Press release

GeNeuro and Servier Announce Promising post hoc Analyses of Six-Month Data from CHANGE-MS Phase 2b Study at MSParis2017

- Anti-inflammatory effect observed in *post hoc* analysis in active population at 24 weeks for highest dose
- Remyelination effect observed already at 24 weeks for highest dose
- Analysis of full 12-month results expected 1Q18

Geneva, Switzerland, and Paris, France, October 28, 2017 – 11:00 CEST – GeNeuro (Euronext Paris: CH0308403085 – GNRO) and Servier announced today post hoc analyses of 6-month data from the CHANGE-MS Phase 2b study of GNbAC1 for the treatment of patients with relapsing-remitting multiple sclerosis (RRMS). The results showed an anti-inflammatory effect in active patients at the highest (18 mg/kg) of the three doses tested at Week 24. In addition, at the same dose, a promising effect on remyelination was observed at 24 weeks.

GNbAC1 is a monoclonal antibody that neutralizes a pathogenic retroviral envelope protein (pHERV-W Env) encoded by a member of the HERV-W family. CHANGE-MS 6-month results of GNbAC1 were presented today by Prof. Hans-Peter Hartung, chairman of the Department of Neurology of the University Hospital Düsseldorf (Germany) and principal investigator of the CHANGE-MS study at MSParis2017, the 7th Joint ECTRIMS-ACTRIMS meeting. The slides presented by Prof. Hartung are available on GeNeuro's web site.

The analysis on active patients was conducted on the 121 patients (45% of the patients included), who had at least one gadolinium-enhancing (Gd+) T1 lesion on their Baseline brain MRI scan. A positive effect of GNbAC1 at Week 24 was seen for the highest dose (18 mg/kg) in significantly reducing Gd+ T1 lesions (p=0.008). Similar effects were seen across other MRI measures of neuroinflammation, including new and/or enlarging T2, and combined unique active lesions. The 18 mg/kg dose appeared to consistently outperform both lower doses and placebo across MRI endpoints. These results support the hypothesis of a late onset of action of GNbAC1 seen at 6 months, which could be due to its mode of action through neutralizing a pathogenic protein (pHERV-W Env), without directly modulating or suppressing patients' immune systems, as well as to the time taken to reach a therapeutic concentration of the antibody in the brain.

Remyelination following treatment with GNbAC1 was measured by MRI with magnetization transfer ratio (MTR) analyses performed in the normal appearing white matter (NAWM) and cerebral cortex of patients. Recent studies have observed that there is a reduction in MTR signal in NAWM and cerebral cortex in patients with MS versus controls, with a pathological gradient of MTR signal loss.

Despite the variability inherent in a 50-center MTR study, the Baseline data reproduced the pathological gradients observed in prior studies. At the highest dose (18 mg/kg), MTR signal increased throughout NAWM and cerebral cortex, from Baseline to Week 24, with statistical trends for GNbAC1 18 mg/kg versus placebo (p=0.06) across each NAWM and cerebral cortical band. The 18 mg/kg dose demonstrated an increase of approximately 2 MTR % units versus placebo, across each NAWM and cerebral cortical band, while placebo had either mild reductions or no change (depending on the specific band observed) through Week 24.

"The effect of GNbAC1 on inflammation and remyelination observations for the highest dose at Week 24 are very encouraging. This is a novel mechanism of action trying to block a potential cause of the disease, so these analyses help us understand how GNbAC1 works in the patient setting and what benefits it could bring to patients. We now look forward to confirmation at the 48-week readout," **explained Prof Hans-Peter Hartung.**

"These positive analyses provide additional support to pursue the development of this new approach for patients with MS, in close collaboration with GeNeuro. We are very excited about potentially providing MS patients with a breakthrough therapy," **stated Dr. Christian de Bodinat, Director of Servier's Neuro-psychiatry Centre for Therapeutic Innovation.**

"GeNeuro has undertaken the challenge of developing a new option for treating MS patients, parallel to the existing immunomodulation / immunosuppression pathways, with the ambition to bring new benefits to patients," **stated Jesús Martin-Garcia, CEO of GeNeuro.** *"The analyses performed show promise, especially in the critical unmet medical need for therapies that promote remyelination. We now look forward to confirming these potential benefits with the final results from this 12-month study, expected in the first quarter of 2018."*

CHANGE-MS Phase 2b study is a randomized, double-blind, placebo-controlled study of 270 RRMS patients in 50 clinical centers in 12 European countries. The primary endpoint is an assessment of the efficacy of GNbAC1 based on the number of inflammatory lesions on brain MRI. Secondary endpoints at 12 months will also include MRI measures of inflammation and neurodegeneration, clinical parameters, and biomarkers, including pHERV-W Env. The protein is thought to be a causal factor of multiple sclerosis, with an impact of inflammation and on the inhibition of remyelination. As announced in August 2017, the initial 6 month data from the CHANGE-MS study failed to reach significance in achieving the primary neuroinflammation endpoint which covered weeks 12 to 24. The analysis of the full 12-month Phase 2b data is expected to become available in 1Q18.

GNbAC1 is a monoclonal antibody which neutralizes a retroviral envelope protein encoded by a pathogenic member of the HERV-W family (pHERV-W Env). Human endogenous retroviruses (HERVs) are ancestral retroviral DNA insertions in the human genome, thought to account for up to 8% of the total. The pHERV-W Env protein is thought to be a causal factor in the development of multiple sclerosis and Type 1 diabetes. GeNeuro is also currently conducting a Phase 2a study in Type 1 diabetes, with results expected during the third quarter of 2018.

Conference call:

Jesús Martin-Garcia, Chairman and CEO and the company management will host a conference call in English, on Monday, October 30, 2017 at 02:00pm CET / 09:00am EDT followed by a Q&A session. Details will be provided on Monday morning.

About magnetization transfer ratio (MTR):

MTR measures the amount of magnetization energy that is transferred from protons that are "fixed" (in tissue) to nearby protons that are "free" (in water molecules), after administration of an "off-resonant pulse" by the MRI scanner. This amount of transferred signal can be measured in each voxel of the MRI scan and, in the white matter of the brain, the MTR signal has been shown to directly correlate to the amount of structural myelin contained within that voxel.

Recent studies have observed that there is a reduction in MTR signal, both in NAWM and cerebral cortex, in patients with MS versus controls. These studies have shown that the amount of structural damage to myelin (as measured by reduction in MTR signal) in otherwise normal appearing white matter and the cerebral cortex of MS patients is worse in people with secondary progressive MS (SPMS) than in people with relapsing-remitting MS (RRMS). This loss of MTR signal is not uniform but occurs with a "pathological gradient" from the surface of the ventricles outward (in white matter) and surface of the brain inward (in the cerebral cortex). Taken together (and along with neuropathological studies showing structural damage to the cerebral cortex of MS patients, which follows a similar pathological gradient), these data suggest a diffusible, pathological factor in the cerebrospinal fluid of MS patients, as the cause of this damage.

About CHANGE-MS

(**C**linical trial assessing the **H**ERV-W Env **An**tagonist **G**NbAC1 for **E**fficacy in **M**ultiple **S**clerosis)

- Randomized, double-blind, placebo-controlled study of 270 RRMS patients in 50 clinical centers in 12 European countries
- 6-month study with extension up to one year for secondary endpoints
- Primary endpoint: assess the efficacy based on the number of inflammatory lesions on brain MRI, assessed at the end of the placebo-controlled period
- Secondary endpoints: MRI measures of neurodegeneration and remyelination, clinical parameters at 6 and 12 months, and biomarkers, including pHERV-W Env

As announced in August 2017, the initial 6-month data from the CHANGE-MS study failed to reach significance in achieving the primary neuroinflammation endpoint which covered weeks 12 to 24. GNbAC1 showed an excellent tolerability and safety over these first 6 months. The analysis of the full 12-month Phase 2b data is expected to become available in 1Q18.

CHANGE-MS is fully funded through the partnership with Servier signed in 2014, in which Servier is involved in the development and potential commercialization of GNbAC1 in MS in territories ex USA and Japan. Under this agreement and depending on achievement of development milestones, GeNeuro could receive a maximum of €362.5M, excluding royalties.

About Multiple Sclerosis (MS)

MS is a disease of the central nervous system (brain, optic nerves and spinal cord) that affects more than two million people worldwide, with most people being diagnosed between the ages of 20 and 40 years. MS is the consequence of inflammatory processes directed against the myelin sheath, a protective sleeve surrounding axons, the communication channels for neurons. Myelin damage prevents the axons from functioning properly and leads to their degeneration and neuronal loss. It slows down or prevents nerve impulses from travelling between the brain and the rest of the body, thereby causing the symptoms associated to this disease. Relapsing-remitting multiple sclerosis (RRMS) is characterised by infrequent, acute exacerbations with full or partial recovery between attacks. It is the most common form of MS and accounts for around 85% of all cases at onset.

About GNbAC1

The development of GNbAC1 is the result of more than 25 years of research into human endogenous retroviruses (HERVs), including 15 years at Institut Mérieux and INSERM, a French national medical research institute. Found in the human genome, certain HERVs have been linked to various autoimmune and neurodegenerative diseases. Researchers have demonstrated that the retroviral envelope protein associated with a pathogenic form of HERV-W [pHERV-W, formerly referred to as the Multiple Sclerosis RetroVirus (MSRV)] has been identified in brain lesions of patients with MS, particularly in active lesions, and in the pancreas of T1D patients. By neutralizing pHERV-W Env, GNbAC1 could at the same time block these pathological inflammatory processes and restore remyelination in MS patients and maintain insulin production in T1D patients. As pHERV-W Env has no known physiological function, GNbAC1 is expected to have a good safety profile, without directly affecting the patient's immune system, as observed in all clinical trials to date.

About GeNeuro

GeNeuro's mission is to develop safe and effective treatments against neurological disorders and autoimmune diseases, such as multiple sclerosis or Type 1 Diabetes, by neutralizing causal factors encoded by HERVs, which represent 8% of human DNA.

GeNeuro is based in Geneva, Switzerland and has R&D facilities in Lyon, France. It has 30 employees and rights to 16 patent families protecting its technology.

For more information, visit: www.geneuro.com

About Servier

Servier is an international pharmaceutical company governed by a non-profit foundation, with its headquarters in France (Suresnes). With a strong international presence in 148 countries and a turnover of 4 billion euros in 2016, Servier employs 21,000 people worldwide. Entirely independent, the Group reinvests 25% of its turnover (excluding generic drugs) in research and development and uses all its profits for development. Corporate growth is driven by Servier's constant search for innovation in five areas of excellence: cardiovascular, immune-inflammatory and neuropsychiatric disease, oncology and diabetes, as well as by its activities in high-quality generic drugs.
Servier has a solid commitment to neuropsychiatry and to proposing innovative therapies to patients suffering from neurological conditions. Its research teams are investigating new ways of treating diseases such as Alzheimer's and Parkinson's, as well as a broad range of neurodegenerative disorders, by targeting the toxic proteins that lead to neuron degeneration. The priority is to focus on the causes of the diseases rather than their symptoms. Currently, there are 5 projects at different stages of research in this promising area. Regarding development, where Servier's team has a strong expertise in international clinical development and in investigator training in neurology and psychiatry, current phase II/III projects focus on autism, major depressive disorder, post-stroke functional recovery and multiple sclerosis.

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