



FOR IMMEDIATE RELEASE

to-BBB Publishes Nonclinical Data on Lead Product 2B3-101

A Potential New Treatment Option for Patients with Brain Cancer

Leiden, the Netherlands, 10 January 2014 - 2B3-101, glutathione pegylated liposomal doxorubicin, is being developed as a new treatment option for patients with brain cancer. In nonclinical studies it was shown that 2B3-101 enhanced the delivery of the active compound doxorubicin to the brain. Furthermore, 2B3-101 significantly inhibited tumor growth in an experimental brain cancer model. These studies have now been published in the open access peer-reviewed scientific journal [PLOS ONE](#).

Pieter Gaillard, founder and Chief Scientific Officer at to-BBB, indicates the importance of the [published results](#): “These proof-of-concept data, showing the efficacy of 2B3-101 in a brain cancer model, provided the backbone of the clinical development plan, and have resulted in the initiation of a clinical trial in patients with brain cancer.”

Olaf van Tellingen, Research Scientist at The Netherlands Cancer Institute / Antoni van Leeuwenhoek Hospital (NKI-AVL), adds: “In two independent experiments, treatment with 2B3-101 resulted in a significant inhibition of brain tumor growth, and this effect was stronger than the effect of pegylated liposomal doxorubicin (as marketed as Doxil®/Caelyx®). Furthermore, treatment with 2B3-101 resulted in a significantly increased median survival time compared to Doxil/Caelyx.”

Furthermore, this improved efficacy of [2B3-101](#) was supported by additional *in vitro* and *in vivo* experiments. Using an *in vitro* model, it was shown that 2B3-101 was actively and specifically taken up by blood-brain barrier endothelial cells, while Doxil/Caelyx mainly remained bound to the cells without substantial evidence of an active uptake process. These findings were confirmed *in vivo*, showing a higher brain retention with 2B3-101 compared to Doxil/Caelyx four days after the administration, while the plasma levels were comparable.

The brain is a well-protected organ. The so-called blood-brain barrier selectively allows nutrients to enter the brain, and keeps harmful substances and also most drugs out of the brain. This makes treatment of brain tumors much more challenging compared to treatment of tumors outside the brain. By use of to-BBB's proprietary G-Technology®, the blood-to-brain delivery of drugs is enhanced by using active transport processes at the blood-brain barrier. The 2B3-101 product is based on the G-Technology and the existing pegylated liposomal doxorubicin (Doxil/Caelyx).

Full reference to the publication

Gaillard PJ, Appeldoorn CCM, Dorland R, van Kregten J, Manca F, et al. (2014) Pharmacokinetics, Brain Delivery, and Efficacy in Brain Tumor-Bearing Mice of Glutathione Pegylated Liposomal Doxorubicin (2B3-101). *PLoS ONE* 9(1): e82331. doi:10.1371/journal.pone.0082331

About to-BBB

to-BBB is a clinical stage biotechnology company developing novel treatments for devastating brain disorders, such as brain cancer and neuroinflammatory diseases. The Company combines existing drugs with to-BBB's proprietary G-Technology to enhance drug delivery across the blood-brain barrier. to-BBB currently has two products in clinical trials: its lead product 2B3-101 is in a Phase IIa trial in Europe and the US for the treatment of primary brain tumors as well as brain metastases; the second product 2B3-201 for MS relapses and other neuroinflammatory diseases entered a Phase I clinical study in December 2013.

to-BBB is based in the Netherlands and its subsidiary to-BBB Taiwan Ltd. is based 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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