A causal approach to changing the course of neurodegenerative diseases

Investor teleconference

June 2, 2020

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GeNeuro's mission

To change the course of neurodegenerative and autoimmune diseases

- Leveraging the biology of human endogenous retroviruses (HERVs) to neutralize causal factors associated with these disorders
- Approach validated through 2-year Phase II results on key markers of disease progression in Multiple Sclerosis
- Clear path to deliver full value of its approach to all stakeholders
  - Trial with Karolinska Institutet on patients with disability progression without relapses
  - Preclinical program against Amyotrophic Lateral Sclerosis in partnership with the NIH

Summary of AGM

74.37% of shares represented, 95%+ approval

1. Approval of 2019 Annual Report
2. Appropriation of Result
3. Appropriation of Reserves
4. Information on capital loss and remediation measures
5. Release of Board od Directors members and management
6. Compensation
    1. Consultative vote on Compensation Report
    2. Approval of Aggregate Compensation for Board of Directors
    3. Approval of Aggregate Compensation for Management
7. Election/re-election of Directors
8. Re-election of Chairman of the Board
9. Election/re-election of members of Compensation Committee
10. Re-election of Auditor
11. Re-election of Independent Proxy
12. Authorized capital

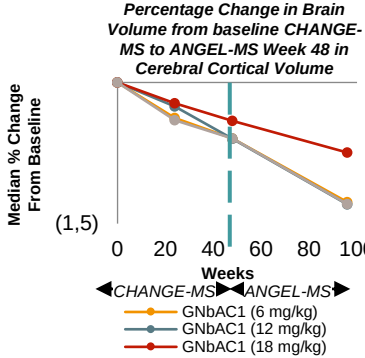
Full results available on http://www.geneuro.com/en/investors/general-meetings

2019 highlights

- Successful Phase Ic, assessing the administration of temelimab up to 110mg/kg to treat MS and other auto-immune diseases.
- Positive results from the ANGEL-MS study of temelimab in MS, confirming and extending at 96 weeks the data reported at Week 48 in the CHANGE-MS Phase IIb study.
- Successful results of the six-month extension of the Phase IIa study of temelimab in T1D confirmed all observations in the trial, meeting its primary objective.
- New academic publications supporting GeNeuro's approach in MS
- 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.

Clinical data show positive effects of temelimab (*GNbAC1*)

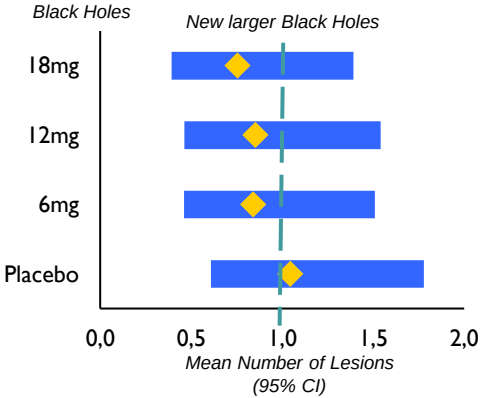
1 Evolution of Cortical Atrophy over 96 weeks



Group	Median % reduction at week 48 in ANGEL-MS	Relative reduction of atrophy
Control	(1.29)	42%
6mg/kg	(1.27)	41%
18mg/kg	(0.75)	

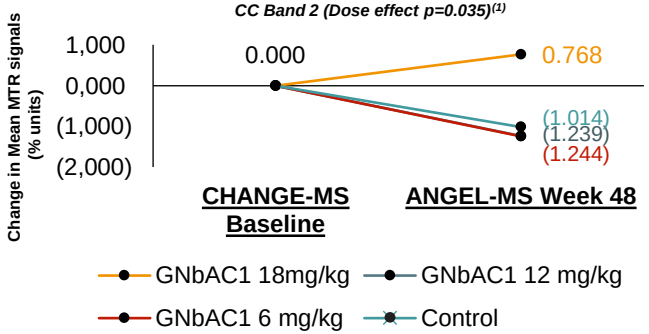
Dose effect p=0.058[1]

3 Reduction of Black Holes at week 48 (not computed at week 96 for technical reasons)



Median reduction between 18mg/kg group and control group in new larger T1 Black Holes[3] *=* ***63%*** *(p=0.014)*

2 Evolution of Cortical MTR[2] signal over 96 weeks



4 Very well tolerated drug

# 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[4]	1 (1.3%)	0	0

(1) Dose effect analyzed by linear regression, SAS analysis proc GLM; (2) ***MTR*** = Magnetization transfer ratio; (3) T1 hypointense lesion ≥ 14mm3 volume;
(4) Patient had previously voluntarily exited the study; the Investigator considered the event as unrelated.

New publications supporting GeNeuro's approach

Including for example

PNAS

pHERV-W envelope protein fuels microglial cell-dependent damage of myelinated axons in multiple sclerosis

D. Kremer et. Al., May 2019

cells

Review

The Molecular Basis for Remyelination Failure in Multiple Sclerosis

J. Gruchot et Al., August 2019

Recent two-year clinical data validates GeNeuro's approach against disease progression in MS

Supporting pre-clinical data

- **Neurodegeneration reduced** by
  - directly **acting on** proinflammatory **microglia,** the key immune cells in PMS, responsible for lesion growth and exacerbation
- **Neuroregeneration enabled** by
  - rescuing the negative impact of pHERV-W Env on **OPC** maturation - the key cells in the remyelination process.
- **No direct effect on T/B lymphocytes** and thereby not compromising adaptive immunity
- **Excellent preclinical safety package** based on a stabilized IgG4 backbone, low immunogenicity and a linear PK at all doses

Clinical observations

- **Reduction of Brain Atrophy**
- **Reduction in new T1 Black Holes**
- **Benefit on Magnetization Transfer Ratio**
- **Effects on markers associated with disease progression not due to immune modulation**
- **Excellent tolerability in clinical trials**

➢ Clear positioning against **disability progression**, the key unmet medical need in MS

Sources: Kremer et al., Ann Neurol 2013; Kremer et al., Mult Scler J 2015; *Luo et al., Neuropsychiatr Dis Treat 2017; Göttle et al. Glia 2018; Küry et al., Trends Mol Med; Kremer, Gruchot et al., PNAS May 2019

ALS program aiming at obtaining IND in 2021

- Research partnership in 2017, extended in 2019, with the National Institute of Neurological Disorders and Stroke (NINDS), part of the U.S. National Institutes of Health (NIH)
  - GeNeuro provides antibodies designed to block the activity of HERV-K envelope protein
  - NINDS tests antibodies in cellular and animal models of HERV-K associated ALS
  - Results validate the potential of GeNeuro's anti pHERV-K antibodies as a new therapeutic approach against ALS

- Following successful results of the research partnership with NIH in ALS models, GeNeuro has signed in October 2018 an exclusive worldwide license with the NIH covering the development rights of an antibody program to block the activity of pHERV-K Env, a potential key factor in the development of ALS

  GeNeuro is executing on the preclinical development of the lead antibody, aiming at IND by 2H2021

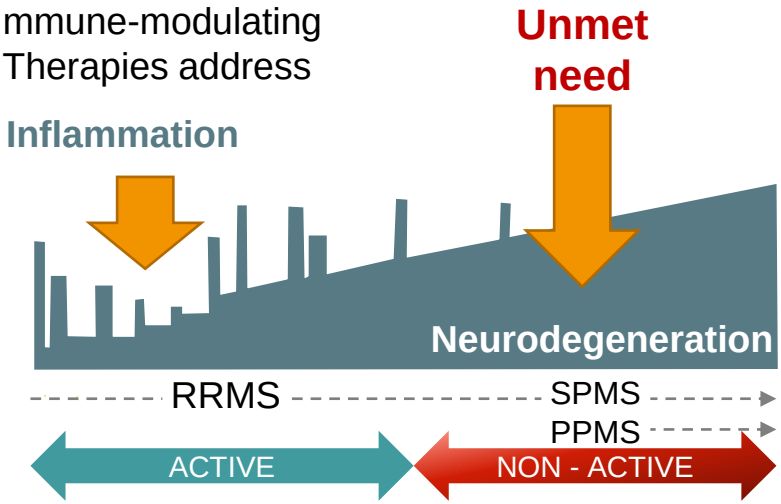
First mover in HERV-mediated diseases

Program	Pre-clinical	Phase I	Phase IIa	Phase IIb	Phase III
1. Temelimab Multiple Sclerosis CHANGE-MS / ANGEL-MS **Karolinska/ASC trial**	Planning next stage developments based on positive neurodegeneration 96-week results **CHANGE-MS : 270 patients in RRMS indication** - completed 03/2018 **ANGEL-MS : 219 patients extension** - Completed 03/2019 **Phase II study in Non-Active Progressive /** Launch initially planned Q1 2020*				
2. Anti-HERV-K ALS	**R&D Agreement with NIH, IND submission planned for 2021** Preclinical program underway, candidate humanized				
Other opportunities	***Subject to ad-hoc funding / partnering***				
3. Temelimab Type 1 Diabetes	Safety & signal finding Phase IIa, completed 05/2019 New study subject to development of temelimab in MS				
4. Temelimab CIDP	ODD granted by the US FDA No study planned presently.				
5. New anti HERV-W Ab Inflammatory Psychosis	Research collaborations with Academic labs, murine candidate selected No study at present without ad-hoc non-dilutive funding				

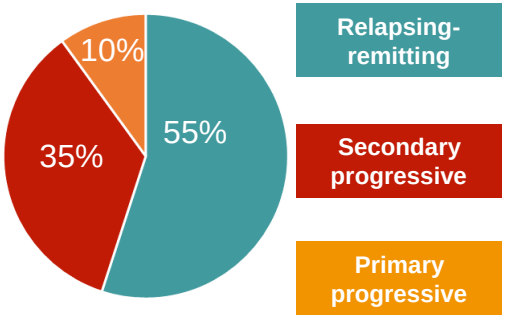
* : launch initially planned Q1 2020, delayed by COVID-19 pandemic

GeNeuro targets the key unmet medical need in MS

Immune-modulating Therapies address



Total MS population



"It is evident that currently available disease modulatory therapies for MS exert very limited effects on the progressive aspect of MS and that this phase starts early in the disease course. A role of pHERV-W Env in progressive disease worsening is supported by accumulating preclinical and clinical evidence. We are excited to explore the therapeutic potential of temelimab in patients progressing without relapses [--] to push the boundaries of current therapeutic possibilities,"

Prof. Fredrik Piehl, Professor of Neurology at the Department of Clinical Neurosciences of the Karolinska Institutet, *Press release, November 25, 2019*

The “Karolinska” study - Endpoints bridge to previous studies and explore markers of myelin and axonal integrity

Primary endpoints

- Safety and tolerability of temelimab

Secondary endpoints (bridged to CHANGE and ANGEL-MS studies)

- MRI measurements documenting baseline versus week 48 in:
  - Volume of thalamus, cortex + globus pallidum
  - Number and volume of black holes
  - Change in myelin integrity by magnetization transfer ratio (MTR)
- Markers of neurodegeneration / neuroprotection in biofluids (NfL, neurogranin, MBP, etc.)

Exploratory endpoints (based on novel myelin and lesion imaging)

- MRI measurements documenting baseline versus week 48 in:
  - Markers of myelin integrity, myelin fraction (REMyDI) and axonal density (multi shell diffusion) in lesions and slowly evolving lesions vs normal appearing white matter (NAWM)
- Clinical assessments documenting baseline versus week 48 in:
  - Overall Disability Response Score (ODRS) – multicomponent clinical endpoint

COVID-19 has delayed the start of the trial, initially planned for March 2020

- GeNeuro announced on March 19 the temporary postponement of its planned Phase 2 trial of temelimab in multiple sclerosis (MS) at the Karolinska Institutet
  - to prioritize healthcare resources behind the fight of COVID-19 and
  - to reduce the risk for MS patients

- The 1-year trial will enroll patients whose disability progresses without relapses
- GeNeuro has previously announced that its cash runway will last until mid-2022, well beyond the end of the Phase II trial as long as the recruitment of its 40 patients is finalized in 2020.

High unmet medical need with multiple options for Phase II/III and/or Phase III development

Development options

- **As a monotherapy or on top of existing DMTs**
  - Extension and enlargement of the Karolinska trial, seeking clinical endpoints at two years
  - As monotherapy**,** in non-active progressive MS patients, as clear regulatory entry point; and / or
  - On top of a number of existing DMTs, to enlarge addressable patient population (but also increasing trial's number of patients due to baseline diversity)

- **Combination with a Partner's existing DMT**
  - Temelimab's safety profile allows a combination with existing anti-inflammatory drug, to slow-down / prevent progression on treated Relapsing MS patients (rendered "non-active" by their anti-inflammatory treatment)

Reinforcement of GeNeuro's team

Recruitment of Dr. David Leppert, MD, as Chief Medical Officer of GeNeuro

In addition to his academic accomplishments, David has had a long and distinguished industry career, where he has notably led the development of ocrelizumab as Global Development Team Leader at Roche, and subsequently led clinical development activities of ofatumumab and siponimod as Therapeutic Area Head Neuroinflammation at Novartis

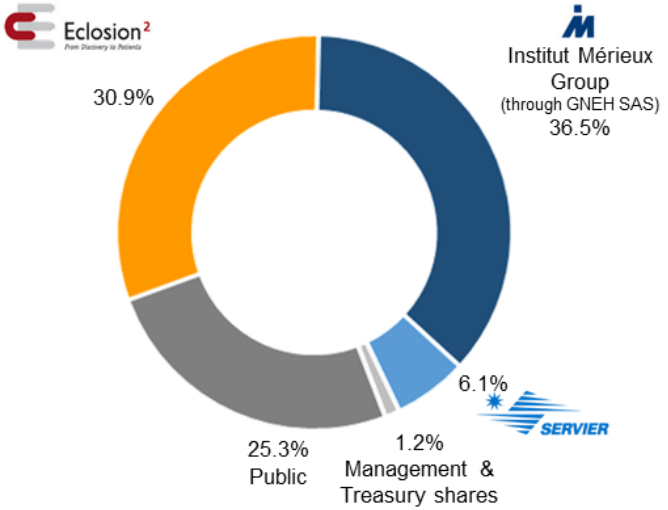
http://www.geneuro.com/en/about/management

Recap Capital increase

- International private placement to selected institutions
- Raised €17.5 mln in gross proceeds through:
  - Issuance of 5.9 mln new shares
  - At issue price of €2.95, i.e. 7% discount to closing price on Jan. 30
- Key participants in Private Placement:
  - GNEH SAS/ Institut Mérieux
  - Invesco
  - Invus
  - Van Herk Investment Group

Financial Summary
Successful Jan. 2020 PIPE extends runway to 1H2022

Share capital as of February 2020



Note: excludes stock options, representing a maximum 4.5% dilution, with an average exercise price of €9.89 per share

P&L and cash balance (in € '000)

	FY 2019	FY 2018	FY 2017
Income	-	7,463	14,949
R&D Expenses	(5,262)	(10,930)	(16,161)
G&A	(3,744)	(4,686)	(4,597)
Operating loss	(8,990)	(8,089)	(5,740)
Cash & Equivalents	15,2M[(1)]	8,961	26,602

(1) : pro forma including net proceeds from Jan. 2020 PIPE

Cash at end Q1 2020 was €11.8 million

Financial Agenda

Next investor meetings

- June 18: Gilbert Dupont "SMALL & MIDCAPS” Forum - All Digital
- June 23-24: European Spring ‘MidCap Event Paris – All Digital

Capturing the full value of the HERV platform

- Clear path to deliver value in Multiple Sclerosis
  - Effort on track to finalize dose and confirm benefit on patients whose disability is progressing despite treatment reducing relapses
  - Open options for development going forward in MS
- ALS program on track, in partnership with NIH, aiming for IND in 2021
- Programs in T1D and inflammatory psychosis sidelined, only with ad-hoc funding / partners

A causal approach to changing the course of neurodegenerative diseases

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Temelimab's strong results pave the way for the continued development against disease progression

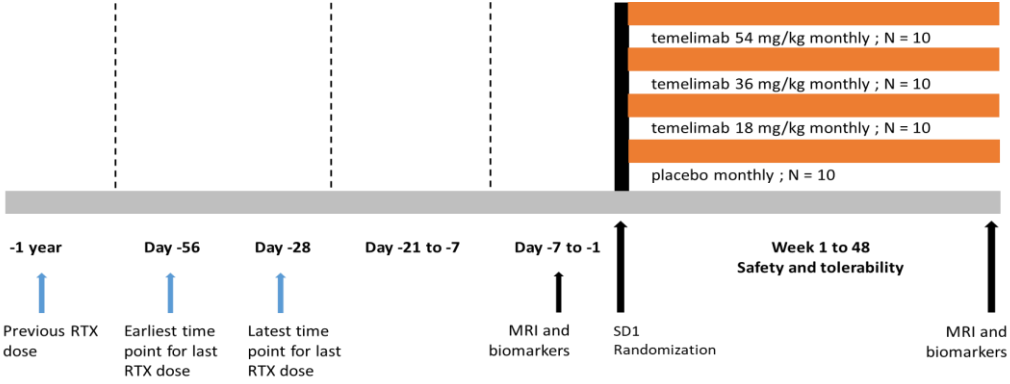
Strengths of the program

- Robust and consistent impact on the MRI markers associated with disease progression, confirmed at 96 weeks
  - Reduction of atrophy of brain volumes (Thalamus, Cortex, whole brain),
  - Reduction of Black Holes
  - Maintained MTR values
- Activity appears to be independent of anti-inflammatory effect
- Excellent safety for long term treatment, as monotherapy or in combination
- Corroborated by accumulating scientific evidence of the pertinence of the mode of action

Further data to be generated

- Generation of data in progressing MS population
- Define the optimal dose

The “Karolinska” study – A bridging study to explore doses and effect on the target population



Phase II study outline:

- Karolinska’s Academic Specialist Center; PI: Fredrik Piehl MD PhD
- RMS patients with confirmed disability progression in the absence of relapse activity (PIRA)
- Relapse activity is managed thanks to B-cell depletion with rituximab (anti-CD20 mAb)
- Monthly administration of temelimab 18, 36, 54 mg/kg vs placebo
- Initially 40 patients with confirmed progression over the last year, with EDSS of 3.0-5.5
- Bridging CHANGE-MS and ANGEL-MS MRI endpoints, and adding novel biomarkers linked to disease progression, myelin integrity and axonal density

RAINBOW-T1D Summary

Successful study, opening way to early-onset T1D trials

- 12 month study with a 6-month double blind period and a 6-month extension with all patients on temelimab, including patients previously on placebo
- Excellent safety / tolerability of temelimab observed over one year
- Positive temelimab pharmacodynamic observations at 6 months are confirmed in the second period
- No conclusions possible on C-peptide, insulin consumption and HbA1C: small cohort size from a late onset adult population, well treated with low insulin needs, stable during trial
- Study completes its objective of demonstrating safety and pharmacodynamic response in adult T1D patients, opening door to further development in larger early-onset pediatric population

Rainbow T1D Week 48 PD Outcomes - Hypoglycemia

Confirmed decrease of hypoglycemic episodes

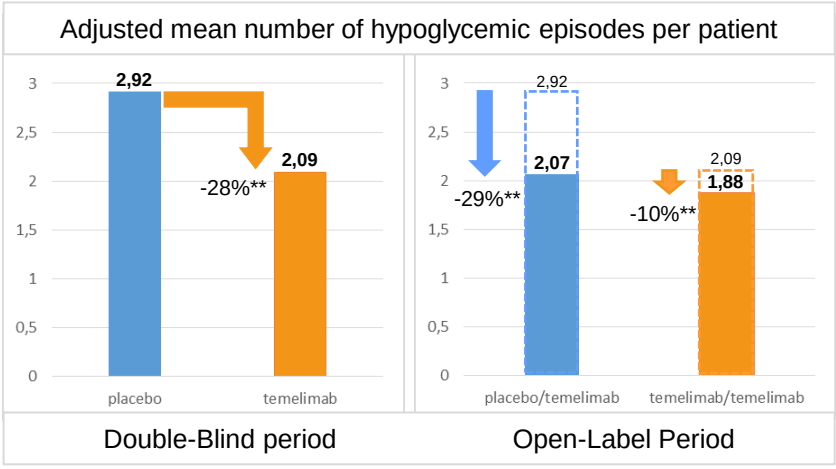
Adjusted mean number of hypoglycemic episodes per patient	Temelimab/temelimab (N=31 out of 43**)	Placebo/temelimab (N=14 out of 21**)	Rate ratio	P-value*
Double-blind Period	2.09	2.92	0.75	0.0001
Extension Period	1.88	2.07	0.91	0.82

Group treated by temelimab 12 months:

- Reduction of frequencies of hypoglycemia under temelimab in first 6-month (-28%, p<0.0001 vs placebo),
- Further reduction of 10% in the second 6 month period

Group switching to temelimab from placebo:

- Reduction of hypoglycemia frequency in this group vs the previous placebo period (-29%), reaching the level of reduction observed with temelimab in the first 6 months of treatment



* Poisson regression analysis

** Patients who continued in the Open-Label period