

Press release

GeNeuro presents data supporting pathogenic role of an endogenous retroviral protein (HERV-W ENV) in post-COVID neuropsychiatric syndrome

Enters collaboration with the FondaMental Foundation to speed development of diagnostic and therapeutic options for patients

- Data provides a biologic rationale to the long-term neuropsychiatric symptoms affecting an important subset of post-COVID-19 patients
- Fondation FondaMental and GeNeuro aim to develop one of the first treatment options for these patients

Paris, France and Geneva, Switzerland, July 5, 2021 – 7:30am CEST – GeNeuro (Euronext Paris: CH0308403085 - GNRO), a biopharmaceutical company developing new treatments for neurodegenerative and autoimmune diseases, such as multiple sclerosis (MS), presented new data showing that the **neuropsychiatric symptomatology seen in “post-COVID” patients may be due to activation of HERV-W ENV expression in these individuals by SARS-CoV-2, and to its persistence long after the acute COVID phase.** These data, presented at the first “**Neuro Sciences Psychiatry and Neurology Days**” held in Paris, France, on July 1-2, provide a biologic rationale explaining why so many COVID-19 patients develop long-term neurological and psychiatric symptoms. This could open the door for a therapeutic intervention with temelimab targeting HERV-W ENV.

According to recent large-scale studies, **more than 10% of people infected by SARS-CoV-2 fail to fully recover and/or develop new symptoms, with a high proportion of neurological and/or psychiatric affections.** Of note, in more than 90%¹ of the cases the original COVID-19 symptoms were not severe enough to warrant hospitalization. With more than 176 million confirmed COVID-19 cases worldwide², of which more than 80 million in the USA and Europe, this problem is now being recognized as a **major public health emergency**, as it could affect millions of persons.

“We are confronted with a wave of depressive and cognitive disorders occurring sometimes several months after a COVID-19 infection, regardless of the severity of their acute phase,” said Prof. Marion Leboyer, Head of Psychiatry at Henry Mondor University Hospitals (Paris Est Creteil University) and Director of the FondaMental Foundation. “[Previous publications](#) have established a link between the occurrence of psychotic disorders in patients carrying markers of inflammation and the envelope protein of the endogenous human retrovirus (HERV-W ENV). Finally, preliminary data have shown a significant increase in the levels of this HERV-W ENV protein in post-COVID patients presenting neuropsychiatric symptoms. This finding, which we will test on a large cohort of patient samples, could be a key element in understanding the problem and opening up treatment options.”

Recent publications have shown that expression of HERV-W ENV [was triggered by SARS-CoV-2 in vitro](#) in white blood cells of approximately 20% of healthy donors, suggesting individual susceptibility. This protein was also detected in the blood of hospitalized COVID-19 patients where the amount of expression in lymphocytes was [associated with the severity of disease progression](#).

¹ Source: United Kingdom Office for National Statistics

² Source: European Centre for Disease Prevention and Control. Only accounting for reported cases, not extrapolating for undiagnosed/unreported cases.

The data presented by Dr. Hervé Perron, CSO of GeNeuro, at the conference reveal that upon infection with **COVID-19, HERV-W ENV expression can also be triggered in the brain, specifically in microglial cells that are also innate immune cells residing in the brain.** The expression of HERV-W ENV in this organ had previously only been observed in the context of chronic neurological diseases, such as multiple sclerosis or certain inflammatory forms of schizophrenia, where it fuels local inflammation and neurodegenerative mechanisms. In the aftermath of COVID-19, the analysis of preliminary data from patients with post-COVID depressive and/or cognitive disorders now also shows the persistence of HERV-W ENV in the blood.

Under the umbrella of and with funding from the FondaMental Foundation, Prof Leboyer has federated leading European university neuropsychiatric hospitals in France, Belgium and Italy to assemble **a cohort of over 300 samples from post-COVID patients with neuropsychiatric disorders, which** will be analyzed this summer for HERV-W ENV and inflammatory biomarkers at the INSERM “We-Met” laboratory of the University of Toulouse. *“Our objective is to quantify more precisely the link between these biomarkers and the depressive and cognitive disorders suffered by post-COVID patients, in order to pave the way for what would be one of the first diagnostic and therapeutic approaches in this indication,”* said Prof. Leboyer.

GeNeuro’s most advanced drug candidate, temelimab, has been developed to neutralize HERV-W ENV and may offer a first therapeutic option for patients affected by post-COVID neuropsychiatric syndromes. Temelimab has shown very promising results in Phase II trials against MRI markers of neurodegeneration in MS, with excellent safety and tolerability in more than 200 patients treated for 2 years or more.

“Post-COVID is emerging as a key global health issue following COVID-19 infection,” stated Jesús Martin-Garcia, CEO of GeNeuro. “We thank Prof. Leboyer and her academic partners for their fast, generous and thorough reaction to the post-COVID crisis and if, as we expect, the analysis of these large-cohorts confirms the result of the pilot studies, we are committed to conduct a clinical trial with these partners to offer patients a therapeutic option against these highly disabling conditions.”

About HERV-W ENV and COVID-19

SARS-CoV-2 has been shown to trigger the expression of HERV-W ENV in the blood of about 20% of healthy donors, suggesting a genetic and/or epigenetic susceptibility to the production of this pathogenic protein when exposed to the virus.

HERV-W ENV expression was detected in the lymphocytes of hospitalized COVID-19 patients, versus none in healthy subjects, and the level of HERV-W ENV was correlated with the severity of the evolution of the disease.

Post-mortem studies of COVID-19 patients have now shown that the expression of HERV-W ENV can be triggered in the brain, in particular on microglial cells as well as in endothelial cells of brain blood vessels. Previously, an expression of HERV-W ENV in the brain had only been observed in patients who have died from diseases such as multiple sclerosis, consistent with a role in fueling long-term neurodegeneration. HERV-W ENV is not found in the brain of other neurological controls, such as patients suffering from Alzheimer or Parkinson diseases.

Analyses of samples from the first pilot cohorts of patients with post-COVID depressive and cognitive symptoms have shown that the HERV-W ENV protein is still present at consistently detectable, and sometimes high, levels in the blood. This may allow early identification and treatment of patients who could benefit from an anti-HERV-W ENV therapy such as temelimab.

The new data presented at the “Neuro Sciences Psychiatry and Neurology Days” were generated in partnership with the CIRI (International Center for Infectiology Research), in Lyon, France, a leading research institute against infectious diseases. The CIRI and GeNeuro announced on June 24 that they had agreed to extend their collaboration agreement on the link between HERVs and COVID, with an expanded focus on post-COVID.

References:

- E. Balestrieri et al, *“Evidence of the pathogenic HERV-W envelope expression in T lymphocytes in association with the respiratory outcome of COVID-19 patients”*, The Lancet EBioMedicine, April 2021 [https://www.thelancet.com/journals/ebiom/article/PIIS2352-3964\(21\)00134-1/fulltext](https://www.thelancet.com/journals/ebiom/article/PIIS2352-3964(21)00134-1/fulltext)

- B. Charvet et al, “SARS-CoV-2 induces transcription of human endogenous retrovirus RNA followed by type W envelope protein expression in human lymphoid cells”, Research Square, April 2021
<https://www.researchsquare.com/article/rs-301236/v1>
- M. Garcia-Montojo et al, “HERV-W envelope expression in blood leukocytes as a marker of disease severity of COVID-19”, The Lancet EBioMedicine, May 2021
[https://www.thelancet.com/journals/ebiom/article/PIIS2352-3964\(21\)00156-0/fulltext](https://www.thelancet.com/journals/ebiom/article/PIIS2352-3964(21)00156-0/fulltext)

About HERV-W ENV and Psychotic Disorders

The association between the occurrence of psychotic disorders in patients carrying markers of inflammation and the endogenous human retrovirus envelope protein (HERV-W ENV) has been previously documented, and a link has been established between the presence of HERV-W ENV and altered neural pathway development. The effect of HERV-W ENV leads to a disruption of synaptic glutamatergic communication and results in the development of psychotic symptoms *in vivo*. These results have recently been confirmed by the same teams.

- E.M. Johansson et al, “Human endogenous retroviral protein triggers deficit in glutamate synapse maturation and behaviors associated with psychosis”, Science Advances, July 2020
<https://advances.sciencemag.org/content/6/29/eabc0708>

About Fondation FondaMental

The FondaMental Foundation is a research foundation dedicated to the fight against mental illness. It combines care and cutting-edge research to promote personalized, multidisciplinary patient care and to support research and innovation in the improvement of diagnostic and therapeutic strategies for mental illness. It can receive donations and legacies.

www.fondation-fondamental.org

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 rights to 17 patent families protecting its technology. For more information, visit: www.geneuro.com

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