

***BRAIN* Publication Demonstrates Significantly Improved Therapeutic Window of Deep Brain Stimulation Using directSTIM™ Directional Electrode**

- Study confirms proof-of-concept for innovative DBS lead developed by Aleva Neurotherapeutics -

Lausanne, Switzerland, May 28, 2014 – Aleva Neurotherapeutics, a company developing next-generation implants for Deep Brain Stimulation (DBS) in major neurological indications such as Parkinson’s disease, today announced the publication of the results of an intraoperative study with its novel directSTIM™ directional lead. Data were published in the peer-reviewed journal *Brain - A Journal of Neurology*.*

The data presented in *Brain* are based on 11 patients with Parkinson’s Disease and 2 patients with essential tremor. In the study, clinical investigators assessed the intraoperative clinical effect of directional stimulation using Aleva’s directSTIM™ lead. This device features two rings consisting of three independent electrodes each. The angular position of the electrodes allows stimulation at 0°, 120° and 240° directions. Directional stimulation was tested at the target determined for the permanent lead. The clinical investigators compared the therapeutic window (defined as the electrical current at which side-effects occur minus the current at which a significant therapeutic effect is observed) of directional and classical stimulation. Compared to omnidirectional stimulation, the therapeutic window in the best direction was 41% wider. Furthermore, the current threshold producing meaningful therapeutic effects in the best direction was 43% lower than in omnidirectional stimulation. No complication was observed due to the insertion and removal of the directional lead or during testing.

“Side effects are often limiting the delivery of adequate current necessary to reach the maximum benefit of DBS,” said Dr. Claudio Pollo, Head of Functional Neurosurgery at the University Hospital in Bern, Switzerland and Principal Investigator of the study. “Our data demonstrate that directional stimulation with the directSTIM™ lead has a strong potential to reduce side effects, widen the therapeutic window, and lower the therapeutic current. This new approach may pave the way for improved DBS by increasing the selectivity of stimulation and by prolonging battery life. Furthermore, it provides an access to even smaller and complex regions that are difficult to stimulate with the currently available electrodes”.



Alain Dransart, Aleva's Clinical and Regulatory Director, commented: "We are very pleased with the results of this intraoperative study with our directional DBS lead. This is a major milestone for our company. Our next step is the validation of directSTIM™ for long-term implantation so that we can offer this new device to patients suffering from Parkinson's Disease and essential tremor".

* Reference:

Pollo C, Kaelin-Lang A, Oertel MF, Stieglitz L, Taub E, Fuhr P, Lozano AM, Raabe A, Schüpbach M - Directional deep brain stimulation: an intraoperative double-blind pilot study. Brain 2014; doi:10.1093/brain/awu102.

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About Aleva Neurotherapeutics:

Aleva Neurotherapeutics develops next-generation neurostimulation technologies and devices for Deep Brain Stimulation (DBS) therapy. Its solutions are designed to be more versatile, more precise and more efficient than currently available DBS approaches while causing fewer side effects and complications. Based on its proprietary microDBS™ technology, Aleva develops two novel, brain stimulating products with different properties. The first, called directSTIM™, is a directional electrode compatible with existing DBS systems; the second, called spiderSTIM™, is a full solution for both intra-surgical and long-term therapeutic use. All of Aleva's products are fully compatible with existing DBS technologies and devices.

The company is a spin-off from the Ecole Polytechnique Fédérale de Lausanne (EPFL) Microsystems Laboratory of Prof. Philippe Renaud. Aleva Neurotherapeutics has raised EUR 14.5 million from renowned private and institutional investors, among them BioMedInvest AG, BB Biotech Ventures LP, Banexi Ventures Partners, Initiative Capital Romandie and selected private investors.

About Deep Brain Stimulation (DBS)

Deep brain stimulation is approved worldwide for the treatment of Parkinson's disease (PD), essential tremor, dystonia, obsessive-compulsive disorder (OCD) and for the treatment of epilepsy. It is also under investigation for major depression. It is a therapy that relies on the delivery of mild electrical pulses to specific areas in the brain via an implanted lead that is connected to a battery-powered implantable pulse generator. Several clinical groups are currently investigating the application of DBS



for other neurological and psychiatric disorders. At present, it is carried out using electrodes that send the electrical current in all directions around the lead.

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