FOR IMMEDIATE RELEASE

to-BBB Initiated Phase I Study in Healthy Volunteers with 2B3-201

Improved Anti-Inflammatory Therapy for Acute MS Relapses

Leiden, the Netherlands, 17 December 2013 - Last week, the First-in-Human study with 2B3-201, to-BBB's second product, was initiated at the Centre for Human Drug Research (CHDR) in Leiden, the Netherlands. This Phase I trial is designed to determine the safety profile, and will also give a first glance at the pharmacological profile. In this double-blind crossover study, 18 healthy volunteers are assigned to three cohorts in which they will receive an ascending single dose of 2B3-201, as well as placebo and standard of care methylprednisolone.

2B3-201 is being developed for treatment of diseases with neuroinflammation, such as acute relapses of multiple sclerosis (MS). The current standard of care methylprednisolone is effective, yet it requires high dose infusions for several days. This often results in side effects and inconvenience for the patient. Therefore, there is a high medical need for an effective treatment that could be given at lower doses with a more convenient dosing regimen.

"to-BBB's G-Technology® provides a safe method to enhance the slow and sustained delivery of drugs to the brain," says Werner Gladdines, Head of Development at to-BBB. "By combining this technology with methylprednisolone, 2B3-201 was developed and tested in nonclinical models with neuroinflammation, in which it showed a similar efficacy at single administration with a 10 times lower dose compared to multiple high doses of methylprednisolone."

Following an extensive nonclinical development program, to-BBB initiated the Phase I clinical trial. The aim of this First-in-Human study is to assess the safety, tolerability, pharmacokinetics and pharmacodynamics of 2B3-201 in healthy volunteers, in comparison to placebo and methylprednisolone. Using a double-blind crossover design, each healthy volunteer receives an infusion of 2B3-201, placebo and methylprednisolone with 1-week intervals, thereby acting as his own control.

"Next to the standard safety parameters and pharmacokinetics, assessments of effects on cognition, behavior, and glucose tolerance will be evaluated," adds Dr. Geert Jan Groeneveld, Research Director Neurology & Pain at CHDR. "By including specific neurological tests in CHDR's NeuroCart and therapeutic dose levels of methylprednisolone in the control arm, this study allows for an extensive read-out of pharmacological and neurological effects."

2B3-201 is expected to follow a relatively short route towards marketing authorization. In addition to acute MS relapses, there is significant therapeutic potential in related inflammatory diseases, such as optic neuritis, neuromyelitis optica (NMO), uveitis, Behçet's disease, sarcoidosis, and neuropathic pain.

About Methylprednisolone

Methylprednisolone (and to a lesser extent prednisone) has become the standard of care for diseases with neuroinflammation, such as acute MS relapses. As an acute pulse therapy, methylprednisolone treatment is given as a daily intravenous infusion of high doses (500-1000

mg) for 3-5 consecutive days. At these high doses, methylprednisolone is effective, yet side effects like sodium retention-related weight gain and fluid retention, glucose intolerance with hyperglycemia, gastrointestinal side effects, and mood changes including insomnia and anxiety, occur frequently.

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 for enhanced drug delivery across the blood-brain barrier. This platform 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. to-BBB's lead product 2B3-101 is investigated in a Phase IIa trial for the treatment of primary brain tumors as well as brain metastases. to-BBB's second product 2B3-201 for MS relapses and other neuroinflammatory diseases has entered into a Phase I clinical study in December 2013.

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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