Agenda

- Fondazione AriSLA

- Strategic Plan 2023-2025_ where we are

- AriSLA 2025 Call for Letter of Intent

  - Objectives

  - Features

- Suggestions for grant writing

- Time for discussion

AriSLA, Fondazione Italiana di Ricerca per la Sclerosi Laterale Amiotrofica ETS

AriSLA, since 2008 alongside the research

The Foundation is **the leading Italian non-profit body that supports and promotes ALS research.**

It was born in 2008 thanks to the foresight of our 4 founding members, **AISLA Aps** – Associazione italiana Sclerosi Laterale Amiotrofica, **Fondazione Cariplo**, **Fondazione Telethon ETS**, **Fondazione Vialli e Mauro** per la Ricerca e lo Sport Onlus.

Since then AriSLA has been working with the **aim of promoting excellent research,** to give concrete answers to those who live every day with this disease.

AriSLA, Fondazione Italiana di Ricerca per la Sclerosi Laterale Amiotrofica ETS

AriSLA, mission and vision

Mission: To support **excellent research** towards the cure of ALS

Vision: To become the **landmark for the Italian scientific community**, playing the role of catalyst and driving force to fight ALS, **providing the necessary economical, scientific and technical support**
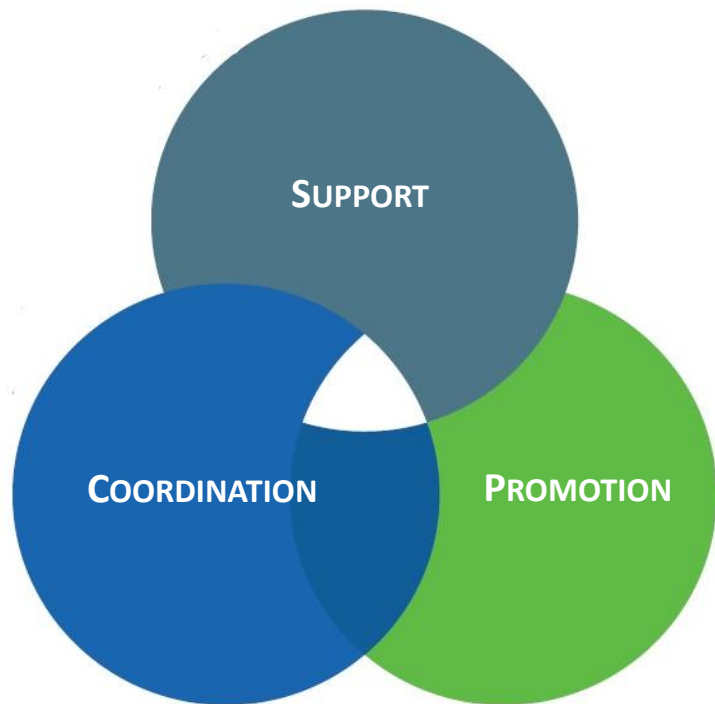
→ **SUPPORT**

Investing in research excellence, through the launch of **competitive calls for projects** and a **rigorous selection process**.

→ **COORDINATION**

Monitoring output/outcome of the projects, not only their economic performance.

→ **PROMOTION**

Dissemination of the scientific results derived from the funded projects and of the advancements on ALS research for the scientific community, patients and their families, associations and donors that support the Foundation's activities.

Numbers reflect a real commitment

→ SUPPORTING RESEARCH

16.980.138 €
invested in research programs since 2009

17
Calls for research projects on ALS

115
funded projects

160
research groups involved

306
scholarships to young researchers

→ SHARING RESULTS

45
scientific dissemination events

400+
publications derived from AriSLA- funded projects (2010-2024)

→ ENGAGING PEOPLE

101
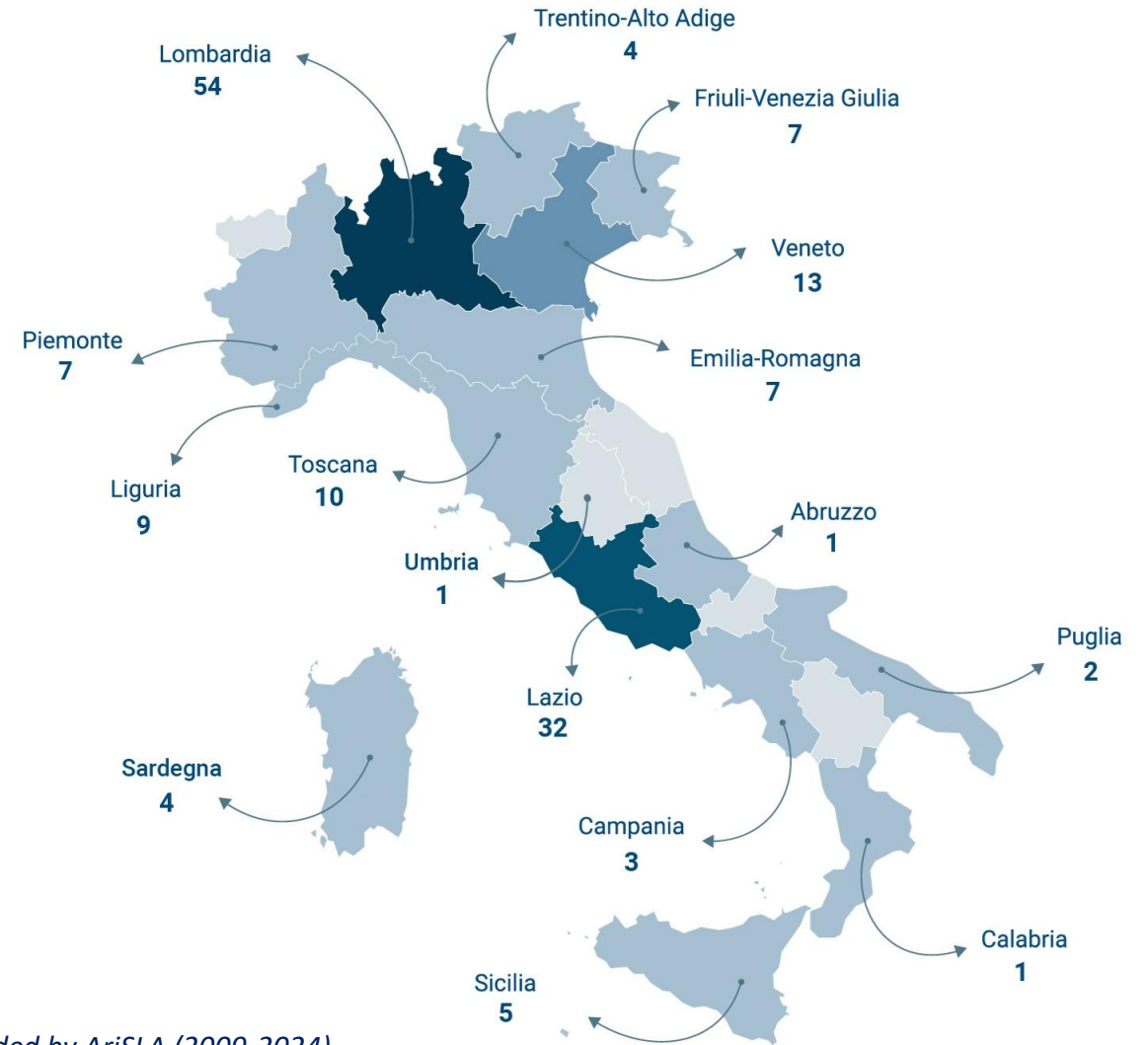fundraising events promoted by groups of volunteers

25+
companies and organizations adopted our projects

13
editions of the AriSLA Book reporting our scientific achievements and the activities implemented each year

Funding research in Italy

AriSLA supports the Italian scientific community, providing investigators with funds for development of their projects and promoting interactions and collaborations.

Lombardia
54

Trentino-Alto Adige
4

Friuli-Venezia Giulia
7

Veneto
13

Piemonte
7

Emilia-Romagna
7

Liguria
9

Toscana
10

Abruzzo
1

Umbria
1

Puglia
2

Lazio
32

Sardegna
4

Campania
3

Calabria
1

Sicilia
5

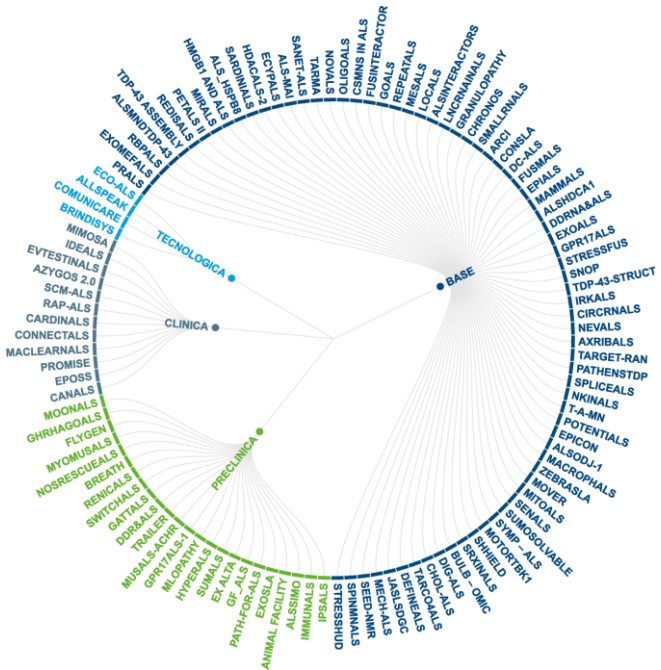*National distribuition of research groups funded by AriSLA (2009-2024)*

Monitoring the funded projects to assess their impact and define strategic activities

Given the complexity of the disease, AriSLA funds research in different areas

AriSLA's aim is to identify effective therapeutic strategies and new, reliable biomarkers for diagnosis and prognosis.

Funded research areas

Basic: 74 projects

Preclinical: 24 projects

Clinical: 13 projects

Technological: 4 projects

The Foundation analyzes the funded projects to assess their impact and defines strategic activities

Funded research has generated knowledge on ALS and contributed to the growth of the Italian scientific community

> Front Res Metr Anal. 2023 Aug 4:8:1067981. doi: 10.3389/frma.2023.1067981. eCollection 2023.

The positive impact on translational research of Fondazione italiana di ricerca per la Sclerosi Laterale Amiotrofica (AriSLA), a non-profit foundation focused on amyotrophic lateral sclerosis. Convergence of ex-ante evaluation and ex-post outcomes when goals are set upfront

Stefania Guareschi [#] [1], Maddalena Ravasi [#] [1], Tiziana Zaffino [1], Mario Melazzini [1], Anna Ambr

Affiliations + expand

PMID: 37601533   PMCID: PMC10436489   DOI:

MINI REVIEW article

Front. Med., 10 June 2024
Sec. Regulatory Science
Volume 11 - 2024 | https://doi.org/10.3389/fmed.2024.1407912

This article is part of the Research Topic
Repurposing for Small Population Needs
View all 4 Articles >

New clinical insight in amyotrophic lateral sclerosis and innovative clinical development from the non-profit repurposing trial of the old drug guanabenz

Anna Ambrosini [1,2*]   Eleonora Dalla Bella [3]   Maddalena Ravasi [1]   Mario Melazzini [1]   Giuseppe Lauria [4,5]

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[4] IRCCS 'Carlo Besta' Neurological Institute, Milan, Italy
[5] Department of Medical Biotechnology and Translational Medicine, University of Milan, Milan, Italy

Bibliometric assessment of AriSLA-derived articles

***Publications*: <u>366 total publications</u>** derived from 78 AriSLA-funded projects (Web of science 2010-2023 - www.webofscience.com)

- 267 original papers
- 89 reviews

***Relative Citation Ratio (RCR)*:**

- Method to measure the influence of a research article by using its co-citation network to field and time-normalize the number of citations it has received. It provides **an alternative to journal impact factor to identify influential papers**.

- NIH-funded papers are the benchmark for RCR. Any paper with **RCR 1.0 belongs to the top 50% of NIH-funded papers**.

*Dataset = **325 AriSLA papers** (71 projects) - (2010-2021) indexed in the NIH iCite platform*

	RCR mean	N. publications
All publications	2.48±0.27	325
Original articles	2.17±0.19	248
Review	3.45±0.96	77

(Source: iCite 2010-2021, analysis March 2023 - https://icite.od.nih.gov/analysis
WoS term=amyotrophic+lateral+sclerosis)

➡ **67%**
(218 papers) are in the top 50% NIH percentile

Data from: Guareschi et al. Frontiers in Research Metrics and Analytics, 2023

The outcomes of AriSLA's research (2010-2023)

	Research topics	No. funded projects	No. original Articles	Key outcomes	
	Autophagy and stress response	13	64	Progress from basic to preclinical research	
	Genetics and genomics	9	48	Contribution to gene discovery	
	Non cell autonomous mechanisms	30	51	Progress from basic to preclinical research	
	RNA metabolism and epigenetics	25	73	Progress from basic to preclinical research IP generation	
	Excitation and energy metabolism	6	17	Preclinical POC (repurposing drug) has led to an international Phase 2 trial (same drug) IP generation	
	Clinical research	15	28	4 interventional clinical trials Clinical POC (repurposing drug) has led to an industry-sponsored international Phase 2 trial (new small molecule) Imaging biomarkers	

AriSLA new Vision: Strategic plan 2023-2025

We aim for research that has greater impact on patients' lives.

Our new strategic plan took inspiration from the 2022 ALS Strategic plan of the National Institute of Neurological Disorders and Stroke (NINDS) and from the interaction with AriSLA advisory board members, researchers and patients

More impact on ALS patients' clinic

✓Accelerate the identification of effective interventions for the diagnosis, treatment and prevention of ALS

Clinically informed basic research

✓Support a research that starts from the patient features, in order to obtain results with potential impact on ALS patients

Promote the collaboration between clinical and basic researchers

✓Seminars, workshops, encouraging the collaboration between scientist within the call

2023-2025 AriSLA Strategic Plan

1. Optimizing CLINICAL RESEARCH and ACCELERATE RESEARCH on the pathophysiology underlying ALS

- **PRIORITIES IN THE CALL**
- **PILOT GRANT PROGRAM**
- **MEETINGS AND WEBINARS WITH BASIC AND CLINICAL SCIENTISTS**

SCIENTIFIC RESEARCH

2. Improving QoL of ALS patients

CLINICAL STUDIES ON BULBAR SYMPTOMS

3. Creating new PARTNERSHIP opportunities between academia, associations and industry

- **AriSLA MEETING**
- **THE INTERNATIONAL ALLIANCE Of ALS/MND ASSOCIATIONS**

4. Strengthening the commitment to SCIENTIFIC DISSEMINATION

COMMUNICATION **INITIATIVES**

RESEARCH SUPPORT

AriSLA, Fondazione Italiana di Ricerca per la Sclerosi Laterale Amiotrofica ETS

2023-2025 AriSLA Strategic Plan – where we are

Strategic plan priorities and themes	2023 Call	2024 Call
Development of effective clinical measures for ALS, including both diagnostic and theragnostic **biomarkers**	FG: **MIMOSA**, Andrea Bandini; **IDEALS**, Nilo Riva PG:**CHOL-ALS**, Laura Calabresi **TARCO4ALS**, Marcello Manfredi **MyoMusALS**, Rosanna Piccirillo	FG: **DEFINALS**, Gianluigi Zanusso; **MoonALS**, Giovanni Nardo PG: **Seed-NMR**, Linda Cerofolini
Definition of the **natural history** of ALS from the pre-symptomatic to the disease state, to improve the knowledge of how the disease begins and progresses	FG: **DIG-ALS**, Sandra d'Alfonso	PG: **JALSDGC**, Antonio Orlacchio **FLYGEN**, Arianna Manini **MECH-ALS**, Marco Foiani
Setting and characterization of **model systems** that can provide information on human sporadic ALS		PG: **SpiMNALS**, Carmelo Milioto **StressHud**, Alessandro Rosa
Unravel the molecular pathophysiological mechanisms of **clinical heterogeneity in ALS** with the aim of classifying ALS into subgroups and define different forms of sporadic ALS based on distinct molecular mechanisms leading to neurodegeneration	FG: **BULB-OMIC**, Eleonora Dalla Bella	PG: **SpiMNALS**, Carmelo Milioto
New treatment Identification	PG: **MyoMusALS**, Rosanna Piccirillo	FG: **MoonALS**, Giovanni Nardo PG: **GHRHagoALS**, Riccarda Granata

Promoting research

AriSLA **disseminates scientific results** of funded projects and provides constant updates on scientific progress at national and international level.

- Annual **scientific conference**
- **Webinar** and seminars

Disclosure on ALS research for **patients, donors and society**

- **Institutional communication:** website, social reports, press office, social networks, newsletter
- **Popular events dedicated to ALS patients: Symposium ALS, Focus ALS (in cooperation with the Association of patients**
- **Local initiatives:** promoted by volunteer groups and open to citizens

AriSLA 2025 Call: Features

- ❑ CBIM web application

- ❑ Opening: 18 February 2025

- ❑ Letter of Intent (LOI) + Full Proposal (FP)

- ❑ Full Grant and Pilot Grant

- ❑ Manteinance of strategic plan priorities

LOI submission
18/2-25/3

LOI evaluation
15/4-20/5

FP submission
12/6- 29/7

FP Evaluation
31/7-30/9

Consensus Meeting
By October

CDA
By December
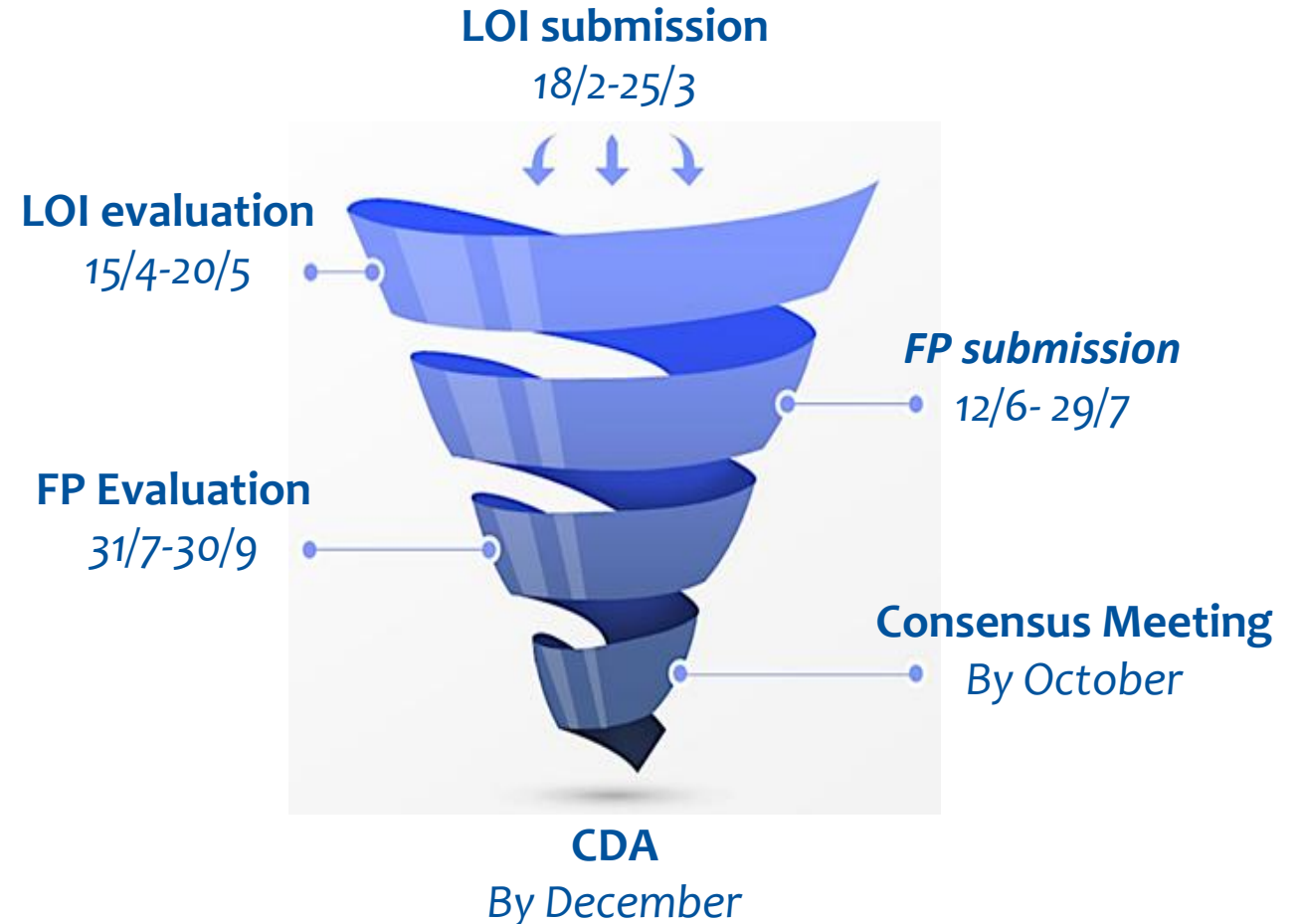
AriSLA 2025 Call: Features

1. Basic research is expected to be **clinically informed**, integrating clinical characteristics to the interpretation of mechanistic studies.

2. AriSLA set **priority topics**

   Applications not respondent to the priority topics may proceed to the full evaluation only if evaluated in the excellent /outstanding ranges

   -> Interaction between basic research scientists and clinicians is highly encouraged.

   In case of a Multi-centre project the PI may be a basic researcher or a clinician

Top priority topics of our calls

✓ **Effective clinical measures for ALS,** including both diagnostic and theragnostic biomarkers

✓ **Natural history of ALS** from the pre-symptomatic to the disease state, to improve the knowledge of how the disease begins and progresses

✓ **Model systems** to provide information on human sporadic ALS.

    -> multiple models

✓ **Molecular pathophysiological mechanisms of clinical heterogeneity in ALS** with the aim of classifying ALS into subgroups

The peer-review evaluation process of project proposals

Each year AriSLA selects the best proposals following a **rigorous process** entrusted to **international experts** who judge their scientific merit.

LOI SUBMISSION	PHASE 1 TRIAGE	PHASE 2 FULL PROPOSAL SUBMISSION AND EVALUATION	CONSENSUS MEETING	BOARD OF DIRECTORS
Researchers from Italian non-profit Universities and Research Institutes, either public or private, send their LOI proposals.	Each LOI is independently evaluated by 3 international reviewers.	The top ranking LOIs are invited to submit a full proposal (FP). FPs are remotely and independently evaluated by 3 international reviewers.	The Scientific Committee involved in Phase 2 participates in a plenary discussion to select the projects to be funded.	The Board of Directors accepts the reviewers' suggestions and decides on the allocation of funds depending on the availability of economic resources.

The actors of the selection process

→ **INTERNATIONAL SCIENTIFIC COMMITTEE**

The Committee conducts the evaluation process and makes funding recommendations on the basis of the criteria of the Call for Proposals to guarantee

- **impartiality** of judgement (no CoI) and confidentiality
- transparency and fairness of the evaluation
- **scientific excellence of the project** proposal
- attention to the **return of results on patients' quality of life.**

Geographical distribution of members of the AriSLA International Scientific Committee

The International Scientific Committee (ISC)

Participation is on **rotation** basis, and it is regulated by a contract with AriSLA

Confidentiality is preserved for a further period of 5 years after the end of the contract

Composition may vary according to the type of applications being reviewed

Composition is **publicly available**. The identity of reviewers involved in each application is not disclosed to the applicant

➢ In order to minimize conflicts of interest (financial or otherwise), reviewers should not:

- have published together with the applicants at least in the past 3 years

- be engaged in active collaborations with the applicants

- be professional associates of the applicants

➢ During the Consensus Meeting, reviewers with a conflict of interest with any application will leave the room during the discussion

➢ Experts are expected to inform AriSLA of any related interests, that might be perceived as relevant.

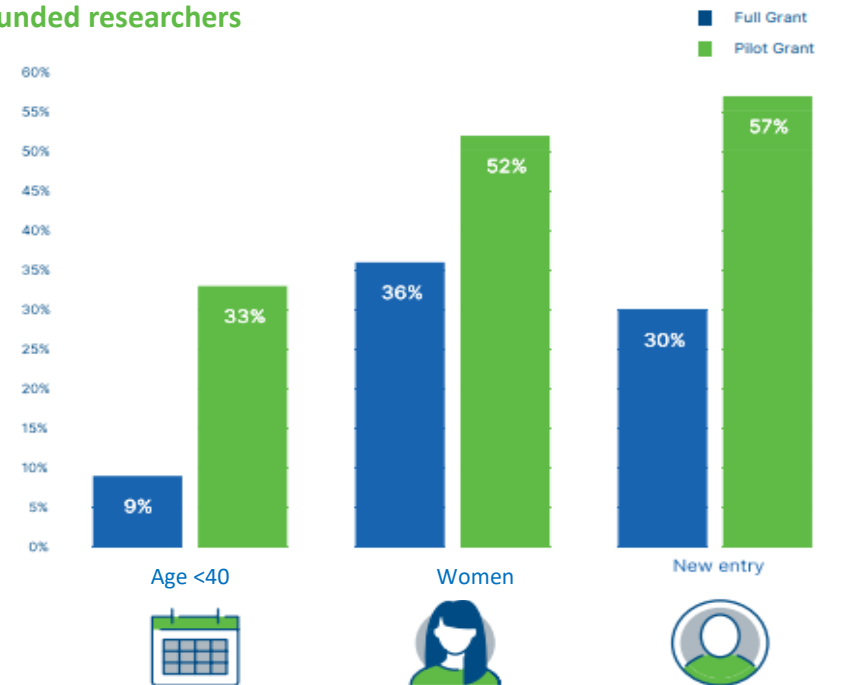# Two types of grant for two different purposes

→ **FULL GRANTS:** research projects with a **solid background and consistent preliminary data**

- Maximum amount of **240.000 euro**

- Maximum duration of **36 months**

- Mono- or multicentric

→ **PILOT GRANT:** research projects with highly **innovative** and **original** hypotheses, without preliminary data

- Maximum amount of **60.000 euro**

- Maximum duration **12 months**

- Only monocentric

Funded researchers

	Full Grant	Pilot Grant
Age <40	9%	33%
Women	36%	52%
New entry	30%	57%

Web application for submission

- CBIM provider
- Use 2024 credentials or create new account

Scientific contents – Guidelines

- SCOPE OF THE PROJECT/SUMMARY STATEMENT

- CENTRAL HYPOTHESIS, BACKGROUND AND RATIONALE

- RESEARCH PLAN

- SIGNIFICANCE AND NOVELTY

- PRELIMINARY DATA

- ROLE OF COORDINATOR AND PARTNERS

- ADHERENCE TO THE CALL'S PRIORITIES

- INDICATE HOW THE PROPOSED STUDY ADDRESSES THE PRIORITIES SET IN THE CALL

Eligibility Criteria

Eligible Host Institutions and applicants

- **Italian non-profit Institutes**, either public or private

- Applicants: **scientific competence**, **independence**, **capability** to self-manage the proposed project and **must operate in the Host Institution for the entire duration of the Grant**.

- Investigators: **maximum of 2 Grants** and can be **Principal Investigator (PI) of 1 Application only**.

Actual grantees

Applicants of ongoing AriSLA projects that are not expected to end by December 31, 2025, the following rules apply:

- a PI is not eligible to submit a new Application as PI, but can apply as Partner in one Multi-centre Application;

- a Partner of one ongoing project can apply for one new Grant, either as PI or Partner;

- a Partner of two ongoing projects is not eligible for the current Call.

Please note: If there are any changes during the evaluation process in the PI's and partner's Host institution and/or **position please contact promptly** AriSLA Offices

Eligibility Criteria

Definition

- **Principal Investigator (PI)** is the scientific coordinator of the project, either in case of a Single-centre or a Multi-centre project.

- Project **Partners** are researchers directly involved in the project that will synergistically undertake part of the scientific work; they can ask for a budget to cover their expenses.

- **Collaborators** are researchers whose specific support is needed for the completion of minor parts of the project, for example providing specific cell cultures, animal models or tools not available in the PI/Partner's laboratory, or any kind of support to the project. (During the Full Proposal Phase Collaborators must sign a collaboration letter). **Economic coverage for collaborators is not provided by AriSLA.**

Declaration

- The Host Institution declares

  - That the Applicant is authorised to submit the Application on its behalf (*General Information* page)

  - That will provide the necessary facilities and personnel to carry out the submitted research project**. If the Applicant is not holder of a permanent position, her/his salary needs to be provided through other means.**

Renewal, revised or new application?

Renewal Application by a former grantee

- A "Renewal Application" is a new funding request **based on data from a previously funded AriSLA Grant**

- **Renewal Applications of previously funded Grants are encouraged, and the effective exploitation of the results obtained with the previous Grant will be matter of evaluation.**

- The "Renewal Application" of a previously funded Pilot Grant can only be submitted as Full Grant Application.

- The holder of a previously funded Pilot Grant may apply for another Pilot Grant as a "New Application" specifying the reasons of changing the research topic.

Revised Applications

- The "Revised Application" should be modified in accordance with the comments received during the evaluation process and with the 2024 AriSLA Call criteria.

- **Only up to two resubmissions** of a previously unsuccessful Application, not necessarily in consecutive years, are allowed.

Evaluation criteria: Pilot Grants

LOI evaluation

- **Innovation and originality**

- **Quality and feasibility**

Full proposal evaluation

- **Innovation**

- **Relevance** of the project for ALS

- **Significance and expected impact** of the results **on the disease** knowledge and treatment

- **Objectives** and **methodologies**

- **Capability to successfully carry out the project**

- **Potential** for expected results **to attract large-scale funding**

Evaluation criteria: Full Grants

LOI evaluation

- **Innovation and originality**

- **Quality and feasibility and experience** of the applicant in the field

> **NOTE:**
> - Partner's contribution, <u>complementarity</u> of approaches and <u>synergy</u> are assessed by the Reviewers
> - No indication of maximum number of centers

Full proposal evaluation

- Strength of the **background** and **rationale.**

- **Availability of solid preliminary data**

- **Objectives and methodologies**

- **Significance and expected impact** of the results **on the disease** knowledge and treatment

- **Investigator experience and synergy with Partners (if any)**:

- Sound and effective exploitation of the **results derived from previously funded AriSLA Pilot/Full Grant** (if applicable)**.**

Suggested Reviewers

- They should <u>not currently work in Italian Institutions</u>

- Avoid friends (not associated with your work)

- Highly qualified Scientists, with specific interest in the argument of your grant proposal (if the topic is not within their specific interest, they may refuse to participate in the review process)

- It is better if AriSLA can rely on your suggestions, you are the one that knows better if a Reviewer may have a conflict of interest with your work

- You can also indicate reviewers you prefer don't see your application for a given conflict.

How to write the Letter of Intent

Tell a compelling story:

- Generate interest in your scientific question

- Demonstrate the importance of your study

- Describe **concise** and **convincing** aims

- Indicate that you know what the expected results are

How to write the Letter of Intent

- **Explain always the rationale**

- If your proposal is highly innovative, you'll need to make a very strong case for why you are challenging the **existing paradigm** and have **data to support** your innovative approach

- Make the review easier, **don't be redundant** with the content

- **Define statistic analysis and power for significance**

- **Avoid/limit experiments too dependent on success** and specify alternative approaches

→ You have to convince reviewers that your proposal will work. If this is a completely new approach, no matter how exciting it might be, the grant panel will require some **evidence for its credibility**

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How to write the Letter of Intent – Rationale

Background, rationale and objectives

- AriSLA funds only ALS related projects: **clearly and concisely introduce the disease characteristics you are proposing to investigate**

- **What is still missing?** capture the reviewers' attention by making an argument for why you should be funded. Tell the reviewers why testing your hypothesis is worth funding, why you are the person to do it!

- Define limited and specific Aims. **<u>Do not propose too much</u>**

- Your hypothesis must be demonstrable and the goals achievable with the required resources

How to write the Letter of Intent - Applicant section

Personal statement

- Good records in the topic

- Good records in the methods

- Experience in foreign laboratories

Independence of young investigators

- How many papers with the first name (or corresponding author)

- Any other/previous grants?

- How large is your group?

- Will you have the authorship of the proposed study?

Be honest and convincing!

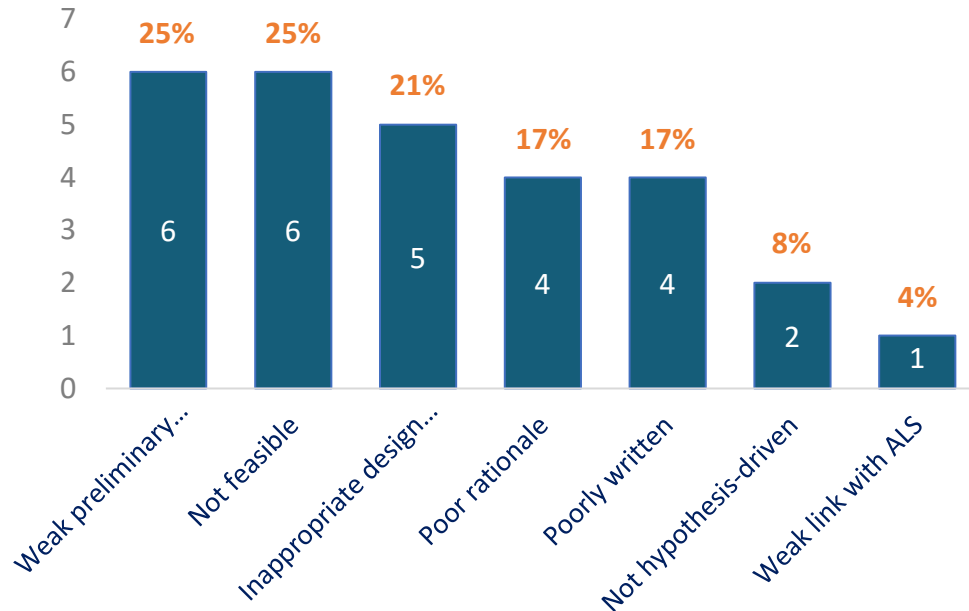# Most common reasons cited by reviewers for an application's failure

- **Not** specific **for ALS**

- **Poorly articulated hypotheses** / Lacking solid scientific basis

- **Weak preliminary data** / **Weak Rationale**

- Incremental research, **not a step change**

- **Not innovative** / Lack of original ideas

- **Unsuited methods and model systems**

- Too little detail - **no potential problems and pitfalls**

- **Over-ambitious research plan**

- **Insufficient** consideration of **statistical needs**. Sample sizes not justified
  with power calculations

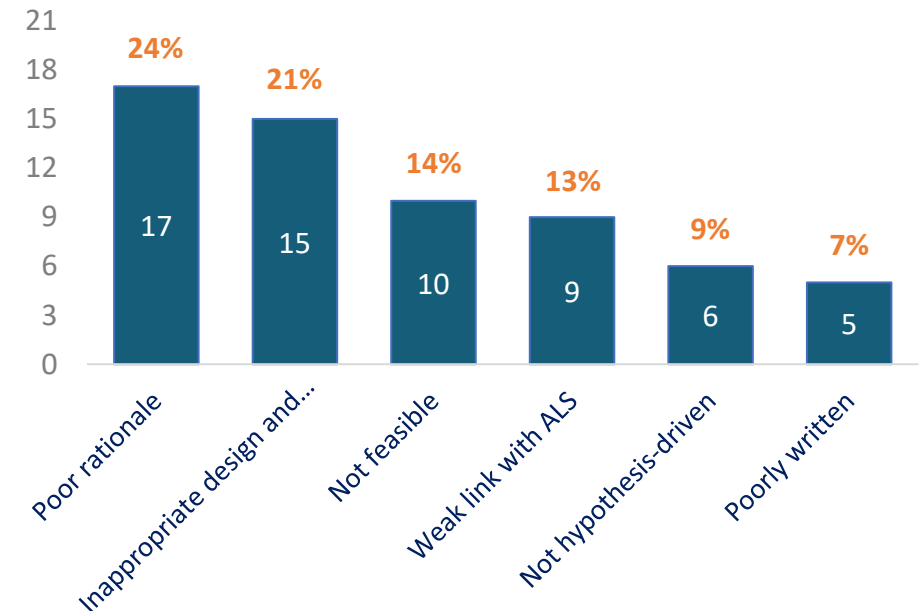# 2024 Call - Weaknesses outlined by reviewers

LOI WEAKNESSES

- Not feasible
- Poor rationale
- Inappropriate design and methods
- Poorly written
- Not hypothesis-driven
- Weak link with ALS
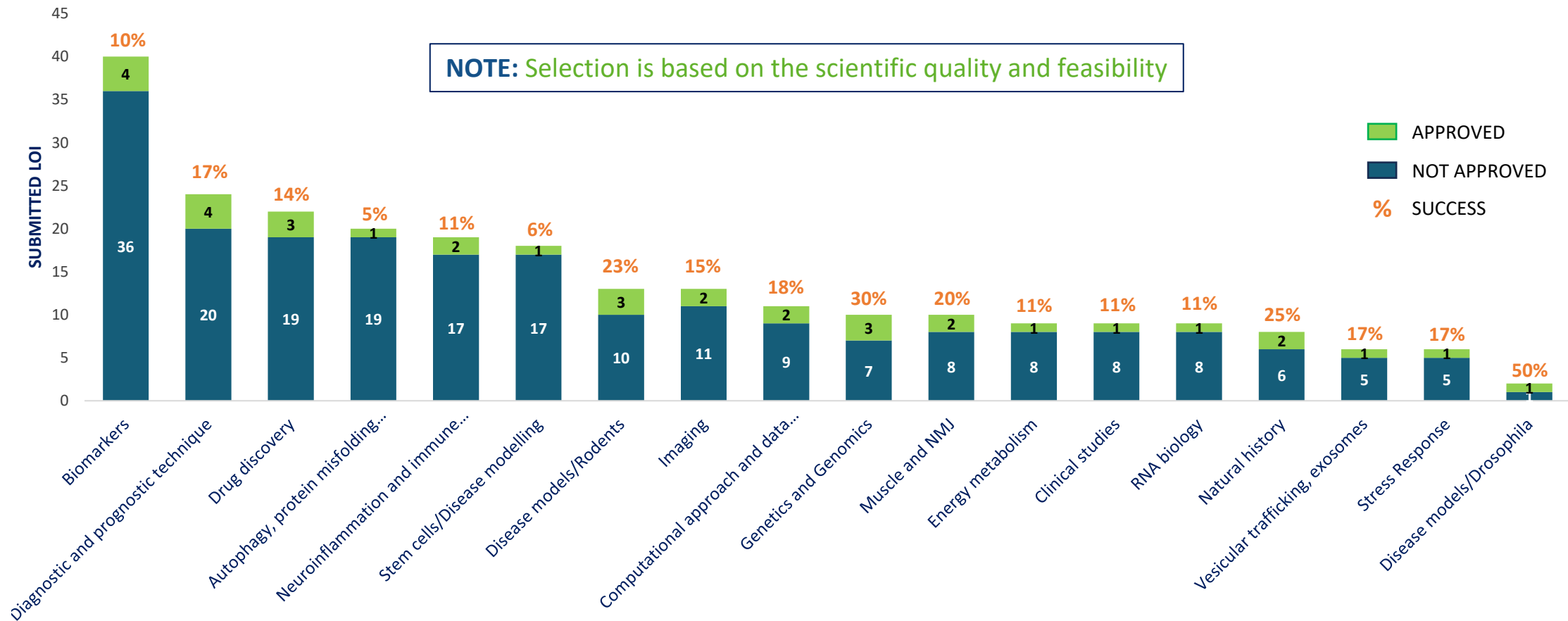- Weak preliminary studies

FULL GRANT

Category	Count	%
Weak preliminary...	6	25%
Not feasible	6	25%
Inappropriate design...	5	21%
Poor rationale	4	17%
Poorly written	4	17%
Not hypothesis-driven	2	8%
Weak link with ALS	1	4%

PILOT GRANT

Category	Count	%
Poor rationale	17	24%
Inappropriate design and...	15	21%
Not feasible	10	14%
Weak link with ALS	9	13%
Not hypothesis-driven	6	9%
Poorly written	5	7%

The **percentage** indicates the share of submitted projects reported with the specific weakness by at least one reviewer.

2024 Call - Keywords success

- 94 LOIs submitted (24 Full Grants and 70 Pilot Grants)
- 29 keywords associated with the AriSLA Strategic Plan 2023-25

NOTE: Selection is based on the scientific quality and feasibility

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If you are not funded....

Don't get discouraged. You are not the only one!

Listen to your Reviewers

- Read the Review feedback carefully. It is meant to provide you with suggestions to improve your grant application

- Perhaps if reviewers did not understand your work is because you did not make it clear and proved to be feasible

- You should learn from comments to re-write a more appealing grant the next year

- Try to understand and solve all the pitfalls

- Maybe you need collaborators with specific expertise, especially if your application is rejected more than one time

Suggestions for readings

- AriSLA Call for Research projects 2025

- Application guidelines 2025 Full Grant / Pilot Grant

PLEASE READ THEM CAREFULLY AND CONTACT US IF YOU NEED SUPPORT

bandi@arisla.org

- *Guidebook for New Principal Investigators (Institute of Genetics, CIHR. By R. McInnes, B. Andrews & R Rachubinski) https://cihr-irsc.gc.ca/e/documents/ig_guide_for_new_pis_e.pdf*

- *Hossein Ardehali. How to write a successful grant application and research paper. Circ Res. 2014 Apr 11;114(8):1231-4. https://www.ahajournals.org/doi/epdf/10.1161/CIRCRESAHA.114.303695*

- *Masud Husain. How to write a successful grant or fellowship application. Pract Neurol. 2015 Dec;15(6):474-8. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4680180/pdf/practneurol-2015-001206.pdf*

- *https://writingcenter.uagc.edu/writing-letter-intent*

Buon lavoro
dal
Team AriSLA!!