A Swiss joint stock company (*société anonyme)* with share capital of 1,029,515.95 Swiss francs
Registered and principal office: 3 chemin du Pré-Fleuri – 1228 Plan-les-Ouates – Geneva – Switzerland
CHE-112.754.833 *Registre du commerce* (commercial register) of Geneva

2020
UNIVERSAL REGISTRATION DOCUMENT
including the Annual Financial Report

This Universal Registration Document was filed on April 30, 2021 with the Autorité des marchés financiers ("AMF") as competent authority under Regulation (EU) 2017/1129, without prior approval in accordance with Article 9 of the said Regulation.

This Universal Registration Document may be used for the purpose of a public offer of securities or the admission of securities to trading on a regulated market if it supplemented by a securities note and, as the case may be, by a summary and all the amendments to the Universal Registration Document. These documents are being together approved by the AMF in accordance with Regulation (EU) 2017/1129.

Copies of this Universal Registration Document are available at no cost at the headquarters of GeNeuro SA (3 chemin du Pré-Fleuri - 1228 Plan-les-Ouates / Geneva – Switzerland), as well as electronically on the GeNeuro website (www.geneuro.com) or on the AMF website (www.amf-france.org).

GENERAL OBSERVATIONS

Unless otherwise indicated, in this universal registration document (the "**Universal Registration Document**") the terms "**Company**" or "**GeNeuro**" mean GeNeuro SA and the term "**Group**" means the Company and its subsidiaries GeNeuro Innovation SAS ("**GeNeuro Innovation**"), in France, and GeNeuro Australia Pty Ltd ("**GeNeuro Australia**"), in Australia.

This Universal Registration Document was prepared pursuant to Annex 1 and Annex 2 of the delegated regulation (EU) 2019/980 of the Commission of 14 March 2019 which complements Regulation (EU) 2017/2019 of the European Parliament and Counsel and, pursuant to article 19 of the Regulation (EU) 2017/1129, incorporates by reference the Company's consolidated financial statements for the year ended December 31, 2019, prepared in accordance with IFRS, and the auditors' report related thereto presented in section 20.3 of the Registration Document ("*Document de reference*") filed with the AMF on April 30.

This Universal Registration Document contains statements about the Group's objectives. These statements are sometimes identified by the use of the future tense, the conditional tense, and expressions with forward-looking character, such as "think," "has as an objective," "expects," "intends," "should," "with the ambition of," "consider," "believe," "wish," "could," etc. This information is based on data, assumptions, and estimates considered reasonable by the Company. They may change or be changed because of uncertainties related to any business as well as to the economic, financial, competitive and regulatory environment.

Furthermore, the achievement of the Group's objectives assumes the success of its strategy, which is set forth in Section 5.1.2 of the Universal Registration Document. The Company can make no commitment or give any assurance that the objectives set forth in this Universal Registration Document will be achieved.

Investors are urged to give consideration to the risk factors set forth in Chapter 3 "Risk Factors" of this Universal Registration Document before making their investment decision. The occurrence of such risks could have a negative effect on the Group's business, financial condition, results of operations, or prospects. Furthermore, other risks, not presently identified or not considered material by the Company, could have the same negative effect, and investors could lose all or part of their investment.

This Universal Registration Document also contains information about the markets in which the Group competes, some of which information was obtained from sources external to the Company. Unless otherwise indicated, the information relating to the markets in which the Company competes or its competitive position contained in this Universal Registration Document comes from the Company's internal estimates. These internal estimates are based on reports of analysts, specialized studies, industry publications, any and all information published by market survey companies, and public and governmental sources, as well as internal knowledge of the market by the Company. Even though such information is considered reliable, it has not been independently verified by the Company. Furthermore, in light of the very rapid changes occurring in France, in the world, and in the industry in which the Group competes, it is possible that such information may prove erroneous or not be up-to-date. The Group's business, accordingly, could evolve in a different way from the one described in this Universal Registration Document. The Company has not committed or agreed to publish any update of the information contained herein, except in connection with any legal or regulatory obligation that may apply to it.

A glossary that contains definitions of certain technical terms used in this Universal Registration Document, as well as an index of abbreviations used, are set forth in Appendix of this Universal Registration Document.

A reconciliation table with the Annual Financial Report is located at the end of this Universal Registration Document.

This Universal Registration Document has been prepared on the basis of the Company's annual financial statements for the financial years ending December 31, 2019 and 2020.

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CHAPTER 1. PERSONS RESPONSIBLE FOR THIS UNIVERSAL REGISTRATION DOCUMENT

1.1 Person Responsible For The Universal Registration Document

Mr. Jesús Martin-Garcia, Chairman of the Board of Directors and Chief Executive Officer of GeNeuro.

1.2 Certificate Of The Person Responsible For The Universal Registration Document

"I certify that, to the best of my knowledge, the information contained in this Universal Registration Document is in accordance to the facts and that the Universal Registration Document makes no omission likely to affect its import.

I certify that, to my knowledge, the financial statements of GeNeuro have been prepared in accordance with applicable accounting standards and give a fair view of the assets, liabilities, financial position and results of the Company and all the subsidiaries included in the scope of consolidation, and that the management report of the board of directors, as referenced in the cross reference list included on page 242 gives a true and fair view of the business trends, results and financial position of the Company and all the subsidiaries included in the scope of consolidation and describes the main risks and uncertainties with which they have to contend".

Mr. Jesús Martin-Garcia, Chairman of the Board of Directors and Chief Executive Officer of GeNeuro.

1.3 Information From Third Parties, Experts' Statements or Reports

Certain market information set forth in Chapter 6, "Description of the Group's Business" of this Universal Registration Document, come from third-party sources. The Company certifies that such information has been faithfully reproduced and that, to the Company's knowledge, on the basis of data published or provided by such sources, no fact has been omitted that would make the information reproduced inaccurate or misleading.

1.4 Declaration relating to the registration document

Not applicable.

1.5 Person Responsible For The Financial Information

Mr. Miguel Payró
Group Chief Financial Officer
3 chemin du Pré-Fleuri, CH-1228 Plan-les-Ouates, Switzerland
Telephone: +41 22 552 4800
info@geneuro.com
www.geneuro.com

1.6 Indicative Timetable for Financial Communication

April 6, 2021	2020 annual results
April 9, 2021	Q1 2021 cash position
May 27, 2021	Annual general meeting of shareholders
July 23, 2021	Q2 2021 cash position
September 29, 2021	1H 2021 results
October 22, 2021	Q3 2021 cash position

* This timetable is indicative and the Company reserves the right to amend the above-mentioned dates should it deem it necessary to do so.

CHAPTER 2.
STATUTORY AUDITORS OF THE FINANCIAL STATEMENTS

2.1 Principal Statutory Auditor

The Company's statutory auditor is:

PricewaterhouseCoopers SA
Avenue Giuseppe-Motta 50
CH-1202 Geneva

The auditor in charge is Mr. Michael Foley.

PricewaterhouseCoopers SA, Geneva branch, is registered at the *Registre du commerce et des sociétés* (Registry of Commerce and Companies) of Geneva under number CHE-390.062.005.

PricewaterhouseCoopers SA is a member of EXPERTsuisse – Swiss Expert Association for Audit, Tax and Fiduciary.

The auditors were appointed at the General Shareholders' Meeting held on May 27, 2020, for a term of one (1) financial year; their engagement is to end at the close of the General Shareholders' Meeting to be held to approve the financial statements for the financial year ended December 31, 2020.

2.2 Subsidiary Statutory Auditor

None. GeNeuro is a Swiss company, and the concept of a subsidiary statutory auditor does not exist in Switzerland.

CHAPTER 3.
RISK FACTORS

The Company operates in a changing environment that involves risks, some of which are out of its control. Investors are advised to take into consideration all the information contained in this Universal Registration Document, including the risk factors set forth in this chapter. Pursuant to Article 16 of Regulation (EU) 2017/1129 and of Delegated Regulation (EU) 209/980, this chapter only presents the risks that the Company believes, as of the date of approval of this Universal Registration Document, in the event they should occur, might have a material adverse effect on the Group's business and operations, its results of operations, its financial position, earnings, prospects or ability to hit its targets.

In order to identify and assess such risks, the Company has mapped the risks associated to its activity and has grouped them into five categories below, it being stipulated that within each category and sub-category, risk factors are presented by order of decreasing importance with an evaluation of their probability (high, medium, low), negative impact (high, medium, low), and the net level of criticality, estimated by combining for each risk its probability of occurrence and its negative impact, as assessed by the Company as at the date on which the Registration Document was filed, together with taking into account the potential actions and preventive measures undertaken by the Company at that date. The occurrence of new events, both internal and external to the Company, may however alter this order of importance in the future.

Impact of COVID-19 Pandemic

In addition to these risks and in the context of the COVID-19 outbreak, which was declared a "pandemic" by the World Health Organization (WHO) on March 12, 2020, the Company has undertaken a full review of the impact of the outbreak on its business and has strictly followed the recommendations issued by the World Health Organization and by local governments in terms of health & hygiene and organizational standards, in order to ensure the health and safety of its staff and their families.

The Company's 40-patient Phase II Karolinska Trial in MS with temelimab, its main product, saw its launch postponed by three months to prioritize healthcare resources behind the fight of COVID-19 and to reduce the risk for MS patients. On June 25, 2020, the Company announced the initiation of the trial following the inclusion of the first patient in the trial and announced the completion of recruitment on February 18, 2021, compared to an earlier publicly stated target date of end 2020. On this basis, the Company now expects that results will be communicated in Q1 2022. Whilst the impact of COVID-19 has no bearing on the Company's financial situation over the next 12 months, should the pandemic continue and prevent the smooth completion of the Karolinska Trial, this could have a material adverse effect on the Company's business, results of operations, financial condition and cash flows.

On April 15, 2021, GeNeuro announced the publication of data by the University of Rome "Tor Vergata" in the Lancet's EBioMedicine showing that HERV-W ENV is found on lymphocytes of hospitalized patients with COVID-19, and that its level of expression is associated with disease severity. The Company also announced the publication of data from research led by it and by the International Center for Infectiology Research (CIRI) in Lyon, France, showing that when human peripheral blood mononuclear cells from healthy donors were cultured and exposed to SARS-CoV-2, about 20% of donors responded by expressing HERV-W ENV in lymphocytes, cells in which the virus did not replicate. This expression was triggered specifically by the spike protein of SARS-CoV-2, independently from cytokine release. This research suggests a genetic and/or epigenetic susceptibility associated to the activation of HERV-W ENV in blood lymphoid cells, which could be important in understanding how SARS-CoV-2 infection may lead to severe forms of COVID-19 in some patients.

Until these studies, the highly pro-inflammatory HERV-W, usually found in specific disease situations, mostly in the brain, had never before been observed circulating in the body at high levels and, in particular, was never seen expressed in T-lymphocytes. Understanding the mechanisms leading from SARS-CoV-2 infection to severe disease is critical for the development of effective treatments. The identification of the association between HERV-W ENV expression and inflammatory and immune dysfunction in COVID-19 opens an avenue for further investigation of its role as a trigger of detrimental immune response and potential target for therapy.

Considering the rapidly evolving situation, the Company will update its assessment on a regular basis.

Section	Risks Factors	Proba-bility	Negative impact	Net level of criticality
3.1	**Risks Related To The Development and Potential Future Commercialization of the Group's Product Candidates**			
3.1.1	GeNeuro has developed a new approach, the therapeutic benefit of which has not yet been demonstrated, that is not based on confirmed pathways such as the immunomodulation and immunosuppression approaches used by existing therapies for the treatment of autoimmune diseases.	*High*	*High*	*High*
3.1.2	The Company's products, including its most advanced product candidate, temelimab, may never be approved for marketing due to the need to obtain satisfactory results in clinical trials (including its Phase II Karolinska/ASC clinical trial in MS, now with top line results expected in Q1 2022) and obtain marketing authorization from regulatory authorities.	*High*	*High*	*High*
3.1.3	The Company's product candidates may never be approved for marketing due to operational reasons.	*High*	*High*	*High*
3.1.4	The Company may not be competitive in its market.	*High*	*High*	*High*
3.1.5	The Company has limited visibility on its future prospects and financial results.	*Medium*	*High*	*High*
3.1.6	The uncertainty about reimbursement rates and measures to reform healthcare systems could delay or compromise acceptance of products by the market.	*Medium*	*High*	*Medium*
3.1.7	Other clinical applications of temelimab for conditions such as T1D are based solely on pre-clinical work or on limited clinical data, and the Company may never succeed in developing and marketing effective treatments based on such technology.	*High*	*Medium*	*Medium*
3.2	**Risks Related To The Company's Financial Situation and Capital Needs**			
3.2.1	The €17.5 million gross proceeds of the capital increase completed in January 2020 are expected to provide the Company with the means to continue its development until Q2 2022 but the Company may not succeed in obtaining additional funds needed to continue its clinical development in the future.	*High*	*High*	*High*
3.2.2	The Company should continue to sustain operating losses (following losses of € €9.5 million and €7.5 million, respectively, in 2019 and 2020) in relation to its research and development activities.	*High*	*High*	*High*
3.2.3	The Group benefits from Research Tax Credits from the French government which regime may be challenged or modified in the future.	*Medium*	*Low*	*Low*
3.2.4	The Company could be unable to carry tax losses forward.	*Medium*	*Low*	*Low*
3.2.5	Full exercise of all securities carrying the right to acquire shares granted and outstanding would result in a dilution of existing shareholders.	*Medium*	*Low*	*Low*
3.2.6	Exchange Rate Risk.	*Medium*	*Low*	*Low*
3.3	**Risks Related To The Company, Its Operations and Organization**			
3.3.1	The Company is dependent on its key employees and, as such, could fail to continue attracting and retaining its key employees and scientific advisors.	*Medium*	*High*	*Medium*
3.3.2	The Company faces the risk of liability linked to its products or operations and it may not be able to obtain adequate insurance coverage at an acceptable cost.	*Medium*	*High*	*Medium*
3.3.3	Shareholders might be unable to achieve a control premium in the event of a change of control of the Company based on the fact that French and Swiss regulations concerning mandatory public takeover offers are not applicable.	*Low*	*Low*	*Low*
3.4	**Risks Related To The Company's Dependency on Third Parties**			
3.4.1	The Company does not have manufacturing capabilities and is exposed to the risks associated with relying on third party manufacturers for its most advanced product candidate temelimab and its other products.	*Medium*	*High*	*Medium*
3.4.2	The Company does not have experience in the areas of sales, marketing and distribution and may be required to rely on third parties and/or mobilize new internal resources for this purpose.	*High*	*Medium*	*Medium*
3.4.3	The Company relies on external scientific collaborators.	*Medium*	*Medium*	*Medium*
3.5	**Risks Relating To The Company's Intellectual Property Rights**			
3.5.1	If the Company is unable to maintain or protect its intellectual property rights, it could lose its competitive advantage and be unable to operate profitably.	*Medium*	*High*	*Medium*

3.5.2	The Company's products and technologies could infringe or be claimed to infringe patents and patent applications held or controlled by third parties.	*Medium*	*High*	*Medium*
3.5.3	If the Company does not comply with its obligations under the license agreement with bioMérieux, it could lose rights that are very important for its business.	*Medium*	*High*	*Medium*
3.5.4	The Company's business could be affected if it is unable to protect the confidentiality of its information and know-how.	*Medium*	*High*	*Medium*

3.1 Risks Related To The Development and Potential Future Commercialization of The Group's Product Candidates

3.1.1 GeNeuro has developed a new approach, the therapeutic benefit of which has not yet been demonstrated, that is not based on confirmed pathways such as the immunomodulation and immunosuppression approaches used by existing therapies for the treatment of autoimmune diseases.

The Company has developed a new approach to the treatment of multiple sclerosis ("**MS**"), which differentiates itself from therapies being sold on the date hereof.

The Company is exploring a new medical path that involves HERV genes that constitute approximately 8% of the human genome. The capacity for the abnormal expression of various elements of a HERV of the W family ("**HERV-W**") has been detected in chronic diseases like MS. The Company seeks to develop, on the basis of this finding, a treatment designed to block the deleterious properties of a protein, HERV-W ENV, which is encoded by genes of the HERV-W family. Recent publications have demonstrated that HERV-W ENV may directly inhibit remyelination and that axonal injury in MS can be significantly driven by HERV-W ENV through activation of microglia and that this contributes to neurodegeneration, particularly in progressive forms of MS. Publications from April 2021 show that HERV-W ENV can be expressed by SARS-CoV-2 and that it is present in the blood of COVID-19 patients, with a correlation between the level of its expression and the severity of the evolution of the disease.

As of the filing date of this Universal Registration Document, there is no treatment that targets endogenous retroviral genes approved for sale by the competent authorities, and such a treatment intended to block a protein expressed by a HERV is, therefore, unproven.

The Company's Phase IIb clinical trials in the MS indication have shown that temelimab has only modest effects on neuroinflammation in the "active inflammatory patients" population as a monotherapy, but also that temelimab has positive impacts on key MRI biomarkers associated with disease progression; as a result, GeNeuro is now focusing on neurodegeneration and disease progression, with temelimab either as a monotherapy for "non-active" progressive patients, and/or as an adjunctive therapy for remitting patients in combination with existing immunomodulatory drugs addressing neuroinflammation.

Accordingly, the prospects for the development and profitability of the Company's most advanced product candidate, temelimab, for MS or other indications, its safety, its effectiveness, and its acceptance by patients, prescribers, and paying agencies, are uncertain. The positive results observed for temelimab for MS in connection with Phase I, on the one hand, and Phases IIa and IIb, on the other hand, and more generally, those relating to existing or future products in the Company's portfolio or based on its technology at the time of the research or preclinical phase, may not be confirmed by future trial phases. Such a situation could have a very material adverse impact on the Company's business, results, financial situation, and prospects.

3.1.2 The Company's products, including its most advanced product candidate, temelimab, may never be approved for marketing due to regulatory reasons.

The Company is subject to regulations that are numerous and evolving and it may not be able to obtain the necessary approvals to market and sell its products, including its product candidate at the most advanced stage of development, temelimab. To obtain a product license for its candidate products, the Company must show, through long, numerous and very expensive clinical trials with uncertain outcomes, that the use of the candidate products is without danger and is effective in humans. Clinical trials are subject to supervision by regulatory authorities as well as by ethics committees, in order to protect the persons participating in the medical research. If the Company does not meet its development calendar (please see Section 5 of this Universal Registration Document), or if it is unable to conduct the expected clinical trials successfully within applicable time limits, its business and operations could be materially and adversely affected.

The Company's ability to obtain product licenses for its products will depend on several factors, including, but not limited to:

- the possibility of pursuing the development of those of its products presently in early clinical trials, or presently in pre-clinical development to a clinical stage;
- its ability, or that of its partners, to conduct clinical trials successfully and within relevant time periods without having to devote significantly greater resources than initially expected;
- its clinical trials showing the efficacy and safety of its products;
- its products being approved for the indication they are intended to treat, or for any indication of any kind; and
- an announcement by its competitors of more promising clinical results with their own products, which makes the Company's economic equation unfavorable.

Traditionally in the biotechnology and pharmaceutical industries, it often happens that favorable results of pre-clinical trials and Phase I/II clinical trials are not confirmed by later stage clinical trials. Regulatory authorities in various countries in which the Company intends to market its products could block initiation of clinical trials, or the pursuit of clinical developments, if the proposed clinical trials do not meet applicable regulatory standards. Such authorities could likewise interpret results differently from the Company and, in any event, request additional tests, on a discretionary basis (relating, among other things, to the study protocols, the characteristics and number of patients, the length of treatment, the analytical methods, the preclinical safety, and post-treatment follow-up), or impose additional or unexpected requirements at the time of such trials. Furthermore, the Company might decide, or might be required by regulatory agencies, to suspend or terminate clinical trials, if new evidence suggests that patients are exposed to unexpected risks. Deaths or other adverse events could occur during a clinical trial, because of medical problems both linked and not linked to the treatments administered, forcing the Company to delay or interrupt the trial. Also, on the basis of the trial's results, the Company could decide to abandon development projects that were initially identified as promising. Finally, products already approved could turn out to be unsafe and then be withdrawn from the market, or they could produce different effects from those initially expected, which could, in turn, limit or prevent them having any commercial use. The occurrence of all or some of these events could have material adverse effects on the Company's business, results, and prospects.

As of the date hereof, none of the Company's products, including its most advanced product candidate, temelimab for MS, has received a marketing authorization from any regulatory authority. The Company cannot be sure that it will receive the necessary approvals to market and sell any of its products. The products may be subject to very stringent laws, and regulatory requirements that are uncertain and subject to change and amendment (for a summary presentation of such laws and regulations in the United States and Europe, please see CHAPTER 9 "Regulatory Environment") of this Universal Registration Document). The FDA and the European Medicines Agency (the "**EMA**") as well as their counterparts in other countries regulate, among other things, research and development, pre-clinical tests, clinical trials, manufacturing, safety, efficacy, records retention, labeling, and the marketing, sale, and distribution of therapeutic products. In particular, without the FDA's approval, it would be impossible for the Company to access the U.S. market, which is the largest pharmaceutical market in the world, particularly for the therapeutic areas targeted by the Company (MS, COVID-19, Amyotrophic Lateral Sclerosis ("**ALS**"), Type1 Diabetes ("**T1D**"), etc.).

These regulatory steps are costly; they may take several years; and their results are unpredictable. The data from pre-clinical and clinical developments may give rise to different interpretations, which could delay obtaining or restrict the scope of regulatory approval. The requirements of the regulatory process vary greatly from one country to another, so that the Company or its strategic partners may not be able to obtain approval on a timely basis in each relevant country. Since the Company's products are based on new, constantly changing technologies and have not been tested on an in-depth basis in humans, the applicable regulatory requirements remain uncertain and could be subject to significant differences of interpretation and changes. Changes in laws and regulations during the development of a product and its regulatory review could cause delays in or the denial of approval.

In the United States, in Europe, and in other countries, applicable laws and regulations and changes to them could:

- delay and/or significantly increase the cost of developing, testing, manufacturing, and marketing the Company's products;
- limit the indications for which it might be authorized to market and sell its products;
- impose new, stricter requirements, suspend approval of the Company's products, or require the Company to stop the clinical trials it is conducting or stop the marketing and sales of the products (for example, if unexpected results are obtained during clinical trials by other researchers of products similar to those of the Company); or
- impose restrictive labeling.

If the Company does not comply with the laws and regulations applicable to its business and operations, it could incur sanctions or penalties, which could include refusals to authorize pending applications, product recalls, restrictions on sales, or the temporary or permanent suspension of its operations as well as civil and criminal proceedings.

The Company has already completed for temelimab, its product candidate at the most advanced stage of development, three clinical Phase I trials[1] to define the pharmacological, immunogenic, and safe use on healthy volunteers. The results of these trials have been published in scientific journals and are considered positive regarding temelimab's safety and tolerability.

The Company has also completed three Phase II trials on a patient population having MS and one Phase II trial on a patient population having T1D:

- a Phase IIa clinical trial for MS[2], intended principally to show temelimab's tolerance over a period of one year by the injection of potentially therapeutic doses and, secondarily, to take initial measurements on the clinical evolution of treated patients; and
- a Phase IIb clinical trial (CHANGE-MS) for MS[3] in patients with the remitting relapsing form of MS ("**RRMS**"), with a primary endpoint evaluating the efficacy of repeated doses of temelimab versus placebo in patients based on the cumulative number of Gadolinium-enhancing ("**Gd+"**) T1 lesions on brain MRIs and with secondary endpoints to evaluate measures of MRI markers associated with neuroprotection, notably brain atrophy, hypointense T1 lesions ("black holes") and magnetization transfer ratio ("**MTR**"), considered to be an indirect measure of the integrity of myelin; and
- a Phase II extension study (ANGEL-MS) of the above Phase IIb clinical trial[4], which allowed patients who took part in the Phase IIb study to benefit from two additional years of treatment; following the decision from the Company's former development partner, in September 2018, not to exercise its option for a license on temelimab, this extension study underwent an early termination and topline results were presented on March 12, 2019;
- In addition, the Company has completed a Phase IIa clinical trial for T1D in adult patients, which has met its primary endpoint of safety at six months, and whose full 12-month results were announced in May 2019.

The Company has also launched a new single center, Phase II clinical study of temelimab in MS, at the Karolinska Institutet / Academic Specialist Center (ASC) of Stockholm, Sweden. The trial, to be conducted at the Center for Neurology of ASC (which, with approximately 2,400 patients, is the largest MS center in Sweden), will be a one-year study that has enrolled 40 patients whose disability progresses without relapses, and will document the safety and tolerability of temelimab following higher doses, as well as measures of efficacy based on the latest biomarkers associated with disease progression. The start of this study (the "Karolinska Trial"), initially aimed for Q1 2020, was delayed to the end of June 2020 due to the COVID-19 crisis, as the Company decided to postpone this trial to prioritize healthcare resources behind the fight of COVID-19 and to reduce the risk for MS patients. Initiation of the trial was announced on June 25, 2020, following the inclusion of the first patient in the trial; the Company announced the completion of recruitment on February 18, 2021, compared to an earlier publicly stated target date of end 2020. On this basis, the Company now expects that results will be communicated in Q1 2022. Whilst the impact of COVID-19 has no bearing on the Company's financial situation over the next 12 months, the pandemic could disrupt the trial and have a material adverse effect on the Company's business, results of operations, financial condition and cash flows.

The use of temelimab for MS requires additional clinical development to be completed, including Phase III clinical trials. Accordingly, if the Company does not receive approval of temelimab for the treatment of MS, its financial condition, results of operations, and prospects will be significantly and adversely affected.

3.1.3 The Company's product candidates may never be approved for marketing due to operational reasons.

The Company's clinical trials, especially for its leading product candidate, temelimab, could be delayed or not occur in a satisfactory manner.

The Company's ability to conduct clinical trials successfully depends on many factors, especially on the pace of patient recruitment, the size of the eligible patient population, the type of clinical protocol, the proximity of patients to clinical sites, eligibility criteria, possible secondary effects, and competition with other clinical trials conducted on product candidates developed by competing companies with, among other things, financial resources that may be greater than the Company's.

In general, the Company could encounter difficulties in recruiting and retaining patients to participate in future clinical trials of its products, in particular for its most advanced product candidate for MS and T1D, temelimab. The strict criteria for inclusion in the trials could also make recruitment of patients difficult. Once recruited, the patients participating in such trials could suspend or terminate their participation at any time without cause, or might be unable to continue participating in a trial if medical, or other, emergencies (such, for example as the current COVID-

[1] "Preclinical" and "clinical" phases are defined in the Appendix.
[2] Source: Derfuss T et al Mult Scler. 2015 Jun;21(7):885-93.
[3] Source: Hartung HPH et al ECTRIMS Congress Berlin 2018; Hartung HPH et al Manuscript in preparation 2019
[4] Source: Hartung HPH et al ECTRIMS Congress Stockholm 2019

19 pandemic) lead governments to impose quarantines or enforced isolation or require existing medical human resources or medical amenities to be solely dedicated to the treatment of such emergencies. Delays in patient recruitment could also increase the costs, delay, or even cause the cancellation of clinical trials (including in relation to the potential need to adjust existing protocols and have such adjustments be agreed by the regulators). Finally, if too many patients terminate their participation in a clinical trial, the analysis of the results of such trial could lack sufficient statistical significance.

Furthermore, large-scale clinical trials could lead to complexity in the management and supply of inventories of the product candidate temelimab. Logistical difficulties and errors in storing and shipping products, and/or poor management of inventories and their supply could cause delays in the completion of the trials.

Likewise, clinical trials designed and coordinated by the Company are conducted by medical and hospital centers and companies that specialize in the organization of trials (a contract research organization or "**CRO**") and the quality of their work (the selection of populations, base-line measurements, compliance with protocols, doses, the number of administrations, intermediate delays and the collection of data) is determinant in the analysis and precision of results. In addition, because Phase II and Phase III clinical trials are typically conducted in numerous centers located in multiple countries, the Company cannot rule out heterogeneity and errors in the performance of such centers, which could impact the precision of the results.

Furthermore, the Company has limited experience in conducting clinical trials at multiple centers and has turned or will turn, now and in the future, to third parties to assist it in supervising and monitoring its trials. A breach or failure by one of such third parties or CROs in performing their task or their failure to comply with applicable regulatory standards could cause delays or even the premature termination of the trials.

3.1.4 The Company may not be competitive in its market

The market for MS treatments for which temelimab is intended, as well as the markets for which its other products are intended, are characterized by rapid technological change, the predominance of protected products, and intense competition. Many organizations, including pharmaceutical and biotechnology companies, academic institutions, and other research entities, are actively engaged in the discovery, research, development, and marketing and sale of products intended to treat MS. If the Company were to obtain a marketing license for temelimab, it might compete with other presently prescribed therapies and/or those under development. Whilst there are today in MS no approved drugs that address disease progression (as opposed to reducing the number of inflammatory relapses, which is the area for which the existing immunotherapies such as immunomodulators and immunosuppressors drugs have been approved), it is possible that new drugs under development could prove effective against neurodegeneration and disease progression and thus be direct and strong competitors to temelimab.

A great number of companies developing immunomodulators or immuno-suppressors for MS, when compared with GeNeuro, have much greater resources and experience in management, manufacturing, marketing and sales, and research. In particular, major pharmaceutical companies like Bayer, Biogen, Bristol-Myers Squibb, Johnson & Johnson, Merck KGaA, Novartis, Roche Sanofi and Teva, which market and sell medications for MS, have much greater experience than GeNeuro in conducting clinical trials and obtaining regulatory approvals. All such companies could also compete with the Company to acquire rights to promising antibodies as well as other complementary technologies. The Company can give no assurance that its products:

- will be granted regulatory approval, protected by patents, or marketed sooner than those of its competitors;
- will remain competitive against other products developed by its competitors that are safer, more effective, or less costly;
- will be competitive against products of companies that might be more efficient in their production, marketing and sales;
- will be a commercial success; or
- will not be made obsolete or unprofitable by technological progress or other therapies developed by its competitors.

If the Company succeeds in obtaining regulatory approval to introduce products based on its technology, it will also need time to gain the support of the medical community, including healthcare providers, patients, and third-party payors. The degree of acceptance by the market will depend on many factors, including:

- the safety and efficacy of its therapeutic products, as demonstrated during clinical trials;
- the existence of undesirable side effects;
- ease of administration;
- the success of its marketing, sales, and public relations strategy;
- the availability of alternative treatments;
- pricing;

- the reimbursement policies of governments and other third parties;
- the effective adoption and implementation of a publication strategy; and
- obtaining the support of recognized external opinion leaders.

Even if temelimab for MS is approved for marketing, the market targeted by the Company could turn out to be less significant than previously thought. The revenues that the Company may receive in connection with the marketing and sale of temelimab may be limited by the number of patients with MS, by the categories of patients who respond well to treatment, by the perception of health providers as to the therapeutic benefit, by its ability to achieve appropriate pricing and reimbursement levels, and by the impact of competition.

If the Company does not market and sell temelimab successfully, its revenues could not materialize and / or decrease as a result, and it could find itself unable to finance the development and marketing of other products for other indications.

3.1.5 The Company has limited visibility on its future prospects and financial results.

GeNeuro has a limited operating history, which does not allow it to estimate its prospects and future revenues. The Company's operations have been so far limited to developing a humanized monoclonal antibody technology aimed at a pathogenic protein expressed by a HERV and, on the basis of such technology, to conduct with the assistance of CROs pre-clinical and clinical trials for the purpose of developing, marketing and selling therapeutic solutions.

Notwithstanding the experience and abilities of its management and scientific team, the Company has not yet shown an ability to overcome the high number of risks and uncertainties that are frequently encountered by biopharmaceutical companies in a rapidly evolving, highly uncertain and speculative industry. The Company's ability to evaluate its future results or commercial prospects with precision, similarly, is more limited than if it had a long operating history or products that had already received marketing approval.

As a result, the likelihood of the Company's success must be evaluated in light of the numerous potential challenges and contingencies that are faced, at an early stage, by a company operating in the business of developing medications, most of which are beyond its control. In light of its development schedule and, assuming the receipt of relevant regulatory authorizations and the commercialization and marketing of its product candidate, GeNeuro estimates as of the date of this Registration Document that the potential sale of its most advanced product candidate, temelimab for MS, could commence between 2025 and 2027. This timing is however dependent on the success of the Phase III trial, or possibly of a Phase II/III trial that could be registration enabling subject to its results, the absence of any event or setback delaying the proper conduct of the trials, and the absence of other events which the Company is currently unable to identify or anticipate.

3.1.6 The uncertainty about reimbursement rates and measures to reform healthcare systems could delay or compromise acceptance of products by the market.

The uncertainty about reimbursement rates and measures to reform healthcare systems could delay or compromise acceptance of products by the market.

If the Company succeeds in marketing and selling the products developed in collaboration with partners, or by itself, their acceptance in the market will depend, in part, on the rate at which government health funds and private insurers reimburse them. Primary insurance health funds and other third-party payors often attempt to limit the cost of care by restricting or refusing to cover costly products and therapies. At present there are several immunomodulating products for the treatment of MS, but none specifically targets a causal factor or the progression of the illness, so that there is little or no experience relating to potential payments for such a treatment by insurance providers.

In some foreign markets, the price of prescription pharmaceuticals is subject to control by the government. The Company's ability to market and sell its products successfully will depend, in part, on the establishment by governmental authorities, private insurers, and other agencies in the United States and Europe of a sufficient reimbursement rate for its products and related treatments. In addition, the determination of the price and the reimbursement rate for the Company's products could be influenced by an announcement by competitors of more promising clinical results than those of the Company's products. Such a situation could have an adverse effect on the conditions for setting the price and the reimbursement rate of products that could lose their competitive advantage over other competing products. Third-party payors are questioning the price of therapeutic products and medical services more and more frequently. Cost control measures that healthcare service providers and reimbursement agencies adopt and healthcare system reforms could adversely affect the Company's operating results. Also, as a result of the current COVID-19 current Pandemic, it may be expected that healthcare will be an important public policy subject of focus and that associated increase of healthcare spending will be more carefully monitored. The Company could thus fail to obtain satisfactory reimbursement for its products, which could impede their acceptance by the market, in which case the Company would be unable to earn a sufficient return on its research and development investments.

The Company's relations with clients and third-party payors are subject to U.S. anti-corruption (anti-kickback), anti-fraud, and anti-abuse laws or other laws and regulations relating to healthcare which could expose it to civil penalties and sanctions, damages, and interest, injury to its reputation, and diminution of its profits and future income. Healthcare professionals, doctors, and third-party payors play a key part in the recommendation and prescription of any product for which the Company may obtain a product license. Its future agreements with third-party payors and customers could expose it more broadly to U.S. anti-fraud and anti-abuse laws and regulations, or other laws and regulations relating to healthcare that may restrict business or financial agreements as well as relationships on the basis of which the Company markets, sells, and distributes any product for which it may hold a product license. Restrictions in accordance with U.S. federal anti-kickback, anti-fraud, and anti-abuse or other laws relating to healthcare are as follows:

- the U.S. federal anti-kickback statute prohibits people from, among other things, deliberately and knowingly soliciting, offering, receiving, or supplying compensation, directly or indirectly, in cash or in kind, to induce or compensate a business connection, or from purchasing, ordering, or recommending any product or service payment which could be made in connection with a healthcare program in the United States, such as Medicare and Medicaid;
- U.S. federal law intended to prevent fraud by companies that are parties to public contracts (the "**U.S. False Claims Act**") provides, among other things, for civil and criminal sanctions against individuals or companies that knowingly present false or fraudulent requests for payment to the U.S. federal government, or make false statements to avoid, reduce, or hide an obligation to pay money to the U.S. government. Such specific actions are open to whistleblowers or any other entity (qui tam actions);
- under the U.S. Health Insurance Portability and Accountability Act of 1996 ("**HIPAA**") a perpetrator of actions intended to defraud any program for providing healthcare services or who makes false statements relating to healthcare problems may be held civilly or criminally liable;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act and regulations thereunder, also imposes obligations, including mandatory contractual language, to protect the confidentiality, security, and transmission of personally identifiable health information;
- U.S. federal law requires that manufacturers of medications report payments and other transfers of value to doctors and university hospitals; and
- analogous laws and regulations of U.S. or foreign states, such as anti-kickback laws, and those prohibiting false claims, could apply to sales or commercial agreements as well as to claims about health products or services reimbursed by non-governmental third-party payors, including private insurers.

If the Company's operations are deemed to be contrary to applicable U.S. law and regulations, the Company could be liable for significant sanctions and penalties, including fines, damages, imprisonment, civil and criminal prosecution, or exclusion of its products from governmental healthcare programs, such as Medicare or Medicaid, or even the restructuring of its business. Any doctor, healthcare professional, or company involved in commercial activities found to violate applicable laws and regulations could be exposed to civil or criminal actions or administrative sanctions, including exclusion from government healthcare programs.

3.1.7 Other clinical applications of temelimab for conditions such as COVID-19 or T1D are based solely on pre-clinical work or on limited clinical data, and the Company may never succeed in developing and marketing effective treatments based on such technology.

Temelimab has been tested pre-clinically for its effect on chronic inflammatory demyelinating polyradiculoneuropathy ("CIDP"), for which temelimab has received Orphan Drug Designation from the U.S. Food and Drug Administration (the "FDA") in February 2018. Temelimab has also been tested in a Phase IIa trial for T1D in adult patients, which has met its primary endpoint of safety at six months, and whose full 12-month results were announced in May 2019[5]. Research data recently published also opens the potential of temelimab as a therapeutic candidate in COVID-19, given the discovery of a correlation between the expression of HERV-W ENV and the severity of the evolution of the disease.

The Company is also using the technology it has developed in the area of endogenous retroviruses to develop new approaches through pre-clinical programs that target, for example, inflammatory psychoses (schizophrenia and bipolar disorders) and amyotrophic lateral sclerosis ("**ALS**"). In 2017, the Company entered into a research agreement with the US NIH for developing new approaches against pHERV-K Env protein as a target in the treatment of ALS, following which the Company has signed in October 2018 an exclusive worldwide license with the National Institute of Neurological Disorders and Stroke (NINDS), part of the U.S. National Institutes of Health (NIH). The agreement covers the development of an antibody program to block the activity of pHERV-K Env (pathogenic envelope protein of the HERV-K family of Human Endogenous Retroviruses), a potential key factor in the development of ALS (see CHAPTER 20 of this Universal Registration Document).

[5] Source: Curtin et al Diabetes Obesity and Metabolism, submitted 2019

If the Company wishes to complete the development of its products and sell them for such indications, it will have to devote significant research effort and undertake numerous tests and clinical trials, obtain regulatory approvals, and make significant financial investments. In developing and marketing products based on its technology, the Company is confronted with a high degree of risk and uncertainty that could slow or even suspend its efforts to develop its products and have a material adverse effect on its business and operations. Even if the Company were in a position to obtain and maintain regulatory approvals for marketing its products, it is possible that:

- it may not obtain the regulatory approvals required for it to conduct clinical trials for such indications;
- it may neither develop nor obtain a marketing approval for its products quickly enough to ensure a competitive position in the target markets;
- it may not be in a position to manufacture and market its future products successfully at a price, reimbursement rate, or scale that allow them to be profitable;
- its future products may not be accepted by medical centers, hospitals, practitioners, and patients, nor be preferred to existing treatments at the time they are introduced, nor, more generally, meet with the expected commercial success;
- its future products may lose their competitive advantage and may become obsolete by the development of new competing products; or
- its future products may not be marketable because of third-party property rights.

If the Company is not successful in developing and marketing other products resulting from its technologies, its revenues will continue to be limited, and its operating results could be significantly affected.

3.2 Risks Related To The Company's Financial Situation and Capital Needs

3.2.1 The Company may not succeed in obtaining additional funds needed to continue its clinical development in the short term and the future.

All of the Company's products are currently in the pre-clinical or clinical trial phase and the Company will need to finance additional studies necessary for the development of temelimab for MS or other indications until the Company may eventually apply for and receive a marketing authorization.

Since its incorporation, the Company has mainly financed its growth by capital increases, including notably the capital increase completed at the time of its initial public offering and listing on the regulated market of Euronext Paris and is not exposed to liquidity risk resulting from indebtedness. The Company will be required to seek additional funding to continue its development in MS which may include, without exclusion, revenues from new partnership agreements, funds from capital increases or other funding, such as subsidies, grants, or other forms of financing.

As of December 31, 2020, cash and cash equivalents of the Company amounted to €6.8 million, with an outstanding debt of a nominal amount of €185 K from BPIFrance. On April 9, 2021, the Company reported on its unaudited cash and cash equivalent position for the first quarter of 2021 of €4.8 million.

Following the specific review of its liquidity risk as of the filing date of this Universal Registration Document, the Company considered that on that date its financial resources are sufficient to cover its upcoming deadlines and operational expenses and investments for at least 12 months after the filing date of this Universal Registration Document and the Company expects that its current cash will suffice to fund its operations and remaining pre-clinical programs until Q2 2022.

The Company's historical cash burn was €7.2 million during 2020, following €9.9 million during 2019 and €17.5 million during 2018, whereas the Company expects that its cash burn for 2021 will be significantly lower than in 2020 based on its current research and development programs. As of the date of this Universal Registration Document, the Company's clinical development program includes only one single-center trial, the Karolinska Trial. However this is not necessarily indicative of future cash burn that will largely depend on future R&D programs actually undertaken.

Although management continues to pursue its plans to finance the development of its products, there is no assurance that the Company will be successful in obtaining sufficient funding in the future, when needed or at all, on terms acceptable to the Company to fund its continuing operations.

The Company will have to bear, if it obtains approval from a country's authorities to test its product candidate in humans in that territory, the significant cost of development of temelimab, which would likely exceed €40 million for

a multi-center Phase II/III registration supportive or enabling (depending on results) study and would likely exceed €100 million for a Phase III study.

In order to finance the continued clinical development of temelimab, the Company is seeking to enter into licensing and distribution, or other, agreements with pharmaceutical companies which will be expected to have sufficient capability for conducting the Phase II and/or III trials, manufacturing on an industrial scale, and distributing, marketing and selling the product. GeNeuro is engaged in these partnering discussions but there is no certainty that these discussions may result in a new partnership.

The Company also believes that the negative cash flow from its operations may increase significantly during future years as a result of conducting clinical trials, manufacturing its products, and extending its research and development programs. It will need considerable funding to pursue its research and development programs, conduct other pre-clinical and clinical trials of its products, and extend its manufacturing, quality control capabilities, and regulatory and administrative capabilities.

The Company's future capital needs will depend on many factors, such as, among others:

- the progress of its research and development programs;
- the scale of such programs;
- the extent of the costs and results of pre-clinical and clinical trials;
- the time and costs necessary for obtaining regulatory approvals, including the time to prepare the application files for regulatory bodies;
- the marketing and sale of product, especially temelimab for MS;
- the Company's ability to establish and maintain collaboration agreements with new partners;
- the cost of improving its manufacturing and marketing capabilities; and/or
- its need to acquire additional technologies or products, as the case may be.

The Company's level of financing needs and their scheduling over time also depends on matters that are largely beyond the Company's control, including:

- costs associated with possible requests or requirements (for example if trials are interrupted by emergencies such as the current COVID-19 epidemic) to change studies, or to include a greater number of patients;
- costs of preparing, filing, defending, and maintaining its patents and other intellectual property rights;
- competing technological developments; and/or
- higher costs and longer lead times than those anticipated to obtain regulatory approvals for the marketing of its products and access to reimbursement.

Finally, if the necessary funds should not be available or not available on a timely basis, the Company may be forced to:

- delay, reduce, or eliminate the number and scope of its pre-clinical and clinical trials;
- grant licenses to technologies to partners or third parties;
- enter into new collaboration agreements on terms and conditions less favorable to it that those that it might have been able to obtain in different circumstances.
- obtain funds through alliance, collaboration or partnering agreements that could force the Company to give up rights to certain of its technologies or its products, rights which it would not have given up in different circumstances; and/or
- delay, reduce, or even cancel research and development programs, or reduce the number of its employees;

The occurrence of one or more of the risks mentioned above could have a material adverse effect on the Group's business, financial condition, results, development, and prospects.

3.2.2 The Company should continue to sustain operating losses in relation to its research and development activities.

The Company has sustained operating losses since its formation, except for the 2014 financial year. Such losses, which amounted to €9.5 million for the 2019 financial year and €7.5 million for the 2020 financial year, reflect both the significance of the expenses incurred in research and development and the absence of its revenues. The Company foresees that such losses will continue over the next few years, at least until the potential marketing and sale of its products, because of the significant investments required for research, development, manufacture, quality

control, and distribution of its products, pre-clinical and clinical trials, administrative activities, and activities linked to the development of intellectual property, as well as license agreements for new products and for the acquisition of new technologies that may become necessary, as the case may be.

The Company expects that its operating losses will increase in the near future, particularly when:

- some of its products move beyond the stage of pre-clinical development to clinical development;
- it is confronted with increased regulatory requirements for manufacturing, and trials for its product candidates (including temelimab for MS, which is its only product in an advanced stage of development);
- it begins to pay fees in connection with applications for product licenses from regulatory bodies;
- it increases its portfolio of products by adding new products for future development;
- it makes milestone payments to third parties (such as bioMérieux) which have already licensed their technologies to it;
- it develops its research and development activities and buys new technologies, products or licenses, as the case may be;
- it develops its business worldwide; and
- it has to finance structural expenses consistent with the growth of its business.

The amount of net losses and the time needed to reach sustained profitability are difficult to estimate and will depend on several factors, including:

- the degree of advancement of the Company's research and development activities, particularly pre-clinical developments and clinical trials;
- the calendar of regulatory procedures in connection with the preparation, review, and protection of patents and intellectual property rights;
- changes in collaboration arrangements made by the Company; and
- other factors, a great number of which are beyond the Company's control.

Given the development stage of its most advanced product, the Company has not yet received any revenue from product sales and the Company's operating revenue and operating profit (or loss) have fluctuated in the past and could continue to do so in the future. Accordingly, its revenues for a given period are not a reliable indicator of its future performance and the Company may never market or sell any products and, as a result, may never become profitable. The Company expects that its main sources of revenue and funds until the potential marketing and sale of its first product candidate, temelimab for MS, will be:

- payments that may be made by future partners of the Company, if the Company enters into one or more agreements with future partners relating to the development and/or marketing and sale of temelimab for MS worldwide (i.e., now including territories that were previously covered by the Company's Collaboration Agreement with Servier) or other revenue of the Company;
- public and private subsidies; and
- potential net proceeds of funds raised by the Company through capital markets transactions.

Any interruption of such financing sources could have a material impact on the operating revenue and operating profit (loss) of the Company.

3.2.3 The Group benefits from Research Tax Credits from the French and Australian governments which regime may be challenged or modified in the future.

One of the two subsidiaries of the Company, GeNeuro Innovation, a French company, benefits from the French Research Tax Credit (*Crédit Impôt Recherche*, "**CIR**") that provides a tax incentive to support the scientific and technical research efforts of French companies. The research expenses that are eligible for the CIR include, under certain conditions, the salaries and compensation of researchers and research technicians, the amortization of fixed assets dedicated to research, services subcontracted to approved research entities (public or private), and expenses for maintaining patents.

The amounts received by GeNeuro Innovation in respect of the CIR are as follows:

- payment of the CIR for financial years 2011 to 2015 of €3,553 K, all of which was received;
- payment of the CIR for financial year 2016 of €519 K, received in September 2017;
- payment of the CIR for financial year 2017 of €791 K, received in March 2019;

- payment of the CIR for financial year 2018 of €593 K, received in August 2019; and
- payment of the CIR for financial year 2019 of €680 K, received in April 2020.

The Company expects to receive payments of the CIR for financial year 2020 during the second half of 2021; the amount accrued at December 31, 2020, for activities in 2020, was € 556 K.

Companies must provide evidence to the French tax authorities, upon request, of the outstanding amount of the CIR and the eligibility of the operations taken into account to benefit from this aid.

GeNeuro Innovation benefits from the early payment of the CIR (i.e., immediately, rather than three years following application). If in the future it should no longer receive amounts under the CIR, or its status or calculations should be questioned, this could have a material adverse effect on the Group's business, prospects, ability to achieve its objectives, financial condition, cash position, or operating profit (loss).

The other subsidiary of the Company, GeNeuro Australia Pty Ltd, an Australian company, has benefited from the Australian Research Tax Credit that provides a tax incentive to support scientific research efforts in Australia. Research expenses that are eligible for the Australian RTC include essentially all costs related to the Company's clinical trial conducted in Australia. Due to the absence of future activities to be conducted in Australia in the foreseeable future, the Company has decided to liquidate its Australian subsidiary and will accordingly not be eligible for future Australian Research Tax Credit benefits.

3.2.4 The Company could be unable to carry tax losses forward.

As of December 31, 2020, the Company had carried-forward tax losses amounting to € 44,196 K (being CHF 47,969 K converted at the December 31, 2019 closing rate). In Switzerland, tax carryforwards may be used within seven years of incurrence and are as follows:

- € 10,698 K originated in 2020 and expiring in 2028
- € 4,440 K originated in 2019 and expiring in 2027
- € 5,858 K originated in 2018 and expiring in 2026
- € 4,755 K originated in 2017 and expiring in 2025
- € 13,746 K originated in 2016 and expiring in 2024
- € 6,160 K originated in 2015 and expiring in 2023
- € 4,450 K originated in 2013 and expiring in 2021

A tax carryforward of €4,614 K generated in 2012 has expired in 2020 as the Company was unable to use it to offset net income.

It is possible that future changes to tax law could alter such provisions by limiting or eliminating the possibilities for attributing the tax loss carryforwards, which could have a material adverse effect on the Group's business, prospects, ability to achieve its objectives, financial condition, cash position, or operating profit (loss).

3.2.5 Dilution Risk

Since its formation, the Company has granted stock options to its management and employees. On February 25, 2021, the Board of Directors awarded an additional 176,800 stock options to executive managers and selected employees of the Company. Accordingly, as of the filing date of this Universal Registration Document and taking into account the expiration of unexercised stock options and the cancelation of unvested stock options for departing employees, full exercise of all securities carrying the right to acquire shares granted and outstanding as of the date hereof would lead to the issuance of 1,064,973 shares, resulting in a potential dilution of 4.9% (such options are described in section 13.1.3 of the Universal Registration Document). The weighted average exercise price of all such securities is €8.25, compared to the market closing price for the Company's shares on Euronext Paris of €5.12 on April 26, 2020.

In connection with its incentive strategy for motivating its executives and employees and to attract additional skills, the Company could issue or award shares or new equity securities carrying the right to acquire shares in the future, which could cause further dilution, potentially material, for present and future shareholders of the Company. Dilution could cause a drop in the price of the Company's shares.

3.2.6 Exchange Rate Risk

The Company is exposed to exchange rate risks relating to changes in the exchange rate between the euro ("**EUR**") and the Swiss franc ("**CHF**") because a portion of the Company's operating expenses is incurred in the latter

currency. Due to the activities of its Australian subsidiary being terminated and there being no assets in AUD, there is no exchange rate risk with the AUD.

If the Company succeeds in marketing and selling its products in the United States, it could earn a portion of its revenue in U.S. dollars and, therefore, would be exposed to an exchange rate risk relating to changes in the exchange rate between the U.S. dollar and the euro.

The Company will follow changes in its exposure to exchange rate risks on the basis of changes in its situation. If the Company does not manage to take effective hedging steps in the future, its results of operations could be negatively impacted.

3.3 Risks Related To The Company, Its Operations and Organization

3.3.1 The Company is dependent on its key employees and, as such, could fail to continue attracting and retaining its key employees and scientific advisors.

The Company's success depends largely on the work and experience of its executive management and its key scientific personnel, especially its Chairman and Chief Executive Officer (*Président Directeur Général*), Mr. Jesús Martin-Garcia; its Chief Medical Officer, Dr. David Leppert; its Chief Scientific Officer, Dr. Hervé Perron; its Chief Financial Officer, Mr. Miguel Payró; and its Chief Development Officer, Dr Jean-François Arrighi. The loss of their expertise could alter the Company's ability to reach its objectives. Furthermore, the Company will need to recruit new qualified executives and scientific staff as it expands in areas that require additional abilities, such as marketing, manufacturing, clinical trials, and regulatory affairs. The Company competes with other companies, research organizations, and academic institutions to recruit and retain highly qualified scientific, technical, and management staff. To the extent such competition is very intense, the Company could be unable to attract or retain such key staff on terms and conditions that are acceptable from an economic point of view. Its inability to attract and retain such key personnel could prevent it from reaching its overall objectives.

3.3.2 The Company faces the risk of liability linked to its products or operations and it may not be able to obtain adequate insurance coverage at an acceptable cost .

The Company is exposed to the risk of liability, particularly product liability, arising in connection with the manufacture and sale of therapeutic products for use in humans. Liability against the Company may also result from clinical trials in connection with the testing of therapeutic products or unexpected adverse side effects resulting from the administration of such products. Complaints or legal proceedings could be filed or brought against the Company by patients, regulatory authorities, biotechnology and biopharmaceutical companies, and other third parties using or selling its products. Such actions could include complaints resulting from actions by its partners, licensees, and subcontractors over which it has little or no control. The Company can give no assurance that its present insurance coverage will suffice to respond to liability actions that could be brought against it. If its partners, licensees, and subcontractors or the Company itself are not in a position to obtain and maintain appropriate insurance coverage at an acceptable cost or protect themselves in some way against product liability actions, they could be held significantly liable, which could have the consequence of seriously affecting marketing and sale of the Company's products and, more generally, harm its business.

The Company is also subject to environmental protection and health and safety laws and regulations that could expose it to liability and restrict its operations. In its research and development programs and pre-clinical tests, the Company uses hazardous substances and biological materials such as human cell lines. Accordingly, in countries in which the Company operates, it is subject to environmental protection and safety laws and regulations governing the use, storage, manipulation, production, and disposal of hazardous substances, including chemical and biological products. The Company is also subject to laws and regulations relating to the use and manipulation of genetically modified organisms under French, European, and U.S. laws and regulations.

In the event of a failure to comply with applicable laws and regulations, the Company could be subject to fines and might have to suspend part or all of its operations. To comply with environmental, and health and safety laws and regulations, the Company would incur additional costs and it could, in the future, incur significant expenses in doing so in the relevant jurisdictions in which it operates. In complying with environmental, health and safety laws and regulations, the Company may have to acquire equipment, modify facilities, and more generally, incur other material expenses. In the event of accidental contamination, injuries, or any kind of damage, the Company could be held liable for damages, which might not be paid by or covered under its insurance policies and which could harm the Company's business.

3.3.3 Shareholders might be unable to achieve a control premium in the event of a change of control of the Company based on the fact that French and Swiss regulations concerning mandatory public takeover offers are not applicable.

In so far as the Company's registered office is in Switzerland whilst its shares are listed only on Euronext Paris's regulated market, neither French regulations on mandatory public tender offers and buyouts, nor Swiss regulations on public takeover offers (purchase or exchange offer) are applicable to public tender offers concerning the Company's shares.

Under these conditions, a person might acquire shares in the Company to an extent representing a controlling stake as defined under Swiss or French law without a legally enforceable obligation to file a public tender offer to all the shareholders.

Similarly, because of the unenforceability of French and Swiss law on compulsory public tender offers, a person could issue a public tender offer to some, but not all, shareholders.

3.4 Risks Related To The Company's Dependency on Third Parties

3.4.1 The Company does not have manufacturing capabilities and is exposed to the risks associated with relying on third party manufacturers for its most advanced product candidate Temelimad and its other products

The Company has chosen to outsource the manufacturing of its products. Its dependence on third parties to manufacture and assemble certain of its products and its lack of experience in manufacturing other products on an industrial scale could affect its ability to develop and sell its products within a reasonable timeframe and on a competitive basis. In particular, the Company depends on third parties to produce its most advanced product candidate, temelimab for MS. In this respect, it has entered into an agreement with the contract manufacturing organization ("**CMO**") Polymun Scientific GmbH ("**Polymun**"), to manufacture its antibody on the basis of good manufacturing practices ("**GMP**"), for determined quantities of product at a pre-determined cost, without future royalties. The Company will also depend on subcontracting agreements for the fill and finish of its products, both for future clinical trials and for subsequent stages of sales and marketing.

The Company could also be unable to enter into subcontracting agreements for the future commercial supply of temelimab, or to do so on acceptable terms and conditions. If it is unable to enter into acceptable subcontracting agreements, the Company may be unable to market and sell temelimab successfully.

Furthermore, dependency on third-party manufacturers involves additional risks to which the Company might not be exposed if it manufactured temelimab itself, such as:

- non-compliance of such third parties with regulatory and quality control standards;
- the violation of such agreements by such third parties;
- the termination or non-renewal of such agreements for reasons beyond its control; and
- the insolvency of such third parties.

If the products manufactured by such third-party suppliers do not comply with regulatory standards, sanctions and penalties could be imposed. Such sanctions could include fines; court orders; civil penalties; refusal of regulatory authorities to grant product licenses; delays, suspension or withdrawal of approvals; revocation of product licenses; product recalls or seizures; operating restrictions and criminal prosecutions, all of which are measures that could have a material adverse effect on the Company's business, operations, its financial position and its financial results.

If the Company is unable to maintain its collaboration agreements with its existing partners, including the CMO Polymun, or enter into new agreements on acceptable terms and conditions, it will have to develop and sell its products at its own expense, or it will have to turn to other partners. This could increase its capital needs and limit its growth and marketing and sales efforts to other areas. In addition, even if the Company, in connection with its agreements, has included provisions designed to impose strict compliance by its partners with their commitments, it cannot control either the extent or the timing of the resources that its existing and future partners will devote to the development or sale of the Company's products. Such partners might also not meet their obligations as set out in the contracts that the Company has, or may have, with them or under the terms it is expecting. In such cases, the Company could be confronted with significant delays and not achieve success in obtaining the support of third parties for the Company's new technology based on the neutralization of HERV-W ENV, or support for the introduction of the Company's products in various markets.

Even though the Company tries to include non-competition clauses in its collaboration agreements, no assurance can be given that such restrictions will ensure sufficient protection to the Company. The Company's partners could develop technologies alone or together with others, including its competitors.

3.4.2 The Company relies on external scientific collaborators

The Company relies on external scientific collaborators, including researchers attached to CROs or universities, to successfully conduct relevant research activities, including in connection with development programs for products, such as the conduct of clinical trials. The competition to maintain such networks is intense, and it may not be possible to maintain them on acceptable conditions. In general, such external collaborators may terminate their commitments at any time. Accordingly, the Company can control their activities only within certain limits and cannot prevent them from devoting a portion of their time to research on and development of other products. Furthermore, such scientific collaborators may be subject to intellectual property rights agreements, or other rights in relation to the results of tests or research and development conducted jointly. Furthermore, they may not wish to grant a license to such intellectual property rights on acceptable terms.

3.4.3 The Company does not have experience in the areas of sales, marketing and distribution and may be required to rely on third parties and/or mobilize new internal resources for this purpose

The Company also lacks experience in the areas of sales, marketing and distribution. If it secures a marketing authorization for its products, it will therefore have to develop its own marketing and sales capabilities either alone, or with strategic partners. In connection with its strategy, it could, therefore, be led to search for partners for the sale, marketing, and distribution of some of its products. In the event of the direct marketing and sale of temelimab by the Company, it will have to develop its own sales and marketing infrastructure, which would involve incurring additional expenses, mobilizing management resources, organizing new skills and taking the time needed to create the appropriate organization and structure to support the product in accordance with applicable law and, more generally, optimizing its marketing and sales efforts. The Company is evaluating the strategic and financial advantages of an alliance with one or several partners for the marketing and sale of temelimab for MS in worldwide markets, if the opportunity should arise. It is possible that the Company may not succeed in entering into an alliance for the marketing and sale of temelimab or any of its products on economically reasonable terms and conditions or maintaining such alliances or marketing and selling its products itself.

The Company expects growth in all areas of its business while it develops and, subject to obtaining required regulatory approvals, markets and sells its products, directly or through potential partners. It will therefore need to recruit staff and expand its capabilities, which could significantly increase its managerial, operating, financing, and other resources. To remain competitive and control its growth, the Company would have to:

- train, motivate, and retain a growing number of employees;
- forecast with precision the demand for its products and the revenue that they may be capable of generating; and
- increase the size of its existing operating, computer, and financial and management systems.

The inability to manage its growth effectively could harm the Company's business and prospects.

3.5 Risks Relating To The Company's Intellectual Property Rights

3.5.1 If the Company is unable to maintain or protect its intellectual property rights, it could lose its competitive advantage and be unable to operate profitably.

The Company's rights under existing agreements, some of which give it access to future products and proprietary processes belonging to third parties (such as its rights to various patents targeting the HERV-W ENV envelope protein under its agreement with bioMérieux-INSERM) or jointly owned with third parties (such as its rights to the HERV-K patent targeting the pHERV-K Env envelope protein under its agreement with the NINDS/NIH) could expire or be terminated. In addition, it might not be able to obtain licenses to other rights which it might need. If it is unable to secure such rights or licenses, or to preserve them, it will have to search for other alternatives or develop the necessary products itself so as to avoid infringing patents or technology rights belonging to third parties. It is possible that such alternatives would not exist or that this could cause a significant increase in costs as well as development time for its products.

It is important to the success of its business that the Company, as well as the licensor and any future licensees, be able to obtain, maintain, and enforce its patent and other intellectual property rights in Europe, the United States, and other countries. It cannot be ruled out that:

- the Company may fail to develop new inventions that are patentable;
- patent applications that are being reviewed, including certain important patents in several jurisdictions, are not granted;
- the patents granted or licenses to its partners or itself are contested or held to be invalid, or the Company may be unable to enforce them;
- the scope of protection granted by a patent is not sufficient to protect the Company from competition; or
- third parties may claim proprietary rights to the patents or other intellectual property rights that the Company owns outright or to which it holds a license.

The grant of a patent does not guarantee its validity or scope, and third parties may challenge both aspects. The validity and scope of a patent in the area of biotechnology are highly uncertain and raise complex legal and scientific questions. Until now, no uniform policy has emerged at a worldwide level in terms of the content of patents granted in the area of biotechnology and the scope of individual claims. Legal action may be necessary to enforce the Company's intellectual property rights, protect its trade secrets, or determine the validity and scope of its intellectual property rights. Any dispute could entail considerable expense, reduce profits, and not provide the protection sought. The Company's competitors could successfully challenge in court or through other proceedings the patents the Company has been granted or has had licensed to it, which could have the consequence of reducing the scope of its patents. In addition, such patents could be infringed or successfully avoided as a result of innovations.

3.5.2 The Company's products and technologies could infringe or be claimed to infringe patents and patent applications held or controlled by third parties.

The Company's products and technologies could infringe or be claimed to infringe patents and patent applications held or controlled by third parties. The Company's success depends on its ability to avoid the infringement or misuse of patents or other intellectual property rights of third parties. The growth of biotechnology and the increase in the number of patents granted in the field increase the risk that third parties will take the position that the Company's products and technologies, including its processes, infringe their patents. In general, a patent application is not published until 18 months after the priority date of the application. In the United States, some patent applications are not published prior to issuance of the patent itself and may be granted on the basis of the date of invention, which does not always result in the issuance of a patent to the party that was the first to file the application. Discoveries or patent applications are made sometimes only months or often even years after the discovery. For this reason, the Company cannot be certain that third parties have not been the first to invent products or file patent applications for inventions covered by its own patent applications or those of its partners. In such cases, the Company could need to obtain licenses to such third-party patents (licenses which it might not be able to obtain on reasonable terms and conditions, if at all), terminate the production and sale of certain product lines, or develop alternative technologies.

In addition, the Company uses antibodies and cells that are available on the market to manufacture certain products, and the use of such antibodies and cells could infringe third-party rights, in which case the Company could be obligated to acquire a license to such rights (a license that it may not be able to obtain on reasonable terms and conditions, if at all), become involved in costly litigation, or stop using such antibodies or cells.

Any litigation or claim brought against the Company, regardless of the outcome, could involve substantial costs and compromise its reputation. Some of the Company's competitors have greater resources than the Company and could be in a better position to bear the cost of complex proceedings. Any dispute of this type could seriously affect the Company's ability to continue in business. More specifically, intellectual property disputes could force the Company to:

- stop selling or using one or more of its products that depend on the challenged intellectual property rights, which could reduce revenue;
- obtain a license from the holder of intellectual property rights deemed infringed, a license that it may not be able to obtain on reasonable terms and conditions, if at all; and
- redesign or, in the event of claims relating to trademarks, rename its products to avoid violating intellectual property rights of third parties. This may not prove to be possible or, in any event, given the time and financial resources that would have to be dedicated to doing so, it may prove to be too costly and, as a result, it could disrupt the Company's sales and marketing efforts.

3.5.3 If the Company does not comply with its obligations under the license agreements with bioMérieux or the NINDS/NIH, it could lose rights that are very important for its business.

If the Company does not comply with its obligations under the license agreement with bioMérieux or under the license agreement with the NINDS/NIH, it could lose rights that are very important for its business. The Company's business depends on a license agreement to use various significant patents relating to temelimab that was granted to the Company by bioMérieux and INSERM, and on a license agreement to use the first HERV-K patent that was

granted to the Company by the NINDS/NIH. The patent licenses granted to the Company may be revoked if the Company does not comply with various terms and conditions set forth therein (in particular, milestone and other payments). To comply with such conditions, the Company could be required to increase the resources dedicated to development projects contemplated by such licenses. Such license agreements also include provisions with which the licensor must comply. Among other things, the Company is counting on its licensor to prosecute any infringement of the licensed patents by third parties. The Company can, however, give no assurance that its licensor is or will be willing to undertake such proceedings.

3.5.4 The Company's business could be affected if it is unable to protect the confidentiality of its information and know-how.

The Company's business could also be affected if it is unable to protect the confidentiality of its information and know-how. The Company provides information and materials from time to time to researchers at academic institutions as well as other public or private entities (including CMO manufacturers) with which it seeks to have various tests or clinical trials conducted.

In both cases, the Company relies on the execution of confidentiality agreements. Its business also depends on non-patented proprietary technology, processes, know-how, and data that it treats as trade secrets and that it protects, in part, through confidentiality agreements with its employees, consultants, and various subcontractors. These agreements and other means of protecting trade secrets may not provide the protection sought or may be violated, the Company may not have effective recourse against such violations, or its trade secrets may be disclosed to its competitors or developed independently by them.

CHAPTER 4.
INFORMATION ABOUT THE COMPANY AND THE GROUP

4.1 History And Development Of The Company And The Group

4.1.1 Legal and commercial name of the Company

Company legal name: GeNeuro SA
Company commercial name: GeNeuro

4.1.2 Place and number of registration and legal identity identifier (LEI)

The Company is registered at the *Registre du commerce* (commercial register) of Geneva, Switzerland, under number CHE-112,754,833. The legal entity identifier (LEI) of GeNeuro is 213800FUJCKXO9LK3444.

4.1.3 Date of incorporation and length of life

The Company was incorporated on February 6, 2006 for an indefinite term.

4.1.4 Registered/principal office, legal form and applicable law

Registered/principal office: 3 chemin du Pré-Fleuri, CH-1228 Plan-les-Ouates, Switzerland
Telephone: +41 22 552 4800
Electronic address: contact@geneuro.com
Web page: www.geneuro.com

The Company is a *société anonyme* (company limited by shares) organized under Swiss law and governed by its Articles of Association and, in particular, Title XXVI of the Swiss Code of Obligations.

4.1.5 Major events in the development of the Company's and the Group's business

2021 On April 15, 2021, the Company announced recent research data on the detection of HERV-W ENV in COVID-19 patients and linking its expression to disease severity. A publication in the Lancet's EBioMedicine by researchers from the "Tor Vergata" University of Rome, Italy, has shown that the pathogenic envelope protein of the human endogenous retrovirus W (HERV-W ENV) is found on lymphocytes of hospitalized patients with COVID-19, and that its level of expression is associated with disease severity. HERV-W ENV's pro-inflammatory properties are thought to act as an "accelerant" of the activation of the innate immune system, fueling the severity of COVID-19 evolution and impacting long term recovery. In addition, through the parallel effort supported by the ANR, preliminary data generated by GeNeuro and the CIRI in Lyon (International Center for Research in Infectious Diseases), made available on Research Square, also shows HERV-W ENV expression in lymphocytes following in vitro exposure to SARS-CoV-2 in about 20% of healthy blood donors, suggesting individual susceptibility. With HERV-W ENV as a possible aggravating agent of COVID-19, GeNeuro's temelimab, an anti-HERV-W ENV monoclonal antibody already in a Phase II clinical trials with an excellent tolerability and safety, could, without any prejudice to its existing programs, start tests against COVID-19 as early as this summer.

On April 9, 2021, the Company announced that its cash position at March 31, 2021, was €4.8 million.

On April 6, 2021, the Company announced its 2020 financial results and provided a corporate update.

On March 2, 2021, GeNeuro announced that the independent Drug Safety Monitoring Board (DSMB) had concluded that the Phase 2 ProTEct-MS trial of temelimab in MS patients should continue as planned without modification as the higher doses of temelimab in ProTEct-MS Phase 2 study are well tolerated.

On February 18, 2021, the Company announced the completed patient recruitment in its Phase 2 ProTEct-MS trial of temelimab in MS patients, conducted at the Karolinska Institutet's Academic Specialist Center (ASC), in Stockholm (Sweden).

On January 26, 2021, GeNeuro announced it had received an award from the French national research agency, ANR (Agence Nationale de Recherche), for its COVERI project focused on understanding the role of human endogenous retrovirus (HERV) proteins in the abnormal immune-inflammation or the neurological damages suffered by important subsets of COVID-19 patients.

On January 11, 2021, the Company announced that its cash position at December 31, 2020, was €6.8 million.

2020 On September 14, 2020, GeNeuro presented the rationale and outline of its Phase 2 ProTEct-MS clinical study of temelimab at MSVirtual2020 (8th Joint ACTRIMS-ECTRIMS Meeting).

On July 20, 2020, GeNeuro announced the publication in Science Advances of data establishing a clear link between human endogenous retroviral proteins and psychotic disorders.

On June 25, 2020, the Company announced the recruitment of the first patient in its Phase 2 trial of temelimab in MS at the Karolinska Institutet's Academic Specialist Center (ASC), in Stockholm, Sweden.

On April 21, 2020, the Company announced the nomination, effective May 1, 2020, of its new Chief Medical Officer, Dr. David Leppert, who is a highly experienced medical and industry professional.

On March 19, 2020, the Company announced that it was postponing the launch of its Karolinska Trial to prioritize healthcare resources behind the fight of COVID-19 and to reduce the risk for MS patients.

On January 31, 2020, the Company announced that it had completed a €17.5 million capital increase through a share offering to certain qualified and institutional investors. Its shareholder GNEH SAS participated for €7.5 million in this offering and paid for its new shares by way of set-off with the €7.5 million loan it had granted to the Company in 2019.

2019 On November 25, 2019, GeNeuro announced an agreement with the Karolinska Institutet / Academic Specialist Center (ASC) of Stockholm to launch a new single center, Phase II clinical study of temelimab in multiple sclerosis. The trial, to be conducted at the Center for Neurology of ASC (which, with approximately 2,400 patients, is the largest MS center in Sweden), will be a one-year study that will enroll, initially, 40 patients whose disability progresses without relapses, and will document the safety and tolerability of temelimab following higher doses, as well as measures of efficacy based on the latest biomarkers associated with disease progression. The study aimed to start enrolling patients in Q1 2020 with last patient out and top line results expected in H2 2021; however, due to the COVID-19 crisis, the Company announced on March 19, 2020, that it was temporarily postponing this trial to prioritize healthcare resources behind the fight of COVID-19 and to reduce the risk for MS patients. Assuming recruitement can be completed by the end of 2020, the Company expects that results would still be communicated in H2 2021.

On September 16, 2019, GeNeuro presented at the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS 2019) Congress in Stockholm, Sweden the full results of the Phase II CHANGE-MS trial and ANGEL-MS extension trial in relapsing-remitting MS (RRMS), which confirmed that the neuroprotective effects of temelimab in MS patients extend to 96 weeks and that temelimab is safe to use and well tolerated for a prolonged period.

In June 2019, GeNeuro announced that data supporting the mode of action of its lead product (temelimab) in treating MS was published in the Proceedings of the National Academy of Sciences (PNAS). Temelimab is a monoclonal antibody designed to neutralize a pathogenic, viral envelope protein, pHERV-W Env, which plays a causal role in the development of MS. The PNAS paper, entitled "pHERV-W envelope protein fuels microglial cell-dependent damage of myelinated axons in multiple sclerosis", demonstrates that axonal injury in MS can be significantly driven by pHERV-W Env through activation of microglia and this contributes to neurodegeneration, particularly in progressive forms of MS. In addition to the already published data demonstrating that pHERV-W Env may directly inhibit remyelination, these data provide additional neurobiological rationale for the results from recently completed CHANGE-MS and ANGEL-MS Phase IIb trials. In these studies, performed in patients with relapsing remitting MS, temelimab showed consistent neuroprotective effects on MRI measures known to be associated with disability progression in MS, through neutralization of pHERV-W Env.

On June 3, 2019, the Company announced that it had drawn the full amount of €7.5 million available under the GNEH Credit Facility as of May 31, 2019.

On May 7, 2019, the Company announced that a six-month extension of its Phase IIa study of temelimab (GNbAC1) in T1D confirmed all previously-observed positive observations in the trial, meeting its primary objective. GeNeuro believes these data open the door to further development in early-onset T1D pediatric patient population.

On March 12, 2019, the Company announced positive results from the ANGEL-MS study of its lead product, temelimab (GNbAC1), in MS. The ANGEL-MS data confirmed that treatment with temelimab for 2 years (96 weeks) 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 IIb 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.

In January 2019, GeNeuro announced positive safety and tolerability results from a Phase 1 study assessing the administration of high doses of temelimab (GNbAC1) to treat MS and other auto-immune diseases. These results suggest that higher dose regimens or a front-loading could be evaluated in a future next clinical study of temelimab in MS and other potential therapeutic indications.

2018 In December 2018, the Company signed a financing agreement with GNEH SAS, a subsidiary of Institut Mérieux, to establish a €7.5 million credit line, allowing it to extend the Company's runway with all ongoing programs until Q3 2020.

On October 17, the Company announced that following a successful collaboration in preclinical amyotrophic lateral sclerosis (ALS) models, GeNeuro has signed an exclusive worldwide license with the National Institute of Neurological Disorders and Stroke (NINDS), part of the U.S. National Institutes of Health (NIH). The agreement covers the development of an antibody program to block the activity of pHERV-K Env (pathogenic envelope protein of the HERV-K family of Human Endogenous Retroviruses), a potential key factor in the development of ALS.

On October 11, the Company presented at ECTRIMS 2018 in Berlin the results from its 48-week CHANGE-MS Phase IIb clinical trial in the MS indication, confirming a robust and coherent impact on the key MRI markers associated with disease progression. Moreover, the benefits have also been observed in patients with lower inflammatory burden, which are not served by existing anti-inflammatory treatments.

On September 26, the Company released the six-month results from the RAINBOW-T1D Phase IIa clinical trial of temelimab in the T1D indication. The data showed that the study met the primary endpoint, with temelimab showing an excellent safety and tolerability profile in T1D patients; some encouraging signals were observed, such as a 32% reduction in the total number of hypoglycemic episodes in the treated group versus placebo ($p<0.0001$), and a 21% decrease of anti-insulin antibodies in the treatment group, versus an increase of 23% in the placebo group ($p<0.01$). But given the low occurrence of events in this well-controlled population and the small size of the Phase IIa cohort, these signals require confirmation at Week 48, as well as through investigation in larger populations with a more recent onset.

On September 17, Servier, based on R&D strategic reasons and its international development priorities, decided to decline the option to license temelimab in MS and to return worldwide rights ex US and Japan for temelimab in MS. Should Servier have had exercised its option, it would have had to finance the global development of temelimab, including in the USA and Japan. As a result, GeNeuro engaged in new partnership discussions for its lead MS program. Following this notification by Servier, the ANGEL-MS two-year extension study, undertaken at Servier's request and with Servier's funding, was terminated one year before its expected end, with Servier bearing the study's closure costs. This early termination allowed to generate 48-week results for ANGEL-MS, which were presented on March 12, 2019.

In March, the Company released the full results from its 48-week CHANGE-MS Phase IIb clinical trial in the MS indication. The 12-month data of this 270-patient study, conducted in 12 European countries, confirmed that there was a modest effect on most MRI measures of neuroinflammation, with no significant separation between treatment groups. Full study results however showed robust and coherent impact at the highest dose of 18 mg/kg on the key MRI markers associated with disease progression. Moreover, the benefits are also observed in patients with lower inflammatory burden, which are not served by present anti-inflammatory treatments. Safety of temelimab is confirmed.

In February, the Company's temelimab drug received the Orphan Drug Designation from the US FDA for the chronic inflammatory demyelinating polyradiculoneuropathy ("**CIDP**") indication.

2017 Publication of the six-month results from the 48-week CHANGE-MS Phase IIb clinical trial on temelimab. The data showed that temelimab is well tolerated and that there is no statistical difference at 6 months between temelimab and placebo in the study's primary endpoint of reducing the number of cerebral Gad-enhancing lesions as measured by MRI, nor on the other MRI measures of neuroinflammation. Post hoc analyses of 6-month data however 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.
Launch of a Phase IIa clinical trial with temelimab in the Type 1 diabetes indication, with 60 recently diagnosed adult patients, in over 10 centers in Australia. The primary endpoint will be the safety of temelimab in this new patient population.
The Company entered into a research agreement with the US NIH for developing new approaches against pHERV-K protein as a target in the treatment of Amyotrophic Lateral Sclerosis (ALS).

2016 At the end of December 2016, completion of the recruitment of the 260 patients of the CHANGE-MS Phase IIb clinical trial on temelimab, 4 months ahead of planning. A Data Safety Monitoring Board reviewed the 3-month data for the first 30 patients and confirmed the very good tolerance profile of temelimab.
Servier decides to finance a new ANGEL study which will allow patients having taken part in the Phase IIb study to benefit from two additional years of treatment.
In April 2016, Initial Public Offering on Euronext's regulated market in Paris, coupled with a capital increase, allowing the Company to raise gross proceeds of €33 million.
Launch of the CHANGE-MS Phase IIb clinical trial on temelimab, contemplating the recruitment of 260 patients initially through 69 clinical centers in 13 European countries. The trial's main endpoint is the cumulative number of brain lesions evidenced by MRI at 6 months, then 12 months together with patients' clinical evaluation.

2015 Servier International B.V. (owned 100% by Servier) acquires 8.6% of GeNeuro's outstanding shares through a sale by Eclosion2 for €15 million on December 11, 2015. Servier exercises its first option under the Collaboration Agreement to finance the Phase IIb trial of temelimab and makes a milestone payment of €17.5 million to GeNeuro.
GeNeuro conducts a pharmacological study controlled against placebo to confirm the safety and penetration in the central nervous system of high doses of the immunoglobulin temelimab on healthy volunteers in preparation for launching a Phase IIb study.

2014 A Collaboration Agreement is signed by GeNeuro, Servier and Institut de recherches internationales Servier for the development of a drug targeting a suspected causal factor of multiple sclerosis.
Completion of the one-year Phase IIa trial on 10 patients with good results in safety as well as pharmacodynamic effects and the first signs of therapeutic responses in patients.

2013 The Swiss drug agency (Swissmedic) authorizes GeNeuro to undertake a Phase IIa clinical trial with extensions for a total of 12 months.

2012 GeNeuro announces the commencement of the Phase IIa clinical trial of temelimab.

2011 GeNeuro announces the completion of the Phase I clinical trial of temelimab, showing that the product is well tolerated.

2010 GeNeuro obtains a favorable opinion from the German committee for scientific regulation, the Paul Ehrlich Institute, on the pre-clinical file for the temelimab monoclonal antibody to treat MS.
GeNeuro Innovation obtains the status of small and medium-sized company ("**SME**") from the EMA.

2009 GeNeuro Innovation, the subsidiary of the Company, is organized in Lyon, France.

2008 A capital increase of CHF 12 million is underwritten by Eclosion and Institut Mérieux to broaden GeNeuro's operations and develop its medicines portfolio through clinical trials.

2006 GeNeuro, a spin-off of French diagnostics company bioMérieux, is founded in Switzerland by Dr. Hervé Perron, Dr. Christophe Mérieux, and Jesús Martin-Garcia, with Eclosion, a Swiss start-up incubator and long-term investor in biotechnology, and bioMérieux as principal shareholders.

CHAPTER 5.
DESCRIPTION OF THE GROUP'S BUSINESS

5.1 General Presentation

GeNeuro is a clinical-stage biopharmaceutical company focused on understanding and stopping the causal factors driving the progression of neurodegenerative and autoimmune diseases. GeNeuro's most advanced therapeutic candidate, temelimab, is a humanized monoclonal antibody that neutralizes a pathogenic protein of the HERV-W family ("**HERV-W ENV**") that has been identified as a potential causal factor in Multiple Sclerosis ("**MS**") and Type 1 Diabetes ("**T1D**"), and has already completed Phase II clinical trials in both indications with an excellent tolerability and safety. In addition, GeNeuro's temelimab has received an Orphan Drug Designation ("**ODD**") from the US Food and Drug Administration ("**FDA**") in the treatment of chronic inflammatory demyelinating polyneuropathy ("**CIDP**"), a rare autoimmune disorder of the peripheral nervous system; and HERV-W ENV has been identified as a potential causal factor in Inflammatory Psychosis.

HERV-W ENV has also been found on lymphocytes of hospitalized patients with COVID-19, and its level of expression is associated with disease severity. HERV-W ENV's pro-inflammatory properties are thought to act as an "accelerant" of the activation of the innate immune system, fueling the severity of COVID-19 evolution and impacting long term recovery. Preliminary data also shows the expression of HERV-W ENV in lymphocytes following in vitro exposure to SARS-CoV-2 in about 20% of healthy blood donors, suggesting individual susceptibility. With HERV-W ENV as a possible aggravating agent of COVID-19, GeNeuro's temelimab could start tests against COVID-19.

More broadly, GeNeuro is leveraging the potential of HERVs through research and academic partnerships to develop new treatments for poorly understood autoimmune and neurodegenerative diseases, such as the Cooperative Research and Development Agreement ("**CRADA**") signed in 2017 with The National Institute of Neurological Disorders and Stroke ("**NINDS**"), part of the U.S. National Institutes of Health ("**NIH**"), to develop novel therapeutic antibodies for the treatment of amyotrophic lateral sclerosis ("**ALS**").

GeNeuro's novel approach against HERVs

The immune system is a complex set of defense mechanisms that seek to protect the body by identifying and destroying potential threats, including infectious agents. Autoimmune diseases are defined as conditions where the immune system of the patient is activated without known cause, and attacks and damages its own tissues. There are many autoimmune diseases, affecting many organ classes, such as rheumatoid arthritis, juvenile (type 1) diabetes, psoriasis, and multiple sclerosis. Since there is no known cause for autoimmune diseases, treatments in these indications target the immune system of the patient to reduce the damage caused by the immune attack and/or provide relief for the damage inflicted to an organ.

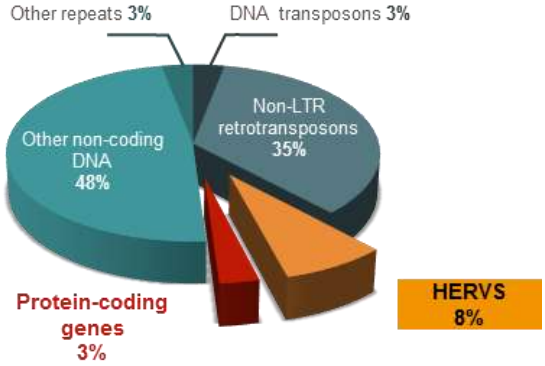
GeNeuro is developing a novel approach against autoimmune and neurodegenerative diseases by trying to block potential causal factors of these disorders. This novel approach is the result of more than 25 years of research on human endogenous retroviruses ("**HERV**"), 15 of which at Institut Mérieux and INSERM before the creation of GeNeuro in 2006.

HERV DNA, which represents up to 8% of the human genome (see Figure 1 below), has originated from infections by viruses whose DNA was integrated into the human germline during evolution. Since HERV DNA is normally silent, HERVs are generally not expressed. In certain disease settings, however, such as multiple sclerosis, HERV genes are reactivated, which leads to significant levels of some HERV proteins in affected tissues.[6] In COVID-19, the International Center for Infectiology Research in Lyon, France (CIRI) has shown, in preliminary findings[7], that when human peripheral blood mononuclear cells from healthy donors were cultured and exposed to SARS-CoV-2, about 20% of donors responded by expressing HERV-W ENV in lymphocytes, cells in which the virus did not replicate. This expression was triggered specifically by the spike protein of SARS-CoV-2, independently from cytokine release.

These proteins, considered as "self" by the body as encoded by its own cells, may retain some of their original viral properties, which could explain in some disease settings the triggering of the immune system and local toxicity.

6 Source: Engel & Hiebert, *Nature Med*. 2010, May; 16(5): 517-8.
7 Source: Charvet, Mazelier et al., Research Square

Figure 1 : DNA breakdown of the human genome



As detailed below, GeNeuro and some leading academic centers have developed and published strong evidence suggesting that the envelope (ENV) protein of the HERV-W family could play a causal role in MS, T1D and Inflammatory Psychosis, and an accelerant role in COVID-19. The NINDS, part of the US NIH, has also published the potential causal role of the ENV protein of the HERV-K family in ALS. And the amount of evidence for the involvement of HERV proteins in poorly understood diseases keeps building up. If these proteins do indeed play a causal role in these pathologies, neutralizing them through therapeutic molecules could, for the first time, allow medicine to have a direct impact on the onset and progression of these diseases. GeNeuro leads the effort of leveraging these promising discoveries into novel and effective treatments for patients, with its research and clinical work currently focused on a number of key indications shown below.

Figure 2 : GeNeuro development pipeline

Program	Pre-clinical / Phase I / Phase IIa / Phase IIb / Phase III
1. **Temelimab** **Multiple Sclerosis**	Planning next stage developments based on positive neurodegeneration 96-week results
CHANGE-MS / ANGEL-MS	**CHANGE-MS : 270 patients in RRMS indication** - completed 03/2018 **ANGEL-MS : 219 patients extension** - Completed 03/2019
Karolinska/ASC trial	**Phase II study in Non-Active Progressive** / fully recruited, results expected Q1 2022
2. **Temelimab** **COVID-19**	**Opportunity for clinical trials in Acute COVID and Long COVID** *Research showing interaction between SARS-CoV-2 and HERV-W ENV, and correlation between HERV-W ENV levels and disease severity*
3. **Anti-HERV-K** ALS	**R&D Agreement with NIH** Preclinical program underway, open for partnership to lead to IND
Other opportunities subject to ad-hoc funding	
4. *Temelimab* *Type 1 Diabetes*	Safety & signal finding Phase IIa, completed 05/2019 New study subject to funding & development of temelimab in MS
5. *Temelimab* *CIDP*	ODD granted by the US FDA No study planned presently.
6. *New anti HERV-W Ab* *Inflammatory Psychosis*	Research collaboration & publication with Academic labs, murine candidate selected No study at present without ad-hoc non-dilutive funding

RRMS: Relapsing-Remitting form of MS; SPMS: Secondary Progressive form of MS.
CIDP: Chronic inflammatory demyelinating polyradiculoneuropathy; ODD: Orphan Drug Designation
ALS: Amyotrophic Lateral Sclerosis; NIH: United States National Institutes of Health

Multiple Sclerosis

MS is a long-term, degenerative disease that affects the central nervous system (consisting of the brain and spinal cord) in which the immune system attacks the myelin sheath that protects nerve fibers and is characterized by neuroinflammation and neurodegeneration. Without the protection of myelin, nerves lose functionality, become damaged and are ultimately destroyed, which leads to the formation of scar tissue (sclerosis). In 85% of the cases at the original diagnosis, MS presents itself in a form called relapsing-remitting MS (RRMS), which will usually degenerate over time into a more aggressive form of the disease: the secondary progressive form (SPMS) during

which the loss of neuronal function increases. Approximately 15%[8] of patients present from the outset with a progressive form of the disease called primary progressive MS (PPMS). There is currently no cure for MS, and no treatment presently available has shown a determining impact on the progression of long-term disability resulting from the disease. Present treatments work by reducing the number of relapses, speeding recovery from attacks, and managing the symptoms of the disease, and are approved for the relapsing-remitting forms of MS (which include the "active secondary progressive" form, which the FDA[9] has defined as one of the relapsing forms of MS). In fact, based on the recent definition by the FDA[10], it is even possible to split MS patients in two broad categories: patients with inflammatory relapses (or "active inflammatory" patients), and patients with progression of their disability without inflammatory relapses ("non-active progressive" patients).

Sales of medications for the treatment of MS in 2020 have been estimated at USD 22 billion[11]. Since MS is an autoimmune disease, all present medications target the immune system of the patient by altering or suppressing the functions of the patient's immune system in order to reduce the number of relapses. While new-generation immuno-suppressive treatments show a reduction of 50% to 80% in the number of relapses, such treatments may also result in significant adverse consequences for patients, because they suppress parts of the immune system. These adverse side effects include opportunistic infections, which could turn out to be serious, as well as an increased risk of cancer. Older immunomodulator treatments, such as interferon and Copaxone®, which, on average, cause a reduction of 30% in the number of relapses and have a more manageable risk profile, held 23% of the global MS market in 2020, down from 42% in 2017, primarily as a result of the pricing pressure exerted by biosimilars of older treatments that have moved off-patent. The reduction in the number of relapses in the RRMS form, however, seems to have little or no long-term impact on the progression of disability[12]. Treating all forms of MS with safe and effective medications able to stop this slowly evolving chronic disease, therefore continues to represent a huge unmet medical need.

In MS, HERV-W ENV has been identified as a potential key factor fueling the inflammatory and neurodegenerative components of the disease in all its forms, most recently in a publication in the Proceedings of the National Academy of Science[13]. The Company believes that temelimab is the first treatment against a suspected causal factor of MS, and, as such, temelimab has the potential to offer a safe and effective treatment that does not affect the patient's immune system, and which could slow or even stop disease progression in all major forms of MS.

GeNeuro initiated in early 2016 a 48-week, multicentric Phase IIb double-blind placebo-controlled study to test its temelimab drug candidate in 270 patients in 50 clinical centers and 12 countries in Europe. This clinical trial, called "CHANGE-MS", was funded through GeNeuro's former partnership with Servier. Three doses were tested: 6 mg/kg, 12 mg/kg and 18 mg/kg, via intravenous injections every 4 weeks. The Company presented 24-week results (including the study's primary endpoint) in August and October 2017, as well as full 48-week results in March 2018.

Whilst the CHANGE-MS study confirmed the safety profile of temelimab, the primary outcome at 24 weeks, which measured inflammation through the reduction of the cumulative number of Gd+ lesions[14], did not reach statistical significance. This could be due to the mode of action of the drug, which neutralizes a pathogenic factor but does not have an immediate impact on active adaptive immunity cells. However, at CHANGE-MS completion at 48 weeks, data showed that temelimab administration had a significant, consistent positive impact on key neuroprotection markers known to be linked to disease progression, such as reduction of brain atrophy, reduction of the number of chronic black holes (permanent tissue damage) and stabilization of MTR values (a measure of myelin integrity). At the ECTRIMS congress in Berlin in October 2018, the Company presented further analysis of the CHANGE-MS 48-week results that showed that the neuroprotective effects of temelimab were at least as prominent in the inactive subpopulation, i.e., without inflammation, which is the precise group of patients who are not served well with currently-available disease modifying treatments.

Furthermore, the patients who had completed CHANGE-MS were offered to continue treatment with temelimab in an extension study called ANGEL-MS. 95% of these patients elected to continue treatment, or a total of 219 patients. The study was originally planned to last two years, but had to be interrupted when Servier stepped out of its partnership with GeNeuro. Nevertheless, 154 patients had already completed 96 weeks of treatment (including the 48 weeks of CHANGE-MS), and over 90% had over 86 weeks of treatment, providing a solid basis for evaluating the effect of longer treatment with temelimab.

The topline results of ANGEL-MS after a total of 96-weeks[15] of treatment were presented on March 12, 2019. These results showed 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 IIb study. This includes reductions in brain atrophy, particularly in the cortex and thalamus, and maintenance in myelin integrity, as

8 Source: United States National MS society
9 FDA Press release on Siponimod approval, March 26, 2019
10 ibid
11 Source: 2019 annual reports of companies active in this field
12 Source: Ebers et al.: study of 730 patents over a period of 28 years
13 Kremer, Gruchot et al., PNAS, May 2019
14 Gd+: gadolinium-enhancing lesions, as measured by MRI
15 48 weeks of CHANGE-MS + 48 weeks of ANGEL-MS

measured by magnetization transfer ratio ("**MTR**") imaging, a marker of remyelination. 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. At the same time, confirming the missed primary endpoint results at 24-weeks, the study showed that temelimab had only a modest effect on neuroinflammation, as evidenced by a non-significant reduction in the number of T2 lesions. As a result, the positive results observed on reduction of neurodegeneration and maintenance of neuro-regeneration appear to indicate that the effect of temelimab is not mediated by inflammation and that, in a highly encouraging way, temelimab appears to be active against the clear unmet medical need in MS, which is neurodegeneration in all forms of the disease. The CHANGE-MS and ANGEL-MS results also provide the first evidence of the effect from neutralizing a pathogenic HERV protein in an autoimmune disease, opening the way to multiple applications in other autoimmune and neurodegenerative diseases. For a more detailed review of the results, please refer to sections 5.2.4.4 and 5.2.4.8 of the Universal Registration Document.

Based on the 96-week results of CHANGE-MS and ANGEL-MS, the Company has defined the development path forward for temelimab in MS. As the impact of temelimab on MRI markers associated with disease progression indicate a very high potential against the key unmet medical need in MS: curbing the progression of disability.

GeNeuro is therefore focusing on neurodegeneration and disease progression, which could be as a monotherapy for "non-active"[16] progressive patients, or as an adjunctive therapy for remitting patients in combination with existing immunomodulatory drugs addressing neuroinflammation, such paths being non-exclusive. In conjunction with this assessment, the Company has completed a Phase 1c pharmacology study of temelimab at high doses, up to 110 mg/kg, supporting the use of higher doses or temelimab in future clinical trials.

In this connection, GeNeuro announced on November 20, 2019, an agreement with the Karolinska Institutet / Academic Specialist Center (ASC) of Stockholm to launch a new single center Phase II clinical study of temelimab in multiple sclerosis. This new trial is conducted at the Center for Neurology of ASC, which, with approximately 2,400 patients, is the largest MS center in Sweden. The one-year trial has enrolled 40 patients whose disability progresses without relapses, and will document the safety and tolerability of temelimab following higher doses, as well as measures of efficacy based on the latest biomarkers associated with disease progression, including MRI measurements of brain atrophy, black holes (permanent damage), change in myelin integrity by magnetization transfer ratio, markers of myelin integrity and myelin fraction (REMyDI[17]), and markers of neurodegeneration and neuroprotection in biofluids such as Neurofilament Light Chains. The study (the "Karolinska Trial") aimed to start enrolling patients in Q1 2020 with last patient out and expected top line results in H2 2021; however, due to the COVID-19 crisis, the launch of the trial was delayed by approximately three months. The first patient was included in the study in June 2020 and the Company announced on February 18, 2021, that it had completed patient recruitment ; the Company now expects that results will be communicated in Q1 2022.

GeNeuro is in parallel continuing its partnership discussions that could, if positive, lead to the launch of an additional Phase II/III combination or "on top of" trial in MS, in patients with disease progression but without relapses due to a treatment with an existing anti-inflammatory drug.

In all cases, a successful Phase II or II/III trial would open the way to a Phase III registration trial in MS.

Given the high costs of the international clinical trials necessary to confirm efficacy and register a product in MS with both the FDA and the EMA, which the Company estimates to exceed €100 million per Phase III trial, exclusive of additional registration costs, the Company is actively pursuing partnership discussions for the MS indication at the same time as it is working on the design of potential future clinical trials in the progressive forms of MS, aiming to further validate the Company's therapeutic potential in the unmet medical need of stopping disease progression. These trials could include a Phase II in "non-active progressive patients" to extend the knowledge of temelimab's action in this untreated population, a Phase II/III registration supportive or enabling trial (depending on results) or Phase III trials. Subject to the results of a Phase II/III trial, the Company could be required to conduct an additional Phase III clinical trial before it would be in a position to file for registration.

COVID-19

COVID-19 is the most severe global pandemic since the influenza pandemic of 1918. As of April 20, 2021, there have been over 140 million confirmed cases and over 3 million global deaths from COVID-19. The risk of mortality increases with age (estimated to be ~0.1% for individuals aged 0-19, ~6% for individuals over age 60). Risk of severe disease and mortality increase for persons with pre-existing diseases or comorbid conditions (e.g. cardiovascular disease, diabetes, chronic lung disease, obesity), and hospitals worldwide continue to face the increasing demand of patients requiring oxygen supply, ventilators, and intensive care. SARS-CoV-2 is the novel coronavirus first identified in humans in December 2019 and is the cause of COVID-19. Coronaviruses are a large family of viruses that can cause illness in animals or humans. In humans there are several known coronaviruses

[16] Defined as MS patients experiencing progression of disability independent of the relapse activity
[17] Rapid Estimation of Myelin for Diagnostic Imaging, an MRI based method for automatic quantification of myelin volume in the brain.

that cause respiratory infections. These coronaviruses range from the common cold to more severe diseases such as severe acute respiratory syndrome (SARS), Middle East respiratory syndrome (MERS), and COVID-19.

Both pulmonary and extra-pulmonary SARS-CoV-2-related forms have been recognized[18], which predominantly involve the impairment of immune functions[19]. Innate immune hyper-activation combined with adaptive immune dysregulation has been recognized to play a critical role in the progression of the disease and thus in the clinical outcome of COVID-19 patients,[20,21] suggesting the critical evolution driven by exacerbated innate immunity and associated inflammation and lymphopenia[22,23]. The immunological involvement includes hyper-immune reactions such as the "cytokine storm" syndrome (mostly occurring in pulmonary forms), the pediatric multisystem inflammatory syndrome, and immune-mediated cutaneous or neurological diseases along with various autoimmune manifestations such as the dysregulation of coagulation mechanisms[24,25].

In addition, large numbers of patients who have been infected with SARS-CoV-2 continue to experience a constellation of symptoms long past the time that they've recovered from the initial stages of COVID-19 illness. Often referred to as "Long COVID", these symptoms, which can include fatigue, shortness of breath, "brain fog", sleep disorders, fevers, gastrointestinal symptoms, anxiety, and depression, can persist for months and can range from mild to incapacitating. These present before, during, and after respiratory symptoms and are unrelated to respiratory insufficiency, suggesting independent brain damage. In some cases, new symptoms arise well after the time of infection or evolve over time. Follow-ups conducted in Germany and the United Kingdom found post–COVID-19 neuropsychiatric symptoms in 20% to 70% of patients, even in young adults, and lasting months after respiratory symptoms resolved[26].

A recent study, published in the Lancet's EBioMedicine under the title "Evidence of the pathogenic HERV-W envelope expression in T lymphocytes in association with the respiratory outcome of COVID-19 patients", shows that HERV-W ENV is found on lymphocytes of hospitalized patients with COVID-19, and that its level of expression is associated with disease severity[27]. Until this study, the highly pro-inflammatory HERV-W, usually found in specific disease situations, mostly in the brain, had never before been observed circulating in the body at high levels and, in particular, was never seen expressed in T-lymphocytes. Understanding the mechanisms leading from SARS-CoV-2 infection to severe disease is critical for the development of effective treatments. The identification of the association between HERV-W ENV expression and inflammatory and immune dysfunction in COVID-19 opens an avenue for further investigation of its role as a trigger of detrimental immune response and potential target for therapy.

In a parallel effort supported by the French National Research Agency (ANR), GeNeuro, working in collaboration with the International Center for Infectiology Research in Lyon, France (CIRI) started research to understand why HERV-W ENV was found at high levels in the blood of hospitalized COVID-19 patients. Preliminary findings, available online on Research Square[28], show that when human peripheral blood mononuclear cells from healthy donors were cultured and exposed to SARS-CoV-2, about 20% of donors responded by expressing HERV-W ENV in lymphocytes, cells in which the virus did not replicate. This expression was triggered specifically by the spike protein of SARS-CoV-2, independently from cytokine release. This research suggests a genetic and/or epigenetic susceptibility associated to the activation of HERV-W ENV in blood lymphoid cells, which could be important in understanding how SARS-CoV-2 infection may lead to severe forms of COVID-19 in some patients.

These findings, combined with the known pro-inflammatory properties of the HERV-W ENV protein, may shed a new light on the development of severe forms of COVID-19, and may also offer an unforeseen opportunity to stop this evolution through a novel therapeutic approach.

HERV-W ENV is found in specific disease situations, and its presence is always tied to negative disease outcomes for the patient. The pro-inflammatory effects of HERV-W ENV are mediated through the activation of the TLR4 innate immune receptor, a pathway closely associated with some of the key features of COVID-19, such as hyper-activation of immune functions, endothelial cell activation, vasculitis as well as coagulopathy. HERV-W ENV has mostly been studied in neurodegenerative diseases, with widely observed pathogenic effects on peripheral and central nervous system cells. The presence of HERV-W ENV in COVID-19 patients may have a double effect: in

18 Gupta et al. Extrapulmonary manifestations of COVID-19. Nat Med 20202
19 Vardhana SA, Wolchok JD. The many faces of the anti-COVID immune response. J Exp Med 2020;
20 Wang J, Jiang M, Chen X, Montaner LJ. Cytokine storm and leukocyte changes in mild versus severe SARS-CoV-2 infection: Review of 3939 COVID-19 patients in China and emerging pathogenesis and therapy concepts. J Leukoc Biol 2020
21 Cao X. COVID-19: immunopathology and its implications for therapy. Nat Rev Immunol 2020
22 Zhang et al. Viral and host factors related to the clinical outcome of COVID-19. Nature 2020
23 Huang I, Pranata R. Lymphopenia in severe coronavirus disease-2019 (COVID-19): systematic review and meta-analysis. J Intensive Care 2020
24Mehta et al. COVID-19: consider cytokine storm syndromes and immunosuppression. Lancet 2020
25 Nath A, Smith B. Neurological issues during COVID-19: An Overview. Neurosci Lett 2021
26 Woo et al. Frequent neurocognitive deficits after recovery from mild COVID-19. Brain Commun. 2020
27 Balestrieri E, Matteucci C et al, Evidence of the pathogenic HERV-W envelope expression in T lymphocytes in association with the respiratory outcome of COVID-19 patients, Lancet EBioMedicine, April 2021
28 Charvet B, Horvat B et al, SARS-CoV-2 induces transcription of human endogenous retrovirus RNA followed by type W envelope protein expression in human lymphoid cells, ResearchSquare, April 2021.

the short-term, when activated in genetically susceptible individuals, HERV-W ENV could act as an accelerant to the innate immune response, fueling complications and leading to the need for ventilation. But even after the primary infection is over, if HERV-W ENV has reached a self-fueling expression level, it could cause persistent damage to endothelial cells in blood vessels and also to cells from the peripheral and central nervous system, which could explain many of the long-term neurological symptoms experienced by patients long after SARS-CoV-2 infection.

As the leaders in the HERV field and with HERV-W ENV as a possible aggravating agent of COVID-19, GeNeuro has started working with leading medical centers in Europe and the USA to evaluate temelimab as a therapeutic treatment, both to prevent immune system hyper-activation in recently infected patients, as well as to tackle severe neurological and psychiatric syndromes in long-COVID patients.

Type 1 Diabetes

Type 1 diabetes is a chronic disease that results from the autoimmune destruction of the insulin-producing beta cells in the pancreas. As a result, the pancreas produces little or no insulin, a hormone needed to allow sugar (glucose) to enter cells and produce energy. T1D is the major type of diabetes in children, accounting for over 85% of all diabetes cases in people under the age of 20 worldwide. In general, the incidence rate increases from birth and peaks between the ages of 10–14 years during puberty. Data from large epidemiologic studies worldwide indicate that the incidence of T1D is increasing and that the prevalence of T1D is approximately one person out of 300 in the United States by 18 years of age, with approximately 1.8 million cases diagnosed in the United States. T1D is distinct from the more common type 2 diabetes, which occurs when the body becomes resistant to insulin, a condition generally associated with lifestyle, with onset predominantly in adulthood.

There is no cure today for T1D, but insulin replacement therapy for life allows patients to manage the condition. Yet even with careful management, long-term complications generally develop over decades as a result of fluctuations in blood sugar levels. Serious long-term complications include heart disease, stroke, kidney failure, foot ulcers, and damage to the eyes. Due to the absence of a disease modifying therapy in T1D, this could position temelimab as a first line treatment in this indication.

In T1D, HERV-W ENV was detected post-mortem in the pancreas over 60% of patients, was observed to cause a dose dependent disruption of insulin production in vitro, and was demonstrated to be able to induce hyperglycemia and hypoinsulinemia in rodents. These findings were published in 2017 in the Journal of Clinical Investigation Insights[29]. By blocking pHERV-W in the pancreas of affected patients, GeNeuro hopes to slow down or stop the process of destruction of the pancreas' insulin-producing beta cells. Attenuating the decline in beta cell function should improve glycemic control and reduce the risk of hyperglycemia. If the effect is profound and sustained, reduction or delay of severe diabetic complications could be expected.

GeNeuro completed a Phase IIa clinical trial of temelimab in 64 T1D patients in Australia. The primary endpoint of this Phase IIa trial was safety in this new patient population, but key secondary endpoints included pharmacodynamic measures to assess the number of hypoglycemic episodes, the maintenance of insulin production (C-peptide) and other T1D-related biomarkers such as insulin consumption, glycated hemoglobin, glycaemia, and anti-beta cells antibodies. Results at the end of the 24-week study period, confirmed at 48 weeks at the end of the extension period, showed a very good safety and tolerability profile of temelimab in T1D patients, in addition to the observation of some encouraging signals, such as a 32% reduction in the total number of hypoglycemic episodes in the treated group versus placebo ($p<0.0001$) or a 21% decrease of anti-insulin antibodies in the treatment group, versus an increase of 23% in the placebo group ($p<0.01$). But given the low occurrence of events in this well-controlled population and the small size of the Phase IIa cohort, these positive signals require confirmation through investigation in larger pediatric populations with a more recent onset of disease.

CIDP

Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) is a rare autoimmune disorder of the peripheral nervous system ("**PNS**") characterized by the destruction of the fatty protective covering (myelin sheath) around nerves due to local inflammation of the nerve roots. As transmission of nerve signals is affected, patients suffer from weakness and impairment of motor function, particularly in the arms and legs. CIDP is related to multifocal inflammation and demyelinating lesions of the proximal PNS. Existing CIDP therapies are intravenous human immunoglobulins ("**IVIG**"), corticosteroids and plasma exchange. Long-term therapy is often limited by side effects and one-third of patients are refractory to existing treatments. This illustrates a critical unmet medical need for new treatments of CIDP and diagnostic biomarkers in this indication, which could position temelimab as a first line treatment in CIDP.

In the PNS, Schwann cells play a central physiological role. Whilst they are the myelinating cells of the PNS, they can also be activated by pathogenic agents to recruit proinflammatory immune cells. Several studies have confirmed

[29] Source: Levet S, Medina J, Joanou J et al. An ancestral retroviral protein identified as a therapeutic target in type-1 diabetes. JCI Insight. 2017 Sep 7;2(17). pii: 94387.

that HERV-W ENV is found in half of CIDP patients and that this protein is expressed on Schwann cells in CIDP lesions[30]. The effects of HERV-W ENV expression have been studied in vitro on cultured human Schwann cells. Cells expressing HERV-W ENV presented a strong and significant increase in IL-6 and CXCL10 transcript levels, which are both pro-inflammatory. In the US, based on a prevalence rate of 9 cases per 100,000, the total estimated prevalence of CIDP in 2010 was 27,810 patients.

Temelimab has received an Orphan Drug Designation ("**ODD**") from the US FDA in the treatment of CIDP, which allows GeNeuro to consider its next steps. An ODD may enable its recipient to obtain the following advantages for the development of the product:

- a 50% tax credit on the cost of clinical trials undertaken in the USA;
- a seven year period of marketing exclusivity following the marketing approval;
- some written recommendations provided by the FDA concerning clinical and preclinical studies to be completed in order to register the new drug;
- a fast-track procedure for the FDA to evaluate registration files.

Inflammatory Psychosis

Inflammatory psychosis includes schizophrenia ("**SCZ**") and bipolar disorder ("**BD**") observed in patients presenting an inflammatory syndrome marked with an increase in C-reactive protein[31]. Schizophrenic symptoms include hallucinations, delusions, paranoïa leading to social withdrawal; BD is characterized by episodes of agitation and elation or depression.

About 1% of the population worldwide suffers from psychotic disorders, and no curative treatments exist today: antipsychotic drugs or mood stabilizers are symptomatic treatments but frequently these drugs do not prevent mental handicap and social withdrawal, and have severe side effects.

HERV-W ENV and GAG proteins are increased in the PBMC and serum of 50% to 60% of patients with SCZ and BD correlated with an increase of C-reactive protein. HERV-W genes and proteins are expressed in the cortex of patients with psychotic disorders[32]. It has also been evidenced that demyelination due to HERV-W Env could participate in the neuropsychiatric dysfunction [33]. HERV-W can be triggered by viruses or bacteria such as Influenza, Herpes or T gondii, germs which are epidemiologically associated with SCZ.

GeNeuro has ongoing collaborations with research centers in France (Créteil and Bordeaux) on epidemiological studies and animal models of psychotic disorders, with the objective to achieve a preclinical proof-of-concept with a clear strategy to enter clinical trials. This has led to a translational study, published in Science Advances [34], which found that HERV-W proteins, which have been previously found in patients with inflammatory psychosis, such as schizophrenia and bipolar disorders, induce glutamate receptor disorganization and behavioral deficits in vitro and in vivo. This leads to disruption of synaptic glutaminergic communication and results in the emergence of psychosis symptoms, allowing to establish a clear link between the presence of a human endogenous retrovirus envelope protein and corruption of nerve pathway development. This leads to disruption of synaptic glutaminergic communication and results in the emergence of inflammatory psychosis symptoms.

ALS

The scientific corpus supporting the involvement of HERVs in poorly understood diseases is growing, and GeNeuro is working with leading research centers in the United States and Europe to apply this technology to the treatment of other human diseases where HERVs could also be playing a key role and which are still incurable, such as amyotrophic lateral sclerosis ("**ALS**"), which is a motor neuron disease that occurs most often as a sporadic disease with no known cause or inheritance pattern. In ALS, the Company entered into a Cooperative Research And Development Agreement with the US National Institutes of Health in February 2017 and has signed in October 2018 an exclusive worldwide license with the National Institute of Neurological Disorders and Stroke (NINDS), part of the U.S. National Institutes of Health (NIH). The agreement covers the development of an antibody program to block the activity of pHERV-K ENV (pathogenic envelope protein of the HERV-K family of Human Endogenous Retroviruses), a potential key factor in the development of ALS.

[30] Source: Faucard R, Madeira A, Gehin N et al. Human Endogenous Retrovirus and Neuroinflammation in Chronic Inflammatory Demyelinating Polyradiculoneuropathy. EBioMedicine. 2016 Apr;6:190-198

[31] Source: Huang et al. Human endogenous retroviral pol RNA and protein detected and identified in the blood of individuals with schizophrenia. Schizophr Res. 2006

[32] Source: Karlsson et al. Retroviral RNA identified in the cerebrospinal fluids and brains of individuals with schizophrenia. Proc Natl Acad Sci U S A. 2001

[33] Source: Qin et al. Elevation of Ser9 phosphorylation of GSK3beta is required for HERV-W env-mediated BDNF signaling in human U251 cells. Neurosci Lett. 2016.

[34] Science Adv. Human endogenous retroviral protein triggers deficit in glutamate synapse maturation and behaviors associated to psychosis. E. M. Johansson, D. Bouchet, R. Tamouza, P. Ellul, AS. Morr, E. Avignone, R. Germi, M. Leboyer, H. Perron, L. Groc

Possible commercialization and marketing timelines
GeNeuro estimates that the potential sale of its lead product candidate, temelimab for MS, could, considering its development schedule, the receipt of regulatory authorizations and the commercialization and marketing of its product candidate, commence between 2025 and 2027, subject to the success of one or several Phase III trials, the absence of any event delaying the proper conduct of the trials, and the absence of other events that the Company is currently unable to identify or anticipate.

5.1.1 Competitive Advantages

GeNeuro's competitive strengths are rooted in its novel approach against autoimmune and neurodegenerative diseases, supported by strong IP and an experienced executive team with a strong track record.

- **Temelimab has the potential to slow down or stop the progression of the disease in several autoimmune indications**. By neutralizing HERV-W ENV, a protein believed to be a causal factor in pathologies such as MS, T1D and CIDP, GeNeuro could open a new avenue for safe and effective treatments addressing the key common unmet medical need in these indications: tackling the progression of the disease. As such, temelimab targets a huge unmet medical need and, in case of success, would have a clear differentiation relative to and/or in combination with existing treatments.
- **Temelimab has demonstrated its potential to offer a therapeutic option of great value for patients suffering from MS**. No presently available treatment has yet demonstrated a major impact on the progression of long-term disability for any form of MS. By blocking upstream a potential key factor present in all types of MS that fuels both inflammation and neurodegeneration, temelimab may provide a safe and effective treatment for all major forms of the disease, with the potential to reduce or stop progression towards disability. The 96-week Phase II data showed that temelimab administration had a significant, consistent positive impact on key neuroprotection markers known to be linked to disease progression. This is the first time that the benefit of a treatment targeting endogenous retrovirus protein is shown in a clinical trial.
- **Recent findings on the link between HERV-W ENV and COVID-19 open the avenue to a new potential target for therapy.** With HERV-W ENV as a possible aggravating agent of COVID-19, temelimab, with its excellent safety and tolerability profile, might be used as a therapeutic treatment, both to prevent immune system hyper-activation in recently infected patients, as well as to tackle severe neurological and psychiatric syndromes in long-COVID patients. While vaccination and the early administration of neutralizing SARS-CoV-2 drugs (e.g., anti-spike-protein antibodies) will diminish the number of severe cases in the medium term, the world will have to continue living with the virus and its variants over the long-term; furthermore, the very high number of already infected patients displaying long-term symptoms, mostly neurological, represent a huge unmet medical need.
- **Temelimab could become the first disease-modifying-therapy in T1D**. While insulin therapy helps patients to control their glucose levels, there is no disease-modifying therapy in this indication today. 50% of adults with T1D have a glycated hemoglobin above 8%, which is a prognosis for severe consequences including renal, ophthalmic, cardiac, vascular and nervous system dysfunctions and deficiencies. The key unmet medical need targeted by temelimab is to help preserve the endogenous-insulin production capacity of the patient, by neutralizing a causal factor of the disease.
- **GeNeuro has full worldwide rights to temelimab**. GeNeuro has full worldwide ownership of all rights to temelimab and has all options open for geographic and/or indication-specific partnerships to develop its lead compound worldwide, as a single agent for patients with progressive forms of MS, or in combination with existing therapies for relapsing forms of the disease.
- **Broad and strong intellectual property supports GeNeuro's first mover advantage in the HERV space**. GeNeuro's leadership position in the HERV space is supported by its acknowledged expertise in the field and a portfolio of 17 patent families that cover Europe, the United States, and other major markets. These patents (owned or under exclusive license from bioMérieux-Inserm, or with the NIH for HERV-K) cover antibodies targeting HERV-W ENV in the treatment of a wide range of therapeutic indications including MS, CIDP and T1D and targeting pHERV-K ENV in the treatment of ALS. GeNeuro believes that the scope and quality of its patent portfolio give it a strong competitive position in the area of HERV-W ENV and contribute to protecting GeNeuro's first-mover advantage as a leader in HERV-mediated diseases.
- GeNeuro has an experienced and highly synergistic management team assisted by internationally renowned scientific and medical advisors. GeNeuro has assembled a talented team of professionals with complementary skills who have demonstrated during the last ten years their ability to move research from the laboratory to the clinic. The Company's management is supported by a team of internationally renowned experts who assist on scientific and strategic matters. As key opinion leaders ("KOLs") in their respective fields, they help to promote temelimab in the scientific, medical, and patient communities.
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5.1.2 Company Strategy and Objectives

GeNeuro's strategy is to continue the development of temelimab to make it available as soon as possible to patients affected with MS, to initiate clinical trials in COVID-19, subject to funding, and to continue leveraging its lead in the HERV field to bring closer to the clinic new products in areas of high unmet medical need such as ALS or T1D.

GeNeuro's assessment of the 96-week results of its MS trials, in discussions with potential partners and key medical opinion leaders, makes clear that the impact of temelimab on MRI markers associated with disease progression indicates a very high potential against the key unmet medical need in MS: curbing the progression of disability.

GeNeuro is therefore focusing on neurodegeneration and disease progression, which could be either as a monotherapy for "non-active" progressive patients, or as an adjunctive therapy for remitting patients in combination with existing immunomodulatory drugs addressing neuroinflammation, such paths being non-exclusive. In conjunction with this assessment, the Company has completed a Phase 1c pharmacology study of temelimab at high doses, up to 110 mg/kg, supporting the use of higher doses or temelimab in future clinical trials.

Given the high costs of the international clinical trials necessary to confirm efficacy and register a product in MS with both the FDA and the EMA, which the Company estimates to exceed €100 million per Phase III trial, the Company continues to pursue partnership discussions for the MS indication at the same time as it is working on the design of potential future clinical trials in the progressive forms of MS, aiming to further validate the Company's therapeutic potential in the unmet medical need of stopping disease progression. These trials include the karolisnka Trial, a currently on-going Phase II study on a small cohort of "non-active progressive patients" to extend the knowledge of temelimab's action in this untreated population, or Phase III trials.

Key elements of the Company's strategy include:

- **Continue the development of temelimab in MS**. Since publication in March 2019 of the 2-year results of its Phase IIb clinical trials (CHANGE-MS and ANGEL-MS), which were presented in more detail in September 2019 at the ECTRIMS congress in Stockholm, Sweden, GeNeuro has worked on the design of further Phase II and Phase III studies in the progressive forms of MS, likely to include higher doses of temelimab as supported by the results of the Phase 1c pharmacology study which have been communicated in January 2019. Such further studies would aim at furthering temelimab towards registration in MS with both the FDA and the EMA. GeNeuro is currently working on the development plan for temelimab in MS, which, subject to the outcome of partnership discussions and/or to its financial resources, could include:
- A monotherapy approach, in non-active progressive MS patients, where the unmet medical need is the highest; and
- A combination approach, in conjunction with an existing anti-inflammatory drug, to slow-down or prevent progression for relapsing MS patients, an area in which current treatments have modest impact.
- Regulatory authorities, such as the FDA, and the MS community have clearly identified "progression without relapses" as the urgent medical need in MS. GeNeuro's temelimab results indicate a true potential in this area where there is no medication available, and thus has a wide number of options on how to continue development in MS. Yet developing a drug against progressive forms of MS is a complex endeavor, as patients' condition evolves slowly over time, and clinical trials require large cohorts treated for long periods of time. Inclusion criteria for such trials aimed at having homogenous patient populations are a key success factor, and GeNeuro may have to execute smaller Phase II trials to ensure that it maximizes the chances of success of its future global Phase II/III or Phase III trials.
- In this connection, GeNeuro has launched a new clinical study of temelimab in multiple sclerosis, conducted at the Center for Neurology of the Karolinska Institutet / Academic Specialist Center (ASC) of Stockholm, Sweden, (which, with approximately 2,400 patients, is the largest MS center in Sweden). The one-year trial has enrolled 40 patients whose disability progresses without relapses, and will document the safety and tolerability of temelimab following higher doses, as well as measures of efficacy based on the latest biomarkers associated with disease progression, including MRI measurements of brain atrophy, black holes (permanent damage), change in myelin integrity by magnetization transfer ratio, markers of myelin integrity and myelin fraction (REMyDI[35]), and markers of neurodegeneration and neuroprotection in biofluids such as Neurofilament Light Chains. The study aimed to start enrolling patients in Q1 2020 with last patient out and top line results expected in H2 2021; however, due to the COVID-19 crisis, the Company postponed this trial to prioritize healthcare resources behind the fight of COVID-19 and to reduce the risk for MS patients. Recruitment was eventually initiated in June 2020 and was completed on February 18, 2021; the Company now expects results for Q1 2022.
- **Initiate clinical trials with temelimab in COVID-19**. Recent findings published in the Lancet's EBioMedicine have shown the presence of HERV-W ENV on lymphocytes of hospitalized patients with COVID-19 and the correlation of the level of expression with disease severity; furthermore, recent data showed that SARS-CoV-2 is able to induce in vitro HERV-W ENV expression in human blood cells of approximately 20% of healthy

[35] Rapid Estimation of Myelin for Diagnostic Imaging, an MRI based method for automatic quantification of myelin volume in the brain.

volunteers. The known pro-inflammatory properties of HERV-W ENV are thought to act as an "accelerant" of the activation of the innate immune system, fueling the severity of COVID-19 evolution and impacting long term recovery. With HERV-W ENV as a possible aggravating agent of COVID-19, GeNeuro's temelimab could start tests against COVID-19 as early as the summer of 2021, subject to funding.

- **Advance new products into clinical trials**. The preclinical developments in ALS, conducted in partnership with the NIH, and in Inflammatory Psychosis, conducted in partnership with French academic research centers, have yielded positive results that are expected to validate the approach for new products with a clear clinical strategy. Following the signing in October 2018 of an exclusive worldwide license with the U.S. NIH, which covers the development of an antibody program to block the activity of pHERV-K ENV (pathogenic envelope protein of the HERV-K family of Human Endogenous Retroviruses), a potential key factor in the development of ALS, GeNeuro has initiated a preclinical development program for its pHERV-K ENV antibody. Given the current progress of this technologically difficult program and the development delays caused by the COVID-19 pandemic, the Company now believes that this product could enter the clinical stage in the second half 2022, subject to funding or to a partnership agreement.
- **Postpone the development of temelimab in T1D**. The full 12-month results of the Phase IIa trial were presented in May 2019; based on these results and having achieved the safety primary endpoint of this study, the Company is considering to engage with regulatory authorities to define the best way to bring forward a treatment that could be the first disease-modifying therapy in T1D. However, given that temelimab might be developed in two significantly different indications, T1D and MS, and given the current state of partnership discussions about temelimab in MS, the Company is not currently planning a study in T1D in the near term.
- **Postpone temelimab development in CIDP**. The Orphan Drug Designation granted by the US Food and Drug Administration in February 2018 is expected to facilitate interactions with the authorities to design a proof-of-concept study in this rare indication. However, given the difficulty of recruiting patients affected by this rare disease, the Company is not planning a study in CIDP in the near term.
- **Leverage the Company's HERV platform to develop other product candidates**. An increasing body of scientific literature suggests that different HERV families, such as HERV-W and HERV-K, may be involved in a variety of pathologies, as confirmed by the recent findings on COVID-19. GeNeuro will continue to proactively engage with leading academic teams worldwide to translate their discoveries into new treatments to serve very large unmet medical needs or to identify indications where temelimab might become a possible therapeutic approach.

5.1.3 A Novel Approach To Human Endogenous Retroviruses

When GeNeuro was formed in 2006, the idea that the non-coding part of human DNA ("junk" DNA) could express proteins was not broadly accepted by the scientific community. It was thought that junk DNA had no significance, and even today the majority of studies involving DNA focus on "coding" genes. It is now commonly accepted that the mobile genetic elements of junk DNA play a significant role in the evolution of the genome during a lifetime and have become a suspect in the development of numerous unexplained pathologies, such as cancer and autoimmune disorders.

HERVs are part of this family of mobile genetic elements and represent 8% of human DNA. HERV DNA sequences are probably the result of the integration of exogenous retroviruses into the genome and their transmission by the human germline during evolution. It is now understood that these genetic sequences have physiological and pathological effects. Although most HERV sequences do not code for functional proteins, the human genome does contain HERV sequences that have the potential to create functional proteins[36].

GeNeuro has taken advantage of the pioneering work of Dr. Hervé Perron, its founder and present Chief Scientific Officer, in the area of HERVs to develop the first drug against HERV-W ENV (initially called MSRV env), a HERV protein that appears to be strongly expressed in organs only in pathological conditions. GeNeuro was formed in 2006 on the basis of work done during 15 years at INSERM and Institut Mérieux on MSRV env, which is an envelope protein of a human endogenous retrovirus of the HERV-W family and which has been identified as a potential cause of MS.

5.2 HERV-W ENV in MS

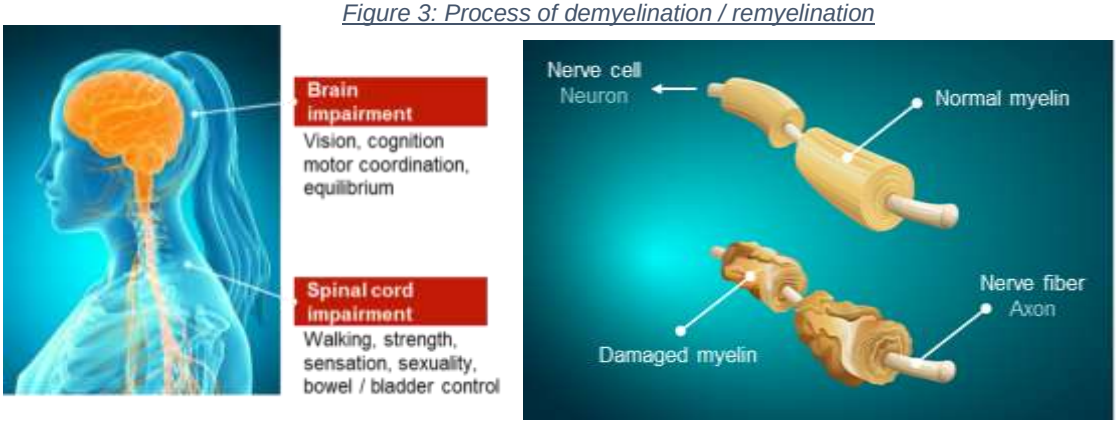
5.2.1 What is Multiple Sclerosis?

MS is a degenerative, inflammatory and chronic disease that affects the central nervous system, consisting of the brain and spinal cord. It generally first manifests itself in patients who are between 20 and 40 years of age. It is considered to be an autoimmune disease: persons suffering from MS have a disorder of the body's defense system. The immune system attacks the myelin sheath that protects nerve fibers and facilitates the transmission of nerve

[36] Source: "HERVs, the Enemy within", Nature Medicine, 2010, 15,415-422, Engel and Hiebert.

signals. The disorder causes complex autoimmune mechanisms to occur, the operation of which is still poorly understood, which attack cells responsible for creating the myelin sheath that protects the central nervous system. Thus, with MS, the myelin sheath does not facilitate the rapid transmission of nerve signals, which are slowed or even stopped: this situation is called demyelination.

Figure 3: Process of demyelination / remyelination



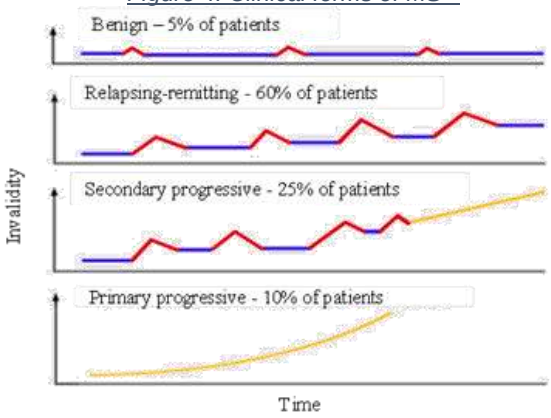
In 85% of cases, the disease takes the form of an initial phase of outbursts of inflammation that cause demyelination and provoke the appearance of various symptoms: motor problems tied to muscular weakness, sensitivity problems, cognitive problems, visual symptoms, or equilibrium problems. These various clinical signs may occur within hours or over a few days and disappear totally or partially in a few weeks as a result of neuronal function restoration. This biphasic disease course marked by alternating episodes of neurological disability and recovery is designated as relapsing remitting (the **relapsing remitting** form of MS or "**RRMS**").

After a few years, approximately 8 patients out of 10 diagnosed with RRMS see their condition evolve toward a **secondary progressive form** ("**SPMS**"). Isolated outbursts then occur, as with RRMS, but they are not followed by new remissions. In the first few years of this process, many patients continue to experience relapses, a phase of the disease described as active SPMS, which is one of the relapsing forms of MS. Later, many patients with SPMS stop experiencing new relapses, but disability continues to progress, a phase called non-active SPMS[37].

In approximately 10% of cases, the initial phase of outbursts and remissions does not exist, and symptoms worsen linearly from the onset of the disease. This clinical form of MS is called the **primary progressive form of MS** ("**PPMS**").

For 5% of patients, MS is benign.

Figure 4: Clinical forms of MS[38]



(i) Origin and Prevalence of the Disease

The exact origin of MS is still uncertain, despite significant research efforts for 20 years. Certain researchers assume that a combination of various infectious genetic or environmental factors could be the cause of MS. Some research suggests that a genetic predisposition could cause MS (more than 20 genes potentially involved have been identified in recent years). This would explain a more marked prevalence of the disease in European populations

[37] Source: https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm634469.htm
[38] Source: Figure taken from Sadiq S, Multiple Sclerosis, in Merrit's Neurology by Louis ED, Mayer SA, Rowland SP, Wolters Kluwer ed. 2015.

compared to Asia or Africa. Likewise, the risk of developing the disease for a first-degree relative of a MS patient is approximately 1.5% to 2.6%, whereas it is only 0.001% in the general population.[39]

Along with this genetic vulnerability, some environmental and infectious factors could influence the development of the disease. Even if it has not been possible to show a direct causal link between infection and MS, infectious factors such as the herpes virus family, including the Epstein Barr virus, which have a strong tropism for the brain, have been the subject of much research because of the frequent detection of them in patients suffering from MS.[40] These viruses of the herpes family have become the focus of attention of several epidemiological studies and, in particular, by observation of the occurrence of a high number of cases of MS in the Shetland Islands and Sardinia beginning in the second half of the twentieth century, when these populations are thought to have been exposed to viruses of the herpes family for the first time.[41]

It has also been observed recently that such viruses, particularly the Epstein Barr virus,[42] may activate endogenous retrovirus genes and trigger a process of expression of endogenous retrovirus proteins.[43] Endogenous retroviruses, therefore, could be the missing link between infectious factors and the onset of MS.

The prevalence of the disease differs rather significantly depending on geographic area:

- High prevalence zones (greater than 100 per 100,000)[44]: Canada, the United States, Scandinavia, Scotland, and northern Europe
- Average prevalence zones (approximately (approximately 50 to 100 per 100,000): Russia, France, central Europe, and the south Pacific
- Low prevalence zones (less than 20 per 100,000): southern Mediterranean, South America, and Asia.

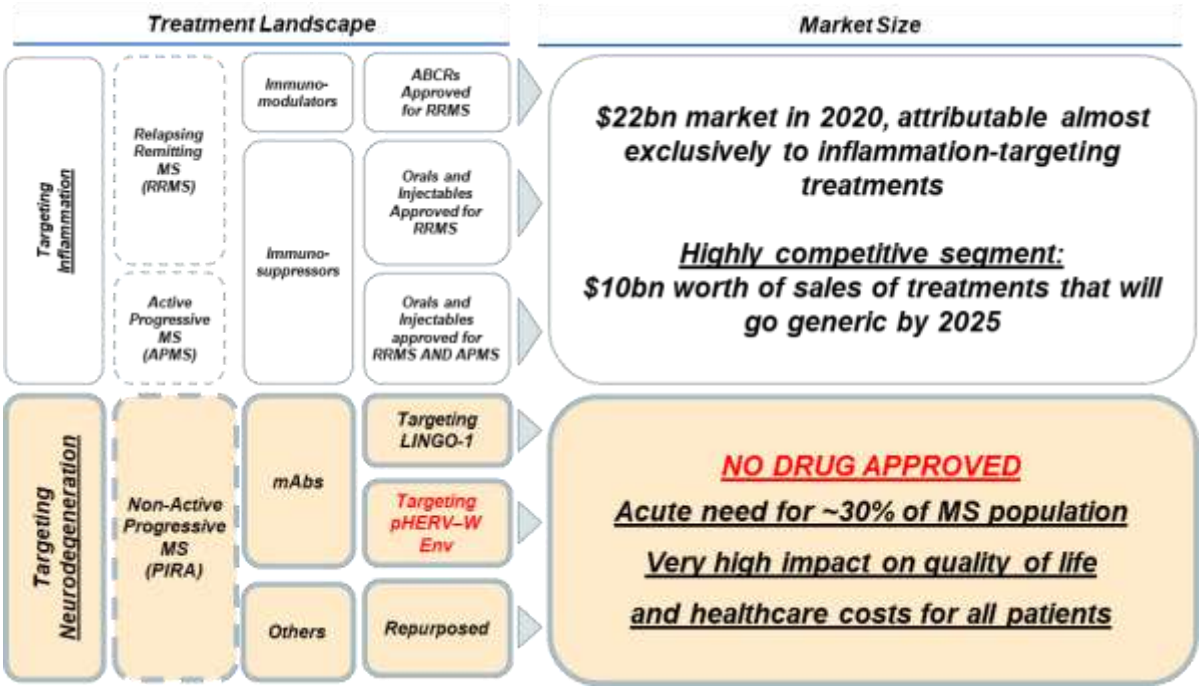
Causal factors such as passive exposure to tobacco during childhood or certain nutritional deficiencies are also suspected.

It is estimated that the number of patients in the world suffering from MS is approximately 2.5-3.0 million[45] with an average occurrence of one person out of 1,000 in Western countries. In the United States, a recently completed prevalence study, funded by the National MS Society, has estimated that nearly 1 million people over the age of 18 live with a diagnosis of MS[46]. MS mainly affects young adults and, more generally, women (in a ratio of two women for every one man affected with RRMS), and is the primary cause of non-traumatic severe handicap among 30-year-olds. The average age for the onset of symptoms is 30, and the first symptoms appear seven out of 10 times between the ages of 20 and 40 years.

It is believed that the progression of MS is fueled by a neuroinflammatory and a neurodegenerative process. During the Remitting phase of the disease, relapses are caused by inflammation in clinically-relevant areas of the brain, which remit partially or in full with the resolution of the inflammatory episode. In parallel, there is a neurodegenerative process from the start of the disease, characterized by axonal loss and brain atrophy, which drives the long term evolution of disability. The neurodegenerative process becomes paramount during the progressive phases of the disease, where MS patients suffer from the progression of their disability with very limited contribution from inflammatory episodes.

[39] Source: Sadiq, Multiple Sclerosis, in Merrit's Neurology by Louis ED, Mayer SA, Rowland SP, Wolters Kluwer ed. 2015.
[40] Source: Belbasis L, Bellou V, Evangelou E, Ioannidis JP, Tzoulaki I. "Environmental risk factors and multiple sclerosis: an umbrella review of systematic reviews and meta-analyses". *Lancet Neurol*. 2015 Mar;14(3):263-73. doi: 10.1016/S1474-4422(14)70267-4.
[41] Source: Sadiq 2015 *ibid*.
[42] Source: Mameli G, Madeddu G., Mei A, Uleri E, Poddighe L, Delogu LG, Maida I, Babudieri S, Serra C, Manetti R, Mura MS, Dolei A.: Activation of MSRV-type endogenous retroviruses during infectious mononucleosis and Epstein-Barr virus latency: the missing link with multiple sclerosis? *PLoS One*. 2013 Nov. 13; 8(11):e78474. doi: 10.1371.
[43] Source: Mameli *et al.*, 2013 *ibid*.
[44] Source: Atlas of MS 2013.
[45] Source: UK Multiple Sclerosis Trust, www.mstrust.org.uk.
[46] Source: US National MS Society

Figure 5– treatment landscape for Multiple Sclerosis



(ii) Present Treatments for MS

There is presently no treatment capable of curing MS or preventing its progression to disability in patients, but the treatments approved for this indication can treat symptoms and improve the quality of life. There are two major categories of approved medications, but there is no approved therapy targeting the neurodegenerative process of MS:

Disease Modifying Treatments ("DMTs") for MS mainly focus on the Remitting phase of the disease and belong to two therapeutic classes: the immunomodulators and the immunosuppressors, these two classes differentiating themselves by their risk-benefit profile.[47] The immuno-modulative and immunosuppressant treatments reduce inflammation by their action on immune system cells and have a role in the prevention of attacks in recurring-remitting forms. On the other hand, their long-term effect on neuro-degeneration, i.e., the progressive destruction of neurons, the dominant phenomenon of the progressive form of MS, has not been shown. As for the primary or secondary[48] progressive forms of the disease, only ocrelizumab has received, in March 2017, the FDA approval for the primary progressive form of MS, as well as for remitting relapsing forms of MS, followed by the approval in Europe in January 2018. Treatments for the relapsing-remitting forms of MS accounted for approximately USD 22 billion in sales in 2020.

Symptomatic treatments, which reduce the intensity of MS's symptoms, include: corticosteroids, like methyl prednisone, for example, which are used to attenuate symptoms in connection with an MS attack; baclofen or dantrolene or cannabinoids, which are used against spasticity; or fampridine, which is used to improve walking speed. These treatments are often given in addition to basic treatments, in a transitory or long-term manner. They have no proven impact, however, on the evolution of the disease.

Neuroprotective treatments, trying to address the neurodegenerative component of MS, are the frontier in the development of new therapies as they target the key unmet medical need in this disease: slowing down or stopping the progression of disability. There are a few treatments currently in clinical development, including temelimab, but none has been yet approved.

[47] Source: Curtin and Hartung, Expert Rev Clin Pharmacol. 2014 Jan;7(1):91-104.

[48] It should be noted that even though some treatments (beta-interferon) are registered for the treatment of RRMS, they are sometimes used to treat MS patients transitioning into SPMS, but who continue to have relapses; those treatments are only administrated on a transitional basis. Furthermore, the Mitoxantrone (Novantrone®) treatment, used in oncology (cytotoxic chemotherapy) for years, is prescribed for some SPMS patients showing severe progression between relapses, but only over a short period of a few months and with a defined maximum dose, considering its severe side effects (particularly with the increased risk of a subsequent occurrence of chronic lymphocytic leukemia and cardiac damage).

Presently available anti-inflammatory DMTs

Table 1: main treatments in the MS indication[49] - 2020

Self injectable (ABCRs)		
Name	Sales (in USD million)	Date of launch in Europe
Betaferon	485	1995
Avonex / Plegridy	1,878	1997 / 2014
Rebif	1,357	1998
Copaxone	1,356	2000
(incl. Generics)		2016
Total:	**5,076**	

Oral and intravenous		
Name	Sales (in USD million)	Date of launch in Europe
Tysabri	1 946	2006
Gilenya	3 003	2011
Aubagio	2 454	2013
Tecfidera	3 905	2014
Lemtrada	136	2013
Ocrevus	4 702	2017
Mavenclad	637	2017
Mayzent	170	2019
Kesimpta	15	2021
Zeposia	12	2021
Total:	**16 980**	

Neuroprotective «Add-ons»		
Name	Sales (in USD million)	Date of launch in Europe
Ampyra	98	n.a.
Fampyra	103	2011
Total:	**201**	

GLOBAL TOTAL	**22 256**

The medications that have the least effect on the number of flare-ups, the self-injectables, (Avonex©, Betaferon©, Copaxone©, and Rebif© — the so-called "**ABCRs**"), introduced more than 15 years ago, are still fairly widely prescribed by neurologists, with 23% of sales in 2020 (with Plegridy©, included in the chart set forth above). Such products are immunomodulators, considered to be first-line treatments that change the inflammatory response, but which do not appear to reduce the immune response strongly and, therefore, have shown to have little impact on the patient's resistance to infections or cancers. The efficacy on the frequency of attacks is moderate, but the adverse effects profile is relatively favorable for this category of treatment.

Oral and intravenous medications that arrived more recently on the market (for example, Tysabri© in 2006, Gilenya© in 2011, Tecfidera© in 2014, Ocrevus in 2017, Mavenclad and Mayzent in 2019, Kesimpta in 2020 in the USA) appear to offer more effective results for the management of flare-ups, but their stronger effect on the immune system also involves potentially larger issues with side effects, by reducing a patient's defenses against opportunistic infections that can become serious and may also be associated with an increased risk of cancer.

Finally, while some of these treatments have shown a delay in the risk of disability progression during clinical trials, these results appear to be driven by inflammation and none of these DMTs appears to diminish in a determining manner the long-term progression of the disease towards disability. The total number of attacks does not seem to influence the moment of evolution to the secondary progressive phase in patients or the accumulation of disabilities over the long term.[50]

Concerning the treatment of progressive forms of MS, to date only one anti-inflammatory DMT (ocrelizumab) has been approved for the primary progressive form of MS. New treatments recently approved, such as cladribine (Mavenclad) in 2017, siponimod (Mayzent) in 2019, ponesimod (Ponvory), ofatumumab (Kesimpta) or ozanimod (Zeposia) in 2020 are approved for patients with active secondary progressive MS, which the FDA considers to be one of the relapsing forms of MS[51]. The mechanism of action of these products is based on immunosuppression, and the publication of their clinical trial results[52] has shown that their effectiveness is driven by the level of inflammatory activity of the patient.

[49] Source : companies' 2020 annual reports.
[50] Source: Scalfari *JAMA Neurol*. 2013 Feb;70(2):214-22: study on 730 patients followed over a period of 28 years.
[51] Source: https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm634469.htm
[52] Source: Mulero et al., *Ther Adv Neurol Disord*. 2018 May 10.; Montalban et al., *N Engl J Med* 2017; Dumitrescu et al., Expert Opin Pharmacother. 2019 Feb

GeNeuro's management believes that these new products, while highly effective at reducing inflammation and the damage it creates, should not radically change the paradigm of MS treatment as they work exclusively through the inflammatory component of the disease. GeNeuro's lead candidate temelimab is not positioned as a competitor in this category of products, as it targets the neurodegenerative process that may be the key driver of disease progression.

New therapies targeting neurodegeneration

Treatment of neurodegeneration, particularly in progressive forms of MS, remains a very significant unmet medical need. In progressive forms of the disease, the inflammatory component seems to play a less significant part than in RRMS, as illustrated by the fact the recent immunomodulators such as ocrelizumab or siponimod have shown statistically significant results in progressive MS patients only in patient subgroups with an active inflammation[53], and thus appear to be beneficial only to patient subgroups which have some brain inflammatory activity. New approaches outside the known paths of immunosuppression and seeking to enhance remyelination, such as those represented by GeNeuro's temelimab will probably be necessary in order to provide new therapeutic solutions that specifically target the neurodegenerative component of the disease. Other efforts in this area include:

- **Ibudilast,** an anti-inflammatory drug, approved in Japan for asthma since 1989, is being developed by MediciNova for several neurodegenerative indications, including progressive forms of MS. Its proposed mode of action is through the inhibition of macrophage migration, decrease of TNFα, enhancing survival and maturation of oligodendrocytes. In the latest MS trial results presented at MSParis2017, the SPRINT-MS Phase IIb study recruited a total of 255 patients and showed that treatment with up to 100 mg/day led to a reduction in whole-brain atrophy of approximately 2.5 ml by 96 weeks, the primary endpoint. To our knowledge, further studies in MS have not yet been initiated.
- **Masitinib,** an orally administered tyrosine kinase inhibitor, is developed by AB Science for RRMS and progressive forms of MS and a number of other neurological, oncology and inflammatory diseases indications. In February 2020, AB Science announced the results of a study enrolling primary progressive and non-active secondary progressive MS, testing masitinib 4.5mg/kg/day and 6mg/kg/day vs placebo. Masitinib 4.5mg/kg/day versus placebo induced less progression in a statistically significant way on the primary endpoint which was a non-classical EDSS measure. The results were negative when comparing the highest dose of masitinib at 6 mg/kg/day vs placebo. A confirmatory Phase 3 study of masitinib in progressive MS patients is reportedly planned by AB Science.

2020 also saw the discontinuation of two major efforts in this area:

- **Opicinumab** was a monoclonal antibody neutralizing the protein LINGO-1 developed by Biogen with a remyelination and axonal protection objective. In October 2010, Biogen announced that the Phase II study of opicinumab failed to meet both its main and secondary goals and that Biogen was discontinuing the program.
- **D-Biotin** oral was vitamin B7 given at high dose (MD1003 or Qizenday© and was developed by the French company MedDay. In March 2020, the company announced that its second pivotal Phase III trial (SPI2) of its investigational product MD1003 had not met its primary and secondary endpoints.

With highly efficient anti-inflammatory drugs on the market, treating the neurodegenerative component of MS to slow down or hopefully be able to stop disease progression is the key unmet medical need in MS.

5.2.2 Pre-clinical research in Multiple Sclerosis

i) HERV-W ENV is Found in All Active MS Brain Lesions

HERV-W ENV was first isolated on the surface of leptomeningeal cells and macrophages from MS patients[54]. Immuno-histological and immuno-histochemical studies have since repeatedly shown that HERV-W ENV is found in 100% of the plaques of MS patients analyzed to date[55], in all forms of MS, from the earliest to the latest stages of disease. These studies have also shown that there is a correlation between the level of expression of the protein and the intensity of the lesion.

The illustration below shows how HERV-W ENV is present in the initial stage of a newly formed lesion. In Figure 6, the onset of demyelination may be observed by pallor in the enveloping cerebral tissue colored in brown, a phenomenon associated with the strong expression of HERV-W ENV positive macrophages, as shown in Figure 7.

[53] Source: FDA approval on siponimod: "In the subgroup of patients with non-active SPMS, the results were not statistically significant"
[54] Source: Perron, et al., Lancet 1991.
[55] Sources: Anthony et al. 2004; Garson et al., 2005; Mameli et al., 2007; Perron et al., 2012.

Figure 6: Zone of Demyelination

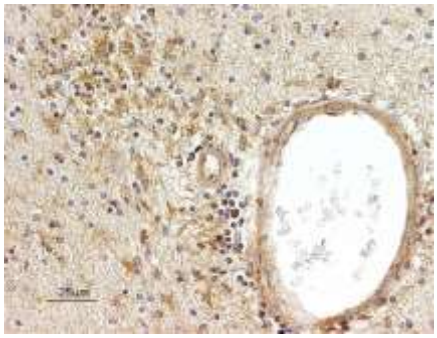
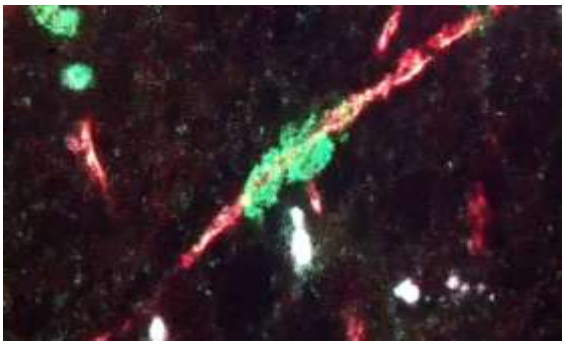
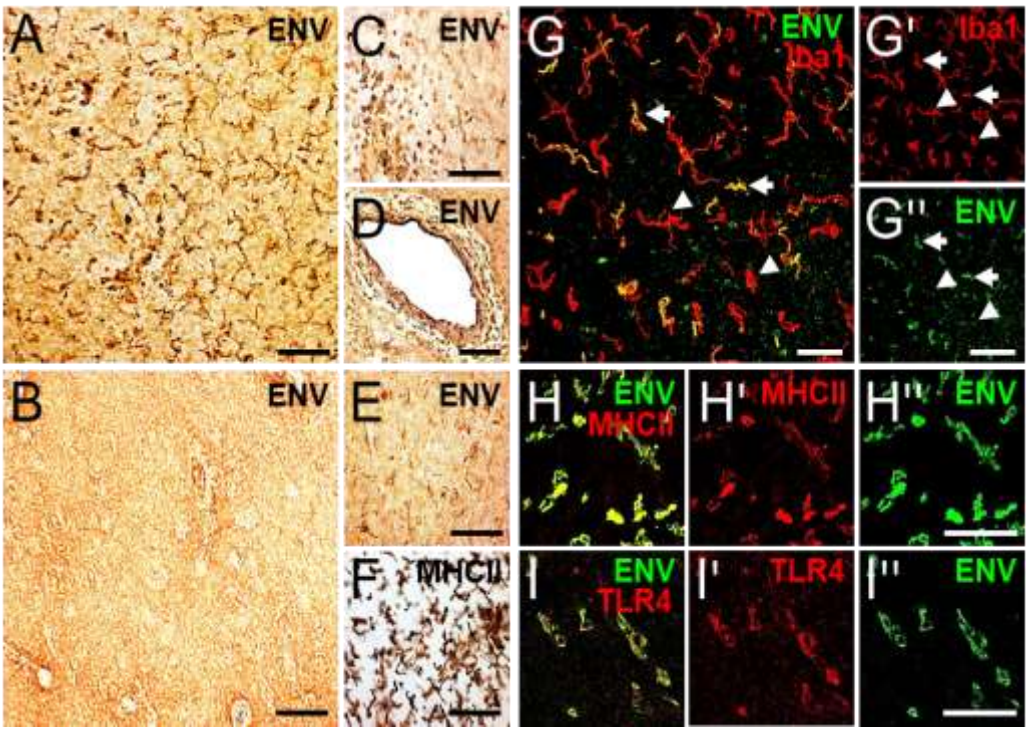


Figure 7: Macrophages Expressing HERV-W ENV



The illustration below shows HERV-W ENV positive microglial/monocytic cells in MS lesions:

Figure 8: HERV-W ENV positive microglial/monocytic cells in MS lesions



ii) A Strong Epidemiological Association Between HERV and MS also in the Periphery (blood and cerebrospinal fluid)

Presence of HERV-W ENV in cerebrospinal fluid

An observational study of a cohort of 26 MS patients followed for 10 years has shown that the presence of HERV-W ENV in the cerebrospinal fluid ("**CSF**") of early MS patients is associated with a significant increase in both the disability level of the HERV-W ENV positive patients (see the differences in the EDSS score in the figure below) and the incidence of progression of the disease into the secondary progressive form of MS after 10 years, as presented in Figure 9 and Table 2 below.

Figure 9: EDSS scores at study entry and after 10 years

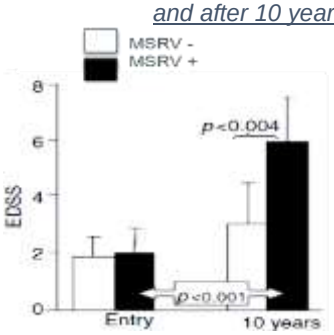


Table 2: Conversion to SPMS according to MSRV status by MSRV status[56]

After 10 years	MSRV+	MSRV-	
	n=18	n=8	
mean EDSS score	6.2	3.3	p<0.004
rate of conversion into the secondary progressive phase of the disease	8/18 (44%)	0/8 (0%)	p<0.0001

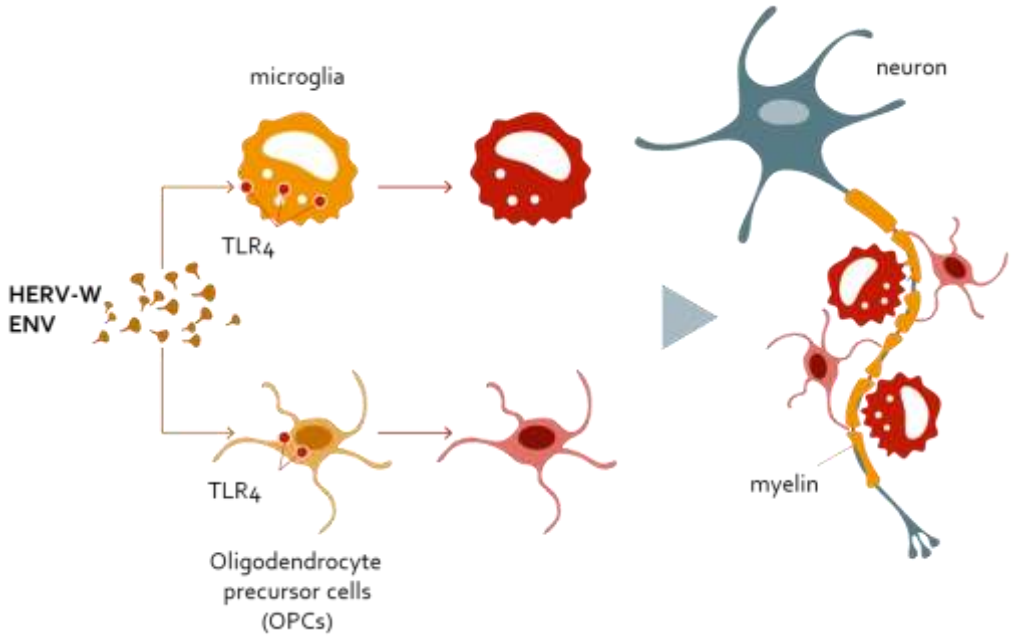
EDSS: Expanded Disability Status Scale

iii) HERV-W ENV fuels two key components of disease progression in MS

Pre-clinical studies using isolated cells have shown that HERV-W ENV has a dual mode of action which is relevant to the two main drivers of disease progression in MS: the activation of microglial cells into aggressive phenotypes causing direct damage to brain tissue, and the inhibition of the maturation of oligodendrocyte precursor cells (OPC), which are responsible for myelin repair and are known to be impaired in MS patients. Although it was originally thought that stopping the activation of microglial cells (the resident innate immune system cells in the brain) would have an indirect effect on adaptive immunity (the inflammatory activity of B and T cells), temelimab clinical results have now demonstrated that this effect is in fact modest.

Stopping HERV-W ENV mediated activation of microglia and allowing OPC maturation through temelimab should potentially reduce direct damage to brain tissue and improve the myelin repair system, which is fully in line with the clinical results observed in CHANGE-MS and ANGEL-MS in reducing MRI markers associated with disease progression (see below under 5.2.4.6 and 5.2.4.8).

Figure 10 : mode of action of HERV-W ENV

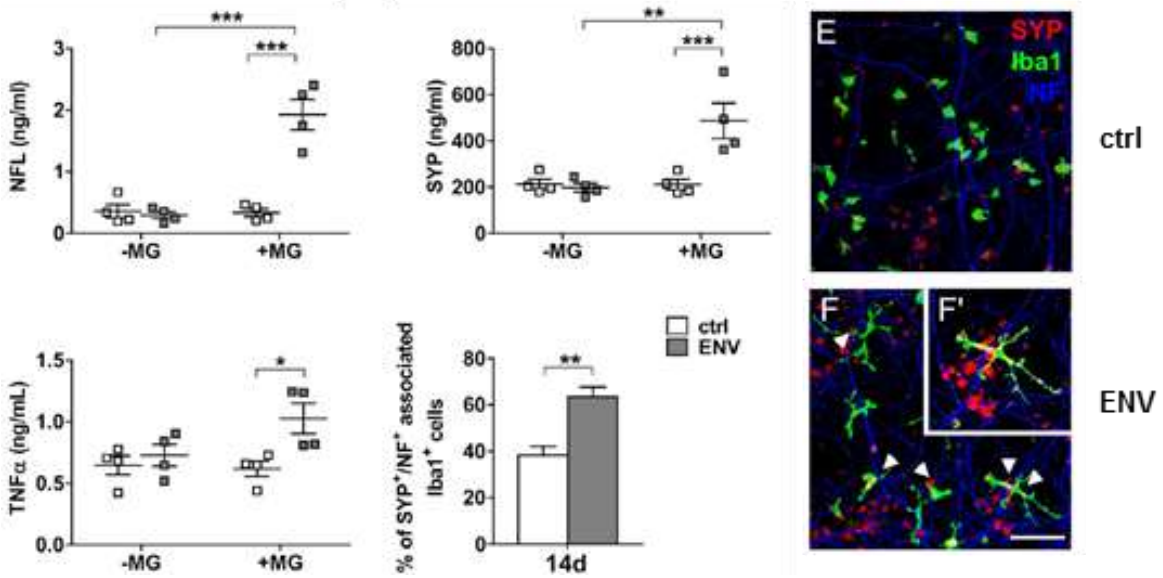


Activation of microglial cells via an interaction with the TLR4 receptor

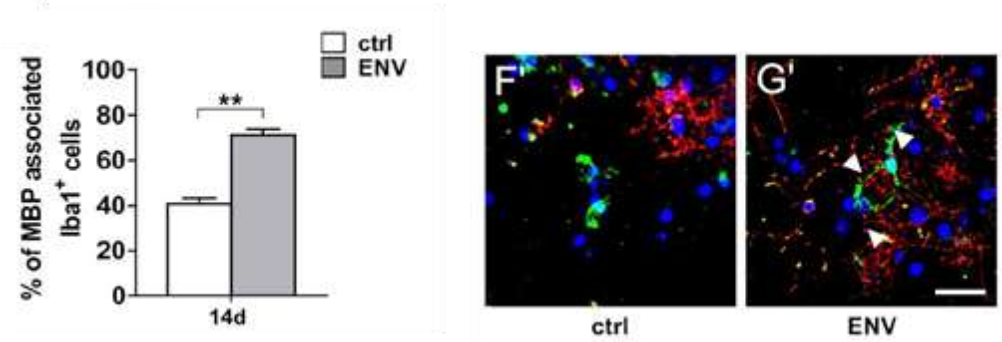
Recent studies[57] have shown that HERV-W ENV appears to be a major factor fueling microglial cell mediated neurodegeneration in MS, which is considered as a major engine of disease progression in MS:

in vitro, HERV-W ENV interaction with microglia activates those cells which become an aggressive phenotype, leading to axonal injury due to increased TNF. This was confirmed by the release of axonal neurofilament light chain (NFL) and of synaptophysin (SYP).

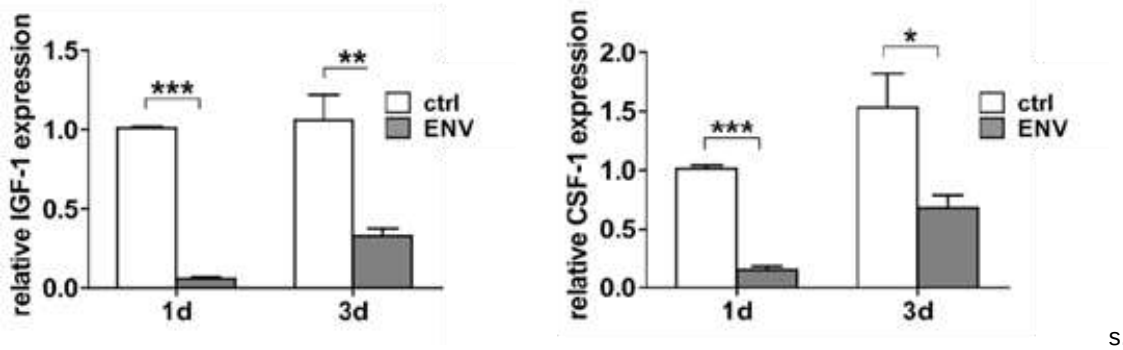
[56] Source: Sotgiu et al., 2010 ibid.
[57] Source: Kremer et al., Ann Neurol 2013; Kremer, Gruchot et al. PNAS May 2019



Activated microglia are directed towards myelinated axons, as observed in neuron / oligodendrocyte / microglia co-cultures, where HERV-W ENV induces microglia to associate themselves with axonal structures.



Finally, the stimulation of microglia with HERV-W ENV leads to significant decrease of regenerative genes transcription (IGF-1, CSF-1, FGF-2) in these cells.



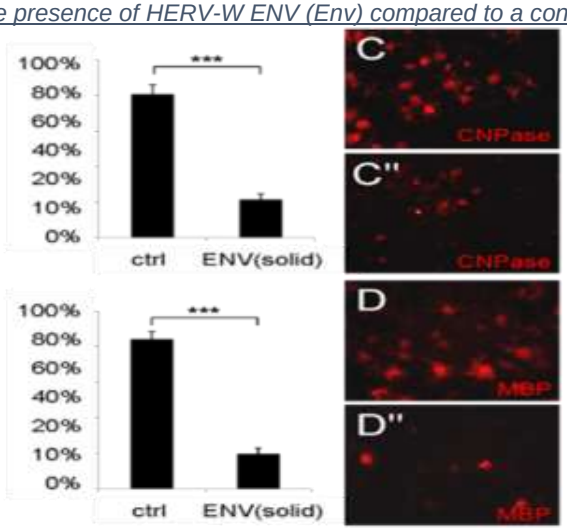
s.

Neurodegenerative action, inhibiting the normal myelin repair process

Recent studies[58] have shown *in vitro* a neurodegenerative action of HERV-W ENV by inhibiting the normal myelin repair process of the brain. In the presence of HERV-W ENV, oligodendrocyte precursor cells ("OPCs"), which migrate to the myelin lesions and are essential for repairing the damage caused by MS, cannot differentiate into mature oligodendrocytes capable of producing myelin. OPCs express TLR4 receptors, and the interaction with HERV-W ENV induces the production of nitric oxide radicals (NO stress) and a decreased expression of myelin maturation markers.

[58] Source: Kremer et al., *Ann Neurol* 2013.

Figure 11: In vitro inhibition of myelin synthesis detected by CNPase and MBP in the presence of HERV-W ENV (Env) compared to a control[59]



The neurodegenerative effects of HERV-W ENV *in vitro* provide a possible explanation of mechanisms driving MS disease progression. These effects are replicated in the animal models discussed below.

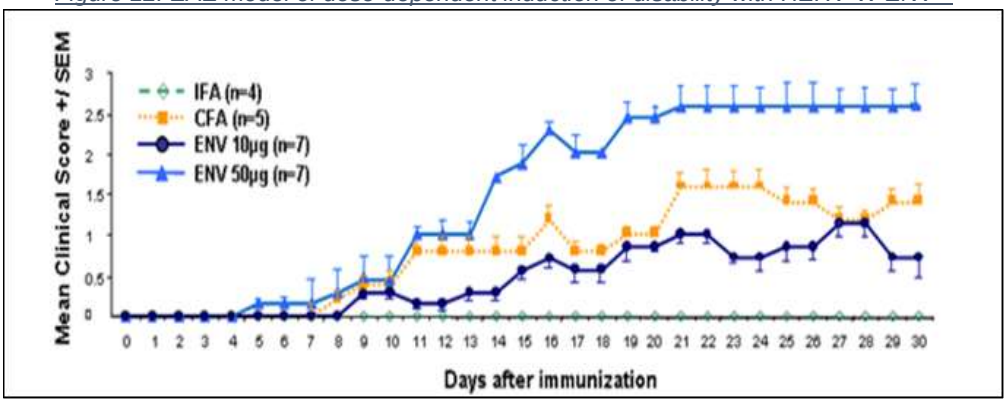
iv) HERV-W ENV Leads to a Form of MS in Animals

MS is described as a chronic and degenerative inflammatory disease of the central nervous system. From a pathological point of view, MS is characterized by the infiltration of auto-reactive T-cells and macrophages into the central nervous system, ultimately leading to demyelination and axonal loss. In this process, dysregulation of the innate immune system is regarded as one of the triggering or exacerbating co-factors in MS.[60] MSRV particles elicit strong inflammatory responses in mice[61] by activating TLR4 and its mediated inflammatory mechanisms.[62]

The reference animal model in MS is the experimental autoimmune encephalomyelitis ("**EAE**") model. Many of the MS drugs that are in current use or under development have been developed, tested, or validated on the basis of EAE studies, but in order to induce autoimmunity, the classical EAE model uses Complete Freund's Adjuvant ("**CFA**"), consisting of inactivated and dried mycobacteria (usually M. tuberculosis).

GeNeuro has developed and published an EAE-like animal model,[63] where mycobacteria are replaced by HERV-W ENV, the protein found in patients. In this animal model, HERV-W ENV induces autoimmunity, neuro-inflammation and demyelination, as well as the loss of mobility, thus recapitulating the human disease using the relevant factor found in patients.

Figure 12: EAE model of dose-dependent induction of disability with HERV-W ENV[64]



[59] Source: Kremer et al., 2013 ibid.
[60] Source: Weiner, *Ann Neurol.* 2009 Mar;65(3):239-48.
[61] Source: Firouzi *et al*., *J Neurovirol.* 2003 Feb;9(1):79-93.
[62] Sources: Perron *et al*., *Virology.* 2001 Sep 1;287(2):321-32; Rolland *et al*., 2006 *ibid.*
[63] Source: Perron *et al*., 2013 *ibid.*
[64] Source: Perron *et al*., 2013 *ibid.*

Note: CFA is the Complete Freund's Adjuvant; IFA is the Incomplete Freund's Adjuvant (without the mycobacteria, used as a control); Env is the HERV-W ENV protein.[65]

The amount of preclinical evidence developed by GeNeuro and third parties provides a very strong link between HERV-W ENV and MS. The presence of HERV-W ENV plaques in MS lesions, the well characterized neurodegenerative mode of action, and the induction of MS-like symptoms by HERV-W ENV in animal models, strongly suggest a causal link between this protein and MS. This opens the field for potentially treating MS through the neutralization of a causal factor of the disease, which could address the key unmet medical need of reducing the progression of the disease.

5.2.3 Temelimab Product Characteristics And Preclinical Results

5.2.3.1 Temelimab: A High Performance Humanized Monoclonal Antibody

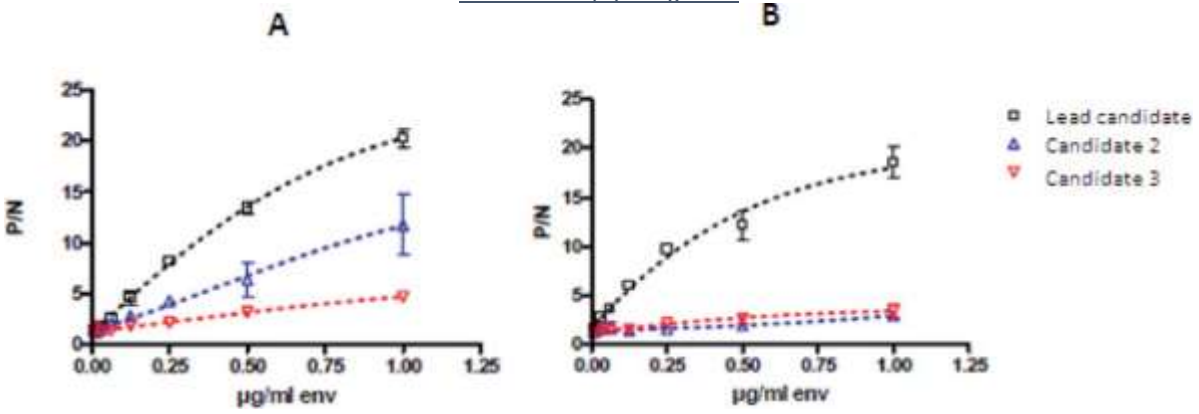
The selection of the humanized monoclonal antibody ("mAb") temelimab from among a panel of molecule candidates was based on quality criteria.

Figure 13: An IgG4 monoclonal antibody similar to temelimab

IgG4

The parent HERV-W ENV-specific agonist mAb mu-temelimab (a type IgG1/kappa immunoglobulin) was obtained by immunizing mice with recombinant HERV-W ENV protein. The precursor of the lead product, mu-temelimab, was selected based on its ability to neutralize the induction of pro-inflammatory cytokines by HERV-W ENV in peripheral mononuclear blood cell ("**PMBC**") cultures and on its high binding capacity with the target.

Figure 14: Illustration of the binding activity of the mAb candidates towards HERV-W ENV transmembrane (A) and surface (B) antigens[66]



Before the final humanization step, interim forms were produced that consisted of a chimeric IgG1 immunoglobulin (ch-temelimab-IgG1) and a chimeric IgG4 immunoglobulin (ch-temelimab-IgG4). Finally, a humanized version of the antibody, temelimab, which fully retains the binding properties of the parent murine form, was developed via an in silico design based on the amino acid sequence of the murine parental antibody. Temelimab is a full-length antibody of the IgG4/kappa subclass.

A site-directed mutagenesis was also performed to increase the stability of the IgG4. Temelimab has a molecular weight of approximately 147 kDa and is linked with HERV-W ENV with an affinity (KD) of 2.2 nM. The stability of the product has been estimated as of the date hereof at 36 months.

[65] Source: Perron *et al.*, *PlosOne* 2013.
[66] Source: Curtin *et al.*, *MABS* 2015,7, 265-275.

5.2.3.2 Manufacturing a Product with High Yield

GeNeuro's current stock of temelimab was manufactured by the Austrian company Polymun pursuant to a contract development and manufacturing agreement dated December 1, 2012 between GeNeuro and Polymun.

Pursuant to amendments to the contract dated March 18 and December 8, 2016, Polymun has produced additional batches of temelimab for use in Phase II trials (including for the ANGEL-MS extension study). Under the contract, GeNeuro owns all improvements concerning the manufacturing of temelimab developed during the execution of the agreement while Polymun retains the right to use any improvements to manufacture other proteins. This Polymun contract also allows GeNeuro to purchase the manufacturing process and to transfer the technology to third parties, as needed.

Polymun developed both cell culture and downstream purification processes suitable for the manufacture of the antibody under GMP conditions at clinical-grade quality. The production and purification of temelimab were performed using established production protocols for a monoclonal antibody.

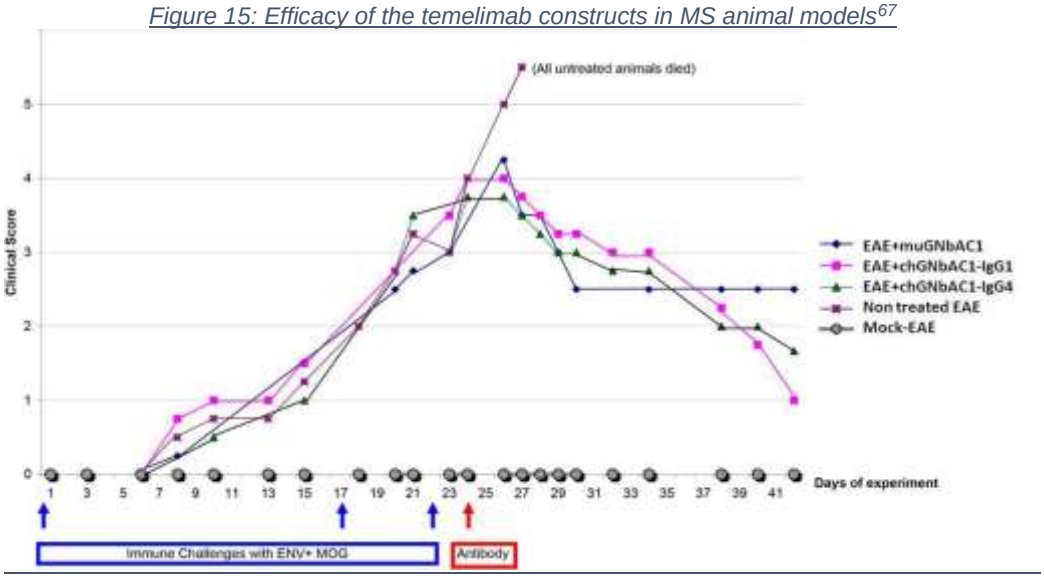
A master cell bank ("**MCB**") was established and tested for sterility, identity, the absence of adventitious agents, and stability. All of GeNeuro's specifications were met following qualification analyses. The MCB cell line was, therefore, considered suitable for the generation of a working cell bank suitable for the large-scale production of temelimab.

A fermentation process was developed by Polymun, with a view to obtaining a stable process with high product yield. This process can be used for large-scale production and establishing a robust and high-yielding purification process. Two manufacturing runs were performed in Polymun's former facility. The original process was subsequently modified when Polymun relocated to a new facility. The modified process was developed by Cellca GmbH ("**Cellca**") pursuant to a service and license agreement that grants to GeNeuro a worldwide, perpetual, non-exclusive and non-transferable right to use a new production cell line developed by Cellca and related intellectual property for the development, manufacture and, commercialization of temelimab The current process for the manufacture of temelimab is based on the cell line developed by Cellca and includes a fermentation process optimized for this new cell line, resulting in shorter process times and higher productivity compared to the prior process. An additional purification step is also included in the downstream sequence. Extensive testing of the drug products produced by the former and current manufacturing processes has shown the products to be equivalent.

5.2.3.3 Temelimab is a Highly Specific and Effective Antibody in Preclinical Models of MS

An assessment of the therapeutic efficacy of temelimab in HERV-W ENV-induced EAE was conducted. The efficacy of intermediate constructs created during the mAb humanization process was assessed and the efficacy of IgG4 versus IgG1 was compared. As shown in the figure below, mice treated with temelimab mAbs survived and showed improved clinical scores. The efficacy of the temelimab-IgG4 antibody was similar to that of the temelimab-IgG1 antibody, suggesting that the IgG1 effector function is not necessary for therapeutic efficacy. The IgG4 molecule, therefore, was selected for humanization.

Figure 15: Efficacy of the temelimab constructs in MS animal models[67]

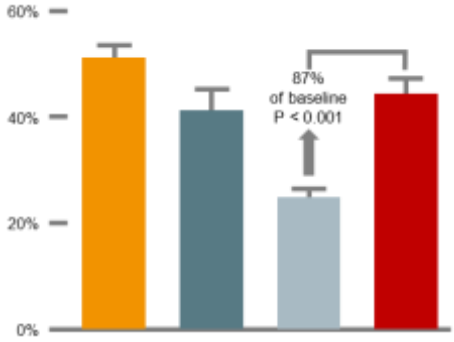


[67] Source: Curtin *et al.*, *MABS* 2015,7, 265-275.

The efficacy of temelimab was also assessed in an *in vitro* model of neurodegeneration that showed the molecule is capable of decreasing the toxic neurodegenerative effect of HERV-Env on oligodendrocytes.[68] This outcome supports the use of temelimab as a treatment for the neurodegenerative component of MS, in particular in progressive forms of MS.

The *in vitro* effect of temelimab on OPCs was tested. It was shown that temelimab significantly diminishes the induction of nitrosative stress due to MSRV-Env in OPCs, and allowed the expression of myelin proteins by differentiated OPCs, which are reduced by HERV-W ENV, to be rescued. This additional effect on glial cell pathology therefore indicates that temelimab can provide a protective effect on OPCs and this suggests a potential to prevent the defect in remyelination associated with MS lesions. In this experiment, temelimab also decreases proinflammatory cytokines, notably TNFα, which is known to induce myelin and oligodendroglial damages. These findings indicate that temelimab can display a double therapeutic effect, protecting OPC differentiation capacity and inhibiting the proinflammatory signaling cascades induced by HERV-W ENV in the CNS[69].

Figure 16: the neutralizing antibody temelimab abrogates HERV-W ENV protein-mediated oligodendroglial maturation blockade



Exp #	Relative rescue of MBP expression
1	88%
3	81%
2	92%
4	88%
5	87%

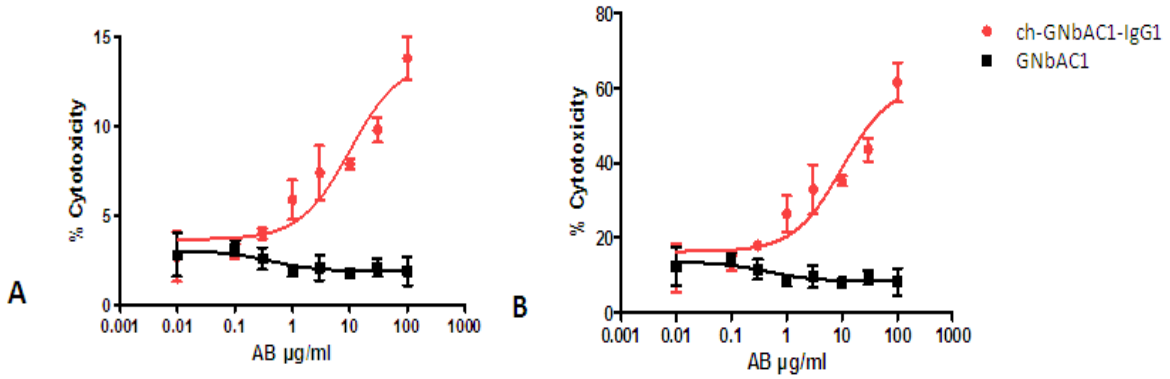
5.2.3.4 Temelimab is a non-cytotoxic mAb with high safety

Although temelimab is an IgG4 and, therefore, unlikely to induce antibody dependent cell-mediated cytotoxicity ("**ADCC**") or complement-dependent cytotoxicity ("**CDC**"), these toxicities cannot be formally ruled out when HERV-W ENV is expressed on the cell surface. *In vitro* experiments were performed in which complement activation in the presence of transfected human cells expressing the antigen on their surface was investigated. In a similar experimental setup, PMBC or natural killer ("**NK**") cell-mediated antibody-dependent cytotoxicity against such antigen-expressing transfectants was analyzed.

The analysis of ADCC and CDC mediated by temelimab was performed using cultured HEK293 cells. The protein HERV-W ENV is expressed on the surface of the transfected HEK293 cells and functions as the antigen recognized and bound by temelimab antibodies. As a positive control, a temelimab of IgG1 isotype was used. The CDC-dependent dose-response curves of temelimab isotype IgG1 (ch-temelimab-IgG1) and isotype IgG4 (temelimab), respectively, are shown in the table below. The isotype IgG1 induced a dose-dependent signal response while isotype IgG4 did not. Cytotoxicity was calculated based on the total number of cells to transfected cells only (14% vs. 62% and 8% vs. 52%, respectively). No significant change in cytotoxicity was observed when comparing different incubation times.

[68] Source: Kremer *et al.*, *Mult Scler.* 2015 Aug;21(9):1200-3.
[69] Source: Kremer D, Förster M, Schichel T, Göttle P, Hartung HP, Perron H, Küry P. The neutralizing antibody Temelimab abrogates HERV-W envelope protein-mediated oligodendroglial maturation blockade. Mult Scler. 2015 Aug;21(9):1200-3.

Figure 17: CDC and ADCC with GNbAC+ IgG1 and IgG4 molecules[70]



These results support an absence of ADCC and CDC cytotoxicity with temelimab, which provides support for a positive safety profile.

5.2.3.5 A Very Low Potential for Immunogenicity

To assess potential immunogenicity, the sequence of temelimab was scanned for the presence of putative human leukocyte antigen (HLA) class II restricted epitopes, also known as T helper (Th)-cell epitopes (T CD4+), for the purpose of detecting immunoglobulin regions that could trigger an immunogenous action to the product.

Table 3: HLA binders of temelimab corresponding to the DRB1, DQ, DP, and DRB3/4/5 genes (epitope counts)[71]

	DRB1	DRB3/4/5	DQ/DP
VH	5	0	3
CH1	0	0	0
Hinge	0	0	0
CH2	0	0	0
CH3	0	0	0
VL	4	1	1
CL	0	0	0
Entire Protein	9	1	4

Table 3 above shows the number of binders corresponding to the DRB1, DQ, DP, and DRB3/4/5 genes (epitope counts). The results show that no binders were found within the constant regions or the hinge region of the antibody; overall nine strong potential DRB1 binders were found within the variable regions VH and VL of temelimab. As in the humoral response raised against an antigen, the observed Th cell activation/proliferation was interpreted in terms of the DRB1 specificity. An analysis of the results showed that all nine strong potential DRB1 binders were within the complementarity-determining regions of the antibody and none was found within the framework. These data support a very low potential for immunogenicity, which has been confirmed so far in clinical trials.

5.2.3.6 No Findings in the Toxicology Program

Since HERV-W ENV is expressed only in humans, the development of a relevant toxicology program was defined from the early stages with the scientific advice of the Paul Ehrlich Institute in Frankfurt. No relevant animal models being available, the program defined maximum tolerated doses in rodents, and was focused on human *in vitro* toxicology.

Temelimab was evaluated in two two-week toxicity studies in mice following a single intravenous administration of temelimab at 6 mg/kg and 30 mg/kg doses, and at 30 mg/kg and 100 mg/kg doses, representing 1x, 5x, and 17x respectively the maximal dose administered in healthy volunteers in the Phase 1a trial. Temelimab serum concentrations were still quantifiable 312 hours after injection. Temelimab serum exposures were similar in male and female mice and increased proportionally between the doses of 6 and 100 mg/kg. No temelimab-related clinical signs, including ophthalmological findings, were observed during these studies and body weight and food consumption appeared to be unaffected by the treatment. No temelimab treatment-related organ weight changes, or macroscopic or microscopic post-mortem findings were observed. In conclusion, in both studies, no effects were

[70] Source: Curtin *et al.*, *MABS* 2015,7, 265-75.
[71] Source: Curtin *et al.*, *MABS* 2015,7, 265-75.

observed on clinical signs, body weight, food consumption, or pathology. The no observed adverse effect level of temelimab was established at 100 mg/kg.

In a repeated dose toxicity study in monkeys, temelimab was evaluated following weekly i.v. administrations (2-hour infusion) to cynomolgus monkeys over a period of 6 months. Each animal was checked at least twice a day during the study for mortality and morbidity. Electrocardiography examinations as well as systolic and diastolic blood pressure measurements were performed on all animals before the beginning of the treatment period and after the end of infusion on Days 1 and 180. Ophthalmological examinations were performed on all animals. Blood sampling (for blood chemistry, hematology and TK and anti-drug antibody (ADA) detection) and urine collection were carried out according to a pre-defined schedule. A complete macroscopic post-mortem examination was performed on all animals. There were no moribund or prematurely sacrificed animals. No relevant clinical signs were observed at 30 and 100 mg/kg/day. There were no changes in body weight, food consumption, electro cardiac assessment, blood pressure, and ophthalmology examination findings during the study. Gross pathology analysis of organs did not reveal any changes in organ weight, physical aspect, and size. No relevant changes were observed in both genders in hematology, blood chemistry or urinalysis parameters during the study. Consequently, under the experimental conditions of the study, no observed adverse effect level for temelimab was established at 300 mg/kg/administration.

Two concentrations of temelimab (2 µg/ml and 10 µg/ml) were tested on 42 different human tissues. At the high (10 µg/ml) concentration, a temelimab-related staining considered to be specific was noted in the mature urothelium (umbrella cells) of the ureter and the urinary bladder, syncytiotrophoblasts/ trophoblasts of the placenta, and superficial endometrial epithelial cells of the uterus of one single panel only. Staining of minor importance, most likely non-specific, was noted in the crypt epithelium of the intestinal tract, canaliculi of the breast, and tails of spermatids in the testis. At the optimal concentration of temelimab (2 µg/ml), no staining was considered to be related to the mAb.

5.2.4 Temelimab: Clinical Development as of the Date Hereof

To date, eight clinical studies of temelimab have been or are being conducted on humans, which are summarized in Table 4:

Table 4: Summary of clinical studies[72]

Clinical Study N°	Design	Subjects	temelimab dose, regimen, route of administration	Formu-lation	Placebo or compara tor	Key results
GNC-001 Clinicaltrials.gov identifier: NCT01699555	Randomized placebo-controlled first-in-human study with temelimab	33 healthy male subjects (cohorts 0.1 5 to 6.00 mg/kg were analyzed for PK)	Single doses, 0.0025 mg/kg 0.025 mg/kg 0.15 mg/kg 0.60 mg/kg 2.00 mg/kg 6.00 mg/kg intravenous	Liquid	Placebo	Well tolerated with all adverse events mild or moderate
GNC-002 Clinicaltrials.gov identifier: NCT01639300	Randomized placebo-controlled first-in-human study with temelimab Repeated dose phase Open label	10 MS patients (cohorts 2 and 6 mg/kg)	Single doses, 2 mg/kg 6 mg/kg Intravenous Open label: repeated doses 2 mg/kg, 6 mg/kg intravenous	Liquid	Placebo No Placebo in open label phase	Single dose phase: well tolerated, linear PK and t½:17 – 49 days Repeated dose phase: well tolerated, AR: ~3.0, overall stability of MRI
GNC-001B Clinicaltrials.gov identifier: NCT02452996	Randomized placebo-controlled pharmacology study with temelimab	21 healthy male subjects	Single doses, 6 mg/kg 18 mg/kg 36 mg/kg Intravenous	Liquid	Placebo	Well tolerated with all adverse events mild or moderate
GNC-003 CHANGE-MS 24-week and 48 week completed NCT02782858	Phase IIb, randomized, placebo-controlled, parallel-group, multicenter study with two treatment periods in RRMS patients: Period 1 (Day 1 to Day 169)	270 RRMS patients	Period 1: 4 cohorts in, receiving either placebo or temelimab i.v every 4 weeks for 24 weeks with 69 subjects in the placebo group and 67 subjects in	Liquid	Placebo	Well tolerated with all adverse events mild or moderate. Significant and consistent positive impact on key neuroprotection

[72] Source: GeNeuro.

Clinical Study N°	Design	Subjects	temelimab dose, regimen, route of administration	Formu-lation	Placebo or compara tor	Key results
	and Period 2 (Day 169 to Day 337). Period 2 is dose-blind with all placebo patients re-randomized to 1 of the temelimab dose cohorts		each of the following temelimab groups: 6 mg/kg, 12 mg/kg, and 18 mg/kg Period 2: 3 cohorts receiving temelimab (same doses as in Period 1) i.v. every 4 weeks for 24 weeks			markers known to be linked to disease progression.
GNC-004 ANGEL -MS extension study 48 weeks completed NCT03239860	Two-year open-label extension study to GNC-003 in RRMS patients; early termination in October 2018.	219 RRMS patients	3 cohorts receiving temelimab at 6 mg/kg, 12 mg/kg and 18 mg/kg i.v. over 2 hours every 4 weeks until optimal dose is decided based on GNC-003 results; then all patients to be shifted to this dose	Liquid	none	Well tolerated with all adverse events mild or moderate. Continued positive impact on key MRI measures of disease progression in MS patients, with encouraging dose-dependent effects on clinical measures of disease progression.
GNC-301 RAINBOW 24-week, extended to 48-week, completed NCT03179423	Randomized placebo-controlled first-in-human multicenter study with temelimab in T1D. The first part of the trial is double-blind and the second part is open-label with all participants receiving the active treatment.	60 T1D adult patients	Period 1: 2 cohorts, receiving either placebo or temelimab i.v every 4 weeks for 24 weeks with 20 subjects in the placebo group and 40 subjects temelimab 6 mg/kg group. Period 2: open-label with all participants receiving the active treatment	Liquid	Placebo	Safety demon-strated in T1D patients, posi-tive pharmaco-dynamic signs with decrease in hypoglycaemia frequencies and in anti-insulin antibody levels in patients treat-ed with temelimab
GNC-006 completed	Randomized placebo-controlled high-dose pharmacology study	24 healthy male subjects	Single doses, 36 mg/kg, 60 mg/kg, 85 mg/kg, 110 mg/kg intravenous	Liquid	Placebo	Well tolerated with all adverse events mild or moderate
GNC-401 ProTEct-MS 48-week, Ongoing NCT04480307	Phase IIa, randomized, double-blind, placebo-controlled, parallel-group, single center study in RRMS patients following treatment with rituximab	40 RRMS patients	4 cohorts in, receiving either placebo or temelimab i.v every 4 weeks for 48 weeks with 10 subjects in the placebo group and 10 subjects in each of the following temelimab groups: 18 mg/kg, 36 mg/kg, and 54 mg/kg	Liquid	Placebo	Ongoing. DSMB confirmed higher doses of temelimab are well tolerated

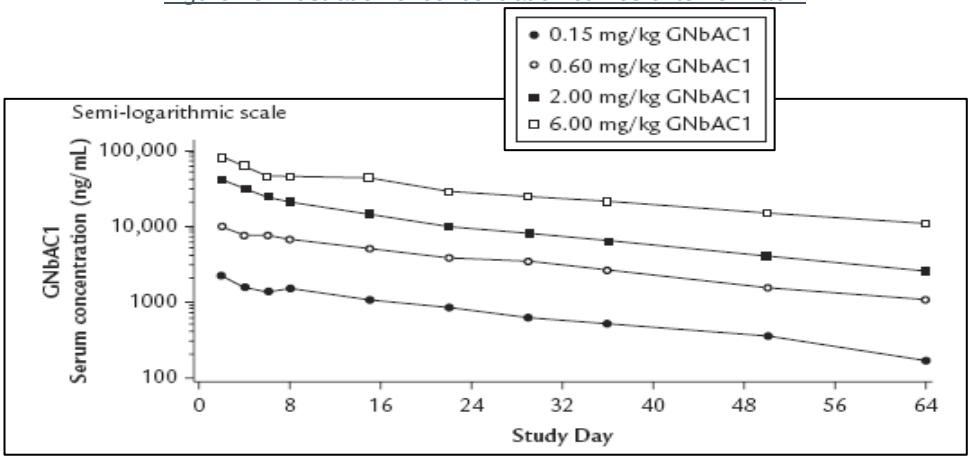
5.2.4.1 Study GNC-001: A First-in-Humans Study Supporting the Safety of temelimab[73]

The safety and pharmacokinetics of temelimab were investigated for the first time in humans in study GNC-001 in healthy male volunteers.[74] The study included 33 subjects of which 23 healthy male subjects received doses of temelimab varying from 0.0025 mg/kg to 6 mg/kg while 10 healthy male subjects received a placebo during the trial. Temelimab was well tolerated with no serious adverse events observed. Twenty-eight total adverse events were reported by 15 subjects. The incidence of adverse events having a suspected relationship to the study drug was low across all treatment groups. Four possible or probable drug-related adverse events were reported at the 2.00 mg/kg and 6.00 mg/kg dose levels by single subjects and comprised sore throat, headache, and jaw pain. No clinically significant changes related to treatment were observed on vital signs, urinalysis, EKG, or laboratory evaluations.

There was no evidence of antibody production against temelimab during the entire study period of 64 days and no treatment-emergent antibodies against temelimab appeared in any of the treated subjects. The data, therefore, indicated that single ascending intravenous infusions of temelimab induced no antibody response.

The pharmacokinetics of temelimab were as expected with this class of molecules. The observed geometric mean half-life values ranged from 18.8 to 25.7 days across all dose levels and maximum serum concentrations were observed 1.5 to 2.5 hours after administration. The concentration curves appear Figure 18 below.

Figure 18: Illustration of concentration curves of temelimab[75]



5.2.4.2 Study GNC-002: First Signs of a Therapeutic Response in Patients

The GNC-002 study was a Phase IIa clinical study, completed in April 2014, which had the main goal of confirming the safety of temelimab in MS patients. The safety and tolerability of temelimab were considered to be good. The majority of the adverse events were mild or moderate in severity. Only one serious adverse event consisting of acute pancreatitis was reported in the 6 mg/kg cohort during the study but was considered to be unrelated to the study treatment. The affected patient had a medical history of recurrent biliary calculi, which explained the condition. The patient recovered fully and received nine additional doses of temelimab without recurrence of this pathology. Otherwise, the most frequently emergent adverse events experienced were gait disturbance reported by two patients in the 2 mg/kg group and one patient in the 6 mg/kg group, nasopharyngitis reported by three patients in the 2 mg/kg group and two patients in the 6 mg/kg group, and leukocyturia reported by one patient in the 2 mg/kg group and two patients in the 6 mg/kg group. The patients reporting leukocyturia were known for repeated urinary tract infections, which is a common pathology in MS patients. There was no evidence of antibody production against temelimab during the study period.

Pharmacokinetic data were also assessed during the study and were in line with those observed during the first clinical study GNC001 and consistent with single monthly administration of the medication. The study also made a possible observation of a pharmacodynamic response to temelimab: the biomarkers linked to HERV diminished in a statistically significant manner during the period of treatment, as shown in Figure 19 below.

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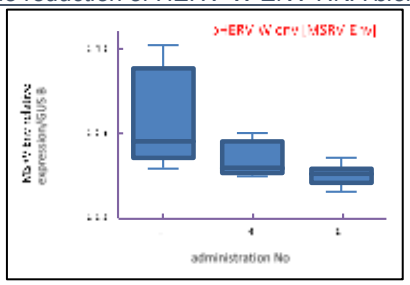
[73] Source: Curtin F, Lang AB, Perron H, Laumonier M, Vidal V, Porchet HC, Hartung HP.: "Temelimab, a humanized monoclonal antibody against the envelope protein of multiple sclerosis-associated endogenous retrovirus: a first-in-humans randomized clinical study". *Clin Ther.* 2012 Dec;34(12):2268-78.

[74] Source: Curtin *et al.*, 2012 *ibid.*

[75] Source: GeNeuro.

Figure 19: Illustration of the reduction of HERV-W ENV RNA biomarker during treatment[76]



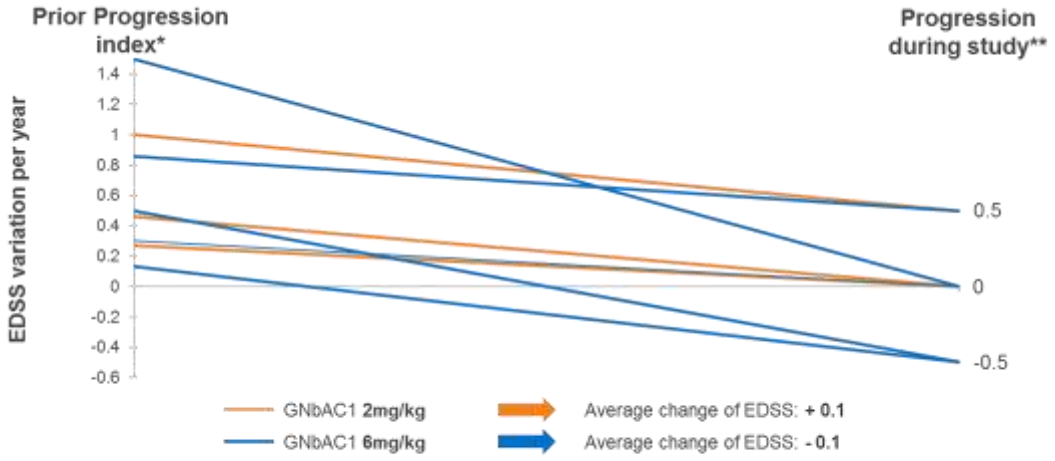
In terms of MRI assessment, eight out of eight patients who completed 12 monthly repeated administrations of temelimab showed globally stable MRI images over the treatment period, with no new lesions or the extension of existing ones. In addition, the EDSS score remained overall stable in patients who completed 12 monthly administrations of temelimab with an increase of 0.2 point on the mean EDSS for the 2 mg/kg temelimab cohort and a decrease of 0.2 point on the mean EDSS for the 6 mg/kg temelimab cohort. The stability of the brain lesions over 12 months is an encouraging sign in terms of the pharmacodynamic response to the treatment. MRI and EDSS results are presented in Table 5 below.

Table 5: Results of MRI and EDSS by dose cohort at 6 and 12 months[77]

	2 mg/kg (n=5)*	6 mg/kg (n=5)	All (n=10)
Brain MRI stability 6 mo.vs baseline	4/5	5/5	9/10
Brain MRI stability 12 mo. vs baseline	3/3*	5/5	8/8*
Mean EDSS change 6 mo. vs baseline	+0.1	+0.1	+0.1
Mean EDSS change 12 mo.vs baseline	+0.2*	-0.2	0.0*

To illustrate these results, the progression index ("**PI**") of the eight patients who completed the study was analyzed and compared to changes in their EDSS during treatment for a year. The PI was calculated by dividing the EDSS score of a patient by the number of years elapsed since he/she was diagnosed with MS. It should be noted that the data used to calculate PI prior to the beginning of the study was based on anamnestic data contained in the file of each patient and, accordingly, not verified in connection with the study. The PI, therefore, is a relative measurement, since the progression of the disability does not always evolve linearly over time, and patients treated have been followed by various doctors before entering the study. It provides a historical indication, however, of the average speed of the progression of the disability score of a patient over one year. Despite the limits of the trial duration in comparison with the pace of the development of the illness, the small sample of patients and the absence of a placebo, a comparison of individual PI with the evolution of the EDSS score during the year of the study allows one to observe in the figure below a change of the trend in the progression of disability of patients treated.

Figure 20: Comparison of PI by patient with changes in EDSS score during the study[78]

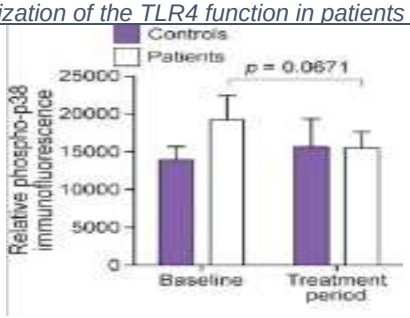


*Notes: * Estimated average individual disease progression before entering the study. Data allowing the calculation of the prior progression index are based on anamnestic data derived from each patient's file and, as a consequence, haven't been checked within the context of the study.*
*** 2 patients stopped the treatment after 6 months for reasons not linked to GNbAC1 safety.*

[76] Source: Derfuss *et al.*, 2014 *ibid.*
[77] Source: Curtin, Derfuss, Lang, Perron, Kappos, Hartung, Lalive. "Temelimab, a monoclonal antibody against the MSRV envelope protein, pharmacodynamic responses in patients with multiple sclerosis" *Poster ECTRIMS* 2014, Boston.
[78] Source: GeNeuro.

Finally, the study shows normalization of the over-activation of TLR4, observed in patients with MS and found in patients in the study at its beginning. After a year of treatment, as shown in the illustration below, over-activation of TLR4 returned to normal for patients treated, which supports the assumed mode of action of temelimab.

Figure 21: Normalization of the TLR4 function in patients during treatment[79]



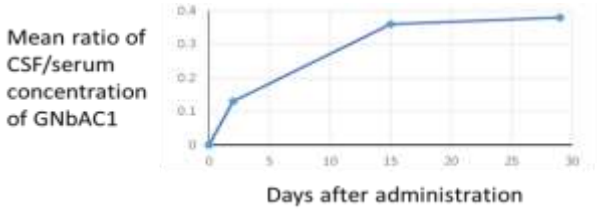
Overall, the study confirmed a very good safety profile for the product over one year, and showed very promising pharmacodynamic signs as well as first signs of a therapeutic response during the first administration of temelimab to MS patients. However, the two different dose regimens, the small sample size, the open nature of the extensions, the short observation period, and the inclusion of primary and secondary progressive patients did not permit conclusions regarding the efficacy of temelimab in this study, the objective of which was to confirm the safety of temelimab in patients.

5.2.4.3 GNC-001B Study: Good Penetration of temelimab in CSF for an antibody

This study was a Phase Ib, single-center, in-patient, randomized, double-blind, placebo-controlled, dose-escalating study to evaluate the safety, tolerability, and pharmacokinetic profiles of single intravenous infusions of temelimab for doses of 6 mg/kg, 18 mg/kg, and 36 mg/kg, respectively, in healthy subjects. Doses of temelimab were administered as an intravenous infusion over one to four hours, depending on the dose.

Twenty-one subjects received a single infusion of temelimab or placebo. Single doses of temelimab were well tolerated. All adverse events were mild or moderate in severity and no subject withdrew as a result of adverse events. There were no notable dose- or treatment-related trends in the number or type of adverse events reported. Temelimab concentrations in the CSF of the study participants were assessed at different points in time. The mean percentage of temelimab in the CSF ranged between 0.3% and 0.4% at 15 and 29 days, which is higher than the ratios observed with other mAbs such as BIIB-033 (*please see* Figure 22 below). [80]

Figure 22: CSF/serum concentration ratios by dose and sampling day[81]



5.2.4.4 CHANGE-MS

5.2.4.5 Study design and objectives

GeNeuro conducted a double-blind placebo-controlled study, called CHANGE-MS, in patients with RRMS. The study based the efficacy evaluation of the drug on MRI brain imaging. The primary objective was to assess the efficacy of repeated doses of temelimab versus placebo in patients based on the cumulative number of Gadolinium-enhanced T1 lesions on brain MRIs — a study end-point recommended by regulatory authorities for this development phase of MS.[82] The study also assessed pre-determined secondary objectives, among which: (i) assess temelimab's efficacy on other brain MRI end points; (ii) assess temelimab's effect on the relapse rate; (iii) assess the safety and tolerability of repeated doses of temelimab; (iv) determine the pharmacokinetics of repeated doses of temelimab in a subgroup of patients; (v) identify an optimal dose for Phase III studies based on

[79] Source: Derfuss et al., 2015 ibid., and Zimmermann, Neurol Neuroimmunol Neuroinflamm. 2015 Aug. 20;2(5):e144. doi.
[80] Source: Tran *et al.*, *Neurol Neuroimmunol Neuroinflamm.* 2014 Aug. 21;1(2):e18. doi.
[81] Source: GeNeuro.
[82] Source: EMA 2015.

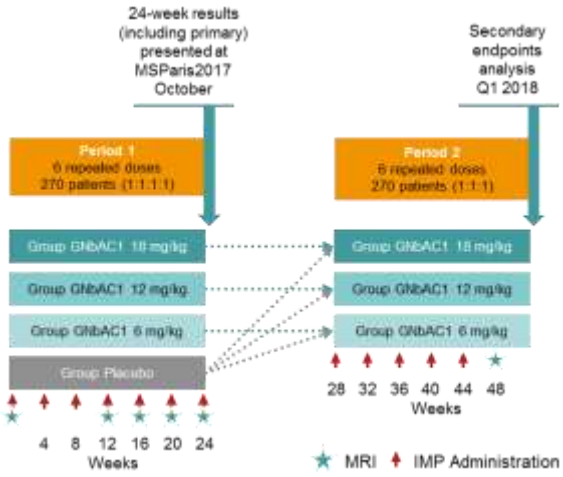
efficacy and safety findings; (vi) study the pharmacodynamic response on biomarkers, including HERV-W ENV markers; (vii) assess the immunogenicity of temelimab; and (viii) assess the health-related quality of life.

The study enrolled a total of 270 patients (*please see* the illustration below). Patients inclusion criteria were: (i) RRMS according to the 2010 revised McDonald criteria; (ii) age between 18 and 55 years; (iii) present disease activity characterized by at least one documented relapse within one year or one Gd-enhancing T1 lesion at screening or evidenced within the last three months; and (iv) EDSS score less than 6.0. No other MS treatments were provided during the study other than corticosteroids and symptomatic treatments such as fampridin.

The study was performed over two periods:

- Period 1 (weeks 1–24): a double-blind randomized, placebo-controlled study with the following groups: temelimab 6 mg/kg, 12 mg/kg or 18 mg/kg; or placebo with a randomization ratio (1:1:1:1).
- Period 2 (weeks 25–48): extension where all patients receive only active treatment. In Period 2, patients from the placebo group were re-randomized to temelimab 6 mg/kg, 12 mg/kg or 18 mg/kg (randomization 1:1:1).

Figure 23: Design of CHANGE-MS Study[83]



Temelimab was administered intravenously over a 2-hour infusion in a glucose 5% solution bag at ~2 mL/min.

Centers located in the following countries participate in the study: Bulgaria, Croatia, the Czech Republic, Estonia, Germany, Hungary, Italy, Poland, Russia, Serbia, Spain, and Ukraine. Fifty centers, mainly university hospital centers, participated in the study. The study was launched in November 2015, with a first patient included in May, 2016, and the last ones in December, 2016. The final 48-week results were announced in March 2018.

5.2.4.6 24-week results

On August 28, 2017, GeNeuro announced the first results of CHANGE-MS as they became available. The first output was the excellent safety profile of temelimab as can be seen in Table 6 below.

Table 6: CHANGE-MS safety results at 24 weeks

	GNbAC1 6 mg/kg N=67	GNbAC1 12mg/kg N=66	GNbAC1 18 mg/kg N=67	Placebo N=68
24-week completers	60 (90%)	59 (90%)	64 (95%)	66 (97%)
SAE	1	1	0	2
Serious-related AE*	0	1	0	0
AE leading to early termination	2	1	1	0
AE leading to death	0	0	0	0

* Macroscopic hematuria: resolved

[83] Source: GeNeuro.

There was a very good balance in terms of frequencies of serious adverse events or events leading to discontinuation among the different treatment groups and there was no evidence of more frequent or more severe adverse events with higher doses of temelimab, comforting favorable safety results observed so far in the development of temelimab.

Primary endpoint at 24 weeks: results on inflammatory end-points

The primary endpoint was not met and is presented in table below. Although the total number of lesions was reduced by approximately 50% in the 18 mg/kg treatment group compared to placebo, after accounting for Baseline imbalances, there were no statistically significant differences in the number of gadolinium enhancing T1 lesions compared to placebo at 24 weeks for any active dose group.

Table 7: main CHANGE-MS endpoints at 24 weeks

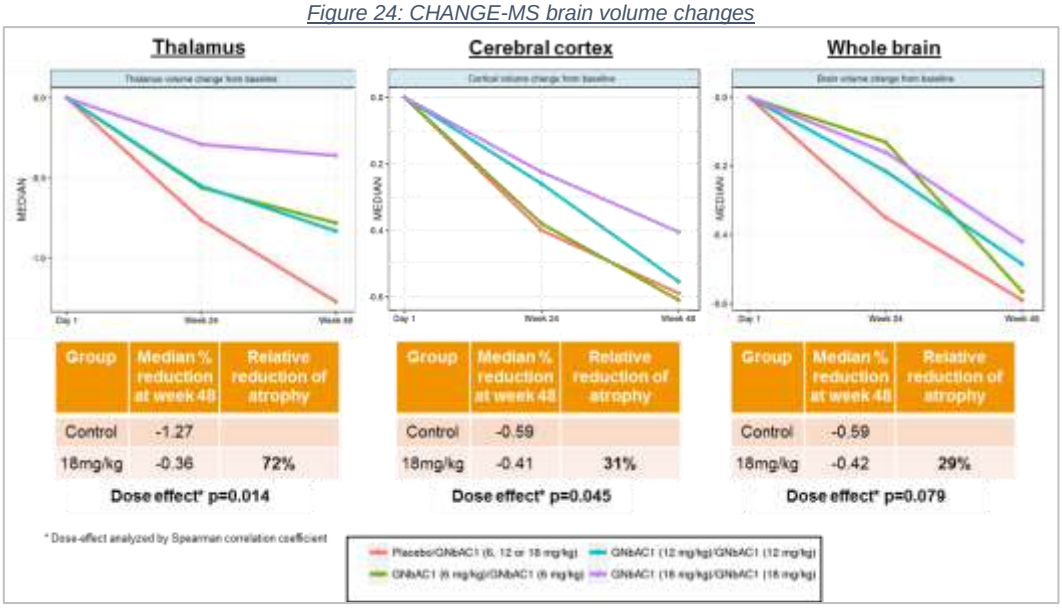
			GNbAC1 6 mg/kg	GNbAC1 12mg/kg	GNbAC1 18 mg/kg	Placebo
Primary Endpoint						
Total Gd+ lesions	Week 12 -24	# of lesions	510	407	339	666
		Mean (Med) P value	8.4 (2.0) p = 0.539	6.9 (2.0) p = 0.704	5.3 (1.0) p = 0.481	10.1 (1.5)
Secondary endpoints include: total # new/enlarging T2 / CUAL / T1 BH; T2 / T1 BH volume, ARR, EDSS, MSFC, MSQOL-54						
% change in whole brain volume	Baseline – week 24	Mean (Med)	-0.32 (-0.13)	-0.35 (-0.22)	-0.24 (-0.16)	-0.34 (-0.35)
# of relapses	Baseline – week 24		18 p = 0.492	21 p = 0.217	21 p = 0.291	15
Total Gd+ lesions	Week 24	Mean (Med) P value	2.7 (1.0) p = 0.103	2.3 (0) p = 0.907	2.0 (0) p = 0.083	4.1 (0)

CHANGE-MS neuroprotection and remyelination endpoints at 48 weeks.

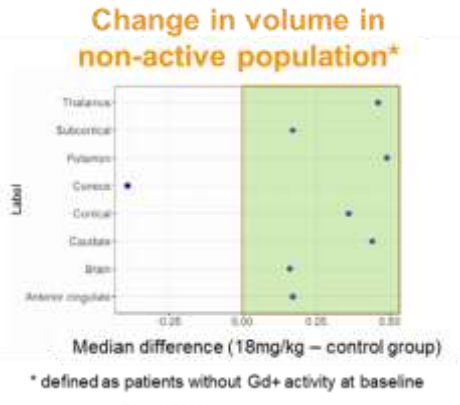
At 48 weeks, pre-specified, key secondary endpoints were assessed. For the second 24-week period, the group of patients originally randomized to placebo and then (at week 24) re-randomized into the three active treatment arms was used as the Control Group in the 48-week analyses.

Brain volume changes were analyzed for the whole brain and several cerebral structures. Benefits of temelimab were seen, with less atrophy in the cerebral cortex and thalamus, with relative reductions of 31% and 72% respectively between the 18 mg/kg (the highest dose studied) and Control Group, with a statistically significant dose-relationship across treatment groups assessed by the Spearman correlation coefficient (p=0.045 for cortex atrophy and p=0.014 for thalamic atrophy). For whole brain atrophy, there was a 29% relative reduction in brain volume loss over 12 months for the 18 mg/kg group versus the Control Group. The Spearman correlation analysis showed a trend for a dose-relationship (p=0.079).

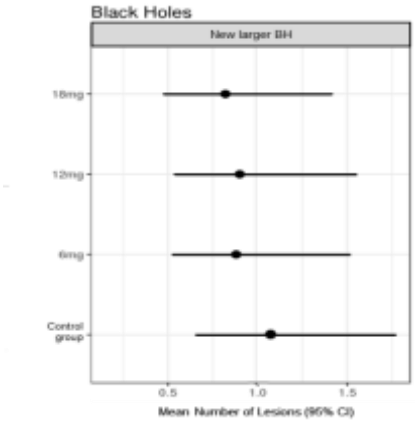
Figure 24: CHANGE-MS brain volume changes



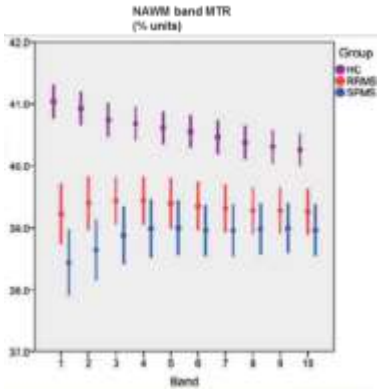
Importantly, the benefits observed were not dependent on reducing inflammatory activity. As illustrated in the figure below, the reductions in atrophy were at least as robust in "non-active" patients (patients with no inflammatory activity at baseline). This is evidence that the effect of temelimab is mediated through its target cells (OPC and microglia) and not through the modulation or suppression of adaptive immunity. This is particularly important as the critical unmet medical need in MS is to treat non-active progressive patients, either because they progress while taking existing, highly effective immunomodulatory DMTs, or because they have reached the stage where adaptive inflammation has a much lower influence on the course of the disease (i.e. "non-active progressive MS").



The number of **T1 hypointense lesions**, or black holes, was a key secondary measure of the study. The number of new T1 black holes of at least 14mm3 volume (3mm in diameter) was reduced by 63% at 48 weeks in the 18mg/kg versus the Control Group (pairwise comparison p= 0.014). Reductions compared to the Control Group were also observed at lower temelimab doses. The figure below shows the average number of black holes by treatment group at 48 weeks. These data were supported by analyses of changes in T1 black hole volume, which were smaller in the groups having received temelimab throughout the 48 weeks of CHANGE-MS compared to the Control Group with a statistically significant dose-response effect (Spearman correlation coefficient p = 0.030).



Magnetization transfer imaging involves the measurement of the transfer of magnetization between the free and bound proton pools in tissue. Images during two sequences are subtracted leading to a magnetization transfer ratio (MTR) image, which is proposed as a measure of myelin. Remyelination following treatment with temelimab 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, as illustrated in the figure above. A decrease of the MTR signal in the NAWM is associated with clinical disability[84]. Despite the variability inherent in a 50-center MTR study, the Baseline data reproduced the pathological gradients observed in prior studies.

A benefit in **Magnetization Transfer Ratio** (**MTR**) signal for 18mg/kg dose group was observed in comparison with the Control Group at 48 weeks, in both normal appearing white matter and cerebral cortex, consistent with a potential benefit on myelin integrity. The table below presents the distributions and medians for MTR signal values by treatment group at 24 and 48 weeks for normal appearing white matter (periventricular bands 1 to 3), showing positive median changes in the 18 mg group (meaning that ≥ 50% of patients had an absolute increase in MTR signal), while all other groups had a decrease in MTR signal, as would be expected in an MS patient population. The results were consistent across all six normal appearing white matter and cerebral cortical bands.

[84] Source: Traboulsee A, Dehmeshki J, Peters Kr et al. Disability in multiple sclerosis is related to normal appearing brain tissue MTR histogram abnormalities Mult Scler 2003;9:566-73

Table 8: CHANGE-MS MTR results

		WEEK 24*		WEEK 48	
Change in MTR signal (% units)		**Mean**	**Median**	**Mean**	**Median**
PV Band 1	18mg/kg	0.68	0.28	0.128	-0.265
	Placebo / 6-12-18mg	-0.35	-0.58	-0.855	-1.01
		Gain vs. placebo	**P value**	**Gain vs. placebo / 6-12-18mg**	**P value**
	18mg vs. Placebo / 6-12-18mg	**1.03**	**0.188**	**0.98**	**0.271**
PV Band 2	18mg/kg	0.64	0.30	0.179	-0.155
	Placebo / 6-12-18 mg	-0.32	-0.64	-0.763	-0.94
		Gain vs. placebo	**P value**	**Gain vs. placebo / 6-12-18mg**	**P value**
	18mg vs. Placebo / 6-12-18 mg	**0.96**	**0.188**	**0.94**	**0.277**
PV Band 3	18mg/kg	0.66	0.34	0.223	-0.145
	Placebo / 6-12-18 mg	-0.28	-0.61	-0.712	-0.91
		Gain vs. placebo	**P value**	**Gain vs. placebo / 6-12-18mg**	**P value**
	18mg vs. Placebo / 6-12-18 mg	**0.94**	**0.194**	**0.94**	**0.269**

MTR: Magnetization Transfer Ratio
* Recalculated with the same number of qualifying MTR scans at 48 weeks

For secondary endpoints related to **MRI measures of neuroinflammation**, patients in all treatment groups improved from Week 24 to Week 48, however there was no significant separation between treatment groups. The effect of temelimab on adaptive immune-mediated inflammation is not clinically relevant, and any reduction in inflammatory activity does not appear to be responsible for the effects seen on neurodegenerative endpoints.

In terms of **safety** at 48 weeks, there were no organ-class specific toxicities and no dose dependent adverse events were observed. As shown in Table 9 below, serious adverse events in general and those potentially related to the treatment were infrequent and well balanced across treatment groups.

Table 9: CHANGE-MS safety results

	GNbAC1 **6 mg/kg N=88**	GNbAC1 **12mg/kg N=90**	GNbAC1 **18 mg/kg N=89**	Overall **N=267**
SAE	3	4	1	8
Serious-related AE*	0	1	0	-
AE leading to early termination	2	2	2	6
AE leading to death	0	0	0	0

Temelimab continued to show an excellent tolerability profile throughout the second part of the CHANGE-MS study.

5.2.4.7 ANGEL-MS Extension

ANGEL-MS (Assessing the HERV-W Env ANtagonist temelimab for Evaluation in an open label Long-term Safety Study in Patients with MS) is an international long-term extension study of the Phase IIb Study GNC-003 (CHANGE-MS) in patients with Relapsing Remitting Multiple Sclerosis (RRMS) with the primary objective of demonstrating the long-term safety of monthly repeated doses of temelimab. The study was planned to last 96 weeks and patients continued their temelimab treatment dose from GNC-003 (i.e. 6 mg/kg, 12 mg/kg or 18 mg/kg, administered intravenously, with 4-week administration intervals). The primary endpoint is the long-term safety of temelimab, based notably on adverse events (AEs) and clinical safety laboratory. The secondary objective is long-term efficacy based on brain MRI markers, annualized relapse rate, disability, disease activity, EDSS and MSFC Scores.

5.2.4.8 Results

The study started on June 6th, 2017 and 219 patients in total enrolled, representing 94% of all patients who completed the CHANGE-MS study. ANGEL-MS was fully funded by Servier and had an early termination due to Servier's decision to end its partnership with GeNeuro, with all patients being offered end-of-study visits. Across the two studies (CHANGE-MS and ANGEL-MS), 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). As there was no longer an administration of placebo during ANGEL-MS, 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).

Brain volume changes were analyzed on the whole brain and different anatomical locations, atrophy of the brain and more specifically of certain of its parts such as the thalamus being often considered as a predictor of the progression of disability. Benefits of temelimab were seen in a lower cortical and thalamic atrophy rate, with relative volume loss reductions of 42% and 43% respectively between the highest dose of 18 mg/kg and the Control group, with a dose-effect across treatment groups assessed by linear regression showing a trend value of p=0.058 for cortical atrophy and a statistically significant value of p=0.038 for thalamic atrophy). Table 10 below presents the evolution of median thalamic atrophy by time and by treatment groups since the original baseline of CHANGE-MS.

In terms of **safety** at 96 weeks (CHANGE-MS + ANGEL-MS), there were no organ-class specific toxicities and no dose dependent adverse events observed. As shown in Table 10 below, serious adverse events in general and those potentially related to the treatment were infrequent and well balanced across treatment groups. Temelimab continued to show an excellent tolerability profile throughout the second part of the study.

Table 10: ANGEL-MS safety results

Number of patients (%)	18 mg/kg (N=77)	12 mg/kg (N=68)	6 mg/kg (N=74)
Adverse Events (AEs)	34 (44.2%)	32 (47.1%)	33 (44.6%)
Serious adverse events (SAEs)	5 (6.5%)	1 (1.5%)	6 (8.1%)
Serious related AEs	3 (3.9%)	0	0
AEs leading to study discontinuation	2 (2.6%)	1 (1.5%)	1 (1.4%)
Fatality*	1 (1.3%)	0	0

* Patient had previously voluntarily exited the study; the Investigator considered the event as unrelated.

In order to ensure consistency, analyses of efficacy endpoints in ANGEL-MS were based on comparing the original randomized groups from 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).
Further, in order to examine the robustness of the efficacy analyses, several sensitivity analyses were performed. First by dose groups, i.e. by the randomized dose received in ANGEL-MS, irrespective of time treated. Then by absolute dose received, separating the total dose of temelimab into quartiles, irrespective of body weight or randomized dose group. And finally separating the patients having received 18mg/kg during 96 weeks against all other treatments. No corrections were performed for multiple testing.

Overall, the ANGEL-MS data confirmed that treatment with temelimab for 2 years had a continued, positive impact on key MRI-based paraclinical measures, associated with disease progression in multiple sclerosis, extending the data reported at Week 48 in the CHANGE-MS study. These include reductions in brain atrophy (notably in the cerebral cortex and thalamus) and maintenance of 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.

In terms of **MRI measures of neuroinflammation**, all groups improved with treatment, however no significant separation between treatment groups was observable. The effects of temelimab are unlikely to be driven by an anti-inflammatory effect.

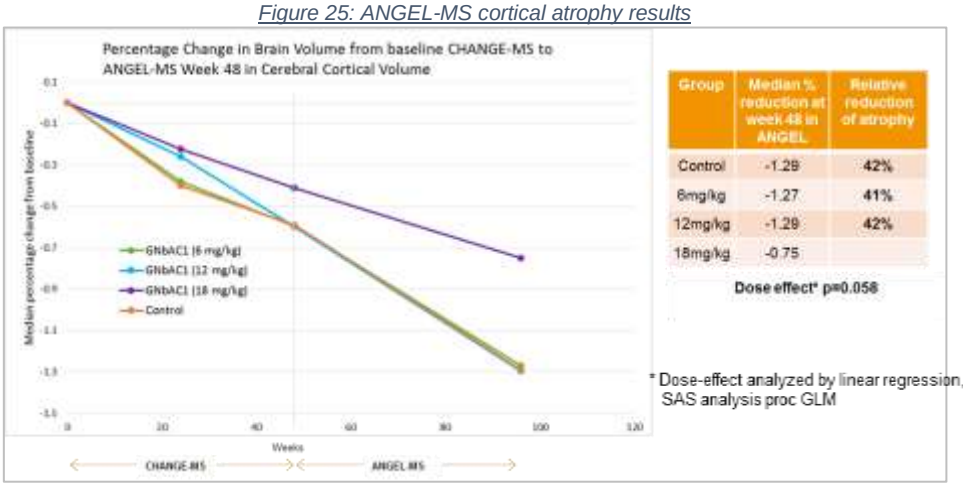
Number of T2 lesions	18 mg/kg	12 mg/kg	6 mg/kg	Control Group	P-value
Median number of new or newly enlarged T2 lesions from ANGEL-MS Baseline	5.0	5.0	6.0	6.0	0.31*
Volume of T2 lesions	**18 mg/kg**	**12 mg/kg**	**6 mg/kg**	**Control Group**	**P-value**
Median % increase of T2 lesion volume from ANGEL-MS Baseline	8.1%	8.7%	13.7 %	11.8 %	0.28**

*Non parametric analysis SAS Proc NPAR1WAY, excluding Control group from analysis

**Regression analysis SAS Proc GLM, excluding Control group from analysis

Effects of temelimab on **brain atrophy measures** observed in CHANGE-MS were confirmed in ANGEL-MS after 96 weeks of total treatment. As illustrated in Figure 25 and Figure 26 below, this was notable in the cerebral cortex and thalamus, with relative reductions in volume loss of 42% and 43%, respectively, between the 18 mg/kg (highest dose studied) and Control Group, with a trend for a dose-response across treatment groups for cortical atrophy (p=0.058) and a statistically significant dose-response for thalamic atrophy (p=0.038).

Figure 25: ANGEL-MS cortical atrophy results



As illustrated in Figure 27, for thalamic atrophy, all sensitivity analyses were consistent on the effect of the 18mg/kg dose versus any other treatment arm.

Figure 26: ANGEL-MS thalamic atrophy results

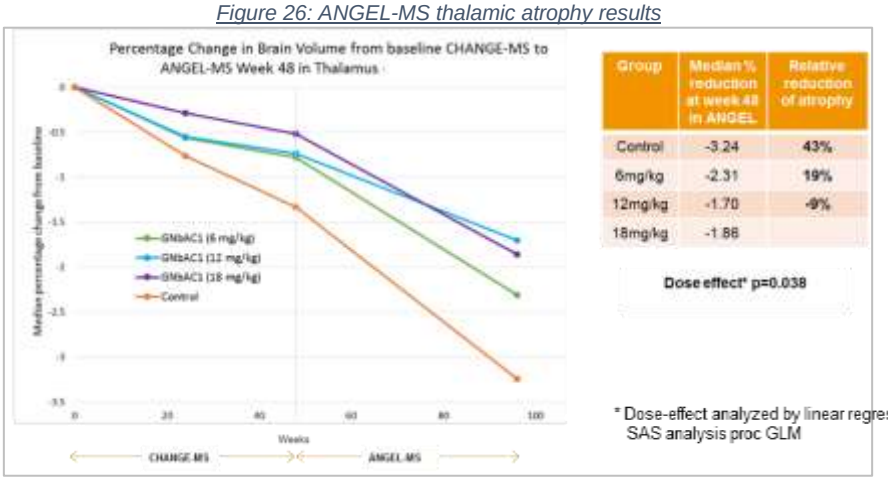
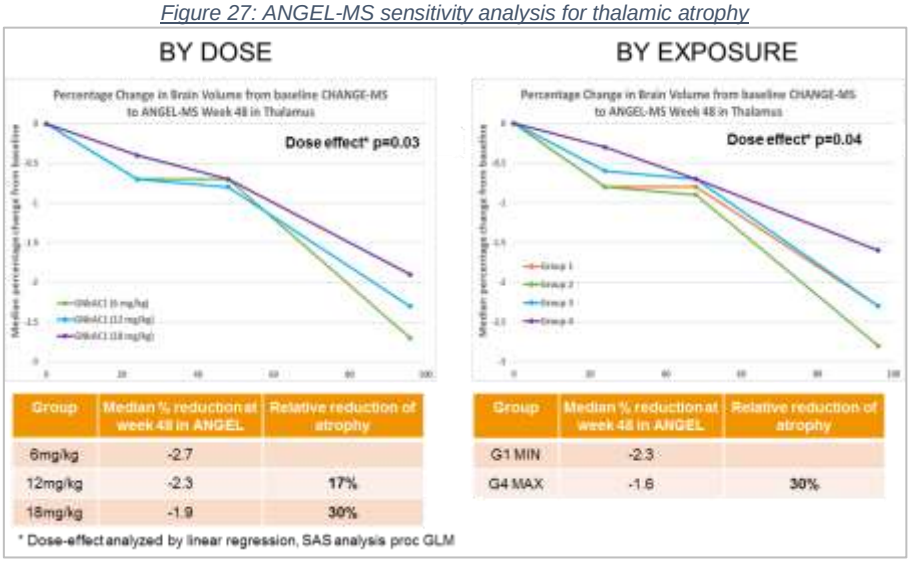


Figure 27: ANGEL-MS sensitivity analysis for thalamic atrophy



The number of **T1 hypointense lesions** was not analyzed at the end of ANGEL-MS. This was because, in order to protect patients from unnecessary exposure to gadolinium, no gadolinium contrast was given in the ANGEL-MS study. As a result, it was technically not possible to differentiate between acute T1 Black Holes (due to edema associated with acute, inflammatory lesions) and chronic T1 Black Holes (due to permanent tissue destruction).

Nonetheless, the effect of temelimab on lesion evolution into permanent tissue destruction was shown, with less increase in mean T1 Black Hole lesion volume in the 18 mg/kg group versus the Control Group.

	18 mg/kg	12 mg/kg	6mg/kg	Control
Median percent increase in T1 hypointense lesion volume	8.7	9.2	14.5	21.3
Pairwise comparisons vs Control, p-values*	0.12	0.80	0.41	

*Analysis of covariance on rank transformed data

The effect on **Magnetization Transfer Ratio** (MTR) signal of 18mg/kg dose group relative to the Control Group, observed at 24 and 48 weeks of CHANGE-MS, was confirmed in comparison with the Control Group at 96 weeks, in both normal appearing white matter and cerebral cortex, consistent with a potential benefit on remyelination. Figure 28 and Figure 29 below present the distributions and medians of MTR signals by treatment group at 48 weeks of ANGEL-MS for periventricular bands and for cortical bands.

Figure 28: ANGEL-MS MTR signal changes in Normal Appearing White Matter

		WEEK 48 ANGEL-MS							
Change in MTR signal from CHANGE-MS BL (% units)		18 mg	12 mg	6 mg	Control	Gain 18 vs 12	Gain 18 vs 6	Gain 18 vs Ctrl	Trend p*
PV Band 1	mean	-0.84	-3.02	-3.76	-3.17	2.18	2.91	2.33	0.022
	median	-1.83	-3.55	-3.39	-3.52	1.72	1.56	1.69	
PV Band 2	mean	-0.12	-2.17	-2.94	-2.13	2.05	2.82	2.01	0.034
	median	-0.99	-2.70	-2.16	-2.65	1.71	1.17	1.66	
PV Band 3	mean	0.74	-1.31	-1.85	-1.11	2.05	2.60	1.86	0.048
	median	-0.32	-1.42	-0.86	-1.35	1.10	0.54	1.03	

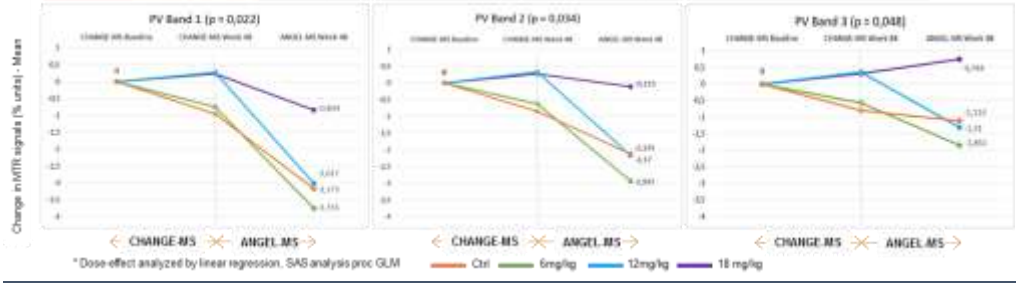


Figure 29: ANGEL-MS MTR signal changes in cortex

		WEEK 48 ANGEL-MS							
Change in MTR signal from CHANGE-MS BL (% units)		18 mg	12 mg	6 mg	Control	Gain 18 vs 12	Gain 18 vs 6	Gain 18 vs Ctrl	Trend p*
CC Band 2	mean	0.77	-1.24	-1.24	-1.01	2.01	2.01	1.78	0.035
	median	0.00	-0.89	-0.73	-0.96	0.89	0.73	0.96	
CC Band 3	mean	0.63	-1.40	-1.42	-1.19	2.03	2.06	1.82	0.033
	median	-0.01	-0.97	-1.07	-1.20	0.96	1.06	1.19	
CC Band 4	mean	0.44	-1.76	-1.78	-1.54	2.20	2.22	1.98	0.024
	median	0.13	-1.11	-1.12	-1.41	1.24	1.25	1.54	

Importantly, and for the first time, encouraging, dose-dependent effects were seen on **clinical measures of disease progression**. This was as measured by a lower proportion of patients with 12-week confirmed EDSS progression, or with 20% worsening in Timed 25-Foot Walk from Baseline of CHANGE-MS to week 96 (or end-of-study) in ANGEL-MS.

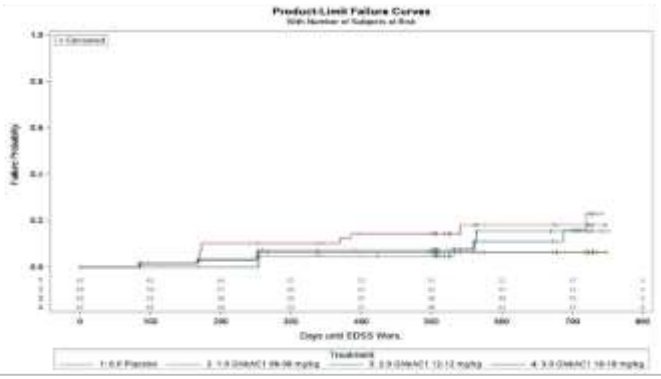
A lower probability of 12-week **confirmed disability progression** in the 18 mg/kg group versus all other groups is illustrated in Figure 30 below.

Figure 30: ANGEL-MS probability of disease progression

	18 mg/kg	12 mg/kg	6 mg/kg	Control
% of patients with 12-week confirmed worsening in neurological disability from CHANGE-MS baseline to week 48 ANGEL-MS	3.8	4.8	8.3	9.1

Slightly lower probability of 12-week confirmed disability progression in the 18 mg/kg group, but not reaching statistical significance:

- Survival Wilcoxon overall test p=0.34
- Log-rank overall test p=0.45
- Hazard ratio 18mg/kg vs control = 0.50, pairwise comparison p=0.27



When pooling all groups against the 18mg/kg group, the result nearly reaches statistical significance. However, the cohort of patients is small, as the study was not designed to examine disability progression, and the number of events recorded is also very low. Therefore, although encouraging, these results are not conclusive.

Also encouraging, and consistent with the EDSS data, is the proportion of patients with a worsening of > 20% or more in the **Timed 25-Foot Walk Test** when comparing CHANGE-MS Baseline to the end of ANGEL-MS, as may be seen in Table 11 below.

Table 11: ANGEL-MS proportion of patients with worsening >20% of Timed 25-foot walk

Timed 25-foot walk – Original CHANGE-MS Groups	18 mg/kg	12 mg/kg	6 mg/kg	Control	P-value**
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	0.03

* Fifteen patients with extreme walking disability removed from analysis –for whom the test was almost impossible to perform – excluded patients distributed equally across treatment groups

** Fisher exact test

At 96 weeks of treatment, a lower proportion of patients in the 18mg/kg group experienced a clinically relevant worsening, than in any other group, with statistical significance of p=0.03. All of the sensitivity analyses performed confirmed the results, as illustrated in Table 12 below.

Table 12: ANGEL-MS – sensitivity analysis of proportion of patients with worsening >20% of Timed 25-foot walk

Timed 25-foot walk – By Dose Groups	18 mg/kg	12 mg/kg	6 mg/kg	P-Value**
Percentage of patients with worsening ≥ 20% in the Timed 25-Foot Walk Test compared to CHANGE-MS Baseline*	3.6	16.9	15.0	0.04
Timed 25-foot walk – By 18 vs Others	**18 mg/kg**	**Others**	**P-value****	
Percentage of patients with worsening ≥ 20% in the Timed 25-Foot Walk Test compared to CHANGE-MS Baseline*	2.4	15.0	0.03	

* Fifteen patients with extreme walking disability removed from analysis –for whom the test was almost impossible to perform – excluded patients distributed equally across treatment groups

** Fisher exact test

The same caution as above holds true, but these results at 96 weeks appear to indicate that the positive effect observed in MRI measures may translate into a clinical benefit.

Overall at 96 weeks of temelimab treatment, there was a consistent and sustained benefit with temelimab at the dose of 18mg/kg on key independent markers of neurodegeneration, such as thalamic, cortex and whole brain volumes, as well as MTR in cortical and normal appearing white matter. These markers are linked to long term disease progression and worsening of disability in MS. 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. Moreover, temelimab appeared safe during the whole duration of the trial.

These results are coherent with the pre-clinical knowledge to date on the mechanisms of action of HERV-W ENV and of temelimab.

5.2.4.9 GNC-006 Study: robust safety confirmed at high doses

This study was a Phase Ic, single-center, randomized, double-blind, placebo-controlled, dose-escalating study in 24 healthy volunteers to assess the administration of high doses of temelimab.

Four cohorts of patients received doses of temelimab ranging from 36 mg/kg to 110 mg/kg. The results of the study, performed in a specialized pharmacology trial unit part of the University Hospital of Sydney, Australia, showed that no adverse events related to drug safety occurred and that pharmacokinetic data were linear for all doses tested.

5.2.5 Continued Clinical Development in MS

The 48-week results of the CHANGE-MS study and the 96-week results of the ANGEL-MS extension trial (resulting from the addition of the 48-week CHANGE-MS study and the 48-week of the ANGEL-MS study) both showed that the 18 mg/kg dose induced a positive response for neuroprotection markers such as brain volumes, black holes and MTR, and showed encouraging dose-dependent effects on clinical measures of disease progression. In addition, the safety profile over 96 weeks of temelimab at all tested doses appeared very favorable. Furthermore, the results of the high-dose pharmacology study completed in January 2019 support and expand the large amount of positive clinical data regarding temelimab's safety, tolerability and efficacy up to 110mg/kg. Based on these results, temelimab may provide a safe treatment option enhancing neuroprotection in all forms of the disease, that could result in the reduction of the disability progression, which is the key unmet medical need in MS.

The two completed Phase IIb clinical trials in MS show that temelimab provides a clear benefit against neurodegeneration through a novel mode of action that does not rely on immunosuppression. This benefit could be particularly relevant for patients in a progressive form of the disease, where there are today few treatment options, all of which rely on immunosuppression pathways. But temelimab could also bring relevant clinical benefits to a remitting-relapsing MS population, as neurodegeneration is believed to start already in the early phases of the disease and as the safety profile of temelimab could allow it to be used in combination with existing therapies targeting the immune system. GeNeuro is thus currently working on two possible avenues for the development of temelimab in MS:

- A monotherapy approach, in non-active progressive MS patients[85], where the unmet medical need is the highest; and
- A combination approach, in conjunction with an existing anti-inflammatory drug, to slow-down or prevent progression for relapsing MS patients, an area in which current treatments have modest impact.

Given the high costs of the international clinical trials necessary to confirm efficacy and register a product in MS with both the FDA and the EMA, which the Company estimates to exceed €100 million, the Company is actively pursuing partnership discussions for the MS indications at the same time as it is preparing a new clinical trial in MS, in patients whose disability progresses without relapses aiming to further validate the Company's therapeutic potential in the unmet medical need of stopping disease progression.

Regulatory authorities, such as the FDA, and the MS community have clearly identified "progression without relapses" as the urgent medical need in MS. GeNeuro's temelimab results indicate a true potential in this area where there is no medication available, and thus has a wide number of options on how to continue development in MS. Yet developing a drug against progressive forms of MS is a complex endeavor, as patients' condition evolves slowly over time, and clinical trials require large cohorts treated for long periods of time. Inclusion criteria for such trials aiming at having homogenous patient populations are a key success factor.

In this connection, GeNeuro announced on November 20, 2019, an agreement with the Karolinska Institutet / Academic Specialist Center (ASC) of Stockholm, Sweden, to launch a new, single-center, Phase II clinical study of temelimab in multiple sclerosis. This new trial is now being conducted at the Center for Neurology of ASC, which, with approximately 2,400 patients, is the largest MS center in Sweden. The one-year trial has enrolled 40 patients whose disability progresses without relapses, and will document the safety and tolerability of temelimab following

[85] Non-active progressive: the MS phase when patients stop experiencing new relapses, but disability continues to progress

higher doses, as well as measures of efficacy based on the latest biomarkers associated with disease progression, including MRI measurements of brain atrophy, black holes (permanent damage), change in myelin integrity by magnetization transfer ratio, markers of myelin integrity and myelin fraction (REMyDI[86]), and markers of neurodegeneration and neuroprotection in biofluids such as Neurofilament Light Chains. The study's initiation was delayed due to the COCID-19 pandemic but recruitment was eventually completed in February 2021. Positive results from this study, expected for Q1 2022, would open the way to a Phase III registration trial in MS.

[86] Rapid Estimation of Myelin for Diagnostic Imaging, an MRI based method for automatic quantification of myelin volume in the brain.

5.3 COVID-19

i) Origin and prevalence

Coronavirus disease (COVID-19) is an infectious disease caused by SARS-CoV-2, a newly discovered coronavirus, whose emergence was first observed when cases of unexplained pneumonia were noted in the city of Wuhan, China, at the end of 2019.

SARS-CoV-2 is the novel coronavirus first identified in humans in December 2019 and is the cause of COVID-19. Coronaviruses are a large family of viruses that can cause illness in animals or humans. In humans there are several known coronaviruses that cause respiratory infections. These coronaviruses range from the common cold to more severe diseases such as severe acute respiratory syndrome (SARS), Middle East respiratory syndrome (MERS), and COVID-19.

COVID-19 is the most severe global pandemic since the influenza pandemic of 1918. As of April 20, 2021, there have been over 140 million confirmed cases and over 3 million global deaths from COVID-19. The risk of mortality increases with age (estimated to be ~0.1% for individuals aged 0-19, ~6% for individuals over age 60). Risk of severe disease and mortality increase for persons with pre-existing diseases or comorbid conditions (e.g. cardiovascular disease, diabetes, chronic lung disease, obesity), and hospitals worldwide continue to face the increasing demand of patients requiring oxygen supply, ventilators, and intensive care.

Both pulmonary and extra-pulmonary SARS-CoV-2-related forms have been recognized[87], which predominantly involve the impairment of immune functions[88]. Innate immune hyper-activation combined with adaptive immune dysregulation has been recognized to play a critical role in the progression of the disease and thus in the clinical outcome of COVID-19 patients,[89,90] suggesting the critical evolution driven by exacerbated innate immunity and associated inflammation and lymphopenia[91,92]. The immunological involvement includes hyper-immune reactions such as the “cytokine storm” syndrome (mostly occurring in pulmonary forms), the pediatric multisystem inflammatory syndrome, and immune-mediated cutaneous or neurological diseases along with various autoimmune manifestations such as the dysregulation of coagulation mechanisms[93,94].

In addition, large numbers of patients who have been infected with SARS-CoV-2 continue to experience a constellation of symptoms long past the time that they’ve recovered from the initial stages of COVID-19 illness. Often referred to as “Long COVID”, these symptoms, which can include fatigue, shortness of breath, “brain fog”, sleep disorders, fevers, gastrointestinal symptoms, anxiety, and depression, can persist for months and can range from mild to incapacitating. These present before, during, and after respiratory symptoms and are unrelated to respiratory insufficiency, suggesting independent brain damage. In some cases, new symptoms arise well after the time of infection or evolve over time. Follow-ups conducted in Germany and the United Kingdom found post–COVID-19 neuropsychiatric symptoms in 20% to 70% of patients, even in young adults, and lasting months after respiratory symptoms resolved[95].

ii) Current treatments

Current treatments for COVID-19 are designed for hospitalized patients and include:

- Corticosteroids: Many doctors have been treating very ill COVID-19 patients with corticosteroids since the pandemic began. It makes biologic sense for those patients who have developed a hyper-immune response (a cytokine storm) to the viral infection. In these cases, it is the immune system's overreaction that is damaging the lungs and other organs, and too often leading to death. Dexamethasone and other corticosteroids (prednisone, methylprednisolone) are potent anti-inflammatory drugs. They are readily available and inexpensive.
- Anticoagulation drugs ("blood thinners"): almost all patients admitted to the hospital with COVID-19 receive medications to help prevent blood clots.
- Antiviral drugs: despite conflicting evidence from early studies on remdesivir's effectiveness, in October 2020, the FDA approved the antiviral drug remdesivir to treat COVID-19 following clinical trials suggesting

87 Source: Gupta et al. Extrapulmonary manifestations of COVID-19. Nat Med 20202
88 Source: Vardhana SA, Wolchok JD. The many faces of the anti-COVID immune response. J Exp Med 2020;
89 Source: Wang J, Jiang M, Chen X, Montaner LJ. Cytokine storm and leukocyte changes in mild versus severe SARS-CoV-2 infection: Review of 3939 COVID-19 patients in China and emerging pathogenesis and therapy concepts. J Leukoc Biol 2020
90 Source: Cao X. COVID-19: immunopathology and its implications for therapy. Nat Rev Immunol 2020
91 Source: Zhang et al. Viral and host factors related to the clinical outcome of COVID-19. Nature 2020
92 Source: Huang I, Pranata R. Lymphopenia in severe coronavirus disease-2019 (COVID-19): systematic review and meta-analysis. J Intensive Care 2020
93 Source: Mehta et al. COVID-19: consider cytokine storm syndromes and immunosuppression. Lancet 2020
94 Source: Nath A, Smith B. Neurological issues during COVID-19: An Overview. Neurosci Lett 2021
95 Source: Woo et al. Frequent neurocognitive deficits after recovery from mild COVID-19. Brain Commun. 2020

that in patients aged 12 and older and weighing at least 40 kilograms, remdesivir may modestly speed up recovery time. Remdesivir remains the sole FDA-approved drug for the treatment of COVID-19.

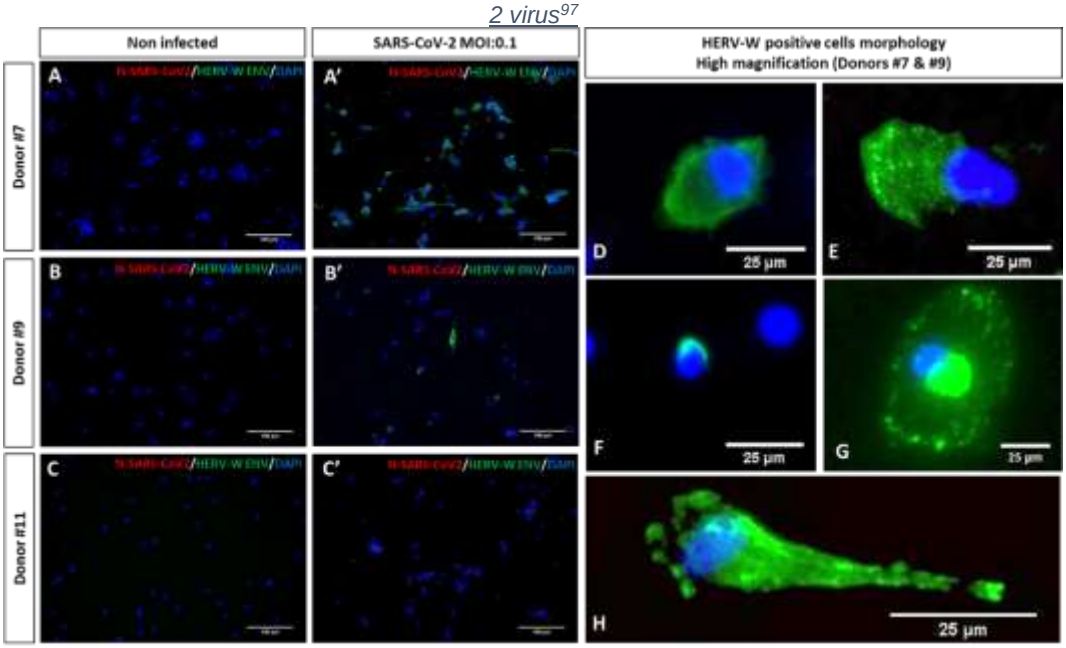
- Monoclonal antibodies: anti-SARS-CoV-2 monoclonal antibodies that target the SARS-CoV-2 spike protein and block virus entry into cells have been evaluated for the treatment of COVID-19. To date, the FDA has issued Emergency Use Authorizations (EUAs) for three anti-SARS-CoV-2 monoclonal antibodies and combinations: bamlanivimab alone, bamlanivimab plus etesevimab, and casirivimab plus imdevimab. However, because of an increasing number of reports of variants that are resistant to bamlanivimab alone, this product is no longer be distributed by the U.S. government.

Neurological symptoms are reported in up to 25 percent[96] of people who develop COVID-19. Currently, the condition they are suffering from is known as "long COVID," although other names are being proposed. Very different chronic illnesses may develop in some people who have had COVID-19, so the US National Institutes of Health has proposed a unifying name: post-acute sequelae of SARS-CoV-2 infection, or "PASC". There appear to be two main groups of symptoms, one that is mainly respiratory, such as a cough and feeling breathless, but also includes fatigue and headaches, and a second group of symptoms that affects many parts of the body, including the heart, brain and the gut, that range from memory, concentration or sleep problems, to fast or pounding heartbeat, lingering loss of smell or taste, depression or anxiety. A smaller number of COVID-19 patients develop severe psychotic symptoms. Due to the variety of symptoms, there is today no specific treatment approved for PASC.

5.3.1 Pre-clinical research in COVID-19

GeNeuro, working in collaboration with the International Center for Infectiology Research in Lyon, France (CIRI) started research to understand why HERV-W ENV was found at high levels in the blood of hospitalized COVID-19 patients. Preliminary findings, available online on Research Square[97], show that when human peripheral blood mononuclear cells from healthy donors were cultured and exposed to SARS-CoV-2, about 20% of donors responded by expressing HERV-W ENV in lymphocytes, cells in which the virus did not replicate – see illustration in Figure 31 below. This expression was triggered specifically by the spike protein of SARS-CoV-2, independently from cytokine release. This research suggests a genetic and/or epigenetic susceptibility associated to the activation of HERV-W ENV in blood lymphoid cells, which could be important in understanding how SARS-CoV-2 infection may lead to severe forms of COVID-19 in some patients.

Figure 31: HERV-W ENV immunodetection in primary PBMC cultures from healthy blood donors with SARS-CoV-2 virus[97]



Heretofore, HERV-W ENV had been found in specific disease situations, and its presence has always been tied to negative disease outcomes for the patient. The pro-inflammatory effects of HERV-W ENV are mediated through the activation of the TLR4 innate immune receptor, a pathway closely associated with some of the key features of COVID-19, such as hyper-activation of immune functions, endothelial cell activation, vasculitis as well as coagulopathy. HERV-W ENV has mostly been studied in neurodegenerative diseases, with widely observed pathogenic effects on peripheral and central nervous system cells. The presence of HERV-W ENV in COVID-19 patients may have a double effect: in the short-term, when activated in genetically susceptible individuals, HERV-

[96] Source: Desai et al, Neurological manifestations of coronavirus disease 2019, Neurol Sci. 2021 Jan
[97] Source: Charvet B, Horvat B et al, SARS-CoV-2 induces transcription of human endogenous retrovirus RNA followed by type W envelope protein expression in human lymphoid cells, ResearchSquare, April 2021.

W ENV could act as an accelerant to the innate immune response, fueling complications and leading to the need for ventilation. But even after the primary infection is over, if HERV-W ENV has reached a self-fueling expression level, it could cause persistent damage to endothelial cells in blood vessels and also to cells from the peripheral and central nervous system, which could explain many of the long-term neurological symptoms experienced by patients long after SARS-CoV-2 infection.

5.3.2 Clinical data linking HERV-W ENV to COVID-19

In a study published in the Lancet's EBioMedicine[98], researchers from the University of Rome "Tor Vergata" have found (i) that HERV-W ENV was highly expressed in the leukocytes of COVID-19 patients but not in those of healthy donors (see Figure 32 below) ; (ii) that the expression of HERV-W ENV correlated with the markers of T-cell differentiation and exhaustion and blood cytokine levels; (iii) that the percentage of HERV-W ENV-positive lymphocytes correlated with inflammatory markers and pneumonia severity in COVID-19 patients; and (iv) that, notably, HERV-W ENV expression reflected the respiratory outcome of patients during hospitalization. Given the known immuno- and neuro-pathogenicity of HERV-W ENV protein, it could promote certain pathogenic features of COVID-19 and therefore serve as a biomarker to predict clinical progression of disease and as a potential therapeutic target.

Figure 32: expression of HERV-W in leukocytes of COVID-19 patients[99]

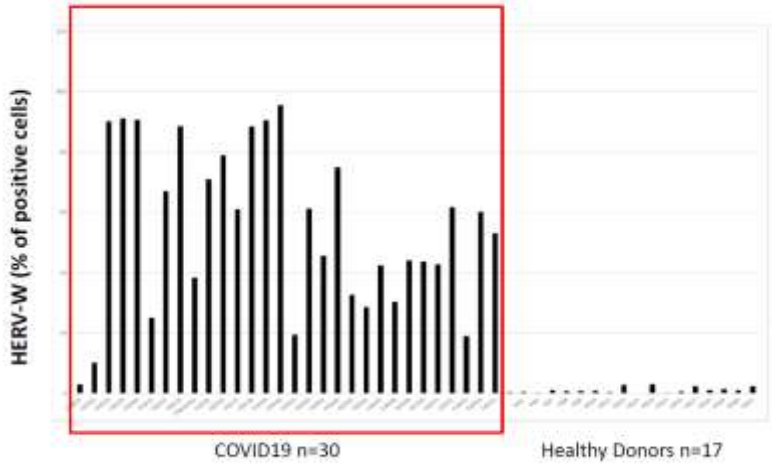
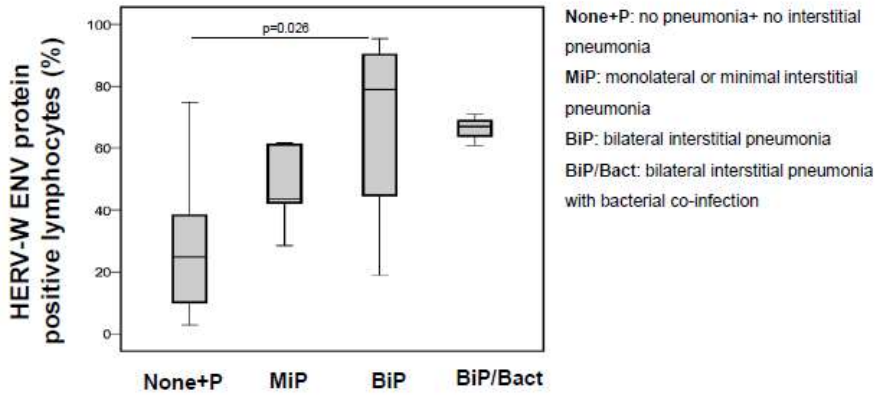


Figure 33: correlation between HERV-W expression in lymphocytes and respiratory outcome[98]



5.3.3 Possible Clinical Development in COVID-19

The scientific rationale for the development of temelimab for the treatment of COVID-19 is supported by the above findings and by the known pro-inflammatory properties of the HERV-W ENV protein. These may shed a new light on the development of severe forms of COVID-19, and may also offer an unforeseen opportunity to stop this evolution through a novel therapeutic approach.

With HERV-W ENV being a possible aggravating agent of COVID-19, and with GeNeuro's temelimab being a humanized monoclonal antibody that specifically neutralizes this pathogenic protein, GeNeuro has started working

[98] Source : Balestrieri E, Matteucci C et al, Evidence of the pathogenic HERV-W envelope expression in T lymphocytes in association with the respiratory outcome of COVID-19 patients, Lancet EBioMedicine, April 2021

[99] Source : University of Rome « Tor Vergata", April 2021

with leading medical centers in Europe and the USA to evaluate temelimab as a therapeutic treatment, both to prevent immune system hyper-activation in recently infected patients, as well as to tackle severe neurological and psychiatric syndromes in long-COVID, or PASC, patients.

For recently infected patients, the contemplated study would follow the guidelines laid out by the WHO, and could be a pilot Phase II, rolling into Proof-Of-Concept Phase II/IIII, beginning with a safety phase with approximately 10 patients, then increasing to 60 patients, and measuring clinical evolution (days of hospitalization, ICU prevention) as the primary endpoint, with 60-day follow-up for post-COVID-19 syndromes.

For "Long COVID, or PASC, patients, as symptoms are heterogeneous, the emerging research cohorts in Europe and the USA are working on stratifying patients to understand the nature of the affections and define treatment options. GeNeuro is working with leading neurological and neuropsychiatric centers in the EU and the USA to participate to this stratification with HERV-W ENV biomarkers, as patients positive to HERV-W ENV would be immediate candidates for a treatment with temelimab, as one of the very few present approaches to treat PASC patients.

5.4 HERV-W ENV in T1D

5.4.1 Type 1 Diabetes

Type 1 diabetes is a chronic disease that results from the autoimmune destruction of the insulin-producing beta cells in the pancreas. As a result, the pancreas produces little or no insulin, a hormone needed to allow sugar (glucose) to enter cells and produce energy. People with T1D need daily insulin injections in order to manage their glucose level and would not be able to survive without insulin.

T1D is the major type of diabetes in children, accounting for over 85% of all diabetes cases in people under the age of 20 worldwide. In general, the incidence rate increases from birth and peaks between the ages of 10–14 years during puberty. T1D is distinct from the more common type 2 diabetes, which occurs when the body becomes resistant to insulin, a condition generally associated with lifestyle, with onset predominantly in adulthood.

There is no cure today for T1D, but insulin replacement therapy for life allows patients to manage the condition. Yet even with careful management, long-term complications generally develop over decades as a result of fluctuations in blood sugar levels. Serious long-term complications include heart disease, stroke, kidney failure, foot ulcers, and damage to the eyes.

i) Origin and prevalence of the disease

The origin of T1D is unknown, but a combination of genetic susceptibility factors and environmental triggers such as viral infection, toxins or some dietary factors have been implicated indifferent studies. T1D accounts for 5–10% of the total cases of diabetes worldwide[100].

There are very wide variations between world regions regarding the incidence of T1D, The World Health Organization's "Multinational Project for Childhood Diabetes", also known as the DiaMond Project, published in 2000 an analysis on the incidence of T1D in children less than 15 years of age in 50 countries worldwide[101]. This study reported a greater than 350-fold difference in the incidence of T1D among 100 populations worldwide, with incidences ranging from a low of 0.1/100,000 per year in China and Venezuela, compared to incidences >20/100,000 in countries such as Sweden, Norway, Portugal, the UK, Canada, New Zealand, to a high of 36.5/100,000 in Finland and 36.8/100,000 per year in Sardinia. In the United States, the "Search for Diabetes in Youth study"[102] showed wide disparities between populations within the country, with the highest incidence of T1D at the age of 10-14 years being of 32.9/100,000 in non-Hispanic white youth, as compared to an incidence of 18.2/100,000 in the Hispanic population, 1.95/100,000 in the Navajo population, and a national incidence of 24.3/100,000. It is estimated that there are approximately 1.8 million cases diagnosed with T1D in the United States.

The reasons for these differences between world regions and ethnicities are unclear, but an interplay between genetic, and environmental factors and behavioral patterns is suspected. All studies report an increase in the incidence of T1D, for example DiaMond noting an increase of up to 4.0% in Asia, 3.2% in Europe, and 5.3% in North America in the period 1995–1999.

Some genes have been implicated in susceptibility studies for T1D, the most important being two haplotypes of the human leukocyte antigen (HLA) complex[103]. But although 90–95% of young children with T1D carry either or both susceptibility haplotypes, approximately 5% or fewer persons with HLA-conferred genetic susceptibility actually develop clinical disease. External factors having been reported as risk factors in the onset of the disease are the

[100] Source: Diagnosis and classification of diabetes mellitus. Diab care. 2009
[101] Source: Incidence of childhood type 1 diabetes worldwide. (DiaMond) Project Group, Diabetes Care. 2000
[102] Source: Incidence of diabetes in youth in the United States. JAMA. 2007
[103] Source: The genetic basis for type 1 diabetes. Br Med Bull. 2008

lack of vitamin D[104] during pregnancy or early childhood, as well as the consumption of cow milk. A number of viruses have been associated with T1D, including enteroviruses such as Coxsackievirus B, rotavirus, mumps virus and cytomegalovirus[105]. A temporal association has been reported between enterovirus infection and the appearance of the first autoantibodies[106], but the role of the virus in the progression of the disease is unclear. Yet the role of these viruses could be to unlock human endogenous retroviral genes in the cells they affect (including pancreas cells for enteroviruses), leading to the encoding of pathogenic HERV proteins, which could be a key factor in triggering local inflammation and toxicity.

ii) Present treatments

In a non-pathological situation, the regulation of blood glucose levels within a very precise range is achieved through a number of metabolic hormones acting in synergy. The key hormones acting in this process are[107]:

- Insulin, which was discovered in the early 20th century, is the first pancreatic beta cell hormone known to lower blood glucose concentrations. It binds to specific receptors present on many cells of the body, including fat, liver, and muscle cells. The primary action of insulin is to stimulate glucose uptake by the cells and therefore lower blood glucose levels. In T1D, the destruction of beta cells impairs insulin production by the patient.
- Amylin, discovered more recently in 1987, is co-produced with insulin by the pancreas beta cells and acts in synergy with insulin by reducing glucagon levels and slowing down the rate of gastric emptying.
- Glucagon, first described in the 1950's, is a key hormone that opposes the effects of insulin by stimulating hepatic glucose production. It plays a key role in maintaining glucose levels in the blood, most notably during fasting periods of the day. When plasma glucose decreases below the required limit, glucagon secretion increases, resulting in the production of glucose by hepatic cells, in order to restore plasma glucose levels to the normal range. Glucagon is produced by pancreatic alfa-cells, which are not affected by T1D, resulting in an excessive glucagon-to-insulin ratio that leads to the release of hepatic glucose, and makes it difficult for patients to control blood glucose levels.
- GLP-1, discovered in the 1960's, is a hormone produced by the L-cells found mainly in the ileum and colon as a response to food absorption. GLP-1 stimulates insulin production and reduces glucagon production only when plasma glucose levels are high. It has a very short half-life of a few minutes in plasma.

The current standard treatment for T1D is frequent measure of blood glucose followed with multiple daily insulin injections, sometimes complemented by other products seeking to improve the hormonal balance to achieve an effective regulation of blood glucose levels.

Insulin replacement therapy has been used for almost one century and has been a life-saving therapy since its introduction by F. Banting in 1921. Before that, patients affected by T1D had a very short life expectancy. Insulin was first harvested from the pancreas of animals, most notably pigs, until late 20th century biotechnology allowed the production of human insulin harvested from cells. Insulin remains the vital and main treatment for patients affected by T1D. The two major forms of insulin are basal and prandial forms.

- Basal insulins are long-acting and injected once or twice a day to provide a constant level of insulin during the day to keep blood glucose within a consistent range. There are numerous basal insulins on the market and the major types of insulins in this space are:
- insulin glargine (Lantus© from Sanofi and Basilar© from Boehringer Ingelheim and Lilly)
- insulin detemir (Levemir© from Novo Nordisk)
- insulin degludec (Tresiba© from Novo Nordisk)

- Prandial insulins are rapid-acting in order to respond to glucose increases after a meal. They act rapidly in the body to counter the increase of sugar levels following food intake. The range of prandial insulins has also considerably increased over the last few years. The major types of insulins in this space are:
- insulin lispro (Humalog © from Eli Lilly and Admelog© from Sanofi)
- insulin aspart (Novolog© and Fiasp© from Novo Nordisk)
- insulin glulisine (Apidra© from Sanofi)

There are large efforts made by the major pharmaceutical companies active in the field of diabetes to improve the benefits provided by the different types of insulin, be it on long-acting forms for basal insulin, or the speed of action for prandial insulins. Since GeNeuro's plans are not to replace insulin but to preserve the patients' remaining

[104] Source: The association between ultraviolet B irradiance, vitamin D status and incidence rates of type 1 diabetes in 51 regions worldwide. Diabetologia. 2008
[105] Source: The role of viruses in human diabetes. Diabetologia45
[106] Source: Enterovirus infection as a risk factor for beta-cell autoimmunity in a prospectively observed birth cohort: the Finnish Diabetes Prediction and Prevention Study. Diabetes 2000
[107] Source: Glucose Metabolism and Regulation: Beyond Insulin and Glucagon, Diabetes Spectrum 2004

endogenous insulin production capacity, the market dynamics for insulin products are largely irrelevant to GeNeuro. But it is important to note the increasing use of other products developed for Type 2 Diabetes ("**T2D**") in the T1D space, especially GLP-1 receptor agonists and SGLT2 inhibitors, and innovations in the delivery of insulin through pumps and "artificial pancreases", which are pumps able to monitor the blood glucose levels and adapt the drug delivery according to needs.

GLP-1 receptor agonists, initially developed for T2D, are sometimes used for T1D patients. This class of molecule interacts with the beta cell GLP-1 receptors and increases glucose-dependent insulin secretion and decreases glucagon secretion, delaying gastric emptying and increasing satiety. They effectively lower glucose and weight while having a low risk of hypoglycemia[108]. Practice has indicated that the use of GLP-1 receptor agonists may improve glucose control levels in T1D patients[109]. Some researchers have suggested that the use of GLP-1 receptor agonists in T1DM may act through the reduction of excessive postprandial glucagon secretion, allowing patients to reduce their total daily dose of exogenous insulin. The leading approved GLP-1 agonists on the market, by date of first approval, are:

- exenatide (Byetta©/Bydureon©), from AstraZeneca, approved in 2005/2012
- liraglutide (Victoza©, Saxenda©), from Novo Nordisk, approved 2010/2016
- dulaglutide (Trulicity©), from Eli Lilly, approved in 2014
- albiglutide (Tanzeum©), from GSK, approved in 2014
- lixisenatide (Lyxumia©), from Sanofi, approved in 2016
- semaglutide (Ozempic), from Novo Nordisk, approved in 2017

SGLT-2 (Sodium glucose cotransporter 2) inhibitors, also developed for T2D, block the SGLT2 protein involved in 90% of glucose reabsorption in the proximal renal tubule, resulting in increased renal glucose excretion and lower blood glucose levels[110]. The leading approved SGLT-2 inhibitors on the market, by date of first approval, are:

- canagliflozin (Invokana©), marketed by Johnson & Johnson, approved the FDA in 2013
- dapagliflozin (Forxiga©), from Bristol-Myers Squibb and AstraZeneca, approved by FDA in 2014
- empagliflozin (Jardiance©) from Boehringer Ingelheim and Eli Lilly and Company, approved by FDA in 2014 for Type-2 diabetes

Estimating the sales of T1D therapies is made difficult by the fact that most drugs in this indication are also marketed for T2D, a far larger indication in terms of number of patients. GlobalData estimated in 2013 that the global T1D market was worth US$6.6 billion, with over 70% of sales in the United States, and projected to grow to a total of over US$13 billion by 2023[111]. But insulin replacement therapies, which are the core of the treatment of T1D patients, are under severe price pressure due to patent cliffs for leading products and the commoditization of the insulin market.

Insulin pumps replace direct injection and/or pens as they deliver the drug through a subcutaneous injection attached to a pump with an insulin reservoir. These pumps are programmed to dispense specific amounts of rapid-acting insulin automatically. This steady dose of insulin is known as the basal rate, and it replaces whatever long-acting insulin the patient was using. The insulin dose has to be complemented by a bolus through the pump after meals, which is made through a calculation by the patient of the impact of the meal on blood glucose. With increasing miniaturization and the wide spread of smartphones, and a very active market dominated by Medtronic, the use of these devices has reached an estimated 35% of T1D users in the United States, and about 15-20% in major European countries[112].

An insulin pump combined with a continuous glucose monitoring device may provide even tighter blood sugar control. These devices, also called "artificial pancreases", are defined by the FDA as a "device that automatically monitors blood glucose and provides appropriate insulin doses in people with diabetes who use insulin"[113]. Recent developments in this field include:

- In September 2016, the FDA approved the first hybrid closed loop system, the Medtronic's MiniMed 670G, intended to automatically monitor blood sugar and adjust basal insulin doses in people with type 1 diabetes. This system is dubbed "hybrid" because it still requires patient input about what they are eating and a calibration of the pump using fingerstick testing.

[108] Source: GLP-1 receptor agonists: a review of head-to-head clinical studies. Ther Adv Endocrinol Metab. 2015
[109] Source: A Systematic review and meta-analysis of randomized controlled trials in use of GLP1 receptor agonists in type 1 diabetes mellitus, AACE 2017
[110] Source: Sodium glucose co-transporter 2 inhibitors—a novel therapy for type 2 diabetes mellitus. *Pract Diabetes Int*. 2010
[111] Source: GlobalData PharmaPoint report 2015
[112] Source: http://www.ntac.nhs.uk
[113] Source: The Artificial Pancreas Device System, www.fda.gov

- At the end of 2017, Abbott launched its FreeStyle Libre, the first continuous glucose monitoring system that does not require any fingerstick tests to calibrate.

As of the date of this Universal Registration Document, it is premature to understand the dynamics of the penetration of these new devices in the T1D market.

Finally, transplantation of beta cells has been tried successfully in T1D[114], but the need to take immunosuppressant drugs for life to avoid rejection, and the scarcity of human beta cells to transplant, have limited the use of this treatment strategy.

All in all, despite the use of effective insulin forms and advances in its delivery, exogenous insulin cannot replicate the level of precision with which human beta cells regulate glucose levels. Add-on therapies, such as GLP-1 agonists and SGLT-2 inhibitors, can contribute to further regulation of glucose levels, but they also carry long-term safety risks. Even with the most diligent insulin use, effects of diabetes include episodes of hyperglycemia and hypoglycemia, and frequent long-term adverse effects such as nerve damage, blindness, kidney damage, limb ulcers and cardiovascular diseases. A recent Australian study[115] has reported that the life expectancy of a person with T1D is reduced by approximately 12 years when compared to the general population. Currently, drugs that can prevent further progression of the disease or restore the function of pancreatic beta cells are not available.

iii) Market dynamics

The clinical manifestation of type 1 diabetes is thought to represent end-stage insulitis, since only 10–20% of the insulin-producing cells have been estimated to still be functioning at the time of diagnosis. Nevertheless, patients with T1D and remaining endogenous insulin reserves may benefit from treatments aimed at preserving insulin secretory capacity. Currently, there are no treatment options to preserve this function. Attenuating the decline in beta cell function should improve glycemic control and reduce the risk of hyperglycemia. If the effect is profound and sustained, reduction or delay of diabetic complications could be expected.

By neutralizing HERV-W ENV, a potential causal factor that promotes inflammation and disrupts insulin production, GeNeuro hopes to preserve the remaining endogenous insulin production of T1D patients.

5.4.2 Pre-clinical research in T1D

i) Mechanisms of HERV activation by exogenous infections

Viruses such as influenza, rhinovirus or Epstein-Barr are epidemiologically linked to T1D, and in particular Coxsackie B virus has been found to be associated with this disorder. In a preliminary experiment, the CVB-4E2 strain of a Coxsackie Virus isolated from T1D pancreas was compared to a control CVB-4 strain isolated from a non-T1D patient in their potential to induce expression of the HERV-W genes in vitro: the CVB-4E2 strain induced a higher magnitude of expression compared to the control strain. These results suggest that only certain enteroviral strains have the potency to transactivate HERV-W and may “turn-on” a self-sustaining and expanding HERV-W expression in cells they have infected, i.e. in the pancreas[116]. This observation is compatible with low-dose infections of target tissues by environmental viruses as a cause of endogenous retroviral-mediated pathogenesis in T1D.

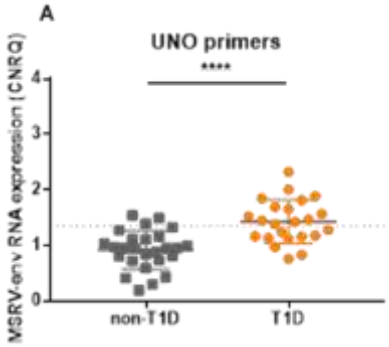
The role of HERV-W ENV has been further investigated by GeNeuro. HERV-W ENV was detected in human Type 1 DM patients by three different methods, and in three different types of human samples. A PCR study was conducted on leucocytes of T1D patients and of non-T1D blood donors (see Figure 34 below). In this T1D cohort, 13 over 23 T1D were positive for HERV-W ENV RNA, showing that the frequency of HERV-W ENV RNA in PBMCs from T1D patients was 56.5% (13/23). In comparison, only about 11.5% (n=3/26) of non-T1D patients also display positivity. The difference of HERV-W ENV RNA levels between T1D and non-T1D patients was found to be statistically significant ($p<0.0001$).

[114] Source: Pancreatic Islet Transplantation, www.nih.gov

[115] Source: Life expectancy of type 1 diabetic patients during 1997-2010: a national Australian registry-based cohort study, Diabetologia. 2016

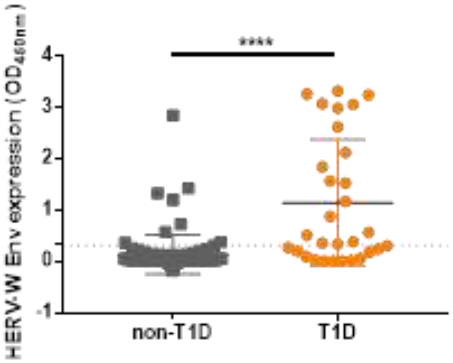
[116] Source: Levet S, Medina J, Joanou J, Demolder A, Queruel N, Réant K, Normand M, Seffals M, Dimier J, Germi R, Piofczyk T, Portoukalian J, Touraine JL, Perron H. “An ancestral retroviral protein identified as a therapeutic target in type-1 diabetes. “ JCI Insight. 2017 Sep

Figure 34: HERV-W ENV RNA comparing PBMC from T1D patients and non-T1D blood donors.



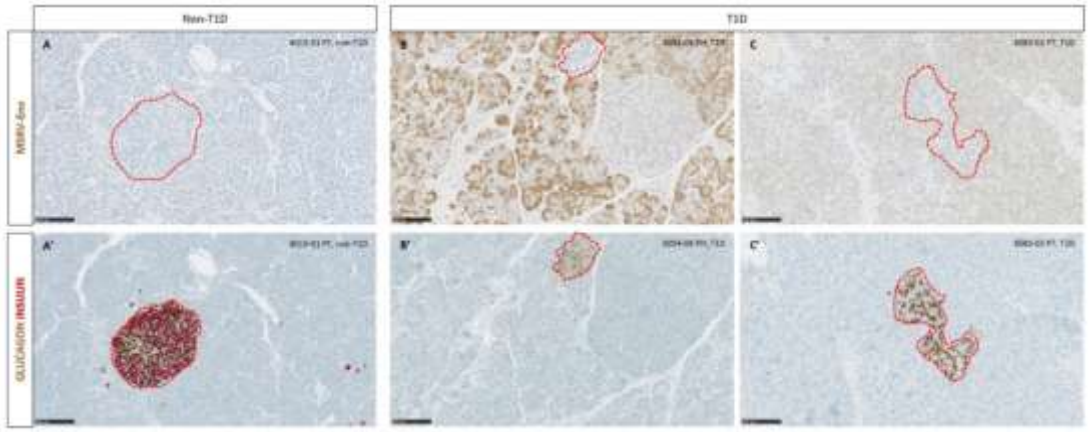
An antigenemia study was conducted with an ELISA method on serum from 30 T1D patients and from 93 non-T1D blood donors. In this T1D cohort, 18 out of 30 T1D samples were positive for HERV-W ENV, showing that the frequency of HERV-W ENV in the serum from T1D patients was 60% (n=18/30). In comparison, only about 8.6% (n=8/93) of non-T1D patients displayed positivity; this difference of HERV-W Env protein detection between T1D and non-T1D patients was found to be statistically significant (p<0.0001), which supports the results obtained on RNA[117] (see Figure 35).

Figure 35: Dosage of HERV-W ENV in sera from T1D patients and non-T1D blood donors.



Thirdly, immunohistochemical analyses were performed on human pancreas biopsies (nPOD repository, University of Florida, USA) and showed that HERV-W ENV protein was highly expressed in the pancreas of 75% of Type 1 D patients (15/20), whereas 16% of non-Type 1 DM controls with various pathologies were weakly positive (3/19). An extensive immuno-histological analysis of human Type 1 DM pancreata further revealed that HERV-W ENV is expressed by acinar cells surrounding Langerhans islets and that this expression correlates with the presence of macrophage infiltrates within the exocrine pancreas[118] (see Figure 36).

Figure 36: Expression of HERV-W ENV in pancreas from T1D patients, in the vicinity of Langerhans islets.



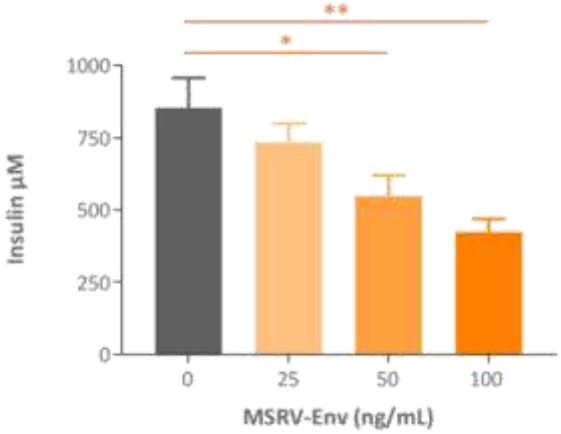
[117] Source: Levet S, Medina J, Joanou J, Demolder A, Queruel N, Réant K, Normand M, Seffals M, Dimier J, Germi R, Piofczyk T, Portoukalian J, Touraine JL, Perron H. "An ancestral retroviral protein identified as a therapeutic target in type-1 diabetes. " JCI Insight. 2017 Sep

[118] Source: ibid.

ii) HERV-W ENV toxicity on beta-cells

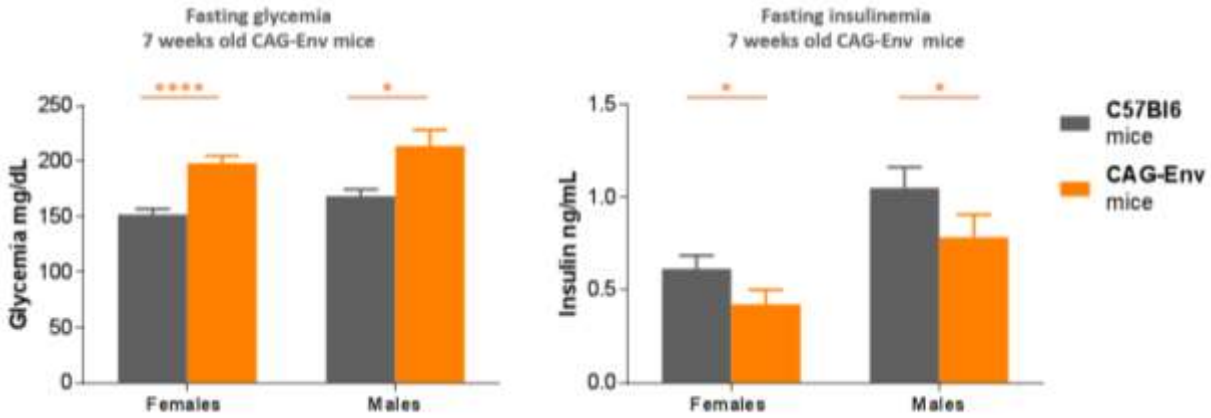
HERV-W ENV protein appears to be toxic on beta-cells. HERV-W ENV directly inhibits insulin secretion in a dose-dependent manner in primary human Langerhans islets and in rat INS1E insulinoma cell line. This inhibition reached 50% at 100ng/mL of HERV-W ENV in human β cells[119]. (see Figure 37).

Figure 37: Insulin secretion inhibition by HERV-W-Env in insulinoma cells.



These *in vitro* data were completed by *in vivo* observation in a transgenic mice model expressing HERV-W ENV. In this model, the MSRV-pV14 Env transgene, originally cloned from MS isolate, is expressed under the control of the ubiquitous CAG promoter and cis-regulated by the autologous HERV-W long terminal repeat. It is inserted in the so-called HPRT locus of the murine X-chromosome and, without upregulation by external factors, can be spontaneously expressed at low levels in permissive cells within various tissues. These transgenic mice, named CAG-Env mice, displayed both hyperglycemia and hypoinsulinemia, as seen in T1D pathology. On average, 7 weeks old CAG-Env transgenic mice displayed insulin levels 28% below that of C57Bl6 mice and a glycemia 29% above the same non-transgenic controls. The hyperglycaemia concomitant with hypoinsulinaemia in CAG-Env mice constitutes an in vivo model with hallmarks of T1D clinical features (see Figure 38). In addition, mice expressing HERV-W ENV displayed immune cells infiltrates in their exocrine pancreas, a feature associated with hyperglycaemia and decreased levels of insulin.

Figure 38: Effect of constitutive expression of HERV-W ENV protein on fasting glycemia and insulinemia in young CAG-Env mice.



In addition, GeNeuro has initiated several collaborations with European and North American academic groups, such as the *Centre Hospitalier Universitaire de Lausanne* (CHUV – the University Hospital of Lausanne) and the University of British Columbia (Vancouver), to further explore the role of HERV-W-Env in T1D physiopathology.

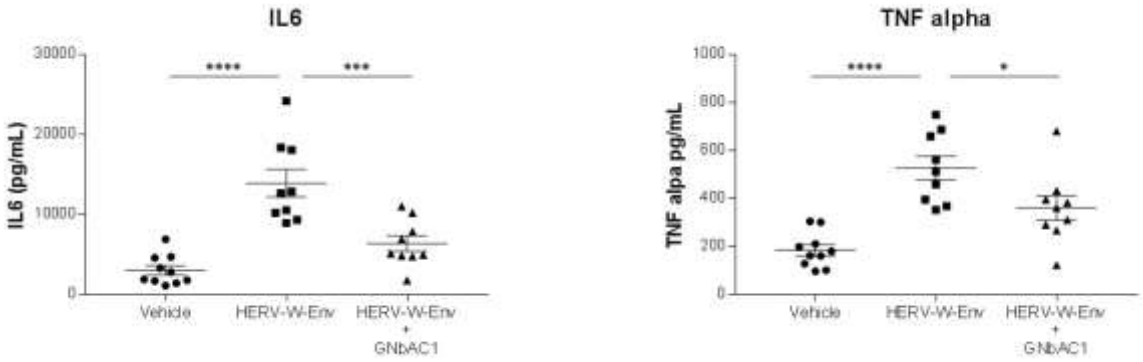
[119] Source: Levet S, Medina J, Joanou J et al. An ancestral retroviral protein identified as a therapeutic target in type-1 diabetes. JCI Insight. 2017 Sep 7;2(17). pii: 94387.

5.4.2.1 Temelimab is a Highly Specific and Effective Antibody in Preclinical Models

(i) Type 1 Diabetes

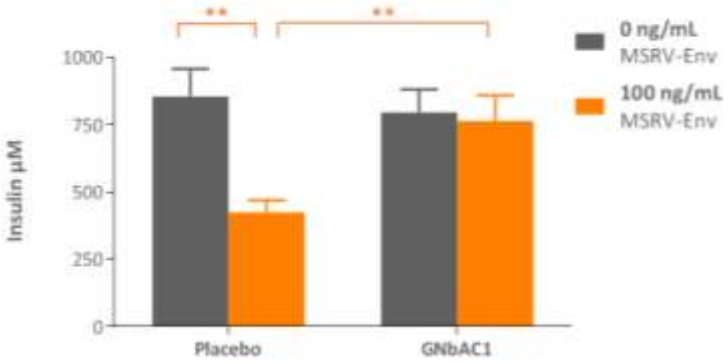
In T1D, it has been shown that HERV-W ENV induces a strong release of pro-inflammatory cytokines such as IL-6 and TNF-α in C57BL/6 mice in the blood, two cytokines found elevated in T1D. HERV-W-Env injected intravenously induces a strong release of IL-6 and TNF-α in mice blood 2 h after its administration, two cytokines expressed in T1D. This general effect is inhibited by the administration of temelimab, indeed a concomitant temelimab administration antagonizes the release of IL-6 and TNF-α induced by HERV-W ENV in mice (see Figure 39).

Figure 39: Release of pro-inflammatory cytokines induced by HERV-W-Env is reversed by temelimab treatment in mice.



The mAb temelimab has been tested in preclinical diabetic models. In the *in vitro* models of T1D, temelimab has been shown to inhibit the toxic effect induced by HERV-W ENV: the dose-proportional toxic effect on primary human pancreatic beta cells in vitro is blocked by temelimab (see Figure 40). Temelimab allows the insulin secretion by human beta cells exposed to HERV-W ENV to be maintained. Indeed, in presence of temelimab, insulin secretion remained stable above 750 µM despite 100 ng/mL of pHERV env, whereas it dropped statistically significantly in absence of temelimab[120].

Figure 40: Effect of temelimab and HERV-W ENV protein on Insulin secretion by pancreatic human βcell in response to glucose.



A summary of the data developed by GeNeuro and academic collaborators in T1D was published in the Journal of Clinical Investigation Insights[121]. These findings have also been presented in oral presentations and posters at international meetings dedicated to diabetes such as the American Diabetes Association (ADA) congress (most recently at its 78th Scientific Session, held June 22-26, 2018 in Orlando, Florida), and have received a very strong response from practitioners that do not have any disease-modifying drugs available today. The safety profile of Temelimab has facilitated the launch of a Phase IIa trial on T1D patients in combination with managed insulin replacement, as described further below.

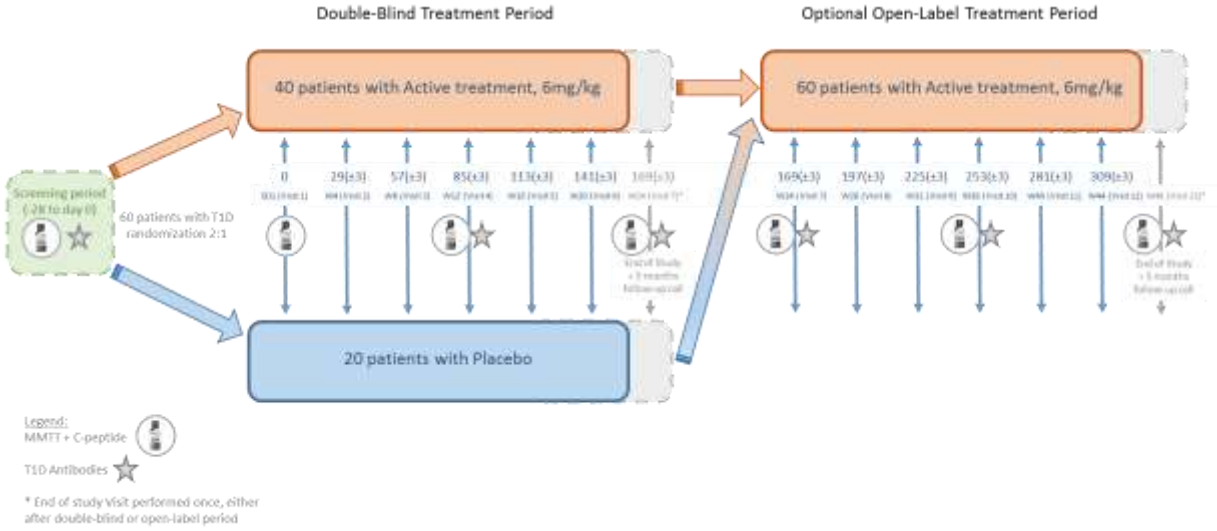
[120] Source: Levet S, Medina J, Joanou J et al. An ancestral retroviral protein identified as a therapeutic target in type-1 diabetes. JCI Insight. 2017 Sep 7;2(17). pii: 94387.

[121] Ibid.

5.4.3 RAINBOW-T1D

In April 2017, GeNeuro launched a Phase IIa clinical trial in Australia on temelimab with T1D patients. The study, called RAINBOW-T1D[122], is assessing the safety of repeated doses of temelimab and assessing the insulin secretion and the autoimmune T1D process. The primary objective of the study was to evaluate the safety and tolerability of temelimab in patients with recent onset of T1D: temelimab was tested versus placebo in a double-blind phase at the dose of 6 mg/kg in 60 patients for 6 repeated 4-weekly doses, followed by an optional open-label extension phase where all patients received temelimab at the dose of 6 mg/kg for 6 additional repeated administrations. Temelimab was given as an add-on to the patient's usual insulin administration. The secondary objective was to determine the pharmacodynamic response to temelimab on biomarkers of T1D, in particular biomarkers assessing the insulin function and biomarkers related to auto-immune processes. The overall design of the study is shown in Figure 41.

Figure 41: Design of the RAINBOW-T1D study with the timing of the main assessments



The included patient population satisfies the following criteria: male or female with a definite diagnosis of T1D made a maximum of 4 years prior to the signed informed consent, with some remaining insulin secretion, assessed by the C-peptide blood level recorded after a standardized meal. The patients must also be positive for at least one diabetes-associated auto-antibody. The primary endpoints are related to safety: Serious Adverse Events (SAE), Adverse Events (AE), physical examination, vital signs and clinical laboratory values. The secondary endpoints were pharmacodynamics endpoints related to diabetes: glycated haemoglobin (HbA1c) blood levels; C-peptide blood levels after standardized meals; Anti-glutamic acid decarboxylase-65 antibody, anti-islet cell antibody, anti-insulin antibody, anti-zinc transporter 8 antibody. HERV-W-Env biomarkers as well as other biomarkers and anti-temelimab antibodies were measured. Planned to include 60 patients, the study actually recruited 64 patients by January 2018 in 13 centers in Australia, of which 61 (95%) completed the double-blind 24-week treatment period. 45 patients entered the 6-month open-label extension phase.

5.4.3.1 Study results

The 24-week interim results of RAINBOW were published in September 2018. The study met its primary endpoint of safety in this new patient population. There were no serious related adverse events in the treatment arm, and the number of adverse events was lower with temelimab than with placebo. No pharmacodynamic parameter showed any detrimental effect of temelimab administration, irrespective of disease duration, concomitant treatment or insulin administration mode. No immunogenicity was observed, and no anti-drug antibodies were measured over the period. This confirms the very good tolerance of temelimab, in combination to standard treatment in this new patient population. The absence of any safety signal seen thus far opens the door to trials in larger diabetic populations, potentially in pediatric patients who represent 80% of cases at onset, and where disease modifying therapies are sorely needed.

All pharmacodynamic markers remained stable over time, without separation between the groups in this small population of adult patients with a well-controlled disease, characterized by high residual C-peptide and moderate HbAc1 levels, and low insulin consumption. Some encouraging signals were observed, such as a 32% reduction in the total number of hypoglycemic episodes in the treated group versus placebo ($p<0.0001$). Also noted was a 21% decrease of anti-insulin antibodies in the treatment group, versus an increase of 23% in the placebo group ($p<0.01$).

[122] Standing for, RAndomIsed, Double-Blind, PlacebO-Controlled Study to Investigate Temelimab in Patients With Onset of Type 1 Diabetes Within 4 Years

But given the low occurrence of events in this well-controlled population and the small size of the Phase IIa cohort, these signals require confirmation through investigation in larger populations with a more recent onset.

The 48-week final results of RAINBOW were announced in May 2019. As mentioned above, at 24 weeks the study had met its primary endpoint of safety in this new patient population and the 48-week results, which were focused on secondary endpoints, confirmed all previously-observed positive observations in the trial. GeNeuro believes these data open the door to further development in early-onset T1D pediatric patient population

In the extension, all patients were treated with temelimab, including those previously on placebo. Data confirmed a very strong safety profile, with no serious related adverse events over the one-year study period, and a continued benefit on the number of hypoglycemic events. The positive effects observed in the 6-month double-blind placebo-controlled period were extended to those patients who switched to temelimab from placebo in the open-label extension period. Pharmacodynamic (PD) markers, such as anti-insulin antibodies, also improved once the placebo population switched to temelimab. The group treated with temelimab for 12 months showed reduction of frequencies of hypoglycemic episodes under temelimab treatment in the initial 6-month double-blind phase (-28%, $p<0.001$ versus placebo), and a further reduction of 10% of hypoglycemic episodes in the second 6-month period. The group switching to temelimab from placebo showed reduction of the frequency of hypoglycemic episodes versus the previous placebo period (-29%), reaching the level of reduction observed with temelimab in the group treated for the first 6 months.

The small cohort size and low occurrence of events confirm the excellent tolerability of temelimab but do not allow for definitive efficacy conclusions. The absence of any safety signal seen thus far opens the door to trials in larger diabetic populations, potentially in pediatric patients who represent 80% of cases at onset, and where disease modifying therapies are sorely needed.

5.4.4 Possible next step in T1D: a pivotal T1D study

Following the full results from its Phase IIa study, GeNeuro is in a position to discuss with the authorities how to conduct pivotal trials in this indication. Such a Phase II/III trial would likely be a placebo-controlled randomized study as add-on to insulin to assess the reduction of the daily use of insulin (unit/kg body weight) and increase in C-peptide production induced by temelimab in pediatric patients with recent (6 months) T1D onset with maintained or reduced glycated hemoglobin after 1 and 2 years versus baseline and collect data on T1D related biomarkers. Temelimab would be administered with a monthly schedule at a dose of 6 mg/kg. A sample size in the range of about 300 T1D patients with recent T1D onset is expected to be included. The need to perform a second pivotal Phase II/III study to allow registration would be discussed with regulatory authorities during scientific advices. However, given that temelimab might be developed in two significantly different indications, T1D and MS, and given the current state of partnership discussions about temelimab in MS, the Company is not currently planning a study in T1D in the near term.

5.5 Chronic Inflammatory Demyelinating Polyradiculoneuropathy (CIDP)

iii) Origin and prevalence

Chronic inflammatory demyelinating polyradiculoneuropathy is a rare autoimmune disorder of the peripheral nervous system ("**PNS**") with a worldwide incidence of approximately one or two for every 100,000[123] persons and with orphan disease status in Europe and the United States. CIDP is related to multifocal inflammation and demyelinating lesions of the proximal PNS. From a pathological and clinical standpoint, CIDP has numerous analogies with MS and is sometimes called the "MS of the peripheral nervous system." Its clinical presentation is heterogeneous and its diagnosis is challenging because of its unknown etiology and the lack of specific biomarkers. Existing CIDP therapies are intravenous human immunoglobulins ("IVIG"), corticosteroids, and plasma exchange. Long-term therapy is often limited by side effects and one-third of patients are refractory to existing treatments. This situation illustrates a critical unmet medical need for alternative treatments for CIDP and diagnostic biomarkers.

Preclinical results examined by the CMPH in a scientific opinion show interest in testing temelimab for CIDP in clinical trials. Indeed, several studies[124] have confirmed the presence of HERV-W ENV in half of the patients with CIDP, and the expression of such protein in Schwann cells in lesions caused by CIDP. The effects of HERV-W ENV expression were studied *in vitro* in cultured human Schwann cells ("HSC"). The cells expressing HERV-W ENV presented a strong and significant increase of IL-6 and CXCL10 transcripts levels, which are both pro-inflammatory.

[123] Sources : GBS/CIDP Foundation International, https://www.gbs-cidp.org/cidp/all-about-cidp/

[124] Sources : Perron et al., 2012 ibid.; Source: Faucard R, Madeira A, Gehin N et al. Human Endogenous Retrovirus and Neuroinflammation in Chronic Inflammatory Demyelinating Polyradiculoneuropathy. EBioMedicine. 2016 Apr;

GeNeuro presented these data to the EMA for a scientific opinion. EMA concluded that the preclinical dossier developed by GeNeuro for CIDP was of sufficient interest to justify the start of clinical development for this indication. In addition, the US FDA granted an Orphan Drug Designation (ODD) for temelimab in CIDP in February 2018.

iv) Current treatments

Current treatments for CIDP can be divided into four categories:
- Glucocorticoid drugs
- Immunoglobulins
- Plasma Exchange
- Alternative treatments

Glucocorticoids such as Prednisone© are commonly used in practice to treat CIDP patients as potent inhibitors of inflammatory processes. But their lack of specificity and potential long-term side effects limit their use mainly to the treatment of relapses in CIDP.

Immunoglobulins (IGs) have been proven effective for CIDP in clinical trials and are the leading category of drugs in this indication. IVIG's help enhancing the immune system of the patient. They require very high doses in the treatment of CIDP, and necessitate continued intermittent treatments every few months. The leading immunoglobulins are:

- Privigen© from CSL Behring is an intravenous IG (IVIG) administered as an infusion. It contains a broad spectrum of antibodies against infectious agents based on pooled plasma from at least 1'000 donors. This product is approved for CIDP, as well as Primary Immunodeficiency (PI) and Immune Thrombocytopenic Purpura (ITP). Sales of Privigen© were reported to be of US$ 1'649 million in 2017, and projected to raise to over US$ 2'700 million in 2022[125]. But these sales cover all indications for which this product has been approved, with no information on specific sales for CIDP, albeit the company reports CIDP is the largest indication for its immunoglobulins[126].

- Hizentra© from CSL Behring is a sub-cutaneous administered humanized immune globulin, approved for CIDP by the EU EMA in 2017 and the US FDA in 2018. This product, which has already been approved for PI since 2010, is the leading subcutaneous immunoglobulin. In the PATH Phase III, it proved effective at lowering CIDP relapses through self-administration by the patient. Sales of Hizentra© were reported to be of US$ 621 million in 2017 and were projected to raise to over US$ 1,200 million in 2022[127]. But these sales cover all indications for which this product has been approved, with no information on specific sales for CIDP.

- Gammunex-C© from Grifols (originally developed by Bayer), was the first immunoglobulin product approved for CIDP in 2008 (US FDA). It is also approved for PI and ITP. This therapy may be administered both IV and subcutaneously, but for CIDP the IV administration is recommended. This product, derived from human blood, provides a broad spectrum of opsonic and neutralizing IgG antibodies against bacterial, viral, parasitic and mycoplasmal agents. It had reported sales of US$ 1,109 million in 2017, projected to raise to over US$1,500 million by 2022[128]. But these sales cover all indications for which this product has been approved, with no information on specific sales for CIDP.

- Other immunoglobulins used for CIDP include Kenketsu Glovenin-I© by Nihon Pharmaceutical and Tegeline© by LBF

Plasma Exchange is a process whereby blood from the patient is taken, cells removed, and plasma from the patient replaced by other human plasma. The result is to remove substances such as toxins, metabolic substances and plasma parts from the patient's blood. This process has shown benefit in CIDP but, as for IVIGs, the benefit only lasts a few weeks and the process has to be repeated.

Alternative treatments are drugs approved for other indications, used on the 25-30% of patients not responding to IGs or plasma exchange. These drugs are mainly immunosuppressive medications and/or monoclonal antibodies. A few to be noted are Cyclosporine© and Rituximab©, the latter also used for years off-label in multiple sclerosis, before the approval of its humanized form Ocrelizumab©.

[125] Source: CIDP Landscape 2018, Delveninsight
[126] Source: CSL 2018 Half Year Results, 14 February 2018
[127] Source: CIDP Landscape 2018, Delveninsight
[128] Source: ibid

v) Emerging therapies and market dynamics

There are a number of new IG therapies currently in Phase III development for CIDP. These therapies include:

- NewGam© from OctaPharma, an IVIG currently in Phase III against CIDP. This treatment is already approved under the brand name of Panzyga© for PID, ITP as well as Guillain-Barré Syndrome (GBS). This study is expected to be completed by the end of 2019.

- HyQvia© from Shire Pharmaceuticals (initially developed by Baxalta before its acquisition by Shire) is an IG which may be administered subcutaneously as well as IV. This drug is already approved for PI in adults, and ongoing two parallel Phase III trials with an estimated completion expected for 2021 and 2022.

There have also been trials with immunosuppressive drugs such as Fingolimod© from Novartis, which underwent a Phase III trial that was abandoned after an independent Data Monitoring Committee estimated that it would be unlikely for this study to show significant benefit of the drug versus placebo at the time of completion[129]. There are reports of clinical practice with other compounds approved for MS, such as Tysabri© and Lemtrada©. But the role for immunomodulation or immunosuppressive drugs in this indication remains still to be defined.

Available treatments in this indication (IG, steroids, plasma exchange and alternative treatments) are not optimal, especially because long-term therapy is often limited by side effects and one-third of patients are refractory to approved therapies. There is, consequently, an unmet medical need which supports testing new therapies into clinical development for CIDP.

5.5.1 HERV-W ENV in CIDP

The scientific rationale for the development of temelimab for the treatment of CIDP is supported by epidemiological and *in vitro* observations.

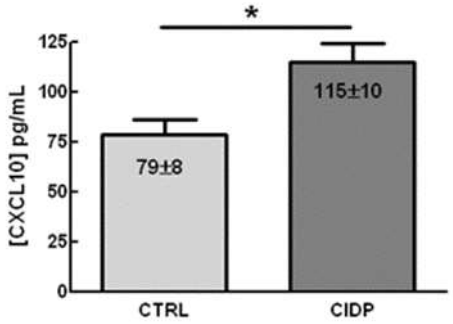
Two independent studies were conducted to confirm the association of CIDP with HERV-W ENV expression (Study 1: 18 CIDP patients vs 20 healthy subjects; study 2: 18 CIDP patients vs 28 healthy subjects[130] . Levels of HERV-W ENV mRNA in peripheral blood mononuclear cells (PBMCs) were analyzed with a highly selective set of primers for pHERV-W RNA.by quantitative real-time polymerase chain reaction (q-RT-PCR). HERV-W ENV RNA expression was significantly higher in CIDP patients than in the control group ($p<0.001$). Essentially, both studies showed that 40-50 % of CIDP patients have statistically significant higher expression levels of HERV-W ENV mRNA compared to healthy controls.

Schwann cells are at the interface of the immune and peripheral nervous system. CIDP affects the peripheral myelin, which is produced by the Schwann cell. Schwann cells' integrity and their interactions with axons are crucial in peripheral nerve physiology, and they represent key targets in inflammatory neuropathies[131]. Schwann cells cumulate the physiological roles of oligodendrocytes, astrocytes, and microglial cells, and can adapt to injury, and promote nerve repair. Thus, Schwann cells play a central role in PNS physiology.

To study whether HERV-W ENV may play in the pathophysiological cascade leading to CIDP, the morphology of human Schwann cells in presence of pHERV-W-Env in primary cultures was explored by contrast-phase microscopy. A strong TLR4 immuno-labeling was detected at the plasma membrane of the cells indicating that they express HERV-W ENV receptors, and have the potential to respond to HERV-W ENV stimulation. Moreover, in several independent experiments, it was shown that low concentrations of HERV-W ENV significantly increases the expression of CXCL10 in primary cultures of human Schwann cells[132]. As numerous reports have highlighted the critical pathological role of CXCL10 in CIDP, CXCL10 is proposed as a key factor involved in the infiltration of spinal nerve roots and peripheral nerves by macrophages and T cells. Moreover, CXCL10 is a relevant peripheral biomarker of CIDP. CXCL10 has been shown to be significantly elevated in the sera of CIDP patients' cohorts where HERV-W ENV is significantly overexpressed (see Figure 42).

[129] Source: Oral Fingolimod in CIDP: Results from a Phase III Randomized Placebo-controlled Trial, Neurology, April 2017.
[130] Source: Faucard R, Madeira A, Gehin N et al. Human Endogenous Retrovirus and Neuroinflammation in Chronic Inflammatory Demyelinating Polyradiculoneuropathy. EBioMedicine. 2016 Apr;6:190-198.
[131] Source: Rosso G, Young P, Shahin V. Implications of Schwann Cells Biomechanics and Mechanosensitivity for Peripheral Nervous System Physiology and Pathophysiology. Front Mol Neurosci. 2017 Oct 25;10:345.
[132] Source: Faucard R, Madeira A, Gehin N et al. Human Endogenous Retrovirus and Neuroinflammation in Chronic Inflammatory Demyelinating Polyradiculoneuropathy. EBioMedicine. 2016 Apr;6:190-198.

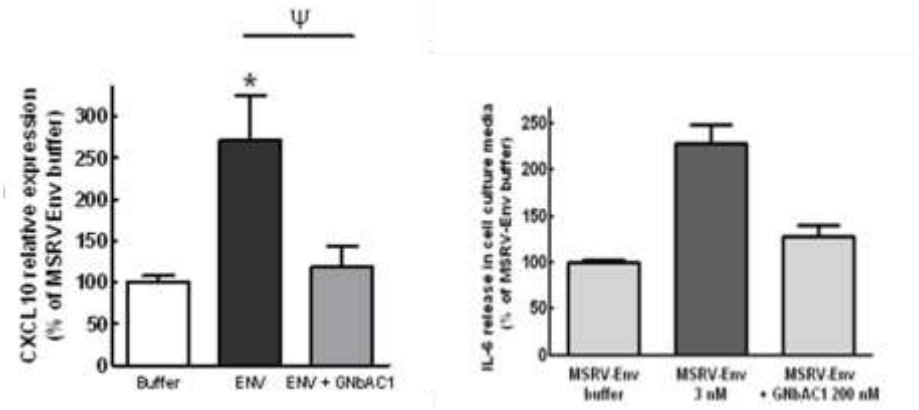
Figure 42: CXCL10 is elevated in sera of CIDP patients



(ii) CIDP

GeNeuro investigated the effects of temelimab on the HERV-W ENV action on human Schwann cells, with a primary focus on CXCL10 and IL-6 expression, two cytokines of importance in CIDP. As it was shown that Schwann cells express TLR4 receptors at their plasma membrane and that HERV-W ENV induces a strong and robust overexpression of CXCL10 and IL6 - a cytokine which is increased in the CSF of CIDP patients and is upregulated in sural nerve biopsies - when applied at very low concentrations on human Schwann cells. HERV-W ENV (3 nM) highly increases CXCL10 as well as Il6 expression, while the addition of temelimab (200 nM) inhibits this effect for both cytokines as shown in Figure 43 below[133].

Figure 43: Inhibition of HERV-W ENV-induced overexpression of CXCL10 or IL-6 by temelimab in human Schwann Cells in primary culture



5.5.2 Phase II study in CIDP

The contemplated study would be an international Phase II/III study which should allow registration of temelimab in this indication. It is likely that it would be a randomized add-on study on top of a usual IVIG treatment received by the patients, recording also a certain number of scores on scales used in CIDP such as the INCAT score. The study would recruit in the range of about 100 CIDP patients positive for pHERV-W-Env and would have a follow-up of at least one year. The design of the study would be discussed with regulatory authorities especially in the framework of the recently obtained Orphan Drug Designation in the USA. However, given the difficulty of recruiting patients affected by this rare disease, the Company is not planning a study in CIDP in the near term.

5.6 Servier Partnership Termination

In 2014, GeNeuro entered into a collaboration agreement with Servier, pursuant to which GeNeuro was responsible for the development of Temelimab for the treatment of MS until the completion of the Phase IIb CHANGE-MS clinical trial, after which Servier could exercise an option to take an exclusive license and take over development of Temelimab for MS in all markets, excluding the United States and Japan. Servier paid a total of €37.5 million to GeNeuro under this agreement; furthermore, in 2016 Servier committed to finance the ANGEL-MS trial, for which it paid an additional €14 million to GeNeuro. The agreement also provided for milestone payments to GeNeuro of up to €362.5 million, the funding of a Phase III clinical trial in MS, and royalties on future sales in Servier's territories.

[133] Source: Faucard R, Madeira A, Gehin N et al. Human Endogenous Retrovirus and Neuroinflammation in Chronic Inflammatory Demyelinating Polyradiculoneuropathy. EBioMedicine. 2016 Apr;6:190-198.

In addition, under an option agreement to purchase shares, also made with Servier in November 2014, Servier International B.V. (a wholly owned subsidiary of Servier) acquired 8.6% of GeNeuro's outstanding shares via a sale by Eclosion2 for €15 million on December 11, 2015 and maintained its stake through subscribing to the April 2016 capital increase concurrent with the initial public offering of the Company on the regulated market of Euronext Paris.

Fin the summer of 2018, Servier notified the Company that it would not exercise its option for strategic priority reasons and has thus reverted to GeNeuro all its rights to temelimab. In addition, the ANGEL-MS extension study, which was ongoing at the time, was terminated during the fourth quarter of 2018, with Servier bearing the closure costs. No costs or penalties were borne by the Company for the termination of the Servier partnership.

5.7 The HERV Platform in other indications

Recent biomedical research has established that most chronic conditions affecting human beings are the consequence of a combination of factors that include genetic, hormonal, and environmental triggers. HERVs belong to this modern view of disease, acting through the combination of genetic predisposition and external factors to become reactivated and function directly as causal agents for disease.

Over 26 families of HERVs have been identified and GeNeuro believes that they represent factors for chronic, multifactorial diseases with an autoimmune component. Developing the knowledge of the role played by HERV proteins in such diseases makes it possible to envision the development of therapies for numerous other human diseases for which there are currently no satisfactory treatments.

GeNeuro has focused its research on the HERV proteins HERV-W ENV and HERV-K ENV and has established relationships with third-party research groups studying this protein and other HERV proteins in different diseases.

5.7.1 Amyotrophic Lateral Sclerosis

Amyotrophic lateral sclerosis ("**ALS**") is a devastating motor neuron disease that occurs most often as a sporadic disease with no known cause or inheritance pattern. It was first described by the French neurologist Jean-Martin Charcot. The name ALS reflects both the degeneration of corticospinal motor neurons, the descending axons of which show altered structure in the lateral spinal cord (lateral sclerosis) and the demise of spinal motor neurons, with secondary denervation associated with muscle wasting (amyotrophy). ALS is a rapidly progressive and ultimately fatal neurodegenerative disease resulting from motor neurons degeneration in the cerebral motor cortex, the brainstem and spinal. ALS can affect people of any age, but usually starts around the age of 60 and in inherited cases around the age of 50. The average survival from onset to death is three to five years. According to research by the ALS Association, a little over 5,000 people in the U.S. are diagnosed with ALS each year, as many as 20,000 Americans have the disease at any given time and as many as 150'000 worldwide[134]. About 10% of ALS cases appear to be genetically transmitted in families (hereditary ALS) in association with specific genomic mutations. ALS is also considered a multisystem neurodegenerative disorder that can include cognitive and behavioral changes in addition to muscle weakness.

Today, no cure for ALS is known. There are three current approved medications that may extend life by about 2-3 months but do not reverse motor neuron death and do little to treat the underlying cause of ALS. Costs associated with ALS are greater than that of other neurological diseases, indicating a continued need for medical advances and financial support for patients and families. Most patients with ALS condition die from respiratory failure.

Increased reverse transcriptase (RT) activity was found in the serum of ALS patients, which led to the speculation that RT activity may derive from inherited active human endogenous retroviruses (HERVs). HERVs represent 8% of the human genome and the HERV-K family comprises recently integrated copies in the human genome. Sequencing studies revealed that HERV-K sequences are more frequently expressed in patients with ALS compared to controls[135]. HERV-K gag- pol and Env RNA have significantly elevated expression in brains from ALS patients compared to controls.

Dr. Nath, Head of the National Institute of Neurological Disorders and Stroke ("**NINDS**"), part of the U.S. National Institutes of Health ("**NIH**"), and his research group recently discovered the targeted expression and the pathogenic effects of the envelope protein from HERV-K in ALS[136]. Their research has evidenced that:

- pathogenic HERV-K ENV proteins are expressed in the brains of ALS patients, and observed in the anterior horn of the spinal cord, the site of lower motor neurons that degenerate in ALS[137].

[134] Sources: alsa.org, arsla.org
[135] Source: Douville, Liu et al. 2011, Douville and Nath 2014
[136] Source: Li W, Lee MH, Henderson L, et al. Human endogenous retrovirus-K contributes to motor neuron disease. Sci Transl Med. 2015 Sep
[137] Source: Douville R et al. Ann Neurol. 2011; Alfahad et al. Antiviral Res. 2013; Li et al. ibid; Dolei A et al. Int J Mol Sci. 2019

- TDP-43 (TAR - transactivation responsive- DNA binding protein 43) deposits which are thought to be critical in motor neuron degeneration are considered the final hallmark of ALS and HERV-K RT expression correlates with TDP-43[138]
- HERV-K ENV expression induces toxicity in human motor neurons. Transgenic mice expressing the HERV-K ENV gene developed an ALS-like motor neuron dysfunction and develop profound weakness of the limbs and spinal muscles, including those for respiration, resulting in 50% mortality by 10 months. These signs of motor dysfunction observed in transgenic mice expressing HERV-K ENV support the pathophysiological role of HERV-K ENV in this disorder[139]
- HERV-K ENV expression is specific for ALS, since it could not be found in patients with multiple sclerosis, Parkinson's or Alzheimer's disease[140]

The possibility that HERV-K plays a crucial role in the pathophysiology of ALS could explain why several researchers have detected RT in ALS brain and blood samples, but have not been able to demonstrate human-to-animal or human-to-human transmission of the disease, because HERVs arise from the genome and not from the environment. Further, it may also explain the anatomical spread of the illness through paracrine activation of permissive autologous cells, which generally starts in one region of the body and then spreads along an anatomical pathway[141].

Taken together, these findings suggest that endogenous retroviral elements and HERV-K in particular are involved in the pathophysiology of ALS and could be the missing link between TDP43 and ALS[142]. Thus, HERV-K ENV protein expression within neurons of patients with ALS may contribute to neurodegeneration and disease pathogenesis.

In February 2017, GeNeuro signed a Cooperative Research and Development Agreement ("**CRADA**") with the NINDS to develop novel therapeutic antibodies for the treatment of amyotrophic lateral sclerosis. The research has evaluated the ability of these antibodies to neutralize a potential causal factor of ALS, the envelope protein of HERV-K (a family of Human Endogenous Retroviruses, HERVs). Under the terms of the agreement, GeNeuro provided antibodies designed to block the activity of HERV-K Envelope protein. These candidate antibodies were tested in cellular and animal models of HERV-K associated ALS by the NINDS, and have achieved preclinical proof-of-concept of this novel therapeutic avenue addressing ALS pathogenesis.

Following the positive results of this pre-clinical work, GeNeuro has in October 2018 entered into an agreement with the NIH granting GeNeuro an exclusive license on the jointly owned HERV-K patent. Based on this, the Company has now launched a preclinical development program for its HERV-K ENV antibody, a high quality preclinical humanized mAb that will ready for GMP production by the summer of 2021. Due to the pre-clinical development work in collaboration with the NIH having been delayed by the COVID-19 pandemic, the objective is now of reaching an IND by the second half of 2022 and initiating a first clinical trial on patients as soon as possible thereafter, subject to funding. Based on its current resources, the Company has decided to open active partnership discussions for this program.

5.7.2 Inflammatory Psychosis

Inflammatory psychosis includes schizophrenia ("**SCZ**") and bipolar disorder ("**BD**") observed in patients presenting an inflammatory syndrome marked with an increase in C-reactive protein[143]. Schizophrenic symptoms include hallucinations, delusions, paranoïa leading to social withdrawal; BD is characterized by episodes of agitation and elation or depression.

About 1% of the population worldwide suffers from psychotic disorders, and no curative treatments exist today: antipsychotic drugs or mood stabilizers are symptomatic treatments but frequently these drugs do not prevent mental handicap and social withdrawal, and have severe side effects.

HERV-W ENV and GAG proteins are increased in the PBMC and serum of 50% to 60% of patients with SCZ and BD correlated with an increase of C-reactive protein. HERV-W genes and proteins are expressed in the cortex of patients with psychotic disorders[144]. It has also been evidenced that demyelination due to HERV-W Env could

138 Source: Manghera M et al. Neurobiol Dis, 2016; Li et al. ibid; Krug et al. PLoS Genet. 2017; Chang et al. Curr Biol. 2019
139 Source : Li et al, ibid
140 Source: Li et al, ibid.; Arru et al. Eur J Neurol. 2018; Douville et al. ibid
141 Source: Kury, Nath, et al. 2018
142 Source: Alfahad et al, ibid
143 Source: Huang et al. Human endogenous retroviral pol RNA and protein detected and identified in the blood of individuals with schizophrenia. Schizophr Res. 2006
144 Source: Karlsson et al. Retroviral RNA identified in the cerebrospinal fluids and brains of individuals with schizo-phrenia. Proc Natl Acad Sci U S A. 2001

participate in the neuropsychiatric dysfunction [145]. HERV-W can be triggered by viruses or bacteria such as Influenza, Herpes or T gondii, germs which are epidemiologically associated with SCZ.

GeNeuro has ongoing collaborations with research centers in France (Créteil and Bordeaux) on epidemiological studies and animal models of psychotic disorders, with the objective to achieve a preclinical proof-of-concept with a clear strategy to enter clinical trials. This has led to a translational study, published in Science Advances [146], which found that HERV-W proteins, which have been previously found in patients with inflammatory psychosis, such as schizophrenia and bipolar disorders, induce glutamate receptor disorganization and behavioral deficits in vitro and in vivo. This leads to disruption of synaptic glutaminergic communication and results in the emergence of psychosis symptoms, allowing to establish a clear link between the presence of a human endogenous retrovirus envelope protein and corruption of nerve pathway development. This leads to disruption of synaptic glutaminergic communication and results in the emergence of inflammatory psychosis symptoms.

5.7.3 Other Opportunities

The number of HERV families has grown to more than 26 to date and much research is underway to better understand their roles in the disease. In May 2015, GeNeuro held the first “HERV and Disease” international congress in Lyon, bringing together research teams working on HERVs as potential driving factors in poorly understood diseases. A summary of the congress was published in the scientific journal Mobile DNA[147] (Perron, Feschotte and collaborator, in press), and relayed by biotech media. Many emerging links to diseases for which there is no treatment were presented, in particular the one by Dr. Avindra Nath supporting a therapeutic rationale for targeting HERV-K in ALS, a devastating neurodegenerative disease for which there is currently no treatment.[148]

GeNeuro believes that it has established a leadership role in both HERV research and in bringing the community of HERV researchers together. GeNeuro wants to play an important part by contributing to a better understanding of the role of HERVs in disease, by being the clear leader in the development of novel therapies targeting disease-causing HERV proteins. GeNeuro’s intention is to continue supporting external research to accelerate the transition of these potential new treatments from the lab to patients.

In order to promote this objective, GeNeuro organized in March 2017 the second “HERV & Disease” congress, in Washington DC, USA. This congress, co-chaired by Dr Avindra Nath, head of the NINDS (National Institute of Neurological Disorders and Stroke), part of the US NIH, was geared solely to neurological pathologies. A third edition of the “HERV & Disease” congress took place in Lyon, France, in November 2019. Excerpts from this congress were released in scientific publications.

145 Source: Qin et al. Elevation of Ser9 phosphorylation of GSK3beta is required for HERV-W env-mediated BDNF signaling in human U251 cells. Neurosci Lett. 2016.

146 Science Adv. Human endogenous retroviral protein triggers deficit in glutamate synapse maturation and behaviors associated to psychosis. E. M. Johansson, D. Bouchet, R. Tamouza, P. Ellul, AS. Morr, E. Avignone, R. Germi, M. Leboyer, H. Perron, L. Groc

147 Source: Nath A, Kury P, Sciascia do Olival G et al. Meeting report: First international workshop on human endogenous retroviruses and diseases, HERVs & disease 2015. Mobile DNA 2015 6:20 (Oct 15). 78.

148 Source: Nath, Science Translational Medicine (Li W, Lee MH, Henderson L, Tyagi R, Bachani M, Steiner J, Campanac E, Hoffman DA, von Geldern G, Johnson K, Maric D, Morris HD, Lentz M, Pak K, Mammen A, Ostrow L, Rothstein J, Nath A. “Human endogenous retrovirus-K contributes to motor neuron disease”. Sci Transl Med. 2015 Sep 30; 7(307):307ra153.

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5.8 Research And Development and Intellectual Property

The Company engages in research and development activities to develop:

- new therapeutic products, especially monoclonal antibodies, for the treatment of diseases associated with the expression of HERVs;
- diagnostic products to act as companions for the therapeutic products; and
- novel solutions for the study and treatment of HERV diseases.

GeNeuro files patent applications to protect its product candidates, technical processes and the processes used to prepare its product candidates, the compounds or molecules contained in these product candidates and medical treatment methods. GeNeuro also licenses rights to patents owned by third parties or jointly owned with third parties.

By 2006, the Mérieux group and INSERM had accumulated 15 years of work on HERVs, which led to a broad intellectual property portfolio. GeNeuro has taken exclusive licenses to and/or holds 16 patent families offering strong coverage of the HERV-W ENV field, ranging from DNA sequences to products and their therapeutic applications, plus one patent in the HERV-K field. GeNeuro's portfolio of patents is divided into four broad categories:

- the "SEP 16" patent family covers HERV-W ENV sequences necessary for the preparation of an antibody, particularly an antibody targeting the identified sequences. Patents in this category have been granted in all major markets and are owned by bioMérieux and INSERM. GeNeuro holds an exclusive license to such intellectual property for therapeutic uses. These patents include HERV-W fusion, SEP 6, SEP 12, SEP 13, SEP 15, SEP 16, SEP 18, SEP 19, SEP 20, SEP 21, and the INTERECO families described below;
- the "TLR4" patent family broadly covers the use of any antibody targeting HERV-W ENV in MS and other neurological indications. This patent, described below, was granted in all principal markets and is owned by bioMérieux and INSERM. GeNeuro has an exclusive license to such intellectual property for therapeutic uses;
- the "MSRV ligand" patent family covers specific epitopes and antibodies against such epitopes (including GeNeuro's first product candidate) and their use in a broad spectrum of therapeutic indications, including MS, CIDP, and T1D. The basic patent, dating from 2009, was granted in the United States and is still pending in Europe. GeNeuro has filed several patents thereafter on its products, the most recent dating from 2014. GeNeuro owns these patents. These patents cover the MSRV ligand, and the endogenous antiviral, remyelination, and the anti-TM family of antibodies described below; and
- the "HERV-K" patent, which covers the anti-HERV-K Envelope antibody and uses thereof.

Based on more than 25 years of work in the field and a systematic effort to optimize and develop intellectual property, GeNeuro believes that its portfolio of intellectual property and its constant efforts to protect new discoveries put the Company in a strong competitive position.

The term of individual patents depends upon the legal term of patents in the countries in which they are obtained. In most countries, including the United States, the patent term is 20 years from the earliest claimed filing date of a non-provisional patent application or its foreign equivalent in the applicable country. In the United States, a patent's term may, in certain cases, be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the USPTO in examining and granting a patent, or may be shortened if a patent is terminally disclaimed over a commonly owned patent or a patent naming a common inventor and having an earlier expiration date. In the United States, a patent may also be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984 (see Section 9.1.9 of this Universal Registration Document).

For information on the accounting for costs related to research and development activities, please refer to section 7.2.1.2 "Operating Expenses by Function", as well as to notes 2, 10, 12 and 14 of the consolidated financial statements for the year ended December 31, 2020 in Chapter 18 of this Universal Registration Document.

5.8.1 Intellectual Property

The table below summarizes the patent families to which the Company has rights.

Table 13: Patent families

Patent Family	Name	Owners/Holder(s)
Family 1	MSRV Ligand	GeNeuro
Family 2	Endogenous antiretroviral	GeNeuro
Family 3	Remyelination	GeNeuro
Family 4	SEP 16	bioMérieux
Family 5	TLR4	bioMérieux & INSERM
Family 6	SEP 12	bioMérieux
Family 7	SEP 15	bioMérieux
Family 8	SEP 18	INSERM
Family 9	INTERECO	bioMérieux
Family 10	AntiTM antibody	GeNeuro
Family 11	HERV-W fusion	bioMérieux & INSERM
Family 12	SEP 6	bioMérieux
Family 13	SEP 13	bioMérieux
Family 14	SEP 19	bioMérieux
Family 15	SEP 20	bioMérieux
Family 16	SEP 21	bioMérieux
Family 17	HERV-K antibody in ALS	GeNeuro and the NIH, with exclusive licence to GeNeuro on jointly owned IP

5.8.1.1 Summary of Patent Families by Products

Antibodies directed against SU region of the ENV envelope protein of MSRV

The Company holds intellectual property rights to the monoclonal antibody being developed at the clinical stage:

- the use of an anti-ENV-SU antibody capable of binding specifically to the soluble fraction of the Env protein of MSRV (Family 5);
- ligands, more specifically an antibody, including sequences corresponding to specific CDRs of the Env envelope protein for MSRV (Family 1);
- the use of such ligands in the treatment of MS, schizophrenia, CIDP, epilepsy, psoriasis, cancer, inflammatory pancreatitis and, diabetes, in particular T1D (Family 1);
- the use of an antibody against the envelope protein of HERV-W/MSRV, its fragment, and its derivatives as a global antiretroviral agent (Family 2); and
- the use of an antibody directed against HERV-W/HERV-W ENV for its use in the prevention of a blockage of the capacity for repairing myelin (Family 3), particularly in pathologies such as RRMS, chronic progressive MS, CIDP, and schizophrenia or bipolar disorders.

MSRV Genetic Sequences

The Company is licensed under several patent families that cover genetic sequences of MSRV, including:

- the Env gene sequence of MSRV (Family 4), as well as the Env gene sequence of the endogenous retrovirus HERV-7q. (Family 8); and
- the gag and pol gene sequences of MSRV (Family 6).

Therapeutic product

The Company holds a license to a patent family that covers a compound that consists of a therapeutic agent capable of inhibiting superantigenic activity and the use of such compound for prophylaxis and/or treatment of a disease, particularly an autoimmune disease such as MS (Family 16).

Diagnostic method

The Company holds a license to two patent families that cover methods for detecting the expression of an envelope protein of an endogenous retrovirus (Family 11) and to detecting the MSRV-1 retrovirus (Family 15).

The Company also holds a license to a patent family that covers a composition of two pathogenic agents and/or infectants associated with MS and which are useful in diagnostic or treatment methods, particularly for MS (Family 12).

The Company holds a license to a patent family that covers nucleic material capable of being used in a diagnostic method, a prophylaxis method, or a method for treating MS or rheumatoid polyarthritis (Family 13).

The Company also holds a license to a patent family that covers an endogenous nucleic fragment that includes at least a part of the gag gene of an endogenous retrovirus and which is useful for detecting autoimmune diseases, particularly MS, or monitoring a pregnancy (Family 14).

5.8.1.2 Patents and Patent Applications

Below is a description of the patents which GeNeuro holds or for which GeNeuro holds a license from a third party or for which an application has been made, with a special reference to the PCT, European, and United States and PCT patents, to which should be added the patents obtained or applied for in certain other countries which are not included below.

Family 1: MSRV Ligand

Family 1 involves ligands including sequences corresponding to specific CDRs of the envelope protein EnSv of MSRV.

In particular, it covers humanized antibodies directed against the envelope protein Env of MSRV.

This family covers, in a particular way, humanized antibodies directed against the epitope of the SU region of the envelope protein Env of MSRV necessary for the activation of TLR4.

It thus covers the antibody presently being tested in MS. It also covers the use of such a humanized antibody in the treatment of MS, schizophrenia, CIDP, epilepsy, psoriasis, cancer, inflammatory pancreatitis and diabetes, particularly T1D.

Family 1 is wholly owned by the Company.

FAMILY 1: MSRV LIGAND	
Owner	GeNeuro
Title	Therapeutic use of particular ligands in diseases associated with the MSRV retrovirus
PCT Extension & Engagements in National and/or Regional Phases Theoretical Expiration Date[149]: July 8, 2029	

Claims subject matters

A: GNbAC1 (Temelimab) Antibody
B: Pharmaceutical composition comprising the GNbAC1 (Temelimab) antibody
C: Method of treatment of a MSRV-associated disease using the GNbAC1 (Temelimab) antibody, in particular treatment of multiple sclerosis, progressive multiple sclerosis, relapsing remitting multiple sclerosis
D: Method of treating multiple sclerosis using the GNbAC1 (Temelimab) antibody
E: Method of treating MSRV-associated diabetes using the GNbAC1 (Temelimab) antibody
F: Method of binding an MSRV-ENV protein using the murine parental version of GNbAC1 (Temelimab) antibody
G: Method of detection of the anti-ligand of the GNbAC1 (Temelimab) antibody in a sample using the murine parental version of GNbAC1
H: Immunoassay kit for the detection of an anti-ligand comprising the murine parental version of GNbAC1 (Temelimab) antibody

Combinations of claims

1 = A + B + C
2 = A + H
3 = A + B + C + D + E
4 = A + B + C + G + H
5 = A + B + G + H
6 = A + B + H
7 = A + C+ G + H
8 = A + G+ H
9 = D + F

Country	Priority date	Country / N° of priority	Filing Date	N° of Application	Issue date	N° of Patent	Expiry Date	Status	Claims
PCT	15/05/2009 13/03/2009 08/07/2008	US 61/213 189 US 61/202 581 US 61/129 613	08/07/2009	EP2009/058663			08/01/2011	Engaged	
Australia	15/05/2009 13/03/2009 08/07/2008	US 61/213 189 US 61/202 581 US 61/129 613	08/07/2009	2009268025	13.11.2014	2009268025	08/07/2029	Granted	**1**
Brazil	15/05/2009 13/03/2009 08/07/2008	US 61/213 189 US 61/202 581 US 61/129 613	08/07/2009	PI 0915667-4				Pending	
Canada	15/05/2009 13/03/2009 08/07/2008	US 61/213 189 US 61/202 581 US 61/129 613	08/07/2009	2,729,869	13.02.2018	2,729,869	08/07/2029	Granted	**7**
China	15/05/2009 13/03/2009 08/07/2008	US 61/213 189 US 61/202 581 US 61/129 613	08/07/2009	200980134828.3	31.12.2014	ZL 200980134828.3	08/07/2029	Granted	**6**
Hong Kong	15/05/2009 13/03/2009 08/07/2008	US 61/213 189 US 61/202 581 US 61/129 613	25/11/2011	11112831.5	16.10.2015	1158232	08/07/2029	Granted	**6**

[149] Subject to the due and punctual payment of applicable maintenance fees. This date does not take into consideration the possibility of obtaining an additional protection certificate.

South Africa	15/05/2009 13/03/2009 08/07/2008	US 61/213 189 US 61/202 581 US 61/129 613	08/07/2009	2011/00446	25.01.2012	2011/00446	08/07/2029	Granted	**7**
USA	15/05/2009 13/03/2009 08/07/2008	US 61/213 189 US 61/202 581 US 61/129 613	08/07/2009	12/997 486	06.05.2014	8,715,656	09/08/2030	Granted	**6**
USA (Division)	15/05/2009 13/03/2009 08/07/2008	US 61/213 189 US 61/202 581 US 61/129 613	08/07/2009	14/221 963	24.01.2017	9,550,824	25/08/2029	Granted	**9**
USA Continuation	15/05/2009 13/03/2009 08/07/2008	US 61/213 189 US 61/202 581 US 61/129 613	08/07/2009	15/367 864	14.11.2017	9,815,888	08/07/2029	Granted	**E**
USA Continuation	15/05/2009 13/03/2009 08/07/2008	US 61/213 189 US 61/202 581 US 61/129 613	26/10/2017	15/794 541	28.08.2018	10,059,758	08/07/2029	Granted	**A**
India	15/05/2009 13/03/2009 08/07/2008	US 61/213 189 US 61/202 581 US 61/129 613	08/07/2009	336/KOLNP/2011	24.12.2018	304912	08/07/2029	Granted	**2**
Israel	15/05/2009 13/03/2009 08/07/2008	US 61/213 189 US 61/202 581 US 61/129 613	08/07/2009	210204	01.07.2015	210204	08/07/2029	Granted	**4**
Japan	15/05/2009 13/03/2009 08/07/2008	US 61/213 189 US 61/202 581 US 61/129 613	08/07/2009	2011-517153	16.12.2016	6058264	08/07/2029	Granted	**5**
Japan (Division)	15/05/2009 13/03/2009 08/07/2008	US 61/213 189 US 61/202 581 US 61/129 613	08/07/2009	2015-048795	17.03.2017	6109869	08/07/2029	Granted	**E**
Japan (Division)	15/05/2009 13/03/2009 08/07/2008	US 61/213 189 US 61/202 581 US 61/129 613	08/07/2009	2017-043877	15.03.2019	6495361	08/07/2029	Granted	**3**
Mexico	15/05/2009 13/03/2009 08/07/2008	US 61/213 189 US 61/202 581 US 61/129 613	08/07/2009	MX/A/2010/014319	21.11.2013	315557	08/07/2029	Granted	**4**
New-Zealand	15/05/2009 13/03/2009 08/07/2008	US 61/213 189 US 61/202 581 US 61/129 613	08/07/2009	590515	30.04.2013	590515	08/07/2029	Granted	**4**
Republic of Korea	15/05/2009 13/03/2009 08/07/2008	US 61/213 189 US 61/202 581 US 61/129 613	08/07/2009	10-2011-7002937	28.11.2016	10-1682040	08/07/2029	Granted	**7**
Ukraine	15/05/2009 13/03/2009 08/07/2008	US 61/213 189 US 61/202 581 US 61/129 613	08/07/2009	a201101404	26.05.2014	105495	08/07/2029	Granted	**7**
Eurasia	15/05/2009 13/03/2009 08/07/2008	US 61/213 189 US 61/202 581 US 61/129 613	08/07/2009	201100160	31.10.2016	24655	08/07/2029	Granted	**7**
Armenia	15/05/2009 13/03/2009 08/07/2008	US 61/213 189 US 61/202 581 US 61/129 613	08/07/2009	201100160	01.11.2016	24655	08/07/2029	Granted	same as Eurasia
Azerbaijan	15/05/2009 13/03/2009 08/07/2008	US 61/213 189 US 61/202 581 US 61/129 613	08/07/2009	201100160	01.11.2016	24655	08/07/2029	Granted	same as Eurasia
Belarus	15/05/2009 13/03/2009 08/07/2008	US 61/213 189 US 61/202 581 US 61/129 613	08/07/2009	201100160	01.11.2016	24655	08/07/2029	Granted	same as Eurasia
Russia	15/05/2009 13/03/2009 08/07/2008	US 61/213 189 US 61/202 581 US 61/129 613	08/07/2009	201100160	01.11.2016	24655	08/07/2029	Granted	same as Eurasia
Kazakhstan	15/05/2009 13/03/2009 08/07/2008	US 61/213 189 US 61/202 581 US 61/129 613	08/07/2009	201100160	01.11.2016	24655	08/07/2029	Granted	same as Eurasia
Kirghizstan	15/05/2009 13/03/2009 08/07/2008	US 61/213 189 US 61/202 581 US 61/129 613	08/07/2009	201100160	01.11.2016	24655	08/07/2029	Granted	same as Eurasia
Moldavia	15/05/2009 13/03/2009 08/07/2008	US 61/213 189 US 61/202 581 US 61/129 613	08/07/2009	201100160	01.11.2016	24655	08/07/2029	Granted	same as Eurasia
Tajikistan	15/05/2009 13/03/2009 08/07/2008	US 61/213 189 US 61/202 581 US 61/129 613	08/07/2009	201100160	01.11.2016	24655	08/07/2029	Granted	same as Eurasia
Turkmenistan	15/05/2009 13/03/2009 08/07/2008	US 61/213 189 US 61/202 581 US 61/129 613	08/07/2009	201100160	01.11.2016	24655	08/07/2029	Granted	same as Eurasia
Europe	15/05/2009 13/03/2009 08/07/2008	US 61/213 189 US 61/202 581 US 61/129 613	08/07/2009	09780311.8	26.04.2017	2315777	08/07/2029	Validated	**8**
Germany	15/05/2009 13/03/2009 08/07/2008	US 61/213 189 US 61/202 581 US 61/129 613	08/07/2009	09780311.8	26.04.2017	2315777	08/07/2029	Validation	same as Europe
Austria	15/05/2009 13/03/2009 08/07/2008	US 61/213 189 US 61/202 581 US 61/129 613	08/07/2009	09780311.8	26.04.2017	2315777	08/07/2029	Validation	same as Europe
Belgium	15/05/2009 13/03/2009 08/07/2008	US 61/213 189 US 61/202 581 US 61/129 613	08/07/2009	09780311.8	26.04.2017	2315777	08/07/2029	Validation	same as Europe
Bulgaria	15/05/2009 13/03/2009 08/07/2008	US 61/213 189 US 61/202 581 US 61/129 613	08/07/2009	09780311.8	26.04.2017	2315777	08/07/2029	Validation	same as Europe
Cyprus	15/05/2009 13/03/2009 08/07/2008	US 61/213 189 US 61/202 581 US 61/129 613	08/07/2009	09780311.8	26.04.2017	2315777	08/07/2029	Validation	same as Europe
Croatia	15/05/2009 13/03/2009 08/07/2008	US 61/213 189 US 61/202 581 US 61/129 613	08/07/2009	09780311.8	26.04.2017	2315777	08/07/2029	Validation	same as Europe
Denmark	15/05/2009 13/03/2009 08/07/2008	US 61/213 189 US 61/202 581 US 61/129 613	08/07/2009	09780311.8	26.04.2017	2315777	08/07/2029	Validation	same as Europe

Spain	15/05/2009 13/03/2009 08/07/2008	US 61/213 189 US 61/202 581 US 61/129 613	08/07/2009	09780311.8	26.04.2017	2315777	08/07/2029	Validation	same as Europe
Estonia	15/05/2009 13/03/2009 08/07/2008	US 61/213 189 US 61/202 581 US 61/129 613	08/07/2009	09780311.8	26.04.2017	2315777	08/07/2029	Validation	same as Europe
Finland	15/05/2009 13/03/2009 08/07/2008	US 61/213 189 US 61/202 581 US 61/129 613	08/07/2009	09780311.8	26.04.2017	2315777	08/07/2029	Validation	same as Europe
France	15/05/2009 13/03/2009 08/07/2008	US 61/213 189 US 61/202 581 US 61/129 613	08/07/2009	09780311.8	26.04.2017	2315777	08/07/2029	Validation	same as Europe
United Kingdom	15/05/2009 13/03/2009 08/07/2008	US 61/213 189 US 61/202 581 US 61/129 613	08/07/2009	09780311.8	26.04.2017	2315777	08/07/2029	Validation	same as Europe
Greece	15/05/2009 13/03/2009 08/07/2008	US 61/213 189 US 61/202 581 US 61/129 613	08/07/2009	09780311.8	26.04.2017	2315777	08/07/2029	Validation	same as Europe
Hungary	15/05/2009 13/03/2009 08/07/2008	US 61/213 189 US 61/202 581 US 61/129 613	08/07/2009	09780311.8	26.04.2017	2315777	08/07/2029	Validation	same as Europe
Ireland	15/05/2009 13/03/2009 08/07/2008	US 61/213 189 US 61/202 581 US 61/129 613	08/07/2009	09780311.8	26.04.2017	2315777	08/07/2029	Validation	same as Europe
Iceland	15/05/2009 13/03/2009 08/07/2008	US 61/213 189 US 61/202 581 US 61/129 613	08/07/2009	09780311.8	26.04.2017	2315777	08/07/2029	Validation	same as Europe
Italy	15/05/2009 13/03/2009 08/07/2008	US 61/213 189 US 61/202 581 US 61/129 613	08/07/2009	09780311.8	26.04.2017	2315777	08/07/2029	Validation	same as Europe
Latvia	15/05/2009 13/03/2009 08/07/2008	US 61/213 189 US 61/202 581 US 61/129 613	08/07/2009	09780311.8	26.04.2017	2315777	08/07/2029	Validation	same as Europe
Lithuania	15/05/2009 13/03/2009 08/07/2008	US 61/213 189 US 61/202 581 US 61/129 613	08/07/2009	09780311.8	26.04.2017	2315777	08/07/2029	Validation	same as Europe
Luxembourg	15/05/2009 13/03/2009 08/07/2008	US 61/213 189 US 61/202 581 US 61/129 613	08/07/2009	09780311.8	26.04.2017	2315777	08/07/2029	Validation	same as Europe
Macedonia	15/05/2009 13/03/2009 08/07/2008	US 61/213 189 US 61/202 581 US 61/129 613	08/07/2009	09780311.8	26.04.2017	2315777	08/07/2029	Validation	same as Europe
Malta	15/05/2009 13/03/2009 08/07/2008	US 61/213 189 US 61/202 581 US 61/129 613	08/07/2009	09780311.8	26.04.2017	2315777	08/07/2029	Validation	same as Europe
Monaco	15/05/2009 13/03/2009 08/07/2008	US 61/213 189 US 61/202 581 US 61/129 613	08/07/2009	09780311.8	26.04.2017	2315777	08/07/2029	Validation	same as Europe
Norway	15/05/2009 13/03/2009 08/07/2008	US 61/213 189 US 61/202 581 US 61/129 613	08/07/2009	09780311.8	26.04.2017	2315777	08/07/2029	Validation	same as Europe
Netherlands	15/05/2009 13/03/2009 08/07/2008	US 61/213 189 US 61/202 581 US 61/129 613	08/07/2009	09780311.8	26.04.2017	2315777	08/07/2029	Validation	same as Europe
Poland	15/05/2009 13/03/2009 08/07/2008	US 61/213 189 US 61/202 581 US 61/129 613	08/07/2009	09780311.8	26.04.2017	2315777	08/07/2029	Validation	same as Europe
Portugal	15/05/2009 13/03/2009 08/07/2008	US 61/213 189 US 61/202 581 US 61/129 613	08/07/2009	09780311.8	26.04.2017	2315777	08/07/2029	Validation	same as Europe
Czech republic	15/05/2009 13/03/2009 08/07/2008	US 61/213 189 US 61/202 581 US 61/129 613	08/07/2009	09780311.8	26.04.2017	2315777	08/07/2029	Validation	same as Europe
Romania	15/05/2009 13/03/2009 08/07/2008	US 61/213 189 US 61/202 581 US 61/129 613	08/07/2009	09780311.8	26.04.2017	2315777	08/07/2029	Validation	same as Europe
San Marino	15/05/2009 13/03/2009 08/07/2008	US 61/213 189 US 61/202 581 US 61/129 613	08/07/2009	09780311.8	26.04.2017	2315777	08/07/2029	Validation	same as Europe
Slovakia	15/05/2009 13/03/2009 08/07/2008	US 61/213 189 US 61/202 581 US 61/129 613	08/07/2009	09780311.8	26.04.2017	2315777	08/07/2029	Validation	same as Europe
Slovenia	15/05/2009 13/03/2009 08/07/2008	US 61/213 189 US 61/202 581 US 61/129 613	08/07/2009	09780311.8	26.04.2017	2315777	08/07/2029	Validation	same as Europe
Sweden	15/05/2009 13/03/2009 08/07/2008	US 61/213 189 US 61/202 581 US 61/129 613	08/07/2009	09780311.8	26.04.2017	2315777	08/07/2029	Validation	same as Europe
Swiss	15/05/2009 13/03/2009 08/07/2008	US 61/213 189 US 61/202 581 US 61/129 613	08/07/2009	09780311.8	26.04.2017	2315777	08/07/2029	Validation	same as Europe
Turkey	15/05/2009 13/03/2009 08/07/2008	US 61/213 189 US 61/202 581 US 61/129 613	08/07/2009	09780311.8	26.04.2017	2315777	08/07/2029	Validation	same as Europe
Europe (Division)	15/05/2009 13/03/2009 08/07/2008	US 61/213 189 US 61/202 581 US 61/129 613	08/07/2009	17159699.2			08/07/2029	Pending	
Hong Kong	15/05/2009 13/03/2009 08/07/2008	US 61/213 189 US 61/202 581 US 61/129 613	28/02/2018	18102934.5			08/07/2029	Pending	

*: As provided under the “Patent Term Adjustment” mechanism, the U.S. Patent and Trademark Office granted an additional term of protection for this patent of 397 days

**: As provided under the “Patent Term Adjustment” mechanism, the U.S. Patent and Trademark Office granted an additional term of protection for this patent of 48 days

Family 2: Endogenous Antiretroviral

Family 2 involves the use of an antibody directed against the envelope protein HERV-W/MSRV, its fragments, and its derivatives as a global antiretroviral agent.

This family also covers the use of the combination of such an antibody, its fragments, or derivatives, with a classic antiretroviral. The Company, has also considered the synergistic effect of such a combination.

Family 2 is wholly owned by the Company.

FAMILY 2: ENDOGENOUS ANTIRETROVIRAL								
Owner/Holder	GeNeuro							
Title	Antiretroviral drug targeting human endogenous retrovirus							
Country	**Priority date**	**Country / N° of priority**	**Filing date**	**N° of Application**	**Issue date**	**N° of Patent**	**Expiry date**	**Status**
Argentina	28/05/2014	EP 14305806.3	28/05/2015	20150101680			28/05/2035	Pending
GCC	28/05/2014	EP 14305806.3	27/05/2015	29474/2015			27/05/2035	Pending
Taiwan	28/05/2014	EP 14305806.3	28/05/2015	104117097			28/05/2035	Pending
PCT	28/05/2014	EP 14305806.3	27/05/2015	EP2015/061691			28/11/2016	Engaged
United Arab Emirates	28/05/2014	EP 14305806.3	27/05/2015	P6000315/2016			27/05/2035	Pending
Australia	28/05/2014	EP 14305806.3	27/05/2015	2015265936			27/05/2035	Pending
Brazil	28/05/2014	EP 14305806.3	27/05/2015	11 2016 027671 0				Pending
Canada	28/05/2014	EP 14305806.3	27/05/2015	2 949 884			27/05/2035	Pending
China	28/05/2014	EP 14305806.3	27/05/2015	201580027652.7			27/05/2035	Pending
Hong-Kong	28/05/2014	EP 14305806.3	21/09/2017	17109624.6			27/05/2035	Pending
Eurasia	28/05/2014	EP 14305806.3	27/05/2015	201692471			27/05/2035	Pending
Ecuador	28/05/2014	EP 14305806.3	27/05/2015	IEPI-2016-91728			27/05/2035	Pending
Egypt	28/05/2014	EP 14305806.3	27/05/2015	1916/2016			27/05/2035	Pending
Europa	28/05/2014	EP 14305806.3	27/05/2015	15725326.1	31.07.2019	3148582	27/05/2035	Granted
Hong-Kong	28/05/2014	EP 14305806.3	28/07/2017	17107531.2			27/05/2035	Pending
Israel	28/05/2014	EP 14305806.3	27/05/2015	249040			27/05/2035	Pending
India	28/05/2014	EP 14305806.3	27/05/2015	201617043958			27/05/2035	Pending
Japan	28/05/2014	EP 14305806.3	27/05/2015	2017-514954			27/05/2035	Pending
Republic of Korea	28/05/2014	EP 14305806.3	27/05/2015	10-2016-7035895			27/05/2035	Pending
Mexico	28/05/2014	EP 14305806.3	27/05/2015	MX/A/2016/015560			27/05/2035	Pending
Malaysia	28/05/2014	EP 14305806.3	27/05/2015	PI 2016002061			27/05/2035	Pending
New Zealand	28/05/2014	EP 14305806.3	27/05/2015	726568			27/05/2035	Pending
Russia	28/05/2014	EP 14305806.3	27/05/2015	2016151471	27.05.2019	2 689 326	27/05/2035	Granted
Saudi Arabia	28/05/2014	EP 14305806.3	27/05/2015	516380343			27/05/2035	Pending
Singapore	28/05/2014	EP 14305806.3	27/05/2015	11201609886S			27/05/2035	Pending
Thailand	28/05/2014	EP 14305806.3	27/05/2015	1601007115			27/05/2035	Pending
Ukraine	28/05/2014	EP 14305806.3	27/05/2015	a201613240			27/05/2035	Pending
USA	28/05/2014	EP 14305806.3	27/05/2015	15/314 017			27/05/2035	Pending
Vietnam	28/05/2014	EP 14305806.3	27/05/2015	1-2016-04728			27/05/2035	Pending
South Africa	28/05/2014	EP 14305806.3	27/05/2015	2016/08050			27/05/2035	Pending

Family 3: Remyelination

This application covers compounds and compositions for the prevention and/or treatment of a mechanism that blocks the endogenous myelin repair capability of the adult nervous system in disorders associated with the expression of the envelope protein HERV-W Env, particularly its subtype, MSRV.

This family also covers the use of an antibody directed against HERV-W Env for use in the prevention of the blockage of the endogenous myelin repair capability, particularly in disorders such as RRMS, chronic progressive MS, CIDP, and schizophrenia or bipolar disorders.

Family 3 is wholly owned by the Company.

FAMILY 3: REMYELINATION	
Owner/Holder	GeNeuro
Title	Compound for treatment of inhibition of remyelination in diseases and disorders associated with expression of the envelope protein HERV-W
PCT Extension & Engagements in National and/or Regional Phases Theoretical Expiration Date[150]: October 1, 2033	

Claims subject matters

A Composition comprising the antibody GNbAC1 (temelimab) and a nitric oxide inhibitory drug or Combined composition (kit) comprising the antibody GNbAC1 (temelimab) and a nitric oxide inhibitory drug

B Method for preventing or treating diseases associated with HERV-W ENV using the antibody GNbAC1 (temelimab), in particular multiple sclerosis, progressive multiple sclerosis, relapsing remitting multiple sclerosis

C Method for preventing or treating diseases associated with HERV-W EN using the antibody GNbAC1 (temelimab) and a nitric oxide inhibitory drug or using a composition comprising the antibody GNbAC1 (temelimab) and a nitric oxide inhibitory drug, in particular multiple sclerosis, progressive multiple sclerosis, relapsing remitting multiple sclerosis

D Method for preventing or treating progressive multiple sclerosis using the antibody GNbAC1(temelimab)

Country	Priority date	Country / N° of priority	Filing date	N° of Application	Issue date	N° of Patent	Expiry date	Status	Claims
PCT	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	EP2013/070452			02/04/2015	Engaged	
Saudi Arabia	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	515360207	18/09/2018	6097	01/10/2033	Granted	**A**
Australia	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	2013326552	06/09/2018	2013326552	01/10/2033	Granted	**A**
Australia (Division)	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	2018217328			01/10/2033	Pending	
Brazil	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	1120150071503				Pending	
Canada	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	2 882 781			01/10/2033	Pending	
China	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	201380051713.4	18.06.2018	ZL 201380051713.4	01/10/2033	Granted	**B**
China (Division)	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	201610152679.5			01/10/2033	Pending	
Hong Kong	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/08/2016	16109172.3			01/10/2033	Pending	
Colombia	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	15-095895	01.10.2013	33485	01/10/2033	Granted	**A**
Egypt	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	282/2015			01/10/2033	Pending	
United Arab Emirates	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	P431/15			01/10/2033	Pending	
USA	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	14/429 199	12.12.2017	9,840,550	01/10/2033	Granted	**A**
USA (Division)	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	15/812 745			01/10/2033	Pending	
Eurasia	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	201590678	31.10.2017	028245	01/10/2033	Granted	**A** **C**
Eurasia (Division)	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	201791525			01/10/2033	Pending	
Armenia	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	201590678	31.10.2017	028245	01/10/2033	Granted	as in Eurasia
Azerbaijan	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	201590678	31.10.2017	028245	01/10/2033	Granted	as in Eurasia
Belarus	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	201590678	31.10.2017	028245	01/10/2033	Granted	as in Eurasia
Russia	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	201590678	31.10.2017	028245	01/10/2033	Granted	as in Eurasia
Kazakhstan	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	201590678	31.10.2017	028245	01/10/2033	Granted	as in Eurasia
Kirghizstan	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	201590678	31.10.2017	028245	01/10/2033	Granted	as in Eurasia
Tajikistan	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	201590678	31.10.2017	028245	01/10/2033	Granted	as in Eurasia
Turkmenistan	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	201590678	31.10.2017	028245	01/10/2033	Granted	as in Eurasia
Israel	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	237474			01/10/2033	Pending	
Israel (Division)	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	264382			01/10/2033	Pending	
Japan	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	2015-533633	10.08.2018	6379331	01/10/2033	Granted	**D**
Japan (Division)	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	2017-214696	14/06/2019	6538138	01/10/2033	Granted	**A**
Malaysia	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	PI 2015700643			01/10/2033	Pending	
Mexico	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	MX/A/2015/003572			01/10/2033	Pending	

150 Subject to the due and punctual payment of applicable maintenance fees. This date does not take into consideration the possibility of obtaining an additional protection certificate.

Mexico (Division)	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	MX/A/2019/008916			01/10/2033	Pending	
Singapore	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	11201501274V	06.04.2017	11201501274V	01/10/2033	Granted	**A C**
Thailand	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	1501001128			01/10/2033	Pending	
South Africa	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	2015/01491			01/10/2033	Pending	
Europe	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	13770926.7	21.11.2018	2904009	01/10/2033	Granted	**A**
Europe (Division)	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	18198309.9	24.02.2021	3447070	01/10/2033	Granted	
Albania	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	13770926.7	21.11.2018	2904009	01/10/2033	Granted	**A**
Germany	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	13770926.7	21.11.2018	2904009	01/10/2033	Granted	**A**
Austria	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	13770926.7	21.11.2018	2904009	01/10/2033	Granted	**A**
Belgium	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	13770926.7	21.11.2018	2904009	01/10/2033	Granted	**A**
Bulgaria	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	13770926.7	21.11.2018	2904009	01/10/2033	Granted	**A**
Cyprus	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	13770926.7	21.11.2018	2904009	01/10/2033	Granted	**A**
Croatia	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	13770926.7	21.11.2018	2904009	01/10/2033	Granted	**A**
Denmark	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	13770926.7	21.11.2018	2904009	01/10/2033	Granted	**A**
Spain	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	13770926.7	21.11.2018	2904009	01/10/2033	Granted	**A**
Estonia	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	13770926.7	21.11.2018	2904009	01/10/2033	Granted	**A**
Finland	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	13770926.7	21.11.2018	2904009	01/10/2033	Granted	**A**
France	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	13770926.7	21.11.2018	2904009	01/10/2033	Granted	**A**
Great Britain	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	13770926.7	21.11.2018	2904009	01/10/2033	Granted	**A**
Greece	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	13770926.7	21.11.2018	2904009	01/10/2033	Granted	**A**
Hungary	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	13770926.7	21.11.2018	2904009	01/10/2033	Granted	**A**
Ireland	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	13770926.7	21.11.2018	2904009	01/10/2033	Granted	**A**
Iceland	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	13770926.7	21.11.2018	2904009	01/10/2033	Granted	**A**
Italy	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	13770926.7	21.11.2018	2904009	01/10/2033	Granted	**A**
Latvia	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	13770926.7	21.11.2018	2904009	01/10/2033	Granted	**A**
Lithuania	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	13770926.7	21.11.2018	2904009	01/10/2033	Granted	**A**
Luxembourg	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	13770926.7	21.11.2018	2904009	01/10/2033	Granted	**A**
Macedonia	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	13770926.7	21.11.2018	2904009	01/10/2033	Granted	**A**
Malta	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	13770926.7	21.11.2018	2904009	01/10/2033	Granted	**A**
Monaco	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	13770926.7	21.11.2018	2904009	01/10/2033	Granted	**A**
Norway	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	13770926.7	21.11.2018	2904009	01/10/2033	Granted	**A**
Netherlands	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	13770926.7	21.11.2018	2904009	01/10/2033	Granted	**A**
Poland	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	13770926.7	21.11.2018	2904009	01/10/2033	Granted	**A**
Portugal	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	13770926.7	21.11.2018	2904009	01/10/2033	Granted	**A**
Czech Republic	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	13770926.7	21.11.2018	2904009	01/10/2033	Granted	**A**
Romania	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	13770926.7	21.11.2018	2904009	01/10/2033	Granted	**A**
San Marino	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	13770926.7	21.11.2018	2904009	01/10/2033	Granted	**A**
Serbia	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	13770926.7	21.11.2018	2904009	01/10/2033	Granted	**A**
Slovakia	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	13770926.7	21.11.2018	2904009	01/10/2033	Granted	**A**
Slovenia	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	13770926.7	21.11.2018	2904009	01/10/2033	Granted	**A**
Sweden	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	13770926.7	21.11.2018	2904009	01/10/2033	Granted	**A**
Switzerland	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	13770926.7	21.11.2018	2904009	01/10/2033	Granted	**A**
Turkey	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	13770926.7	21.11.2018	2904009	01/10/2033	Granted	**A**
Russia	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	2015116149	22.11.2017	2,636,355	01/10/2033	Granted	**A C**
India	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	2397/DELNP/2015			01/10/2033	Pending	
New Zealand (Division)	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	740726			01/10/2033	Pending	
Republic of Korea	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	10-2015-7011152			01/10/2033	Pending	
Ukraine	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	a201504292	25/04/2019	119032	01/10/2033	Granted	**A**

Ukraine (Division)	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	a201809345			01/10/2033	Pending	
Vietnam	28/12/2012 02/10/2012	US 61/746 792 US 61/708 779	01/10/2013	1-2015-01547			01/10/2033	Pending	

Family 4: SEP 16

Patent family 4 covers the sequence of the env gene.

This family covers the sequence necessary for the development of humanized antibodies directed against the epitope of the envelope protein Env of MSRV necessary for the activation of TLR4.

Family 4 is wholly owned by bioMérieux.

FAMILY 4: SEP 16				
Owner/Holder	bioMérieux			
Title	Retroviral nucleic material and nucleotide fragments, in particular associated with multiple sclerosis and/or rheumatoid arthritis, for diagnostic, prophylactic and therapeutic uses			
Extensions Theoretical Expiration Date[151]: July 7, 2018				
Country	Filing date and number	Publication date and number	Issue date and number	Status
Canada	CA 2 295 935 July 7, 1998		CA 2 295 935 Sep. 9, 2014	Patent issued
Europe	EP 98936467.4 July 7, 1998	EP 0 996 731 May 3, 2000	EP 0 996 731 Aug. 31, 2005	Patent issued and confirmed in FR, SP, IT, GB, GER, SW
Europe (division)	EP 05017735.1 July 7, 1998	EP 1 612 270 Jan. 4, 2006	EP 1 612 270 Sep. 2, 2009	Patent issued and confirmed in FR, SP, IT, GB, GER, SW
Japan	JP 11-508255 July 7, 1998	JP 2002-509437 March 26, 2002	JP 4 272 264 March 6, 2009	Patent issued
United States	US 09/319 156 July 7, 1998		US 7 771 927 Aug. 10, 2010	Patent issued
United States (division)	US 12/776 893 July 7, 1998		US 8 088 910 Jan. 3, 2012	Patent issued

Family 5: TLR4

This patent family covers the use of an anti env-SU antibody capable of binding itself to the soluble fraction of the Env protein of MSRV for preparation of a medication intended to treat MS or schizophrenia by inhibiting the pro-inflammatory cascade involving the soluble fraction of Env of MSRV and such receptor.

This patent family, therefore, broadly covers an antibody directed against Env-SU of MSRV for use in the treatment of MS or schizophrenia.

Family 5 is owned by bioMérieux and INSERM.

FAMILY 5: TLR4				
Owner/Holder	bioMérieux and INSERM			
Title	Composition for treating pathology associated with MSRV/HERV-W			
Priority				
Country	Filing date and number	Publication date and number	Issue date and number	Status
France	FR 04 00675 Jan. 23, 2004	FR 2 865 403 June 1, 2005	FR 04 00675 June 12, 2009	Patent issued
PCT Extension & Engagements in National and/or Regional Phases Theoretical Expiration Date: [152] January 24, 2025				
PCT	PCT/FR2005/00156 Jan. 24, 2005	WO2005/080437 Sep. 1, 2005		Application engaged

151 Subject to the due and punctual payment of applicable maintenance fees.
152 Subject to the due and punctual payment of applicable maintenance fees.

Canada	CA 2 554 263 Jan. 24, 2005		CA 2 554 263 Aug. 5,2014	Patent issued
China	CN 20058006462.3 Jan. 24, 2005	CN 1926153 A March 7, 2007	ZL200580006462.3 May 4, 2011	Patent issued
Europe	EP 05717480.7 Jan. 24, 2005	EP 1 709 082 Oct. 11, 2006	EP 1 709 082 March 12, 2014	Patent issued and confirmed in SW, GER, SP, FR, GB, IT, AU, BE, BG, CY, DK, EE, FI, GR, HU, IE, IS, LT, LU, MC, NL, PL, PT, CZ, RO, SI, SK, SE, TR
Europe (division)	EP 10183899.3 Jan. 24, 2005	EP 2 365 002 Sep. 14, 2011		Examination pending
India	IN 3065/CHENP/2006 Jan. 24, 2005		IN 241 921 July 30, 2010	Patent issued
Japan	JP 2006-550240 Jan. 24, 2005	JP 2008-505847 Feb. 28, 2008	JP 4 991 314 May 11, 2012	Patent issued
United States	US 10/586 742 Jan. 24, 2005	US-2008-0038279 Feb. 14, 2008	US 7 666 420 Feb. 23, 2010	Patent issued*.

*: As provided under the "Patent Term Adjustment" mechanism, the U.S. Patent and Trademark Office granted an additional term of protection for this patent of 103 days.

Family 6: SEP 12

This patent family covers the gag and pol sequences of MSRV. Family 6 is wholly owned by bioMérieux.

FAMILY 6: SEP 12				
Owner/Holder	bioMérieux			
Title	Viral material and nucleotide fragments associated with multiple sclerosis useful for diagnostic, preventive and therapeutic purposes			
PCT Extensions & Engagements in National and/or Regional Phases Theoretical Expiration Date[153]: August 2, 2016				
Country	Filing date and number	Publication date and number	Issue date and number	Status
PCT	PCT/FR1996/01244 Aug. 2, 1996	WO1997/06260 Feb. 20, 1997		Application engaged
Canada	CA 2 201 282 Aug. 2, 1996		CA 2 201 282 01 April 2013	Patent issued
Europe	EP 96420265.9 Aug. 2, 1996	EP 0 789 077 Aug. 13, 1997	EP 0 789 077 Sep. 26, 2007	Patent issued and confirmed in FR, GER, IT, SP, SW, GB
Europe (division)	EP 07018564.0 Aug. 2, 1996	EP 1 916 304 April 30, 2008	EP 1 916 304 Jan. 18, 2012	Patent issued and confirmed in FR, GER, IT, SP, SW, GB
Japan	JP 9-508179 Aug. 2, 1996		JP 4 444 372 Jan. 22, 2010	Patent issued
Japan (division)	JP 2009-265658 Aug. 2, 1996		JP 5 143 814 Nov. 30, 2012	Patent issued
United States	US 08/691 563 Aug. 2, 1996		US 6 001 987 Dec. 14, 1999	Patent issued
United States (division)	US 09/374 766 Aug. 2, 1996		US 6 579 526 June 17, 2003	Patent issued
United States (division)	US 11/463 109 Aug. 2, 1996		US 7 932 350 May 24, 2007	Patent issued."

*: As provided under the "Patent Term Adjustment" mechanism, the U.S. Patent and Trademark Office granted an additional term of protection for this patent of 1133 days.

Family 7: SEP 15

This patent family covers a particular sequence that is expressed in the placenta.

Family 7 is wholly owned by bioMérieux.

153 Subject to the due and punctual payment of applicable maintenance fees.

FAMILY 7: SEP 15

FAMILY 7: SEP 15				
Owner/Holder	bioMérieux			
Title	Endogenic retroviral sequences associated with autoimmune diseases or with pregnancy disorders			
PCT Extension & Engagements in National and/or Regional Phases Theoretical Expiration Date[154]: July 6, 2018				
Country	Filing date and number	Publication date and number	Issue date and number	Status
PCT	PCT/FR1998/01442 July 6, 1998	WO1999/02696 Jan. 21, 1999		Application engaged
Canada	CA 2 298 834 July 6 1998		CA 2 298 834 March 23, 2015	Patent issued
Europe	EP 98935106.9 July 6, 1998	EP 1 000 158 May 17, 2000	EP 1 000 158 Nov. 22, 2006	Patent issued and confirmed Abandoned in confirmed countries
Japan	JP 11-508244 July 6, 1998	JP 2002-512530 April 23, 2002	JP 4 249 269 Jan. 23, 2009	Patent issued

Family 8: SEP 18

This patent family covers the env gene of the HERV-7q endogenous retrovirus.

Family 8 is wholly owned by INSERM.

FAMILY 8: SEP 18				
Owner/Holder	INSERM			
Title	Nucleic sequence and deduced protein sequence family with human endogenous retroviral motifs, and their uses			
Priority				
Country	Filing number and date	Publication number and date	Issue number and date	Status
France	FR 98 07920 June 23, 1998	FR 2 780 069 Dec. 24, 1999	FR 98 07920 June 28, 2002	Patent issued
Extensions Theoretical Expiration Date[155]: June 23, 2019				
Canada	CA 2 331 923 23 June 23, 1999		CA 2 331 923 Feb. 18, 2014	Patent issued
Europe	EP 99926538.2 June 23, 1999	EP 1 090 122 April 11, 2001	EP 1 090 122 July 16, 2008	Patent issued and confirmed in GER, FR, NL, GB
United States	US 09/719 554 June 23, 1999		US 6 919 438 July 16, 2005	Patent issued
United States (division)	US 11/028 539 June 23, 1999	US 2005-0118573 June 2, 2005	US 7 534 439 May 19, 2009	Patent issued. *

*: As provided under the "Patent Term Adjustment" mechanism, the U.S. Patent and Trademark Office granted an additional term of protection for this patent of 235 days.

Family 9: INTERECO

This patent family covers the peptide domain required for interaction between the envelope of a virus pertaining to the HERV-W interference group and an hASCT receptor. This area plays a part in the transmission of information and the merger of cells.

Family 9 is wholly owned by bioMérieux.

FAMILY 9: INTERECO	
Owner/Holder	bioMérieux
Title	Peptide domain required for interaction between the envelope of a virus pertaining to the HERV-W interference group and an HASCT receptor

154 Subject to the due and punctual payment of applicable maintenance fees.
155 Subject to the due and punctual payment of applicable maintenance fees.

Priority				
Country	Filing date and number	Publication date and number	Issue date and number	Status
France	FR 06 50468 Feb. 9, 2006	FR 2 897 062 Aug. 10, 2007	FR 06 50465 Nov. 4, 2011	Patent issued
PCT Extension & Engagements in National and/or Regional Phases Theoretical Expiration Date[156]: February 9, 2027				
PCT	PCT/FR2007/000236 Feb. 9, 2007	WO2007/090967 Aug. 16, 2007		Application engaged
Australia	AU 2007213591 Feb. 9, 2007		AU 2007213591 Feb. 19, 2012	Patent issued
Canada	CA 2 640 793 Feb. 9, 2007		CA 2 640 793	Patent issued Awaiting official deed
China	CN 200780004699.7 Feb. 9, 2007	CN 101379079 A March 4, 2009	ZL200780004699.7 Nov. 14, 2012	Patent issued
Europe	EP 07730950.8 Feb. 9, 2007	EP 1 981 904 Oct. 22, 2008		Examination pending
India	4129/CHENP/2008 Feb. 9, 2007			Examination pending
Israel	IL 193 353 Feb. 9, 2007			Examination pending
Japan	JP 2008-553798 Feb. 9, 2007	JP 2009-525741 July 16, 2009		Examination pending
Japan (division)	JP 2015-200607 Feb. 9, 2007			Examination pending
United States	US 14/847 941 Feb. 9, 2007			Examination pending

Family 10: Ac AntiTM

This patent family covers a humanized antibody directed against the HERV-W envelope protein, in particular the C-terminal extremity of the SU region of the envelope protein of HERV-W, to the exclusion of any antibody specifically directed against the liaison site of such Env protein and the hASCT1 or hASCT2 receptor. Such antibodies can be advantageous for monitoring pathological pregnancies.

Family 10 is wholly owned by the Company.

FAMILY 10: Ac ANTITM				
Owner/Holder	GeNeuro			
Title	Pharmaceutical composition containing antibodies directed against the HERV-W envelope			
Priority				
Country	Filing number and date	Publication number and date	Issue number and date	Status
France	FR 07 00952 Feb. 9, 2007	FR 2 912 314 Aug. 15, 2008	FR 07 00952 Aug. 3, 2012	Patent issued – theoretical expiration date157: February 9, 2027
PCT Extension & Engagements in National and/or Regional Phases				
PCT	PCT/FR2008/000166 Feb. 11, 2008	WO2008/113916 Sep. 25, 2008		Application engaged
Europe	EP 08761866.6 Feb. 11, 2008	EP 2 117 594 Nov. 18, 2009		Application abandoned
United States of America	US 12/449,327 Feb. 11, 2008	US 2010-0074894 March 25, 2010		Application abandoned

The extensions of the patent filed subsequently were abandoned, because the MSRV ligand patent, providing broader protection, was filed in the meantime; such extensions, therefore, were no longer of interest.

Family 11: HERV-W fusion

This patent family covers a process for detecting the expression of the envelope protein of a HERV based on the detection of the fusogenic power of such protein in a cellular tissue or of a cellular culture, by showing the formation of syncytia.

156 Subject to the due and punctual payment of applicable maintenance fees.
157 Subject to the due and punctual payment of applicable maintenance fees.

Family 11 is owned by bioMérieux and INSERM.

FAMILY 11: HERV-W FUSION	
Owner/Holder	bioMérieux and INSERM
Title	Method for detecting the expression of an envelope protein of a human endogenous retrovirus and uses of a gene coding for said protein

PCT Extension & Engagements in National and/or Regional Phases theoretical expiration date[158]: September 1, 2020				
Country	**Filing number and date**	**Publication number and date**	**Grant number and date**	**Status**
PCT	PCT/FR00/02429 Sep. 1, 2000	WO01/16171 Sep. 8, 2011		Application engaged
Europe	EP 00960783.9 Sep. 1, 2000	EP 1 212 359 June 12, 2002	EP 1 212 359 Nov. 12, 2011	Patent granted
Europe	EP 10 183 612.0 Sep. 1, 2000	EP 2 385 058 Nov. 9, 2011	EP 2 385 058 Nov. 6, 2013	Patent granted
Japan	JP 2001-519732 Sep. 1, 2000	JP 2003-510032 March 18, 2003	JP 4 283 475 March 27, 2009	Patent granted
Japan	JP 2008-244988 Sep. 1, 2000	JP 2009-72194 April 9, 2009	JP 4 824 731 Sep. 16, 2011	Patent granted
Canada	CA 2 383 877 Sep. 1, 2000		CAK 2 383 877 April 15, 2014	Patent granted
United States of America	US 10/069,883 Feb. 11, 2008	US 2010-0074894 March 25, 2010	7 442 550 Oct. 28, 2008	Patent granted

Family 12: SEP 6

This patent family covers a composition that consists of two pathogenic agents and/or infectants associated with MS.

These agents are, respectively:

- a first agent being a human virus possessing reverse transcriptase activity and which is related to a family of endogenous retroviral elements or a variant of such virus, and
- a second agent or variant of such agent.

Both of these pathogenic and/or infectant agents come from the same viral source chosen from the sources called, respectively, POL-2.

This composition may be used in a diagnostic method, a prophylaxis method, or as a treatment method, particularly for MS.

FAMILY 12: SEP 6				
Owner/Holder	bioMérieux			
Title	MMSRV1 virus linked to multiple sclerosis, its nucleic components and their applications			
PCT Extension & Engagements in National Phase				
Country	Filing number and date	Publication number and date	Grant number and date	Status
PCT	PCT/FR95/00142 Feb. 6, l995	WO95/21256 Aug. 10, 1995		Application engaged
United States	US 08/384 137 Feb. 6, 1995		US 5 871 996 Feb. 6, 1999	Patent granted
United States	US 08/470 006 Feb. 6, 1995		US 5 962 217 Jan. 5, 1999	Patent granted
United States	US 09/133 411 Feb. 6, 1995		US 6 342 383 Jan. 29, 2002	Patent granted
United States	US 08/471 969 Feb. 6, 1995		US 5 871 745 Feb. 16, 1999	Patent granted
United States	US 09/200 990 Feb. 6, 1995		US 6 184 025 B1 Feb. 6, 2001	Patent granted

158 Subject to the due and punctual payment of applicable maintenance fees.

Family 13: SEP 13

This patent family relates to nucleic medicine capable of being used in a diagnostic mode, a method for prophylaxis, or as a method for treating MS or rheumatoid polyarthritis.

Family 13 is wholly owned by bioMérieux.

FAMILY 13:SEP 13				
Owner/Holder	bioMérieux			
Title	Viral material and nucleotide fragments associated with multiple sclerosis, for diagnostic, prophylactic and therapeutic purposes			
PCT Extension & Engagements in National and/or Regional Phases theoretical expiration date[159]: November 26, 2017				
Country	**Filing number and date**	**Publication number and date**	**Grant number and date**	**Status**
PCT	PCT/IB97/01482 Nov. 26, 1997	WO98/23755 June 4, 1998		Application engaged
Europe	EP 97 911 411.3 Nov. 26, 1997	EP 0 942 987 Sep. 22, 1999	EP 0 942 987 Aug. 19, 2009	Patent granted
Canada	CA 2 272 845 Nov. 26, 1997		CA 2 272 845 Jan. 12, 2010	Patent granted
Japan	JP 10-524475 Nov. 26, 1997	JP 2001-505768 May 8, 2001	JP 4 226 657 Dec. 5, 2008	Patent granted
United States	US 08/979 847 Nov. 26, 1997		US 6 582 703 June 24, 2003	Patent granted
United States	US 11/581 030 Nov. 26, 1997	US 2007-0031452 Feb. 8, 2007	US 7 674 888 Nov. 26, 1997	Patent granted

Family 14: SEP 19

This patent family relates to endogenous nucleotide fragments having at least one part of the gag gene of an endogenous retrovirus associated with an autoimmune disorder or a failed pregnancy or pregnancy disorders.
This family also covers the use of such a fragment to detect, in a biological sample, susceptibility to an autoimmune disease, especially MS, or for monitoring or following a pregnancy.

Family 14 is wholly owned by bioMérieux.

FAMILY 14: SEP 19				
Owner/Holder	bioMérieux			
Title	Process for the detection of an endogenous nucleic acid fragment associated with an autoimmune disease			
PCT Extension & Engagements in National and/or Regional Phases theoretical expiration date[160]: January 21, 2020				
Country	Filing number and date	Publication number and date	Grant number and date	Status
PCT	PCT/FR00/00144 July 21, 2000	WO00/043521 July 27, 2000		Application engaged
Europe	EP 00 900 645.3 Jan. 21, 2000	EP 1 147 187 Oct. 24, 2001	EP 1 147 187 June 27, 2012	Patent granted
United States	US 10/632 793 Jan. 21, 2000	US 2004-0048298 March 11, 2004	US 7 632 931 Dec. 15, 2009	Patent granted

Family 15: SEP 20

This family relates to a nucleic fragment of the LTR-RU5 region. This patent family also covers probes and methods capable of hybridation with such fragment, the protein it encodes, an antibody directed against such protein, and a protein for detecting the MSRV-1 retrovirus though such probe or the antibodies described in the invention.
Family 15 is wholly owned by bioMérieux.

FAMILY 15: SEP 20	
Owner/Holder	bioMérieux

159 Subject to the due and punctual payment of applicable maintenance fees.
160 Subject to the due and punctual payment of applicable maintenance fees.

Title	The LTR region of MSRV-1 and the proteins it encodes, and probes and methods for detecting the MSRV-1 retrovirus			
PCT Extension & Engagements in Regional Phase theoretical expiration date[161]: February 15, 2020				
Country	Filing number and date	Publication number and date	Grant number and date	Status
PCT	PCT/IB00/00159 Feb. 15, 2000	WO00/47745 Aug. 17, 2000		Application engaged
Europe	EP 00 902 825.9 Feb. 15, 2000	EP 1 151 108 Nov. 7, 2001	EP 1 151 108 Nov. 30, 2005	Patent granted

Family 16: SEP 21

This invention covers, in particular, a method for detecting superantigenic activity in a biological sample, including demonstration of a majority expansion of lymphocytes.
This application also covers a composition consisting of a therapeutic agent capable of inhibiting superantigen activity and the use of such composition for prophylactic steps and/or the treatment of a disease, particularly an autoimmune disease, such as MS.

Family 16 is wholly owned by bioMérieux.

FAMILY 16: SEP 21				
Owner/Holder	bioMérieux			
Title	Method for detecting MSRV-1 induced superantigen activity in a biological sample			
PCT Extension & Engagements in Regional Phase theoretical expiration date[162]: March 20, 2020				
Country	Filing number and date	Publication number and date	Grant number and date	Status
PCT	PCT/FR00/00691 March 20, 2000	WO00/57185 Sep. 28, 2000		Application engaged
Europe	EP 00 912 720.0 March 20, 2000	EP 1 163 522 Sep. 28, 2000	EP 1 163 522 Nov. 22, 2006	Patent granted

Family 17: HERV-K"

This invention covers an antibody directed against the HERV-K Envelope protein, and uses thereof.
Family 17 is jointly owned by GeNeuro and the NIH; the NIH has entered into an exclusive license of its rights to GeNeuro.

FAMILY 17: HERV-K	
Owner/Holder	GeNeuro and the NIH
Title	Pharmaceutical composition containing antibodies directed against the HERV-K Envelope

Country	Priority date	Country / N° of priority	Filing date	N° of Application	Issue date	N° of Patent	Expiry date	Status
Europe			20/01/2017	17305062.6			20/01/2037	Pending
Argentine	20/01/2017	EP 17305062.6	19/01/2018	20180100129			19/01/2038	Pending
Taiwan	20/01/2017	EP 17305062.6	22/01/2018	107102219			22/01/2038	Pending
PCT	20/01/2017	EP 17305062.6	19/01/2018	US2018/014489			20/07/2019	Engaged
South Africa	20/01/2017	EP 17305062.6	19/01/2018	2019/04587			19/01/2038	Pending
Australia	20/01/2017	EP 17305062.6	19/01/2018	2018210388			19/01/2038	Pending
Brazil	20/01/2017	EP 17305062.6	19/01/2018	not yet allocated			19/01/2038	Pending
Canada	20/01/2017	EP 17305062.6	19/01/2018	not yet allocated			19/01/2038	Pending
China	20/01/2017	EP 17305062.6	19/01/2018	not yet allocated			19/01/2038	Pending
Eurasia	20/01/2017	EP 17305062.6	19/01/2018	not yet allocated			19/01/2038	Pending
Japan	20/01/2017	EP 17305062.6	19/01/2018	not yet allocated			19/01/2038	Pending
Korea	20/01/2017	EP 17305062.6	19/01/2018	not yet allocated			19/01/2038	Pending

161 Subject to the due and punctual payment of applicable maintenance fees.
162 Subject to the due and punctual payment of applicable maintenance fees.

Ukraine	20/01/2017	EP 17305062.6	19/01/2018	not yet allocated			19/01/2038	Pending
US	20/01/2017	EP 17305062.6	19/01/2018	16/478 576			19/01/2038	Pending
Europe	20/01/2017	EP 17305062.6	19/01/2018	18713060.4			19/01/2038	Pending
India	20/01/2017	EP 17305062.6	19/01/2018	201917027958			19/01/2038	Pending
Israel	20/01/2017	EP 17305062.6	19/01/2018	267955			19/01/2038	Pending
Mexico	20/01/2017	EP 17305062.6	19/01/2018	MX/A/2019/008648			19/01/2038	Pending
New Zealand	20/01/2017	EP 17305062.6	19/01/2018	755432			19/01/2038	Pending

5.9 Organization of the Company

5.9.1 Operating Organization Chart

GeNeuro is managed by its management under the supervision of its Board of Directors, which is composed of internationally known persons. The Company also has a scientific committee that contributes significant expertise in MS.

Detailed biographies of the members of the Board of Directors and management are set forth in Chapter 14, "Corporate Governance, Administration, Management and Supervisory and General Management Bodies" of this Universal Registration Document.

Present Organization

The Company is led by Jesús Martin-Garcia, CEO, to whom report:

- Dr. David Leppert, Chief Medical Officer (effective May 1, 2020);
- Dr. Hervé Perron, Chief Scientific Officer;
- Dr. Jean-François Arrighi, Chief Development Officer; and
- Mr. Miguel Payró, Chief Financial Officer, also in charge of human resources.

Mr. Martin-Garcia, Dr. Leppert, Dr. Arrighi, Mr. Payró and Dr. Perron are part of GeNeuro's Executive Committee.

Dr. Thomas Rückle, the Company's former Chief Development Officer, resigned effective August 31, 2020, and was succeeded by Dr. Jean-François Arrighi in September 2020.

5.9.2 Product and Manufacturing

GeNeuro SA has substantial experience in the development of biopharmaceutical products such as therapeutic monoclonal antibodies. This experience includes a broad scientific background, which incorporates the application of analytical and bioanalytical technologies in the quality control of therapeutic antibodies, in the technical assessment of the immunogenicity of such products, and in the humanization of therapeutic monoclonal antibodies and its optimized manufacturability. Experience in the development of antibody-based technologies led to strong interest from third parties.

GeNeuro has a mix of in-house expertise and working with highly qualified CMOs. Dr. Alois B. Lang is a biopharmaceutical product development specialist, with particular expertise in the development of therapeutic monoclonal antibody-based products. He has long-term industrial experience and successfully led the development of several antibody-based products from the pre-clinical phase to the clinical trial phase. Having reached the legal age for retirement in Switzerland at the end of 2018, he continues to serve GeNeuro as a consultant to the Company.

GeNeuro's temelimab is manufactured by Polymun. Polymun developed both cell culture and downstream purification processes suitable for the manufacture of the antibody in accordance with GMP and with clinical-grade quality. The production and purification of temelimab uses established production protocols. The manufacturing process is typical for a monoclonal antibody.

The Company believes that Polymun has sufficient capacity in terms of net fermentation volume as well as matching capacity in downstream processing for the manufacturing of GeNeuro's antibody temelimab up to a Phase III clinical trial or marketing application. Polymun has been successfully audited by the FDA. The process is optimized and well characterized and was successfully presented by GeNeuro to relevant regulatory authorities, such as the Paul Ehrlich Institute and Swissmedic. Polymun is already manufacturing other biopharmaceuticals for Phase III clinical

studies or for drugs which are already on the market and thus has the experience and know-how for related procedures such as process validation and documentation for all stages of clinical development and applications for market approval with the relevant authorities.

5.9.3 Clinical Development Expertise

The clinical development team includes seven experts, including one senior physician and a senior pharmacist who have long experience in clinical research and development and in obtaining product licenses for medications and biological products. In particular, they have participated directly in the development and/or registration of three products indicated for MS: beta interferon (Rebif©), mitoxantrone (Novantrone©), cladribine (Cladribine©), and ocrelizumab (Ocrevus©).

As for clinical trials, the Company has already completed three Phase I clinical trials, two Phase IIa trials, one Phase IIb trial and a Phase IIb extension trial, all in different countries in Europe and Australia, as described elsewhere in this Universal Registration Document. These trials were the subject of several publications and communications in international congresses and conferences in Europe and the United States as well as several scientific articles[163] published in international medical literature.

The clinical team also receives high-quality expertise on a consultative basis from Dr. Gordon S. Francis, who has more than 30 years' experience in industrial development and who has played an important role in the registration of three of the most important reference treatments for MS: beta interferon (Rebif©); natalizumab (Tysabri©); and fingolimod (Gilenya©).

Academic experts recognized in related pharmacological or biostatistical areas are also regularly sought by the Company for specific issues linked to clinical development.

5.9.4 Regulatory Expertise

GeNeuro has one senior person in regulatory affairs with extensive experience in regulatory matters. She has substantial knowledge of regulatory development for pharmaceutical products, which is reflected in the regulatory activities of the Company. GeNeuro focuses its regulatory activities on strategic planning and decisions, and uses highly regarded industry consultants as required to assist it. Some of the regulatory matters successfully conducted by the Company include:

- Organization of scientific advice meetings/requests with the following Health Authorities: Paul-Ehrlich Institute (PEI) Germany in 2010 and in 2014 (with respect to Quality, Non-Clinical and Clinical aspects); and Swissmedic in 2012 (with respect to Non Clinical and Clinical aspects) and the European Medicines Agency (EMA), London, UK in 2013. The scientific advice sought from PEI and Swissmedic concerned development of temelimab in MS and from EMA relating to quality, non-clinical and clinical issues with respect to another intended indication (chronic inflammatory demyelinating polyneuropathy).
- SME status with the EMA: GeNeuro Innovation SAS, a subsidiary of GeNeuro SA, has obtained SME status from the EMA (EMA SME number: EMA/SME/080/10/R3).
- Approval by the EMA of the Pediatric Investigation Plan for temelimab in MS in 2017
- Orphan Drug Designation for temelimab for CIDP by the FDA in 2018.

To support the experienced team at GeNeuro, the Company has been working for years with external regulatory service groups and experts, such as NDA Regulatory Services Europe (one of Europe's leading regulatory drug development), pharmacovigilance, and HTA consultancy groups, which support the Company in the CMC part of development as well as in the pediatric investigational plan for the Company's lead product.

Advyzom (Berkeley Heights, New Jersey) is supporting GeNeuro in the IND filing in the United States. Among GeNeuro's regulatory experts are:

163 Sources: Curtin F, Lang AB, Perron H, Laumonier M, Vidal V, Porchet HC, Hartung HP. "Temelimab, a Humanized Monoclonal Antibody Against the Envelope Protein of Multiple Sclerosis-Associated Endogenous Retrovirus: A First-in-Humans Randomized Clinical Study". Clin Ther 2012, 34:2268-78.
Derfuss T, Curtin F, Guebelin C, Bridel C, Rasenack M, Matthey A, Du Pasquier R, Schluep M, Desmeules J, Lang AB, Perron H, Faucard R, Porchet H, Hartung HP, Kappos L, Lalive PH. "A phase IIa randomized clinical study testing Temelimab, a humanized monoclonal antibody against the envelope protein of multiple sclerosis associated endogenous retrovirus in multiple sclerosis patients — a twelve month follow-up". J Neuroimmunol. 2015 Aug. 15; 285:68-70.
Derfuss T, Curtin F, Guebelin C, Bridel C, Rasenack M, Matthey A, Du Pasquier R, Schluep M, Desmeules J, Lang AB, Perron H, Faucard R, Porchet H, Hartung HP, Kappos L, Lalive PH. "A phase IIa randomised clinical study of Temelimab, a humanised monoclonal antibody against the envelope protein of multiple sclerosis-associated endogenous retrovirus in multiple sclerosis patients". Mult Scler. 2015 Jun; 21(7):885-93.
Curtin F, Vidal V, Bernard C, Lang AB, Porchet H. "Serum and Cerebrospinal Fluid Pharmacokinetics of the new IgG4 Monoclonal Antibody Temelimab to treat multiple sclerosis: a Phase I Study". MAbs. 2016 Jul; 8(5): 854–860.

- Paul Chamberlain, who has acted as an expert for the preclinical package and CMC development of biopharmaceutical products. He serves on the Advisory Board of NDA Regulatory Science, where he collaborates with former senior CMPH European regulators; and
- Jennifer Sims, who is an expert in the preclinical safety toxicology of therapeutic proteins. She has vast experience in preclinical drug development from both the regulatory (UK MHRA, as UK delegate to the CMPH Safety Working Party) and industry perspectives, with an emphasis on biotechnology products. She is Past Vice Chair of the BioSafe leadership group and was EFPIA topic leader and Rapporteur for ICH S6 revision.

5.10 Material Events having an Impact on the Information set forth in Sections 5.1 to 5.3

None.

5.11 Degree of the Company's Dependence on Patents, Licenses, Manufacturing and Commercial or Financial Agreements or new Manufacturing Processes

For a description of the risk factors relating to manufacturing agreements with CROs and CMOs, and patent licenses with bioMérieux and INSERM, please see Section 3.4, "Risks Related To The Company's Dependency on Third Parties Risks" and Section 3.5, "Risks Relating To The Company's Intellectual Property Rights of this Universal Registration Document.

5.12 Factual Basis for any Statement by the Company about its Competitive Position

Except for estimates made by the Group as of the date of this Universal Registration Document, the facts on which statements about the Group's competitive position are derived come principally from the following sources:

- Atlas Multiple Sclerosis 2013; UK Multiple Sclerosis Trust; US National MS Society
- Sorensen S. "New Management Algorithms in Multiple Sclerosis", Current Opinion Neurology 2014
- www.clinicaltrials.gov
- Scientific publications about clinical trial results
- Annual reports of companies active in the field; and
- BioMed tracker.

5.13 Investments

5.13.1 Historical Investments

Investments in tangible fixed assets have historically been limited to specific laboratory equipment as well as information technology equipment. The first-time application of IFRS 16 as of January 1, 2019 using the modified retrospective approach resulted in a € 913 thousand increase in the Company's financial liabilities and an increase in property, plant and equipment for the same amount Intangible property investments include the cost of exclusive licenses to bioMérieux patents in 2006 and the 2016 milestone payment, the cost of the exclusive license to NIH for the jointly owned patent in 2018 as well as the acquisition costs of various software programs. Please see Notes 3 and 4 to the consolidated financial statements for the year ended 31 December 2019 set forth in CHAPTER 18 of this Universal Registration Document.

5.13.2 Pending Investments

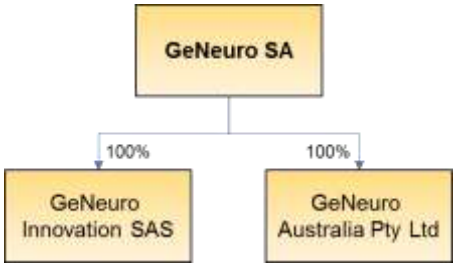
None.

5.13.3 Future Investments

The Group does not expect at this stage to have to undertake investments over €250 thousand, to keep its computer equipment and its laboratories in line with its growth and development.

CHAPTER 6.
ORGANIZATION CHART

6.1 Organization



6.2 Subsidiaries And Equity Stakes

The Company has :

- a 100%-owned subsidiary (shares and voting rights) in France, based in Lyon.

  GeNeuro Innovation, organized in December 2009 and registered in 2010, is a French société par actions simplifiée (simplified stock company) with its registered office at 60 avenue Rockefeller (69008) in Lyon, France. The purpose of GeNeuro Innovation is research and development, especially involving experiments on models and products used, in particular, for therapeutic purposes in the healthcare field as well as providing services in connection with its research and development.

- a 100%-owned subsidiary (shares and voting rights) based in Sydney, Australia.

  GeNeuro Australia Pty Ltd, established in November 2016 and active since January 2017, is a “proprietary company”, i.e. a company with fewer than 50 shareholders. The purpose of GeNeuro Australia Pty Ltd is unlimited but the company was established to conduct the T1D clinical trial in Australia. Due to the absence of planned activities in Australia in the foreseeable future, the Company has decided to liquidate this subsidiary, which is expected to be completed in Q2 2021. No significant costs are expected to be generated by this liquidation.

6.3 Restructurings

Due to the absence of planned activities in Australia in the foreseeable future, the Company has decided to liquidate its subsidiary GeNeuro Australia, which is expected to be completed in Q2 2021. No significant costs are expected to be generated by this liquidation.

CHAPTER 7.
ANALYSIS OF FINANCIAL CONDITION AND RESULTS

Readers are urged to read the following information and comments relating to the financial condition and results of the Company and of its subsidiary together with this entire Universal Registration Document and especially the Group's consolidated financial statements and the notes thereto prepared in accordance with IFRS for the years ended December 31, 2019 and 2020, reproduced with the notes thereto in CHAPTER 18 of this Universal Registration Document.

The discussion of the financial statements set forth in this CHAPTER 7, "Analysis of Financial Condition and Results" and CHAPTER 8, "Cash and Equity" of this Universal Registration Document has been prepared solely on the basis of the consolidated financial statements prepared in accordance with IFRS, as issued by the IASB, included in CHAPTER 18, "Information Regarding the Company's Assets, Financial Situation and Results" of this Universal Registration Document.

7.1 Financial Condition

7.1.1 General Discussion

GeNeuro is a clinical-stage biopharmaceutical company focused on the development of novel treatments of Human Endogenous Retroviruses (or HERV)-mediated diseases, including diseases or disorders of the central nervous system and other diseases induced by HERVs. Since its formation, GeNeuro has devoted its resources primarily to the development of novel treatments for multiple sclerosis (MS). GeNeuro's most advanced candidate, temelimab, is a humanized monoclonal antibody that neutralizes a HERV protein called pHERV-W Env which has been identified as a potential key factor fueling the inflammatory and neurodegenerative components of MS. The Company believes that temelimab is the first treatment against a suspected causal factor of MS and, as such, temelimab has the potential to offer a safe and effective treatment that does not affect the patient's immune system, and which could slow or even stop disease progression in all major forms of MS.

The Company was formed on February 6, 2006 and, in 2009, formed a French subsidiary, GeNeuro Innovation, to pursue research, then in 2016 formed an Australian subsidiary, GeNeuro Australia Pty Ltd, to conduct a clinical trial in that country starting in 2017. Following completion of trial activities in Australia, this latter subsidiary will be liquidated during 2021.

At this stage, research and development has absorbed the majority of the resources of the Group, which has devoted approximately 62% of its financial resources in 2019, and 59% in 2020, to research and development. Research, development, and pre-clinical studies led the Company, in November 2014, to sign the Collaboration Agreement with Servier regarding the treatment of multiple sclerosis (please see Chapter 20, "Material Agreements" of the Universal Registration Document).

Since its formation, the Group has been financed primarily by successive capital increases, including the €33 million capital increase completed in 2016 in connection with the Company's initial public offering (IPO) on Euronext's regulated market in Paris, and the €17.5 million capital increase completed in January 2020 through a private placement. The Group has also received limited research subsidies, particularly from Bpifrance and the European Union in connection with the Psych-Aid program, as well as research tax credits for work conducted by its French and Australian subsidiaries.

Since the Group is active only in research and development, its operations during the various periods discussed are organized under a single segment, "Research and Development of Pharmaceutical Products."

7.1.2 Principal Factors Having an Impact on the Group's Business and Profit (Loss)

In light of the Group's stage of development, historical results principally reflect the research and development expenses of its product, temelimab.

The principal factors having an impact on the Group's business and operations, financial condition, profit and loss, growth and development, and prospects are:

- the scale of the Group's research and development programs, adherence to their development schedule, and opportunities for developing new indications;
- the generation of new pre-clinical and clinical data making it possible to confirm the therapeutic potential of treatments based on the neutralization of HERVs;
- the ability of the Group to finance its operations, including by equity increases and research subsidies.

7.1.3 Summary of Key Accounting Principles and Methods

The Group's financial statements for the financial years ended December 31, 2019 and 2020, which are reproduced with the notes thereto in CHAPTER 18, "Information Regarding the Company's Assets, Financial Situation and Results" of this Universal Registration Document, have been prepared in accordance with IFRS, as issued by the IASB. Such financial statements have been prepared in accordance with historical cost convention, except for certain financial instruments which are measured at fair value and the plan assets included in the calculation of the defined benefit pension plan liability, which are also measured at fair value.

In connection with the preparation of the Group's financial statements in accordance with IFRS, the Company has exercised judgments and made estimates that could influence the amounts presented in respect of assets and liabilities on the date of preparation of the financial statements and of revenue and expense for the period. Such estimates have been made by the Company on a going concern basis in accordance with information available at the time when such judgments and estimates were made. Such estimates are continuously evaluated and are based on past experience as well as various other factors that have been deemed reasonable and that constitute the basis for analyzing the book value of assets and liabilities. These estimates may be revised, if the circumstances on the basis of which they were made change, or if new information becomes available. The Company's actual results of operations may differ significantly from such estimates, if the assumptions or conditions should change.

The Company believes that the most significant estimates or judgments involved in the preparation of the financial statements are described below. For a more detailed description of the accounting principles and methods applied by the Group, please see Note 2 of the consolidated financial statements included in CHAPTER 18 of this Universal Registration Document.

Recognition of Revenue from Collaborative Agreements

There were no revenues from Collaborative Agreements recognized in 2019 or 2020.

When applicable, the Company recognizes income from license fees, the provision of R&D services and management fees on the arrangement of R&D services. Income is recognized when control of the goods or services passes to the customer. For the provision of a license, this is dependent on whether the license conveys a right of use or right of access to the underlying intellectual property. The R&D services are recognized over time as the Company performs the clinical trials and the customer benefits from those services. The Company identifies the performance obligations in each contract with a customer. A performance obligation is a promise to deliver goods and services that is distinct from other promises in the contract.

Where a contract contains more than one performance obligation, the Company allocates the transaction price based on the stand-alone selling price of each separate performance obligation. The Company receives upfront payments and variable consideration in the form of milestones. The Company uses the most likely method to estimate variable consideration and includes such consideration in the transaction price and income if it is not highly probable of reversal.

Income from licenses that convey a right to use intellectual property is recognized when the customer is able to use that intellectual property. R&D services are recognized over the clinical study period based on an input method. This method is calculated by the clinical trial costs incurred over the estimated costs to complete the study.
The Company provides management services, where it arranges clinical trials with an external provider on behalf of a customer. In these arrangements, the Company is acting as agent and recognizes the management fee as income as the management services are delivered.

Revenues generated by collaboration agreements are recognized under "Income".

Intangible Assets

Research and development expenses
Research and development costs are recognized as expenses when they are incurred. Costs incurred on development projects are recognized as intangible assets when the following criteria are fulfilled:

- it is technically feasible to complete the intangible asset so that it will be available for use or sale;
- management intends to complete the intangible asset and use it or sell it;
- there is an ability to use or sell the intangible asset;
- it can be demonstrated how the intangible asset will generate probable future economic benefits;
- adequate technical, financial, and other resources necessary to complete the development and to use or sell the intangible asset are available; and
- the expenditure attributable to the intangible asset during its development can be reliably measured.

In the opinion of management, due to uncertainties inherent in the development of the Group's products, the criteria for development costs to be recognized as an asset, as prescribed by IAS 38, "Intangible Assets," are not met.
As a result, internal development expenses incurred (mainly consisting of the cost of pre-clinical experiments, clinical trials, and the production cost of temelimab) are recognized under "research and development expenses" when they are incurred.

Licenses
Licenses acquired by the Company to access intellectual property are recognized under intangible assets. The amortization of such licenses over their useful lives shall start upon marketing approval of the related products (please see Notes 19.3 and 19.4 of the Notes to the Group's consolidated financial statements set forth in CHAPTER 18, "Information Regarding the Company's Assets, Financial Situation and Results" of the Universal Registration Document).

Subsidies and Grants

Grants received from public entities to subsidize certain types of expenditure are recognized when there is reasonable assurance that the entity will comply with the conditions attached to obtaining the grants. They are recognized as a reduction in the related expenditure, in this case research and development ("**R&D**") expenses.

Contributions received from academic institutions are recognized as a reduction in R&D expenses, in a constant proportion to the corresponding expenditure so as to maintain the principle of matching income with related expenses.

Research Tax Credits
The Group receives certain specific project-related research tax credits ("**RTC**") that are granted to companies incorporated in France as an incentive for technical and scientific research. Companies with expenses that meet the eligibility criteria receive a tax credit that (i) can offset against corporate income tax due in the year in which it is granted, as well as in the following three financial years, or, (ii) under certain circumstances, can be paid to the Company.

Until 2019, the Group has also benefited from research tax credits for its activities in Australia for the research of new treatments against Type 1 diabetes linked to endogenous retroviruses. This research tax credit scheme provided a tax credit of 43.5% of admissible research expenses. No Australian research tax credits were recognized in 2020.

The Group considers the research tax credits received from French and Australian tax authorities as government grants as the tax credits are received independently from tax payments of the Group. The Group recognizes these credits in the consolidated statement of financial position within other current receivables given the expected time of collection, and in the consolidated income statement under research and development subsidies. The credits are recognized in the year in which the eligible expenses giving rise to the tax credit are incurred.

Competitiveness and Employment Tax Credit
The Competitiveness and Employment Tax Credit (the "**CETC**") is granted to companies located in France to encourage employment. The amounts of the CETC are accounted for as a reduction of employee expense.

Bpifrance repayable advance
A repayable advance was granted to the Company's subsidiary, GeNeuro Innovation, by Bpifrance in September 2011 to provide financial support to the Group in conducting a clinical trial and developing a diagnostic test for CIDP.

As of December 31, 2019, this advance was recorded as a non-current liability of €190K, whereas at December 31, 2020, it was recorded as current liabilities / non-current liabilities of €49K and €130K, respectively. The repayment schedule is described in Note 10.1 of the Notes to the Group's consolidated financial statements set forth in CHAPTER 18 of the Universal Registration Document.

Evaluation of Purchase Options Granted to Employees, Executives, and Outside Service Providers

The determination of the fair value of payments made to employees, executives, and outside service providers based on shares is based on the Black & Scholes option valuation model which makes assumptions about complex and subjective variables. Such variables include notably the value of the Company's shares, the expected volatility in the share price over the lifetime of the instrument, and the present and future behavior of the holders of those instruments. There is a high, inherent risk of subjectivity when using an option valuation model to measure the fair value of share-based payments in accordance with IFRS 2.

The fair value of the options is thus measured by taking into consideration the following valuation assumptions, which are set forth in Note 9 of the consolidated financial statements:

- the price of the underlying shares is deemed to be equal to the investor's subscription price, or is calculated by reference to internal valuations;
- the risk-free rate is selected by reference to on the average lifetime of the instruments; and
- volatility is estimated by reference to a sample of listed companies in the biotechnology sector, at the date when instruments are granted and over a period equivalent to the lifetime of the option.

The table below sets forth the assumptions used to calculate the fair value of the share purchase options in accordance with IFRS 2 for the financial years ended December 31, 2019 and 2020:

Allocation date	Number of options issued / Shares granted with a restriction period	Exercise price	Market price at time of grant	Exercise period	Vesting period	Volatility	Risk-free rate	Fair value at grant date per option / share
Stock-options 04/2010	123,000	4.00 CHF	N/A	5.5 years		50.5%	1.11%	1.46
Stock-options 04/2013	3,000	4.00 CHF	N/A	5 years		50.3%	0.05%	1.40
Shares granted to Board members 11/2015	45,000	N/A	N/A	N/A		N/A	N/A	27.99
PSOU 06/2016 (1)	606,400	13.00 €	9.28 €	5 years		58.8%	-1.09%	2.29
PSOU 01/2017 (1)	35,000	13.00 €	10.19 €	5 years	3 years	53.6%	-0.86%	2.48
PSOU 02/2017 (1)	15,000	13.00 €	9.29 €	5 years	2 years	53.6%	-0.87%	1.74
PSOU 02/2018 (1)	20,000	13.00 €	6.28 €	5 years	2 years	50.0%	-0.77%	0.14
Stock-options 02/2017 - part 1	42,500	13.00 €	9.67 €	5 years	3 years	53.6%	-0.94%	2.50
Stock-options 02/2017 - part 2	7,500	13.00 €	9.39 €	5 years	3 years	53.6%	-0.94%	2.35
Stock-options 02/2018	22,500	13.00 €	6.20 €	5 years	3 years	50.0%	-0.75%	0.80
Stock-options 09/2018	158,540	2.73 €	3.66 €	10 years	4 years	50.0%	0.00%	1.74
Stock-options 03/2020 - part 1	75,750	3.34 €	3.07 €	10 years	4 years	49.4%	-0.63%	0.73
Stock-options 03/2020 - part 2	75,750	3.34 €	3.07 €	10 years	4 years	45.8%	-0.52%	1.20
Stock-options 12/2020 - part 1	15,000	2.95 €	2.82 €	10 years	4 years	59.6%	-0.78%	0.86
Stock-options 12/2020 - part 2	15,000	2.95 €	2.82 €	10 years	4 years	53.6%	-0.64%	1.32

(1) Reflects the number of PSOUs granted originally; the actual number of stock options granted in February 2019, at the expiry of the PSOU Plan, is 602,335 for the 2016 Plan, 36,400 and 15,000, respectively, for the 2017 Plans and 18,500 for the 2018 Plan.

7.1.4 Presentation of Principal Items of Consolidated Profit and Loss Statement

7.1.4.1 Revenue and Operating Profit and Loss

Given the stage of clinical development of its most advanced product, the Group has not earned any revenue from product sales as of the date hereof.

The Group's research and development activities, given the significant financial resources involved, have generated operating losses and have not generated operating revenue other than that resulting from the execution of partnering and licensing agreements providing for lump-sum payments and royalties.

In December 2015, the Company received a first milestone payment of €17.5 million under the Collaboration Agreement entered into with Servier in November 2014 (please see Chapter 20, "Material Agreements" of the Universal Registration Document), followed by a second milestone payment of €12.0 million in December 2017. These milestone payments were recognized as revenues as follows: €1.8 million during 2015, €5.9 million during 2016; €14.6 million during 2017; and €7.2 million during 2018. The Servier Agreement was terminated in 2018 and no further milestone payments will be received under it. Rebillings made to Servier in connection with the ANGEL-MS study, for which the Company acted as an agent, were accounted for through a reduction of the studies and research costs, representing €7.9 million during 2018 and €1.9 million during 2019, the year in which the ANGEL-MS study was completed; there were no such rebillings in 2020.

7.1.4.2 Research and Development

The Company conducts research and development on therapies associated with the presence of HERVs with a first indication for MS.

During the years under review, the Company has devoted a significant part of its resources to the development of such therapies. Research and development expenses are set forth in Note 14 of the annual financial statements, which are reproduced set forth in CHAPTER 18 of the Universal Registration Document.

In accordance with IAS 38, development expenses may be recorded as intangible assets only if the Company can show that the six criteria (described in Section 7.1.3 of the Universal Registration Document) for recording an asset

have been met. The Company has determined that these criteria are not met at this stage. Accordingly, internal development expenses, consisting principally of expenses for pre-clinical and clinical studies, are recorded as expenses in the line item Research and Development, when incurred.

Principal research and development expenses are:

- the cost of research and conducting pre-clinical and clinical studies on temelimab for MS;
- the cost of developing and manufacturing the monoclonal antibody temelimab in accordance with GMP;
- personnel expenses for members of the research and development team; and
- expenses for protection of intellectual property.

Product candidates at advanced stages of clinical development generally have higher development costs than those in the initial stages of clinical development, principally because of the increase in the size and duration of such clinical trials. The Company expects that its research and development expense will continue to increase inasmuch as it intends to initiate clinical trials for various product candidates while pursuing the later stages of clinical development for temelimab for MS and T1D.

7.1.4.3 General and Administrative Expenses

General and administrative expenses consist principally of:

- compensation for administrative staff;
- the fees of outside advisors; and
- overhead costs for the rental of office space and the general expenses of the management of the Company, including travel expense.

The Company applies a strict policy for incurring expenses, particularly for general and administrative expense, so that it can devote its resources primarily to pre-clinical and clinical development.

7.1.4.4 Financial Income and Expenses

Net financial income and expenses consist essentially of:

- interest on time deposits; and
- currency exchange gains and losses in connection with payments made to foreign service providers in local currencies.

7.2 Comparison Of The Financial Statements For The Two Years Ended December 31, 2019 and 2020

7.2.1 Constitution of Operating Loss and Net Loss

SIMPLIFIED INCOME STATEMENT (in K of EUR)	31 Dec. 2020 Audited 12 months	31 Dec. 2019 Audited 12 months
Income	**-**	**-**
Research and development expenses	**(4,713.1)**	**(6,174.7)**
Subsidies	**556.0**	**912.4**
General and administrative expenses	**(3,302.0)**	**(3,744.1)**
Operating expenses	**(7,459.1)**	**(9,006.4)**
Other income	**-**	**16.2**
Operating loss	**(7,459.1)**	**(8,990.2)**
Net loss	**(8,962.3)**	**(9,460.8)**

7.2.1.1 Revenue

Given that its product is still at an early stage of development, the Company did not earn any revenue from product sales during the financial years ended December 31, 2019 and 2020.

INCOME (in K of EUR)	31 Dec. 2020 Audited 12 months	31 Dec. 2019 Audited 12 months
Income	**-**	**-**
Total Income	**-**	**-**

There was no revenue in 2019 or 2020.

7.2.1.2 Operating Expenses by Function

Research and development expenses

Research and development expenses during the financial years presented were as follows:

RESEARCH AND DEVELOPMENT (in K of EUR)	31 Dec. 2020 Audited 12 months	31 Dec. 2019 Audited 12 months
Studies and research	(1,930.3)	(2,645.4)
Intellectual property	(339.9)	(538.3)
Raw materials and consumables	(28.1)	(36.0)
Rental expenses	(39.7)	(39.8)
Professional fees	(239.4)	(355.0)
Payroll expense	(1,935.1)	(2,261.7)
Amortization and depreciation	(176.4)	(197.7)
Share based payment expense	(37.6)	(60.2)
Other	13.4	(40.6)
Research and Development expenses	**(4,713.1)**	**(6,174.7)**
Research tax credit	553.9	912.4
Other subsidies	2.1	-
Subsidies	**556.0**	**912.4**
Net research and development expense	**(4,157.1)**	**(5,262.3)**

Research and development expenses continued to decrease significantly in 2020 compared to 2019, due to the completion in 2019 of the Company's Phase II clinical trials in MS and T1D and the completion of the Phase 1 high-dose pharmacology study; during 2020, the Company had only one active clinical trial, in MS at the Karolinska Institutet in Stockholm, Sweden, whose launch was delayed by three months until end June 2020 as a result of theCOVID-19 pandemic. Accordingly, costs for studies and research decreased by €0.7 million from 2019, or 27%.

Research & development personnel costs also decreased by €0.3 million, or 15%, in 2020, as a continued reduction in personnel resulting from the slow-down in the research and clinical trial activities. Generally, the Group has continued to devote its research and development efforts primarily to clinical trials of its monoclonal antibodies in the treatment of MS and ALS, as well as, in 2020, in COVID-19 research. Following new patent filings that were made in 2018 and 2019, this cost decreased by €0.2 million in 2020 (please see Chapter 5.8, "Research And Development and Intellectual Property" of the Universal Registration Document).

The Group's significant research and development expenses permit it to benefit from research tax credits in relation to the work carried out. Variations in the amounts of these research tax credits between years result from the nature of the work undertaken, the timing of clinical or pre-clinical studies and the profiles of the personnel assigned to conduct research and development during the relevant periods; the completion of the clinical trials conducted in Australia during 2019 explains why the research tax credits claims reduced to €554 K in 2020.

Professional fees decreased by €126 K in 2020 due to the reduction in research and clinical trial activities, whereas share based payment expense also decreased by €22 K.

General and administrative expenses

General and administrative expenses during the financial years presented were as follows:

GENERAL AND ADMINISTRATIVE EXPENSES (in K of EUR)	31 Dec. 2020 Audited 12 months	31 Dec. 2019 Audited 12 months
Travel and assignments expenses	(102.1)	(381.2)
Office expenses	(39.7)	(47.9)
Rental expenses	(37.4)	(22.6)
Professional fees	(994.0)	(1,255.2)
Payroll expense	(1,755.4)	(1,753.0)
Tax expense	(38.2)	(26.5)
Insurance expense	(25.5)	(29.4)
Postal and telecom expenses	(78.2)	(47.8)
Amortization and depreciation	(158.2)	(157.1)
Share based payment expense	(68.9)	(22.7)

Other	(4.4)	(0.7)
General and administrative expenses	**(3,302.0)**	**(3,744.1)**

In 2020, general and administrative expenses decreased a further 12% from 2019, after a decrease of 20% from 2018, thanks to a continued across the board cost control. Payroll was stable in euros, in spite of the 3.8% weakening of the euro versus the Swiss franc in which the majority of payroll expense is incurred, reflecting stable fixed salaries and lower variable cash bonuses, while the share-based payment item increased by €46 K. Travel expenses decreased markedly, by 73%, due to curtailment of travel and investor-related activities due to the COVID-19 pandemic. Professional fees declined by € 261 K, primarily due to lower investor relations costs.

7.2.1.3 Financial Income (Expenses)

FINANCIAL INCOME (EXPENSES), NET (Amounts in K of EUR)	**31 Dec. 2020** Audited **12 months**	**31 Dec. 2019** Audited **12 months**
Other financial income	3.1	6.0
Interests on shareholder loan	(72.3)	(441.9)
Share-based expense related to capital increase at discount to market	(1,364.4)	-
Other financial expenses	(7.9)	(6.6)
Foreign exchange gains (losses)	(61.7)	(28.1)
Financial income (expenses), net	**(1,503.2)**	**(470.6)**

The Group reimbursed its GNEH shareholder loan in connection with its January 2020 capital increase, which explains the reduction in interest charges. The share-based expense is related to the capital increase completed in January 2020 through a private placement; because the capital increase was not open to all existing shareholders but was restricted to certain selected institutional investors, pursuant to IFRS 2 the discount between the share price prior to the capital increase (€3.18 per share) and the actual issue price (€2.95 per share) is considered a share based payment, resulting in a charge of € 1,364 K within financial expenses, with a corresponding amount added to reserves within shareholders' equity.

The Group's financial income derives essentially from interest earned on its euro and AUD cash balances.

7.2.1.4 Income Tax

INCOME TAX (EXPENSE) / INCOME (Amounts in K of EUR)	**31 Dec. 2020** Audited **12 months**	**31 Dec. 2019** Audited **12 months**
Deferred tax	-	-
Withholding tax	-	-
Income tax (expense) / income	**-**	**-**

Deferred tax assets are recorded when it is probable that the Company will have future taxable earnings against which cumulative tax loss carryforwards may be used. In application of this principle, in light of the Group's earnings prospects, no deferred tax assets were recorded as of December 31, 2019 or 2020.

7.2.1.5 Earnings Per Share

RESULT PER SHARE	**31 Dec. 2020** Audited **12 months**	**31 Dec. 2019** Audited **12 months**
Weighted average number of outstanding shares	19,969.3	14,562.2
Net result for the period (in K of EUR)	(8,962.3)	(9,460.8)
Basic losses per share (EUR/share)	**(0.45)**	**(0.65)**
Diluted losses per share (EUR/share)	**(0.45)**	**(0.65)**

During the 2020 financial year, the Group recorded a decrease of €0.5 million in its net loss, resulting primarily from a decrease in its operating costs offset by the share-based expense of the capital increase of January 2020.
Losses per share were also impacted by the increase in the weighted average number of shares due to the capital increase completed in January 2020.

Excluding the share-base expense, the loss per share in 2020 would have been EUR 0.38 per share.

7.2.2 Analysis of Statement of Financial Position

7.2.2.1 Non-currents Assets

NON-CURRENT ASSETS (in K of EUR)	31 Dec. 2020 Audited	31 Dec. 2019 Audited
Intangible assets	1,148.8	1,155.1
Property, plant and equipment	1,442.0	677.5
Non-current financial assets	257.2	285.5
Total non-current assets	**2,848.0**	**2,118.1**

Intangible assets consist essentially of license rights acquired from bioMérieux in 2006, upon the formation of the Company, and of milestone payments related thereto and due at the time of launching clinical trials.

Property, plant and equipment consist principally of laboratory equipment specific to the Group's research operations and reflects the application of IFRS 16 as of January 1, 2019. The increase in 2020 is attributable to the 5-year extension of the Company's lease for its main office, in Geneva.

Non-current financial assets include the cash reserve related to the liquidity contract (see Note 8 of the financial statements for the year ended 31 December 2020) and security deposits related to the leases of the Company's premises.

7.2.2.2 Current Assets

CURRENT ASSETS (in K of EUR)	31 Dec. 2020 Audited	31 Dec. 2019 Audited
Other current assets	819.9	1,349.8
Cash and cash equivalents	6,842.9	5,931.4
Total current assets	**7,662.8**	**7,281.2**

Other current assets consist essentially of the French and, for 2019, Australian research tax credit and value added tax receivables (€0.9 million and €0.55 million, respectively, in 2019 and 2020).

Cash and cash equivalents consist of excess cash in bank accounts; the increase recorded in 2020 is due to the capital increase completed in January 2020.

7.2.2.3 Equity

EQUITY (in K of EUR)	31 Dec. 2020 Audited	31 Dec. 2019 Audited
Capital	892.3	614.7
Additional paid-in capital	14,702.3	53,648.7
Cumulative translation adjustments	265.8	284.1
Accumulated comprehensive loss	(324.0)	(2,328.0)
Accumulated deficit attributable to owners of the parent	(10,021.9)	(57,428.0)
Equity attributable to owners of the parent	**5,514.5**	**(5,208.5)**
Total Equity	**5,514.5**	**(5,208.5)**

The Company's equity was restored following the €17.5 million capital increase completed in January 2020.

As mentioned in 7.2.1.3, the IFRS 2 share-based expense of € 1,364 K, accounted for within financial expenses, is offset by a corresponding amount added to reserves within shareholders' equity.

The Company's capital as of December 31, 2019 was CHF 732,905.90 (€614,721) and as of December 31, 2020 was CHF 1,029,515.95 (€ 892,300), divided into 20,590,319 fully paid shares each with a nominal value of CHF 0.05.

Net changes in the Group's net equity during the dates presented result principally from the annual losses for the periods under review, reflecting research and development expenses incurred by the Group.

7.2.2.4 Non-current Liabilities

NON-CURRENT LIABILITIES (in K of EUR)	31 Dec. 2020 Audited	31 Dec. 2019 Audited
Employee benefit obligations	1,391.8	3,135.4
Non-current financial liabilities	1,273.4	483.4
Other non-current liabilities	3.4	6.8
Total non-current liabilities	**2,668.6**	**3,625.6**

Obligations to employees include a provision for retirement obligations for GeNeuro's employees located in Switzerland as well as retirement indemnities for employees of its French subsidiary, GeNeuro Innovation (please see CHAPTER 18 of the Universal Registration Document). The reduction of €1.7 million in 2020 is predominantly attributable to staff departures, only partly offset by actuarial changes arising from changes in the financial assumptions, notably the discount rate used, due to the prevailing interest rate environment in Swiss francs.

Non-current financial liabilities consist of a repayable advance by Bpifrance to GeNeuro Innovation in 2011 (please see Section 8.1.3, "Funding Through Repayable Advances and Subsidies" of the Universal Registration Document), and of the long-term portion of the lease liabilities pursuant to IFRS 16; the increase is due to the signing of a new lease for the Company's headquarter premises.

7.2.2.5 Current Liabilities

CURRENT LIABILITIES (in K of EUR)	31 Dec. 2020 Audited	31 Dec. 2019 Audited
Current financial liabilities	293.3	8,025.6
Trade payables	540.4	1,247.1
Other current liabilities	1,494.0	1,709.5
Total current liabilities	**2,327.7**	**10,982.2**

The reduction in current financial liabilities is due to the repayment in January 2020 of the €7.5 million loan from GNEH SAS, one of the Company's main shareholders, by way of set-off with GNEH SAS's subscription to the capital increase completed at that time.

The evolution in trade payables in 2020 reflects the reduced level of the Group's activities during the periods presented.

7.3 Group's Market Risks

GeNeuro strives to implement measures in line with the Company's size to minimize the potentially adverse effects of market risks on its financial performance.

7.3.1 Interest Rate Risk

The Company does not have any significant exposure to interest rate risk. Please see Note 20 of the consolidated financial statements for the year ended 31 December 2020 for additional information.

7.3.2 Foreign Currency Exchange Rate Risk

The Company is exposed to foreign currency exchange rate risk with respect to changes in the exchange rate between the euro and the Swiss franc, and the U.S. dollar. As the Company has completed its clinical trials in Australia and does not presently plan any further activities in that country, it considers it is no longer exposed to a foreign currency exchange risk with the Australian dollar. Please see Section 3.2.6 "Exchange Rate Risk" and Note 20 of the consolidated financial statements for the year ended 31 December 2020.

7.3.3 Key Performance Indicators

The Company has not defined key performance indicators.

CHAPTER 8.
CASH AND EQUITY

Readers are urged to review Notes 6, 7, and 10 of the Notes to the Group's consolidated financial statements prepared in accordance with IFRS for the financial years ended December 31, 2019 and 2020 set forth in CHAPTER 18 of this Universal Registration Document.

8.1 Information About Equity, Liquidity, And Sources Of Funds

As of December 31, 2019 and 2020, the net amount of cash and cash equivalents owned or held by the Group (consisting of excess cash assets) as well as liquid investments (in the form of short-term deposits) was €5.9 million and €6.8 million, respectively.

CASH AND LIQUID INVESTMENTS (in K of EUR)	**31 Dec. 2020** Audited	**31 Dec. 2019** Audited
Cash and cash equivalents	6,842.9	5,931.4
Total cash and liquid investments	**6,842.9**	**5,931.4**

Since its formation, the Group has been financed primarily by successive capital increases. Please see Section 3.2.1, and Note 22 to the Group's consolidated financial statements for the financial years ended December 31, 2019 and 2020 set forth in CHAPTER 18 of this Universal Registration Document for further details of the Company's cash strategy, its financing and funding strategy, and its exposure to risks linked to financial instruments and securities.

The Group has also received research subsidies, particularly from Bpifrance and the European Union in connection with the Psych-Aid program, as well as research tax credits for work conducted by its French and Australian subsidiaries.

8.1.1 Financing by Equity Capital

Until 2015, the Group had raised, by contributions from the founders and successive capital increases, a total of CHF 28.7 million (€23.4 million at the applicable historical exchange rates between 2006 and 2014). Capital increases from 2008 to 2015 have been fully subscribed by the Group's two historical shareholders, Eclosion2 & Cie SCPC and Institut Mérieux. In 2016, in the context of its initial public offering on Euronext's regulated market in Paris, the Group completed a new capital increase of €33 million, increasing the total amount of funds raised from capital increases to €56.4 million.

On February 4, 2020, the Group completed a €17.5 million capital increase through an international private placement open only to certain qualified and institutional investors (the "Offering") at an issue price of €2.95 per share, determined through a book-building process. After deduction of the loan set-off (see below) and issuance expenses and taxes, the net amount raised by the Company was € 9 million.

8.1.2 Debt Financing

At December 31, 2019, the Company had fully drawn down a €7.5 million Credit Facility provided by its shareholder GNEH SAS. This loan was fully repaid by way of set-off through the 2020 capital increase.

8.1.3 Financing by Leases

The first-time application of IFRS 16 as of January 1, 2019 using the modified retrospective approach resulted in a € 913 increase in the Company's financial liabilities and an increase in property, plant and equipment for the same amount (see Note 7 and Note 4, respectively). The weighted average incremental borrowing rate applied by the Company to lease liabilities recognized in the consolidated financial statements as of January 1, 2019 was between 1.5% to 2% for property leases and 5% for the other leases

8.1.4 Funding Through Repayable Advances and Subsidies

Bpifrance Repayable Advance

A repayable advance was made to the Company's subsidiary, GeNeuro Innovation, by Bpifrance on September 16, 2011 to support the Group financially in conducting a clinical trial and for development of a diagnostic test for CIDP.

The following table shows the changes in such repayable advance during the periods discussed.

(in K of EUR)	Bpifrance reimbursable advance
At 31 December 2018	**186.2**
Subsidies	-
Financial expenses	4.2
At 31 December 2019	**190.4**
Reimbursement	(15.0)
Subsidies	(2.1)
Financial expenses	5.7
At 31 December 2020	**179.0**

The repayment schedule is described in Note 10.1 of the Notes to the Group's consolidated financial statements prepared in accordance with IFRS for the year ended 31 December 2020 set forth in CHAPTER 18 of this Universal Registration Document.

8.1.5 Financing by Research Tax Credits

The Company's French and Australian subsidiaries have benefitted from research tax credits ("**RTC**") for their research and development work. The amount of the RTC reported for financial year 2019 was repaid during the first six months of 2020. Payment of the amount of RTC accrued as at December 31, 2020 is expected during the second half of 2020.

8.2 Description Of The Group's Cash Flows

As of December 31, 2020, cash and cash equivalents were €6.8 million, compared to €5.9 million as of December 31, 2019.

Cash flow from operating activities

Cash flows from operating activities were negative in 2020 and 2019, as a result of the still significant expenses of the Company's research and development activities and despite the decrease in general and administrative expenses. These cash outflows from operating activities amounted to -€7.2 million and -€9.9 million for the year ended December 31, 2020 and 2019, respectively. The decrease in cash outflows from operating activities during 2020 was due primarily to:

- the negative change in working capital of €0.45 million in 2020, compared to a negative €1.4 million in 2019; the favorable variation of €0.9 million results primarily from:
  - a negative variation of €1.6 million in other current assets during 2020; and a
  - a €1.0 million negative variation in other current liabilities, primarily due to the repayment of the balance of unused the advances received from Servier to fund the ANGEL-MS clinical trial; offset by
  - a positive variation of €3.4 million in trade payables and related accounts during 2020, resulting primarily from the completion of the clinical trials and payments to related suppliers;
- the share-based expense of €1.5 million, of which €1.4 million is linked to the IFRS 2 accounting of the discount at which the capital increase of January 2020 was completed related to the prior market price;
- the decrease by €0.5 million in the Company's net loss.

Cash flow from investing activities

Cash flows from investing activities were negative by €23 K and by €46 K in 2020 and 2019, respectively.

The Group's operations generally do not require investments in tangible assets given that the Company subcontracts the major part of production to third parties. Acquisitions of tangible assets are not significant and relate essentially to laboratory equipment and office equipment.

Cash flow from financing activities

Cash flow from financing activities was positive by €8.1 million and €6.9 million, respectively, for the year ended December 31, 2020 and 2019, resulting from the capital increase completed in 2020 and repayment, by way of set-off, of the GNEH shareholder loan that was drawn down in 2019.

Cash burn

The Group considers its cash burn to approximate its cash outflow from operating activities, given its low level of capital expenditures and investment in intangible assets. Accordingly, its cash burn for 2020 was €7.2 million, compared to an estimate of €8.0 million communicated in April 2020, and an actual cash burn of €9.9 million for 2019.

As the Company only has one single center clinical trial underway in 2021, it expects its cash burn to further decrease in 2021. Taking into account the Karolinska/ASC clinical trial in Sweden in 2021, the completion of the Company's pre-clinical program in ALS and its COVID-19 program, the Company expects that its current cash will suffice to fund its operations and remaining pre-clinical programs into Q2 2022. The Company continues to be actively engaged in seeking a new partner for temelimab in the MS indication, but will also seek other sources of financing, such as capital increases, debt or non-dilutive funding, such as grants or subsidies, to allow it to continue its program in indications such as MS, ALS and COVID-19.

In addition, the following factors will continue to contribute to the Company's cash burn:

- some of the Company's other products move beyond the stage of pre-clinical development to clinical development;
- the Company is confronted with increased regulatory requirements for manufacturing and trials for its product candidates (including temelimab for MS, which is its only product in an advanced stage of development);
- the Company begins to pay fees in connection with applications for product licenses from regulatory bodies;
- it increases its product portfolio by adding new products for future development;
- it makes milestone payments to third parties (such as bioMérieux) which have already licensed their technologies to it;
- it develops its research and development activities and buys new technologies, products or licenses, as the case may be;
- it develops its business; and
- it finances structural expenses consistent with the growth of its business.

8.3 Borrowing Conditions And Financing Structure

With respect to the year ended December 31, 2020, the Group's financial debts essentially consisted of research subsidies received in the form of repayable advances granted by Bpifrance amounting to €185 K on the date hereof.

(amounts in K of EUR)	**Dec. 31, 2020**			
	Gross amount	**Less than 1 year**	**1 to 5 years**	**More than 5 yrs**
Shareholder loan	-	-	-	-
Reimbursable advances	179.0	49.2	129.8	-
Lease liabilities	1,387.7	244.1	1,143.6	
Total financial liabilities	**1,566.7**	**293.3**	**1,273.4**	**-**
Current financial liabilities	*293.2*			
Non-current financial liabilities	*1,273.4*			
Trade liabilities	**540.4**	**535.5**	**-**	**-**
Other current liabilities	**1,494.0**	**1,494.0**	**-**	**-**

Please see Notes 7 and 12 to the audited consolidated financial statements as at and for the year ended December 31, 2020 reproduced in CHAPTER 18 of this Universal Registration Document, for further details.

8.4 Information About Any Restriction On The Use Of Funds Significantly Influencing, Or Potentially Influencing, The Group's Business, Directly Or Indirectly

None.

8.5 Sources Of Funds Expected For Future Investments

To cover the Company's future needs, the Company listed its shares in Euronext's regulated market in Paris in April 2016 and at the same time completed a capital increase.

At that time, the former Collaboration Agreement with Servier provided for Servier to finance the totality of the costs of the ANGEL-MS extension study. Following Servier's decision to exit the Collaboration Agreement and its full payment of all amounts due to the Company, no future milestone payments are due from Servier.

Since it began operations, the Company has sustained operating losses, except for the 2014 financial year, when the upfront payment from Servier allowed it to generate a positive operating result of €2.2 million. Such losses reflect both the significance of the expenses incurred in research and development and the weakness of the Company's revenues. The Company foresees that such losses will continue over the next few years, at least until the marketing and sale of its products (should that occur), because of the significant investments required for research, development, manufacture, quality control, distribution of its products, pre-clinical and clinical trials, administrative activities, and activities linked to the development of intellectual property, as well as license agreements for new products and for the acquisition of new technologies that may become necessary, as the case may be. The Company may never market or sell any products and, as a result, may never become profitable. Its operating loss has increased from €4.3 million in 2015 to €14.0 million in 2016, before reducing to €5.7 million in 2017 as a result of the €12.0 million milestone payment from Servier, and increasing again to €8.1 million in 2018 ; the operating loss was €7.5 million in 2020 compared to €9.0 million in 2019.

Following Servier's decision not to exercise its option to license temelimab in MS, the Company has recovered all its worldwide rights on its temelimab program and it has initiated partnership discussions for this program. The Company is also planning to seek grants or subsidies to support its development efforts in indications such as ALS, MS and COVID-19 in order to allow it to launch subsequent clinical trials in these indications and will also seek other sources of financing, such as capital increases, debt or non-dilutive funding, such as grants or subsidies, to allow it to continue its program in indications such as MS, ALS and COVID-19.

The Company expects that its operating losses will increase in the near future, particularly when:

- some of its products move beyond the stage of pre-clinical development to clinical development;
- it is confronted with increased regulatory requirements for manufacturing and trials for its product candidates (including temelimab for MS, which is its only product in an advanced stage of development);
- it begins to pay fees in connection with applications for product licenses from regulatory bodies;
- it increases its portfolio of products by adding new products for future development;
- it makes milestone payments to third parties (such as bioMérieux or the NIH) which have already licensed their technologies to it;
- it develops its research and development activities and buys new technologies, products or licenses, as the case may be;
- it develops its business in different parts of the world; and
- it has to finance structural expenses consistent with the growth of its business.

The amount of net losses and the time needed to reach sustained profitability are difficult to estimate and will depend on several factors, including:

- the degree of advancement of the Company's research and development activities, particularly pre-clinical developments and clinical trials;
- the calendar of regulatory procedures in connection with the preparation, review, and protection of patents and intellectual property rights;
- changes in collaboration arrangements made by the Company; and
- other factors, a great number of which are beyond the Company's control.

8.6 Off-Balance Sheet Commitments

Off-balance sheet commitments consist of individual rights to training, commercial leases, and covenants under the license agreement with bioMérieux and the NIH. These off-balance sheet commitments are described in Note 19 to the consolidated financial statements prepared in accordance with IFRS for the year ended 31 December 2020. prepared in accordance with IFRS, set forth in CHAPTER 18 of this Universal Registration Document.

CHAPTER 9.
REGULATORY ENVIRONMENT

Governmental authorities in Europe, the United States and other countries, at the federal, state and local levels extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, post-approval monitoring and reporting, marketing, and the export and import of drug and biological products, or biologics, such as the Company's product candidates. Generally, before a new drug or biologic can be marketed, considerable data demonstrating its quality, safety and efficacy must be obtained, organized into a format specific to each regulatory authority, submitted for review, and approved by the regulatory authority.

9.1 In the United States

9.1.1 U.S. Biological Product Development

In the United States, the FDA regulates biologics under the Federal Food, Drug, and Cosmetic Act (the "**FDCA**"), and the Public Health Service Act, and their implementing regulations. Biologics are also subject to other federal, state, and local statutes and regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local, and foreign statutes and regulations require the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, the approval process, or after approval, may subject an applicant to administrative or legal sanctions. These sanctions could include, among other actions, the FDA's refusal to approve pending applications, the withdrawal of an approval, a clinical hold, untitled or warning letters, product recalls or withdrawals from the market, product seizures, the total or partial suspension of production or distribution injunctions, fines, refusals of government contracts, restitution, disgorgement, or civil or criminal penalties. Any agency or judicial enforcement action could have a material adverse effect on the Company.

The Company's product candidates must be approved by the FDA through the Biologics License Application (the "**BLA**") process before they may be legally marketed in the United States. The process required by the FDA before a biologic may be marketed in the United States generally involves the following:

- the completion of extensive non-clinical (sometimes referred to as "pre-clinical") laboratory tests, pre-clinical animal studies and formulation studies in accordance with applicable regulations, including the FDA's Good Laboratory Practice ("**GLP**") regulations;
- submission to the FDA of an IND, which must become effective before human clinical trials may begin;
- the performance of adequate and well-controlled human clinical trials in accordance with applicable IND and other clinical trial-related regulations (sometimes referred to as good clinical practices ("**GCPs**")), to establish the safety and efficacy of the proposed product candidate for its proposed indication;
- submission of a BLA to the FDA;
- the satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities where the product is produced to assess compliance with the FDA's current good manufacturing practices ("**cGMP**"), requirements to assure that the facilities, methods, and controls are adequate to preserve the product's identity, strength, quality, purity, and potency;
- a potential FDA audit of the pre-clinical and/or clinical trial sites that generated the data in support of the BLA; and
- FDA review and approval of the BLA prior to any commercial marketing or sale of the product in the United States.

The data required to support a BLA are generated in two distinct development stages: pre-clinical and clinical. The pre-clinical development stage generally involves laboratory evaluations of drug chemistry, formulation, and stability, as well as studies to evaluate toxicity in animals, which support subsequent clinical testing. The conduct of the pre-clinical studies must comply with federal regulations, including GLPs. The sponsor must submit the results of the pre-clinical studies, together with manufacturing information, analytical data, any available clinical data or literature, and a proposed clinical protocol to the FDA as part of the IND. An IND is a request for authorization from the FDA to administer an investigational drug product to humans. The central focus of an IND submission is on the general investigational plan and the protocol(s) for human trials. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA raises concerns or questions regarding the proposed clinical trials and places the IND on clinical hold within that 30-day time period. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. The FDA may also impose clinical holds on a product candidate at any time before or during clinical trials due to safety concerns or noncompliance. Accordingly, the Company cannot be sure that submission of an IND will result in the FDA allowing clinical trials to begin, or that, once begun, issues will not arise that could cause the trial to be suspended or terminated.

The clinical stage of development involves the administration of the product candidate to healthy volunteers or patients under the supervision of qualified investigators, generally physicians not employed by or under the trial sponsor's control, in accordance with GCPs, which include the requirement that all research subjects provide their informed consent for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria, and the parameters to be used to monitor subject safety and assess efficacy. Each protocol, and any subsequent amendments to the protocol, must be submitted to the FDA as part of the IND. Further, each clinical trial must be reviewed and approved by an independent institutional review board ("IRB"), at or servicing each institution at which the clinical trial will be conducted. An IRB is charged with protecting the welfare and rights of trial participants and considers such items as whether the risks to individuals participating in the clinical trials are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the informed consent form that must be provided to each clinical trial subject or his or her legal representative, and must monitor the clinical trial until completed.

There are also requirements governing the reporting of ongoing clinical trials and completed clinical trial results to public registries. Sponsors of certain clinical trials of FDA-regulated products, including biologics, are required to register and disclose specified clinical trial information, which is publicly available at www.clinicaltrials.gov. Information related to the product, patient population, phase of investigation, study sites and investigators, and other aspects of the clinical trial is then made public as part of the registration. Sponsors are also obligated to discuss the results of their clinical trials after completion. Disclosure of the results of these trials can be delayed until the new product or new indication being studied has been approved.

Clinical trials are generally conducted in three sequential phases that may overlap, known as Phase I, Phase II and Phase III clinical trials. Phase I clinical trials generally involve a small number of healthy volunteers who are initially exposed to a single dose and then multiple doses of the product candidate. The primary purpose of these clinical trials is to assess the metabolism, pharmacologic action, side effect tolerability, and safety of the product candidate and, if possible, to gain early evidence on effectiveness. Phase II clinical trials typically involve studies in disease-affected patients to determine the dose required to produce the desired benefits. At the same time, safety and further pharmacokinetic and pharmacodynamic information is collected, as well as the identification of possible adverse effects and safety risks and preliminary evaluation of efficacy. Phase III clinical trials generally involve large numbers of patients at multiple sites, in multiple countries (from several hundred to several thousand subjects) and are designed to provide the data necessary to demonstrate the efficacy of the product for its intended use and its safety in use, to establish the overall benefit/risk relationship of the product, and to provide an adequate basis for product approval. Phase III clinical trials may include comparisons with placebo and/or other comparator treatments. The duration of treatment is often extended to mimic the actual use of a product during marketing. Generally, two adequate and well-controlled Phase III clinical trials are required by the FDA for approval of a BLA.

Post-approval trials, sometimes referred to as Phase IV clinical trials, may be conducted after initial marketing approval. These trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication. In certain instances, the FDA may condition approval of a BLA on the sponsor's agreement to conduct additional clinical trials to further assess the biologic's safety and effectiveness after BLA approval.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and written IND safety reports must be submitted to the FDA and the investigators for serious and unexpected suspected adverse reactions, findings from other studies suggesting a significant risk to humans exposed to the drug, and findings from animal or in vitro testing suggesting a significant risk to humans. Phase I, Phase II, and Phase III clinical trials may not be completed successfully within any specified period, if at all. The FDA, the IRB, or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial if the clinical trial is not being conducted in accordance with the IRB's requirements, or if the drug has been associated with unexpected serious harm to patients. Additionally, some clinical trials are overseen by an independent group of qualified experts organized by the clinical trial sponsor, known as a data safety monitoring board. This group provides authorization for whether or not a trial may move forward at designated intervals based on access to certain data from the trial. The company may also suspend or terminate a clinical trial based on evolving business objectives and/or competitive climate. Concurrent with clinical trials, companies usually complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the product candidate as well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, must develop methods for testing the identity, strength, quality, and purity of the final product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life.

9.1.2 BLA and FDA Review Process

Following trial completion, trial data are analyzed to assess safety and efficacy. The results of pre-clinical studies and clinical trials are then submitted to the FDA as part of a BLA, along with proposed labeling for the product and

information about the manufacturing process and facilities that will be used to ensure product quality, the results of analytical testing conducted on the chemistry of the product candidate, and other relevant information. The BLA is a request for approval to market the biologic for one or more specified indications and must contain proof of safety, purity, potency, and efficacy, which is demonstrated by extensive pre-clinical and clinical testing. The application includes both negative or ambiguous results of the pre-clinical and clinical trials as well as positive findings. Data may come from company-sponsored clinical trials intended to test the safety and efficacy of a use of a product, or from a number of alternative sources, including studies initiated by investigators. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety and efficacy of the investigational product to the satisfaction of the FDA. FDA approval of a BLA must be obtained before a biologic may be marketed in the United States.

Under the Prescription Drug User Fee Act (the "**PDUFA**"), as amended, each BLA must be accompanied by a significant user fee, which is adjusted on an annual basis. The PDUFA also imposes an annual product fee for human drugs and an annual establishment fee on facilities used to manufacture prescription drugs. Fee waivers or reductions are available in certain circumstances, including a waiver of the application fee for the first application filed by a small business.

Once a BLA has been accepted for filing, which occurs, if at all, 60 days after the BLA's submission, the FDA's goal is to review BLAs within ten months of the filing date for standard review or six months of the filing date for priority review, if the application is for a product intended for a serious or life-threatening condition and the product, if approved, would provide a significant improvement in safety or effectiveness. The review process is often significantly extended by FDA requests for additional information or clarification.

After the BLA submission is accepted for filing, the FDA reviews the BLA to determine, among other things, whether the proposed product candidate is safe and effective for its intended use, and whether it is being manufactured in accordance with cGMP to ensure and preserve the product candidate's identity, strength, quality, purity, and potency. The FDA may refer applications for novel drug product candidates or drug product candidates which present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation, and a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions. The FDA will likely re-analyze the clinical trial data, which could result in extensive discussions between the FDA and the company during the review process. The review and evaluation of a BLA by the FDA is extensive and time consuming, and may take longer than originally planned to complete, and the company may not receive a timely approval, if at all.

Before approving a BLA, the FDA will conduct a pre-approval inspection of the manufacturing facilities for the new product to determine whether they comply with cGMPs. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. In addition, before approving a BLA, the FDA may also audit data from clinical trials to ensure compliance with GCP requirements. After the FDA evaluates the application, the manufacturing process, and the manufacturing facilities, it may issue an approval letter or a Complete Response Letter. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A Complete Response Letter indicates that the review cycle of the application is complete and the application will not be approved in its present form. A Complete Response Letter usually describes all the specific deficiencies in the BLA identified by the FDA. The Complete Response Letter may require additional clinical data and/or an additional pivotal Phase III clinical trial(s), and/or other significant and time-consuming requirements related to clinical trials, pre-clinical studies, or manufacturing. If a Complete Response Letter is issued, the applicant may either resubmit the BLA, addressing all the deficiencies identified in the letter, or withdraw the application. Even if such data and information are submitted, the FDA may ultimately decide that the BLA does not satisfy the criteria for approval. Data obtained from clinical trials is not always conclusive and the FDA may interpret data differently from the way the Company interprets the same data.

There can be no assurance that the FDA will ultimately approve a product for marketing in the United States, and the Company may encounter significant difficulties or costs during the review process. If a product receives marketing approval, the approval may be significantly limited to specific populations, severities of allergies, and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the product. Further, the FDA may require that certain contraindications, warnings, or precautions be included in the product labeling or may condition the approval of the BLA on other changes to the proposed labeling, the development of adequate controls and specifications, or a commitment to conduct post-market testing or clinical trials and surveillance to monitor the effects of approved products. For example, the FDA may require Phase IV testing, which involves clinical trials designed to assess the product's safety and effectiveness further and may require testing and surveillance programs to monitor the safety of approved products that have been commercialized. The FDA may also place other conditions on approvals, including the requirement for a Risk Evaluation and Mitigation Strategy ("**REMS**"), to ensure the safe use of the product. If the FDA concludes a REMS is needed, the sponsor of the BLA must submit a proposed REMS. The FDA will not approve the BLA without an approved REMS, if required. A REMS could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries, and other risk minimization tools. Any

of these limitations on approval or marketing could restrict the commercial promotion, distribution, prescription, or dispensing of products. Product approvals may be withdrawn for noncompliance with regulatory standards or if problems occur following initial marketing.

9.1.3 Orphan Drug Designation

The FDA may grant an orphan drug designation to drugs intended to treat a rare disease or condition that affects fewer than 200,000 individuals in the United States, or if it affects more than 200,000 individuals in the United States, there is no reasonable expectation that the cost of developing and marketing the drug for this type of disease or condition will be recovered from sales in the United States. Orphan product designation must be requested before submitting a BLA. After the FDA grants orphan product status, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan product designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

In the United States, orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages, and user-fee waivers. In addition, if a product receives the first FDA approval for the indication for which it has orphan designation, the product is entitled to orphan drug exclusivity, which means the FDA may not approve any other application to market the same drug for the same indication for a period of seven years, except in limited circumstances, such as a showing of clinical superiority over the product with orphan exclusivity or where the manufacturer with orphan exclusivity is unable to assure sufficient quantities of the approved orphan-designated product. Competitors, however, may receive approval for different products, the indication for which the orphan product has exclusivity or obtain approval for the same product but for a different indication for which the orphan product has exclusivity. Orphan product exclusivity also could block the approval of one of the Company's products for seven years, if a competitor obtains approval of the same biological product as defined by the FDA. If a drug or biological product designated as an orphan product receives marketing approval for an indication broader than that so designated, it may not be entitled to orphan product exclusivity.

9.1.4 Expedited Development and Review Programs

The FDA has a Fast-Track program that is intended to expedite or facilitate the process for reviewing new drugs and biological products that meet certain criteria. Specifically, new drugs and biological products are eligible for fast-track designation if they are intended to treat a serious or life-threatening condition and non-clinical or clinical data demonstrate the potential for addressing an unmet medical need. Fast-Track designation applies to the combination of the product and the specific indication for which it is being studied. The sponsor of a new drug or biologic may request the FDA to designate the drug or biologic as a Fast-Track product concurrently with the submission of an IND or at any time before a pre-BLA meeting, and the FDA must determine if the product qualifies for Fast-Track designation within 60 days of receipt of the sponsor's request. Unique to a fast-track product, the FDA may consider for review sections of the marketing application on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the application, the FDA agrees to accept sections of the application and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the application.

Any product submitted to the FDA for marketing, including under a Fast-Track program, may be eligible for other types of FDA programs intended to expedite development and review, such as priority review and accelerated approval. Any product is eligible for priority review, or review within a six-month time-frame from the date a complete BLA is accepted for filing, if it treats a serious condition and has the potential to provide a significant improvement in safety or effectiveness. The FDA will attempt to direct additional resources to the evaluation of an application for a new drug or biological product designated for priority review in an effort to facilitate the review.

Additionally, a product may be eligible for accelerated approval. Drug or biological products studied for their safety and effectiveness in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit over existing treatments may receive accelerated approval, which means that they may be approved on the basis of adequate and well-controlled clinical trials establishing that the product has an effect on a surrogate end point that is reasonably likely to predict a clinical benefit, or on the basis of an effect on a clinical end point other than survival or irreversible morbidity. As a condition of approval, the FDA may require that a sponsor of a drug or biological product receiving accelerated approval perform adequate and well-controlled post-marketing clinical trials.

If the FDA concludes that a drug shown to be effective can be safely used only if distribution or use is restricted, it will require such post-marketing restrictions as it deems necessary to assure the safe use of the drug, or elements to assure safe use ("**ETASU**"), such as:

- distribution being restricted to certain facilities or physicians with special training or experience; or
- distribution being conditioned on the performance of specified medical procedures.

The limitations imposed would be commensurate with the specific safety concerns presented by the product. In addition, the FDA currently requires as a condition for accelerated approval the pre-approval of promotional

materials, which could adversely impact the timing of the commercial launch of the product. Fast-track designation, priority review, and accelerated approval do not change the standards for approval but may expedite the development or approval process.

9.1.5 Breakthrough Designation

The Food and Drug Administration Safety and Innovation Act (the "**FDASIA**") amended the FDCA to require the FDA to expedite the development and review of a Breakthrough Therapy. A product can be designated as a Breakthrough Therapy if it is intended to treat a serious or life-threatening condition and preliminary clinical evidence indicates that it may demonstrate substantial improvement over existing therapies on one or more clinically significant end points. A sponsor may request that a product candidate be designated as a Breakthrough Therapy concurrently with the submission of an IND or any time thereafter, and the FDA must determine if the product candidate qualifies for Breakthrough Therapy designation within 60 days of receipt of the sponsor's request. If so designated, the FDA must act to expedite the development and review of the product's marketing application, including by meeting with the sponsor throughout the product's development, providing timely advice to the sponsor to ensure that the development program to gather pre-clinical and clinical data is as efficient as practicable, involving senior managers and experienced review staff in a cross-disciplinary review, assigning a cross-disciplinary project head for the FDA review team to facilitate an efficient review of the development program and to serve as a scientific liaison between the review team and the sponsor, and taking steps to ensure that the design of the clinical trials is as efficient as practicable.

9.1.6 Pediatric Trials

Under the Pediatric Research Equity Act, a BLA or supplement to a BLA must contain data to assess the safety and efficacy of the product for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDASIA requires that a sponsor who is planning to submit a marketing application for a drug or biological product that includes a new active ingredient, a new indication, a new dosage form, new dosing regimen or a new route of administration submit an initial Pediatric Study Plan ("**PSP**") within 60 days of an end-of-Phase II meeting or as may be agreed between the sponsor and the FDA. The initial PSP must include an outline of the pediatric study or studies that the sponsor plans to conduct, including study objectives and design, age groups, relevant end points, and statistical approach, or a justification for not including such detailed information, and any request for a deferral of pediatric assessments or a full or partial waiver of the requirement to provide data from pediatric studies along with supporting information. The FDA and the sponsor must reach agreement on the PSP. A sponsor can submit amendments to an agreed-upon initial PSP at any time if changes to the pediatric plan need to be considered based on data collected from non-clinical studies, early phase clinical trials, and/or other clinical development programs. The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of data or full or partial waivers.

9.1.7 Post-Marketing Requirements

Following approval of a new product, a manufacturer and the approved product are subject to continuing regulation by the FDA, including, among other things, monitoring and recordkeeping activities, the reporting to the applicable regulatory authorities of adverse experiences with the product, providing the regulatory authorities with updated safety and efficacy information, product sampling and distribution requirements, and complying with promotion and advertising requirements, which include, among others, standards for direct-to-consumer advertising, restrictions on promoting products for uses or in patient populations that are not described in the product's approved labeling (known as "off-label use"), limitations on industry-sponsored scientific and educational activities, and requirements for promotional activities involving the internet. Although physicians may prescribe legally available drugs and biologics for off-label uses, manufacturers may not market or promote such off-label uses. Modifications or enhancements to the product or its labeling or changes of the site of manufacture are often subject to the approval of the FDA and other regulators, which may or may not be received or may result in a lengthy review process. Prescription drug promotional materials must be submitted to the FDA in conjunction with their first use. Any distribution of prescription drug products and pharmaceutical samples must comply with the U.S. Prescription Drug Marketing Act, or the PDMA, a part of the FDCA.

In the United States, once a product is approved, its manufacture is subject to comprehensive and continuing regulation by the FDA. The FDA regulations require that products be manufactured in specific approved facilities and in accordance with cGMP. cGMP regulations require, among other things, quality control and quality assurance as well as the corresponding maintenance of records and documentation, and provide an obligation to investigate and correct any deviations from cGMP. Manufacturers and other entities involved in the manufacture and distribution of approved products are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP and other laws. Accordingly, manufacturers must continue to expend time, money, and effort on production and quality control in order to maintain cGMP compliance. These regulations also impose certain organizational, procedural, and documentation requirements with respect to manufacturing and quality assurance activities. BLA holders using contract manufacturers, laboratories, or packagers are responsible for the

selection and monitoring of qualified firms and, in certain circumstances, qualified suppliers to these firms. These firms and, where applicable, their suppliers are subject to inspections by the FDA at any time, and the discovery of violative conditions, including failure to conform to cGMP, could result in enforcement actions that interrupt the operation of any such facilities or the ability to distribute products manufactured, processed, or tested by them. The discovery of problems with a product after approval may result in restrictions on the product, manufacturer, or holder of an approved BLA, including, among other things, the recall or withdrawal of the product from the market.

The FDA also may require post-approval testing (sometimes referred to as Phase IV testing), risk minimization action plans, and post-marketing surveillance in order to monitor the effects of an approved product or place conditions on an approval that could restrict the distribution or use of the product. The discovery of previously unknown problems with a product or the failure to comply with applicable FDA requirements can have negative consequences, including adverse publicity, judicial or administrative enforcement, warning letters from the FDA, mandated corrective advertising or communications with doctors, and civil or criminal penalties, among others. Newly discovered or developed safety or efficacy data may require changes to a product's approved labeling, including the addition of new warnings and contraindications, and also may require the implementation of other risk management measures. New government requirements, including those resulting from new legislation, may also be established, or the FDA's policies may change, which could delay or prevent the regulatory approval of products under development.

9.1.8 Other Regulatory Matters

Manufacturing, sale, promotion, and other activities following product approval are also subject to regulation by numerous regulatory authorities in addition to the FDA, including the Centers for Medicare & Medicaid Services other divisions of the Department of Health and Human Services, the Drug Enforcement Administration, the Consumer Product Safety Commission, the Federal Trade Commission, the Occupational Safety & Health Administration, the Environmental Protection Agency, and state and local governments. In the United States, sales, marketing, and scientific or educational programs must also comply with state and federal fraud and abuse laws, data privacy and security laws, transparency laws, and pricing and reimbursement requirements in connection with governmental payor programs, among others. The handling of any controlled substances must comply with the U.S. Controlled Substances Act and Controlled Substances Import and Export Act. Products must meet applicable child-resistant packaging requirements under the U.S. Poison Prevention Packaging Act. Manufacturing, sales, promotion, and other activities are also potentially subject to federal and state consumer protection and unfair competition laws.

The distribution of pharmaceutical products is subject to additional requirements and regulations, including extensive record-keeping, licensing, storage, and security requirements intended to prevent the unauthorized sale of pharmaceutical products.

Failure to comply with regulatory requirements can subject firms to possible legal or regulatory action. Depending on the circumstances, failure to meet applicable regulatory requirements can result in criminal prosecution, fines or other penalties, injunctions, the recall or seizure of products, the total or partial suspension of production, the denial or withdrawal of product approvals, or refusal to allow a firm to enter into supply contracts, including government contracts. In addition, even if a firm complies with FDA and other requirements, new information regarding the safety or efficacy of a product could lead the FDA to modify or withdraw product approval. Prohibitions or restrictions on sales or the withdrawal of future products marketed by the Company could materially adversely affect its business.

Changes in regulations, statutes, or the interpretation of existing regulations could impact the Company's business in the future by requiring, for example: (i) changes to its manufacturing arrangements; (ii) additions or modifications to product labeling; (iii) the recall or discontinuance of its products; or (iv) additional record-keeping requirements. If any such changes were to be imposed, they could adversely affect the operation of the Company's business.

9.1.9 U.S. Patent Term Restoration and Marketing Exclusivity

Depending upon the timing, duration, and specifics of the FDA approval of the Company's product candidates, some of its U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984 (also called the Hatch-Waxman Amendments). The Hatch-Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date. The patent term restoration period is generally one-half the time between the effective date of an IND and the submission date of a BLA plus the time between the submission date of a BLA and the approval of that application, except that the review period is reduced by any time during which the applicant failed to exercise due diligence. Only one patent applicable to an approved drug is eligible for the extension, and the application for the extension must be submitted prior to the expiration of the patent. The U.S. PTO, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. In the future, the Company may apply for the restoration of the patent term for its currently

owned or licensed patents to add patent life beyond their current expiration date, depending on the expected length of the clinical trials and other factors involved in the filing of the relevant BLA.

An abbreviated approval pathway for biological products shown to be similar to, or interchangeable with, an FDA-licensed reference biological product was created by the Biologics Price Competition and Innovation Act of 2009 ("**BPCIA**"). Biosimilarity, which requires that the biological product be highly similar to the reference product notwithstanding minor differences in clinically inactive components and that there be no clinically meaningful differences between the product and the reference product in terms of safety, purity, and potency, can be shown through analytical studies, animal studies, and a clinical trial or trials. Interchangeability requires that a biological product be biosimilar to the reference product and the product can be expected to produce the same clinical results as the reference product in any given patient and, for products administered multiple times, the product and the reference product may be alternated or switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biological product. A reference biological product is granted twelve years of exclusivity from the time of first licensure of the product, and the FDA will not accept an application for a biosimilar or interchangeable product based on the reference biological product until four years after the date of first licensure. "First licensure" typically means the initial date the particular product at issue was licensed in the United States. This does not include a supplement for the biological product or a subsequent application by the same sponsor or manufacturer of the biological product (or licensor, predecessor in interest, or other related entity) for a change that results in a new indication, route of administration, dosing schedule, dosage form, delivery system, delivery device, or strength, unless that change is a modification to the structure of the biological product and such modification changes its safety, purity, or potency. Whether a subsequent application, if approved, warrants exclusivity as the "first licensure" of a biological product is determined on a case-by-case basis with data submitted by the sponsor.

Pediatric exclusivity is another type of regulatory market exclusivity in the United States. Pediatric exclusivity, if granted, adds six months to existing exclusivity periods and patent terms. This six-month exclusivity, which runs from the end of other exclusivity protection or patent term, may be granted based on the voluntary completion of a pediatric trial in accordance with an FDA-issued "Written Request" for such a trial.

9.2 In the European Union

9.2.1 European Union Drug Development

In the European Union, the Company's future product candidates may also be subject to extensive regulatory requirements. As in the United States, medicinal products can only be marketed if a marketing authorization from the competent regulatory agencies has been obtained.

As in the United States, the various phases of pre-clinical and clinical research in the European Union are subject to significant regulatory controls. Although the EU Clinical Trials Directive 2001/20/EC has sought to harmonize the EU clinical trials regulatory framework, setting out common rules for the control and authorization of clinical trials in the European Union, the EU Member States have transposed and applied the provisions of the Directive differently. This has led to significant variations in the Member State regimes. To improve the current system, Regulation No. 536/2014 on clinical trials of medicinal product candidates for human use, which repealed Directive 2001/20/EC, was adopted on April 16, 2014 and published in the European Official Journal on May 27, 2014. This Regulation aims at harmonizing and streamlining the clinical trials authorization process, simplifying adverse event reporting procedures, improving the supervision of clinical trials, and increasing their transparency. Although the Regulation entered into force on June 16, 2014, it will not be applicable until six months after the full functionality of the IT portal and database envisaged in the Regulation is confirmed. This is not expected to occur until January 2022. Until then Clinical Trials Directive 2001/20/EC will still apply.

Under the current regime, before a clinical trial can be initiated it must be approved in each of the EU countries in which the trial is to be conducted by two distinct bodies: the National Competent Authority ("**NCA**") and one or more Ethics Committees, ("**ECs**"). Under the current regime all suspected unexpected serious adverse reactions, to the investigated drug that occur during the clinical trial have to be reported to the NCA and ECs of the Member State in which they occurred.

9.2.2 European Union Drug Review and Approval

In the European Economic Area (the "EEA") (which is now comprised of the 27 Member States of the European Union plus Norway, Iceland, Liechtenstein), medicinal products can only be commercialized after obtaining a Marketing Authorization ("**EU MA**"). There are two types of MAs:

- the EU MA, which is issued by the European Commission through the Centralized Procedure, based on the opinion of the Committee for Medicinal Products for Human Use ("**CHMP**"), of the EMA, and which is valid throughout the entire territory of the EEA. The Centralized Procedure is mandatory for certain types of products, such as biotechnology medicinal products, orphan medicinal products, and medicinal products that contain a

new active substance indicated for the treatment of AIDS, cancer, neurodegenerative disorders, diabetes, or autoimmune and viral diseases. The Centralized Procedure is optional for products that contain a new active substance not yet authorized in the EEA, or for products that constitute a significant therapeutic, scientific, or technical innovation or which are in the interest of public health in the European Union; and

- national MAs, which are issued by the competent authorities of the Member States of the EEA and only cover their respective territories, are available for products that do not fall within the mandatory scope of the Centralized Procedure. Where a product has already been authorized for marketing in a Member State of the EEA, this National MA can be recognized in another member state through the Mutual Recognition Procedure. If the product has not received a National MA in any Member State at the time of application, it can be approved simultaneously in various Member States through the Decentralized Procedure. Under the Decentralized Procedure an identical dossier is submitted to the competent authorities of each of the Member States in which the MA is sought, one of which is selected by the applicant as the Reference Member State ("**RMS**"). The competent authority of the RMS prepares a draft assessment report, a draft summary of the product characteristics ("**SmPC**"), and a draft of the labeling and package leaflet, which are sent to the other Member States (referred to as the Concerned Member State (the "**CMSs**") for their approval. If the CMSs raise no objections, based on a potential serious risk to public health, to the assessment, SmPC, labeling, or packaging proposed by the RMS, the product is subsequently granted a national MA in all Member States (i.e., in the RMS and the CMSs).

Under the above-described procedures, before granting the MA, the EMA or the competent authorities of the Member States of the EEA make an assessment of the risk–benefit balance of the product on the basis of scientific criteria concerning its quality, safety, and efficacy.

9.3 Registration procedures outside of Europe and the United States

In addition to regulation in the United States and Europe, a variety of foreign regulations govern clinical trials, commercial sales and distribution of drugs. Pharmaceutical firms who wish to market their medicinal drugs outside the European Union and the United States must submit marketing authorization application to the national authorities of the concerned countries, such as the Pharmaceutical and Medical Device Agency, or PMDA in Japan. The approval process varies from jurisdiction to jurisdiction and the time to approval may be longer or shorter than that required by the FDA or European Commission.

9.4 Reimbursement

Sales of the Company's products will depend, in part, on the extent to which the Company's products, once approved, will be covered and reimbursed by third-party payors, such as government health programs, commercial insurance, and managed healthcare organizations. These third-party payors are increasingly reducing reimbursements for medical products and services. The process for determining whether a third-party payor will provide coverage for a drug product typically is separate from the process for setting the price of a drug product or for establishing the reimbursement rate that a payor will pay for the drug product once coverage is approved. Third-party payors may limit coverage to specific drug products on an approved list (also known as a formulary) which might not include all the approved drugs for a particular indication.

In order to secure coverage and reimbursement for any product candidate that might be approved for sale, the Company may need to conduct expensive pharmaco-economic studies in order to demonstrate the medical necessity and cost-effectiveness of the product candidate, in addition to the costs required to obtain FDA or other comparable regulatory approvals. Whether or not the Company conducts such studies, its product candidates may not be considered medically necessary or cost effective. A third-party payor's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a product does not ensure that other payors will also provide coverage, and adequate reimbursement, for the product. Third-party reimbursement may not be sufficient to enable the Company to maintain price levels high enough to realize an appropriate return on its investment in product development.

The containment of healthcare costs has become a priority of federal and state governments, and the prices of drugs have been a focus in this effort. The U.S. government, state legislatures, and foreign governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement, and requirements for the substitution of generic products. The adoption of price controls and cost-containment measures, and the adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit the Company's net revenue and results. Decreases in third-party reimbursement for the Company's product candidate or a decision by a third-party payor not to cover the Company's product candidate could reduce physician usage of the product candidate and have a material adverse effect on the Company's sales, results of operations, and financial condition.

In addition, in some countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. In Europe, the requirements governing drug pricing vary widely from country to country. Some countries provide that products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost-effectiveness of a particular product candidate to currently

available therapies or so called health technology assessments, in order to obtain reimbursement or pricing approval. For example, the European Union provides options for its Member States to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A Member State may approve a specific price for the medicinal product, or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. Recently, many countries in the European Union have increased the amount of discounts required on pharmaceuticals and these efforts could continue as countries attempt to manage healthcare expenditures, especially in light of the severe fiscal and debt crises experienced by many countries in the European Union. For example, in France, effective access to the market assumes that the Company's future products will be supported by a hospital (through an agreement for local communities) or reimbursed by a healthcare or social security administration and the price of medications is negotiated with the Economic Committee for Health Products.

There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of the Company's product candidates. Historically, products launched in the European Union do not follow price structures of the United States and generally tend to be significantly lower.

The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act (collectively the "**ACA**") enacted in the United States in March 2010, has already had, and is expected to continue to have, a significant impact on the healthcare industry. The ACA has expanded coverage for the uninsured while at the same time containing overall healthcare costs. With regard to pharmaceutical products, among other things, the ACA expanded and increased industry rebates for drugs covered under Medicaid programs and made changes to the coverage requirements under the Medicare Part D program.

Since its enactment there have been judicial and Congressional challenges to certain aspects of the ACA, as well as recent efforts by the Trump administration to repeal or replace certain aspects of the ACA. Since January 2017, President Trump has signed two Executive Orders and other directives designed to delay the implementation of certain provisions of the ACA or otherwise circumvent some of the requirements for health insurance mandated by the ACA. Concurrently, Congress has considered legislation that would repeal or repeal and replace all or part of the ACA. While Congress has not passed comprehensive repeal legislation, it has enacted laws that modify certain provisions of the ACA such as removing penalties, starting January 1, 2019, for not complying with the ACA's individual mandate to carry health insurance, delaying the implementation of certain ACA-mandated fees, and increasing the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D. In July 2018, the Centers for Medicare and Medicaid Services, or CMS, published a final rule permitting further collections and payments to and from certain ACA-qualified health plans and health insurance issuers under the Affordable Care Act risk adjustment program in response to the outcome of federal district court litigation regarding the method CMS uses to determine this risk adjustment. On December 14, 2018, a U.S. District Court Judge in the Northern District of Texas, ruled that the individual mandate is a critical and inseverable feature of the ACA, and therefore, because it was repealed as part of the Tax Cuts and Jobs Act, the remaining provisions of the ACA are invalid as well. While the Texas U.S. District Court Judge, as well as the Trump Administration and CMS, have both stated that the ruling will have no immediate effect, it is unclear how this decision, subsequent appeals, and other efforts to repeal and replace the ACA will impact the ACA.

In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted. On August 2, 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least USD 1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction of several government programs, including aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, begun in April 2013. On January 2, 2013, President Obama signed into law the American Taxpayer Relief Act of 2012 (the "**ATRA**") which delayed for another two months the budget cuts mandated by these sequestration provisions of the Budget Control Act of 2011. The ATRA, among other things, also reduced Medicare payments to several providers, including hospitals, imaging centers, and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. . Recently, there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products. Such scrutiny has resulted in several recent U.S. Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the cost of drugs under Medicare and reform government program reimbursement methodologies for drug products. At the federal level, the Trump administration's budget proposal for fiscal year 2019 contains further drug price control measures that could be enacted during the 2019 budget process or in other future legislation, including, for example, measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid, and to eliminate cost sharing for generic drugs for low-income patients. Additionally, the Trump administration released a "Blueprint" to lower drug prices and reduce out of pocket costs of drugs that contains additional proposals to increase manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products and reduce the out of pocket costs of drug products paid by consumers. Additionally, on January 31, 2019, Office of Inspector General of the U.S. Department of Health and

Human Services proposed modifications to federal Anti-Kickback Statute safe harbors which, among other things, will affect rebates paid by manufacturers to Medicare Part D plans, the purpose of which is to further reduce the cost of drug products to consumers. Although a number of these, and other proposed measures may require additional authorization to become effective, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

On May 30, 2018, the Right to Try Act, was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational new drug products that have completed a Phase I clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a drug manufacturer to make its drug products available to eligible patients as a result of the Right to Try Act.

9.5 Other Healthcare Laws and Compliance Requirements in the United States

Business operations in the United States and arrangements with clinical investigators, healthcare providers, consultants, third-party payors and patients may expose the Company to broadly applicable federal and state fraud and abuse and other healthcare laws. These laws may impact, among other things, the Company's research, proposed sales, marketing, and education programs for the Company's product candidates that obtain marketing approval. The laws that may affect the Company's ability to operate include, among others:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, receiving, offering, or paying remuneration (including any kickback, bribe, or rebate), directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, lease, order, or recommendation of, an item, good, facility, or service reimbursable under a federal healthcare program, such as the Medicare and Medicaid programs. Practices that involve remuneration that may be alleged to be intended to induce prescribing, purchases or recommendations may be subject to scrutiny if they do not qualify for an exception or safe harbor. Several courts have interpreted the statute's intent requirement to mean that if any one purpose of an arrangement involving remuneration is to induce referrals of federal healthcare covered business, the Anti-Kickback Statute has been violated;
- federal, civil and criminal false claims laws and civil monetary penalty laws, which impose penalties and provide for civil whistleblower or qui tam actions against individuals and entities for, among other things, knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other third-party payors that are false or fraudulent, or making a false statement or record material to the payment of a false claim or avoiding, decreasing, or concealing an obligation to pay money to the federal government, including, for example, providing inaccurate billing or coding information to customers or promoting a product off-label;
- the federal Health Insurance Portability and Accountability Act of 1996 ("**HIPAA**") created additional federal criminal statutes that prohibit knowingly and willfully executing or attempting to execute a scheme to defraud any healthcare benefit program, knowingly and willfully falsifying, concealing or covering up a material fact or making false statements relating to healthcare matters, knowingly and willfully embezzling or stealing from a healthcare benefit program, or willfully obstructing a criminal investigation of a healthcare offense;
- the federal Physician Payments Sunshine Act, enacted as part of the ACA, which requires applicable manufacturers of covered drugs, devices, biologics, and medical supplies to track and annually report to the CMS payments and other transfers of value provided to physicians and teaching hospitals and certain ownership and investment interests held by physicians or their immediate family members in applicable manufacturers and group purchasing organizations;
- HIPAA, as amended by the Health Information Technology and Clinical Health Act ("**HITECH**"), and its implementing regulations, which impose certain requirements on covered entities and their business associates relating to the privacy, security, and transmission of individually identifiable health information; and
- state law equivalents of each of the above federal laws, such as state anti-kickback and false claims laws which may apply to items or services reimbursed by any third-party payor, including commercial insurers, state marketing, and/or transparency laws applicable to manufacturers that may be broader in scope than the federal requirements, state laws that require biopharmaceutical companies to comply with the biopharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect as HIPAA, thus complicating compliance efforts.

The ACA broadened the reach of the federal fraud and abuse laws by, among other things, amending the intent requirement of the federal Anti-Kickback Statute and the applicable federal criminal healthcare fraud statutes.

Pursuant to the statutory amendment, a person or entity no longer needs to have actual knowledge of this statute or specific intent to violate it in order to have committed a violation. In addition, the ACA provides that the government may assert that a claim that includes items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil U.S. False Claims Act or the civil monetary penalties statute.

Efforts to ensure that the Company's business arrangements with third parties will comply with applicable healthcare laws will involve substantial costs. It is possible that governmental authorities will conclude that the Company's business practices may not comply with current or future statutes, regulations, or case law involving applicable fraud and abuse or other healthcare laws. If the Company's operations are found to be in violation of any of these laws or any other governmental regulations that may apply to it, the Company may be subject to significant administrative, civil, and/or criminal penalties, damages, fines, disgorgement, individual imprisonment, exclusion from government funded healthcare programs, (such as Medicare and Medicaid), and the curtailment or restructuring of its operations. If the physicians or other healthcare providers or entities with whom or which the Company expects to do business are found to be not in compliance with applicable laws, they may be subject to administrative, civil, and/or criminal sanctions, including exclusions from government-funded healthcare programs.

9.6 Data protection Rules in Europe

European Union Regulation (EU) 2016/679, known as the General Data Protection Regulation (GDPR), which entered into force on 25 May 2018, as well as EU Member States implementing legislations, apply to the collection and processing of personal data, including health-related information, by companies located in the EU, or in certain circumstances, by companies located outside of the EU and processing personal information of individuals located in the EU. These laws impose strict obligations on the ability to process personal data, including health-related information, in particular in relation to their collection, use, disclosure and transfer.

CHAPTER 10.
INFORMATION ON TRENDS

10.1 Recent Changes Since The End Of Financial Year 2020

Completion of recruitment of Karolinska Trial

On February 18, 2021, the Company announced it had completed the patient recruitment in its Phase 2 trial of temelimab in MS patients, conducted at the Karolinska Institutet's Academic Specialist Center (ASC), in Stockholm (Sweden). On March 2, 2021, the Company announced that the independent Drug Safety Monitoring Board has concluded the Phase 2 trial of temelimab in MS patients should continue as planned without modification. Accordingly, GeNeuro now anticipates the results of this trial will be available during Q1 2022. Should the COVID-19 pandemic worsen and prevent the smooth completion of this 40-patient clinical trial by the end of 2021, this could have a material adverse effect on the Company's business, results of operations, financial condition and cash flows.

Cash Position as at March 31, 2021

On April 9, 2021, the Company reported on its unaudited cash and cash equivalent position for the first quarter of 2021 of €4.8 million. The available cash resources provide GeNeuro with solid visibility until Q2 2022 in terms of financing all its planned activities.

The Company indicated that the cash consumption related to GeNeuro's operating and investing activities in Q1 2021 was €2.1 million, compared to €3.3 million for the same period of 2020. The Q1 2021 cash consumption was in line with the Company's expectations and included the payment of outstanding invoices from suppliers and accruals at end December 2020; accordingly, the Q1 2020 cash consumption is not indicative of ongoing cash consumption, which the Company expects to continue decreasing during 2021, to approximately €5.2 million for the full year, compared to €7.2 million in 2020.

COVID-19 project

On January 26, 2021, GeNeuro announced it had received an award from the French national research agency, ANR (Agence Nationale de Recherche), for its COVERI project focused on understanding the role of human endogenous retrovirus (HERV) proteins in the abnormal immune-inflammation or the neurological damages suffered by important subsets of COVID-19 patients.

On April 15, 2021, the Company announced recent research data on the detection of HERV-W ENV in COVID-19 patients and linking its expression to disease severity.

In a publication in the Lancet's EBioMedicine, researchers from the "Tor Vergata" University of Rome, Italy, have shown that the pathogenic envelope protein of the human endogenous retrovirus W (HERV-W ENV) is found on lymphocytes of hospitalized patients with COVID-19, and that its level of expression is associated with disease severity. HERV-W ENV's pro-inflammatory properties are thought to act as an "accelerant" of the activation of the innate immune system, fueling the severity of COVID-19 evolution and impacting long term recovery.

In addition, through the parallel effort supported by the ANR, preliminary data generated by GeNeuro and the CIRI in Lyon (International Center for Research in Infectious Diseases), made available on Research Square, also shows HERV-W ENV expression in lymphocytes following in vitro exposure to SARS-CoV-2 in about 20% of healthy blood donors, suggesting individual susceptibility.

With HERV-W ENV as a possible aggravating agent of COVID-19, GeNeuro's temelimab, an anti-HERV-W ENV monoclonal antibody already in a Phase II clinical trials with an excellent tolerability and safety, could, without any prejudice to its existing programs, start tests against COVID-19 as early as this summer, subject to financing.

10.2 Known Trends, Uncertainties, Requests For Commitment Or Event Reasonably Likely To Influence The Company's Prospects

Given the high costs of Phase III clinical trials in MS, likely to exceed to €100 million, GeNeuro has launched the Karolinska Trial to provide additional data, notably on the optimal dose, to support its partnering discussions. The results of the Karolinska Trial are expected in Q1 2022.

Impact of COVID-19 Pandemic

In the context of the COVID-19 outbreak, which was declared a "pandemic" by the World Health Organization (WHO) on March 12, 2020, the Company has undertaken a full review of the impact of the outbreak on its business and has strictly followed the recommendations issued by the World Health Organization and by local governments in terms of health & hygiene and organizational standards, in order to ensure the health and safety of its staff and their families.

The launch of the Karolinska Trial was initially delayed due to the pandemic to prioritize healthcare resources behind the fight of COVID-19 and to reduce the risk for MS patients. However, on June 25, 2020, GeNeuro announced that thanks to the Karolinska Institutet, the trial had resumed promptly after the situation allowed, with the first patient being included in the study, and on February 18, 2021, the Company announced it had completed the patient recruitment.

COVID-19 therapeutic program

On January 26, 2021, the Company announced it had received an award from the French national research agency, ANR (Agence Nationale de Recherche), for its COVERI project focused on understanding the role of human endogenous retrovirus (HERV) proteins in the abnormal immune-inflammation or the neurological damages suffered by important subsets of COVID-19 patients.

In June 2020, GeNeuro signed a research agreement with the CIRI (International Center for Research in Infectiology), in Lyon, France, a leading research institute against infectious diseases. This research effort concentrates on understanding the viral-host DNA interplay that is known to be able to derepress HERV gene locking mechanisms and produce pathogenic HERV proteins. It is suspected that proteins of the HERV-W family, with known pro-inflammatory and neurodegenerative properties, may be used by SARS-CoV-2 as a Trojan horse, which would bring new light in understanding syndromes associated to COVID-19 as well as a new opportunity to treat some of its worst consequences.

Based on initial results provided to the ANR, GeNeuro was awarded the grant as part of COVID-19 Research Action, which aims to support short-term research work in connection with the pandemic. GeNeuro will receive €137,000 to cover costs in the continuation of the collaborative research project, at and with the CIRI, to analyze a larger number of samples from multicenter cohorts of COVID-19 patients in Europe. With this project, GeNeuro aims to expand the understanding of COVID-19 immunoinflammatory syndromes and neuronal damage to identify how to best tackle the disease through this novel pathway.

On April 15, 2021, the Company announced recent research data on the detection of HERV-W ENV in COVID-19 patients and linking its expression to disease severity.

In a publication in the Lancet's EBioMedicine, researchers from the "Tor Vergata" University of Rome, Italy, have shown that the pathogenic envelope protein of the human endogenous retrovirus W (HERV-W ENV) is found on lymphocytes of hospitalized patients with COVID-19, and that its level of expression is associated with disease severity. HERV-W ENV's pro-inflammatory properties are thought to act as an "accelerant" of the activation of the innate immune system, fueling the severity of COVID-19 evolution and impacting long term recovery.

In addition, through the parallel effort supported by the ANR, preliminary data generated by GeNeuro and the CIRI in Lyon (International Center for Research in Infectious Diseases), made available on Research Square, also shows HERV-W ENV expression in lymphocytes following in vitro exposure to SARS-CoV-2 in about 20% of healthy blood donors, suggesting individual susceptibility.

With HERV-W ENV identified as a possible aggravating agent of COVID-19, GeNeuro's temelimab, an anti-HERV-W ENV monoclonal antibody already in a Phase II clinical trials with an excellent tolerability and safety, could, without any prejudice to its existing programs, start tests against COVID-19 as early as this summer, subject to financing. This would provide a new and complementary approach in the treatment of SARS-CoV-2-infected patients.

Considering the rapidly evolving situation, the Company will update its assessment on a regular basis.

CHAPTER 11.
FORECASTS OR ESTIMATES OF PROFIT OR LOSS

The Company does not plan to make forecasts or estimates of profits and losses.

CHAPTER 12.
ADMINISTRATIVE, MANAGEMENT, SUPERVISORY, AND SENIOR MANAGEMENT BODIES

12.1 Members Of The Administration, Management, And Supervisory Bodies

12.1.1 Board of Directors

12.1.1.1 Membership of the Board of Directors

On the filing date of this Universal Registration Document, the members of the Company's Board of Directors were as follows:

Name	Position	First appointment	Expiration
Jesús Martin-Garcia	Chairman of the Board of Directors	Feb. 6, 2006	General Shareholders' Meeting to consider and act on the financial statements for FY 2020
Hedi Ben Brahim	Independent* Director	May 27, 2020	General Shareholders' Meeting to consider and act on the financial statements for FY 2020
Michel Dubois	Independent* Director	July 16, 2008	General Shareholders' Meeting to consider and act on the financial statements for FY 2020
Giacomo Di Nepi	Independent* Director	July 21, 2015	General Shareholders' Meeting to consider and act on the financial statements for FY 2020
Eric Falcand	Independent* Director	Nov. 19, 2015	General Shareholders' Meeting to consider and act on the financial statements for FY 2020
Gordon S. Francis	Independent* Director	March 17, 2015	General Shareholders' Meeting to consider and act on the financial statements for FY 2020
Christophe Guichard	Independent* Director	Nov. 19, 2015	General Shareholders' Meeting to consider and act on the financial statements for FY 2020

* Independent directors for purposes of the Swiss Code of Good Practices for company governance organized in Switzerland (economiesuisse).

During 2020, one of the former directors, Mr Jean-Jacques Laborde, announced that he would not seek reelection at the 2020 AGM held on May 27, 2020; in his place, GNEH SAS proposed Mr Hedi Ben Brahim as a director and Mr Ben Brahim was duly elected at the AGM. Also, on September 25, 2020, Mr Marc Bonneville announced his resignation from the Board to focus on other professional activities. GNEH SAS, which is an Institut Mérieux subsidiary, has informed the Company that it intended to propose Dr. Philippe Archinard, a director and former CEO of Transgene SA, as a candidate for the Board of Directors at the next shareholders' meeting. There has been no other change in the members of the Company's Board of Directors during 2020 nor is there is any family relationship between any of them.

- Other offices or positions presently held

Companies that are not part of the Group in which members of the Company's Board of Directors have served as a member of the board of directors or a supervisory body, or are general partners of a limited partnership during the last five years are as follows:

Name	Position	Company/Entity
Jesús Martin-Garcia	Managing Director	Eclosion2 & Cie SCPC
	Director	GenKyoTex SA
	Director	DepGen SA

Name	Position	Company/Entity
Hedi Ben Brahim	Chief Executive Officer Chairman of the Board Chairman of the Supervisory Board	Transgene SA ABL Inc. Fab'entech SA
Giacomo Di Nepi	Director Senior Advisor	Zambon SpA, Peptomyc SA NTC Srl, Handicap International KKR Inc.
Michel Dubois	Chairman	GeNeuro Innovation SAS
Eric Falcand	-	-
Gordon S. Francis	-	-
Christophe Guichard	Shareholder and Managing Director Director Managing Director Director Director	Eclosion2 SA Kylane SA KH Medtech SàrL Scientis Pharma APAC Netris Pharma SA

- Offices held during the last five fiscal years and which have terminated as of the date hereof

Companies that are not part of the Group in which members of the Company's Board of Directors served as member of an administration, management, or supervisory body or were partners in a limited partnership during the last five years are as follows:

Name	Office	Company/Entity
Jesús Martin-Garcia	Director	Fondation Eclosion
Hedi Ben Brahim	-	-
Michel Dubois	-	-
Giacomo Di Nepi	CEO Director	Polyphor SA Kuros Biosciences AG
Eric Falcand	-	-
Gordon S. Francis	-	-
Christophe Guichard	Chairman of the Board	Neurix SA

For purposes of Company directorships, the members of the Board of Directors are domiciled at the Company's registered and principal office.

During the last five years, no member of the Company's Board of Directors:

- was convicted of fraud, perjury, or any other official sanction or penalty against him/her/it by governmental or regulatory authorities;
- was involved in an insolvency, bankruptcy, receivership, or liquidation as an executive or officer; or
- has been prevented by a court from acting as a member of an administration, management, or supervisory body or from being involved in the management or conduct of the business and affairs of an issuer.

12.1.1.2 Biographies of Members of the Board of Directors

Jesús Martin-Garcia – Chairman of the Board of Directors and Chief Executive Officer, Swiss national, 57 years old

Jesús began his career in 1983 at the World Economic Foundation, then in 1989 joined McKinsey & Co, where he directed studies in the pharmaceutical and food industries.

Beginning in 1993, he became an entrepreneur by creating, investing in, and managing numerous start-ups in Switzerland and the United States. He was the co-founder of LeShop in 1996, a company that became the e-commerce leader in Switzerland and was sold to Migros. He was also an initial equity investor and participated in the development of other start-ups such as Silverwire and VTX, during more than 10 years.

In 2003, he organized Eclosion, a public–private partnership, to transform potentially disruptive academic discoveries in the area of life science into medications. This original structure was instrumental in the launch of GeNeuro, of which Jesús took the leadership in 2006.

Jesús Martin-Garcia holds a degree in Economics and in Law from the University of Geneva. He also holds an MBA from Harvard Business School. He serves on the boards of biotech companies and industrial and management associations.

Hedi Ben Brahim – Director, French national, 40 years old

Hedi Ben Brahim became Chairman & Chief Executive Officer of Transgene SA on January 1st, 2021. He joined Transgene from Institut Mérieux where he was Vice-President for Immunotherapy since September 2018. He is the Chairman of ABL Inc., a contract research & development, and contract biomanufacturing organization (CRO/CMO) that is a subdiary of Institut Mérieux, and is also Chairman of the Supervisory Board of Fab'entech SA, a privately owned French pharmaceutical company. Prior to joining the Institut Mérieux, he was General Manager at a subsidiary of Vallourec, a solutions provider to the energy sector. Hedi began his career in the public sector at the Ministry of the Economy, Action and Public Accounts, then at the Ministry of Social Affairs and Health. He is a graduate of the École Polytechnique and the École Nationale Supérieure des Mines de Paris.

Giacomo Di Nepi – Director, Italian national, 68 years old

Mr. Giacomo Di Nepi, Director of the Company, has very broad experience in the pharmaceutical industry, having been an executive both in large companies and in successful start-ups.

Mr Di Nepi is currently Senior Advisor to KKR, a leading global investment firm, which he advises on Healthcare investment opportunities and supports existing portfolio companies. He is also a director of Zambon and NTC. He was previously Chief Executive Officer of Polyphor Ltd., a Swiss biotechnology company at the clinical stage which did an IPO on the SIX Swiss Exchange in May 2018. From 2009 to 2015, Mr. Giacomo Di Nepi was Executive Vice President and Chief Executive Officer for Europe at InterMune, until its acquisition by Roche in September 2014, and prior to that was Head of Europe at Takeda.

Mr. Giacomo Di Nepi was also a Partner with McKinsey & Co and a Vice President of Farmindustria in Italy. He was also a member of the Comité des Responsables Européens (Committee of European Managers) of the Fédération européenne des associations et industries (European Federation of Associations and Industries). Mr. Giacomo Di Nepi holds a degree in economics from the University of Bocconi in Milan and an MBA from the Institut européen d'administration des affaires – (European Institute of Business Administration) (INSEAD) in Fontainebleau.

Mr. Di Nepi is the Chair of the Nomination and Remuneration Committee.

Michel Dubois – Director, French national, 77 years old

Michel Dubois spent 25 years with Institut Mérieux, with increasing responsibility until he became the Chief Executive Officer of the Institut Mérieux holding company. He began his career as a consultant with McKinsey & Company and with Arthur Andersen.

Michel Dubois is Chairman of GeNeuro Innovation, the French subsidiary of GeNeuro.

Eric Falcand – Director, French national, 59 years old

Mr. Eric Falcand has been a Director of the Company since November 19, 2015. He holds a degree from the *Ecole Nationale Vétérinaire* (National Veterinary School) of Lyon. He also holds a master's degree in pharmaceutical management from the *Institut de Pharmacie Industrielle* (Institute of Industrial Pharmacy) of Lyon, and an MBA from the Ecole de Management (management school) of Lyon.

He initially worked at Virbac from 1988 to 1991 in marketing and sales before becoming COO for sales at Synthelabo (Sanofi) between 1991 and 1997.

He then joined Laboratoires Servier, first as Managing Director of the subsidiary in Russia, then as CEO of Servier UK, then joining the business development and licensing team in 2008 before becoming Vice President, Global Head of Business Development & Licensing of Servier Monde in 2015.

Gordon S. Francis – Director, Canadian national, 71 years old

Dr. Gordon Francis, Director of the Company, is a recognized neurologist in the field of MS.

Gordon Francis has dedicated most of his career to developing treatments for multiple sclerosis and has played a key part in marketing three important treatments against this condition.

Dr. Gordon Francis served as Vice President and Chief of the Neurological division at Novartis and was in charge of developing and registering Gilenya®, the first oral treatment for MS to be registered in the United States in 2010 and in Europe in 2011. Prior to that, he managed the group responsible for the marketing of Tysabri® with Elan from 2004 to 2006 and, before then, the group responsible for the approval procedure for Rebif® in the United States for Serono in 2002.

He has a degree from the Medical School of Queen's University in Kingston and completed his training in internal medicine and neurology at McGill University. In addition, he undertook post-doctoral research in neuro-immunology at the University of California at San Francisco. He has published more than 100 articles in the field of neurology.

Dr. Gordon Francis also managed the clinic for clinical research on MS at McGill and the clinical research center of the *Institut neurologique* (neurological institute) of Montréal.

Christophe Guichard – Director, French national, 51 years old

Mr. Christophe Guichard is a Director of the Company, and holds a degree from the EDHEC Business School. He also holds a *Diplôme d'Etudes Supérieures Comptables et Financières (*Superior Accounting and Finance studies) and from the Harvard Business School.

He began his professional career with Salustro Reydel (KPMG) between 1994 and 1998 as Audit Manager before joining, in November 1998, the group Trader Classified Media and held various positions in its Finance Department before becoming its CFO in 2006.

In connection with its business, he completed several financing transactions including two IPOs (simultaneously on Euronext and Nasdaq in March 2000 and in 2006 on the London Stock Exchange), several bank financings of senior debt, and acquisitions and sales of assets.

He joined Eclosion in March of 2008 and participates actively in managing the investment fund Eclosion2 & Cie SCPC as a Shareholder and Managing Director as well as several portfolio companies as CFO, including GeNeuro, where he was responsible for financial, legal, and human resource matters until his election to the Company's Board of Directors in November 2015. Mr. Guichard is the Chair of the Audit Committee.

12.1.2 Management

Members of management are appointed by the Board of Directors and are responsible for the management and direction of the Company's business and affairs, subject to the inalienable authority of the Board of Directors (please see Section 19.2.2.1, of this Universal Registration Document) in accordance with the Articles of Association, the internal rules and procedures of management.

Management performs its responsibilities under the supervision of the Board of Directors, assists the Board of Directors in the performance of its responsibilities, and carries out its decisions.

The authority of management and its members is set forth in a Table showing the division of roles and responsibilities approved by the Board of Directors.

The members of the management are registered at the Geneva Commercial Register, and any of them signing together with the Chief Executive Officer or the CFO of the Company have authority to bind the Company.

Management itself determines the procedures applicable to the performance of their responsibilities, in compliance with relevant laws, the Company's Articles of Association and internal rules and procedures.

12.1.2.1 Members of Management

On the filing date of this Universal Registration Document, the members of the Company's management were as follows:

- **Jesús Martin-Garcia**, Chief Executive Officer (CEO)
- **Jean-François Arrighi,** Chief Development Officer (CDO)
- **David Leppert,** Chief Medical Officer (CMO)
- **Miguel Payró**, Chief Financial Officer (CFO)
- **Hervé Perron**, Chief Scientific Officer (CSO)

François Curtin, the Company's former Chief Operating Officer (COO) and acting Chief Medical Officer (CMO), resigned effective April 30, 2020, to pursue an academic appointment at the Swiss Federal Institute of Technology

(ETH) in Zurich; Thomas Rückle, the Company's former Chief Development Officer, resigned effective August 31, 2020, for family reasons in order to return to Germany. There have been no other changes in 2020 or 2021 until the filing date of this Universal Registration Document. There are no family ties or relationships between the members of Management and the Company.

- Other outstanding positions

Companies that are not members of the Group in which members of the Company's management and directors have served as members of an administration, management, or supervisory body or are general partners in a French limited partnership during the last five years are as follows:

Name	Position	Company/Entity
Jean-François Arrighi	-	-
David Leppert	-	-
Miguel Payró	-	-
Hervé Perron	-	-

- Offices held during the last five fiscal years and that have terminated as of the date hereof

Companies not members of the Group in which members of the Company's management have served as a member of an administration, management or supervisory body or have been general partners in a French limited partnership during the last five years are as follows:

Name	Position	Company/Entity
Jean-François Arrighi	-	-
David Leppert	-	-
Miguel Payró	-	-
Hervé Perron	-	-

12.1.2.2 Biographies of Members of Management

Jean-François Arrighi – Chief Development Officer (CDO), French national, 55 years old

Dr. Jean-François Arrighi, PhD, joined GeNeuro as Chief Development Officer on September 1, 2020. Dr. Arrighi has been working in the field of immune-mediated inflammatory diseases for more than 25 years. He studied Biology at the University of Geneva, Switzerland, where he received his PhD in Immunology. He was then Master Assistant at the Department of Dermatology of the University of Geneva before joining Serono International where he led NCE and NBE Discovery Projects for autoimmune and inflammatory diseases and became Global Product Team Leader for early clinical development. After two years as independent consultant to various pharmaceutical companies and biotech startups, he worked on the development of several biosimilars with Merck KGaA and Fresenius Kabi SwissBioSim GmbH as Senior Manager, Nonclinical Pharmacology.

Dr Arrighi has been working in the field of immune-mediated inflammatory diseases for more than 25 years. Over the past 15 years his career has been centered around preclinical and early clinical development and biosimilars development, leading several projects from lead to proof of concept to registration. He is author or co-author of more than 40 scientific publications.

David Leppert– Chief Medical Officer (CMO), Swiss national, 63 years old

Dr. David Leppert joined Geneuro in May 2020 as Chief Medical Officer. David Leppert will steer the development of Geneuro's clinical development strategy and lead execution of its clinical programs. Dr. Leppert is a recognized expert in the worldwide neurology community, having developed pioneering research and worked for over 20 years in clinical development, successfully leading the development of prominent drugs such as ocrelizumab to treat multiple sclerosis while at Roche, and leading the development of all neurology clinical trials while at Novartis. Dr. Leppert is currently Associate professor in Neurology at University of Basel, and will retain his academic appointment.

Dr. David Leppert, who is a board certified neurologist, has a degree from the Medical Faculty of the University of Zürich. He founded the Clinical Neuro-immunology Laboratory at the University Hospital Basel in 1995, and served in parallel as head of the epilepsy outpatient clinic from 1999 to 2004 . He received the 2nd Hoechst-Marion-Roussel prize for MS research (1999), the Ellermann Prize of the Swiss Neurological Society (2001), and the Baasch-Medicus Award (2002) for his research on the role of matrix metalloproteinases and genomics in MS. He began his industry career in 2004 at GlaxoSmithKline in translational medicine and later at in GE Healthcare for diagnostic drug development. Dr Leppert was then Senior Medical Consultant at Novartis and Global Project Medical Director

for the Siponimod MS program, before joining Roche as Global Development Team Leader for the development of ocrelizumab, later becoming Therapeutic Area Head Neuroinflammation. He returned to Novartis in 2015 as Therapeutic Area Head Neuroinflammation, where he was responsible for early and late stage development of MS compounds. Most recently, he was Senior Research Associate at the University of Basel, focusing on research on neurofilaments and other biomarkers of neurological diseases.

Dr Leppert has authored over 100 peer reviewed publications and holds an MD from the University of Zurich, where he also completed his specialty training in neurology. He completed research fellowships in neuroimmunology and neurophysiology at the University of California, San Francisco.

Miguel Payró – Chief Financial Officer, British national, 58 years old

Mr. Miguel Payró has been the Company's Chief Financial Officer since November 2015 and holds a degree from the University of Geneva in Economics and Social Science/Company Management.

Previously, he was Chief Financial Officer of the Swiss Franck Muller watch group, for which he completed a number of mergers and acquisitions and the formation of subsidiaries as well as a restructuring of its shareholders. He was a partner in Value Management Group, a strategic management advisory company, and was responsible for the IPO on the Swiss stock exchange of Unilabs and numerous development projects, including in the field of clinical trials, as well as investor relations. He also worked in the fields of capital markets and acquisition finance for various Swiss banks.

Hervé Perron – Chief Scientific Officer, French national, 62 years old

Dr. Hervé Perron is co-founder and Chief Scientific Officer of the Company.

His research for 15 years at Université Joseph Fourier and INSERM, and his role as research director at bioMérieux led to the discovery of the impact of HERVS on MS. This research served as a basis for the setting up of GeNeuro, which he joined at its formation in 2006.

Hervé is internationally known as a leader in the area of endogenous retroviruses. GeNeuro's research unit, which he directs together with an international network of academic collaborators, is attempting to exploit the enormous potential opened by endogenous retroviruses for understanding and treating serious diseases.

Dr. Hervé Perron holds a doctorate in virology and wrote his doctoral dissertation on neuro-immunology. He is author of more than 120 publications and patents and works as a reference expert for various scientific journals.

12.1.3 Committees of the Board of Directors

The Nominations Committee and the Remuneration Committee consist of:

- Mr. Giacomo Di Nepi, Chairman of the committee;
- Mr. Hedi Ben Brahim, member; and
- Mr. Christophe Guichard, member.

The Audit and Control Committee consists of:

- Mr. Christophe Guichard, Chairman of the committee;
- Mr. Hedi Ben Brahim, member; and
- Mr. Eric Falcand, member.

Following Mr Jean-Jacques Laborde's decision not to seek reelection at the 2020 AGM and the election of Mr Hedi Ben Brahim as a director, Mr Hedi Ben Brahim was elected by the AGM as a member of the Remuneration Committee and was nominated by the Board of Directors as a member of the Nomination Committee and of the Audit and Control Committee.

There has been no other change in the membership of the Nominations, Remuneration and Audit and Control Committees during 2019 or 2020.

For further information about the responsibilities and modus operandi, please see Section 14.3, "Operation of Committees" of this Universal Registration Document.

12.2 Conflicts Of Interest In The Administration, Management, And Supervisory Bodies

Mr. Martin-Garcia, Dr. Arrighi, Mr. Di Nepi, Mr. Dubois, Dr. Francis, Dr. Leppert, Mr. Payró and Dr. Perron are shareholders, directly or indirectly, of the Company and/or owners of securities carrying the right to acquire the Company's shares (please see Section 16.1, "Identification of Shareholders" of this Universal Registration Document).

Furthermore, Messrs. Martin-Garcia and Guichard are also Directors of Eclosion2 SA, a general partner without limited liability of Eclosion2 & Cie SCPC (Société en Commandite - Swiss limited partnership), which is one of the Company's shareholders.

Mr. Hedi Ben Brahim is the Chief Executive Officer of Transgene SA, a French biotechnology company that is 60%-owned by Institut Mérieux and Eric Falcand also holds the position of Director of Business Development & Licensing with Servier. Both Servier and Institut Mérieux are shareholders (in the case of Institut Mérieux through GNEH SAS) of the Company.

Agreements between related parties are described in Section 17.2 of this Universal Registration Document.

To the Company's knowledge and subject to the relationships described above and the personal interests involved in the agreements set forth in Section 17.2 of this Universal Registration Document, there is no present or potential conflict of interest between their responsibility to the Company and the private interests and/or obligations of the persons constituting the management and administration committees of the Company.

The Board of Directors has adopted a set of internal rules and procedures that contain an article relating to conflicts of interest that requires an obligation for a member of the Board of Directors in a conflict of interest situation or in a situation that gives the appearance of a conflict of interest, to inform the Chairman of the Board of Directors thereof. In the event of a conflict of interest, or in the event of an appearance of a conflict of interest (and only at the Chairman's request), the Director may not participate in the discussion or the vote. A person with a conflict of interest may not serve as a member of the Board of Directors.

The agreements or arrangements between the Company and members of the Company's governance bodies or their family or close relations thereof have been made on arm's-length terms and conditions and approved without the involvement of the persons concerned. If necessary, an expert fact-finding may be ordered.

To the Company's knowledge, there is no agreement, arrangement, or contract of any kind between the Company and its shareholders, customers, suppliers, or others pursuant to which any member of management or of the Board of Directors of the Company has been appointed.

CHAPTER 13.
COMPENSATION AND BENEFITS

13.1 Compensation And Benefits Of Any Kind Granted To Executive Officers And Members Of The Administrative, Management, And Supervisory Bodies

As provided in the Swiss ordinance (Decree law) against abusive compensation in publicly traded companies (*sociétés anonymes cotées en bourse*) (as set forth in Section 13.4 of this Universal Registration Document), the Company is required to submit directors' and management's compensation to the approval of its general shareholders' meeting; this approval concerns the maximum global (i.e. collective) fixed and variable compensation of the members of the Board of Directors and of management, respectively. There is no vote on the individual remuneration of each member. The maximum global remuneration is approved ex ante (until the next general shareholders' meeting for the Board of Directors and for the next annual financial years for the members of management). In addition, the Company's Board of Directors is responsible for preparing each year a written compensation report, that must be made available to the shareholders in advance of the general shareholders' meeting in the same manner as the annual financial statements. Pursuant to Swiss law and the Company's articles of incorporation, as amended, the GeNeuro compensation report is submitted to the consultative vote of the general shareholders' meeting; this vote does not affect any global compensation that was approved ex ante by the general shareholders' meeting.

Also as provided in the Swiss ordinance (Decree law) against abusive compensation in publicly traded companies (*sociétés anonymes cotées en bourse*) (as set forth in Section 13.4 of this Universal Registration Document), the Company hereby discloses the overall compensation of members of the Board of Directors and executive management as well as the amount granted to each of the members of the Board of Directors (for more details, see the 2020 Compensation Report presented in section 13.4.3 of this Universal Registration Document) and the amount granted to the highest paid member of management, Mr. Jesús Martin-Garcia in 2020.

The total amount of overall annual compensation for the 2020 financial year paid to members of the Board of Directors was €89 thousand (2019: €109 thousand).

The total amount of overall compensation (including cash compensation, accruals for variable compensation, share-based payments, benefits in kind and social security and pension charges) for 2020 paid (or accrued) to members of management (including the CEO) was €1,913 thousand (2019: €2,035 thousand), including €296 thousand (2019: €314 thousand) of bonus accrual and €164 thousand (2019: nil) of accounting value attributable to stock options granted to members of management. The total amount received by the CEO in 2020 was €716 thousand (2019: €633 thousand), including €133 thousand (2019: €155 thousand) of cash bonus paid in the following year and €87 thousand (2019: nil) of accounting value attributable to the stock options granted to the CEO at an exercise price of €3.34 per share.

13.1.1 Compensation of Any Kind Granted to the Highest-Paid Member of Management

Compensation Table 1: Summary of compensation and stock options granted to the highest-paid member of management

Table summarizing compensation, options, and shares granted to the highest-paid member of management		
Amounts in thousands	2020 financial year	2019 financial year
Jesús MARTIN-GARCIA – CEO (1)		
Compensation in respect of the year *(detailed in Table 2)*	€ 519	€ 528
Valuation of multi-year variable compensation granted during the year	-	-
Valuation of options granted during the year *(detailed in Table 4)*	€ 87	-
Valuation of shares granted without consideration during the year	-	-
Total	€ 606	€ 528

(1) Appointed CEO *(directeur général)* with effect from January 1st, 2016.

Compensation Table 2: Compensation of highest-paid member of management

Table summarizing compensation of the highest-paid member of management				
	2020		**2019**	
Amounts in thousands	Amounts due (1)	Amounts paid (2)	Amounts due (1)	Amounts paid (2)
Jesús MARTIN-GARCIA – CEO (3)				
Base compensation	€ 374 (4)	€ 374 (4)	€ 360	€ 360
Annual variable compensation	€ 133	€ 155 (5)	€ 155	€ 121 (5)
Multi-year variable compensation	-	-	-	-
Exceptional compensation	-	-	-	-
Director's fee	-	-	-	-
Fringe benefits (vehicle)	€ 12	€ 12	€ 13	€ 13
TOTAL	€ 519	€ 541	€ 528	€ 494

(1) For the year.
(2) During the year.
(3) Appointed CEO with effect from January 1st, 2016. Mr MARTIN-GARCIA's variable compensation is defined in connection with the annual performance appraisal with a specific objectives plan (qualitative and quantitative criteria, such as the progress of clinical trials). The bonus is decided by the Board of Directors.
(4) The base compensation is paid in CHF and has remained the same in CHF in 2020 compared to 2019; the increase in the EUR amount is due to the unfavorable evolution of the EUR/CHF exchange rate.
(5) The variable compensation is paid in CHF in the following year.

13.1.2 Compensation and benefits of any kind paid to members of the Board of Directors

The compensation and benefits paid to members of the Board of Directors during the financial years ended December 31, 2019 and December 31, 2020 consist of the following.

Compensation Table 3: Table of directors' fees and other compensation received by members of the Board of Directors

Table of directors' fees and other compensation received by members of the Board of Directors (in thousands of Euros)			
Directors		**Amounts paid in 2020**	**Amounts paid in 2019**
Jesús Martin-Garcia	Director's fees	n.a.	n.a.
	Other compensation	n.a.	n.a.
Christophe Guichard	Director's fees	-	-
	Other compensation	-	-
Michel Dubois	Director's fees	23.8	22.5
	Other compensation	-	-
Eric Falcand	Director's fees	-	-
	Other compensation	-	-
Hedi Ben Brahim	Director's fees	-	-
	Other compensation	-	-
Gordon S. Francis (1)	Director's fees	32.3	31.1
	Other compensation	-	18.4
Giacomo Di Nepi (2)	Director's fees	23.8	22.9
	Other compensation	7.4	9.7

(1) Other compensation relates to compensation paid in shares in 2015 and accounted for over the next 4 years of the vesting period – see also Note 9 to the consolidated financial statements for the year ended 31 December 2020 in Section 18.3.2.
(2) Other compensation for 2019 relates to compensation paid in shares in 2015 and accounted for over the next 4 years of the vesting period – see also Note 9 to the consolidated financial statements for the year ended 31 December 2020 in Section 18.3.218.3.2. Other compensation for 2020 relates to additional consulting services provided. .

13.1.3 Stock Options and Grants of Free Shares

As mentioned in the Compensation Report included in Section 13.4.3, the compensation of the members of the Board of Directors, other than the CEO, Mr. Jesús Martin-Garcia, consists exclusively of a fixed annual monetary compensation per term from one general meeting of shareholders to the next.

Compensation Table 4: Rights convertible into shares of the Company granted by the Group to the CEO during the year ended December 31, 2020

Mr Martin-Garcia received 90,000 stock options during 2020, with an exercise price of €3.34 and a duration of 10 years. No equity incentives were granted to Mr. Jesús Martin-Garcia in 2019.

Compensation Table 5: Rights convertible into shares of the Company exercised by the CEO during the year ended December 31, 2020

None.

Compensation Table 6: Shares granted without consideration to each Board member during the year ended December 31, 2020

None.

Compensation Table 7: Shares granted without consideration becoming available for each Board member during the year ended December 31, 2020

None.

Compensation Table 8: History of grants of rights convertible into shares of the Company

Type of Plan	**Plan 1**	**Plan 2**	**Plan 3 PSOU 2016**[164]	**Plan 4 PSOU 2017**[165]	**Plan 5 Stock Options**[166]	**Plan 6 PSOU 2018** [165]	**Plan 7 Stock Options** [166]	**Plan 8 Stock Options**[167]	**Plan 9 Stock Options**[168]
Date of Board decision	Apr. 16, 2010	Nov. 10, 2015	June 22, 2016	Feb. 23, 2017	Feb. 23, 2017	Feb. 8, 2018	Feb. 8, 2018	July 4, 2018	Mar. 5, 2020 Dec. 11, 2020
Total number of shares to be subscribed for or purchased ***of which by Directors and executive officers*:***	111,000	45,000	602,335 [164]	51,400 [165]	49,000	18,500 [148]	22,500	158,540	181,500
Gordon S. Francis	-	*30,000*	-	-	-	-	-	-	-
Giacomo di Nepi	-	*15,000*	-	-	-	-	-	-	-
Jesús Martin-Garcia	-	-	*242,400*[164]	*15,000*[165]	-	*18,500*[165]	-	-	*90,000*
Point of departure for exercising options	Apr. 16, 2013	Election to the Board	Jan. 1, 2019	Jan. 1, 2019	Feb. 23, 2018	Jan. 1, 2019	Feb. 8, 2019	Feb. 27, 2020	Mar. 5, 2021 Dec. 11, 2021
Expiration date of exercise rights	Apr. 16, 2022	Duration of Board mandate	5 years after option grant	5 years after option grant	5 years after option grant	5 years after option grant	5 years after option grant	10 years after option grant	10 years after option grant
Subscription or purchase price	CHF 4	CHF 0.5	€13	€13	€13	€13	€13	€2.73	€3.34 and €2.95
Terms and conditions of exercise (when the plan has several tranches)	In one time	In one time	-	-	-	-	-	-	-
Cumulative number of exercised subscription and purchase options	5,000	45,000	-	-	-	-	-	-	-
Subscription or purchase options remaining at the end of the year	45,000	-	460,194	15,000 [165]	39,500	18,500 [165]	17,500	110.979	181,500[169]
Parity	1 : 1	1 : 1	1 : 1	1 : 1	1 : 1	1 : 1	1 : 1	1:1	1:1

*: as defined under French law, being the CEO ("*Directeur général*").

[164] Plan 3 was approved in principle by the Board of Directors of November 19, 2015, and the details (participants, number of Performance Share Option Units, or PSOU, assigned, and exercise price) have been established by the Board of Directors on June 22, 2016, date when it decided to grant without consideration 606,400 Performance Share Option Units (PSOUs), which are contingent rights to receive, after a maximum of 3 years and under certain performance conditions, a variable number of options to acquire shares of the Company. The final number of options granted at the expiry of the three-year period was decided by the Board of Directors on February 27, 2019, based on the achievement of personal and social goals. Of the total of 606,400 PSOUs initially awarded, a total of 602'335 stock options were granted.

[165] The Plan 4 PSOU 2017 was approved by the Board of Directors of February 23, 2017. The Plan 6 PSOU 2018 was approved by the Board of Directors of February 8, 2018. PSOUs issued under plans 4 and 6 have the same terms (including exercise price and final maturity) as the Plan 3 PSOUs.

[166] The Plan 5 Stock Options was approved by the Board of Directors of February 23, 2017, and the Plan 7 Stock Options was approved by the Board of Directors on February 8, 2018. Options vest over three years, with one third vesting after one year, then one-sixth vesting every six months thereafter.

[167] The Plan 8 Loyalty Stock Options were approved by the Board on July 4, 2018, with final determination as to the terms and numbers of options granted on February 27, 2019.

[168] The Plan 9 Stock Options were approved by the Board on March 5, 2020, with an additional award to new executives on December 11, 2020.

Compensation Table 9: Options to subscribe for or purchase shares granted during 2020 to the top 10 non-officer*/director employee grantees and options exercised by them

Options to subscribe for or purchase shares granted to the top 10 non-officer/director employee grantees and options exercised by them	Total number of options granted / shares acquired
Number of options granted by the Company and any other company of the Group to the ten non-officer employees of the Company or any company of the Group outstanding on the filing date of this Universal Registration Document	15,000
Total number of shares available for subscription upon exercise of the options on the filing date of this Universal Registration Document	152,140
Subscription price for one share	From EUR 2.73 to EUR 13.00, with a weighted average price of EUR 9.40
Number of options exercised during the last financial year	0

**: as defined under French law, i.e. excluding the CEO ("Directeur général")*

Compensation Table 10: History of grants of free shares

None.

13.1.4 Specifics on Terms and Conditions of Compensation and Other Benefits Granted to Executive Officers

Compensation Table 11: Specifics on terms and conditions of compensation and other benefits granted to executive officers*

Executive officers	**Employment agreement (permanent)**		**Supplemental pension plan**		**Allowances and benefits due or likely to be due upon termination or change of function**		**Indemnities under a non-compete clause**	
	Yes	**No**	**Yes**	**No**	**Yes**	**No**	**Yes**	**No**
Jesús Martin-Garcia – Chairman of the Board of Directors and Chief Executive Officer	X		X (1)			X		X
Beginning date of term of office	January 1, 2016, for Mr Martin-Garcia							
Ending date of term of office	Indefinite							

*: as defined under French law, being the CEO ("*Directeur général*")?

(1): pursuant to the Swiss pension fund system, the Company contributes to an old age retirement and pension plan for its Swiss-based employees consisting of two pillars: the minimum State old age retirement insurance (*Assurance Vieillesse et Survivants*, "**AVS**", the first pillar) and a compulsory company-wide defined benefit scheme ("**LPP**", the second pillar), pursuant to which the Company has made contributions of K€ 69 for the benefit of Mr Martin-Garcia.

13.2 Amounts Provisioned By The Company And Its Subsidiary For Payment Of Pensions, Retirement, Or Other Benefits To Executives

The Company made provisions for for the purpose of paying pensions and retirement benefits to certain Directors and executives under State-mandated compulsory plans; such amounts are calculated on the same basis as for the Group's other employees, which bases are set forth in Note 2.19 of the consolidated financial statements for the year ended 31 December 2020 set forth in CHAPTER 18, "Information Regarding the Company's Assets, Financial Situation and Results" of this Universal Registration Document.

13.3 Loans And Guarantees Granted To Executives

None.

13.4 Legal Framework Relating To Compensation

13.4.1 Swiss Ordinance against Excessive Compensation

The Swiss Ordinance (decree law) against excessive compensation in companies that are publicly traded (*Ordonnance contre les rémunérations abusives*, ORAb or "Ordinance") (Decree law against excessive compensation) took effect on January 1, 2014 and implements a constitutional amendment approved by the Swiss electorate in 2013 following a federal initiative against abusive compensation. The Ordinance's provisions against excessive compensation apply to Swiss corporations that are publicly traded in Switzerland or abroad. The principal provisions of the Ordinance are summarized below.

- **Termination indemnities, premature indemnities, and provisions for the transfer or acquisition of a company**

The Ordinance against excessive compensation prohibits the payment of certain types of indemnities or compensation to members of a board of directors, management, or consultative council of a publicly traded Swiss company, including, among others, termination indemnities, premature indemnities, and provisions for the transfer or acquisition of a company, just as for certain other types of compensation or benefits that may not be expressly contemplated by the articles of association.

The Ordinance against excessive compensation broadly prohibits termination indemnities, regardless of their form, termination notice periods greater than one year, and agreements providing for compensation the maximum time period of which exceeds one year. However, non-competition clauses taking effect after the end of the employment relationship or consulting agreement are not subject to the prohibition against termination indemnities, unless, by their language, they can be considered to be disguised termination indemnities.

The Ordinance against excessive compensation also prohibits or limits certain types of premature indemnities. The determining point making it possible to distinguish prohibited termination indemnities ("golden parachutes") from certain other types of premature indemnities, such as signing bonuses, is the time when payment is made. Accordingly, a signing bonus the purpose of which is to compensate for benefits and other rights that an executive agrees not to receive from his/her preceding employer remain authorized, whereas an advance against salary is not authorized.

The Ordinance against excessive compensation also prohibits compensation for the transfer or acquisition of a company or companies that are controlled by it, directly or indirectly.

- **Approval by the shareholders of compensation for the board of directors, for management, or for advisory board**

The Ordinance against excessive compensation also requires that compensation for the board of directors, for management, or, in the case of Swiss publicly traded companies, for the advisory board, be approved annually by the company's shareholders. Swiss publicly traded companies must state the terms and conditions of voting in their articles of association, while meeting certain minimum conditions:

- the vote must occur annually;
- the vote must be mandatory; and
- the vote must occur separately for the maximum global amounts granted to the Board of Directors, the consultative council (if any), and management, respectively.

The Ordinance allows companies to determine in their Articles of Association whether the compensation is to be approved ex ante or ex post.

The compensation that must be covered by the approved maximum global amounts includes all compensation granted in relation to the position of the recipients of the relevant corporate bodies (Board of Directors, consultative council, if any, and management) for their services to the company. It includes (without limitation) all fees, salaries, bonuses, overtime compensation, credit notes, revenue and profit participation rights, equity and debt securities, as well as the value of option rights for, or conversion rights into such securities. It comprises all types of compensation, whether in cash or in kind through the provision of services or the delivery of any goods, or through any voluntary pension contributions. It further comprises the value of any suretyship, guarantee or security for, or the waiver of, any obligations of the members of the relevant corporate body.

- **Compensation Report**

The Ordinance against excessive compensation requires that the board of directors prepare an annual compensation report that indicates any and all indemnities that a company has paid, directly or indirectly.

In substance, the compensation report must contain any and all compensation, loans, or credit paid during the financial year just ended to members of the board of directors, management, and consultative council as well as to former members of the board, management, and consultative council and to close relatives of present and past members of the board of directors, management, and consultative council.

The compensation report must also indicate compensation, loans, and credit granted to members of the board of directors overall and individually, while compensation, loans, and credit to members of management must only indicate in a general manner the amount granted to the member of management who is the highest paid, mentioning his/her name and position.

- **Articles of Association**

Swiss companies that are publicly traded companies (in Switzerland or elsewhere) must generally ensure that their articles of association and governance rules conform to the Ordinance against excessive compensation.

A Swiss publicly traded company must, at a minimum, include in its articles of association provisions relating to:

- the number of permitted positions occupied by members of the board of directors, management, and advisory board on senior management bodies or on the board of directors of legal entities that are not controlled by the company, or that do not control the company;
- the maximum term and maximum notice period of agreements that provide for compensation of members of the board of directors and management (which may not exceed a year);
- the principles applicable to tasks and abilities of the Remuneration Committee; and
- terms and conditions of votes at general shareholders' meetings on compensation.

- **Election of members of the board of directors, chairman of the board of directors, members of the Remuneration Committee, and of the independent representative**

The Ordinance against excessive compensation requires that members of the board of directors, its chairman, members of the Remuneration Committee (which may be selected only from members of the board of directors) and the independent representative must be elected individually at the general shareholders' meeting for a term ending at the end of the following ordinary general shareholders' meeting. Re-election is possible.

- **Independent Representative**

The Ordinance against excessive compensation prohibits representation of shareholders by a member of the company's governance body or by a custodian.

The provisions of the Ordinance against excessive compensation also state that the board of directors must ensure that shareholders have the right to:

- issue instructions to the independent representative on a proposal mentioned in the notice of meeting and relating to the matters on the agenda;
- issue general instructions to the independent representative on unannounced proposals relating to matters on the agenda; and
- grant authority and instructions to the independent representative also by electronic means.

When the independent representative has not received any instructions, the independent representative may not vote.

- **Criminal provisions**

The criminal provisions of the Ordinance against excessive compensation punishes members of the board of directors, management, and the consultative council who knowingly receive or have been granted illegal compensation. The Ordinance against excessive compensation also provides for criminal liability for certain prohibited actions performed by a member of the board of directors. Intentional violation of the Ordinance against excessive compensation may give rise to a maximum of three years' imprisonment and a fine of up to six times the annual compensation agreed by the perpetrator with the Company at the time of the document.

13.4.2 Adoption of Rules Relating to Compensation

The Company is subject to the Ordinance against excessive compensation since the date of initial admission of the Company's shares on Euronext's regulated market in Paris.

The Articles of Association provide that the members of the Board of Directors receive fixed, or base, compensation (and may also receive variable compensation) and that members of management are to receive fixed, or base, and variable compensation. Variable compensation may be based, among other things, on the individual performance of the individual involved, of the company, of certain business divisions, or on the trading price of the shares.

The Company may make loans to members of management. The loans may not exceed three months' salary. They are to be repayable no later than the end of the employment relationship.

Compensation may be paid by the Company or its subsidiaries for services rendered thereto.

In accordance with the Ordinance against excessive compensation, the Company's Articles of Association provide for an annual vote at a general shareholders' meeting on:

- the maximum global amount of compensation for the members of the Board of Directors until the next ordinary general shareholders' meeting; and
- the maximum global amount of compensation for the members of management for the following annual financial year.

The compensation submitted to the approval of the general shareholders' meeting is the maximum global (i.e. collective) compensation of the members of the Board of Directors and of management, respectively. There is no vote on the individual remuneration of each member. The maximum global remuneration is approved *ex ante* (until the next general shareholders' meeting for the Board of Directors and for the next annual financial years for the members of management).

The Board of Directors, however, may decide to submit the fixed (base) and the variable compensation to two separate votes. In connection therewith, the Board of Directors may further decide to submit the variable compensation, or a part thereof, to a retrospective approval (*ex post*) of the general meeting, which shall be only consultative.

The proposals concerning the compensation of the Board of Directors and the management are submitted to the general shareholders' meeting by the Board of Directors. The general shareholders' meeting has only the competency to approve or reject the proposals made by the Board of Directors. The shareholders are not entitled to make proposals in this respect. In the event of a negative vote on the Board of Directors' proposals, the Board of Directors may immediately submit one or more amendment proposals at the shareholders' meeting until it obtains approval, or organize a new general shareholders' meeting.

In line with the above, the Company's 2020 general shareholders' meeting to be called to approve the 2019 financial year accounts, to be held on May 27, 2020, will be required to vote, pursuant to article 35 of the articles of association, on the Board of Directors' proposals on:

- The maximum global compensation for members of the Board of Directors until the next general shareholders' meeting (i.e. for the period from May 27, 2020, to the 2021 AGM approving the 2020 financial statements); and
- The maximum global compensation for members of the Executive Management for the next financial year (i.e. for the period from January 1, 2021, to December 31, 2021).

In addition, the compensation report for the 2019 financial year will be submitted to a consultative vote (please see the relevant resolutions to be submitted to the shareholders' meeting as described in Chapter 27 of this Universal Registration Document).

If new members of management are appointed after the vote on compensation, and the total amount of compensation already approved at a shareholders' meeting is insufficient to cover the compensation of such new members, their additional compensation not exceeding 40% of the total amount of compensation already approved shall be deemed approved until the next ordinary general shareholders' meeting.

For the purpose of the Ordinance against excessive compensation and the related provisions of the Articles of Association, the members of the Board of Directors are the persons formally elected by the general shareholders' meeting to the Board of Directors. The members of management are the persons to whom the executive management is delegated and who report directly to or are at the next level below the Board of Directors (see Section 12.1.2.1).

As provided in the Articles of Association, contracts providing for the compensation of members of the Board of Directors are limited to a maximum term of the pending term of office, while contracts that provide compensation to members of management, theoretically, are made for an indefinite term with a maximum termination period of one year. Short-term, or definite-term, agreements may also be made, for no more than one year.

In respect of external offices and positions, the Articles of Association provide that members of the Board of Directors may not serve in more than five additional positions in privately held companies, while members of management may not serve in more than one additional office in publicly traded companies and more than five positions in privately held companies.

13.4.3 Compensation Report pursuant to the Swiss Ordinance Against Excessive Compensation in listed joint stock companies of January 1, 2014 ("ORAb")

The Company's Board of Directors is responsible for preparing each year a written compensation report (with the support of the Remuneration Committee, see below Section 14.3.2).

The Board of Directors must make the compensation report available to the shareholders in advance of the general shareholders' meeting in the same manner as the annual financial statements.

The compensation report may be submitted to the consultative vote of the general shareholders' meeting. This vote does not affect any global compensation that was approved ex ante by the general shareholders' meeting (see above Section 13.4.2).

The auditors ensure that this compensation report is in conformity with applicable law and with the ORAb. The auditors prepare a report to the board of directors and to the shareholders' general meeting.

GeNeuro SA

Plan-les-Ouates

Report of the statutory auditor to the General Meeting

on the remuneration report 2020

Report of the statutory auditor

to the General Meeting of GeNeuro SA

Plan-les-Ouates

We have audited the accompanying remuneration report of GeNeuro SA for the year ended 31 December 2020.

Board of Directors' responsibility

The Board of Directors is responsible for the preparation and overall fair presentation of the remuneration report in accordance with Swiss law and the Ordinance against Excessive Compensation in Stock Exchange Listed Companies (Ordinance). The Board of Directors is also responsible for designing the remuneration system and defining individual remuneration packages.

Auditor's responsibility

Our responsibility is to express an opinion on the accompanying remuneration report. We conducted our audit in accordance with Swiss Auditing Standards. Those standards require that we comply with ethical requirements and plan and perform the audit to obtain reasonable assurance about whether the remuneration report complies with Swiss law and articles 14–16 of the Ordinance.

An audit involves performing procedures to obtain audit evidence on the disclosures made in the remuneration report with regard to compensation, loans and credits in accordance with articles 14–16 of the Ordinance. The procedures selected depend on the auditor's judgment, including the assessment of the risks of material misstatements in the remuneration report, whether due to fraud or error. This audit also includes evaluating the reasonableness of the methods applied to value components of remuneration, as well as assessing the overall presentation of the remuneration report.

We believe that the audit evidence we have obtained is sufficient and appropriate to provide a basis for our opinion.

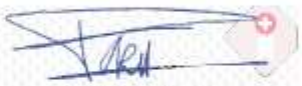
Opinion

In our opinion, the remuneration report of GeNeuro SA for the year ended 31 December 2020 complies with Swiss law and articles 14–16 of the Ordinance.

PricewaterhouseCoopers SA

Michael Foley

Audit expert
Auditor in charge



Florent Rossetto

Genève, 1 April 2021

Enclosure:

- Remuneration report

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2020 REMUNERATION REPORT

1 INTRODUCTION

This Remuneration Report provides the information required by the Swiss Ordinance against excessive compensation in public companies of January 1, 2014 (the "**Compensation Ordinance**"), the Company's Articles of Association (articles 35 and 45) and the Swiss Code of Best Practice for Corporate Governance (status August 28, 2014).

The Compensation Ordinance requires the Company to set out in its Articles of Association the principles for the determination of the compensation of the Board of Directors and the Executive Management. These principles have been included in the Articles which are available on the Company's web site in the French language original under http://www.geneuro.com/data/documents/GeNeuro-SA-statuts-du-27-mai-2020.pdf), together with the organizational rules and policies provided the basis for the principles of compensation.

In addition, we provide information to meet the compensation disclosure requirements under the Swiss Code of Obligations, art. 663 b bis.

2 COMPENSATION POLICY AND GUIDING PRINCIPLES

In light of the Company's resources and of the numerous challenges posed by the COVID-19 pandemic, the key priority for GeNeuro in 2020 was the execution of the Karolinska trial, leading to a reduction in the efforts on other programs. Nevertheless, GeNeuro has continued to make significant progress in 2020. After an initial delay due to the onset of the pandemic, GeNeuro started the trial at the end of June 2020. Whilst patient recruitment was challenging due to the study protocol including the combined administration of a immunosuppressive treatment (rituximab), the additive efforts of the GeNeuro team and the Karolinska/ASC teams allowed recruitment that was completed by mid-February 2021, with an actual delay of only six weeks over the original schedule.

This has been achieved, to a very large extent, thanks to the quality, motivation and commitment of the Geneuro employees and management, which are a key resource to achieve the Company's ambitious goals. In fact, while reducing the overall resources due to the reduced level of activity, GeNeuro was able to strengthen its executive management, for example with the recruitment of its new Chief Medical Officer, David Leppert, who has a very extensive experience and proven track record in clinical development of Multiple Sclerosis drugs.

Geneuro remains committed to have a compensation policy that is designed to attract, motivate and retain its employees and promote the delivery of outstanding individual performance. The award of variable, performance-related compensation, and in particular share-based compensation components, is intended to promote an entrepreneurial mindset and approach whilst aligning long-term employee and shareholder interests.

Given the results of the year, the need to preserve cash and to ensure motivation and retention of the team, the Board of Directors decided, at its February 25, 2021 meeting, to cap cash bonuses relative to 2020 for executive management to 90% of the base bonus, but to grant higher stock options awards in recognition of the efforts made and as tool for retention and motivation.

3 ORGANISATION AND COMPETENCIES

For further details on the organization of the Company, please refer to Chapter 14 of the 2020 Universal Registration Document which provides more information on the Company's governance.

3.1 Remuneration Committee

The Remuneration Committee supports the Board of Directors in establishing and reviewing the compensation strategy and guidelines. Further, the Remuneration Committee supports the Board of Directors in preparing the proposals to the ordinary annual general meeting ("AGM") of shareholders regarding the compensation of the Board of Directors and the Executive Management.

3.2 The Role of the Board of Directors and the Remuneration Committee

Following are the key matters on which the Remuneration Committee provides recommendations to the Board of Directors:

- Compensation strategy, system and guidelines
- Definition of performance criteria (for cash bonus and equity-based incentives)
- Assessment of performance and decision on vesting multiple for equity-based incentive plan
- Compensation of the Board of Directors
- Compensation of the Executive Management (base salary and variable incentive)
- Grant of equity-based incentives to staff other than to the Executive Management
- Proposals to the AGM for maximum compensation of Executive Management and Board of Directors
- Proposals on other compensation-related issues
- Compensation report to the shareholders

3.3 Description of Benchmarks Used, Salary Comparisons and Support from External Consultants

A benchmark review of the total compensation of each member of the Board of Directors and Executive Management was last performed in 2017 by Willis Tower Watson, an independent external consulting firm, to assess market competitiveness of GeNeuro's compensation levels. Compensation data for 2015 and, when available, for 2016 of 14 Swiss and French peer biotechnology companies listed on the SIX Swiss Exchange, Euronext Paris and NASDAQ were collected. Each Executive Management position (except the CSO, who is employed by the French subsidiary) was evaluated by Willis Towers Watson, which found that the base salary of the CEO and Executive Management fell broadly around the 50th percentile point of the peer group and that the total direct compensation fell broadly within a range of the 25th to the 50th percentile of the peer group.

3.4 Shareholders' Vote

As a Swiss legal entity listed on a major foreign stock exchange, the Company is subject to the Swiss Compensation Ordinance, which requires a "say on pay" approval mechanism for the compensation of the Board of Directors and the Executive Management, under which shareholders must vote on the compensation of the Board of Directors and the Management Board on an annual basis.

3.5 Compensation approval process

Beneficiaries	Proposal	Decision[a]	AGMs (Binding approval by shareholders)
Members of the Board of Directors	Remuneration Committee	Board of Directors	*Maximum total compensation:* for the period between two consecutive AGMs
Members of the Executive Management[b]	Remuneration Committee	Board of Directors	*Maximum aggregate compensation:* for the period from January 1 to December 31 of the same year

a: subject to shareholders' binding vote

b : the Executive Management (EM) is defined as the Chief Executive Officer (CEO), Chief Financial Officer (CFO), Chief Scientific Officer (CSO), Chief Development Officer (CDO) and Chief Medical Officer (CMO)

4 COMPENSATION COMPONENTS

4.1 Board of Directors

The compensation of the members of the Board of Directors may, as per the Company's Articles of Association, consist of fixed and variable compensation. Following the Board of Directors' decision of December 7, 2016, the compensation of the members of the Board of Directors today consists exclusively of a fixed annual monetary compensation per term from one general meeting of shareholders to the next. At present only directors who are not linked to one of the large shareholders are remunerated by the Company.

In addition, the Company pays social security contributions where applicable and reimburses members of the Board of Directors for out-of-pocket expenses incurred in relation to their services on an on-going basis. For further information on the compensation for members of the Board of Directors, please refer to the section "Disclosure of 2020 Compensation Paid to the Board of Directors" on page 6.

4.2 Executive Management

The compensation of the members of the Executive Management includes a base salary, variable compensation, pension plan contributions and other benefits such as disability insurance and car allowances. Variable compensation comprises performance-related bonus and equity-based incentives (described in the Universal Registration Document under section 19.1.4 “Conditional capital”). The contractual notice period for members of the Executive Management does not exceed six months.

The variable compensation elements may be subject to the attainment of performance targets (annual corporate and individual targets) that may take into account the achievement of annual operational, strategic, financial or other objectives.

4.2.1 Fixed base salary

The fixed base salary is reviewed based on the position, responsibilities, experience and skills of each member of the Executive Management and takes into account individual performance. The Remuneration Committee reviews the fixed base salaries at the beginning of each year to ensure the Company remains an attractive employer.

4.2.2 Indirect benefits

The Company contributes to the corporate pension plan and provides car allowances and representation allowances for the members of its Executive Management.

4.2.3 Performance-related bonus

Performance-related cash bonuses are reviewed annually and are based on individual and corporate performance. Potential bonuses range from 20 % to 40 % of fixed compensation depending on position and are assessed based on individual and corporate performance.

Corporate goals: Given the current development stage of GeNeuro, the corporate goals for 2020 were closely linked to the continuation of the development program in the multiple sclerosis (MS) indication, with a key focus on the efficient execution of the Karolinska trial. In addition, within the financial constraints imposed by the Company’s limited resources, development continued to make GeNeuro a platform company Both objectives remained largely predicated on the optimal management of budgets and resources.
Corporate development and other goals are also set by the Board of Directors during the last quarter of each year.

Individual goals relate to the roles and responsibilities of the members of the Executive Management and are aligned with the corporate strategy and annual corporate goals. Individual goals are set by the CEO (except in the case of the CEO, where they are set by the Board of Directors) during the first quarter of each year.

For the financial year 2020, due to the Company’s cash position, the Board of Directors decided, at its February 25, 2021, meeting, to cap cash bonuses for executive management to 90% of the base bonus, irrespective of the individual manager’s performance assessment.

4.2.4 Equity Incentive Plans

In June 2016, the Board of Directors formally adopted and granted a long-term equity incentive plan for its Executive Management (the GeNeuro Performance Share Option Units [“PSOU”] program); the goal of the three-year PSOU program was to provide Executive Management members with an opportunity to obtain stock options and benefit from any potential gain in value, thereby providing an additional incentive for participants to contribute to the future success of the Company. The program was therefore aligned with shareholders’ interest to enhance shareholder value and increase the ability of the Company to attract and retain individuals with exceptional skills. On February

27, 2019, following the end of the vesting period, the Board of Directors assessed the performance condition achievement and made its determination of the number of share options to be delivered, which was 635'835 options in total for the Executive Management (or 99% of the number of PSOUs that had been granted initially). For more information about the underlying Plan, see note 9 "Stock Option Plans" in the consolidated financial statements.

In February, 2017, the Board of Directors also adopted the principle and grant of a second long-term equity incentive plan for its Executive Management, based on stock purchase options. The purpose of the GeNeuro Stock Option (SO) plan is to grant Executive Management members stock options to provide them with an opportunity to benefit from any potential gain in value, thereby providing an additional incentive for participants to contribute to the future success of the Company. This program is therefore, like the PSOU program, aligned with shareholders' interest to enhance shareholder value and increase the ability of the Company to attract and retain individuals with exceptional skills. Under this discretionary SO plan, members of the Executive Management are eligible to be granted Stock Options, which vest during the next three years (one third after one year, and therefore one-sixth every six months). Vested options can be exercised during a period of 5 years after the grant date. Any value, income or other benefit derived from any share option is not considered part of the participant's salary or compensation for the purposes of calculating any pension or retirement benefits. The strike price is determined by the Board of Directors at the time of award of the SO.

The Company made two issuances of Stock Options:

- 7'500 Stock Options on February 23, 2017, with a strike price of EUR 13 per share, vs. a market price on February 23, 2017, of EUR 9.39 per share, representing an exercise premium of 38%; and
- 22'500 Stock Options on February 8, 2018, with a strike price of EUR 13 per share, vs. a market price on February 8. 2018, of EUR 6.28 per share, representing an exercise premium of 107%.

For the Stock Options, although there is no cash value of the SOs at grant, their fair value was determined at grant date using a Black & Scholes model and equals to EUR 2.35 per SO for the 2017 grant and to EUR 0.80 for the 2018 grant.

In addition, in July 2018, in order to promote retention throughout the Company, the Board of Directors implemented a "Loyalty Bonus Option Plan" pursuant to which options representing a value of 50% to 100% of the cash bonus would be granted to all employees (including executives) who would have remained with the Company at least until February 28, 2019. The plan was communicated to employees in September 2018 whereas the actual exercise price and number of options was determined on February 27, 2019; due to the plan having been communicated to employees during 2018, the economic value of the Loyalty Bonus Options is considered to be part of the 2018 compensation. The determination of the actual number of Loyalty Bonus options to be granted was made at the Board of Directors' meeting of February 27, 2019.

Finally, during its meeting of March 5, 2020 and with the objective of aligning the equity incentive plan to the strategy and to the value creation timeline and framework for the Company, the Board of Directors implemented a new 4-year Stock Option Incentive Plan that has been benchmarked with the structure of similar programs in the industry. Pursuant to this new Plan, 181,500 new Stock Options were awarded in 2020 to executive management and key employees.

For more information about the underlying Plans, see note 9 "Stock Option Plans" in the consolidated financial statements.

According to the results of the external benchmarking conducted for 2016, the equity-based compensation level for all positions except the CEO were below the 25th percentile of the market, whilst for the CEO it was between the median and the 75th percentile. No benchmarking has been made on the 2020 compensation.

4.3 Structure of compensation

The compensation strategy and split for the period from January 1, 2020 to Dec. 31, 2020 was structured as follows:

• Board of Directors: 100% fixed cash fee;
• Executive Management: for 2020:
  - the compensation structure for the CEO was 63% fixed cash salary (base salary), 22% short-term cash bonus, and 15% equity-based incentives.
  - for the other executive management positions, the compensation structure was 74% fixed cash salary (base salary), 17% short-term cash bonus and 8% equity-based incentive. As a reminder, no equity-based incentives were granted during 2019. As mentioned above, due to the Company's cash position, the Board

of Directors decided, at its February 25, 2021 meeting, to cap cash bonuses for executive management to 90% of the base bonus, irrespective of the individual manager's performance assessment.

Compared to 2019, base salaries for the executive management team have remained stable in local currency terms (but have marginally increased in EUR due to the weakening of the EUR vs CHF in 2020), whereas cash bonuses awarded to the executive management team were 22% lower than in 2019.

5 COMPENSATION DISCLOSURE

5.1 Disclosure of 2020 Compensation to the Board of Directors

The total compensation of the members of the Board of Directors is as follows:

For the period from January 1, 2020 to December 31, 2020 (audited)

in EUR thousands	**Annual cash fee**	**Social security**	**Total compensation**
Jesús Martin Garcia [(1)]	-	-	-
Chairman and CEO			
Hedi Ben Brahim	-	-	-
Giacomo Di Nepi	23.8	0.6	24.4
Michel Dubois	23.4	0.6	24.0
Eric Falcand	-	-	-
Gordon Francis	32.3	1.3	33.6
Christophe Guichard	-	-	-
Total	***79.4***	**2.5**	**81.9**

in CHF thousands	***Annual cash fee***	***Social security***	***Total compensation***
Jesús Martin Garcia [(1)]	-	-	-
Chairman and CEO			
Hedi Ben Brahim	-	-	-
Giacomo Di Nepi	*25.4*	*0.7*	*26.1*
Michel Dubois	*25.0*	*0.6*	*25.6*
Eric Falcand	-	-	-
Gordon Francis	*34.6*	*1.4*	*35.9*
Christophe Guichard	-	-	-
Total	***85.0***	***2.7***	***87.7***

For the period from January 1, 2019 to December 31, 2019 (audited):

in EUR thousands	**Annual cash fee**	**Social security**	**Total compensation**
Jesús Martin Garcia [(1)]	-	-	-
Chairman and CEO			
Marc Bonneville	-	-	-
Giacomo Di Nepi	22.9	0.6	23.5
Michel Dubois	22.5	0.6	23.1
Eric Falcand	-	-	-
Gordon Francis	31.1	1.2	32.3
Christophe Guichard	-	-	-
Jean-Jacques Laborde	-	-	-
Total	***76.4***	**2.4**	**78.8**

in CHF thousands	*Annual cash fee*	*Social security*	*Total compensation*
Jesús Martin Garcia [(1)] *Chairman and CEO*	-	-	-
Marc Bonneville	-	-	-
Giacomo Di Nepi	*25.4*	*0.7*	*26.1*
Michel Dubois	*25.0*	*0.6*	*25.6*
Eric Falcand	-	-	-
Gordon Francis	*34.6*	*1.4*	*35.9*
Christophe Guichard	-	-	-
Jean-Jacques Laborde	-	-	-
Total	***85.0***	***2.7***	***87.7***

Accordingly, total compensation of KEUR 81.9 paid to members of the Board of Directors in 2020 is 49% below the maximum amount approved at the 2020 AGM, held on May 27, 2020 of KEUR 160 for the period from the ordinary General Meeting 2020 until the ordinary General Meeting 2021 (this maximum amount having been decreased from KEUR 185 in 2019). The increase from 2019 to 2020 is entirely due to the weakening of the EUR vs the CHF, as board compensation is paid in CHF.

5.2 Disclosure of 2020 Compensation to the Executive Management

The total compensation of the members of the Executive Management is as follows:

For the period from January 1, 2020 to December 31, 2020 (audited):

In EUR	Base salary	Cash bonus [(1)]	Social Security, pension & others	Total Cash Compensation	Non-Cash Equity incentives[(2)]	Total Compensation	*Number of stock options granted*
Jesús Martin Garcia Chairman and CEO	373,653	133,309	122,256	629,218	86,850	716,068	*90,000*
Other 4 members of the Executive Management	700,289	163,145	256,253	1,119,686	77,573	1,197,259	*76,500*
Total	**1,073,942**	**296,453**	**378,509**	**1,748,905**	**164,423**	**1,913,327**	***166,500***

(1) : cash bonus has been paid in March 2021.
(2) : Based on the value of the entirety of the Stock Options awarded in March 2020 and December 2020, respectively. Social charges on the equity incentives will be due only at the time of exercise of the underlying share option, and will be calculated on the gain realized at that time.

In CHF	*Base salary*	*Cash bonus* [(1)]	*Social Security, pension & others*	*Total Cash Compensation*	*Non-Cash Equity incentives*[(2)]	*Total Compensation*	*Number of stock options granted*
Jesús Martin Garcia Chairman and CEO	*399,996*	*142,707*	*130,875*	*673,578*	*92,973*	*766,551*	*90,000*
Other 4 members of the Executive Management	*749,659*	*174,646*	*274,318*	*1,198,624*	*83,041*	*1,281,665*	*76,500*
Total	***1,149,655***	***317,353***	***405,194***	***1,872,202***	***176,014***	***2,048,217***	***166,500***

For the period from January 1, 2019 to December 31, 2019 (audited):

In EUR	Base salary	Cash bonus (1)	Social Security, pension & others	Total Cash Compensation	Non-Cash Equity incentives(2)	Total Compensation	Number of stock options granted (2)
Jesús Martin Garcia Chairman and CEO	359,579	154,782	118,857	*633,218*	0	*633,218*	0
Other 5 members of the Executive Management	964,945	159,514	277,395	*1,401,854*	0	*1,401,854*	0
Total	**1,324,524**	**314,296**	**396,252**	***2,035,072***	**0**	***2,035,072***	**0**

(1) : cash bonus has been paid in March 2020, with a positive impact of reversal of accruals in 2019.
(2) : Equity incentives awarded in 2016, 2017 and 2018 were already included in prior compensation reports. There were no other equity awards in financial year 2019.
Social charges on the equity incentives will be due only at the time of exercise of the underlying share option, and will be calculated on the gain realized at that time.

In CHF	*Base salary*	*Cash bonus (1)*	*Social Security, pension & others*	Total Cash Compensation	*Non-Cash Equity incentives(2)*	*Total Compensation*	Number of stock options granted (2)
Jesús Martin Garcia Chairman and CEO	*399,996*	*172,179*	*132,217*	*704,392*	*0*	*704,392*	*0*
Other 5 members of the Executive Management	*1,073,405*	*177,443*	*308,574*	*1,559,423*	*0*	*1,559,423*	*0*
Total	***1,473,401***	***349,622***	***440,791***	***2,263,814***	***0***	***2,263,814***	***0***

Aggregate cash compensation paid to members of the Executive Management, including social security, pension and other charges, was KEUR 1,749 for the financial year 2020, i.e. 14% below the 2019 amount. For fixed compensation, the aggregate amount (including related social security payments and pension fund contributions) was KEUR 1,376, i.e. 17% below the total fixed executive management compensation for 2019, due to the resignation of certain executive officers; and 53% below the maximum amount of KEUR 2,900 for 2020, which was approved at the 2019 AGM held on May 24, 2019 (the 2020 fixed compensation was also 31% below the maximum amount of KEUR 2,000 for 2021, which was approved at the 2020 AGM held on May 27, 2020).

As for the variable compensation paid to members of Executive Management, it amounted to KEUR 372 for the cash portion (including related social security payments and pension fund contributions) in 2020, below the amount of KEUR 383 in 2019; the equity incentive component was KEUR 164 for 2010 vs nil for 2019 (and KEUR 185 in 2018). In total, the aggregate variable compensation (cash and non-cash) was KEUR 537, which is 81% below the maximum amount of KEUR 2,900 for 2020, which was approved at the 2019 AGM held on May 24, 2019 (the 2020 fixed compensation was also 73% below the maximum amount of KEUR 2,000 for 2021, which was approved at the 2020 AGM held on May 27, 2020).

LOANS AND CREDITS

As of December 31, 2020, the Company has no outstanding loans, credit lines or post-retirement commitments beyond the occupational benefit schemes to members of the Board of Directors or the Management Board. Furthermore, the Company has not paid any compensation to nor granted any loans or credit lines to former members of the Board of Directors or related persons.

SHARE OWNERSHIP INFORMATION

Disclosure of share awards in the Company to members of the Board of Directors or Executive Management in the year ended

	Dec. 31, 2020		Dec. 31, 2019	
Beneficiaries	**Shares**	**Stock options**	**Shares**	**Stock options**
Jesús Martin Garcia	-	90,000	-	-
Jean-François Arrighi	-	10,000	-	-
David Leppert	-	20,000	-	-
Miguel Payró	-	34,500	-	-
Hervé Perron	-	12,000	-	-
Total	**-**	**166,500**	**-**	**-**

CHAPTER 14.
OPERATION OF ADMINISTRATION AND MANAGEMENT BODIES OF THE COMPANY

The running of the Company's Board of Directors is determined by Swiss law and regulations, by the Company's Articles of Association and by the organizational rules and procedures of the Board of Directors, the principal provisions of which are described in this Chapter 16.

The Articles of Association as well as the organizational rules and procedures of the Board of Directors described in this Universal Registration Document are available on the Company's website www.geneuro.com.

14.1 Organization And Operation Of The Company's Management And Administrative Bodies

14.1.1 Organization and Operation of the Board of Directors

Membership and information on members of the Board of Directors are subject to the developments set forth in Section 12.1.1, "Board of Directors" of this Universal Registration Document.

Membership

In accordance with the Articles of Association, the Board of Directors may consist of between five and ten members elected at a general shareholders' meeting. The chairman of the Board of Directors is also chosen at a general shareholders' meeting.

At the filing date of this Universal Registration Document, the Board of Directors comprises eight members. The names and biographies of such members are set forth in Section 12.1.1 of this Universal Registration Document.

The Board of Directors believes that it has six independent members for purposes of Article III7 of its organizational rules and procedures and Article 14, section 1, of the Swiss Code of Good Company Governance Practices of economiesuisse to which the Company intends to refer (please see Section 14.4, "Statement Regarding Company Governance" of this Universal Registration Document).

The independent members are Messrs. Hedi Ben Brahim, Michel Dubois, Giacomo Di Nepi, Eric Falcand, Gordon S. Francis, and Christophe Guichard, inasmuch as these individuals:

- do not serve in management, nor have they served in management in the last three years; and
- do not have a significant business relationship with the Company or its subsidiaries.

Authority

In accordance with the Swiss Code of Obligations and the Articles of Association and the organizational rules and procedures of the Board of Directors, the Board of Directors exercises the highest authority and supervision of the Company's business and affairs.

The decision-making authority of the Board of Directors applies principally to the following items:

i. exercising the highest levels of management of the Company and issuing necessary instructions, especially to define the Company's strategy and general resources for achieving it, the ultimate supervision of management and of the persons to whom it is delegated, decisions on developing, terminating, acquiring or selling strategic activities, and withdrawal from strategically important court cases;
ii. setting the basic principles in respect of the organization of the Company's administration and management;
iii. appointment and removal of the persons responsible for management and representation;
iv. fixing the compensation of the Directors and management, particularly the compensation strategy and structure of the compensation of Directors and management within the framework provided by law, regulations, and the Articles of Association, guidelines relating to the occupational pensions of members of the Board of Directors and management, proposals at the general shareholders' meeting to consider and act on approving the total compensation of the Board of Directors and management, fixing the individual compensation of the Directors and members of management, and preparing a report on compensation to be submitted at a general meeting of shareholders;
v. creating a system for identifying and handling risks and internal controls and of compliance with law and the Articles of Association;

vi. fixing the principles applicable to bookkeeping and accounting, financial controls, and the strategic financing plan, especially the establishment of the accounting function, and determination of the accounting reference, and the establishment of an appropriate system of financial planning, including, especially, the annual budget;
vii. preparing the management report (which includes the annual report, annual financial statements, and consolidated financial statements);
viii. organizing and giving notice of general shareholders' meetings and preparing proposals by the Board of Directors for the general shareholders' meeting;
ix. carrying out decisions approved at general shareholder meetings taken in compliance with law and the Articles of Association;
x. adopting the rules relating to the Company's communications and public relations strategy; and
xi. informing a court in the event of over-indebtedness.

In addition, the Board of Directors is responsible for ensuring that appropriate measures (such as embargoes or black-out periods) are taken for purchases and sales of the Company's shares or relevant rights at critical moments, such as in connection with an acquisition proposal or prior to a press conference or disclosure of the Group's results.

Finally, on November 19, 2015, the Board of Directors approved organizational rules and procedures by which it delegates management of the Company to members of management.

Terms and conditions of operation

The Board of Directors meets as often as the Company's business and affairs require, but at least four times per year.

Notice of Board meetings or decisions is given by the Chairman in writing (letter, fax, email, or any other similar, form of notice). In the event the Chairman is unable to act, notice of a Board of Directors meeting may also be given by the Vice Chairman.

Any member of the Board of Directors may ask the Chairman at any time to hold a meeting of the Board of Directors for a specific agenda matter, or request that points be included on the agenda.

Notices of meetings are sent 10 days prior to the meeting. In the event of an emergency, the Chairman may fix a shorter period. The notice is to contain the agenda as well as the documents, presented clearly and concisely, needed for the Board of Directors to transact business. If documentation cannot be provided before the meeting, the Chairman is to give the members of the Board of Directors sufficient time to familiarize themselves therewith prior to the commencement of the meeting.

As a general rule, the persons responsible for an item added to the agenda are present at the meeting. The persons who are indispensable for responding to questions for the purpose of illuminating various points must be available. The chairman of the Board of Directors may invite members of management, employees, or third parties to participate in Board of Directors' meetings for all or part of the agenda.

For major matters, the Board of Directors may consult independent outside experts, at the Company's expense.

Action of the Board of Directors may be taken in the form of a meeting, telephone conference, video-conference, or any other means making it possible to transact business.

If the Board of Directors consists of several members, its decisions are to be taken at a meeting by a majority of the votes cast by members present: provided, however, that they form a quorum of a majority of the Board (an attendance quorum).

Actions by the Board of Directors may also be taken by a majority of the votes of the Board members in the form of a written consent (letter, fax, or email) to a proposal by the Chairman, as long as the proposal is submitted to all members, and none of them demands a meeting.

In the event of a tie vote, the Chairman's vote shall be decisive.

Actions relating to formalities in connection with capital increases, future payments for new shares, or an issue of warrants may be taken by a single Director, and no quorum will be required.

Minutes of the deliberations and discussions of the Board of Directors are to be prepared, even when only a single Director takes part, and must be signed by the Chairman and the secretary of the meeting. The minutes must mention the members present. The Chairman shall be responsible for the content and retention of Board minutes.

Each member of the Board of Directors has the right to obtain information about the Company's business and affairs. During meetings, each Board member may ask for information from the other members, as well as from members of management. Outside meetings, Directors are to send their requests for information to the Chairman.

Rate of participation

During the 2020 financial year, the Company's Board of Directors met seven times, and the average attendance of Board members was 96%.

14.1.2 Organization of Management

The membership and information about members of management are set forth in Section 12.1.1.1 "Membership of the Board of Directors" of this Universal Registration Document.

14.2 Agreements Between Members Of Administration Or Management Bodies And The Company Or Any Of Its Subsidiaries

14.2.1 Employment Agreements

Pursuant to Swiss law, Messrs. Martin-Garcia, Arrighi, Leppert, and Payró hold employment agreements with the Company. Dr. Curtin and Mr Rückle resigned from the Company in 2020.

Mr. Perron is party to an employment agreement with GeNeuro Innovation.

14.2.2 Consulting Contracts

Mr. Gordon S. Francis is a consultant to the Company who assists in connection with clinical development projects in the field of neurology.

On February 25, 2015, Mr. Gordon S. Francis and the Company entered into a consulting agreement for a term of three years, terminable at any time upon 30 days' prior notice. For his consulting work, Mr. Gordon S. Francis is paid compensation of CHF 2,000 per day of work. His travel expenses are also reimbursed, in accordance with the Company's internal rules.

14.3 Operation Of Committees

The Board of Directors has delegated to certain of its members, organized in committees, the responsibility for preparing, supervising, or carrying out decisions and actions within the scope of its authority.

Article II.3 of the Company's organizational rules and procedures provides that the Board of Directors will include the following permanent committees:

- a Nominations Committee;
- a Remuneration Committee; and
- an Audit and Control Committee.

In connection with its responsibilities, the Board of Directors may appoint other committees on the basis of ad hoc rules or decisions/actions.

As of the filing date of this Universal Registration Document, the Board of Directors has not used this authority.

14.3.1 Nomination Committee

On November 19, 2015, the Board of Directors approved the rules and procedures for the Nominating Committee, the principal terms of which are set forth below.

Membership

The Nominations Committee has three members. The Board of Directors chooses the Chairman and members of the Nomination Committee.

The members of the Nominations Committee are:

- Mr. Giacomo Di Nepi, Chairman of the committee;
- Mr. Hedi Ben Brahim, member; and
- Mr. Christophe Guichard, member.

Responsibilities

The Nominations Committee has the following responsibilities:

1. it prepares for the action to be taken by the Board of Directors in respect of candidates for the Board of Directors proposed at a general shareholders' meeting;

2. it ensures, taking account of the Company's situation and interests, that, over time, the members of the Board of Directors comply with the recommendations of the Swiss Code of Best Practice for Corporate Governance; and

3. it develops and submits proposals to the Board of Directors in respect of:

    a. planning and scheduling the succession of Directors,
    b. the criteria for selecting candidates for the Board of Directors,
    c. the program to initiate new Directors in their responsibilities, and
    d. continuous training and education of the Directors.

Terms and conditions of operation

The relevant rules and procedures of the organizational rules and procedures are to apply mutatis mutandis to proceedings of the Nominations Committee (please see Section III of the organizational rules and procedures set forth in Section 14.1, "Organization and Operation of the Company's Management and Administrative Bodies" of this Universal Registration Document).

Reports

The Nominations Committee reports to the Board of Directors.

14.3.2 Remuneration Committee

On November 19, 2015, the Board of Directors approved the rules and procedures of the Remuneration Committee, the principal terms of which are set forth below.

Membership

The Remuneration Committee is a body that is mandatory for any Swiss company publicly traded in Switzerland or elsewhere.

As provided in the Articles of Association, the Remuneration Committee has three members.

To the extent possible, the Board of Directors is to propose that at least two independent members be elected, at a general shareholders' meeting, to the Remuneration Committee. If it proposes members that are not independent, the Board of Directors shall so report at the general shareholders' meeting.

The Board of Directors has not proposed that at a general shareholders' meeting there be elected members who are interdependent (i.e., who are under the control or orders of other members of the Board of Directors or management).

The members of the Remuneration Committee are:

- Mr. Giacomo Di Nepi, Chairman of the committee;
- Mr. Hedi Ben Brahim, member; and
- Mr. Christophe Guichard, member.

Prior to the 2020 AGM, Mr Jean-Jacques Laborde was the chairman of the committee. Following Mr Laborde's decision not to seek reelection at the 2020 AGM, Mr Hedi Ben Brahim was elected as a Director and as a member of the Remuneration Committee; the Remuneration Committee members then decided to nominate Mr Giacomo Di Nepi as the new Chair.

Responsibilities

The Remuneration Committee has the following responsibilities:

1. it assists the Board of Directors in establishing and periodically revising the Company's compensation policy, as follows:
   (a) it reports periodically to the Board of Directors on the status of the compensation process in light of applicable law, the Articles of Association, and decisions taken at a general shareholders' meeting,
   (b) it ensures that the Company offers a package of services and benefits consistent with the market and its performance in order to attract and retain persons with the skills and personalities required, and
   (c) it ensures that the compensation system does not contain undesired or undesirable incentives, and that it does not contain items that could be influenced on a targeted basis in a way that is contrary to the objective sought;
2. it assists the Board of Directors in the preparation of proposals for compensation that the Board of Directors is to submit for approval at a general shareholders' meeting;
3. it prepares and submits to the Board of Directors a report on compensation to be submitted at a general shareholders' meeting;
4. at the time of a general shareholders' meetings, acting by and through its Chairman, it provides explanations on the report and the compensation system and answers questions;
5. it chooses outside advisors on compensation and mandates them, determines their fees, and critically assesses their conclusions; and
6. it submits to the Board of Directors any proposal on compensation that it believes is in the Company's interest.

Terms and conditions of operation

The Chairman of the Board of Directors, the Chief Executive Officer and the Chief Financial Officer may be invited to meetings, except when the issue is their own compensation.

The Remuneration Committee is authorized to obtain necessary specialized knowledge, by consulting outside advisors, if necessary.

If the compensation practices of other companies are used for comparison, the Remuneration Committee is to review the membership of the comparison group and the relevance of the comparisons made.

If the Remuneration Committee asks Company employees to undertake comparisons, they shall follow the instructions of the Chairman of the Remuneration Committee for such purpose.

As to other matters, the relevant rules of procedures of the organizational rules and procedures are to apply mutatis mutandis to proceedings of the Remuneration Committee (please see Section III of the organizational rules and procedures set forth in Section 14.1, "Organization and Operation of the Company's Management and Administrative Bodies" of this Universal Registration Document).

Reporting

The Remuneration Committee reports to the Board of Directors.

14.3.3 Audit and Control Committee

On November 19, 2015, the Board of Directors approved the rules and procedures of the Audit and Control Committee, the principal terms of which are set forth below.

Membership

The Audit and Control Committee is composed of three members. The Board of Directors chooses the Chairman and the members of the Audit and Control Committee. The majority of the members of the Audit and Control Committee must be independent.

The members of the Audit and Control Committee are:

- Mr. Christophe Guichard, Chairman of the committee;
- Mr. Hedi Ben Brahim, member; and
- Mr. Eric Falcand, member.

Prior to the 2020 AGM, Mr Jean-Jacques Laborde was a member of the committee. Following Mr Laborde's decision not to seek reelection at the 2020 AGM, Mr Hedi Ben Brahim was elected as a Director and the Board of Directors then decided to nominate him as a member of the Audit and Control Committee.

All members are considered independent under the economiesuisse Code and have particular competences in finance and accounting.

Responsibilities

The Audit and Control Committee has the following responsibilities:

1. it ensures the establishment of a risk management and internal control system appropriate to the size, complexity, and risk profile of the Company and submits necessary proposals to the Board of Directors;
2. it supervises the internal audits;
3. it prepares a report at least once a year containing recommendations to the Board of Directors on:
   (a) the adequacy of the control system with regard to the recognized rules of good practices; and
   (b) the extent of effective implementation of the Company's compliance system;
4. it reviews the effectiveness of the external auditors (auditing firm);
5. it assists the Board of Directors, prepares decisions and makes recommendations in respect of any and all responsibilities of the Board of Directors in respect of financial accounting and planning;
6. it exercises critical control and verification of the Company's financial statements, the consolidated financial statements, and the interim financial statements intended to be published or disclosed;
7. it discusses the financial statements with finance managers as well as separately, as the case may be, with the head of the outside auditing firm;
8. it decides whether to recommend to the Board of Directors that the Company's financial statements and consolidated financial statements be presented at a general shareholders' meeting;
9. it evaluates the performance and fees of the outside auditors, ensures their independence, and verifies, in particular, whether the audit engagement is compatible with any other engagements by the Board; and
10. if the Chairman of the Board of Directors is also a member of management, it takes necessary measures to ensure the control and verification of the management activities of the Chairman of the Board of Directors.

Terms and conditions of operation

The relevant rules and procedures of the organizational rules and procedures are to apply mutatis mutandis to proceedings of the Audit and Control Committee (please see Section III of the organizational rules and procedures set forth in Section 14.1, "Organization and Operation of the Company's Management and Administrative Bodies" of this Universal Registration Document).

Reporting

The Audit and Control Committee reports to the Board of Directors.

14.4 Statement Regarding Company Governance

There are no requirements under Swiss law for a company to present a specific report on corporate governance.

Since the listing of the Company's shares on Euronext Paris, the Company refers to all recommendations of the Swiss Code of Best Practice for Corporate Governance of economiesuisse (the "economiesuisse Code").

The applicable economiesuisse Code to which the Company refers to may be consulted on the Internet at: www.economiesuisse.ch. The Company keeps copies of this Code permanently available to the members of its governance bodies.

The table below presents the Company's position vis-à-vis the recommendations made by the economiesuisse Code:

Recommendations of the Code of Good Practices	Compliance	Noncompliance
I. Shareholders		
R1: As providers of capital, the shareholders have the last word	X	
R2: The Company works to facilitate exercise by the shareholders of their legal rights	X	
R3: The Company ensures that general meetings of shareholders are a venue of communication so that they may discharge their responsibilities as members of a company's supreme governance body on an informed basis	X	
R4: The Company works to facilitate participation of the shareholders at general shareholders' meetings by setting the dates clearly and with sufficient lead time	X	
R5: General shareholders' meetings are to be organized so that shareholders can express themselves factually and concisely on the items set forth in the agenda	X	
R6: The organizational structure ensures the right of the shareholders to obtain information and consult documents	X	
R7: At a general shareholders' meeting, the majority must make its wishes known clearly	X	
R8: The Board of Directors is also to maintain contact with the shareholders between general meetings	X	
II. Board of Directors and Management		
a. Tasks of the Board of Directors		
R9: The board of directors, elected by the shareholders, exercises high-level management and supervision of the Company or group	X	
R10: The principal inalienable and nontransferable tasks of the Board of Directors are set forth in Swiss company law	X	
R11: The Board of Directors in the Articles of Association defines the responsibilities of persons responsible for management	X	
b. Membership		
R12: The membership of the Board of Directors must be balanced (male/female representation, diversity of members and majority of independent members)		Partially[170]
R13: The board of directors plans and schedules the renewal of offices and ensures continuing training and education of its members	X	
c. Independence		
R14: The independence of members of the Board of Directors must meet specific criteria	X	
d. Operation and chairmanship of the Board of Directors		
R15: The Board of Directors defines procedures appropriate to its business	X	
R16: The Chairman is responsible for preparing and presiding at meetings; he/she ensures and vouches for information	X	
e. Management of conflicts of interest and inside information		
R17: Each member of the Board of Directors and of management must manage his or her personal affairs so as to avoid as much as possible conflicts of interest with the Company	X	
R18: The Board of Directors is to adopt very precise principles relating to any disclosure of events and is to take steps to prevent violations of law on insider trading	X	
f. Chairmanship of the Board of Directors and of management		
R19: The principle of the balanced relationship to be reached between the responsibilities of management and control is also valid for the head of the Company		Partially[171]

[170] In accordance with the economiesuisse Code, the Board of Directors is to consist of men and women: at present the Board of Directors consists solely of men. This results from the Company's development and the active role of its founders and historical investors. The Company and its subsidiary promote equality between men and women within the Group. The Board of Directors, however, is opposed to the introduction of quotas in its membership. The Board of Directors should target appropriate diversity among its members: the Board of Directors aims to develop diversity of its members in the Company's interests. The Board of Directors should consist of a majority of independent members: six Directors out of seven are independent.

171 According to the economiesuisse Code, the chairmanship of the Board of Directors and management should be entrusted to two different persons. The Chairman of the Board of Directors, Mr. Jesús Martin-Garcia, also holds the position of Chief

Recommendations of the Code of Good Practices	Compliance	Noncompliance
g. Risk management, compliance with rules, and system of internal controls		
R20: The Board of Directors is responsible for ensuring that management of risks and the system of internal controls are appropriate for the company. Risk management relates to financial, operational, and reputational risks	X	
R21: The Board of Directors is to take steps to ensure compliance with applicable standards	X	
h. Committees of the Board of Directors		
R22: The Board of Directors may appoint committees responsible for specific tasks	X	
1. Audit Committee		
R23: The Board of Directors is to create an Audit Committee	X	
R24: The Audit Committee reaches its own opinion on internal and external audits, the internal control system, and the annual financial statements	X	
2. Remuneration Committee		
R25: The Board of Directors is to propose to the shareholders non-executive and independent parties to be appointed to a Remuneration Committee	X	
3. Nomination Committee		
R26: The Board of Directors shall create a Nomination Committee	X	
i. Specific cases		
R27: The rules of the Swiss Code, depending on the structure of the shareholders and the size of the Company, may be adapted to the circumstances	X	
III. Audit		
R28: Outside audits are conducted by the audit firm appointed by the shareholders	X	
IV. Disclosure		
R29: The Company is to supply in its management report information about corporate governance	X	
ANNEX 1		
I. Recommendations about compensation for members of the Board of Directors and management		
a. Role of the shareholders at a general meeting		
R30: The Board of Directors is to ensure that shareholders at a general meeting are able to exercise their rights and competence	X	
b. Role of the Board of Directors and Remuneration Committee		
R31: The Board of Directors is to decide on the compensation system for the highest-level managers of the Company and the compensation to be proposed at a general shareholders' meeting	X	
R32: With a view to appointment of the Remuneration Committee, the Board of Directors is to propose at the general meeting of shareholders non-executive and independent persons	X	
R33: The Remuneration Committee plays a key part in implementing the requirements of the law, the Articles of Association, and the shareholders' meetings, which require, in the Company's interests, specialized skills	X	
R34: On the basis of indications by the Board of Directors relating to compensation strategy, the Remuneration Committee is to develop a proposal for the creation of a compensation system intended for Company executives	X	
c. Details of system of compensation		
R35: As a general matter, the compensation system is based on fixed and variable components. It rewards service leading to success over the long and medium term through compensation available in the future	X	
R36: The compensation system is organized so as to avoid granting benefits that are not materially justified and negative incentives	X	
R37: The Remuneration Committee critically appraises compensation paid by other companies and the conclusions of internal and external advisors	X	

Executive Officer. The Board of Directors believes that this organization is presently best suited to the Company, given the human competences currently available. Supervision of management actions by Mr. Jesús Martin-Garcia is ensured by the Audit and Control Committee.

Recommendations of the Code of Good Practices	Compliance	Noncompliance
d. Reporting on compensation and transparency		
R38: The Board of Directors prepares a report each year on compensation and ensures transparency of the compensation for members of the Board of Directors and management	X	

14.5 Internal Control And Company Governance

Since the listing of the Company's shares on Euronext Paris, the Company has adopted an internal control system in accordance with Article 728a of the Swiss Code of Obligations.

The Company has thus adopted several internal control procedures relating to accounting and financial information:

- it maintains internal separation between the production and supervision of its financial statements;
- it uses an independent expert to evaluate its retirement obligations for Swiss employees;
- it has outsourced the preparation of its payroll as well as having a specialized firm handle accounting for its subsidiary, GeNeuro Innovation; and
- it has adopted a procedure for delegating authority regarding the approval of purchase orders and purchase invoices.

In accordance with the internal organizational rules and procedures approved on November 19, 2015, the Audit and Control Committee is responsible for creating a risk management and internal control system appropriate to the size, complexity, and risk profile of the Company.

Furthermore, an independent auditor that is responsible for verifying the internal control system is appointed annually at a general shareholders' meeting.

Finally, since the listing of the Company's shares on Euronext Paris, the Company has continued to improve its internal control practices and its adherence to the economiesuisse Code.

CHAPTER 15.
EMPLOYEES

15.1 Human Resources

15.1.1 Headcount

As of December 31, 2020, the Group employed a total of 17 persons. An operational organization chart is presented in Section 1035.9.1, "Operating Organization Chart" of this Universal Registration Document. At the filing date of this Universal Registration Document, the number of employees has remained 24.

15.1.2 Distribution by Department

As of December 31, 2020, 17 professionals (including consultants and temporary workers) worked for the Group, distributed as follows:

Department	Number of employees
Management and administration	6
Research and development	11
TOTAL	**17**

15.1.3 Geographic Distribution

The table below presents the geographic distribution of the 17 professionals working for the Group as of December 31, 2020:

Country	Number of employees
France	8
Switzerland	9
TOTAL	**17**

15.1.4 Structure and Evolution of Employees Within the Group

The tables below present the structure and recent evolution of employees within the Group during the last two years.

15.1.5 Overall Evolution of the Number of the Group's Employees

	December 31, 2020	December 31, 2019
Number of Group employees	17	24

15.1.6 Distribution of Employees by Type of Employment

The table below shows the distribution of the Group's employees by type of employment during the past two years:

(in percentage)	December 31, 2020	December 31, 2019
Permanent	100%	96%
Non-permanent	0%	4%

15.2 Profit Sharing And Participation Of Employees

15.2.1 Profit Sharing and Participation Agreements

None.

15.2.2 Employee Shareholders – Options for the Acquisition of the Company's Shares

Please see Section 13.1.3, "Stock Options and Grants of Free Shares" and Section 16.1.1, "Distribution of Share Capital and Voting Rights" of this Universal Registration Document.

CHAPTER 16.
PRINCIPAL SHAREHOLDERS

16.1 Identification Of Shareholders

16.1.1 Distribution of Share Capital and Voting Rights

As of December 31, 2019 and December 31, 2020, and based on the latest publicly available information, the Company's shareholders were the following:

	At December 31, 2019			At December 31, 2020			At March 31, 2021		
Shareholders	Number of shares and voting rights*	% of capital	% of voting rights	Number of shares and voting rights*	% of capital	% of voting rights	Number of shares and voting rights*	% of capital	% of voting rights
Eclosion2 & Cie SCPC	6,367,608	43.44%	43.76%	6,367,608	30.93%	31.14%	6,367,608	30.93%	31.10%
GNEH SAS (1)	4,965,654	33.88%	34.12%	7,508,026	36.46%	36.71%	7,508,026	36.46%	36.67%
Servier International BV	1,254,596	8.56%	8.62%	1,254,596	6.09%	6.13%	1,254,596	6.09%	6.13%
Treasury shares	105,881	0.72%	0.00%	139,645	0.68%	0.00%	116,395	0.57%	0.00%
Publicly held	1,816,942	12.40%	12.49%	5,174,694	25.13%	25.30%	5,197,944	25.24%	25.39%
Employees & directors	147,437	1.00%	1.01%	145,750	0.71%	0.72%	145,750	0.71%	0.71%
TOTAL	**14,658,118**	**100.00%**	**100.00%**	**20,590,319**	**100.00%**	**100.00%**	**20,590,319**	**100.00%**	**100.00%**

* Shares held in treasury have their voting rights suspended in accordance with Swiss law.

(1): GNEH SAS is held 81.1% by Institut Mérieux and 18.9% by bioMérieux.

Eclosion2 SCPC & Cie is an investment fund under the authority of FINMA (Swiss Financial Markets Surveillance Federal Authority) and is structured according to the Swiss Federal Act on Collective Investment Schemes. Its main investors are either institutional investors (mainly pension funds) or industrial groups or private individuals investing individually or as part of family offices. According to the partnership agreement between Eclosion2 & Cie SCPC and its investors, they delegate to the general partner, Eclosion2 SA, the management of investments. The largest investor in Eclosion2 SCPC & Cie represents less than 12% of the partnership.

Mr. Martin-Garcia is one of Eclosion2 S.A.'s three managing partners and takes part in decisions regarding that company. However, under the organizational regulations of Eclosion2 S.A., all decisions relating to investment policies are made unanimously by the managing partners.

16.1.2 Significant Shareholders Not Represented on the Board of Directors

None.

16.1.3 Changes in Distribution of Equity Capital and Votes During the Last Two Financial Years*

	At December 31, 2019			At December 31, 2020			At March 31, 2021		
Shareholders	Number of shares and voting rights*	% of capital	% of voting rights	Number of shares and voting rights*	% of capital	% of voting rights	Number of shares and voting rights*	% of capital	% of voting rights
Eclosion2 & Cie SCPC	6,367,608	43.44%	43.76%	6,367,608	30.93%	31.14%	6,367,608	30.93%	31.10%
GNEH SAS (1)	4,965,654	33.88%	34.12%	7,508,026	36.46%	36.71%	7,508,026	36.46%	36.67%
Servier International BV	1,254,596	8.56%	8.62%	1,254,596	6.09%	6.13%	1,254,596	6.09%	6.13%
Treasury shares	105,881	0.72%	0.00%	139,645	0.68%	0.00%	116,395	0.57%	0.00%
Publicly held	1,816,942	12.40%	12.49%	5,174,694	25.13%	25.30%	5,197,944	25.24%	25.39%
Employees & directors	147,437	1.00%	1.01%	145,750	0.71%	0.72%	145,750	0.71%	0.71%
TOTAL	**14,658,118**	**100.00%**	**100.00%**	**20,590,319**	**100.00%**	**100.00%**	**20,590,319**	**100.00%**	**100.00%**

* Shares held in treasury have their voting rights suspended in accordance with Swiss law.

(1): GNEH SAS is held 81.1% by Institut Mérieux and 18.9% by bioMérieux.

As mentioned in section **3**.3, in so far as the Company's registered office is in Switzerland whilst its shares are listed only on Euronext Paris's regulated market, neither French regulations on mandatory public tender offers and buyouts, nor Swiss regulations on public takeover offers (purchase or exchange offer) are applicable to public tender offers concerning the Company's shares.

Under these conditions, a person might acquire shares in the Company to an extent representing a controlling stake as defined under Swiss or French law without a legally enforceable obligation to file a public tender offer to all the shareholders.

Similarly, because of the unenforceability of French and Swiss law on compulsory public tender offers, a person could issue a public tender offer to some, but not all, shareholders.

16.2 Shareholder Voting Rights

On the filing date of this Universal Registration Document, each shareholder's votes equal the number of shares each owns. There is no double-voting right, bearing in mind that under Swiss law, each share may carry only one voting right. Furthermore, under Swiss law, voting rights on treasury shares are suspended.

16.3 Shareholders' Agreements, Lock-Up Obligations, And Concerted Action

To the Company's knowledge, there is no shareholders' agreement, retention agreement, or concerted action involving the Company's shares.

16.4 Control Of The Company

On the filing date of this Universal Registration Document, no shareholder holds control over the Company, the main shareholder, GNEH SAS, holding 36.57% of the Company's shares and votes.

16.5 Agreements That Could Cause A Change Of The Company's Control

None. To the Company's knowledge, there is no agreement that might cause a change of control of the Company.

CHAPTER 17.
TRANSACTIONS WITH RELATED PARTIES

17.1 Intragroup Agreements

GeNeuro and GeNeuro Innovation have entered into two agreements, both dated December 19, 2009:

- a subcontracting agreement by which GeNeuro gives a certain number of studies to GeNeuro Innovation among which is the development of animal models to improve the comprehension of the mechanisms causing, and the development of, diseases and disorders linked to endogenous retroviruses, the development of antibodies, and the development of a diagnostic test for the detection of the envelope protein in serum.
- In consideration of such services, GeNeuro is to pay GeNeuro Innovation a price equal to the sum of the costs incurred by it plus 4%.
- The agreement provides that GeNeuro has the option of deciding whether or not to extend the term of the studies during a period of three months preceding the end thereof. This agreement was renewed on November 19, 2015; and
- a mutual services agreement by which GeNeuro and GeNeuro Innovation each make their employees available to the other and bill each other for such services, which reflects the Group's mode of organization, which assigns internal "research and development costs" to GeNeuro Innovation and the remaining expenses to GeNeuro.
- In consideration of such services, each company is to pay to the other a price equal to the amount of the costs and expense incurred plus 3%.
- Each party may terminate this agreement at any time upon one month's notice.

GeNeuro and GeNeuro Australia Pty Ltd have entered into an "Intercompany Working Capital Debt Facility Agreement" effective November 24, 2016, pursuant to which GeNeuro funds the clinical trials undertaken by its Australian subsidiary. On March 17, 2021, GeNeuro and GeNeuro Australia Pty Ltd entered into a Debt Forgiveness Agreement pursuant to which the outstanding balances due by GeNeuro Australia Pty Ltd to GeNeuro were forgiven in order to allow the liquidation of that subsidiary.

17.2 Transactions With Related Parties

Agreements with related parties are discussed in Note 18, "Related Parties", and Note 10.2 "Loan from shareholder" to the Group's consolidated financial statements for the year ended 31 December 2020 set forth in CHAPTER 18 of this Universal Registration Document.

As also described elsewhere in the Universal Registration Document, the GNEH Credit Facility carried an availability fee of 1.30% to be paid to GNEH SAS on the undrawn portion of the Credit Facility. Following draw-down, borrowings carried interest at a rate increasing progressively up to 12% p.a. until the facility's maturity of June 2020. The Company considered the interest rate to be a market rate at the time the facility was concluded. The GNEH Credit Facility was unsecured and provided for certain early repayment scenarios, including if the Company secured financing under partnerships with third parties or in the event of a change in control. The agreement also gave GNEH the option of using any existing drawn down loan in part or in full as a subscription for new shares, or for securities conferring rights to the share capital in the event that GeNeuro issues such securities. This facility, which was fully drawn as of May 31, 2019, was fully repaid by wyof set-off through the January 2020 Offering.

17.3 Special Reports Of Auditors

None. Under Swiss law, there is no obligation to submit transactions with related parties to the auditors' review.

CHAPTER 18.
INFORMATION REGARDING THE COMPANY'S ASSETS, FINANCIAL SITUATION AND RESULTS

18.1 Historical Financial Information

The consolidated financial statements as of and for the years ended December 31, 2020 and 2019 have been prepared in conformity with IFRS standards as issued by the International Accounting Standards Board.

18.2 Pro Forma Financial Information

Not applicable.

18.3 Financial Statements

18.3.1 Independent Auditors' Report on the Consolidated Financial Statements as of and for the year ended December 31, 2020

GeNeuro SA

Plan-les-Ouates

Report of the statutory auditor to the General Meeting

on the consolidated financial statements 2020

Report of the statutory auditor

to the General Meeting of GeNeuro SA

Plan-les-Ouates

Report on the audit of the consolidated financial statements

Opinion

We have audited the consolidated financial statements of GeNeuro SA and its subsidiaries (the Group), which comprise the consolidated statement of financial position as at 31 December 2020 and the consolidated statement of comprehensive income, consolidated statement of changes in equity and consolidated statement of cash flows for the year then ended, and notes to the consolidated financial statements, including a summary of significant accounting policies.

In our opinion, the accompanying consolidated financial statements give a true and fair view of the consolidated financial position of the Group as at 31 December 2020 and its consolidated financial performance and its consolidated cash flows for the year then ended in accordance with the International Financial Reporting Standards (IFRS) and comply with Swiss law.

Basis for opinion

We conducted our audit in accordance with Swiss law, International Standards on Auditing (ISAs) and Swiss Auditing Standards. Our responsibilities under those provisions and standards are further described in the "Auditor's responsibilities for the audit of the consolidated financial statements" section of our report.

We are independent of the Group in accordance with the provisions of Swiss law and the requirements of the Swiss audit profession, as well as the International Code of Ethics for Professional Accountants (including International Independence Standards) of the International Ethics Standards Board for Accountants (IESBA Code), and we have fulfilled our other ethical responsibilities in accordance with these requirements. We believe that the audit evidence we have obtained is sufficient and appropriate to provide a basis for our opinion.

Our audit approach

Overview

Overall Group materiality: EUR 79'000

We tailored the scope of our audit in order to perform sufficient work to enable us to provide an opinion on the consolidated financial statements as a whole, taking into account the structure of the Group, the accounting process-es and controls, and the industry in which the Group operates.

As key audit matter the following area of focus has been identified:

Confirmation of going concern assumption

Materiality

The scope of our audit was influenced by our application of materiality. Our audit opinion aims to provide reasonable assurance that the consolidated financial statements are free from material misstatement. Misstatements may arise due to fraud or error. They are considered material if, individually or in aggregate, they could reasonably be expected to influence the economic decisions of users taken on the basis of the consolidated financial statements.

Based on our professional judgement, we determined certain quantitative thresholds for materiality, including the overall Group materiality for the consolidated financial statements as a whole as set out in the table below. These, together with qualitative considerations, helped us to determine the scope of our audit and the nature, timing and extent of our audit procedures and to evaluate the effect of misstatements, both individually and in aggregate, on the consolidated financial statements as a whole.

Overall Group materiality	EUR 79'000
How we determined it	1% of total R&D and G&A gross expenses
Rationale for the materiality benchmark applied	We chose total expenses as the materiality benchmark because, in our view, it is the benchmark that best reflects the Group, which is a start-up still in a developmental phase and has no recurring revenues.

We agreed with the Audit Committee that we would report to them misstatements above EUR 7'700 identified during our audit as well as any misstatements below that amount which, in our view, warranted reporting for qualitative reasons.

Audit scope

We tailored the scope of our audit in order to perform sufficient work to enable us to provide an opinion on the consolidated financial statements as a whole, taking into account the structure of the Group, the accounting processes and controls, and the industry in which the Group operates.

The Group is comprised of three entities located in three different countries, namely Switzerland, France and Austral-ia. The Group financial statements are a consolidation of these three entities comprising the Group's operating business and centralised functions. Based on the client's operations we have performed full scope audit work on the Swiss entity, and specified procedures on the French and Australian entities.

Key audit matters

Key audit matters are those matters that, in our professional judgement, were of most significance in our audit of the consolidated financial statements of the current period. These matters were addressed in the context of our audit of the consolidated financial statements as a whole, and in forming our opinion thereon, and we do not provide a separate opinion on these matters.

Confirmation of going concern assumption

Key audit matter	How our audit addressed the key audit matter
The Group has prepared its consolidated financial statements on a going concern basis and, as further explained in Note 2.1 and Note 20 to the consolidated financial statements, management has concluded that the Group will be able to cover its cash outflows for at least twelve months from the date of these consolidated financial statements. The Group had cash and cash equivalents of EUR 6.8 million at 31 December 2020, but consumed cash of EUR 7.2 million for the year then ended, prior to investing and financing activities. Management has plans to raise additional financing in the near future and, if necessary, has a	The main audit procedures we performed for assessing the appropriateness of the cash flow projections used by management to confirm the going concern assumption used in preparing the consolidated financial statements included: - obtained the cash flow forecasts of the Group covering at least 12 months from the date of this report, checked mathematical accuracy and ensured they were approved by the Board of Directors; - audited the existence of cash and cash equivalents as of 31 December 2020;

fallback plan to operate at reduced level of activities in the event they are unable to raise those additional funds. Management's assessment of going concern is based on cash flow forecasts approved by the Board of Directors depending on whether additional funds are raised. Each of these plans are dependent on management judgement and could be influenced by management bias.	- assessed that the cash on hand as of the date of this report was sufficient to cover the budgeted cash outflows for the next 12 months under the assumption that no additional funding is received; - performed a lookback analysis to compare the 2020 budget with the actual results for the year ended 31 December 2020 to assess management's ability to make estimates; - assessed whether managements cost-cutting initiatives as per the 2021 budget can be executed; - discussed management's conclusions and the 2021 budget initiatives with the Board of Directors and confirmed they have approved them; - reviewed the adequacy and appropriateness of management's going concern disclosures in the financial statements. As a result of our audit procedures, as discussed with the Board of Directors, we consider management's approach regarding the assessment of the going concern assumption to be adequate.

Other information in the annual report

The Board of Directors is responsible for the other information in the annual report. The other information comprises all information included in the annual report, but does not include the consolidated financial statements, the stand-alone financial statements and the remuneration report of GeNeuro SA and our auditor's reports thereon.

Our opinion on the consolidated financial statements does not cover the other information in the annual report and we do not express any form of assurance conclusion thereon.

In connection with our audit of the consolidated financial statements, our responsibility is to read the other information in the annual report and, in doing so, consider whether the other information is materially inconsistent with the consolidated financial statements or our knowledge obtained in the audit, or otherwise appears to be materially misstated. If, based on the work we have performed, we conclude that there is a material misstatement of this other information, we are required to report that fact. We have nothing to report in this regard.

Responsibilities of the Board of Directors for the consolidated financial statements

The Board of Directors is responsible for the preparation of the consolidated financial statements that give a true and fair view in accordance with IFRS and the provisions of Swiss law, and for such internal control as the Board of Directors determines is necessary to enable the preparation of consolidated financial statements that are free from material misstatement, whether due to fraud or error.

In preparing the consolidated financial statements, the Board of Directors is responsible for assessing the Group's ability to continue as a going concern, disclosing, as applicable, matters related to going concern and using the going concern basis of accounting unless the Board of Directors either intends to liquidate the Group or to cease operations, or has no realistic alternative but to do so.

Auditor's responsibilities for the audit of the consolidated financial statements

Our objectives are to obtain reasonable assurance about whether the consolidated financial statements as a whole are free from material misstatement, whether due to fraud or error, and to issue an auditor's report that includes our opinion. Reasonable assurance is a high level of assurance, but is not a guarantee that an audit conducted in accordance with Swiss law, ISAs and Swiss Auditing Standards will always detect a material misstatement when it exists. Misstatements

can arise from fraud or error and are considered material if, individually or in the aggregate, they could reasonably be expected to influence the economic decisions of users taken on the basis of these consolidated financial statements.

As part of an audit in accordance with Swiss law, ISAs and Swiss Auditing Standards, we exercise professional judgment and maintain professional scepticism throughout the audit. We also:

- Identify and assess the risks of material misstatement of the consolidated financial statements, whether due to fraud or error, design and perform audit procedures responsive to those risks, and obtain audit evidence that is sufficient and appropriate to provide a basis for our opinion. The risk of not detecting a material misstatement resulting from fraud is higher than for one resulting from error, as fraud may involve collusion, forgery, intentional omissions, misrepresentations, or the override of internal control.
- Obtain an understanding of internal control relevant to the audit in order to design audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the Group's internal control.
- Evaluate the appropriateness of accounting policies used and the reasonableness of accounting estimates and related disclosures made.
- Conclude on the appropriateness of the Board of Directors' use of the going concern basis of accounting and, based on the audit evidence obtained, whether a material uncertainty exists related to events or conditions that may cast significant doubt on the Group's ability to continue as a going concern. If we conclude that a material uncertainty exists, we are required to draw attention in our auditor's report to the related disclosures in the consolidated financial statements or, if such disclosures are inadequate, to modify our opinion. Our conclusions are based on the audit evidence obtained up to the date of our auditor's report. However, future events or conditions may cause the Group to cease to continue as a going concern.
- Evaluate the overall presentation, structure and content of the consolidated financial statements, including the disclosures, and whether the consolidated financial statements represent the underlying transactions and events in a manner that achieves fair presentation.
- Obtain sufficient appropriate audit evidence regarding the financial information of the entities or business activities within the Group to express an opinion on the consolidated financial statements. We are responsible for the direction, supervision and performance of the Group audit. We remain solely responsible for our audit opinion.

We communicate with the Board of Directors or its relevant committee regarding, among other matters, the planned scope and timing of the audit and significant audit findings, including any significant deficiencies in internal control that we identify during our audit.

We also provide the Board of Directors or its relevant committee with a statement that we have complied with relevant ethical requirements regarding independence, and communicate with them all relationships and other matters that may reasonably be thought to bear on our independence, and where applicable, actions taken to eliminate threats or safeguards applied.

From the matters communicated with the Board of Directors or its relevant committee, we determine those matters that were of most significance in the audit of the consolidated financial statements of the current period and are therefore the key audit matters. We describe these matters in our auditor's report unless law or regulation precludes public disclosure about the matter or when, in extremely rare circumstances, we determine that a matter should not be communicated in our report because the adverse consequences of doing so would reasonably be expected to outweigh the public interest benefits of such communication.

Report on other legal and regulatory requirements

In accordance with article 728a paragraph 1 item 3 CO and Swiss Auditing Standard 890, we confirm that an internal control system exists which has been designed for the preparation of consolidated financial statements according to the instructions of the Board of Directors.

We recommend that the consolidated financial statements submitted to you be approved.

PricewaterhouseCoopers SA

Michael Foley

Florent Rossetto

Audit expert
Auditor in charge

Genève, 1 April 2021

Enclosure:

- Consolidated financial statements (consolidated statement of financial position, consolidated income statement, consolidated statement of comprehensive income, consolidated statement of changes in equity, consolidated cash flow statement and notes)

18.3.2 Consolidated Financial Statements prepared in accordance with IFRS standards as of and for the Years Ended December 31, 2020 and December 31, 2019

Consolidated Statement of Financial Position

GENEURO Consolidated Statement of Financial Position (in thousands of EUR)	Notes	12/31/2020	12/31/2019
ASSETS			
Intangible assets	3	1,148.8	1,155.1
Property, plant and equipment	4	1,442.0	677.5
Non-current financial assets	5, 7	257.2	285.5
Total non-current assets		**2,848.0**	**2,118.1**
Other current assets	6	819.9	1,349.8
Cash and cash equivalents	7	6,842.9	5,931.4
Total current assets		**7,662.8**	**7,281.2**
Total Assets		**10,510.8**	**9,399.3**
LIABILITIES AND EQUITY			
Equity			
Share capital	8	892.3	614.7
Additional paid-in capital		14,702.3	53,648.7
Cumulative translation adjustments		265.8	284.1
Accumulated other comprehensive loss		(324.0)	(2,328.0)
Accumulated deficit attributable to owners of the parent		(1,059.6)	(47,967.2)
Net loss attributable to owners of the parent		(8,962.3)	(9,460.8)
Equity attributable to owners of the parent		**5,514.5**	**(5,208.5)**
Total equity		**5,514.5**	**(5,208.5)**
Non-current liabilities			
Employee benefit obligations	11	1,391.8	3,135.4
Non-current financial liabilities	7, 10	1,273.4	483.4
Other non-current liabilities		3.4	6.8
Non-current liabilities		**2,668.6**	**3,625.6**
Current liabilities			
Current financial liabilities	7, 10	293.3	8,025.6
Trade payables	7, 12	540.4	1,247.1
Other current liabilities	7, 12	1,494.0	1,709.5
Current liabilities		**2,327.7**	**10,982.2**
Total Liabilities and Equity		**10,510.8**	**9,399.3**

The accompanying notes form an integral part of these consolidated financial statements

Consolidated Income Statement

GENEURO Consolidated Income Statement (in thousands of EUR)	Notes	12/31/2020 12 months	12/31/2019 12 months
Income	13	-	-
Research and development expenses			
Research and development expenses	14	(4,713.1)	(6,174.7)
Subsidies	14	556.0	912.4
General and administrative expenses	14	(3,302.0)	(3,744.1)
Other income	13	-	16.2
Operating loss		**(7,459.1)**	**(8,990.2)**
Financial income		3.1	5.9
Financial expenses	8, 15	(1,506.3)	(476.5)
Financial income (expenses), net		**(1,503.2)**	**(470.6)**
Pre-tax loss		**(8,962.3)**	**(9,460.8)**
Income tax (expense)	16	-	-
Net loss for the period		**(8,962.3)**	**(9,460.8)**
		12/31/2020	**12/31/2019**
Basic loss per share (EUR/share)	17	**(0.45)**	**(0.65)**
Diluted loss per share (EUR/share)		**(0.45)**	**(0.65)**

Consolidated Statement of Comprehensive Income

GENEURO Consolidated Statement of Comprehensive income (in thousands of EUR)		12/31/2020 12 months	12/31/2019 12 months
Net loss for the period		**(8,962.3)**	**(9,460.8)**
Actuarial gains (losses) - employee benefits	**11**	2,004.0	(1,221.7)
Net other comprehensive income (loss) that will not be reclassified to profit or loss in subsequent periods		**2,004.0**	**(1,221.7)**
Currency translation differences		(18.3)	(39.1)
Net other comprehensive income that may be reclassified to profit or loss in subsequent periods		**(18.3)**	**(39.1)**
Total other comprehensive income (loss)		**1,985.7**	**(1,260.8)**
Comprehensive loss		**(6,976.6)**	**(10,721.6)**

The accompanying notes form an integral part of these consolidated financial statements

Consolidated Statement of Changes in Equity

GENEURO Consolidated Changes in Equity	Notes	Capital Number of shares	Share Capital Ordinary shares at nominal value	Additional paid-in capital	Other reserves from capital	Accumulated deficit and net loss attributable to owners of the parent	Cumulative translation adjustments	Other compre-hensive income (loss)	Share-holders' equity
			In thousands of EUR						
At December 31, 2018		*14,658,118*	**614.7**	**53,706.3**	**-**	**(47,983.0)**	**323.2**	**(1,106.3)**	**5,554.9**
Net loss 2019			-	-	-	(9,460.8)	-	-	(9,460.8)
Other comprehensive income			-	-	-	-	(39.1)	(1,221.7)	(1,260.8)
Comprehensive income (loss)			**-**	**-**	**-**	**(9,460.8)**	**(39.1)**	**(1,221.7)**	**(10,721.6)**
Share capital increase costs			-	(57.6)	-	-	-	-	(57.6)
Share-based payments	9		-	-	-	83.1	-	-	83.1
Treasury shares			-	-	-	(67.3)	-	-	(67.3)
At December 31, 2019		*14,658,118*	**614.7**	**53,648.7**	**-**	**(57,428.0)**	**284.1**	**(2,328.0)**	**(5,208.5)**
Net loss 2020			-	-	-	(8,962.3)	-	-	(8,962.3)
Other comprehensive income			-	-	-	-	(18.3)	2,004.0	1,985.7
Comprehensive income (loss)			**-**	**-**	**-**	**(8,962.3)**	**(18.3)**	**2,004.0**	**(6,976.6)**
Shares issued	8	*5,932,201*	277.6	17,222.3	-	-	-	-	17,499.9
Share capital increase costs			-	(1,168.7)	-	-	-	-	(1,168.7)
Reclassification pursuant to shareholders' meeting	8		-	(55,000.0)	42,750.0	12,250.0	-	-	-
Share-based payments	9		-	-	-	1,470.8	-	-	1,470.8
Treasury shares			-	-	-	(102.4)	-	-	(102.4)
At December 31, 2020		*20,590,319*	**892.3**	**14,702.3**	**42,750.0**	**(52,771.9)**	**265.8**	**(324.0)**	**5,514.5**

(1) At the Annual General Meeting of Shareholders of May 27, 2020, the shareholders resolved to offset €12,250 K from the additional paid-in capital against the carried forward loss, and to allocate € 42,750 K from the additional paid-in capital to a new position “Other reserves from capital” within the free reserves.

The accompanying notes form an integral part of these consolidated financial statements

Consolidated Cash Flow Statement

GENEURO Consolidated Cash Flow Statement (in thousands of EUR)	Notes	12/31/2020 12 months	12/31/2019 12 months
Cash flow from operating activities			
Net loss for the period		**(8,962.3)**	**(9,460.8)**
Adjusted by the reversal of:			
Amortization of intangible assets	3	8.2	8.1
Depreciation of property, plant and equipment	4	353.6	346.7
Change in provision for defined benefit obligation	11	248.0	45.1
Share-based payment expense	9	1,470.8	83.2
Capital tax expense		17.7	-
Financial expense, net	15	138.8	470.6
Gains or loss resulting from the disposal of assets	4, 10	0.7	-
Unwinding of advances	10	3.6	4.2
(Increase) / Decrease in Deposits	*5*	5.6	(74.6)
(Increase) / Decrease in Other current financial assets	*5*	-	34.1
Decrease in Other current assets	*6*	526.0	2,095.5
Decrease in Trade payables and related accounts	*12*	(707.2)	(4,076.7)
Decrease in Other non-current liabilities		(3.4)	(125.6)
Increase / (Decrease) in Other current liabilities	*12*	(218.5)	791.1
Effect of lease modifications	*10*	(55.1)	-
Increase / (Decrease) in deposits from sub-rental		-	(33.6)
Cash outflow from operating activities		**(7,173.5)**	**(9,892.7)**
Cash flow from investing activities			
Acquisitions of intangible assets	3	(1.9)	-
Acquisitions of property, plant and equipment	4	(21.4)	(50.4)
Interest received on short term deposits		0.5	4.0
Cash outflow from investing activities		**(22.8)**	**(46.4)**
Cash flow from financing activities			
Capital increase	8	10,000.0	-
Proceeds from borrowings		-	7,500.0
Interest paid	10	(259.8)	(249.0)
Share capital increase costs paid	8	(1,168.7)	-
Repayment of lease liabilities	10	(327.8)	(315.1)
Repayment of advances		(15.0)	-
Repayment of borrowings	10	-	-
Purchase of treasury shares		(80.0)	-
Cash flow from financing activities		**8,148.7**	**6,935.9**
Increase / (Decrease) in cash		**952.4**	**(3,003.2)**
Cash & cash equivalents - beginning of period		5,931.4	8,961.4
Impact of exchange rate fluctuations		(40.9)	(26.8)
Cash & cash equivalents - end of period		**6,842.9**	**5,931.4**

The accompanying notes form an integral part of these consolidated financial statements

Notes to the Consolidated Financial Statements

(Unless indicated otherwise, the amounts mentioned in these Notes are in thousands)

Note 1: Company overview

The following information constitutes the Notes to the consolidated financial statements and forms an integral part of the consolidated financial statements presented for the financial years ended December 31, 2020 and 2019.

Each of these years covers a 12-month period from January 1 to December 31.

Incorporated on January 31, 2006, GeNeuro SA ("GeNeuro") is a clinical-stage biopharmaceutical Swiss limited company (société anonyme) which develops therapies and companion-diagnostic tools. 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 human endogenous retroviruses ("HERV"), which represent 8% of the human DNA. This represents a novel therapeutic approach pioneered by GeNeuro since 2006, based on 15 years of R&D at Institut Mérieux and INSERM. GeNeuro's lead therapeutic candidate, temelimab (previously known as GNbAC1), is a humanized monoclonal antibody that neutralizes a pathogenic HERV protein of the W family called pHERV-W env (previously called MSRV env) that has been identified as a potential key factor in the onset and development of autoimmune diseases such as MS. The Company has been listed on Euronext in Paris since April 18, 2016.

The Company's registered office is at 3, chemin du Pré-Fleuri - CH-1228 Plan-les-Ouates - Geneva – Switzerland. It has two subsidiaries, GeNeuro Innovation SAS, which was established in France in 2009, and GeNeuro Australia Pty Ltd, incorporated in Australia in 2016.

GNEH SAS, a subsidiary of Institut Mérieux in France, is the largest shareholder of the Company as at December 31, 2020, with a stake of 36.46% in the Company, compared to 33.88% at December 31, 2019; Eclosion 2 & Cie SCPC was the largest shareholder of the Company at December 31, 2019, with a stake of 43.44% in the Company; this stake was reduced to 30.93% at December 31, 2020. Refer to Note 22.

GeNeuro is hereinafter referred to as "GeNeuro", the "Company" or the "Group".

Note 2: Significant accounting policies

2.1 Basis of preparation

Compliance with International Financial Reporting Standards

GeNeuro has prepared its financial statements, approved by the Board of Directors on April 1, 2021, in accordance with International Financial Reporting Standards (IFRS) published by the International Accounting Standards Board (IASB) as at the preparation date of the financial statements, for all the periods presented.

New standards, updates and interpretations adopted by the Group

There were no new standards or amendments adopted by the Group in 2020 which had a material impact on its consolidated financial statements. In addition, there are no new standards and amendments published but not yet effective that are expected to have a material impact on the consolidated financial statements of the Group.

Historical cost convention

The Group's financial statements have been prepared in accordance with the historical cost convention, except with respect to the plan assets included in the calculation of the defined benefit pension plan liability, which are measured at fair value.

Going concern

GeNeuro SA is a biopharmaceutical company at the clinical stage developing innovative therapeutics. The Company is exposed to risks and uncertainties inherent in establishing and developing a business that are common to early-stage companies in the biotechnology industry, including, but not limited to, development by competitors of new technological innovations, dependence on key personnel, protection of proprietary technology, compliance with government regulations and the ability to secure additional financing to fund operations. Product candidates currently under development will require significant additional research and development efforts, including preclinical and clinical testing and regulatory approval prior to commercialization. These efforts require significant amounts of additional capital, adequate personnel and infrastructure and extensive compliance-reporting capabilities. Even if the Company's product development efforts are successful, it is uncertain when, if ever, the Company will realize significant revenue from product sales.

The Company's success may also depend on its ability to:

- establish and maintain strong patent position and protection;
- enter into collaborations with partners in the pharmaceutical industry;
- acquire and retain key personnel;
- acquire additional funding to support its operations.

The Company's financial statements have been prepared on the basis of continuity of operations, realization of assets and the satisfaction of liabilities and commitments in the ordinary course of business. Since its incorporation, the Company has primarily funded its growth through issuances of shares, including the capital increase conducted at the time of its initial public offering in 2016 and a €17.5 million capital increase in January 2020; additional funds provided by research collaborations and research tax credits (in France and Australia); and a Credit Facility provided by its shareholder GNEH SAS in 2019, which was repaid by way of set-off through the capital increase of January 2020.

The Company expects that its operating losses and negative cash flows will continue for the foreseeable future, although it expects that negative cash flows will continue to decrease given the Company's current level of activity. Based on its current cash position and activities and taking into account the Company's fallback operating plans in the event it were unable to raise additional plans, the Company expects to be able to cover its cash outflows for at least twelve months from the date of these financial statements. Hence, the financial statements have been prepared on a going concern basis.

The future viability of the Company beyond that date is dependent on its ability to raise additional capital to finance its operations. The Company will seek additional funding through public financings, debt financings, collaboration agreements, strategic alliances and licensing arrangements. The Company may not be able to obtain financing on acceptable terms, or at all, and the Company may not be able to enter into collaborations or other arrangements. The terms of any financing may adversely affect the holdings or the rights of the Company's stockholders. If the Company is unable to obtain funding, the Company could be required to delay, reduce or eliminate research and development programs, product portfolio expansion, or future commercialization efforts, which could adversely affect its business prospects.

Although management continues to pursue these plans, there is no assurance that the Company will be successful in obtaining sufficient funding on terms acceptable to the Company to fund continuing operations, if at all.

Liquidity risk management is assessed in Note 20.

Consistency of accounting policies

The accounting policies applied are consistent with those applied for the preparation of the annual financial statements as at December 31, 2019. There are no new standards, amendments or interpretations mandatory from the beginning of the 2020 financial year that could have a significant impact on the financial statements of the Group.

2.2 Consolidation methods

Subsidiaries are all the entities over which the Company has control. The Company controls an entity when it is exposed to, or has rights to, variable returns from its involvement with the entity and has the ability to affect those returns through its power over the entity. Subsidiaries are fully consolidated from the date on which the Company acquires control. They are deconsolidated from the date on which control ceases.

Intra-group transactions and balances are eliminated. The accounting policies of the subsidiaries have been aligned with those of the Company.

As of the date of the publication of these consolidated financial statements, the Company had two subsidiaries:

- GeNeuro Innovation SAS, 100% of the voting rights and interests held throughout the periods presented.
- GeNeuro Australia Pty Ltd, 100% of the voting rights and interests held throughout the periods presented.

Therefore, GeNeuro SA (parent company based in Switzerland) presents consolidated financial statements that include the financial statements of its subsidiaries GeNeuro Innovation SAS and GeNeuro Australia Pty Ltd for the fiscal years ended on December 31, 2019 and 2020.

2.3 Use of judgments and estimates

To prepare the financial statements in accordance with IFRS, the Company has made judgments and estimates that could affect the amounts presented under assets and liabilities as at the reporting date, and the amounts presented under income and expenses for the period.

Such estimates are made by the Company's management based on the assumption of going concern and on the information available at the time. These estimates are ongoing and are based on past experience as well as diverse other factors judged to be reasonable and form the basis for the assessments of the book value of assets and

liabilities. The estimates may be revised if the circumstances on which they are based change or as a result of new information. Actual results may differ significantly from such estimates if assumptions or conditions change.

The significant estimates or judgments made by the Company relate to the following in particular:

- Measurement of stock-options issued to employees, executives and external service providers:
  - The fair-value measurement of share-based payments is based on the Black & Scholes option valuation model which makes assumptions about complex and subjective variables. These variables notably include the value of the Company's shares, the expected volatility of the share price over the lifetime of the instrument, and the present and future behaviour of the holders of those instruments. There is a high inherent risk of subjectivity when using an option valuation model to measure the fair value of share-based payments in accordance with IFRS 2.
  - The valuation assumptions adopted are disclosed in Note 9.

- Defined benefit plans:
  - Defined benefit schemes are recognized in the statement of financial position based on an actuarial valuation of the obligations at period-end, minus the fair value of the scheme assets. This valuation is determined using the projected unit credit method, taking into account staff turnover, mortality probability and actuarial assumptions based on management estimates.
  - The valuation assumptions adopted are disclosed in Note 11.

2.4 Foreign currency translation

Functional currency

As of January 1, 2016, owing to the evolution of the parent company's financing (initial public offering on Euronext Paris), to the implementation of the cooperation contract with Laboratoires Servier, whose milestone payments are in euros, and to the launch of the Phase IIb clinical trial whose costs are also in euros, the parent company has changed its functional currency to adopt the euro (EUR or €) instead of the Swiss franc (CHF).

All items were converted into the new functional currency by using the exchange rate at the time (rate as of December 31, 2015: 1.0835 CHF for 1 EUR), except for shareholders' equity which was converted at the applicable historical rates.

Reporting currency

The Group uses the euro (EUR or €) as the reporting currency for its consolidated financial statements.

Transactions and balances

Transactions in foreign currencies are initially recorded by the Group's entities at their respective functional currency spot rates at the date the transaction first qualifies for recognition.

Group companies

The financial statements of GeNeuro Australia Pty Ltd, whose functional currency is the Australian dollar and not the euro, are translated as follows:

- Statement of financial position items (excluding shareholders' equity) are translated at the year-end closing rate;
- Income statement items are translated at the average annual rate;
- Equity items are translated at the historical rate.

The exchange differences arising on translation for consolidation are recognized in other comprehensive income.

The exchange rates used for the preparation of the consolidated financial statements are as follows:

Exchange rate (AUD per EUR)	12/31/2020		12/31/2019	
	Weighted average rate	Closing rate	Weighted average rate	Closing rate
Australian dollar (AUD)	1.6549	1.5896	1.6109	1.5995

Based on exchange rates provided by Banque de France

2.5 Distinction between current and non-current

In its statement of financial position, the Group makes a distinction between current and non-current assets and liabilities.

The following rules were applied to distinguish current from non-current items:

- assets and liabilities constituting working capital circulating in the normal course of business are classified as "current";
- assets and liabilities not being turned over in the normal course of business are presented as “current” or “non-current” depending on whether their maturity is longer or shorter than one year from the balance sheet date.

2.6 Intangible assets

Research and development expenses

Research and development costs are recognized as expenses when they are incurred. Costs incurred on development projects are recognized as intangible assets when the following criteria are fulfilled:

- it is technically feasible to complete the intangible asset so that it will be available for use or sale;
- management intends to complete the intangible asset and use or sell it;
- there is an ability to use or sell the intangible asset;
- it can be demonstrated how the intangible asset will generate probable future economic benefits;
- adequate technical, financial and other resources to complete the development and to use or sell the intangible asset are available;
- the expenditure attributable to the intangible asset during its development can be reliably measured.

In the opinion of management, due to uncertainties inherent in the development of the Group’s products, the criteria for development costs to be recognized as an asset, as prescribed by IAS 38, “Intangible Assets”, are not met.

As a result, internal development expenses incurred (mainly consisting of the cost of preclinical experiments, clinical trials and production cost of temelimab) are recognized under research and development (“R&D”) expenses at the point that they are incurred.

Licenses

Licenses acquired by the Company to access intellectual property are recognized under intangible assets. The amortization of such licenses over their useful lives shall start upon marketing approval of the related products.

Contingent payments

The acquisition of certain intangible assets, mainly licenses, may involve additional payments contingent on the occurrence of specific events or milestones. Unless the Group already has a present obligation to make the payment at a future date, the initial measurement of the intangible asset does not include such contingent payments. Instead, such payments are subsequently capitalized as intangible assets when the contingency or milestone occurs.

Software

Software license acquisition costs are recognized as assets on the basis of the costs incurred in acquiring them and in making the software concerned operational.

Amortization

Amortization is calculated using the straight-line method to spread the cost over the estimated useful life, specifically:

Items	Amortization period
Software	1 to 5 years

Amortization expense is recognized in the income statement under “General and administrative expenses”.

2.7 Property, plant and equipment

Property, plant and equipment are stated at their acquisition cost less accumulated depreciation.
Depreciation is calculated on a straight-line basis over the estimated useful life of the asset.

The following depreciation periods are used:

Items	Depreciation period
Office and computer equipment	3 to 5 years
Laboratory equipment	3 to 5 years
General facilities, fixtures and fittings	5 years
Buildings (Right of use)	Duration of lease

The depreciation expense for property, plant and equipment is recognized in the income statement under:

- "General and administrative expenses" for depreciation of general facilities, fixtures and fittings; office and computer equipment;
- "Research and development expenses" for laboratory equipment.

2.8 Lease agreements

Since January 1, 2019, the Group applies IFRS 16 "Leases" for lease agreements and has elected to use the exemption proposed by the standard on lease contracts for which the lease terms end within 12 months as of the date of initial application; and to exclude the low-value assets (with an individual value in USD of less than 5'000 when new).

In 2019, the Group adopted the new IFRS 16 "Leases" standard, effective from January 1, 2019. The impact on its financial statements from the first-time adoption of this new standard is disclosed in the financial report for the year ended December 31, 2019.

At the inception of the lease a right-of-use asset and a lease liability are recognized in the balance sheet. The asset is initially measured at the amount of the lease liability plus any initial direct costs incurred.

The lease liability is initially measured at the present value of the lease payments payable over the lease term, including variable lease payments depending on an index at the commencement date and the exercise price of purchase options if it is reasonably certain that the option will be exercised. The lease liability is discounted at the rate implicit in the lease. If that rate cannot readily be determined the incremental borrowing rate is used. Lease liabilities are subsequently re-measured to reflect possible changes in the lease terms. Right-of-use assets are depreciated over of the duration of the lease contract including contractually agreed optional extension periods, whose exercise are deemed to be reasonably certain. The depreciation is recognized in operating income. The unwinding of the discounting effect is included in the financial expense. Lease payments are accounted for as a repayment of the lease liability. Expenses for lease contracts for objects with a value of less than USD 5 thousand and lease contracts with a duration of up to twelve months are recognized directly in the income statement.

2.9 Recoverable value of non-current assets

Non-current assets that are not yet being amortized or depreciated, such as licenses, are tested for impairment at the end of the period in which they are acquired and subsequently annually, and whenever events or changes in circumstances indicate that the carrying amount may not be recoverable.

Non-current assets that are subject to amortization or depreciation are subjected to an impairment test whenever an internal or external factor indicates that an asset may have lost value.

Impairment is recognized when the book value of an asset exceeds its estimated recoverable value. The recoverable value of an asset is its fair value less selling costs, or its value in use, whichever is higher.

Any impairment charge is recognized in the income statement under the same category as the amortization or depreciation of the same asset.

As at December 31, 2020, none of the non-current assets presented an internal or external indication of impairment.

2.10 Financial assets

The Group's financial assets are classified into two categories depending on their nature and the purpose for which they are held:

- financial assets at fair value through profit or loss;
- financial assets at amortized cost.

At initial recognition, the Group measures a financial asset at its fair value plus, in the case of a financial asset not at fair value through profit or loss, transaction costs that are directly attributable to the acquisition of the financial asset.

All purchases and sales of financial assets are recognized on the settlement date.

Financial assets are derecognized when the rights to receive cash flows from the investments have expired or have been transferred and the Group has transferred substantially all risks and rewards of ownership.

Financial assets at fair value through profit or loss

Financial assets at fair value through profit or loss consist of currency derivatives and are presented in current financial assets.

Gains or losses arising from changes in the fair value of the "financial assets at fair value through profit or loss" category are presented in the income statement within "Financial income (loss)" in the period in which they arise.

The Group may opt to classify other assets within this category.

Financial assets at amortized cost

This category includes other assets (refer to Note 6) and other financial assets (refer to Notes 5 and 7).

Other assets are initially recognized at fair value and subsequently measured at amortized cost using the effective interest rate method. A provision for impairment of receivables is established when there is objective evidence that the Group will not be able to collect all amounts due according to the original terms of the invoice. The amount of the provision is the difference between the carrying amount and the recoverable amount and is recognized in the income statement.

Non-current financial assets include the cash reserve linked to the liquidity contract (Refer to Note 5). These are non-derivative financial assets with fixed or determinable payments that are not listed on an active market.

2.11 Cash and cash equivalents

Cash and cash equivalents recognized in the statement of financial position include cash positions at banks and cash at hand.

Term deposits with an initial maturity of less than three months are classified as cash equivalent. Cash equivalents are held for trading purposes, easily convertible into a known amount of cash and exposed to negligible risk that they will change in value.

For cash flow statement purposes, net cash consists of cash and cash equivalents as defined above.

2.12 Fair value of financial instruments

The nominal values of trade receivables and trade payables are considered to approximate to their fair values, given the very short payment maturities of these receivables. The same principle applies to other receivables and other current liabilities.

The Company has established three categories of financial instruments depending on their valuation methods and uses this classification to disclose some of the information required by IFRS 7:

- Level 1: financial instruments listed on an active market;
- Level 2: financial instruments whose valuation methods rely on observable inputs;
- Level 3: financial instruments whose valuation methods rely entirely or partly on unobservable inputs, an unobservable input being defined as one whose measurement relies on assumptions or correlations that are not based on the prices of observable market transactions for a given instrument or on observable market data on the valuation date.

At December 31, 2019 and December 31, 2020, there were no instruments held by the Company recognized at fair value through profit and loss.

2.13 Public subsidies receivable

The Company benefits from public subsidies and grants as disclosed below.

Subsidies and grants

Grants received from public entities to subsidize certain types of expenditure are recognized when there is reasonable assurance that the entity will comply with the conditions attached to obtaining the grants. They are recognized as a reduction in the related expenditure, in this case research and development (R&D) expenses.

Research tax credits

The Group receives certain specific project-related research tax credits that are granted to companies incorporated in France as an incentive for technical and scientific research. Companies with expenses that meet the eligibility criteria receive a tax credit that (i) can offset against corporate income tax due in the year in which it is granted, as well as in the following three financial years, or, (ii) under certain circumstances, can be paid to the Company.

The Group also benefits from research tax credits for its activities in Australia for the research of new treatments against Type 1 diabetes linked to endogenous retroviruses. This research tax credit scheme provides a tax credit of 43.5% of admissible research expenses.

The Group considers the research tax credits received from French and Australian tax authorities as government grants as the tax credits are received independently from tax payments of the Group. The Group recognizes these credits in the consolidated statement of financial position within other current receivables given the expected time of collection and reasonable assurance of the collectability, and in the consolidated income statement under research and development subsidies. The credits are recognized in the year in which the eligible expenses giving rise to the tax credit are incurred.

2.14 Receivables and other current assets

Receivables are initially recognized at fair value and subsequently measured at amortized cost.

A provision for impairment is established when there is objective evidence that the Company will not be able to collect all amounts due according to the original terms of the invoice. The amount of the provision is the difference between the carrying amount and the recoverable amount and is recognized in the income statement.

Other receivables include the nominal values of research tax credits, which are recognized in assets in the year when the eligible expenses giving rise to the tax credit are incurred.

The Group applies the IFRS 9 simplified approach to measuring expected credit losses which uses a lifetime expected loss allowance for all trade receivables and contract assets.

2.15 Capital

Classification as equity depends on specific analysis of the characteristics of each instrument issued. Ordinary shares are classified under Shareholders' Equity.

Costs directly attributable to the issue of shares in a capital increase or in a capital increase as part of an initial public offering project, are recognized, net of tax, as a deduction from equity. Refer to Note 8.

2.16 Treasury shares

In accordance with IAS 32, GeNeuro treasury shares are deducted from equity, irrespective of the purpose for which they are held. No gain or loss is recognized in the income statement on the purchase, sale or cancellation of treasury shares.

2.17 Share-based payments

Since its incorporation, the Company has implemented a compensation plan settled in equity instruments in the form of stock-options allocated to certain employees.

In accordance with IFRS 2, the cost of transactions settled in equity instruments is charged to expenses in the period in which the rights to benefit from the equity instruments are acquired, and a corresponding amount is credited to equity. The Company has applied IFRS 2 in accounting for all equity instruments granted to employees and Board members.

The fair value of the stock-options granted to employees is measured using the Black & Scholes option valuation model.

All assumptions used in measuring the value of such plans are disclosed in Note 9.

2.18 Provisions

Provisions are recognized for litigation and other risks when the Group has an obligation to a third party resulting from a past event, it is probable that there will be an outflow of resources to settle the obligation and the future outflow of resources can be reliably estimated. The amount recognized in provisions is the estimated expense necessary to extinguish the obligation, discounted if necessary at period-end.

2.19 Employee benefit obligations

The Group provides retirement, death and disability benefits to its employees in line with local customs and requirements through pension payments to Social Security bodies, which are funded by Company and employee contributions in Switzerland and France, the two countries where the Company operates. The Company has no employees in Australia.

The Group also provides retirement, death and disability benefits to its Swiss and French employees through the following defined benefit scheme plans as follows:

- Swiss employees of the Company are members of a compulsory company-wide defined benefit scheme through a plan which is funded through employer (50%) and employee (50%) contributions to "La Bâloise", a Switzerland-based multi-employer plan (foundation). For the purpose of calculating contributions under this plan, salaries are capped at CHF 150K (approximately € 139K). This company-wide plan has been in place since the inception of the Company and all Swiss employees of the Company are eligible for its benefits. In addition, from January 1, 2018, the Company has implemented an additional pension benefit plan for its executive management to cover the portion of their salary in excess of CHF 150K (approximately € 139). All Swiss executive managers of the Company are eligible for its benefits; this plan is funded through employer (60%) and employee (40%) contributions to "La Bâloise". On retirement, each plan participant will receive his / her accumulated savings, which consist of all contributions paid in by the employer and the employee (net of any withdrawals) and the interest granted on those savings, at a rate which is fixed by the law up to a certain minimum level and at the discretion of the Council of the Foundation thereafter. At the age of retirement, the plan participant has the right to choose between a lump-sum payment or an annuity, or a combination thereof.

- For French employees, the Company provides a retirement indemnity, through the payment by the Company of a lump sum upon retirement.

Pension plans, similar compensation and other employee benefits that qualify as defined benefit schemes (in which the Company guarantees an amount or defined level of benefits) are recognized in the statement of financial position on the basis of an actuarial valuation of the scheme obligations at period-end, minus the fair value of the scheme assets.

The defined benefit obligations are calculated annually by independent actuaries using the projected unit credit method, taking into account staff turnover and mortality probability. The present value of the defined benefit obligation is determined by discounting the estimated future cash outflows using the interest rate of high-quality corporate bonds that are denominated in the currency in which the benefits will be paid and that have terms to maturity approximating the terms of the related pension liability.

Current and past services as well as the net interest on the defined benefit obligation are recognized in the income statement in the period in which they are incurred, and are presented as part of payroll expenses in the income statement. Re-measurements of the defined benefit pension plans are recognized in other comprehensive income.

2.20 Financial liabilities

Financial liabilities are split into two categories and include:

- financial liabilities recognized at amortized cost;
- financial liabilities recognized at fair value through profit or loss.

Financial liabilities recognized at amortized cost

The Group's financial liabilities consist of other payables and accruals which are classified as liabilities at amortized cost according to IFRS 9.

Borrowings and other financial liabilities are initially recognized at fair value and subsequently measured at amortized cost using the effective interest rate method. The "less than 1 year" component of financial liabilities is presented under "current financial liabilities".

Amortized cost is calculated by taking into account any discount or premium on acquisition and fees or costs that are an integral part of the effective interest rate. The effective interest rate amortization is included within finance costs in the income statement.

This category generally applies to interest-bearing loans and borrowings.

Financial liabilities recognized at fair value through profit or loss

For the years ended December 31, 2019 and 2020, the Group had no financial liability recognized at fair value through profit or loss.

2.21 Income tax

Current income tax assets and liabilities are amounts expected to be recovered from or paid to the tax authorities. The tax rates and tax laws used to compute the amount are those that are enacted or substantively enacted at the reporting date in the countries where the Group operates and generates taxable income.

Deferred taxes

Deferred taxes are calculated using the liability method on temporary differences between the tax bases of assets and liabilities and their carrying amounts for financial reporting purposes at the reporting date.

The main temporary differences relate to losses carried forward.

Deferred tax assets are recognized for all deductible temporary differences, the carry forward of unused tax credits and any unused tax losses. Deferred tax assets are recognized to the extent that it is probable that taxable profit will be available against which the deductible temporary differences and the carry forward of unused tax credits and unused tax losses can be utilized.

The carrying amount of deferred tax assets is reviewed at each reporting date and reduced to the extent that it is no longer probable that sufficient taxable profit will be available to allow all or part of the deferred tax asset to be utilized. Unrecognized deferred tax assets are re-assessed at each reporting date and are recognized to the extent that it has become probable that future taxable profits will allow the deferred tax asset to be recovered.

Deferred tax assets and liabilities are measured at the tax rates that are expected to apply in the year when the asset is realized or the liability is settled, based on tax rates (and tax laws) that have been enacted or substantively enacted at the reporting date.

Withholding taxes

Withholding taxes which are estimated to be not recoverable are recognized as an expense in the income statement. No amounts have been expensed due to non-recoverability in the years ended December 31, 2019 and December 31, 2020.

2.22 Revenue recognition

The company recognizes income from license fees, the provision of R&D services and management fees on the arrangement of R&D services. Income is recognized when control of the goods or services passes to the customer. For the provision of a license, this is dependent on whether the license conveys a right of use or right of access to the underlying intellectual property. The R&D services are recognized over time as the Company performs the clinical trials and the customer benefits from those services. The Company identifies the performance obligations in each contract with a customer. A performance obligation is a promise to deliver goods and services that is distinct from other promises in the contract.

Where a contract contains more than one performance obligation, the Company allocates the transaction price based on the stand-alone selling price of each separate performance obligation. The Company receives upfront payments and variable consideration in the form of milestones. The Company uses the most likely method to estimate variable consideration and includes such consideration in the transaction price and income if it is not highly probable of reversal.

Income from licenses that convey a right to use intellectual property is recognized when the customer is able to use that intellectual property. R&D services are recognized over the clinical study period based on an input method. This method is calculated by the clinical trial costs incurred over the estimated costs to complete the study.

The Company provides management services, where it arranges clinical trials with an external provider on behalf of a customer. In these arrangements, the Company is acting as agent and recognizes the management fee as income as the management services are delivered.

Revenues generated by collaboration agreements, when applicable, are recognized under “Income”. Refer to Note 13.

2.23 Information by segment

The Group operates in only one activity segment, the research and development of pharmaceutical products, with the objective to market such products subject to the success of the development phases and the obtention of the required regulatory approvals. The Chief Executive Officer (“CEO”) of the Company reviews the consolidated statement of operations of the Group on an aggregated basis and manages the operations of the Group as a single operating segment.

The Group currently generates no revenue from the sales of pharmaceutical products.

The geographical analysis of non-current assets is as follows:

(Amounts in thousands of EUR)	As at December 31,	
	2020	2019
Switzerland	2,630.2	1,992.2
France	217.8	125.9
Australia	-	-
Total non-current assets	2,848.0	2,118.1

The geographical analysis of operating expenses and subsidies is as follows:

(Amounts in thousands of EUR)	Operating expenses		Subsidies	
	As at December 31,		As at December 31,	
	2020	2019	2020	2019
Switzerland	5,347.9	6,598.1	-	-
France	2,659.7	2,722.2	556.0	680.3
Australia	7.5	598.5	-	232.1
Total operating expenses	8,015.1	9,918.8	556.0	912.4

2.24 Presentation of the Income Statement

The Group presents its income statement by function. The nature of the expenses presented in the income statement by function is disclosed in Note 14 of the Notes to the financial statements.

Financial income (expenses), net, includes mainly:

- expenses related to the financing of the Group;
- foreign exchange gains or losses.

2.25 Other comprehensive loss

Other income and expense items in the period recognized directly in equity are presented in “Other comprehensive loss/gain”.

2.26 Earnings per share

Basic earnings per share are calculated by dividing the net income attributable to Company shareholders by the weighted average number of shares outstanding during the financial year.

Diluted earnings per share are calculated by adjusting the net income attributable to the holders of ordinary shares and the weighted average number of the ordinary shares in circulation by the effects of all the potential dilutive ordinary shares.

If, when calculating diluted earnings per share, the inclusion of instruments giving deferred access to capital (stock-options) creates an anti-dilutive effect, those instruments are not taken into account. Refer to Note 17.

Note 3: Intangible assets

Intangible assets consist of license and software assets.

INTANGIBLE ASSETS (Amounts in thousands of EUR)	License	Software	Total
GROSS VALUE			
Statement of financial position at 31 December 2018	**1,139.8**	**66.7**	**1,206.5**
Statement of financial position at 31 December 2019	**1,139.8**	**66.7**	**1,206.5**
Additions	-	1.9	1.9
Disposals	-	(8.9)	(8.9)
Statement of financial position at 31 December 2020	**1,139.8**	**59.7**	**1,199.5**
ACCUMULATED AMORTIZATION			
Statement of financial position at 31 December 2018	**-**	**43.3**	**43.3**
Increase	-	8.1	8.1
Statement of financial position at 31 December 2019	**-**	**51.4**	**51.4**
Increase	-	8.2	8.2
Decrease	-	(8.9)	(8.9)
Statement of financial position at 31 December 2020	**-**	**50.7**	**50.7**
NET BOOK VALUE			
At 31 December 2018	**1,139.8**	**23.4**	**1,163.2**
At 31 December 2019	**1,139.8**	**15.3**	**1,155.1**
At 31 December 2020	**1,139.8**	**9.0**	**1,148.8**

Pursuant to the Exclusive License Agreement entered into with bioMérieux in 2006 and to the Exclusive License Agreement on Companion Diagnostic signed with bioMérieux in 2015, the Group became liable in 2016 to make milestone payments of € 957K relating to the launch of a phase IIb clinical trial, of which € 907K was paid during 2016 and € 50K was paid during 2017.

Pursuant to an Exclusive License Agreement entered into with the National Institute of Neurological Disorders and Stroke (NINDS), part of the U.S. National Institutes of Health (NIH), in October 2018, the Company made an up-front payment of USD 50K (€ 44.2K).

Neither of these licenses is currently amortized as the marketing approval for the relevant products has not yet been obtained.

The Group performed an assessment of its licenses in the context of its annual impairment test. Given the stage of the Group's development activities, the Group concluded that there was no appropriate manner to assess the "Value in use" (VIU) of the intangible assets, as the future cash flows that could be derived from the intangible assets cannot at this stage be reliably assessed.

Given this early stage, the group has performed the impairment test collectively on the basis of the market capitalization for the entire group of €57.7 million at December 31, 2020, less the value of its tangible assets of €9.4 million. The valuation is considered to be Level 1 in the fair value hierarchy. The Group concluded that no impairment was required under the provisions of IAS 36.

The Group's product candidates related to these licences were additionally assessed for impairment by considering their probability of success. This assessment included reviews of the following:

- Historic investments on the clinical trials, future contractual commitments and internal budgets approved by the Board of Directors for ongoing and future trials;
- Consideration of progress of clinical trials, including obtaining primary endpoint readout data, discussions with regulatory authorities for new trials and enrolment status for ongoing clinical trials;
- Consideration of market potential supported where available by external market studies, and assessments of competitor products and product candidates.

Note 4: Property, plant and equipment

Property plant and equipment consist mainly of laboratory equipment, leasehold improvements and IT equipment.

PROPERTY, PLANT AND EQUIPMENT (Amounts in thousands of EUR)	Buildings (right of use)	Machinery and equipment	Fixtures and fittings	Office and computer equipment, furniture	Office and computer equipment (right of use)	Vehicles (right of use)	Total
GROSS VALUE							
Statement of financial position at December 31, 2018	**-**	**254.1**	**33.2**	**195.7**	**-**	**-**	**483.0**
Adjustment on transition to IFRS 16	853.1	-	-	-	4.1	16.0	873.2
Additions	8.0	14.4	-	28.0	-	-	50.4
Exchange effects	(0.1)	-	-	-	-	-	(0.1)
Statement of financial position at December 31, 2019	**861.0**	**268.5**	**33.2**	**223.7**	**4.1**	**16.0**	**1,406.5**
Additions	165.0	1.8	13.7	5.9	-	-	186.4
Modifications (1)	987.7	-	-	-	-	-	987.7
Disposals	(140.7)	(44.3)	(5.5)	(17.1)	-	-	(207.6)
Statement of financial position at December 31, 2020	**1,873.0**	**226.0**	**41.4**	**212.5**	**4.1**	**16.0**	**2,373.0**
ACCUMULATED DEPRECIATION							
Statement of financial position at December 31, 2018	**-**	**224.5**	**11.0**	**146.8**	**-**	**-**	**382.3**
Increase	295.1	9.7	5.7	28.4	1.2	6.6	346.7
Statement of financial position at December 31, 2019	**295.1**	**234.2**	**16.7**	**175.2**	**1.2**	**6.6**	**729.0**
Increase	296.8	10.9	5.9	22.2	1.2	6.2	343.2
Disposals	(75.6)	(44.2)	(4.3)	(17.1)	-	-	(141.2)
Statement of financial position at December 31, 2020	**516.3**	**200.9**	**18.3**	**180.3**	**2.4**	**12.8**	**931.0**
NET BOOK VALUE							
At December 31, 2018	**-**	**29.6**	**22.2**	**48.9**	**-**	**-**	**100.7**
At December 31, 2019	**565.9**	**34.3**	**16.5**	**48.5**	**2.9**	**9.4**	**677.5**
At December 31, 2020	**1,356.7**	**25.1**	**23.1**	**32.2**	**1.7**	**3.2**	**1,442.0**

(1): on December 1, 2020, the Company extended the term of the lease for its Geneva headquarters, resulting in an adjustment to the value of the right-of-use asset and the corresponding liability.

No impairment was required under the provisions of IAS 36.

Note 5: Financial assets

FINANCIAL ASSETS (Amounts in thousands of EUR)	12/31/2020	12/31/2019
Liquidity contract	74.9	97.6
Deposits	182.3	187.9
Non-current financial assets	**257.2**	**285.5**

Non-current financial assets include the cash reserve related to the liquidity contract entered into following the initial public offering of the Company in April 2016 (refer to Note 7), and a bank security deposit related to the lease of the Company's premises.

Note 6: Other current assets

OTHER CURRENT ASSETS (Amounts in thousands of EUR)	12/31/2020	12/31/2019
Research Tax Credits (1)	553.9	914.0
Value Added Tax	59.6	191.7
Social receivables	55.2	60.8
Prepaid expenses	80.3	172.7
Advance payments (2)	70.7	10.2
Other	0.2	0.4
Total other current assets	**819.9**	**1,349.8**

(1) Research tax credits (RTC)

GeNeuro Innovation SAS has been granted RTCs pursuant to the provisions of articles 244 quater B and 49 septies F of the French General Tax Code. Amounts due from RTCs are recognized as receivables and result in a corresponding reduction in expense in the period that the qualifying expenses were made. RTCs are settled in cash in the following year; in 2019, the Group recognized € 680K, net, in French RTCs, which were reimbursed in the first half of 2020, and in 2020 the Group recognized € 554K, net, in French RTCs, which are expected to be reimbursed by the fourth quarter of 2021.

The Group also benefitted from RTCs for its activities in Australia. For the 2019 financial year, the company has lodged an RTC claim assessed at AUD 374K (€ 234K at the 2019 closing rate) based on R&D expenses incurred during 2019, which was reimbursed by the Australian Tax Authorities during the first half of 2020. There were no Australian RTCs for 2020 as the Group no longer conducted activities in Australia in 2020.

(2) Advance payments

Advance payments comprise payments made to service providers involved with the Company's clinical trials.

Note 7: Financial assets and liabilities and impact on income statement

The Group's assets and liabilities are measured as follows for each year:

(Amounts in thousands of EUR)	12/31/2020		Value - Statement of financial position as per IFRS 9		
Statement of financial position	Carrying Amount of Financial Position	Fair value	Fair value through profit and loss	Fair value through OCI	Amortized cost
Other non-current financial assets	257.2	257.2	-	-	257.2
Cash and cash equivalents	6,842.9	6,842.9	-	-	6,842.9
Total Assets	**7,100.1**	**7,100.1**	**-**	**-**	**7,100.1**
Non-current financial liabilities	1,273.4	1,273.4	-	-	1,273.4
Other non-current liabilities	3.4	3.4	-	-	3.4
Current financial liabilities	293.3	293.3	-	-	293.3
Trade payables	540.4	540.4	-	-	540.4
Other current liabilities	1,494.0	1,494.0	-	-	1,494.0
Total Liabilities	**3,604.5**	**3,604.5**	**-**	**-**	**3,604.5**

(Amounts in thousands of EUR)	12/31/2019		Value - Statement of financial position as per IFRS 9		
Statement of financial position	Carrying Amount of Financial Position	Fair value	Fair value through profit and loss	Fair value through OCI	Amortized cost
Other non-current financial assets	285.5	285.5	-	-	285.5
Cash and cash equivalents	5,931.4	5,931.4	-	-	5,931.4
Total Assets	**6,216.9**	**6,216.9**	**-**	**-**	**6,216.9**
Non-current financial liabilities	483.4	483.4	-	-	483.4
Other non-current liabilities	6.8	6.8	-	-	6.8
Current financial liabilities	8,025.6	8,025.6	-	-	8,025.6
Trade payables	1,247.1	1,247.1	-	-	1,247.1
Other current liabilities	1,709.5	1,709.5	-	-	1,709.5
Total Liabilities	**11,472.4**	**11,472.4**	**-**	**-**	**11,472.4**

Note 8: Capital

COMPOSITION OF SHARE CAPITAL (number of shares)	12/31/2020	12/31/2019
Common bearer shares	20,590,319	14,658,118
Total	**20,590,319**	**14,658,118**
Nominal value (in CHF)	0.05 CHF	0.05 CHF
Approximate nominal value (in EUR)	0.04 €	

This number of shares excludes stock options granted to certain employees, directors and consultants that have not yet been exercized.

Share capital

On January 31, 2020, the Company completed a capital increase of €17.5 million, through the issuance of 5,932,201 ordinary bearer shares. Accordingly, at December 31, 2020, the Company's share capital amounted to € 892.3K (CHF 1,029.5, converted into euros at the applicable historical exchange rates) and was divided into 20,590,319 common bearer shares with a nominal value of CHF 0.05. All shares are fully paid up.

Because the capital increase was not open to all existing shareholders but was restricted to certain selected institutional investors, pursuant to IFRS 2 the discount between the share price prior to the capital increase (€3.18 per share) and the actual issue price (€2.95 per share) is considered a share based payment, resulting in a charge of € 1,364 K within financial expenses, with a corresponding amount added to reserves within shareholders' equity.

Authorized capital

Following the May 27, 2020, shareholders' meeting, the authorized capital amounts to 10,295,159 bearer shares of CHF 0.05 nominal value each; the approval for this authorized capital lapses on May 27, 2022.

Conditional capital

Following the April 14, 2016, shareholders' meeting, the "part I" conditional capital includes 2,198,717 bearer shares of CHF 0.05 nominal value, to be issued upon exercise of stock options granted to employees, directors and consultants in the context of an incentive plan.

Following the May 24, 2019, shareholders' meeting, the "part II" conditional capital comprises 5,130,141 bearer shares of CHF 0.05 nominal value, to be issued upon exercise of stock options or conversion rights granted to shareholders or strategic partners or linked to loans or similar bond issues.

Capital management

Following its initial public offering on Euronext Paris, the Company entered in May 2016 into a liquidity contract with the Gilbert Dupont brokerage house in Paris, in order to reduce the share price's intra day volatility.

In this context, in 2016 the Company provided € 750K to this broker to enable it to buy and sell the Company's shares. The share of the contract that is invested in treasury shares by this broker is accounted for as a reduction in the Company's consolidated equity. The Company can terminate the contract at any time. Pursuant to this contract, 93,645 treasury shares were accounted for as a reduction in shareholders' equity at December 31, 2020 (84,881 shares at December 31, 2019). Results from the sale of such treasury shares are also directly applied to shareholders' equity.

MOVEMENT OF LIQUIDITY ACCOUNT	12/31/2020	12/31/2019
Initial balance (thousands of shares)	84.9	66.5
Shares purchased (thousands of shares)	128.3	107.0
Shares sold (thousands of shares)	(119.5)	(88.6)
Year-end balance (thousands of shares)	**93.7**	**84.9**
Purchases of shares (thousands of EUR)	397.4	388.3
Sales of shares (thousands of EUR)	(374.7)	(321.0)
Net movement of liquidity contract (thousands of EUR)	**22.7**	**67.3**

Dividends

The Company has paid no dividends in the financial years ended December 31, 2019 and 2020.

Note 9: Stock options and common shares granted as part of an incentive plan

Share awards to directors

Holders of ordinary shares that were obtained as part of an incentive plan created for two board members (11/2015 plan) were subject to a restriction period during which the shares could not be transferred, this restriction being lifted by 25% every twelve months; as a result, this restriction was fully lifted on November 18, 2019.

Upon termination of each director's service, the Company has no present obligation to repurchase or settle the shares in cash.

Stock options

The Company has issued stock options as part of an equity incentive plan.

During the first six months of 2020, the Board of Directors agreed to extend the maturity of stock options granted to employees in 2010. Out of the original 123'000 options, 45'000 options remained outstanding, with an exercise price per share of CHF 4 (approximately €3.64), and an initial maturity date on April 16, 2020; following the Board of Directors's decision, the maturity was extended until April 16, 2022.

Options granted pursuant to Performance Share Option Units ("PSOU")

From 2016 to 2018, the Company has granted Performance Share Option Units ("PSOU") to its management. PSOUs enable the beneficiaries, under conditions of vesting (service period) and non-market performance conditions, to be awarded stock options. The service period condition ended on December 31, 2018; following this and based on the achievement of each recipient's performance conditions, the Board of Directors determined on February 27, 2019, for each recipient the actual number of stock options to be awarded in replacement of the PSOUs originally granted; this number varied between 95% and 107% of the initial grant of PSOUs. Stock options thus awarded may be exercized during the five years until February 27, 2024. All vested options not exercized in the 30-day period following the departure (within the validity period of the options) are cancelled. The Group has no legal or constructive obligation to repurchase or settle any of the stock options in cash.

Share purchase options

In 2017 and 2018, the Company has granted its employees and management share purchase options under an equity incentive plan. The share purchase options vest, without performance conditions, in the following tranches:

- for the 2017 and February 2018 options, over three years as follows: one third on the first anniversary of their grant date, and then one sixth every six months thereafter. They may then be exercized during the five years following the end of the vesting period.
  For the September 2018 options: over four years as follows: 25% on the first anniversary of their grant date, and then 12.5% every six months thereafter. They may then be exercized during the ten years following the end of the vesting period. The September 2018 Option plan was communicated to employees in September 2018 whereas the actual exercise price and number of options was determined by the Board of Directors on February 27, 2019 (start of the vesting period); due to the plan having been communicated to employees during 2018, the economic value of the Loyalty Bonus Options is considered to be part of the 2018 compensation.

In addition, a new stock option plan was implemented during the first half of 2020:

2020 Share purchase options

The Company has granted share purchase options under an equity incentive plan. The share purchase options vest on a staggered basis: one fourth on the first anniversary of their grant date, and then one eighth every six months thereafter. They may then be exercised during the six years following the end of the vesting period. In 2020, the Company granted a total of 151,500 stock options with an exercise price of €3.34 per share and 30,000 stock options with an exercise price of €2.95 per share.

All vested options not exercized in the 12 month-period following the departure (within the validity period of the options) are cancelled. The Group has no legal or constructive obligation to repurchase or settle any of the stock options in cash.

The following tables summarize the assumptions adopted in the IFRS 2 valuation:

Allocation date	Number of options issued / Shares granted with a restriction period	Exercise price	Market price at time of grant	Exercise period	Vesting period	Volatility	Risk-free rate	Fair value at grant date per option / share
Stock-options 04/2010	123,000	4.00 CHF	N/A	5.5 years		50.5%	1.11%	1.46
Stock-options 04/2013	3,000	4.00 CHF	N/A	5 years		50.3%	0.05%	1.40
Shares granted to Board members 11/2015	45,000	N/A	N/A	N/A		N/A	N/A	27.99
PSOU 06/2016 (1)	606,400	13.00 €	9.28 €	5 years		58.8%	-1.09%	2.29
PSOU 01/2017 (1)	35,000	13.00 €	10.19 €	5 years	3 years	53.6%	-0.86%	2.48
PSOU 02/2017 (1)	15,000	13.00 €	9.29 €	5 years	2 years	53.6%	-0.87%	1.74
PSOU 02/2018 (1)	20,000	13.00 €	6.28 €	5 years	2 years	50.0%	-0.77%	0.14
Stock-options 02/2017 - part 1	42,500	13.00 €	9.67 €	5 years	3 years	53.6%	-0.94%	2.50
Stock-options 02/2017 - part 2	7,500	13.00 €	9.39 €	5 years	3 years	53.6%	-0.94%	2.35
Stock-options 02/2018	22,500	13.00 €	6.20 €	5 years	3 years	50.0%	-0.75%	0.80
Stock-options 09/2018	158,540	2.73 €	3.66 €	10 years	4 years	50.0%	0.00%	1.74
Stock-options 03/2020 - part 1	75,750	3.34 €	3.07 €	10 years	4 years	49.4%	-0.63%	0.73
Stock-options 03/2020 - part 2	75,750	3.34 €	3.07 €	10 years	4 years	45.8%	-0.52%	1.20
Stock-options 12/2020 - part 1	15,000	2.95 €	2.82 €	10 years	4 years	59.6%	-0.78%	0.86
Stock-options 12/2020 - part 2	15,000	2.95 €	2.82 €	10 years	4 years	53.6%	-0.64%	1.32

(2) Reflects the number of PSOUs granted originally; the actual number of stock options granted in February 2019, at the expiry of the PSOU Plan, is 602,335 for the 2016 Plan, 36,400 and 15,000, respectively, for the 2017 Plans and 18,500 for the 2018 Plan.

Evolution of the number of outstanding options

Number of options	Stock options 04/2010	PSOU Plan 06/2016	PSOU Plan 01/2017	PSOU Plan 02/2017	Stock options 02/2017- part 1	Stock options 02/2017- part 2	PSOU Plan 02/2018	Stock options 02/2018	Stock options 09/2018	Stock options 03/2020	Stock options 12/2020	Total
December 31, 2019	**106,000**	**531,477**	**36,400**	**15,000**	**37,500**	**6,667**	**18,500**	**20,833**	**137,070**	**-**	**-**	**909,447**
Issued	-	-	-	-	-	-	-	-	-	151,500	30,000	181,500
Exercised	-	-	-	-	-	-	-	-	-	-	-	-
Forfeited / cancelled (1)	(61,000)	(71,283)	(36,400)	-	(3,000)	(1,667)	-	(3,333)	(26,091)	-	-	(202,774)
December 31, 2020	**45,000**	**460,194**	**-**	**15,000**	**34,500**	**5,000**	**18,500**	**17,500**	**110,979**	**151,500**	**30,000**	**888,173**
Number of shares to be issued	**45,000**	**460,194**	**-**	**15,000**	**34,500**	**5,000**	**18,500**	**17,500**	**110,979**	**151,500**	**30,000**	**888,173**
Number of options vested as at December 31, 2020	**45,000**	**460,194**	**-**	**15,000**	**34,500**	**5,000**	**18,500**	**15,833**	**48,802**	**-**	**-**	**642,829**

(1) Forfeited following resignation or cancelled following expiry of exercise period.

Valuation of stock options and common shares granted as part of an incentive plan

The fair value of the options was measured using an adjusted Black & Scholes option pricing model, with included the following factors:

- The price of the underlying shares was deemed to be equal to the investor subscription price or was calculated by reference to internal valuations;
- The risk-free rate was selected by reference to the average lifetime of the instruments;
- Volatility was estimated by reference to a sample of biotechnology companies listed on Euronext and SIX (Switzerland), at the date when the instruments were granted, and over a period equivalent to the lifetime of the option.

The fair value of the common shares granted under an incentive plan is equal to the share price at the grant date less the purchase price paid by the allottee.

Breakdown of charges recognized in accordance with IFRS 2 for the relevant periods

(Amounts in thousands of EUR)	12/31/2020		
Grant date	Accumulated expense at opening	Expense	Accumulated expense at 12/31/2020
Stock options 2011 – extension granted 2020	-	22.8	22.8
Shares granted to board members 11/2015	614.4	-	614.4
PSOUs 06/2016	1,381.6	-	1,381.6
PSOUs 01/2017	89.6	-	89.6
PSOUs 02/2017	27.0	-	27.0
Stock options 02/2017- part 1	92.9	3.3	96.2
Stock options 02/2017- part 2	16.0	0.1	16.1
Stock options 02/2018	14.4	(0.3)	14.1
PSOUs 02/2018	3.0	-	3.0
Stock options 09/2018	118.8	25.7	144.5
Stock options 03/2020	-	54.0	54.0
Stock options 12/2020	-	0.8	0.8
Total	**2,357.8**	**106.4**	**2,464.1**

(Amounts in thousands of EUR)	12/31/2019		
Grant date	Accumulated expense at opening	Expense	Accumulated expense at 12/31/2019
Shares granted to board members 11/2015	586.3	28.1	614.4
PSOUs 06/2016	1,445.3	(63.7)	1,381.6
PSOUs 01/2017	59.8	29.8	89.6
PSOUs 02/2017	27.0	-	27.0
Stock options 02/2017- part 1	81.4	11.5	92.9
Stock options 02/2017- part 2	16.0	-	16.0
Stock options 02/2018	10.0	4.4	14.4
PSOUs 02/2018	3.0	-	3.0
Stock options 09/2018	46.0	72.8	118.8
Total	**2,274.9**	**82.9**	**2,357.8**

Note 10: Financial liabilities

Following the Group's adoption of IFRS 16 "Leases" from January 1, 2019, financial liabilities include the lease liabilities related to lease agreements; research grants received in the form of reimbursable advances (refer to Note 10.1); and the shareholder loan from GNEH SAS (refer also to Notes 10.2 and 22).

CURRENT AND NON-CURRENT FINANCIAL LIABILITIES (Amounts in thousands of EUR)	12/31/2020	12/31/2019
Reimbursable advance (Note 10.1)	129.8	182.9
Lease liabilities	1,143.6	300.5
Non-current financial liabilities	**1,273.4**	**483.4**
Reimbursable advance (Note 10.1)	49.2	7.5
Loan from shareholder (Note 10.2)	-	7,689.0
Lease liabilities	244.1	329.1
Current financial liabilities	**293.3**	**8,025.6**
Total financial liabilities	**1,566.7**	**8,509.0**

This section sets out an analysis of net debt and the movements in net debt for each of the periods presented.

Net debt (amounts in thousands of EUR)	12/31/2020	12/31/2019
Cash and cash equivalents	6,842.9	5,931.4
Borrowings (including reimbursable advance)	(179.0)	(7,879.4)
Lease liabilities	(1,387.7)	(629.6)
Net (debt) / cash	**5,276.2**	**(2,577.6)**
Cash and cash equivalents	6,842.9	5,931.4
Gross debt - fixed interest rates	(1,566.7)	(8,509.0)
Net debt	**5,276.2**	**(2,577.6)**

CHANGE IN LOANS AND BORROWINGS (Amounts in thousands of EUR)	LEASE LIABIILITIES	LOAN FROM SHAREHOLDER	REIMBURSABLE ADVANCE	DEPOSIT	TOTAL LOANS AND BORROWINGS
At December 31, 2018	**-**	**-**	**186.2**	**34.1**	**220.3**
Adjustment on transition to IFRS 16	913.3	-	-	-	913.3
Additions	8.3	7,500.0	-	-	7,508.3
Cash flows	(315.1)	-	-	(34.1)	(349.2)
Interest expense	-	189.0	4.2	-	193.2
Payment of interest	-	-	-	-	-
(+/-) Other (impact of change)	23.1	-	-	-	23.1
At December 31, 2019	**629.6**	**7,689.0**	**190.4**	**-**	**8,509.0**
Additions	173.7	-	-	-	173.7
Modification of lease	970.6	-	-	-	970.6
Cash flows	(327.8)	-	(15.0)	-	(342.8)
Decrease	(66.6)	(7,500.0)	-	-	(7,566.6)
Interest expense	9.1	61.7	5.7	-	76.5
Payment of interest	(9.1)	(250.7)	-	-	(259.8)
(+/-) Other (1)	8.2	-	(2.1)	-	6.1
At December 31, 2020	**1,387.7**	**-**	**179.0**	**-**	**1,566.7**

(1) : others include foreign exchange difference on lease liabilities and subsidies on reimbursable advance.

10.1 Reimbursable advance

CHANGE IN REIMBURSABLE ADVANCE (Amounts in thousands of EUR)	
At December 31, 2019	**190.4**
(-) repayment	(15.0)
Subsidies	(2.1)
Financial expenses	5.7
At December 31, 2020	**179.0**

A reimbursable advance was granted to GeNeuro Innovation SAS by Bpifrance on September 16, 2011 in the form of a maximum € 600K, interest-free, reimbursable innovation loan facility to develop a diagnostic test and a therapeutic solution for polyradiculoneuropathies.

Installments could be drawn down under the Bpifrance contract as follows:

- € 200K at the effective date of the contract (drawn);
- € 250K on project progress (not drawn);
- € 150K at the end of the project (not drawn as project is not completed).

GeNeuro Innovation has only drawn the initial € 200K from this Bpifrance loan facility.

Further to the amendment signed on March 30, 2016, the quarterly repayments, based on the actually drawn amount of € 200K of the loan facility. were rescheduled as follows:

- € 7.5K from June 30, 2020 to March 31, 2021
- € 17.5K from June 30, 2021 to March 31, 2022
- € 27.5K from June 30, 2022 to March 31, 2023
- € 42.5K from June 30, 2023 to March 31, 2024
- € 55.0K from June 30, 2024 to March 31, 2025

Due to pandemic related delays, the first repayment was actually implemented as of September 30, 2020.

The agreement also provided for early repayments based on the ex-tax proceeds from the sale or assignment of licenses, patents or knowhow relating to all or part of the results of the aided project, as well as the ex-tax proceeds generated by the marketing or use by the beneficiary. The company has generated no proceeds in relation to this project and accordingly no early repayment has taken place.

This reimbursable advance does not bear annual interest and, as a result, has been treated under IFRS as an interest-free loan for the company. As the conditions are more favorable than market rates, the difference between the amount of the advance at historical cost and the advance discounted at market rates is considered as a public grant.

10.2 Loan from shareholder

In December 2018, the Company entered into a €7.5 million Credit Facility Agreement with one of its shareholders, GNEH SAS, itself a subsidiary of Institut Mérieux. Pursuant to this Credit Facility, the Company had the right to draw the amount of the amount in up to 4 instalments, until May 31, 2019. The full €7.5 million amount of the facility was drawn down before May 31, 2019. This facility was fully repaid in connection with the €17.5 million capital increase completed on January 31, 2020 and to which GNEH SAS participated by way of set-off with its shareholder loan.

Note 11: Defined benefit obligation

EMPLOYEE BENEFIT OBLIGATIONS Amounts in thousands of EUR	France	Switzerland	Total
At December 31, 2020	123.0	1,268.8	1,391.8
At December 31, 2019	110.4	3,025.0	3,135.4

11.1 French Employees

Defined benefit obligations for French employees result in a provision for a retirement indemnity to be paid by the Group at the date of retirement, measured in accordance with the applicable collective bargaining agreement of the pharmaceutical industry.

The main actuarial assumptions used to measure retirement packages are as follows:

ACTUARIAL ASSUMPTIONS	12/31/2020	12/31/2019
Age at retirement	Voluntary retirement age 65 to 67	
Collective agreements	Pharmaceutical industry	
Discount rate (IBOXX Corporates AA)	0.33%	0.77%
Mortality table	INSEE 2017	INSEE 2017
Salary revaluation rate	1.50%	1.50%
Turnover rate*	High	High
Social security expense ratio Management Non-management	 43% 41%	 43% 41%

* Turnover rates assumptions are summarized as follows:

- From 20 to 30 years old : from 18.3% to 10.9%
- From 30 to 40 years old : from 10.9% to 6.3%
- From 40 to 50 years old : from 6.3% to 4.2%
- From 50 to 65 years old : from 4.2% to 0%
- From 65 to 67 years old : 0%

The following shows the change in retirement indemnity:

POST EMPLOYMENT BENEFIT OBLIGATION (Amounts in thousands of EUR)	Post-employment benefit obligations
At December, 2018	**94.8**
Service costs	11.5
Financial costs	1.4
Sub-total included in profit or loss	**12.9**
Actuarial (gains) losses	2.7
At December, 2019	**110.4**
Service costs	11.9
Financial costs	0.8
Sub-total included in profit or loss	**12.7**
Actuarial (gains) losses	(0.1)
At December, 2020	**123.0**

Sensitivity analysis as at December 31, 2020

(Amounts in thousands of euros)		Turnover	
Sensitivity analysis	Low	Medium	Selected assumption : high
Post-employment benefit obligation	151	146	123
		Salary revaluation rate	
Sensitivity analysis	1%	Selected assumption: 1.5%	2%
Post-employment benefit obligation	118	123	129
		Discount rate	
Sensitivity analysis		Selected assumption: 0.33 %	0.83%
Post-employment benefit obligation		123	118

Sensitivity analysis as at December 31, 2019

(Amounts in thousands of euros)		Turnover	
Sensitivity analysis	Low	Medium	**Selected assumption : high**
Post-employment benefit obligation	143	136	**110**
		Salary revaluation rate	
Sensitivity analysis	1%	**Selected assumption: 1.5%**	2%
Post-employment benefit obligation	105	**110**	116
		Discount rate	
Sensitivity analysis	0.27%	**Selected assumption: 0,77%**	1.27%
Post-employment benefit obligation	116	**110**	105

The Group estimates that changes in other assumptions would cause no significant impact on liabilities.

11.2 Swiss Employees

The defined benefit obligation related to the so-called “Second Pillar” Swiss pension scheme is assessed using the following assumptions:

ACTUARIAL ASSUMPTIONS	12/31/2020	12/31/2019
Age at retirement	Voluntary retirement age : 64 female / 65 male	
Discount rate	0.15%	0.20%
Demographic basis	LPP 2020 generation	LPP 2015 generation
Salary increase	1.00%	1.00%
Pension increase	0.50%	0.50%
Interest credited on saving accounts	1.00%	1.00%
Turnover rate	10.00%	10.00%

Assumptions regarding the discount rate were revised at December 31, 2020 due to market conditions of continuing extremely low CHF corporate bond yields.

Mortality rate

Assumptions regarding future mortality are set based on advice, published statistics and experience. The weighted average duration of the defined benefit obligation included in the statement of financial position date is as follows:

	12/31/2020	12/31/2019
Weighted average duration of the defined benefit obligation	18.3	23.4

Changes in the defined benefit obligation and in the fair value of the plan assets are as follows:

Amounts in thousands of EUR	Defined benefit obligation	Fair value of plan assets	Benefit liability
At December 31, 2018	**5,538.2**	**3,837.5**	**1,700.7**
Service	276.7	-	276.7
Financial interests	46.5	34.5	12.0
Employee Contribution	178.8	178.8	-
Currency effects	224.2	151.1	73.1
Sub-total included in profit or loss	**726.2**	**364.4**	**361.8**
Benefits (paid) / received	**(296.5)**	**(296.5)**	**-**
Return on plan assets (excluding financial interests)	-	6.1	(6.1)
Actuarial changes arising from changes in financial assumptions	1,044.7	-	1,044.7
Other actuarial loss	180.5	-	180.5
Sub-total included in "Other Comprehensive Income"	**1,225.2**	**6.1**	**1,219.1**
Contributions by employer	**-**	**256.6**	**(256.6)**
At December 31, 2019	**7,193.1**	**4,168.1**	**3,025.0**
Service	414.6	-	414.6
Financial interests	12.4	6.5	5.9
Employee Contribution	135.1	135.1	-
Currency effects	29.7	17.2	12.5
Sub-total included in profit or loss	**591.8**	**158.8**	**433.0**
Benefits (paid) / received	**(2,108.9)**	**(2,108.9)**	**-**
Return on plan assets (excluding financial interests)	-	26.2	(26.2)
Actuarial changes arising from changes in demographic assumptions	(558.2)	-	(558.2)
Actuarial changes arising from changes in financial assumptions	46.9	-	46.9
Other actuarial gain	(1,467.2)	-	(1,467.2)
Sub-total included in "Other Comprehensive Income"	**(1,978.5)**	**26.2**	**(2,004.7)**
Contributions by employer	**-**	**184.5**	**(184.5)**
At December 31, 2020	**3,697.5**	**2,428.7**	**1,268.8**

Assumptions regarding the discount rate were revised at December 31, 2019 and 2020, due to market conditions of continuing extremely low CHF corporate bond yields; furthermore, in this context of continuing very low interest rates in CHF, the actuarial model equating discount rate and credit interest was deemed at December 31, 2019 to be no longer appropriate and the credit interest rate was increased to 1%, which is the LPP minimum.

Sensitivity analysis as at December 31, 2020 and as at December 31, 2019

Changes in certain actuarial assumptions could result in substantial changes in the post employment benefit obligation.

They can be summarized as follows on December 31, 2020 and 2019:

	on December 31, 2020			on December 31, 2019		
(Amounts in thousands of EUR)	**Salary revaluation rate**			**Salary revaluation rate**		
Sensitivity analysis	0.50%	**Selected assumption: 1%**	1.50%	0.50%	**Selected assumption: 1%**	1.50%
Post-employment benefit obligation	3,674.7	**3,697.5**	3,721.3	7,141.6	**7,193.3**	7,246.4
	Discount rate			**Discount rate**		
Sensitivity analysis	-0.35%	**Selected assumption: 0.15%**	0.65%	-0.30%	**Selected assumption:0.20 %**	0.70%
Post-employment benefit obligation	4,059.3	**3,697.5**	3,382.2	8,100.5	**7,193.3**	6,416.2
	Rate of pension increase			**Rate of pension increase**		
Sensitivity analysis	0.00%	**Selected assumption: 0.50%**	1.00%	0.00%	**Selected assumption: 0.50%**	1.00%
Post-employment benefit obligation	3,501.4	**3,697.5**	3,915.3	6,703.5	**7,193.3**	7,739.1

The estimated Company contributions to pension plans for the financial year 2021 amount to € 220K (based on the closing rate at December 31, 2020).
The categories of plan assets, based on an asset/liability matching analysis, and their respective allocation, are as follows:

Allocation in K€	12/31/2020	12/31/2019
Cash	53.4	104.2
Bonds	1,394.1	2,338.4
Shares	80.1	683.6
Real estate	359.5	-
Mortgages	332.7	633.5
Alternative investments	208.9	408.5
Total	**2,428.7**	**4,168.2**

The benefit payments for the next ten years (in euros) are broken down as follows:

2021	103.0K
2022	77.4K
2023	74.2K
2024	49.2K
2025	43.1K
2026-2030	1,169.3K

Note 12: Other current liabilities

12.1 Trade payables

The amount of trade payables is consistent with the expenses incurred by the Group as part of its clinical trials program and the payment terms agreed by the suppliers and service providers. The decrease at December 31, 2020 is attributable to the payment in early 2020 of suppliers linked to clinical trials completed during 2019.

12.2 Other current liabilities

OTHER CURRENT LIABILITIES (Amounts in thousands of EUR)	12/31/2020	12/31/2019
Personnel and related accounts	468.5	733.2
Social security and other social institutions	250.5	208.0
Other	9.2	8.0
Accrued liabilities	765.8	576.7
Advances received from Servier - ANGEL-MS study	-	183.6
Total other current liabilities	**1,494.0**	**1,709.5**

The advances received from Servier, in connection with the balance of unused advances for the ANGEL-MS study, were repaid during 2020.

The information presented for the period ended December 31, 2019, has been modified from the one presented in note 12.2 of the annual financial report for the fiscal 2019 financial year, due to referencing errors which led to the omission of certain items in personal and related accounts (for K€ 136.5), to an incorrect value of social security and other social institutions (K€ 302.6 compared to the correct value of K€ 208 as per above) and to the omission of the accrued liabilities item (K€ 576.7). The total amount of other current liabilities shown in the statement of financial condition, for K€ 1,709.5, was however correct.

Note 13: Income

INCOME (amounts in thousands of EUR)	12/31/2020	12/31/2019
Total income	-	-

No income was recognized during 2019 or 2020.

13.1 Other income

Other income in 2019 related to rental income derived from the sub-leasing of the Company's former premises, under a contract that ran until February 2019, when the master tenancy agreement for the premises expired.

Note 14: Breakdown by nature of expenses and income

14.1 Research and development expenses

RESEARCH AND DEVELOPMENT EXPENSES (Amounts in thousands of EUR)	12/31/2020	12/31/2019
Studies and research	(1,930.3)	(2,645.4)
Intellectual property	(339.9)	(538.3)
Raw materials and consumables	(28.1)	(36.0)
Rental expenses	(39.7)	(39.8)
Professional fees	(239.4)	(355.0)
Payroll expense (1)	(1,935.1)	(2,261.7)
Amortization and depreciation	(176.4)	(197.7)
Share-based payment expense	(37.6)	(60.2)
Other	13.4	(40.6)
Research and Development Expenses	**(4,713.1)**	**(6,174.7)**
Research tax credits	553.9	912.4
Other subsidies	2.1	-
Subsidies	**556.0**	**912.4**

(1) After deduction of € 25.4K of partial unemployment indemnities received from the French government in connection with the COVID-19 lockdown restrictions in the spring of 2020.

14.2 General and administrative expenses

GENERAL AND ADMINISTRATIVE EXPENSES (Amounts in thousands of EUR)	12/31/2020	12/31/2019
Travel and assignments expenses	(102.1)	(381.2)
Office expenses	(39.7)	(47.9)
Rental expenses	(37.4)	(22.6)
Professional fees	(994.0)	(1,255.2)
Payroll expense	(1,755.4)	(1,753.0)
Tax expense	(38.2)	(26.5)
Insurance expense	(25.5)	(29.4)
Postal and telecom expenses	(78.2)	(47.8)
Amortization and depreciation	(158.2)	(157.1)
Share-based payment expense	(68.8)	(22.7)
Other	(4.5)	(0.7)
General and administrative expenses	**(3,302.0)**	**(3,744.1)**

Note 15: Financial income (expenses), net

Net financial income (expenses) are broken down as follows:

FINANCIAL INCOME (EXPENSES), NET (Amounts in thousands of EUR)	12/31/2020	12/31/2019
Other financial income	3.1	5.9
Financial income	**3.1**	**5.9**
Interest expense related to the Loan from shareholder	(72.3)	(441.9)
Share based expense related to capital increase at discount to market	(1,364.4)	-
Other financial expenses	(7.9)	(6.5)
Foreign exchange losses	(61.7)	(28.1)
Financial expenses	**(1,506.3)**	**(476.5)**
Financial income (expenses), net	**(1,503.2)**	**(470.6)**

Because the capital increase was not open to all existing shareholders but was restricted to certain selected institutional investors, pursuant to IFRS 2 the discount between the share price prior to the capital increase (€3.18 per share) and the actual issue price (€2.95 per share) is considered a share based payment, resulting in a charge of € 1,364 K within financial expenses, with a corresponding amount added to reserves within shareholders' equity.

Note 16: Income tax

Group income tax (expense) / income

INCOME TAX (EXPENSE) / INCOME (Amounts in thousands of EUR)	12/31/2020	12/31/2019
Deferred tax	-	-
Income tax (expense) / income	-	-

Income tax rates and losses carried forward

Although the Group's functional currency is the euro, the parent company, GeNeuro SA, must establish its Swiss tax returns in CHF. Accordingly, carried-forward tax losses are denominated in CHF and are converted for information purposes hereunder in euros at the December 31, 2020 closing rate.

At December 31, 2020, GeNeuro SA had carried-forward tax losses of € 50,107K (CHF 54,126K converted at the December 31, 2020 closing rate), compared with € 44,196K at December 31, 2019 (CHF 47,969K), split as follows:

€ 10,697.5K	originated in	2020	and expiring in	2028
€ 4,440.3K	originated in	2019	and expiring in	2027
€ 5,858.2K	originated in	2018	and expiring in	2026
€ 4,755.3K	originated in	2017	and expiring in	2025
€ 13,746.2K	originated in	2016	and expiring in	2024
€ 6,159.9K	originated in	2015	and expiring in	2023
€ 4,450.1K	originated in	2013	and expiring in	2021

The income tax rate applicable to the Company is the rate currently applicable in the Canton of Geneva, Switzerland, which is 14% (23.7% in 2019).

GeNeuro Innovation SAS had carried forward tax losses of € 1,100K as at December 31, 2020.
The income tax rate applicable to GeNeuro Innovation SAS is the French income tax rate of 28%. This rate will decrease gradually to reach 25 % in 2022.

GeNeuro Australia Pty Ltd had carried forward tax losses of € 2,946K (AUD 4,680) as at December 31, 2020.
The income tax rate applicable to GeNeuro Australia Pty Ltd is the Australian income tax rate of 27.5%.

Reconciliation between theoretical tax and effective tax

(Amounts in thousands of EUR)	12/31/2020	12/31/2019
Net loss	(8,962.3)	(9,460.8)
Income tax expense	-	-
Loss before tax	**(8,962.3)**	**(9,460.8)**
Current tax rate in Geneva	14.00%	23.70%
Theoretical income tax at current tax rate in Geneva	1,254.7	**2,242.2**
Items not subject to tax	162.9	114.6
Share-based payments (1)	(232.7)	(18.9)
Unrecognized tax losses	(1,091.2)	(2,305.3)
Effect of different tax rates	(93.7)	(32.6)
Income tax (expense)	-	-
Effective tax rate	0.00%	0.00%

(1) Deferred tax asset is not recognized because it is not probable that future profits would arise that would allow the deferred tax asset to be recovered.

Taxes shown on the profit and loss statement are not taxes on income but on the Swiss parent's net capital.
Items not subject to tax include mainly research tax credits (non-taxable operating income in France and Australia).
Unrecognized tax losses take into account for 2019 the fact that the intercompany dividend of €5 million paid in 2019 by the French subsidiary to its Swiss parent is not taxable in Switzerland; and for 2020 the fact that the Swiss parent has recognized an impairment of €2.7 million against its participation in and loans to its Australian subsidiary, which will be liquidated in 2021 due to the lack of activity in that country in the foreseeable future.

In 2020, the effect of different tax rates between the French tax rate of 28% and the Geneva tax rate of 14% is €91.7K, partly offset by the -€0.6K difference in tax rates between the Australian tax rate of 27.5% and the Geneva tax rate of 14%. In 2019, the effect of different tax rates between the French tax rate of 33.33% and the Geneva tax

rate of 23.7% was € 46.7K, partly offset by the €14.1K difference in tax rates between the Australian tax rate of 27.5% and the Geneva tax rate of 23.7%.

Nature of deferred taxes

NATURE OF DEFERRED TAX (Amounts in thousands of EUR)	12/31/2020	12/31/2019
Temporary differences	222.1	775.3
Swiss defined benefit obligation	*183.3*	*734.8*
Other	*38.8*	*40.5*
Loss carryforward Australia	13.1	*23.9*
Loss carryforward France	190.9	272.7
Loss carryforward Switzerland (1)	7,065.7	11,659.2
Total of items with a nature of deferred tax assets	**7,491.8**	**12,731.1**
Unrecognized deferred tax assets	(7,488.1)	(12,727.8)
Net total of deferred tax assets	**3.7**	**3.3**
Temporary differences	(3.8)	(3.3)
Total of deferred tax liabilities	**(3.8)**	**(3.3)**
Net total of deferred tax assets (liabilities)	-	-

(1) Taking into account the fact that the intercompany dividend received by the parent company in 2019 is not taxable in Switzerland, thereby increased the tax loss carryforward.

Given the uncertainty related to the Company's ability to generate profits against which it would be able to apply the carried forward losses, management did not recognize any deferred tax assets on the Group's carried forward losses.

Note 17: Losses per share

Basic losses

"Basic losses per share" is calculated by dividing the net income attributable to the Company's shareholders by the weighted average number of ordinary shares issued during the financial year.
Diluted losses per share are calculated by adjusting basic losses per share for the dilutive effect of instruments giving deferred rights to share capital (warrants, bonds, options). When the Group is in a loss-making position, these instruments are not treated as dilutive since they would reduce the loss per share. For the periods reported, diluted losses per share are therefore identical to basic losses per share.

BASIC LOSS PER SHARE	12/31/2020	12/31/2019
Weighted average number of shares outstanding	19,969,293	14,562,166
Number of potentially dilutive shares from exercise of options (1)	110,979	243,070
Net loss for the period (in thousands of EUR)	(8,962.3)	(9,460.8)
Basic loss per share (EUR/share)	**(0.45)**	**(0.65)**
Diluted loss per share (EUR/share)	**(0.45)**	**(0.65)**

(1): Number of potentially dilutive shares from options outstanding at December 31, 2020 – excluding 777,194 "out of the money" options with a weighted average exercise price of €10.00 per share. The shares resulting from the exercise of "in the money" options are not taken into account in the calculation of diluted loss per share as these shares would have an anti-dilutive effect and would decrease the loss per share.

The loss per share in 2020 includes EUR 0.07 per share due to the share based expense of the capital increase of January 2020 (see notes 8 and 15).

Note 18: Related parties

18.1 Compensation due to members of the Board and Officers

One executive officer of the Company is also a member of the Board of Directors.
Aggregate compensation of the members of the Board and Officers was as follows:

COMPENSATION DUE TO MEMBERS OF THE BOARD AND OFFICERS (Amounts in thousands of EUR)	12/31/2020	12/31/2019
Fixed compensation due	1,073.9	1,324.5
Variable compensation due	296.5	312.9
Benefits in kind	32.4	36.1
Employer contribution to pension scheme and other social contributions	381.1	398.7
Share-based payments	87.8	0.0
Attendance fees	79.5	76.4
TOTAL	**1,951.2**	**2,148.6**

Note : variable compensation due was paid in March of the following year.
The Company has signed contracts with three members of its Board of Directors; two of the contracts were entered into in 2015 and one in 2016. In accordance with these contracts and as compensation for services rendered, the Company recorded attendance fees of € 76K in 2019 and € 79K in 2020.

No post-employment benefits were granted to members of the Board or Officers, with the exception of the mandatory and additional defined benefit scheme applicable for Swiss employees and executives under the second pillar of the Swiss social security system, as described in Note 2.19.

All compensation components were fully paid in the year, except for the share-based payments compensation, which is not due to be settled in cash, and the variable compensation which was paid in each case in the subsequent year.

The variable components of compensation were allocated on the basis of performance criteria.

The methods used to calculate the fair value of share-based payments are explained in Note 9. There were no share-based payments accounted for in the 2019 financial year.

18.2 Related party transaction with Servier

In 2014, the Company signed a cooperation and development agreement (the "Servier Agreement") with Laboratoires Servier, France for its lead compound in the field of multiple sclerosis, which was terminated by Servier in 2018 following its decision not to exercise its option for a license. Servier is a privately-owned French pharmaceutical company that is also a shareholder of GeNeuro SA. Pursuant to the Servier Agreement, Servier bore all costs related to its ANGEL-MS clinical trial and had made advances to GeNeuro in this regard. At December 31, 2019, there remained € 183.6K of unused advances, which GeNeuro reimbursed to Servier in 2020.

18.3 Related party transaction with bioMérieux

The Company signed an exclusive licensing contract with bioMérieux in 2006. BioMérieux is a French listed company, majority-owned by Institut Mérieux; bioMérieux and Institut Mérieux are the sole shareholders of GNEH SAS, which owns 33.88% of GeNeuro SA. The key elements of the licensing contract are disclosed in Note 19.2.

18.4 Related party transaction with GNEH SAS

In December 2018, the Company entered into a €7.5 million credit facility agreement with GNEH SAS, which credit facility was reimbursed through the capital increase completed in January 2020 – refer to Note 10.2. In January 2020, the Company completed a capital increase of €17.5 million through a private placement reserved to selected institutional investors, to which GNEH SAS participated to in the amount of €7.5 million, by way of set-off with its shareholder loan. The discount at which this private placement was completed led to the recognition of a share-based payment – refer to Note 8.

Note 19: Off-balance-sheet commitments

19.1 Contingent liabilities and commitments in respect to the licensing Agreement with bioMérieux

In 2006, the Company signed an exclusive license agreement with bioMérieux, France (the "2006 Agreement"), for the sole purpose of developing, manufacturing and selling products covered under bioMérieux patents, with bioMérieux retaining the rights pertaining to diagnostics.

This 2006 Agreement provides for payments in Swiss francs. Amounts in euros presented below are provided for information only, using the average foreign exchange rate of the related year.

Under this 2006 Agreement, the Company is committed to make the following payments:

- An up-front payment of CHF 150K, paid in 2006 (€ 138K);
- An annual contribution towards patent maintenance fees of CHF 50K (approximately € 46K);
- Milestone payments up to a total sum of CHF 72.6 million (approximately € 67.0 million):
  - On commencement of the Phase IIa clinical trial in 2012, the first milestone was reached, triggering a payment by the Company of CHF 200K (approximately € 185K);
  - The start of the Phase IIb clinical trial in 2016 triggered a payment by the Company of CHF 1,000K (€ 925K).
  - The start of a Phase IIa clinical trial in Type 1 diabetes triggered a contingent payment of CHF 200K (approximately € 185K), to be paid only if certain conditions (such as entering a Phase III clinical trial, or being sub-licensed for that indication) are met.
- Royalties based on GeNeuro net licensing revenues and GeNeuro net sales.

In 2015, pursuant to an exclusive license agreement on companion diagnostics (the "Diagnostics Agreement"), bioMérieux also granted an exclusive license on companion diagnostics. This Diagnostics Agreement commits the Company to make milestone payments of up to € 100K.

On the commencement of the Phase IIb clinical trial in 2016, a first milestone was reached, triggering an amount of € 50K paid by the Group to bioMérieux. The balance of € 50K will be due in the event of the start of a Phase III trial. No royalties are due to bioMérieux under the Diagnostics Agreement.

19.2 Contingent liabilities and commitments in respect to the licensing Agreement with the US National Institutes of Health (NIH).

In October 2018, the Company has entered into an Exclusive License Agreement with the National Institute of Neurological Disorders and Stroke (NINDS), part of the U.S. National Institutes of Health (NIH). The agreement covers the development of an antibody program to block the activity of pHERV-K Env (pathogenic envelope protein of the HERV-K family of Human Endogenous Retroviruses), a potential key factor in the development of ALS. Pursuant to this agreement, the Company made an up-front payment of USD 50K (€ 44K), and is committed to annual minimum payments of USD 25K (approximately € 22K) and milestone payments up to a total sum of USD 11.6 million (approximately € 9.9 million) subject to clinical development achievements; in addition, GeNeuro will have to pay the NIH royalties based on its net licensing revenues and net sales.

Note 20: Financial risk management and assessment

GeNeuro may find itself exposed to various types of financial risk: market risk, liquidity risk and credit risk. GeNeuro is implementing measures consistent with the size of the Group to minimize the potentially adverse effects of those risks on its financial performance.

GeNeuro's policy prohibits the use of financial instruments for speculative purposes.

Market risk

Interest rate risk

Interest rate risk reflects the Group's exposure to fluctuations in interest rates in the market. As the Group has no floating-rate debt, the Group is not at risk of increases in debt servicing costs (refer to Note 10 for extent and nature of fixed rate debt obligations). Changes in interest rate could affect returns achieved on cash and fixed term deposits but this risk is not considered material given the current low returns on deposits held by the Group.

Foreign exchange risk

Foreign currency risk is the risk that the fair value or future cash flows of a financial instrument will fluctuate because of changes in foreign exchange rates. The Group's exposure to the risk of changes in foreign exchange rates relates primarily to the Group's operating activities in Switzerland (when expense is denominated in a different currency from the Group's presentation currency).

No currency derivatives were outstanding at December 31, 2020.

Any major development in the Group activity may result in an increase of its exposure to exchange rate risk. Should such increase materialize, the Group would consider adopting an appropriate policy to hedge such risks.

Equity risk

The Company does not hold long or short-term tradable equities on any regulated market.

Liquidity risk

Since its incorporation, the Group has primarily funded is growth through capital increase and additional funds provided by research collaborations and research tax credits. The Group never had recourse to bank loans. As a result, the Group is not exposed to liquidity risk through requests for early repayment of loans.

Significant R&D expenses have been incurred from the start of the Group's activities, generating negative cash flows from operating activities, except in 2015 following the milestone payment by Servier of € 17.5 million.

Cash outflows related to operating activities amounted to € 7,159K compared with € 9,893K for the financial years ended December 31, 2020 and 2019, respectively.

As at December 31, 2020, the Group's cash & cash equivalents amounted to € 6,843K (December 31, 2019: € 5,931K).

As disclosed in Note 2.1 of the Notes to the consolidated financial statements, the Board of Directors believes that, taking into account the projected lower cash outflow from its operating activities for 2021 based on the operating plans, as well as the eventual mitigation measures it has approved, the Group has sufficient financial resources to cover its operating costs for at least one year from the date these financial statements are issued and, as a result, is presenting the consolidated financial statements of the Group on a going-concern basis.

Breakdown of financial liabilities, trade payable and other current liabilities by maturity

The following table shows the breakdown of financial liabilities, trade payable and other current liabilities in the period presented:

	12/31/2020			
(Amounts in thousands of EUR)	**Gross amount**	**< 1 year**	**1 ≥ 5 years**	**> 5 years**
Shareholder loan	-	-	-	-
Reimbursable advance	185.0	50.0	135.0	-
Amounts due under lease contracts	1,431.0	257.8	993.7	179.5
Sub-total	**1,616.0**	**307.8**	**1,128.7**	**179.5**
Discounted interest on reimbursable advance	*(6.0)*			
Interest component of lease contracts	*(43.3)*			
Net financial liabilities	***1,566.7***			
Current financial liabilities	*293.3*			
Non-current financial liabilities	*1,273.4*			
Trade payables	**540.4**	**540.4**	**-**	**-**
Other current liabilities	**1,494.0**	**1,494.0**	**-**	**-**

	12/31/2019			
(Amounts in thousands of EUR)	**Gross amount**	**< 1 year**	**1 ≥ 5 years**	**> 5 years**
Shareholder loan (including accrued interest)	7,689.0	7,689.0	-	-
Reimbursable advance	200.0	7.5	192.5	-
Amounts due under lease contracts	686.6	337.2	349.3	-
Sub-total	**8,575.6**	**8,033.7**	**541.8**	**-**
Discounted interest on reimbursable advance	*(9.6)*			
Interest component of lease contracts	*(57.0)*			
Net financial liabilities	***8,509.0***			
Current financial liabilities	*8,025.6*			
Non-current financial liabilities	*483.4*			
Trade payables	**1,247.1**	**1,247.1**	**-**	**-**
Other current liabilities	**1,709.5**	**1,709.5**	**-**	**-**

The Group will continue to have major funding requirements in the future to fuel its strategy to develop temelimab and new compounds through clinical trials. The precise extent of funding required is difficult to predict accurately, and will largely depend in part on factors outside the Group's control.

Areas subject to significant uncertainty include but are not limited to:

- the ability to conduct successful clinical trials in multiple sclerosis, type 1 diabetes and other indications, including the capacity to recruit in a timely manner patients for those studies,
- the change in the regulatory landscape,
- the approval for other drugs on the market that would potentially reduce the attractiveness for the approach developed by GeNeuro.

Should the Group find itself unable to finance its own growth through partnership agreements, the Group would be dependent on other sources of financing, including equity funding or research grants. See also Note 22.

Credit risk

The Group's credit risk is associated with deposits at banks and financial institutions and with other receivables. The Group seeks to minimize the risk related to banks and financial institutions by placing cash deposits with highly rated financial institutions. The maximum amount of credit risk is the carrying amount of the financial assets. As outstanding receivables include mainly research tax credits granted by France and Australia, the Group does not carry significant credit risk.

Cash balances held at December 31, 2020		Short-term credit rating of financial institution	
	% of cash balances	Standard & Poors	Moody's
Bank 1	14.0%	A-1+	P-1
Bank 2	44.5%	A-1+	P-1
Bank 3	41.5%	A-1	P-1
Total	100.0%		

Note 21: Auditors' fees

Audit fees due by the Group to its auditors, PricewaterhouseCoopers SA, were the following:

Audit fees (Amounts in thousands of EUR)	2020 Financial Year	2019 Financial Year
Audit Fees	261.4	367.3
Assurance services related to share issuance	94.8	9.2

Note 22: Post balance sheet events

In January 2021, the Company has initiated the process of liquidating its Australian subsidiary due to the lack of clinical trial or other research activities in Australia in the foreseeable future. This liquidation, which is expected to be completed during the second quarter of 2021, is not expected to generate significant costs and will reduce ongoing administrative costs of the subsidiary, which amounted to € 8K in 2020.

CHAPTER 19.
ADDITIONAL INFORMATION

19.1 Equity Capital

19.1.1 Amount of the Equity Capital

The Company's equity capital is CHF 1,029,515.95 divided into 20,590,319 bearer shares, each with a nominal value CHF 0.05, all fully paid.

19.1.2 Securities Not Representing Equity

None.

19.1.3 Buy-back by the Company of its Own Shares

Since May 4, 2016, the Company has entered into a liquidity contract with Gilbert Dupont, a Paris based investment services provider. The main purposes of a liquidity contract on shares, where implemented pursuant to the accepted market practice established by the French Financial Markets Authority (Autorité des marchés financiers - the "**AMF**"), are to improve liquidity of share transactions and regularity daily traded prices of the Company's shares and thus to avoid price swings that would not be justified by the market trend.

During the 2020 financial year, through the liquidity contract the Company purchased 128,306 (2019: 107,032) GeNeuro common shares (of CHF 0.05 nominal value) and sold 119,542 (2019: 88,658) GeNeuro common shares (of CHF 0.05 nominal value), at an average weighted purchase price of €3.10 per share (2019: €3.63) and an average weighted sale price of €3.13 per share (2019: €3.62). In addition, the Company purchased 25,000 (2019: 0) GeNeuro common shares (of CHF 0.05 nominal value) in order to partly cover "in the money" vested stock options granted to employees and management.

At December 31, 2020, the Company held, through the liquidity contract, 93,645 (2019: 84,881) GeNeuro common shares (i.e., 0.455% of its equity at December 31, 2020; 2019: 0.579%).

On December 31, 2020, the Company owned 139,645 (December 31, 2019: 105,881) of its own shares, including shares owned through the liquidity contract and other treasury shares.

Under Swiss law, a company may acquire its own shares only if it has free equity available to it equivalent to the amount of the expense necessary to acquire the shares and if the nominal value (paid-in capital) of all such shares does not exceed 10% of the equity capital.

Voting rights related to treasury shares and the rights attaching to them are suspended as long as the Company owns or holds the shares. In addition, the Company must credit to a special reserve (a reserve for treasury shares) an amount equal to the acquisition value of the treasury shares. This reserve may be reduced only to the extent of the acquisition value of the treasury shares if the shares are sold or cancelled.

Furthermore, when the Company holds or owns a majority stake in a subsidiary, acquisition of the Company's shares by such subsidiary is subject to the same limitations and the same consequences as acquisition by the Company of its own shares.

The Company's Board of Directors has the authority to implement a program to buy back the Company's shares subject to Swiss law, applicable EU regulations, the accepted market practice established by the AMF and the General Rules and Regulations of the AMF.

19.1.4 Conditional Equity Capital

The Company's share capital may be increased by a maximum amount of 2,198,717 shares equivalent to 10.7% of the existing share capital, through the exercise of options granted to the Company's managers, employees, and consultants, as based on rules approved by the Board of Directors. The shareholders' pre-emptive rights do not apply to the new shares issued.

In this connection, the Company's Board of Directors, approved various incentive plans for management and employees, as follows:

- Stock options with an exercise price of €13 per share : these include options under a Performance Share Option Units (PSOU) Plan, for the Company's top management, which matured on December 31, 2018; on February 27, 2019, the Board of Directors reviewed the service condition and the achievement of the performance condition and made a final determination as to the number of options to be granted; as a result, the total of 676,400 PSOUs granted were replaced by a total of 672,235 stock options, with an exercise price of €13 per share and a term of 5 years. The Board also approved an incentive plan for stock options on February 23, 2017, when it granted 7,500 stock options to certain executive managers; on February 4, 2018, it also granted 22,500 stock options to executive managers. All these options have a

term of five years from award date; the options under the PSOU Plan are fully vested whereas the others vest over four years (25% after one year, then 12.% every six months).

- Stock options with an exercise price of €2.73 per share: on July 4, 2018, the Board of Directors approved a Loyalty Bonus Option Plan and on February 27, 2019 made the final determination under this plan and granted a total of 158,540 to the Group's employees; these Loyalty Bonus Options have a 10-year term and vest over four years (25% after one year, then 12.% every six months).
- Stock options with an exercise price of €3.34 per share: on March 5, 2020, the Board of Directors approved a new Option Plan and granted a total of 75,750 to management and certain employees; these options have a 10-year term and vest over four years (25% after one year, then 12.% every six months).
- Stock options with an exercise price of €2.95 per share: on December 11, 2020, the Board of Directors granted a total of 15,000 to certain managers; these options have a 10-year term and vest over four years (25% after one year, then 12.% every six months).

Furthermore, the share capital of the Company may also be increased by a maximum amount of 5,130,341 shares equivalent to 24.9% of the existing share capital by exercising options and conversion rights attaching to the issuance of debt securities or similar securities of the Company or other financial instruments by the Company, as defined in Swiss law. The preferential subscription rights will not apply to the shares so issued.

In the case of debt securities or other similar securities, the preferential subscription right of shareholders may be restricted or eliminated by the Board of Directors, if the issuance is made with a view to financing an acquisition of companies, parts of companies, or equity stakes.

In the event of the elimination of preferential subscription rights, debt securities and similar securities or any other financial instrument will be offered at market conditions. The exercise date for options may not be later than five years from the issue date and for conversion rights 10 years from the issuance of debt or similar securities. The exercise price for the acquisition of new shares will correspond to the market price on the date of issuance.

19.1.5 Securities Convertible into Equity Capital

On the filing date of this Universal Registration Document, the securities and other instruments still outstanding and carrying a right to be converted into equity capital consisted of stock options granted to certain executives and consultants of the Company (such options are described in detail in Section 13.1.3, "Stock Options and Grants of Free Shares" of this Universal Registration Document. In the event of the full exercise of the instruments carrying a right to equity capital granted and issued on this day, this would lead to the issuance and subscription of 1,064,973 shares, resulting in a dilution of 4.9% based on the existing number of shares of the Company on the filing date of this Universal Registration Document (such options and rights are described in section 13.1.3 of the Universal Registration Document).

19.1.6 Authorized but Unissued Shares, Undertakings to Increase Equity Capital

Under Swiss law and pursuant to the resolutions of the shareholders' annual meeting of May 27, 2020, the Board of Directors is authorized to increase the Company's equity securities by a maximum amount of 10,295,159 shares representing 50% of its then-existing capital. The Board of Directors may implement this capital increase entirely or in installments. This authorization, which is recorded in the Company's articles of incorporation, as amended, lapses on May 27, 2022.

Under Swiss law, in the case of authorized capital, the Board of Directors determines freely the issue price, the types of capital contributions, and the date from and after which the new shares will have dividend rights as well as other terms and conditions of the share issue that are not reserved to the shareholders.

The Board of Directors decides on the allocation of the preferential subscription rights of shareholders that are not exercised. However, the Board of Directors may eliminate or limit the preferential subscription right only:

- for warrants granted in the usual way to financial institutions that are firm acquirers involved with the Company's IPO (firm underwriting) (overallotment option);
- to acquire companies, parts of companies, and equity stakes; or
- to place new shares on international capital markets by a public offering or private placement with institutional investors at the price that results from book-building.

19.1.7 Equity Capital of Any Group Company Subject to an Option or Conditional or Unconditional Agreement Placing it Under Option

The Company has granted options or warrants to various executive officers and employees that give them the right to acquire the Company's shares. Such options are described in detail in Section 13.1.3 of this Universal Registration Document.

19.1.8 Changes to Equity Capital

The Company was registered at the commercial register of Geneva, Switzerland on February 6, 2006, with an initial equity capital of CHF 100,000, fully paid up.

The equity capital was thereafter increased, on several occasions, to reach CHF 1,029,515.95 as of the filing date of this Universal Registration Document.

Other than the capital increase described under section 10.3 Recent Financing, there was no change to the Equity Capital during the last two financial years.

19.1.9 Pledges

There is, to the Company's knowledge, no pledge on its share capital.

19.2 Articles Of Association

19.2.1 Company Purposes (Article 3 of the Articles of Association)

The Company's principal purpose is the research, development, manufacture, and sale of products used, in particular, for therapeutic purposes, especially in the field of healthcare.

The Company may engage in any activity linked, directly or indirectly, to its company purpose or that could promote it.

19.2.2 Management and Administration of the Company

The Company is managed and administered by a Board of Directors.

19.2.2.1 Board of Directors (Section 4 of the Articles of Association)

The Company is managed and administered by a Board of Directors consisting of a minimum of five directors and up to 10 directors elected individually at a general shareholders' meeting.

The Swiss Code of Obligations does not allow legal entities to act or serve as members of the Board of Directors, but legal entity's representatives are eligible in its place and stead.

The Board of Directors includes a chairman, and may include a vice chairman and a secretary, who may but need not be members of the Board. If applicable, the vice chairman and secretary are appointed by the Board of Directors.

The Directors' term of office is one year. The term of office of a Director ends at the end of the next ordinary general shareholders' meeting considering and voting on the financial statements for the year just ended.

Directors are eligible for re-election; they may be removed at any time by action taken at a general shareholders' meeting.

The Chairman of the Board of Directors is elected at a general shareholders' meeting.

The term of his/her responsibilities as Chairman is one year. The Chairman's term of office ends at the end of the next ordinary general shareholders' meeting considering and voting on the financial statements for the year just ended.

The Chairman is eligible for re-election; he/she may be removed at any time by action taken at a general shareholders' meeting.

In the event of a vacancy during a term of office, the Chairman shall be appointed by the Board of Directors.

Subject to the responsibilities of the committees and the management delegation set forth in the Company's internal organizational rules and procedures, the Chairman manages and directs the work of the Board of Directors on which he/she reports at a general shareholders' meeting. She/he is responsible for the operation of the Company's management bodies and, in particular, ensures that the Directors are able to perform their responsibilities.

Together with management, the Chairman shall transmit to the Board of Directors, on a timely basis, information on all aspects of the Company that could influence its decisions, actions, and supervision.

The Board of Directors meets as often as the Company's business and affairs require, but at least four times a year.

Meetings of the Board of Directors are called by the Chairman in writing (letter, fax, email, or any other similar notice). If the Chairman is unable to act, meetings of the Board of Directors may also be called by the Vice Chairman.

Each member of the Board of Directors may ask the Chairman at any time to call a meeting of the Board of Directors to consider and act on a special agenda or ask that certain items be placed on the agenda sent with the notice.

Notices of meetings are to be sent upon 10 days' prior notice. In the event of an emergency, the Chairman may set a shorter period. The notice of meeting will contain the agenda items as well as the documents necessary for the Board of Directors to transact business, presented clearly and concisely. If it is not possible to provide the documents before the meeting, the Chairman is to give members of the Board of Directors sufficient time to familiarize themselves therewith before beginning the meeting.

As a general matter, persons responsible for an agenda item are to be present at the meeting. It should be possible to contact persons who are indispensable for answering questions and in a position to provide a better understanding of various points. The Chairman may invite members of management, employees, or third parties to take part in meetings of the Board of Directors for all, or any part, of the agenda.

For important matters, the Board of Directors may consult independent outside experts at the Company's expense.

Decisions by the Board of Directors may be taken at a meeting, telephonic conference, videoconference, or any other means allowing for a discussion.

If the Board of Directors has several members, its actions are to be taken at a meeting by a majority of the votes cast by the members present; provided, however, that they represent a majority of the Board (quorum).

Decisions of the Board of Directors may also be taken by a majority vote of members of the Board of Directors in the form of a written consent (by letter, fax, or email) to a proposal by the Chairman, as long as the proposal is submitted to all members, and none of them requests a discussion.

In the event of a tie vote, the Chairman's vote shall prevail.

Actions relating to formalities linked to capital increases, future payments of paid-in capital, or an issuance of coupons may also be taken by a single Director, and no quorum will be necessary.

Minutes of the deliberations and discussions of the Board of Directors are to be prepared, even when only a single Director takes part, and must be signed by the Chairman and the secretary of the meeting. The minutes must list the members present. The Chairman shall be responsible for the content and retention of Board minutes.

Each member of the Board of Directors has the right to obtain information about the Company's business and affairs. During meetings, each Board member may ask for information from the other members, as well as from members of management. Outside of meetings, Directors are to send their requests for information to the Chairman.

The Board of Directors may take decisions on any and all matters not reserved by law or the Articles of Association to shareholders at a general meeting and manage the Company's business and affairs to the extent there has been no delegation to management.

The Board of Directors represents the Company vis-à-vis third parties. The Board of Directors may give signature authority to its members, on a case-by-case basis, by registration with the commercial register. To the extent a Director is a member of management, management's internal rules will determine his/her authority.

The Board of Directors has the following nontransferable and inalienable attributions:

i. exercising the highest-level management of the Company and issuing necessary instructions, especially for determining the Company's strategy and general resources for achieving it, the ultimate supervision of management and of the persons to whom it is delegated, decisions to develop, terminate, acquire or sell strategic activities, and the initiation of and withdrawal from strategically important litigation;
ii. setting the basic principles in respect of the organization of the Company's administration and management;
iii. appoint and remove the persons responsible for management and representation;
iv. setting the compensation of the Directors and management, particularly the compensation strategy and structure of the compensation of Directors and management within the framework provided by law and regulations and the Articles of Association, by guidelines relating to the workplace pensions of members of the Board of Directors and management, and by proposals at the general shareholders' meeting to consider and act on approving the total compensation of the Board of Directors and management, setting the individual compensation of the Directors and members of management and preparing a report on compensation to be submitted to a general meeting of shareholders;
v. creating a system for identifying and handling risks and internal controls in compliance with law and the Articles of Association;
vi. setting the principles applicable to bookkeeping and accounting, financial controls, and the strategic financing plan, especially the establishment of the accounting principles, and determination of the accounting reference, and the establishment of an appropriate system of financial planning, including, especially, the annual budget;
vii. preparing the management report for the shareholders at an ordinary general meeting including approval of the financial statements);
viii. exercising the highest-level supervision of persons responsible for management to ensure, among other things, compliance with law, the Articles of Association, rules, regulations, and instructions given;
ix. calling and giving notice of general shareholders' meetings and preparing proposals by the Board of Directors;
x. carrying out decisions approved at general shareholders' meetings taken in compliance with law and the Articles of Association;
xi. adopting the rules relating to the Company's communications and public relations strategy; and
xii. informing a court in the event of over-indebtedness.

In addition, the Board of Directors is responsible for ensuring that appropriate measures (such as embargoes or black-out periods) are taken for purchases and sales of the Company's shares or relevant rights at critical moments, such as in connection with an acquisition proposal or prior to a press conference or disclosure of the Group's results (please see the rules and regulations relating to the obligations of Directors linked to the listing of the Company).

Each year the Board of Directors will report on its activity, on the activity of its committees, and on the principles applicable to the organization and delegation of management. On that occasion it will review the relevance of the Board of Directors' organizational rules and procedures and other rules and regulations that it has issued and, if appropriate, adapt them to new requirements.

19.2.2.2 Management[172]

The Company's executive management consists of the following, appointed by the Board of Directors:

- Chief Executive Officer (CEO) ("Directeur Général");
- Chief Financial Officer (CFO) ("Directeur financier");
- Chief Medical Officer (CMO) ("Directeur en charge des affaires médicales");
- Chief Scientific Officer (CSO) ("Directeur en charge des affaires scientifiques");
- Chief Development Officer (CDO) ("Directeur en charge du développement").

Subject to any management roles attributed to members of the Company's Board of Directors, management of the Company is entirely delegated to management. Management, moreover, assists the Board of Directors in discharging its responsibilities and, to the extent provided by law and the Articles of Association, carries out the decisions taken by the Board of Directors.

Management's authority is limited by the allocation of roles and responsibilities approved by the Board of Directors (approval requirements, consultation, or prior information of the Board of Directors, its Chairman or the chairs of various committees) or by any ad hoc action or decision of the Board of Directors reserving the right to grant prior approval.

Management may sub-delegate authority to its members or to others in accordance with an organization chart that establishes the principles and limits of the sub-delegation.

The CEO reports to the Board of Directors, while the other members of management report to the CEO or the COO. Management provides appropriate periodic and special reports on events. Management provides the Board of Directors each month with a brief report which contains key numbers that make it possible for the Board of Directors to monitor the evolution of the business, its affairs, and changes in the cash position.

Members of management may represent the Company vis-à-vis third parties and are registered at the commercial register, with signing authority requiring two signatures — those of the CEO and CFO.

19.2.3 Rights, Privileges, Restrictions and Obligations Attaching to the Shares (Articles 5, 7, and 14 of the Articles of Association)

The Company's shares are in bearer form. Each share is indivisible vis-à-vis the Company, which recognizes only one owner for each share. Since November 1, 2019, pursuant to the Federal Act on Implementation of Recommendations of Global Forum on Transparency and Exchange of Information for Tax Purposes and to the related Guidance, bearer shares are only allowed for Swiss companies if the issuing company has securities that are listed on a stock exchange (and in the case of a foreign stock exchange, that this exchange is subject to principles of transparency that are equivalent to those provided for under Swiss law) or if they are intermediated securities pursuant to the Swiss federal law of 3 October 2008 on intermediated securities and deposited with a Swiss depositary. The Company has provided the required evidence that (i) its shares are listed on Euronext Paris and (ii) that Euronext Paris is subject to principles of transparency that are equivalent to those provided for under Swiss law, and is therefore allowed to continue having bearer shares. So long as GeNeuro's bearer shares remain listed on Euronext Paris or another stock exchange and, in the case of listing on a non-Swiss stock exchange, as long as the Company can demonstrate that this foreign stock exchange is regulated by principles of transparency that are equivalent to those of Swiss law, there will be no requirement to change their form to registered shares.

All the Company's shareholders shall have voting rights proportional to the nominal value of all the shares belonging to them.

Each shareholder has the right to at least one vote, even if the shareholder has only one share.

Distribution of earnings under the Articles of Association (Article 7 of the Articles of Association)
Each shareholder shall have the right to a portion of the earnings reflected on the balance sheet in proportion to contributions to equity capital.

[172] This description of the role and authority of the Company's management, which is provided for information in this Section 19.2.2.2, is not a summary of the Articles of Association of the Company which do govern such role or authority.

Any dividend that has not been claimed within five years of its availability is time-barred automatically and by operation of law ("de plein droit") in favor of the Company.

19.2.3.1 Form of securities issued by the Company (Article 6 of the Articles of Association)

Shares shall be dematerialized and issued in the form of value rights ("droits-valeurs"). The value rights of the shareholders will be recorded in the principal registry and the rights corresponding thereto will be recorded to securities accounts with banks. The Company's shares held as indirectly held securities may be transferred or pledged or put into beneficial ownership ("remises en usufruit") by notice in accordance with the terms and conditions provided under applicable Swiss federal law.

19.2.3.2 Preferential subscription right

The Company's shareholders shall have a preferential right to subscribe for capital increases on the terms and conditions provided by the Swiss Code of Obligations and the Articles of Association.

As provided for under the Swiss Code of Obligations and Article 5b of the Company's Articles of Association (see also Section 19.1.6), the Board of Directors may limit or cancel the shareholders' preferential subscription rights:

- In the case of over-allotment options granted in the usual course of business to banks in the context of a public share issue;
- In the case of shares issued during acquisitions of firms or parts of other firms;
- In the case of the issuance of new shares on international equity markets through a bookbuilding process with institutional shareholders.

19.2.3.3 Limitations on voting rights

No provision of the Articles of Association will restrict the right to vote attaching to shares.

19.2.3.4 Changes to Shareholder Voting Rights

Shareholders' rights as set forth in the Company's Articles of Association may be changed or amended only at a general shareholders' meeting.

19.2.4 General Shareholder Meetings (Section 3 of the Articles of Association)

General shareholders' meetings shall include all shareholders regardless of the number of shares the shareholder owns or possesses.

Ordinary general shareholders' meetings are held in principle each year within six months following the end of the financial year. An extraordinary general meeting may be held as often as necessary.

19.2.4.1 Notices of meetings and holding of general shareholders' meetings (Articles 11 seq. of the Articles of Association)

Notice of meetings for a general shareholders' meeting ("GSM") is given by the Board of Directors or, if needed, by the statutory auditors, liquidators, or representative of debt securities.

One or more shareholders representing together at least a tenth of the equity capital may require that a GSM be called or that an item be put onto the agenda. The notice of meeting and inclusion of an item on the agenda must be requested in writing, indicating the subjects of the discussion and proposals.

The Board of Directors is to communicate the date of the GSM at the earliest possible time. A GSM is called by a notice inserted into the *Feuille Officielle Suisse du Commerce* (official Swiss business gazette) at least 20 days prior to the date of the meeting.

The Company will announce the date until which shareholders may send their requests for inclusion of items on the agenda and their proposals relating thereto. This date should not be more in advance of the date of the GSM than is necessary.

The notice of meeting must indicate the matters on the agenda as well as proposals by the Board of Directors and of shareholders who have sought that a meeting be called and held or who have requested inclusion of a matter on the agenda.

The notice of a GSM must inform the shareholders that the management report, the compensation report, and reports of the auditors are available to them at the registered / principal office of the Company and subsidiaries, if any, no later than 20 days prior to the GSM. Each shareholder may demand that a copy of such documents be provided to the shareholder promptly.

The owners or representatives of all the shares may hold a GSM, if there is no opposition, without using the forms prescribed for the notice of meeting. For as long as they are present, such shareholders have the right to conduct business and validly act with respect to any and all matters within the scope of the GSM.

In order to obtain their admission card and vote at the GSM, the shareholders or their representatives must submit to the Company a bank certificate certifying that the securities are deposited and blocked at the bank. The securities must be blocked until the day after the GSM.

The Board of Directors is free to determine the reference date until which shareholders may request from to the Company their admission and voting card, taking into account practical constraints.

A shareholder may request that the shareholder's shares be represented by another person, whether or not a shareholder, or by an independent proxy. Representation of shareholders by a member of a committee of the Company or by a custodian is prohibited.

At a GSM an independent representative will be elected, and the term of office of such person will terminate at the end of the next ordinary general shareholders' meeting. In the event of a vacancy, the Board of Directors will appoint an independent representative for the next GSM.

The independent representative is to vote on the basis of general or specific instructions given by the shareholders. If no instruction is received, the independent representative is to abstain.

Voting by mail is not a form of vote allowed under Swiss law.

GSMs are chaired by the Chairman of the Board of Directors or, in the Chairman's absence, by another member thereof. If there is none, the shareholders at the general meeting will elect a chairman.

The chairman of the GSM will appoint a secretary who may, but need not, be a shareholder.

The chairman answers questions about the Company or asks competent persons or chairs of committees of the Board of Directors to answer them. Complex matters must be submitted in writing to the Board of Directors sufficiently in advance for it to prepare its answers.

The Board of Directors oversees the preparation of the minutes of GSMs. The minutes shall state (i) the number, type, par value and class of shares represented by shareholders and the independent representative, (ii) the decisions and the outcome of elections, (iii) requests for information and answers given, and (iv) declarations or statements which the shareholders ask to have recorded.

The minutes are signed by the chairman and the secretary of the meeting. The shareholders have the right to consult the minutes. Excerpts thereof that are issued are certified true and correct by a member of the Board of Directors.

19.2.4.2 Quorum (Article 19 of the Articles of Association)

An ordinary or extraordinary shareholders' meeting may be validly held regardless of the number of shares represented.

The Chairman organizes the terms and conditions of voting so that it is possible to determine the will of the majority as clearly and efficiently as possible. If a vote is held with raised hand, the shareholders may require any refusals to vote or abstentions from voting to be recorded; the number of votes is to be disclosed.

The shareholders at a general meeting take decisions and hold elections on the basis of an absolute majority of all of votes attributable to the votes represented.

If, in connection with an election, the first round of voting does not make it possible to secure an absolute majority, a second round is to be held during which a relative majority will be decisive.

In the event of a tie vote the chairman's vote prevails.

On the basis of the requirements of the Swiss Code of Obligations, the Articles of Association provide that it is necessary to secure at least two-thirds of the votes attributable to the shares represented and an absolute majority of the paid-in capital amount in order to (i) change or amend the Company's purposes or legal form, (ii) issue shares with preferred voting rights, (iii) make any change in the clause limiting in percentage terms the registration of a shareholder with the right to vote in the share records, (iv) increase the equity capital by an authorized or conditional increase, or an ordinary increase through equity, contributions in kind or for the purposes of acquiring assets, or a grant of special benefits, (v) limit or eliminate the preferential subscription right, (vi) change the Company's registered and principal office, and (vii) dissolve the Company.

19.2.5 Committees

The Board of Directors has three permanent committees formed pursuant to rules approved by the Board of Directors:

- the Remuneration Committee;
- the Nomination Committee; and
- the Audit and Control Committee.

In connection with its authority, the Board of Directors may create other committees or give various tasks to members on the basis of rules or ad hoc decisions.

19.2.6 Clauses in the Articles of Association that could have an impact on the occurrence of a change of control

The Company's Articles of Association do not contain any provision that would make it possible to delay, defer, or prevent a change of control.

As mentioned in section **Erreur ! Source du renvoi introuvable.**, insofar as the Company's registered office is in Switzerland whilst its shares are listed only on Euronext's regulated market in Paris, neither French regulations on mandatory public tender offers and buyouts, nor Swiss regulations on public takeover offers (purchase or exchange offer) are applicable to public tender offers concerning the Company's shares.

19.2.7 Requirements for holdings exceeding certain percentages

Since the listing of the Company's shares on Euronext Paris, the Company, as a third-country issuer of shares with securities admitted to trading on a regulated market in France and, therefore, having chosen France as an initial member, is subject to applicable French law and regulations requiring reporting when investment thresholds are crossed.

Thus, any individual or legal entity that may possess a number of shares representing more than 5%, 10%, 15%, 20%, 25%, 30%, 33.33%, 50%, 66.66%, 90%, or 95% of the Company's equity capital and voting rights must inform the Company and the AMF thereof before the end of trading no later than on the fourth trading day following the crossing of the investment threshold, and the total number of shares and voting rights it possesses.

This information is also to be provided, in the same time frame, when the equity stake or right to vote falls below the thresholds mentioned above.

The person or entity responsible for providing this information must also specify in the report: (i) the number of shares it possesses convertible into, or carrying the right to acquire, shares and the number of votes attaching thereto, and (ii) the shares already issued that such person or entity may acquire under an agreement or security. The same applies to voting rights that such person or entity may acquire on the same terms and conditions.

A threshold crossing reporting form is available on the AMF's website.

19.2.8 Special provisions applicable to changes in the equity capital

Equity capital and rights attaching to shares constituting equity may be changed on the conditions provided by law and the Articles of Association, although the Company's Articles of Association do not contain specific provisions.

For information, the Swiss Code of Obligations provides that the general shareholders' meeting decision to increase the capital may only cancel the preferential subscription rights for valid reasons. The following are considered as valid reasons: the acquisition of a company, or of parts of a company or of a stake in a company, as well employee incentives. No shareholder must be unfairly advantaged or disadvantaged by the cancellation of preferential subscription rights (art. 652b CO).

19.2.9 Financial year (Article 38 of the Articles of Association)

Each financial year begins on January 1 and end on December 31 of each calendar year.

CHAPTER 20.
MATERIAL AGREEMENTS

License Agreements with bioMérieux

On January 31, 2006, the Company entered into a license agreement with bioMérieux, amended on October 27, 2010 to cover additional indications. The initial agreement granted an exclusive license to GeNeuro for any therapeutic application of the patents involving HERV-W belonging to bioMérieux, whilst leaving to bioMérieux any and all rights to the same patents in the field of diagnostics. However, in connection with the license agreement relating to companion diagnostics, dated October 14, 2015, bioMérieux agreed to waive its rights to develop companion diagnostics linked thereto to temelimab and granted to GeNeuro a non-exclusive license to its rights for which the Company agreed to pay it a maximum of €100,000 (excluding taxes).

As of the date hereof, GeNeuro has paid €1,194 thousand to bioMérieux in respect of milestone payments for the clinical development of temelimab. Other milestone payments as well as royalties are also contemplated.

Exclusive License Agreement with the NIH

In October 2018, GeNeuro announced it had signed an exclusive worldwide license with the National Institute of Neurological Disorders and Stroke (NINDS), part of the U.S. National Institutes of Health (NIH). The agreement covers the development of an antibody program to block the activity of pHERV-K Env (pathogenic envelope protein of the HERV-K family of Human Endogenous Retroviruses), a potential key factor in the development of ALS. Pursuant to this agreement, the Company made an up-front payment of KUSD 50 (K€ 44), and is committed to make annual minimum payments of KUSD 25 (approximately K€ 21) and milestone payments up to a total sum of USD 11.6 million (approximately € 9.7 million) subject to clinical development achievements; in addition, GeNeuro will have to pay the NIH royalties based on its net licensing revenues and net sales.

Credit Facility agreement with GNEH SAS

In December 2018, the Company entered into a €7.5 million Credit Facility Agreement with one of its shareholders, GNEH SAS, itself a subsidiary of Institut Mérieux. Pursuant to this Credit Facility, the Company had the right to draw the amount of the amount in up to 4 instalments, until May 31, 2019. The Credit Facility Agreement provided for an availability fee of 1.30% to be paid to GNEH SAS on the undrawn portion of the Credit Facility. Amounts borrowed carried interest at a rate increasing progressively up to 12% p.a. until the facility's ultimate maturity of June 2020. The Company considered the interest rate to be a market rate at the time the facility was concluded. The GNEH Credit Facility was unsecured and provided for certain early repayment scenarios, including if the Company secured financing under partnerships with third parties or in the event of a change in control. The agreement also gave GNEH the option of using any existing drawn down loan in part or in full as a subscription for new shares, or for securities conferring rights to the share capital in the event that GeNeuro issued such securities. A first draw-down of €2.5 million was made and received on March 25, 2019, and on June 3, 2019, the Company announced that it had drawn the remaining €5 million under the Credit Facility. In connection with the January 2020 capital increase, this Credit Facility was fully repaid by way of set-off.

Agreement for clinical trial at Karolinska Institutet's Academic Specialist Center

On November 25, 2019, GeNeuro announced an agreement with the Karolinska Institutet / Academic Specialist Center of Stockholm (ASC) to launch a new ProTEct-MS clinical study of temelimab in multiple sclerosis. The trial, to be conducted at the Center for Neurology of ASC (which with approximately 2,400 patients, is the largest MS center in Sweden), will be a one-year study that will enroll, initially, 40 patients whose disability progresses without relapses, and will document the safety and tolerability of temelimab following higher doses, as well as measures of efficacy based on the latest biomarkers associated with disease progression. The study aimed to start enrolling first patients in Q1 2020 with last patient out and top line results expected in H2 2021. On March 19, 2020, the Company announced the temporary postponement of its planned Phase 2 trial of temelimab in multiple sclerosis (MS) at the Karolinska Institutet's Academic Specialist Center (ASC), Stockholm, Sweden, to prioritize healthcare resources behind the fight of COVID-19 and to reduce the risk for MS patients but announced, on June 25, 2020, the recruitment of the first patient. On February 18, 2021, the Company announced the completed patient recruitment in its Phase 2 ProTEct-MS trial and that it expected results to be announced in Q1 2022.

Contract Development and Manufacturing Agreement with Polymun Scientific GmbH

On December 1, 2012, GeNeuro entered into a contract development and manufacturing agreement with Polymun. Pursuant to amendments to the contract, the latest being dated December 8, 2016, Polymun has produced additional batches of temelimab for use in Phase II trials. Under the contract, GeNeuro owns all improvements concerning the manufacturing of temelimab developed during the execution of the agreement while Polymun retains the right to use any improvements to manufacture other proteins. A purchase of the manufacturing process and a transfer of the technology to third parties, as needed, are possible under the contract with Polymun. As of the date of this Universal Registration Document, no further payments are due to Polymun.

Former Collaboration Agreement with Laboratoires Servier and Institut de Recherches Internationales Servier

In November 2014, the Company entered into the Collaboration Agreement with Laboratoires Servier and Institut de Recherches Internationales Servier, amended in November 2015 and November 2016. Under this agreement, GeNeuro was responsible for developing temelimab (GNbAC1) to treat MS until the completion of the Phase IIb clinical trial, at which time Servier could exercise its option to take a license as well as to assume responsibility for the development of GNbAC1 for MS in all markets except the United States and Japan. The agreement provided for:

- payments of €37.5 million, in three milestone payments which have all been made in 2014, 2015 and 2017 - these payments covered the costs of the Phase IIb clinical trial in MS;
- the financing of an ANGEL-MS extension study enabling patients having participated in the Phase IIb trial to benefit from two additional years of treatment;
- in the event of the exercise of the license option, the financing of a global Phase III clinical trial for MS, including in the US where GeNeuro had retained all rights, as well as milestone payments to GeNeuro of up to €362.5 million and royalties on future sales in Servier's territories .

Finally, and in accordance with a share purchase option agreement also made with Servier in November 2014, Servier International B.V. (a 100%-owned subsidiary of Group Servier) acquired, on December 11, 2015, 8.6% of GeNeuro's outstanding shares from Eclosion2 for €15 million.

On September 17, 2018, Servier notified the Company that it would not exercise its option to license, fund and conduct the development of GNbAC1 for MS in all markets, including in the United States. As a result of Servier's decision, the ANGEL-MS study, offering all patients who had completed the CHANGE-MS study the possibility to continue the treatment for an additional two years, was terminated in the fourth quarter of 2018, with no financial consequences for GeNeuro. All patients undertook one last, end-of-study visit. The 48-week data from ANGEL-MS was released on March 12, 2019.

CHAPTER 21.
DOCUMENTS AVAILABLE TO THE PUBLIC

Copies of this Universal Registration Document are available, free of charge, from the Company (3 chemin du Pré-Fleuri – 1228 Plan-les-Ouates – Geneva – Switzerland – Tel.: +41 22 552 48 00).

This Universal Registration Document is also available on the websites of the Company (http://www.geneuro.com/en/investors/documentation-2/regulated-information or http://www.geneuro.com/fr/investisseurs-fr/documentation/information-reglementee) and of the AMF (www.amf-france.org).

During the period of validity of this Universal Registration Document, the following documents (or copies of such documents) may be consulted at the Company's registered and principal office:

- the Company's Articles of Association;
- any and all reports, correspondence, and other documents, historical financial information, valuations and estimates, and statements or reports prepared by an expert at the Company's request, some of which are included or referred to in this Universal Registration Document; and
- historical financial information included in this Universal Registration Document.

All legal and financial documents relating to the Company and required to be made available to shareholders in accordance with applicable law and regulations may also be consulted at the Company's principal and registered office.

The regulated information under the meaning of the AMF's General Rules and Regulations is also available on the Company's website.

CHAPTER 22.
INFORMATION ON INVESTMENTS

The information about the companies in which the Company owns or holds a fraction of the equity capital that could have a material impact on an analysis of its assets and liabilities, financial condition, or profit and loss is set forth in Section 6.2, "Subsidiaries and Equity Stakes" of this Universal Registration Document and Note 2.2, "Consolidation Methods" to the Group's financial statements for the two years ended 31 December 2020 and 2019 set forth in CHAPTER 18, "Information Regarding the Company's Assets, Financial Situation and Results" of this Universal Registration Document.

CHAPTER 23.
ANNUAL ACCOUNTS FOR THE YEAR ENDED DECEMBER 31, 2020

GeNeuro SA

Plan-les-Ouates

Report of the statutory auditor to the General Meeting

on the financial statements 2020

Report of the statutory auditor

to the General Meeting of GeNeuro SA

Plan-les-Ouates

Report on the audit of the financial statements

Opinion

We have audited the financial statements of GeNeuro SA, which comprise the balance sheet as at 31 December 2020, income statement and notes for the year then ended, including a summary of significant accounting policies.

In our opinion, the accompanying financial statements as at 31 December 2020 comply with Swiss law and the company's articles of incorporation.

Basis for opinion

We conducted our audit in accordance with Swiss law and Swiss Auditing Standards. Our responsibilities under those provisions and standards are further described in the "Auditor's responsibilities for the audit of the financial statements" section of our report.

We are independent of the entity in accordance with the provisions of Swiss law and the requirements of the Swiss audit profession and we have fulfilled our other ethical responsibilities in accordance with these requirements. We believe that the audit evidence we have obtained is sufficient and appropriate to provide a basis for our opinion.

Our audit approach

Overview

Overall materiality: EUR 77'000

We tailored the scope of our audit in order to perform sufficient work to enable us to provide an opinion on the financial statements as a whole, taking into account the structure of the entity, the accounting processes and controls, and the industry in which the entity operates.

As key audit matter the following area of focus has been identified:

Confirmation of going concern assumption

Materiality

The scope of our audit was influenced by our application of materiality. Our audit opinion aims to provide reasonable assurance that the financial statements are free from material misstatement. Misstatements may arise due to fraud or

error. They are considered material if, individually or in aggregate, they could reasonably be expected to influence the economic decisions of users taken on the basis of the financial statements.

Based on our professional judgement, we determined certain quantitative thresholds for materiality, including the overall materiality for the financial statements as a whole as set out in the table below. These, together with qualitative considerations, helped us to determine the scope of our audit and the nature, timing and extent of our audit procedures and to evaluate the effect of misstatements, both individually and in aggregate, on the financial statements as a whole.

Overall materiality	EUR 77'000
How we determined it	1 % of total R&D and G&A gross expenses
Rationale for the materiality benchmark applied	We chose total expenses as the materiality benchmark because, in our view, it is the benchmark that best reflects the entity, which is a start-up still in a developmental phase and has no recurring revenues.

We agreed with the Audit Committee that we would report to them misstatements above EUR 7'700 identified during our audit as well as any misstatements below that amount which, in our view, warranted reporting for qualitative reasons.

Audit scope

We designed our audit by determining materiality and assessing the risks of material misstatement in the financial statements. In particular, we considered where subjective judgements were made; for example, in respect of significant accounting estimates that involved making assumptions and considering future events that are inherently uncertain. As in all of our audits, we also addressed the risk of management override of internal controls, including among other matters consideration of whether there was evidence of bias that represented a risk of material misstatement due to fraud.

Report on key audit matters based on the circular 1/2015 of the Federal Audit Oversight Authority

Key audit matters are those matters that, in our professional judgement, were of most significance in our audit of the financial statements of the current period. These matters were addressed in the context of our audit of the financial statements as a whole, and in forming our opinion thereon, and we do not provide a separate opinion on these matters.

Confirmation of going concern assumption

Key audit matter	How our audit addressed the key audit matter
The entity has prepared its financial statements on a going concern basis and, as further explained in Note 1 and Note 16 to the financial statements, management has concluded that the entity will be able to cover its cash outflows for at least twelve months from the date of these financial statements. The entity had cash and cash equivalents of EUR 5.4 million at 31 December 2020 but had operating losses of EUR 7.8 million in 2020. Management has plans to raise additional financing in the near future and, if necessary, has a fallback plan to operate at reduced level of activities in the event they are unable to raise those additional funds. Management's assessment of going concern is based on cash flow forecasts approved by the Board of Directors depending on whether additional funds are raised. Each of these plans are dependent on management judgement and could be influenced by management bias.	The main audit procedures we performed for assessing the appropriateness of the cash flow projections used by management to confirm the going concern assumption used in preparing the financial statements included: - obtained the cash flow forecasts covering at least 12 months from the date of this report, checked mathematical accuracy and ensured they were approved by the Board of Directors; - audited the existence of cash and cash equivalents as of 31 December 2020; - assessed that the cash on hand as of the date of this report was sufficient to cover the budgeted cash outflows for the next 12 months under the assumption that no additional funding is received;

- performed a lookback analysis to compare the 2020 budget with the actual results for the year ended 31 December 2020 to assess management's ability to make estimates;

- assessed whether managements cost-cutting initiatives as per the 2021 budget can be executed;

- discussed management's conclusions and the 2021 budget initiatives with the Board of Directors and confirmed they have approved them;

- reviewed the adequacy and appropriateness of management's going concern disclosures in the financial statements.

As a result of our audit procedures, as discussed with the Board of Directors, we consider management's approach regarding the assessment of the going concern assumption to be adequate.

Responsibilities of the Board of Directors for the financial statements

The Board of Directors is responsible for the preparation of the financial statements in accordance with the provisions of Swiss law and the company's articles of incorporation, and for such internal control as the Board of Directors determines is necessary to enable the preparation of financial statements that are free from material misstatement, whether due to fraud or error.

In preparing the financial statements, the Board of Directors is responsible for assessing the entity's ability to continue as a going concern, disclosing, as applicable, matters related to going concern and using the going concern basis of accounting unless the Board of Directors either intends to liquidate the entity or to cease operations, or has no realistic alternative but to do so.

Auditor's responsibilities for the audit of the financial statements

Our objectives are to obtain reasonable assurance about whether the financial statements as a whole are free from material misstatement, whether due to fraud or error, and to issue an auditor's report that includes our opinion. Reasonable assurance is a high level of assurance, but is not a guarantee that an audit conducted in accordance with Swiss law and Swiss Auditing Standards will always detect a material misstatement when it exists. Misstatements can arise from fraud or error and are considered material if, individually or in the aggregate, they could reasonably be expected to influence the economic decisions of users taken on the basis of these financial statements.

As part of an audit in accordance with Swiss law and Swiss Auditing Standards, we exercise professional judgment and maintain professional scepticism throughout the audit. We also:

- Identify and assess the risks of material misstatement of the financial statements, whether due to fraud or error, design and perform audit procedures responsive to those risks, and obtain audit evidence that is sufficient and appropriate to provide a basis for our opinion. The risk of not detecting a material misstatement resulting from fraud is higher than for one resulting from error, as fraud may involve collusion, forgery, intentional omissions, misrepresentations, or the override of internal control.
- Obtain an understanding of internal control relevant to the audit in order to design audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the entity's internal control.
- Evaluate the appropriateness of accounting policies used and the reasonableness of accounting estimates and related disclosures made.
- Conclude on the appropriateness of the Board of Directors' use of the going concern basis of accounting and, based on the audit evidence obtained, whether a material uncertainty exists related to events or conditions that may cast

significant doubt on the entity's ability to continue as a going concern. If we conclude that a material uncertainty exists, we are required to draw attention in our auditor's report to the related disclosures in the financial statements or, if such disclosures are inadequate, to modify our opinion. Our conclusions are based on the audit evidence obtained up to the date of our auditor's report. However, future events or conditions may cause the entity to cease to continue as a going concern.

We communicate with the Board of Directors or its relevant committee regarding, among other matters, the planned scope and timing of the audit and significant audit findings, including any significant deficiencies in internal control that we identify during our audit.

We also provide the Board of Directors or its relevant committee with a statement that we have complied with relevant ethical requirements regarding independence, and communicate with them all relationships and other matters that may reasonably be thought to bear on our independence, and where applicable, actions taken to eliminate threats or safeguards applied.

From the matters communicated with the Board of Directors or its relevant committee, we determine those matters that were of most significance in the audit of the financial statements of the current period and are therefore the key audit matters. We describe these matters in our auditor's report unless law or regulation precludes public disclosure about the matter or when, in extremely rare circumstances, we determine that a matter should not be communicated in our report because the adverse consequences of doing so would reasonably be expected to outweigh the public interest benefits of such communication.

Report on other legal and regulatory requirements

In accordance with article 728a paragraph 1 item 3 CO and Swiss Auditing Standard 890, we confirm that an internal control system exists which has been designed for the preparation of financial statements according to the instructions of the Board of Directors.

We recommend that the financial statements submitted to you be approved.

Furthermore, we draw attention to the fact that half of the share capital and legal reserves is no longer covered (article 725 para. 1 CO).

PricewaterhouseCoopers SA

Michael Foley

Audit expert
Auditor in charge

Florent Rossetto

Genève, 1 April 2021

Enclosure:

- Financial statements (balance sheet, income statement and notes)

2020 Financial statements

GeNeuro SA,
Plan-les-Ouates

GeNeuro SA, Plan-les-Ouates

Balance sheet at December 31

Assets	Notes	2020	*2020*	2019	*2019*
		Audited EUR	*For information (CHF)*	Audited EUR	*For information (CHF)*
Current assets					
Cash and cash equivalents		5,377,373	*5,808,638*	4,447,561	*4,827,383*
Other current receivables from third parties		82,804	*89,445*	113,274	*122,948*
Prepaid expenses		84,184	90,936	153,886	*167,028*
Total current assets		**5,544,361**	***5,989,019***	**4,714,721**	***5,117,359***
Non-Current assets					
Participations	3	2,668,364	*2,882,367*	2,668,371	*2,896,250*
Other non-current financial assets	4	1,225,425	*1,323,704*	4,154,723	*4,509,536*
Property, plant and equipment	5	1,233,587	*1,332,521*	534,539	*580,189*
Intangible assets		1,148,748	*1,240,878*	1,154,066	*1,252,623*
Total non-current assets		**6,276,124**	***6,779,470***	**8,511,699**	***9,238,598***
Total Assets		**11,820,485**	***12,768,489***	**13,226,420**	***14,355,957***

Liabilities and Equity	Notes	2020	*2020*	2019	*2019*
		Audited EUR	*For information (CHF)*	Audited EUR	*For information (CHF)*
Current liabilities					
Trade payables		4,059,372	*4,384,933*	3,503,880	*3,803,111*
third parties		*347,237*	*375,085*	*766,738*	*832,217*
group companies	6	*3,712,135*	*4,009,848*	*2,737,142*	*2,970,894*
Current financial liabilities	7	203,590	*219,918*	7,977,779	*8,659,081*
third parties		*203,590*	*219,918*	*288,738*	*313,396*
shareholders		-	-	*7,689,041*	*8,345,685*
Other current liabilities	8	123,696	*133,616*	76,360	*82,881*
third parties	8	*123,696*	*133,616*	*76,360*	*82,881*
Accrued liabilities	9	919,256	*992,980*	1,324,895	*1,438,041*
Total current liabilities		**5,305,914**	**5,731,447**	**12,882,914**	**13,983,114**
Non-current liabilities					
Non-current financial liabilities	7	1,014,638	*1,096,012*	244,523	*265,405*
Total non-current liabilities		**1,014,638**	***1,096,012***	**244,523**	***265,405***
Total liabilities		**6,320,552**	***6,827,459***	**13,127,437**	***14,248,519***
Equity					
Capital		953,942	*1,029,516*	676,269	*732,906*
Legal reserves from capital	10	17,665,378	*20,396,227*	56,611,745	*62,101,839*
Other reserves from capital	10	42,750,000	*46,400,850*	-	-
Treasury shares	10	-802,491	*-866,851*	-699,815	*-759,579*
Carried forward loss		-44,239,215	*-48,957,079*	-51,843,045	*-56,836,730*
Loss for the year		-10,827,681	*-11,591,031*	-4,646,171	*-5,168,400*
Translation adjustment			*-472,643*		*37,402*
Total equity		**5,499,933**	***5,941,030***	**98,983**	***107,438***
Total Liabilities and Equity		**11,820,485**	***12,768,489***	**13,226,420**	***14,355,957***

The accompanying notes form an integral part of these financial statements

GeNeuro SA, Plan-les-Ouates

Income statement for the 12 months ended December 31

	Notes	2020	*2020*	2019	*2019*
		Audited EUR	*For information (CHF)*	Audited EUR	*For information (CHF)*
Income	11	4,675	*5,005*	92,073	*102,422*
Research and development expenses		-4,948,585	*-5,297,460*	-5,904,230	*-6,567,865*
General and administrative expenses		-2,826,246	*-3,025,496*	-3,431,220	*-3,816,889*
Operating loss before interest and taxes		**-7,770,156**	***-8,317,951***	**-9,243,377**	***-10,282,332***
Financial income	12	130,810	*140,032*	5,047,553	*5,614,898*
Financial expenses	12	-248,530	*-266,051*	-441,874	*-491,541*
Impairment to financial assets	4, 12	-2,922,143	*-3,128,154*	-	*-*
Operating loss before taxes		**-10,810,019**	***-11,572,124***	**-4,637,698**	***-5,158,975***
Pre-tax loss		**-10,810,019**	***-11,572,124***	**-4,637,698**	***-5,158,975***
Direct taxes		-17,662	*-18,907*	-8,473	*-9,425*
Net loss for the period		**-10,827,681**	***-11,591,031***	**-4,646,171**	***-5,168,400***

The accompanying notes form an integral part of these financial statements

GeNeuro SA, Plan-les-Ouates
Appendix to annual financial statements

Additional information

Additional information in the notes to the financial statements, such as the cash flow statement and the management report as required by art. 961d CO is not included in the notes as the entity prepares consolidated accounts in accordance with IFRS.

1. Principles used in preparing the annual financial statements

These annual financial statements have been prepared in conformity with the provisions on commercial accounting of the Swiss Code of Obligations (art. 957 to 963b, applicable since January 1, 2013). The main balance sheet items are accounted for as follows.

Certain amounts from the prior year were reclassified for comparison purposes.

Since January 1, 2016, the Company maintains its accounts in euros, this currency being considered as the functional currency.

The financial statements provided in Swiss francs (CHF) are for information purposes. Amounts have been converted from euros into CHF at the following rates:

	2020	2019
Income statement items	1.0705	1.1124
Balance sheet items	1.0802	1.0854

except for equity items which are converted at the applicable historical rate

Revenue recognition
The "Income" line item includes income derived from collaborative agreements entered into by GeNeuro SA.

The Company recognizes income from license fees, the provision of R&D services and management fees on the arrangement of R&D services. Income is recognized when control of the goods or services passes to the customer. For the provision of a license, this is dependent on whether the license conveys a right of use or right of access to the underlying intellectual property. The R&D services are recognized over time as the Company performs the clinical trials and the customer benefits from those services. The Company identifies the performance obligations in each contract with a customer. A performance obligation is a promise to deliver goods and services that is distinct from other promises in the contract.

Where a contract contains more than one performance obligation, the Company allocates the transaction price based on the stand-alone selling price of each separate performance obligation. The Company receives upfront payments and variable consideration in the form of milestones. The Company uses the most likely method to estimate variable consideration and includes such consideration in the transaction price and income if it is not highly probable of reversal.

Income from licenses that convey a right to use intellectual property is recognized when the customer is able to use that intellectual property. R&D services are recognized over the clinical study period based on an input method. This method is calculated by the clinical trial costs incurred over the estimated costs to complete the study.

The Company provides management services, where it arranges clinical trials with an external provider on behalf of a customer. In these arrangements, the Company is acting as agent and recognizes the management fee as income as the management services are delivered.

Going concern

GeNeuro SA is a biopharmaceutical company at the clinical stage developing innovative therapeutics. The Company is exposed to risks and uncertainties inherent in establishing and developing a business that are common to early-stage companies in the biotechnology industry, including, but not limited to, development by competitors of new technological innovations, dependence on key personnel, protection of proprietary technology, compliance with government regulations and the ability to secure additional financing to fund operations. Product candidates currently under development will require significant additional research and development efforts, including preclinical and clinical testing and regulatory

approval prior to commercialization. These efforts require significant amounts of additional capital, adequate personnel and infrastructure and extensive compliance-reporting capabilities. Even if the Company's product development efforts are successful, it is uncertain when, if ever, the Company will realize significant revenue from product sales.

The Company's success may also depend on its ability to:

- establish and maintain strong patent position and protection;
- enter into collaborations with partners in the pharmaceutical industry;
- acquire and retain key personnel;
- acquire additional funding to support its operations.
-

The Company's financial statements have been prepared on the basis of continuity of operations, realization of assets and the satisfaction of liabilities and commitments in the ordinary course of business. Since its incorporation, the Company has primarily funded its growth through issuances of shares, including the capital increase conducted at the time of its initial public offering in 2016 and a €17.5 million capital increase in January 2020, and a Credit Facility provided by its shareholder GNEH SAS in 2019, which was repaid by way of set-off through the capital increase of January 2020.

The Company expects that its operating losses and negative cash flows will continue for the foreseeable future, although it expects that negative cash flows will continue to decrease given the Company's current level of activity. Based on its current cash position and activities and taking into account the Company's fallback operating plans in the event it were unable to raise additional plans, the Company expects to be able to cover its cash outflows for at least twelve months from the date of these financial statements. Hence, the financial statements have been prepared on a going concern basis.

The future viability of the Company beyond that date is dependent on its ability to raise additional capital to finance its operations. The Company will seek additional funding through public financings, debt financings, collaboration agreements, strategic alliances and licensing arrangements. The Company may not be able to obtain financing on acceptable terms, or at all, and the Company may not be able to enter into collaborations or other arrangements. The terms of any financing may adversely affect the holdings or the rights of the Company's stockholders. If the Company is unable to obtain funding, the Company could be required to delay, reduce or eliminate research and development programs, product portfolio expansion, or future commercialization efforts, which could adversely affect its business prospects.

Although management continues to pursue these plans, there is no assurance that the Company will be successful in obtaining sufficient funding on terms acceptable to the Company to fund continuing operations, if at all.

Liquidity risk management is assessed in Note 16.

Non-current assets

Property, plant and equipment are carried in the balance sheet at their purchase cost, less the appropriate economic depreciation. As from January 1, 2019, the Company has applied IFRS 16 "Leases", pursuant to which, at the commencement date of a lease, a lessee recognizes a liability to make lease payments (i.e., the lease liability) and an asset representing the right to use the underlying asset during the lease term (i.e., the right-of-use asset). Lessees are required to separately recognize the interest expense on the lease liability and the depreciation expense on the right-of-use asset. In applying the new standard, a lessee determines each lease's term including any lessee's extension or termination option that is deemed reasonably certain. The assessment of such options is performed as of the commencement of each lease and requires judgment by management. Measuring the lease liability at the present value of the remaining lease payments requires using an appropriate discount rate in accordance with IFRS 16. The discount rate is the interest rate implicit in the lease or, in the event it cannot be determined, the incremental borrowing rate at the date of the lease commencement. The incremental borrowing rate can have a significant impact on the net present value of the right-of use asset and lease liability recognized and requires judgement.

As per IFRS 16, lessees must remeasure the lease liability upon the occurrence of certain events (e.g., a change in the lease term, a change in future lease payments resulting from a change in an index or

rate used to determine those payments). The lessee generally recognizes the amount of the remeasurement of the lease liability as an adjustment to the right-of-use asset.

Intangible assets primarily comprise license rights on patents.

Research and development expenses are accounted for as expenses when incurred, based on the fact that the criteria for recognizing them as intangible assets are not fulfilled.

Lease agreements

Since January 1, 2019, the Company applies IFRS 16 “Leases” for lease agreements and has elected to use the exemption proposed by the standard on lease contracts for which the lease terms end within 12 months as of the date of initial application; and to exclude the low-value assets (with an individual value in USD of less than 5’000 when new).

In 2019, the Company the new IFRS 16 “Leases” standard, effective from January 1, 2019. The impact on its financial statements from the first-time adoption of this new standard is disclosed in the financial report for the year ended December 31, 2019.

At the inception of the lease a right-of-use asset and a lease liability are recognized in the balance sheet. The asset is initially measured at the amount of the lease liability plus any initial direct costs incurred.

The lease liability is initially measured at the present value of the lease payments payable over the lease term, including variable lease payments depending on an index at the commencement date and the exercise price of purchase options if it is reasonably certain that the option will be exercised. The lease liability is discounted at the rate implicit in the lease. If that rate cannot readily be determined the incremental borrowing rate is used. Lease liabilities are subsequently re-measured to reflect possible changes in the lease terms. Right-of-use assets are depreciated over of the duration of the lease contract including contractually agreed optional extension periods, whose exercise are deemed to be reasonably certain. The depreciation is recognized in operating income. The unwinding of the discounting effect is included in the financial expense. Lease payments are accounted for as a repayment of the lease liability. Expenses for lease contracts for objects with a value of less than USD 5 thousand and lease contracts with a duration of up to twelve months are recognized directly in the income statement.

Information, detailed structure and comments on the annual financial statements

2. The annual average full-time employee number was 10.7 employees for 2019 and 9.5 employees for 2020.

3. Participations

		2020		2019	
Name and legal form	Headquarter	Capital	Voting rights	Capital	Voting rights
GeNeuro Innovation SAS	Lyon, France	100%	100%	100%	100%
GeNeuro Australia (Pty) Ltd	Sydney, Australia	100%	100%	100%	100%

4. Other financial assets

	2020	*2020*	**2019**	*2019*
	Audited EUR	*For information (CHF)*	Audited EUR	*For information (CHF)*
Currency derivatives	-	-	-	-
Loans granted to employees	-	-	-	-
Current financial assets	-	-	-	-
Rent deposit	**173,007**	*186,882*	179,365	*194,683*
Cash reserve for liquidity contract	**74,876**	*80,881*	97,552	*105,883*
Advances to subsidiaries	**977,542**	*1,055,941*	3,877,806	*4,208,971*
Other non-current financial assets	**1,225,425**	1,323,704	4,154,723	4,509,537

The reduction in "advances to subsidiaries" is to the recognition of an impairment of financial assets - refer to note 12.

5. Property, plant and equipment

	2020	*2020*	**2019**	*2019*
	Audited EUR	*For information (CHF)*	Audited EUR	*For information (CHF)*
Gross value				
Building (right of use)	1,749,424	*1,889,728*	787,036	*854,249*
Right of use adjustment on transition to IFRS 16	-26,684	*-28,824*	-41,238	*-44,760*
Office and computer equipment, furniture	179,378	*193,764*	176,149	*191,192*
Fixtures and fittings	12,120	*13,092*	12,120	*13,155*
Total Gross Value	**1,914,238**	*2,067,760*	**934,067**	*1,013,836*
Accumulated depreciation				
Building (right of use)	-522,567	*-564,477*	-262,621	*-285,049*
Office and computer equipment, furniture	-148,186	*-160,071*	-129,433	*-140,487*
Fixtures and fittings	-9,898	*-10,692*	-7,474	*-8,112*
Total Gross Value	**-680,651**	*-735,239*	**-399,528**	*-433,648*
Net Book Value				
Building (right of use)	1,200,173	*1,296,427*	483,177	*524,440*
Office and computer equipment, furniture	31,192	*33,694*	46,716	*50,706*
Fixtures and fittings	2,222	*2,400*	4,646	*5,043*
Total Net Book Value	**1,233,587**	*1,332,521*	**534,539**	*580,189*

The variation in property, plant and equipment in 2020 is attributable to the extension of the Company's office lease for a further 5 years at a lower annual rent, as of December 1, 2020.

6. Trade payables

The increase in trade payables to group companies from 2019 to 2020 is attributable to the invoice of services provided by the Company's French subsidiary, less any payments made during the year. Trade payables to third parties have decreased during the year due to the reduction in the activities of the Company.

7. Current and non-current financial liabilities

During 2020, the Company repaid in its entirety the shareholder loan from GNEH SAS. At December 31, 2020, current financial liabilities are comprised of the current portion of the lease liability corresponding to the right of use.

The non-current financial liabilities at December 31, 2020, are comprised of the non-current portion of the lease liability corresponding to the right of use. The increase is due to the new lease agreement entered into as of December 1, 2020.

8. Other current liabilities

At December 31, 2020, other current liabilities are mostly comprised of accrued liabilities for directors' fees, which were paid in January 2021.

Amounts due to pension institutions
At December 31, 2019 and 2020, there were no amounts due to the Swiss occupation pension scheme.

9. Accrued liabilities

At December 31, 2020, the reduction in accrued liabilities was due principally to the reduction in the Company's activities during 2020.

10. Equity

On January 31, 2020, the Company completed a €17.5 million share capital increase through an international private placement reserved to qualified institutional investors, through the issuance of 5,932,201 new ordinary bearer shares. The Company's major shareholder, GNEH SAS, participated to this capital increase for the full principal amount of the loan it had provided to the Company, i.e. €7.5 million, which amount was paid by way of debt set-off.
Accordingly, at December 31, 2020, the Company's share capital amounted to € 892.3K (CHF 1,029.5, converted into euros at the applicable historical exchange rates) and was divided into 20,590,319 common bearer shares with a nominal value of CHF 0.05. All shares are fully paid up.
At the May 27, 2020, annual general meeting of shareholders ("AGM 2020"), the shareholders approved the Board of Directors' proposal to allocate EUR 12'250'000 (CHF 13'296'150 at the December 31, 2019 exchange rate) from the sub-position "Legal reserves from capital" to the sub-position "Carried forward loss" ; and to transfer EUR 42'750'000 (CHF 46'400'850 at the December 31, 2019 exchange rate) from the sub-position "Legal reserves from capital" to a new sub-position "Reserves from capital contributions", within the free reserves.

Own shares of the Company held by the Company or its subsidiaries (book values)

	2020			2019	
	Number	Value (EUR)	*Value in CHF for information*	Number	Value (EUR)
January 1	105,881	699,815	*759,579*	87,507	632,578
Exercise of stock options	-	-	-	-	-
Purchases	153,306	477,372	*511,027*	107,032	388,265
Sales	-119,542	-374,696	*-401,112*	-88,658	-321,028
Currency translation	-	-	*-2,643*	-	-
December 31	139,645	802,491	*866,851*	105,881	699,815
Nominal value of own shares	*CHF 6,982*			*CHF 5,294*	

11. Income

The Company recognized no revenues during the 2020 reporting period; reported income for 2020 relates to withholding tax administrative payments. In 2019, income related primarily to the invoicing of services to the Company's French subsidiary.

12. Financial income and expenses

In 2019, the Company received a dividend of EUR 5 million from its wholly-owned subsidiary GeNeuro Innovation SAS, which was recognized as financial income. No dividend was received in 2020. The balance of financial income is derived from currency gains and income on bank balances.

Financial expenses decreased in 2020 compared to 2019 primarily due to the reduction in interest charges on the shareholder loan of EUR 7.5 million from GNEH SAS, which was repaid on January 31, 2020 in a debt set-off with the amount due by GNEH SAS for its participation to the capital increase.

Impairment of financial assets: due to lack of foreseeable activity for the Company's Australian subsidiary following the completion of the clinical trials it conducted, the Company decided to liquidate this subsidiary during 2021. Accordingly, the Company has taken an impairment of EUR 2,922,143 against the equity participation and the advances granted to the subsidiary, corresponding to the net expected loss on these assets.

13. Commitments

As mentioned in Note 1, as of January 1, 2019, the Company has applied IFRS 16 "Leases", pursuant to which it recognizes a liability to make lease payments in connection with its current premises.

14. Participation rights and options granted to Management, Board of Directors and employees

	Nominal value (2020 grants)		Number of options	
			2020	2019
	EUR	*CHF*		
Board of Directors/Management	7,706.91	*8,325.00*	166,500	112,451
Employees	694.32	*750.00*	15,000	45,999

During 2020, the Company's Board of Directors approved a new Equity Incentive Stock Option Plan, pursuant to which it made initial grants of 181,500 stock options during 2020 to management and employees, with an average exercise price of EUR 3.32 per share and an exercise term of 10 years.

In addition to the above information, a total of 202,274 stock options were cancelled due to non-exercise during their term or forfeited by departing employees.

The Group has no legal or constructive obligation to repurchase or settle any of the stock options in cash.

15. Information required in the case of income statement presentation by function

	2020	*2020*	**2019**	*2019*
	EUR	*For information (CHF)*	EUR	*For information (CHF)*
Personnel expense	-2,537,903	*-2,664,352*	2,948,684	*3,280,116*
Amortization, depreciation and impairment on non-current assets	-3,251,937	*-3,481,199*	297,709	-331,171

16. Other information

Based on the fact that the Company presents consolidated financial statements established pursuant to IFRS accounting standards, the Company does not present in its statutory accounts a cash flow statement nor a statement of change in net equity.

Contingent liabilities

GeNeuro SA is not involved in any litigation.

In 2006, the Company entered into an exclusive license agreement with bioMérieux (France) (the "2006 Agreement") with the sole aim to develop, manufacture and sell products covered by bioMérieux patents, with bioMérieux retaining in this 2006 Agreement the rights related to diagnostics.

The 2006 Agreement mainly provides for:

- an initial payment of KCHF 150, paid in 2006 (EUR 138 K at the January 1, 2016 exchange rate used at the time the Company changed its functional currency from the CHF to the euro);
- an annual contribution of KCHF 50 (approx. EUR 43 K) for the maintenance costs of the patents;
- milestone payments based on development stages of up to CHF 72.6 million in total (approx. EUR 62 million);
- royalties based on net license income and net sales of GeNeuro

On commencement of the Phase IIa clinical trial in multiple sclerosis in 2012, the first milestone was reached, triggering a payment by the Company of KCHF 200 (approx. EUR 171 K at then applicable exchange rate). The opening of the first investigational site of the Phase IIb clinical trial in multiple sclerosis in the first half of 2016 triggered a payment by the Company of KCHF 1,000 (EUR 907 K at the then applicable exchange rate). In addition, the start of the Phase IIa clinical trial in type 1 diabetes triggered a contingent payment of KCHF 200 (approx. EUR171 K), to be paid only if certain conditions (such as entering a phase III clinical trial in this indication, or sub-licensing the product for that indication) are met. Owing to the uncertainties surrounding the results of this type 1 diabetes clinical trial, the Company treats this milestone as a contingent liability.

In 2015, pursuant to an exclusive license agreement on companion diagnostics (the "Diagnostics Agreement"), bioMérieux also granted an exclusive license on companion diagnostics. This Diagnostics Agreement commits the Company to make milestone payments of up to EUR 100 K. On the commencement of the Phase IIb clinical trial in 2016, the first milestone was reached, triggering a payment of EUR 50 K to bioMérieux. The balance of EUR 50 K will be due in the event of the start of a Phase III. No royalties are due pursuant to the Diagnostics Agreement.

In 2018, pursuant to an exclusive license agreement entered into with the National Institutes of Health of the USA for the development of an antibody program to block the activity of pHERV-K Env (pathogenic envelope protein of the HERV-K family of Human Endogenous Retroviruses), a potential key factor in the development of ALS (Amyotrophic Lateral Sclerosis), the Company made an up-front payment of KUSD 50 (approximately EUR 43 K), and is committed to make annual minimum payments of KUSD 25 (approximately EUR 22 K) and milestone payments up to a total sum of USD 11.6 million (approximately EUR 9.9 million) subject to clinical development achievements; in addition, GeNeuro will have to pay the NIH royalties based on its net licensing revenues and net sales.

Liquidity risk

Since its incorporation, the Company has primarily funded is growth through capital increase and additional funds provided by research collaborations. The Company has never had recourse to bank loans. As a result, the Company is not exposed to liquidity risk through requests for early repayment of loans.

Significant R&D expenses have been incurred from the start of the Company's activities, generating negative cash flows from operating activities.

As at December 31, 2020, the Company's cash & cash equivalents amounted to € 5,377 K (December 31, 2019: € 4,448 K).

As disclosed in Note 1 of the Notes to the financial statements, the Board of Directors believes that, taking into account the projected lower cash outflow from its operating activities for 2021 based on the operating plans, as well as the eventual mitigation measures it has approved, the Company has sufficient financial resources to cover its operating costs for at least one year from the date these financial statements are issued and, as a result, is presenting the financial statements of the Company on a going-concern basis.

Post balance sheet events

Following the completion of the clinical trials conducted in Australia and due to the absence of further activity expected for the Company's Australian subsidiary, the Company has initiated the liquidation of this subsidiary, which is expected to be completed in the second quarter of 2021. At December 31, 2020, the Company has taken an impairment of EUR 2,922,143 against the equity participation in and advances to this subsidiary and no further impact resulting from the liquidation is expected in 2021.

CHAPTER 24.
RESOLUTIONS TO BE SUBMITTED TO THE MAY 27, 2021, ANNUAL GENERAL SHAREHOLDERS' MEETING

The Company's annual Ordinary General Meeting will be held on May 27, 2021, at 09:30 at the Company's head office, Chemin du Pré-Fleuri 3, CH-1228 Plan-les-Ouates, Geneva – Switzerland.

Based on article 27 of the Swiss Ordinance 3 on Measures to Combat the Coronavirus of 19 June 2020 (COVID-19 Ordinance 3, status as of April 15, 2021), the Company has decided that shareholders of the Company may exercise their rights at the Ordinary General Meeting **exclusively** through the independent proxy. This measure allows the Company to hold the Ordinary General Meeting as planned despite the pandemic. The conduct of the Ordinary General Meeting remains subject to additional measures issued by the Swiss authorities.

1 Approval of the 2020 Annual Report

The Board of Directors proposes to approve the 2020 annual financial statements, group financial statements and annual report.

Comment: the 2020 Annual Report includes the IFRS Consolidated Financial Statements and the Statutory Financial Statements, both included within the Company's Universal Registration Document in pages 173-211 and 223 -238.

2 Appropriation of Balance Sheet Results

The Board of Directors proposes to carry forward the balance sheet loss of EUR 55'066'896.

3 Information concerning the loss of capital and remediation measures

The Company has shareholder's equity of EUR 5'499'933. This amount is less than half its share capital (EUR 953'942) plus legal reserves (EUR 17'665'378), amounting to EUR 9'309'660 (which Swiss law qualifies as a situation of loss of capital).
During the Annual Shareholders' Meeting, the Board of Directors will discuss the contemplated remediation measures, which may include, amongst others, financial, structural, strategic or operational measures

4 Release of the members of the Board of Directors and of Management

The Board of Directors proposes to release the members of the Board of Directors and of the Management.

5 Compensation

5.1 Consultative Vote on the Remuneration Report

The Board of Directors proposes to approve the 2020 Remuneration Report (consultative vote).

Comment: the 2020 Remuneration Report is included in the Company's Universal Registration Document in pages 149 to 158. Pursuant to the Swiss Code of Best Practice for Corporate Governance, the Board of Directors has decided to submit the Remuneration Report to shareholders for a separate consultative vote in addition to the binding approvals of compensation under agenda item 5.2.

5.2 Standard Annual Approvals

5.2.1 Approval of the Aggregate Compensation of the Board of Directors from the 2021 Ordinary General Meeting until the 2022 Ordinary General Meeting

The Board of Directors proposes to approve a maximum aggregate compensation (including related social security payments) of EUR 160'000 from the 2021 Ordinary General Meeting (approving the 2020 annual accounts) until the 2022 Ordinary General Meeting (approving the 2021 annual accounts).
Comment: the maximum aggregate compensation payable to directors would be unchanged at EUR 160'000.

5.2.2 Approval of the Aggregate Compensation of Management for the Financial Year 2022

(a) Fixed Compensation
The Board of Directors proposes to approve a maximum aggregate fixed compensation (including related social security payments and pension fund contributions) of EUR 2'000'000 for the 2022 financial year.
(b) Variable Compensation
The Board of Directors proposes to approve a maximum aggregate variable compensation (including related social security payments) of EUR 2'000'000 for the 2022 financial year.

Comment: the maximum aggregate compensation payable to management of EUR 2'000'000, for each of the fixed and variable compensation, would be unchanged as it reflects the Company's current development stage.

6 Election and Re-election of the Members of the Board of Directors

The Board of Directors proposes to individually re-elect:

- Mr. Jesús Martin-Garcia,

- Mr Hedi Ben Brahim
- Mr. Giacomo Di Nepi,
- Mr. Michel Dubois,
- Mr. Eric Falcand,
- Mr. Gordon Selby Francis, and
- Mr. Christophe Guichard.

Following Mr Marc Bonneville's resignation from the Board in September 2020, the Board of Directors proposes to elect:

- Mr. Philippe Archinard

Each election would be for a new term until the end of the next ordinary General Meeting.

Comment: The Board of Directors thanks Mr. Marc Bonneville, who was elected as a director on November 19, 2015, for his service and his commitment to the Company. In his stead, the Board of Directors proposes to elect Mr Philippe Archinard, Directeur Général Délégué at Institut Mérieux, which through its GNEH SAS subsidiary owns 36.46% of the Company's share capital.

7 Re-election of the Chairman of the Board of Directors

The Board of Directors proposes to re-elect Mr. Jesús Martin-Garcia as Chairman of the Board of Directors for a new term until the end of the next ordinary General Meeting.

8 Re-election of the Members of the Remuneration Committee

The Board of Directors proposes to individually elect or, as the case may be, re-elect:

- Mr. Hedi Ben Brahim,
- Mr. Giacomo Di Nepi and
- Mr. Christophe Guichard

Each for a new term until the end of the next ordinary General Meeting.

9 Re-election of the Auditor

The Board of Directors proposes to re-elect PricewaterhouseCoopers SA, Geneva branch, avenue Giuseppe-Motta 50, 1201 Geneva, as statutory auditor for the 2021 financial year.

10 Re-election of the Independent Proxy

The Board of Directors proposes to re-elect the notary firm GAMPERT DEMIERRE MORENO – 19, rue du Général-Dufour – Case Postale 5326 - 1211 Geneva 11, as independent proxy for a term until the end of the next Ordinary General Meeting.

Appendix

Abbreviation / Term	Definition
ABCR	Beta interferons and glatiramer acetate (immunomodulators) are a class of first-line treatments that modify the inflammatory response, but do not appear to reduce significantly the immune response and, therefore, resistance to infections or cancers ("ABCR" is derived from the brand names of the medical products: Avonex©, Betaferon©, Copaxone©, Rebif©).
ADCC	Antibody-dependent cell-mediated cytotoxicity
ALS	Amyotrophic lateral sclerosis
Beta interferons	Self-injectable product that reduces the rate of relapse or flare-up in RRMS patients by approximately 30% compared to placebo
BSC	Banks of stem cells
CDC	Complement dependent cytotoxicity
CDR	Regions for determining the complementarity of antibodies
CFA	Complete Freund adjuvant used by the EAE consisting of inactivated and dried mycobacteria (typically M tuberculosis)
CIDP	Chronic inflammatory demyelinating polyradiculoneuropathy: a rare autoimmune disorder of the peripheral nervous system and orphan disease that is also called "Peripheral MS"
Clinical phases	Phase I: Study of the behavior of a molecule tested in an organism on the basis of time (the pharmacokinetics of absorption and elimination) and analysis of safety and tolerance in humans. This phase is conducted on a small number of healthy volunteers.
	Phase II: Assessment of the safety and efficacy of the molecule and determination of the therapeutic dose of the molecule.
	Phase III: Comparison of the efficacy of a new drug to the treatment of reference. This phase involves a large number of patients. The patients are selected on the basis of precise criteria that will make it possible to ascertain the efficacy and benefit of the drug tested as a new treatment for the targeted disease.
CMC	Chemistry, Manufacturing and Controls
CMO	Contract Manufacturing Organization, a company that acts as an external contract manufacturer
CMPH	Committee for Medicinal Products for Human Use, which is a committee of the European Medicines Agency (EMA)
Coronavirus	Coronaviruses are a large family of viruses that can cause illness in animals or humans. In humans there are several known coronaviruses that cause respiratory infections. These coronaviruses range from the common cold to more severe diseases such as severe acute respiratory syndrome (SARS), Middle East respiratory syndrome (MERS), and COVID-19.
CRO	Contract Research Organization, a company specializing in the organization and conduct of clinical trials
DRB1, DQ, DP, DRB 3, 4 and 5	Types of histocompatibility antigens
EDSS	Expanded disability status scale; a scale of disability for measuring the severity of MS
EAE	Experimental autoimmune encephalomyelitis model, animal model of reference in MS
FDA	US Food and Drug Administration
Glatiramer acetate	A copolymer composed of several amino which might interfere with the activation of T lymphocytes, monocytes and dendritic cells. It is administered by subcutaneous injections.
GMP	Good manufacturing practices
GNbAC1 (now temelimab)	A humanized monoclonal antibody that neutralizes a HERV protein called HERV-W ENV
HERV	Human endogenous retrovirus
HERV-K	Human endogenous retrovirus of the K family
HERV-W	Human endogenous retrovirus of the W family
HLA (or T CD4+)	Human leukocyte antigen
HSC	Human Schwann cells
IgG1 / IgG4	Immunoglobulins, also called antibodies
IL-6	IL-6, or interleukin-6, is an interleukin that acts as both a pro-inflammatory cytokine and an anti-inflammatory myokine.

Abbreviation / Term	Definition
INCAT	Inflammatory Neuropathy Cause and Treatment, clinical scale for CIDP
IND	Investigational New Drug application with the US Food and Drug Administration
Interleukin	Interleukin (IL), any of a group of naturally occurring proteins that mediate communication between cells. Interleukins regulate cell growth, differentiation, and motility. They are particularly important in stimulating immune responses, such as inflammation.
IVIG	Intravenous human immunoglobulins
KOL	Key opinion leaders
mAb	Monoclonal antibody
MS	Multiple sclerosis: degenerative, inflammatory and chronic disease that affects the central nervous system, consisting of the brain and spinal cord
MSFCS	Multiple sclerosis functional composite scale
MSRV-ENV	Previous name of HERV-W ENV. Envelope protein of the endogenous retrovirus MSRV or HERV-W and the target of the monoclonal antibody temelimab
OPC	Oligodendrocyte precursor cell
PBMC	Peripheral blood mononuclear cells
HERV-W ENV	Envelope protein of the endogenous retrovirus MSRV or HERV-W and the target of the monoclonal antibody temelimab
Pre-clinical phases	Laboratory tests to evaluate the principal effects of a molecule and its toxicity
PK	Pharmacokinetic
PNS	Peripheral nervous system
PPMS	Primary progressive multiple sclerosis: a clinical form of MS in which the symptoms of the disease get progressively worse in a linear way from the onset of the disease
RRMS	The most common form of MS, called relapsing-remitting MS; characterized by repeated occurrences or attacks of neurological symptoms
SARS-CoV-2	Novel coronavirus first identified in humans in December 2019 that is the cause of COVID-19.
SHC	Schwann human cells
SPMS	A more aggressive form of MS; the secondary progressive form during which the loss of neuronal function gets worse
T CD4+ (or HLA)	Auxiliary lymphocyte cellular epitope
T1D	Type 1 diabetes: A chronic disease that results from the autoimmune destruction of insulin-producing beta cells in the pancreas. The pancreas, therefore, produces little or no insulin, the hormone necessary for the penetration of sugar (glucose) into cells for conversion into energy.
Temelimab (previously GNbAC1)	A humanized monoclonal antibody that neutralizes a HERV protein called HERV-W ENV

Annual Financial Report Cross-reference Table

In accordance with Article 222-3 of the AMF's General Regulations, the Annual Financial Report referred to in Article L. 451-1-2 of the French Monetary and Financial Code contains the information described in the following sections of the Registration Document:

Information required in the Annual Financial Report	Corresponding sections and chapters of the Registration Document
1. Statutory financial statements 2020	Chapter 23
2. Consolidated financial statements 2020	18.3.2
3. Management report	
a) True and fair presentation of business evolution, results and financial situation of the Company and of the Group it consolidates	Chapter 3-5-7-8
b) Major events occurring after the year-end closing	10.1
c) Foreseeable development of the Company	5.1.2
d) Research and development activities	Section 5.8
e) Information about shares buy-backs	19.1.3
4. Statement of the person responsible for the annual financial report	1.2
5. Statutory auditors' report on the statutory financial statements	Chapter 23
6. Statutory auditors' report on the consolidated financial statements	18.3.1