Press release

GeNeuro's ANGEL-MS Phase 2b extension study confirms and extends the neuroprotective effects of temelimab in MS

Data Supports Temelimab's Potential to Treat Disease Progression in MS

- Long-term neuroprotective effects confirmed in patients treated up to two years
- Sustained benefits on cortical and thalamic atrophy and myelin integrity
- Encouraging, dose-dependent effects seen on clinical measures of disease progression
- Excellent tolerability continued to be observed, with no dose-limiting safety signals
- GeNeuro will hold a conference call and webcast today Tuesday, March 12 at 2:30 pm CET / 9:30 am EDT, to share results

Geneva, Switzerland, 12 March 2019 – 07:00am CET – GeNeuro (Euronext Paris: CH0308403085 - GNRO), a biopharmaceutical company developing new treatments for neurodegenerative and autoimmune diseases such as multiple sclerosis (MS), type-1 diabetes (T1D) and amyotrophic lateral sclerosis (ALS), today announced positive results from the ANGEL-MS study of its lead product, temelimab in MS. Temelimab is a humanized, monoclonal antibody designed to neutralize pHERV-W, a pathogenic protein thought to be a causal factor in the development of multiple sclerosis.

The ANGEL-MS data confirmed that treatment with temelimab for 2 years had a continued, positive impact on key MRI measures of disease progression in multiple sclerosis patients, confirming and extending the data reported at Week 48 in the CHANGE-MS Phase 2b study. This includes reductions in brain atrophy, particularly in the cortex and thalamus, and maintenance in myelin integrity, as measured by magnetization transfer ratio (MTR) imaging. Importantly, for the first time, encouraging dose-dependent effects were seen on clinical measures of disease progression. This has been evidenced by a lower proportion of patients with 12-week confirmed EDSS progression, or with 20% worsening in 25-foot timed walk.

Jesús Martin-Garcia, CEO of GeNeuro, said: "We are extremely pleased with this data, which clearly confirm the robust and consistent effects of temelimab on key MRI markers of neuroprotection, and we are excited by the early signs of clinical benefit. The results of ANGEL-MS confirm the potential of temelimab to act against disease progression, the largest unmet medical need in this indication. It further reinforces our determination to continue the development of temelimab in MS."

"These results are remarkable, and they are coherent with temelimab's novel mode of action seeking to stop the activation of the brain's innate immunity and restoring the myelin repair system", noted Prof Hans-Peter Hartung, chairman of the Department of Neurology of the University Hospital Düsseldorf and Lead Investigator of the study. "It offers promise to treat progressive patients with low inflammatory activity, and could have potential synergies with existing anti-inflammatory drugs in relapsing MS patients."

ANGEL-MS (*Assessing the HERV-W Env ANtagonist GNbAC1 (temelimab) for Evaluation in an open label Long-term Safety Study in patients with Multiple Sclerosis*) was a 2-year safety and efficacy extension study to CHANGE-MS, which offered continued treatment to those patients who had completed the 12-month primary study. Ninety-four percent of eligible patients (n=219) entered ANGEL-MS and continued treatment at the same dose of temelimab they were receiving at the end of CHANGE-MS. ANGEL-MS was fully funded by Servier. Although the study had an early termination due to Servier's decision to end the partnership with GeNeuro, all patients were offered end-of-study visits. Across the two studies, a total of 154 patients received temelimab treatment for 96 weeks or more. For patients not having completed 96 weeks, the end-of-study visit results were used in the analysis (last observation carried forward).

To ensure consistency, analyses of efficacy endpoints in ANGEL-MS were based on comparing the original groups in the CHANGE-MS study: temelimab (18mg/kg, 12mg/kg, 6mg/kg) and Control Group (i.e. patients originally randomized to placebo for 6 months in CHANGE-MS and re-randomized into the three active treatment arms for the last 6 months of CHANGE-MS).

ANGEL-MS confirmed that the 18mg/kg dose of temelimab continued to have remarkably consistent benefits over all other groups on key MRI measures linked to MS disease progression, confirming and extending the results of CHANGE-MS at Week 48.

Paraclinical MRI Measures	**Comparison 18 mg/kg temelimab versus Control Group**
Reduction of brain atrophy	
Cortex	42% relative reduction, dose effect[1] p=0.058
Thalamus	43% relative reduction, dose effect[1] p=0.038
Maintaining myelin integrity	
MTR signal across cerebral cortical bands	Consistent improvement of 1.5-2 MTR % units, dose effect[1] p<0.03 in all bands
MTR signal across normal appearing white matter bands	Consistent improvement of 1.5-2.3 MTR % units, dose effect[1] p<0.02 in all bands

The 18mg/kg treatment arm also showed lower probability for 12-week confirmed disability progression (Survival Wilcoxon test p=0.34).

12-week confirmed EDSS progression	**18 mg/kg**	**12 mg/kg**	**6 mg/kg**	**Control**
Percentage of patients with 12-week confirmed worsening in neurological disability from Baseline CHANGE-MS to Week 48 ANGEL-MS	3.8	4.8	8.3	9.1

The measure of 25 foot timed-walk also showed remarkable stability for the 18mg/kg cohort, with only 2.4% of patients worsening ≥20% over two years (dose effect[2] p=0.03).

Timed 25-foot walk	**18 mg/kg**	**12 mg/kg**	**6 mg/kg**	**Control**
Percentage of patients with worsening ≥ 20% in the Timed 25-Foot Walk Test compared to CHANGE-MS Baseline	2.4	23.1	13.3	10.2

While these clinical measures are very encouraging, the limited size and relapsing nature of the cohort for clinical progression measures does not allow to derive any definitive conclusion.

Sensitivity analyses were performed, repeating all efficacy analyses by dose groups (irrespective of the length of treatment) and by total exposure to temelimab (independently of body weight) across the combined CHANGE-MS and ANGEL-MS studies. These sensitivity analyses all provided the same conclusions, demonstrating the robustness of the results seen on MRI measures linked to disease progression, as well as the encouraging dose-dependent clinical effects.

1 Dose-effect analyzed by linear regression on all groups, SAS analysis proc GLM
2 Fisher exact test; fifteen patients with extreme walking handicap removed from analysis

GeNeuro will hold a conference call and webcast on Tuesday, March 12 at 2:30pm CET / 9:30am EDT, to discuss results, followed by a Q&A session.

The call is accessible via the below teleconferencing numbers, followed by the Conference ID#: **43761937#**

- France: +33 172727403
- Switzerland: +41445831805
- UK: +44 2071943759
- USA: +1 6467224916

The webcast can be followed live online via the link: https://www.anywhereconference.com?Conference=418838056&PIN=43761937&UserAudioMode=DATA

Following the live call, a replay will be available on the GeNeuro website: www.geneuro.com

About Temelimab

The development of temelimab (GNbAC1) is the result of more than 25 years of research into human endogenous retroviruses (HERVs), including 15 years within Institut Mérieux and INSERM before GeNeuro was founded in 2006. HERVs are present in the human genome and some have been associated with various auto-immune diseases. The viral envelope protein encoded by a HERV in the HERV-W family (pHERV-W Env) has been found in the brains MS patients, and particularly in active lesions, as well as in the pancreas of patients with in type-1 diabetes on pathological examination. By neutralising pHERV-W Env, temelimab could simultaneously block a pathological, neurodegenerative process and help to restore myelin integrity in MS patients, as well as to maintain insulin production in T1D patients. Given that the pHERV-W Env protein has no known physiological function, temelimab was expected to have a good safety profile, with no effect on the patient's immune system and importantly this has been borne out by all clinical trials carried out to date.

About GeNeuro

GeNeuro's mission is to develop safe and effective treatments against neurological disorders and autoimmune diseases, such as multiple sclerosis, 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 26 employees and rights to 17 patent families protecting its technology.

For more information, visit: www.geneuro.com

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