint of the trial is safety, tolerability and determination of the maximum tolerated dose (MTD). Secondary endpoints include determination of the pharmacokinetic profile of 2B3-101 as well as a preliminary assessment of efficacy in women with brain metastases of breast cancer. While new therapies are increasing the success of treating systemically metastasized breast cancer, brain metastases still represent an increasing problem for these patients.

“We are gratified to investigate 2B3-101 and to explore whether enhanced brain delivery of doxorubicin can result in safe and more effective treatment of patients with brain metastases” says Dr. Dieta Brandsma, Principle Investigator of the study.

“In this trial with 2B3-101 in patients we aim to confirm the positive efficacy and tolerability profile we observed in preclinical studies,” says Werner Gladdines, Head of Clinical Operations at to-BBB. “Furthermore, this trial supports our efforts to further validate our G-Technology<sup>®</sup> to treat patients with brain diseases.”

Brain cancer affects up to 400,000 patients annually in Europe and the United States together. Treatment options for this devastating disease are limited and overall prognoses are poor. The neuroprotective blood-brain barrier (BBB) is limiting the delivery of many anti-cancer drugs to tumors in the brain, especially to micrometastases and invasively growing tumor sprouts.

## About to-BBB

to-BBB is a clinical stage biotechnology company focusing on enhanced drug delivery across the blood-brain barrier. The Company is developing novel treatments for devastating brain disorders, such as brain cancer, neurodegenerative diseases and lysosomal storage diseases, by combining existing drugs with the G-Technology<sup>®</sup>, to-BBB's proprietary brain delivery platform. This technology combines the widely used drug delivery approach of pegylated liposomes with the endogenous tripeptide glutathione as targeting ligand in a novel and safe way. Together with several top tier pharma and biotech companies, to-BBB is investigating the versatility of the G-Technology<sup>®</sup> for drugs that are unable to reach the brain within a tolerable therapeutic window. to-BBB is applying the G-Technology<sup>®</sup> for the delivery of doxorubicin for the treatment of brain cancer as its internal lead product 2B3-101.

to-BBB is headquartered in The Netherlands at the Leiden Bio Science Park and established a fully owned subsidiary, to-BBB Taiwan Ltd., in Taipei, Taiwan. Investors in to-BBB include Aescap Venture, Antea Participaties, Jonghoud International and the Industrial Bank of Taiwan Management Corporation (IBTM).

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