



# ANNUAL REPORT

2023



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## Letter to the EUpALS community

Dear EUpALS community,

2023 was an exciting year in our common fight to find a cure for ALS.

In light of recent developments, we like to provide an update on the evaluation of potential ALS therapies by the European Medicines Agency (EMA) that started in 2023. Indeed, after decades of setbacks in clinical trials, there is now a glimmer of hope for ALS patients.

By fostering productive dialogues and sharing essential information, we can collectively work towards brighter prospects for people living with ALS.

Unfortunately, Amylyx received negative opinion from CHMP on its conditional Marketing Authorization Application for AMX0035 (ALBRIOZA) based on data from the CENTAUR Phase 2 trial. Amylyx is now analysing the data of its PHOENIX Phase 3 trial to present to EMA in Q2 2024.

As for the ASO therapy Tofersen (QUALSODY) from BIOGEN, we anticipate CHMP opinion in H1 of 2024.

Recognizing the significance of a well-informed evaluation, it is paramount that CHMP members possess a comprehensive understanding of ALS and its profound impact on patients and their families. To facilitate this, we strongly encourage our member national ALS/MND Associations to arrange meetings with the CHMP delegates representing your country.

We also like to extend an invitation to engage with the Key Opinion Leaders in your country. This collaboration would greatly aid in gathering the essential support required for the approval process of therapies.

Whenever feasible, these discussions should involve the presence of an individual living with ALS, allowing for a personal testimony of the challenges faced.

Your unwavering dedication and commitment to the ALS community are sincerely appreciated. Let us continue to stand united in our mission to improve the lives of those affected by this challenging condition.

Evij Reviens  
Chairwoman EUpALS





## What is ALS?

ALS stands for Amyotrophic Lateral Sclerosis, an incurable and deadly neuromuscular disease characterized by progressive paralysis.

In Europe, ALS is also known as

SLA, for Sclérose Latérale Amyotrophique (France and French-speaking Belgium) and for Sclerosi Laterale Amiotrofica (Italy)

MND, for Motor Neuron Disease (UK, Ireland, Iceland)

ELA, for Esclerosis Lateral Amiotrófica (Spain and Portugal)

Maladie de Charcot (France and French-speaking Belgium): less used than SLA

In the US the illness is often called Lou Gehrig disease, named after a legendary baseball player who passed away from this disease in 1941.

## Symptoms of ALS

In brief, the following symptoms can be observed in patients with ALS. Not all symptoms occur in an individual ALS-patient.

- Weak and thin muscles, resulting in paralysis
- Joint and muscle pains; muscle contractions
- Fatigue, tiredness
- Reduced appetite resulting in weight loss
- Difficulty chewing, swallowing and speaking; drooling
- Problems with bowel movement
- Reduced lung vital capacity, resulting in difficult breathing
- Compulsive crying, laughing or yawning

## Occurrence and heredity of ALS

ALS is not a rare disease as it affects 6 to 7 people out of every 100.000. It occurs all over the world. Most people are affected by ALS between the age of 50 and 75 but there are also teenagers with ALS.

The diagnosis can only be determined after all other neurologic conditions have been excluded. The course of the disease is progressive but the evolution varies from one person to another.

In Europe, ALS affects about 50.000 individuals of middle age, killing about 10.000 people on a European level each year. Worldwide 450.000 people suffer from ALS. Each year 120.000 people are diagnosed with ALS. This means that every day there are 328 new known cases, which equals 2 new diagnoses of ALS per 100.000. Every year 120.000 patients die from ALS worldwide.



In about 10% of the ALS cases there is a familial pattern. When it concerns the familial type, ALS is usually genetically dominant, which means that a child has a 50% chance of becoming ill. The symptoms of familial ALS are the same as those of the sporadic form. The only difference is that people with familial ALS are usually younger when the first symptoms arise.

### About EUpALS

#### Mission

EUpALS is a European association taking the interests of European ALS patients to heart. We want to obtain equal rights for all European ALS patients and provide them better access to research and information on ALS. We are willing to assume and carry out our role for these 3 aspects.

#### Vision








Our organization aims to fight against ALS in Europe and make everybody aware of this terrible disease. This is why we want to unite all the European ALS/MND associations: to fight harder together on a European scale.

#### Objectives

- Stand up for the rights of all European ALS patients
- Create awareness about ALS on a European scale
- Improve access to and information about ALS research and clinical trials
- Obtain the same rules for ALS research and clinical trials across Europe









## EupALS Board of Directors

 <p>Evy Reviere <i>Chairwoman</i> CEO ALS Liga Belgium</p>	 <p>Sabine Turgeman <i>Treasurer</i> CEO ARSLA France</p>	 <p>Prof. Christian Lunetta <i>Director</i> Post Fata Resurgo Italy</p>
 <p>Joaquin de la Herrán <i>Director</i> Executive Committee member Fundación Luzón Spain</p>	 <p>Dr. Aylin Yaman <i>Director</i> Antalya Branch of ALS/MND Association Turkey</p>	 <p>Guðjón Sigurðsson <i>Secretary</i> Chairman MND Iceland</p>
 <p>Limore Noach <i>Director</i> CEO Stichting ALS The Netherlands</p>	<p>EupALS Board of Directors meetings in 2023</p> <ul style="list-style-type: none"><li>• March 1 (webmeeting)</li><li>• July 11 (Barcelona satellite to ENCALS or webmeeting)</li><li>• September 13 (webmeeting)</li><li>• October 24 (webmeeting)</li></ul>	





EupALS Patients and Carers Expert Board (PCEB)

 <p>Alper Kaya <i>ALS/MND Association Turkey</i></p>	 <p>Mia Möllberg <i>ALS Sweden</i></p>	 <p>Jan Bastiaens <i>ALS Liga Belgium</i></p>
 <p>Angélique van der Lit – van Veldhuizen <i>ALS patiëntenvereniging</i></p>	 <p>Josefina Garcia Pastor <i>Fundació Miquel Valls Spain</i></p>	 <p>Ywan Dierick <i>ALS Liga Belgium</i></p>
<p>Major activities 2023 of the EupALS PCEB</p>	<ul style="list-style-type: none"> <li>• March 15 (webmeeting)</li> <li>• July 11 (Barcelona satellite to ENCALS or webmeeting)</li> <li>• September 20 (webmeeting)</li> <li>• December 13 (webmeeting)</li> </ul>	<ul style="list-style-type: none"> <li>• Feedback to 4 EupALS Industry Partners</li> <li>• Testimonies at TRICALS Masterclass 2023 Amsterdam</li> </ul>







## EupALS Scientific Expert Board (SEB)

		
<p>Prof. Philip Van Damme <i>UZ Leuven, Belgium</i></p>	<p>Prof. Leonard van den Berg <i>UMC Utrecht, The Netherlands</i></p>	<p>Prof. Philippe Corcia <i>CHRU Tours, France</i></p>
		
<p>Prof. Caroline Ingre <i>Karolinska Institutet Stockholm, Sweden</i></p>	<p>Prof. Adriano Chiò <i>University of Torino, Italy</i></p>	<p>Prof. Ammar Al-Chalabi <i>Kings College London, UK</i></p>
		<p><i>Major activities 2023 of the EupALS SEB</i></p> <p><i>EupALS is represented in bi-weekly TRICALS Executive Board webmeeting</i></p> <p><i>Co-drafting EupALS Position Paper on Genetic Testing</i></p>
<p>Prof. Orla Hardiman <i>Trinity College Dublin, Ireland</i></p>	<p>Prof. Monica Povedano <i>IDIBELL Barcelona, Spain</i></p>	







## EupALS Member Associations 2023

Uniting 28 ALS/MND Associations from 22 European countries

















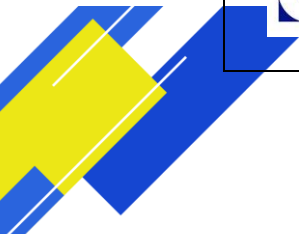


 <p><b>MUSKELSVINDFONDEN</b> plads til forskelle!</p>	 <p><b>POST FATA RESURGO</b></p>	 <p>FUNDACIÓN <b>LUZÓN</b> UNIDOS CONTRA LA ELA</p>
 <p>ULLA-CARIN LINDQUISTS STIFTELSE FÖR ALS-FORSKNING</p>	 <p><b>rmmn</b> Research Motor Neurone</p>	 <p><b>MDA ΕΛΛΑΣ</b> ΣΩΜΑΤΕΙΟ ΕΡΓΟΝΟΜΙΑΣ ΑΤΟΜΩΝ ΜΕ ΝΕΥΡΟΜΥΚΕΣ ΠΑΘΗΣΕΙΣ</p>  <p><b>MDA HELLAS</b> MUSCULAR DYSTROPHY ASSOCIATION</p>
 <p><b>MUSCULAR DYSTROPHY ASSOCIATION OF SLOVENIA</b></p>	 <p>conSLAno</p>	 <p><b>eamda</b> European Alliance of Neuromuscular Disorders Associations</p>
 <p><b>LIVE NOW</b> RUSSIA</p>		

EupALS Industry Partners 2023

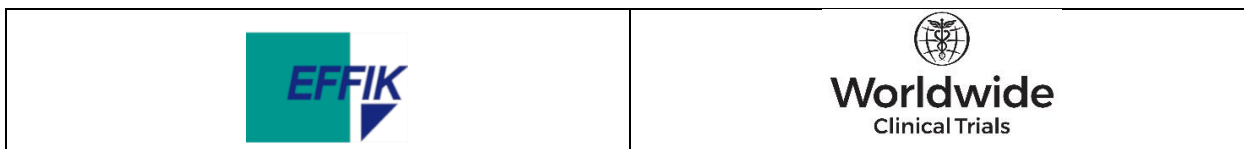
Gold

 <p><b>AMYLYX</b></p>	 <p>Apellis</p>	 <p>argenx</p>
 <p><b>Biogen</b></p>	 <p><b>Corcept</b> THERAPEUTICS</p>	 <p><b>CYTOKINETICS</b></p>
 <p><b>ferrer</b> for good</p>	 <p><b>NOVARTIS</b></p>	 <p><b>REGENERON</b></p>
 <p><b>sanofi</b></p>	 <p><b>TRANQUIS</b> THERAPEUTICS</p>	 <p><b>WAVE</b> LIFE SCIENCES</p>
 <p>Inspired by patients. Driven by science.</p>	 <p><b>ZBiotech</b> Zambon Biotech</p>	





Silver

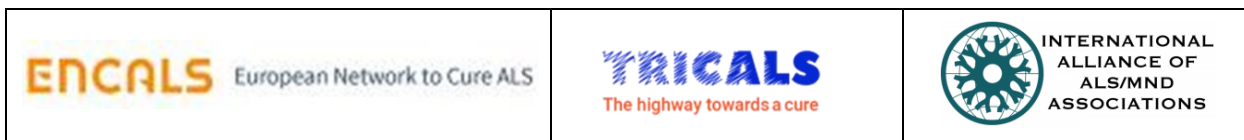


Bronze



Academic partners

Close collaboration



EUpALS activities 2023

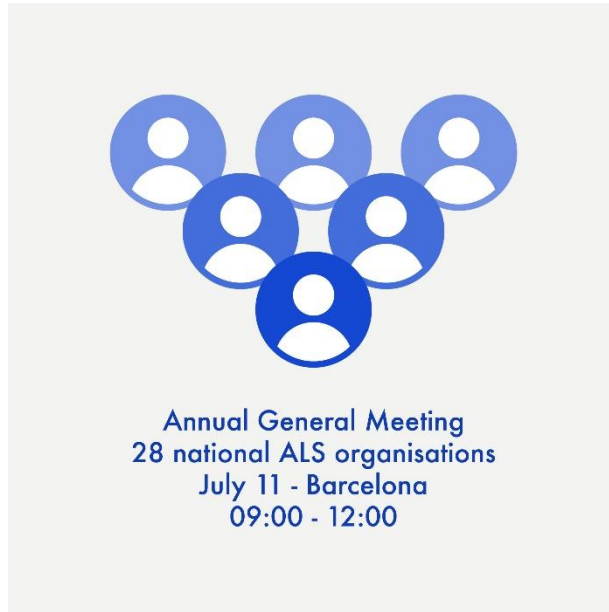
March 1	Board of Directors
March 15	Patients and Carers Expert Board
March 21	Newsletter Spring edition
March 29	Scientific webinar
April 19	Board of Directors
May 10	Brainstorm session on topics Round Table July 11 satellite to ENCALS Barcelona
June 7	Patients and Carers Expert Board
June 14	Board of Directors
June 21	Newsletter Summer edition
July 11	Satellite to ENCALS Barcelona : 09h-12h : Annual General Meeting
July 11	Satellite to ENCALS Barcelona : 12h-13h : Board of Directors
July 11	Satellite to ENCALS Barcelona : 16h-19h : Round Table
September 13	Board of Directors
September 20	Patients and Carers Expert Board
September 21	Newsletter Autumn edition
November 22	Board of Directors
December 6-8	Satellite to Int. ALS-Symposium Basel : Board of Directors
December 13	Patients and Carers Expert Board
December 21	Newsletter Winter edition





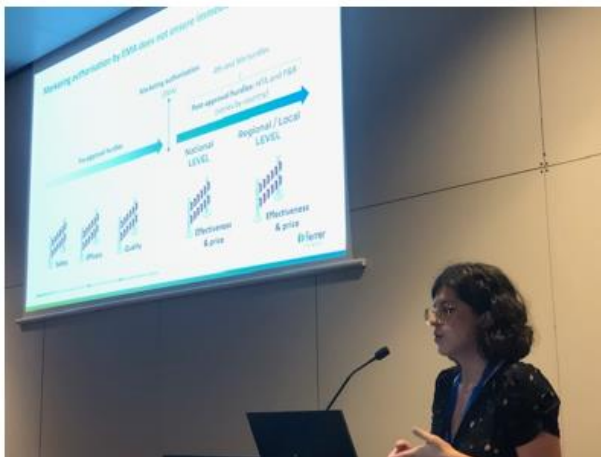
## EupALS Annual General Meeting 2023

On July 11, EupALS organised its **Annual General Meeting 2023** satellite to ENCALS in Barcelona. Thank you all our Member Associations, Industry Partners and other stakeholders who attended in person or virtually.



## EupALS Round Table 2023

On July 11, EupALS organised its **Round Table on Market Access** satellite to ENCALS 2023 in Barcelona. Thank you all our Member Associations, Industry Partners and other stakeholders who attended in person or virtually. Your active participation and valuable input is greatly appreciated.





## EupALS Position Paper 2023

Following the EupALS Round Table 2023, an EupALS Working Group on Market Access was set up. In close collaboration with the EupALS Scientific Expert Board, the EupALS Position Paper 'Need of EU harmonisation of ALS patient genetic testing' was drafted by the Working Group.

On March 23 2023, the Position Paper was communicated to Members of the European Parliament.



### Position Paper

#### Need of EU harmonization of ALS patient genetic testing

##### Hope emerges for ALS patients as ASO-based therapies for genetic subgroups become successful

After decades of repeatedly negative clinical trial results, hope is emerging for ALS patients as a clear milestone in ALS research has been reached, showing that ALS is a treatable disease after all.

Indeed, positive data from the Biogen's VALOR OLE study of the antisense oligonucleotide (ASO) Tofersen in patients with ALS based on an SOD1 mutation were published in the prestigious journal *The New England Journal of Medicine* (edition 2022; 387:1099-1110). The study shows that the therapy reduces motor nerve cell damage and that patients show stabilization in their disease progression. Based on these study results, the FDA approved QALSODY (Tofersen) on April 25, 2023.

Tofersen is currently under evaluation by EMA for market authorization in the EU. Meanwhile, Biogen initiated a Compassionate Use - Early Access Program for Tofersen in the EU.

Having shown the therapeutic potential of an ASO to treat ALS, Biogen and several other companies are currently conducting similar ASO-based clinical trials in other genetic subgroups of ALS patients.

##### My genetic profile: an ALS patient's access key to ASO-based clinical trials and therapy

To gain access to an ASO-based trial and therapy, it is critical to an ALS patient to know his/her genetic profile. In addition to previous scientific knowledge that gene mutations are the underlying cause of familial ALS only (approximately 10% of patients), it becomes nowadays widely accepted that genes also play a role in sporadic ALS (90% of patients), as some of the ALS genes have a reduced penetrance.

Genetic profiling should therefore be offered to all ALS patients as part of the standard clinical practice at diagnosis.

##### Need of EU harmonization of ALS patient genetic testing

In accordance with the right of freedom of movement of EU citizens, genetic profiling should be harmonized throughout all EU member states, and preferentially expanded to the additional EEA and EFTA countries, as well as the UK.

In practice, results performed by a certified ALS genetic testing facility of a certain EU member state should be accepted in all other member states. Most appropriate, this can be implemented through an existing European network of centers of excellence, e.g. ENCALS.







To facilitate this, a pan-EU agreement on the genetic profile that should be analyzed (ranging from a well-defined set of ALS causative genes, to whole-genome sequencing also revealing ALS risk genes), and the according unified technical method to be used, should be agreed upon by the European scientific ALS community as soon as possible. As the initiation of new therapies depends on the outcome of the gene testing, the turn-around time of gene testing should be short.

EU harmonized ALS genetic testing with minimum out of pocket contribution charged to the patient

As ALS therapy and care brings along a substantial economic burden for most patients, the out of pocket contribution that is charged to the ALS patient to have genetic testing should be minimized.

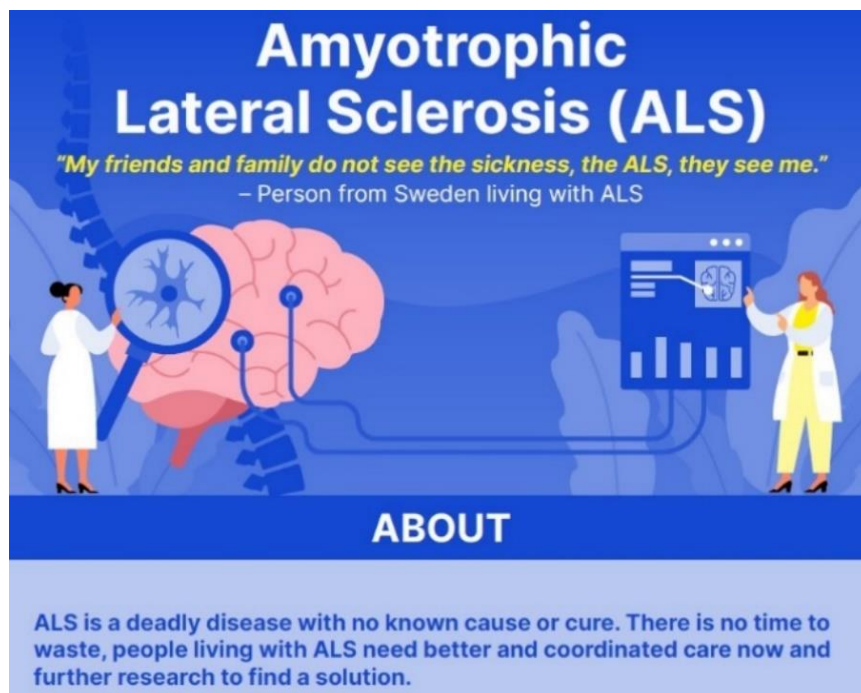
Therefore, we call upon the MEPs and all stakeholders involved in HTA, pricing negotiation, and reimbursement decision processes of all EU member states to align the personal financial contribution by the ALS patient.

**Call to action**

- Genetic profiling with short turn-around time should be offered to all ALS patients as part of the standard clinical practice at diagnosis.
- Results of ALS genetic testing in a certain EU member state should be accepted in all other member states. This harmonization should preferentially be expanded to the additional EEA and EFTA countries.
- Reimbursement of genetic testing should align among all EU member states, to minimize the out-of-pocket financial contribution by the ALS patient.

*EUpALS awareness campaigns 2023*

- February 28 2023: On the occasion of **Global Rare Disease Day**, EUpALS launched a social media campaign with an infographic/video on ALS







- June 21 2023: On the occasion of **Global ALS Awareness Day**, EupALS launched a social media campaign with compilation video of messages by our member ALS Associations



## EupALS and EU policy impact 2023

- February 8 2023: Co-organisation of the event 'Care for persons with Amyotrophic Lateral Sclerosis (ALS) in Europe' in the European Parliament Brussels in collaboration with Fundación Francisco Luzon and MEP Jordi Cañas (Renew Europe).

On this occasion, the document 'Comparative analysis of care for people with ALS in Europe' was presented and discussed by a panel in which EupALS Chairwoman Evy Reviérs participated.





- September 7 2023: Participation in the event 'Time to improve the lives of people with ALS' in the European Parliament Brussels in organisation of the EU ALS Coalition of which EupALS is a partner.

On this occasion, the document 'ALS, a rare neurodegenerative disease: European landscape assessment and policy recommendations for improved diagnosis, care and treatment' was presented and discussed by a panel in which EupALS Chairwoman Evy Reviërs participated.



## ALS clinical trials in 2023

In 2023, the following ALS clinical trials were conducted by EupALS Industry Partners (alphabetical):

- PHOENIX Phase 3 study with AMX-0035, conducted by Amylyx
- MERIDIAN Phase 2 study with pegcetacoplan, conducted by Apellis
- VALOR Open Label Extension study with Tofersen (SOD-1 ASO), conducted by Biogen
- DAZALS Phase 2 study with dazucorilant, conducted by Corcept
- COURAGE-ALS Phase 3 study with reldesemtiv, conducted by Cytokinetics
- ADORE Phase 3 study with FAB122 (oral edaravone), conducted by Ferrer
- HIMALAYA Phase 2 study with SAR443820, conducted by Sanofi
- FOCUS-C9 Phase 1b/2a study with WVE-004 (C9orf72 ASO), conducted by Wave





## EUpALS entered partnership in EU project Real4Reg

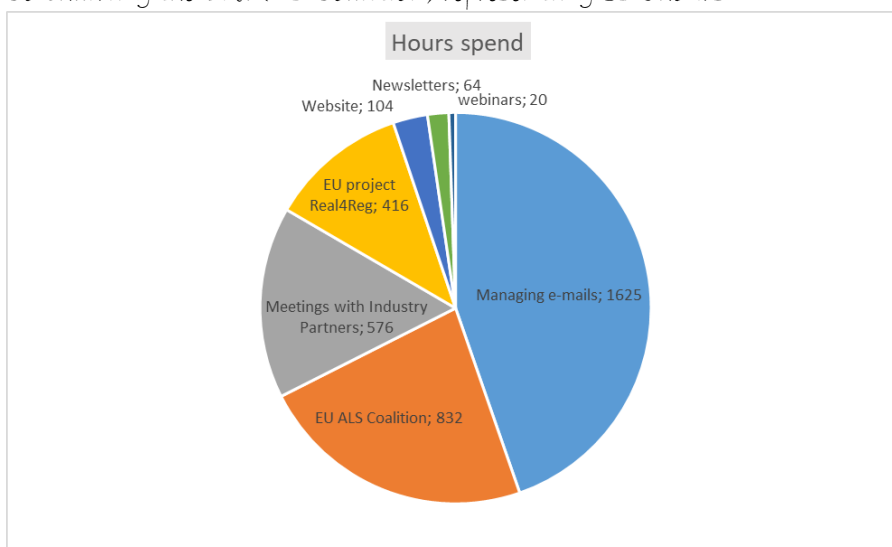
In 2023, EUpALS entered partnership in the EU Horizon project Real4Reg that develops Artificial Intelligence methods for Real World Data analysis in regulatory decision making.



## EUpALS 2023 in numbers

In 2023, EUpALS invested resources and time in

- updating the EUpALS website, representing 104 hours
- Production of 4 Newsletters, representing 64 hours
- Organisation of 2 webinars, representing 20 hours
- Catch-up meetings with Industry Partners, representing 576 hours
- Managing 6625 e-mail contacts, representing 1625 hours
- Managing partnership in EU project Real4Reg, representing 416 hours
- Co-chairing the EU ALS Coalition, representing 832 hours





## Contact

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