2025

The Foundation for Sarcoidosis Research (FSR)
Research Agenda

Prioritizing Progress, Catalyzing Innovation

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01

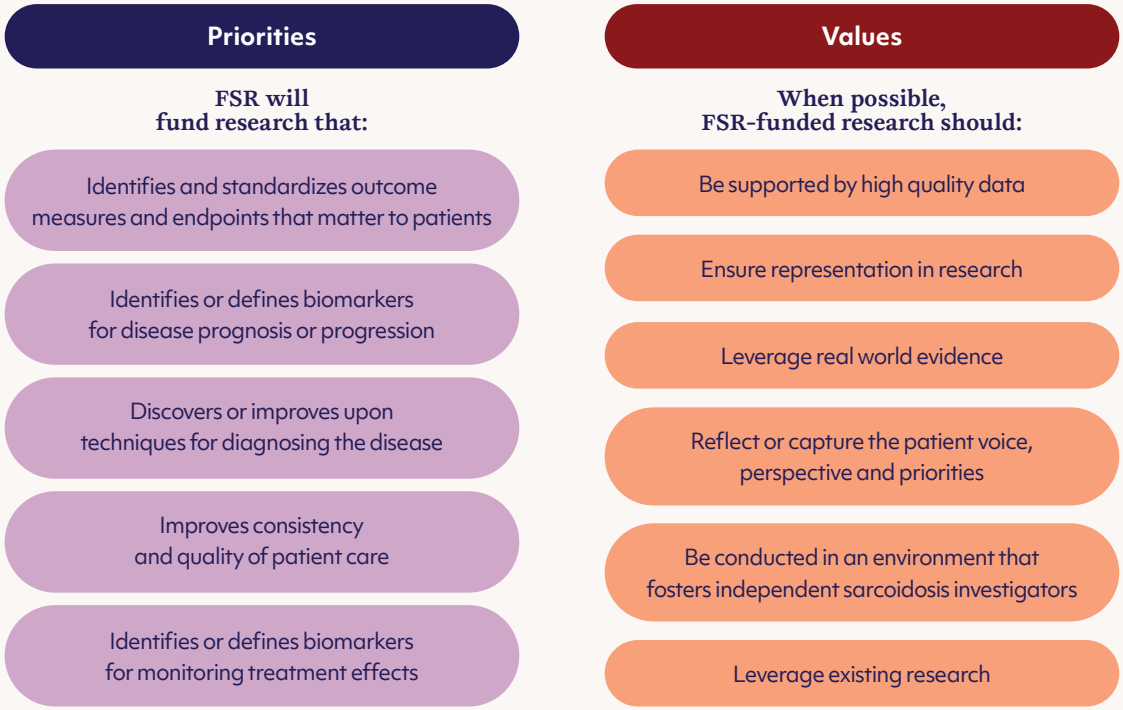
Executive Summary

The **Foundation for Sarcoidosis Research (FSR)** has undertaken a comprehensive process to develop a new Research Agenda that will guide its funding priorities and strategic direction. This initiative comes at a critical time, as sarcoidosis affects approximately 1.2 million people worldwide,[1] and approximately 175,000–200,000 in the United States.[2,3] The disease disproportionately impacts African Americans, particularly women, who experience mortality rates 12 times higher than Caucasians,[2] with rates increasing dramatically over the last thirty years.[4]

Sarcoidosis was first discovered over 150 years ago and yet little progress has been made toward a significant breakthrough in the scientific understanding of the disease and the therapeutic options. To address this concern, FSR has endeavored to create a robust Research Agenda aimed at addressing gaps in sarcoidosis research. By identifying and prioritizing clinical and scientific goals, we aim to take bold strides towards transformational advancements that will improve the lives of patients, deepen our understanding of sarcoidosis, and produce a promising pathway to the development of better therapies and improved patient outcomes.

In the development of this Research Agenda, FSR worked with world-renowned researchers, patients, caregivers, industry partners, and our esteemed **Governing Board of Directors** to employ a rigorous four-stage process (conducted a literature review; held a brainstorming workshop with key stakeholders including physicians, patients, and caregivers; conducted stakeholder interviews; and facilitated a quantitative prioritization survey of the FSR community) in order to establish consensus on priorities which will be used to analyze and drive future research.

Through this process, FSR established five primary research priorities and six research values.



Utilizing these priorities, FSR will work with the **FSR Scientific Advisory Board (SAB)** to implement a revised application review process incorporating priority/value scoring to ensure that FSR-funded research aligns with the consensus-based priorities. We view this Research Agenda as dynamic and evolving. Over the next five years, FSR will evaluate the progress we have made toward these priority goals by measuring them against key performance metric indicators. Recognizing that research is dynamic and non-linear, starting in 2026, FSR will work with its SAB to evaluate progress on an annual basis allowing us to adjust priority goals to reflect the most current state of the research at that time.

This Research Agenda represents a strategic and measurable approach toward the achievement of our mission to accelerate progress toward improved treatments and a possible cure for sarcoidosis. In achieving the goals mapped out in this Research Agenda, FSR will have aided in the acceleration of research through the creation and establishment of universalizable clinical outcome measures and in therapeutic improvement strategies. FSR's Research Agenda will also promote work to establish endpoints that will accelerate clinical trials. This Research Agenda will take steps towards the creation and identification of molecular signatures that will help to better predict the course of the disease and likelihood that a patient will progress in a particular way. Further, it will aid in improved diagnosis and will take significant steps toward a more individualized precision medicine approach to individualized patient care and therapy deployment.

02

Introduction & Background

A Rare and Challenging Disease

Sarcoidosis is a rare inflammatory disease affecting approximately 1.2 million people worldwide,[1] with an estimated prevalence of 60 per 100,000 in the United states.[2] The disease shows notable demographic patterns, disproportionately affecting African Americans, particularly women, who experience mortality rates 12 times higher than Caucasians and 1.5 times higher than African American men.[5] While sarcoidosis can develop in anyone, it typically emerges in middle-aged adults, with peak incidence occurring between ages 30-50 for men and 50-60 for women.[5] The disease's impact is significant despite its rarity, with an average age-standardized mortality rate of 5.19 persons per million in the US.[5]

What makes sarcoidosis particularly challenging from a medical perspective is its complex etiology, heterogenous presentation and disease course. Progress in the management of sarcoidosis is limited by our current understanding of biological processes which result in highly variable disease manifestations and limited tools for diagnosing, and measuring impact and success of therapeutic interventions. Sarcoidosis is believed to be caused by some type of genetic predisposition coupled with exposure to environmental, occupational, or microbial triggers. Sarcoidosis is marked by the formation of granulomas - microscopic clusters of inflammatory cells - that can affect any organ in the body, most commonly the lungs. The disease's course varies significantly among patients with some experiencing spontaneous remission, while others live with complex, chronic symptoms that significantly affect quality of life. As high as 30% of patients may develop advanced, potentially life-threatening complications from sarcoidosis over the course of their lives.[7]

About the Foundation for Sarcoidosis Research

The Foundation for Sarcoidosis Research (FSR), established in 2000, is the leading international organization dedicated to finding better treatment options for sarcoidosis and improving patient care through research, education, and support. Founded by a sarcoidosis patient and her husband after her own challenging journey with multi-system sarcoidosis, FSR has fostered over $7.2 million in sarcoidosis-specific research efforts. FSR has a five-pillar approach to our efforts.

- **Advancing Research:** Supporting and funding research through competitive peer-reviewed grants for academic research, partnering with biotech and pharmaceutical companies to advance and accelerate clinical trials, and conducting qualitative and quantitative research to ensure the patient's voice is at the center of and drives academic, clinical, and industry-driven research efforts.

- **Supporting Clinical Education and Engagement:** Creating the 40+ member FSR Global Sarcoidosis Clinic Alliance, FSR supports over 3,000 clinicians through CME clinician education such as peer-created educational programs, journal clubs, peer case review programs and early career mentoring webinars. By creating a safe space for collaboration and innovation, FSR supports individual providers and institutions committed to finding a cure and offering evidence-based, patient-centric care to improve patient outcomes for all impacted by sarcoidosis.

- **Providing Psycho-Social Support to Patients and Caregivers:** Driving national and local support groups, FSR provides in-person and virtual support for patients and caregivers navigating the journey of living with sarcoidosis. Through the creation of the FSR patient navigator program, FSR provided 1:1 support to newly diagnosed patients and those with new manifestations of the disease as a means of providing them with the tools and resources to find the care and support needed.

- **Creating Educational Events and Materials:** Hosting webinars, wellness series, and townhalls, FSR reaches thousands of patients and caregivers around the globe, providing them access to world-renowned leading experts and providing them with the latest information on emerging research to empower them to advocate for their own care.

- **Working alongside Federal Agencies to Advance Research and Accelerate Drug Development:** Working alongside Congress and Federal Agencies like the NIH and FDA, FSR aims to ensure that research funding and clinical trial design is reflective of patients' needs and desires and that patients have access to needed therapies.

The organization's comprehensive approach includes maintaining a physician directory, facilitating clinical trials, operating a patient ambassador program, hosting conferences, and developing standardized clinical endpoints. Through these initiatives, FSR works tirelessly to bridge the gap between patients, healthcare providers, and researchers while promoting awareness and advancing scientific understanding of this rare disease.

FSR's Research Agenda

FSR's previous Research Agenda was published in 2017 and placed its emphasis on taking bold steps towards de-risking clinical trials. The following strategies were used to reach these goals.

DISEASE MODELS

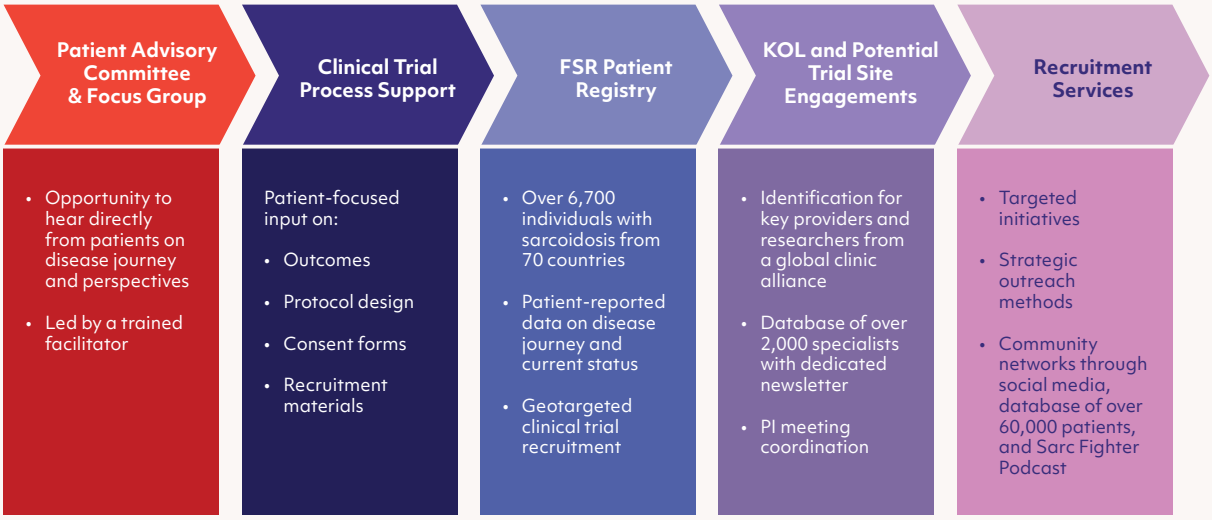
In 2017, FSR awarded $750,000 to five innovative projects designed to investigate possible **disease models for sarcoidosis.** In 2020, three of the five disease model awardees were selected for additional bridge funding totaling $300,000 in support. This bridge funding continued until the end of 2021 and aimed to further develop, characterize, or improve the models and our understanding of the mechanism of sarcoidosis.

This funding has yielded exciting advancements as our awardees are currently working with industry partners to test potential therapeutics in preparation for potential clinical trials in the space. Dr. Elliott Crouser's model, which expands on his NIH-funded pilot project, has received particular attention and is now being used by industry partners to support clinical trials.

CLINICAL TRIAL SUPPORT

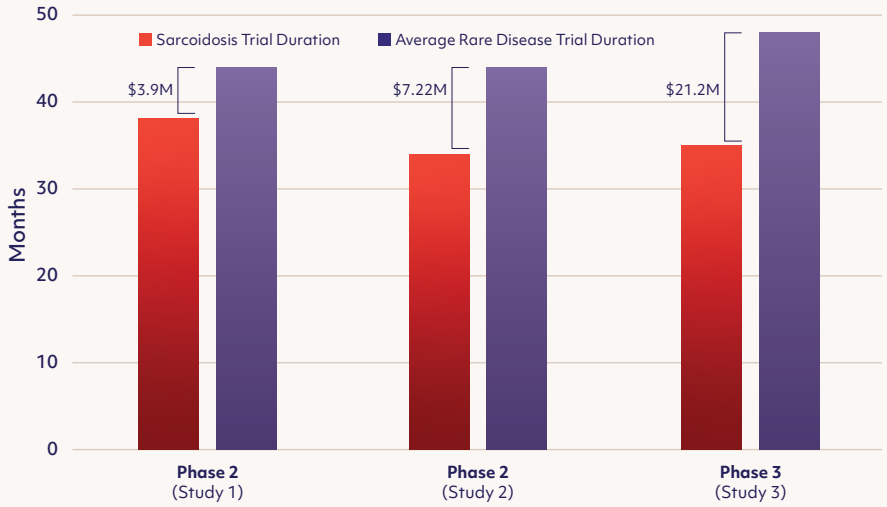
In the establishment of FSR's **SARConnect™ program**, FSR works to ensure that any sarcoidosis and related trial and studies are fully recruited and have patient engagement support to ensure fulfillment of trial requirements. Through a variety of significant outreach efforts, FSR serves as a recruitment specialist connecting academia, industry, and physicians to patients by serving as the message, while at no time risking the patient's privacy or contact information. As a patient-centric third-party, FSR connects stakeholders to their desired constituents by providing direct information and links for them to participate in the trial, study, or project. This is a massive resource-saving mechanism that not only de-risks trials through recruitment but also through education on the importance of patient engagement in research.

FSR SarConnect™
Clinical Trial Support and Recruitment Services



The purpose of this project is to assist industry in pulmonary sarcoidosis and cardiac sarcoidosis clinical trials. With the support of FSR's Patient Advisory Committee, FSR's Clinical Studies Network (CSN), Sarcoidosis Clinics, and FSR's Patient Registry, FSR provides support services throughout the clinical trial processes and recruitment phase.

Average FSR-Partnered Sarcoidosis Trial Duration (Phase 2 and 3) and Associated Cost-Savings Compared to the Average for Rare Disease



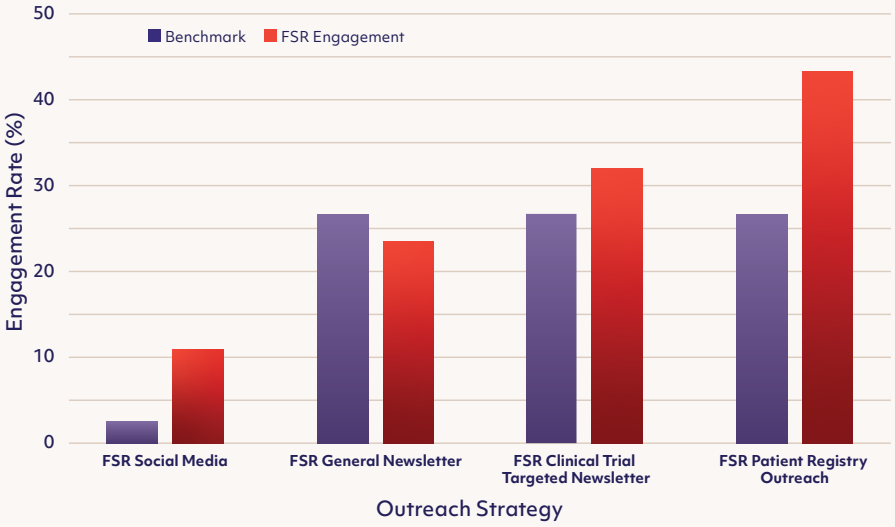
Cost saving based on average direct cost to conduct a clinical trial per day

$23,737 for Phase 2

$55,716 for Phase 3

All noted trials completed enrollment in 2023 or 2024; for some, study completion was estimated and confirmed on clinicaltrials.gov. FSR also partners with Phase 1, observational, and biorepository studies; they were not featured due to limitations in average clinical trial duration and cost of clinical trial source material. FSR has also collaborated with partners who did not meet enrollment in the past before maturity of the SARConnect program.

FSR SarConnect™ Engagement Rates Compared to Reported Benchmarks[8, 9]



FSR Social Media saw better engagement (maximum click-through rates) compared with reported clinical trial benchmark

FSR Email Marketing saw better engagement (average open rates) with two strategies compared with reported nonprofit benchmark

FSR Patient Registry showed excellent engagement, indicating that it is a strong resource for supporting clinical trial recruitment.

Benchmark References:

Social media benchmark:
clinical trial maximum click-through rate - 2%

Email benchmark:
Nonprofit average open rates - 26.6%

Data is from 4 separate FSR partnered clinical trial campaigns

FSR's SarConnect™ patient outreach strategies used in four separate clinical trials, including social media and email outreach, were compared against reported benchmarks to assess the difference in engagement rates. Social media engagement is defined as maximum click-through rate and is compared against reported clinical trial benchmarks, while email engagement is defined as average open-rate and is compared against reported nonprofit benchmarks. This graph illustrates the engagement that patient advocacy groups can achieve using these strategies to directly support clinical trial recruitment in rare disease. All four clinical trials represented in this graph completed enrollment.

Through this program and these efforts, FSR has made significant progress in efforts to de-risk the clinical trial space in sarcoidosis. The average trial duration, including the enrollment period, in rare disease is a little less than four years,[10] yet FSR clinical trial partners who completed enrollment in 2023-2024 through FSR engagement will have trial durations below 2.5 years. This translated to savings between $3.9-7.2 million for Phase 2 studies in sarcoidosis, and over $21 million for Phase 3.[11, 12]

Utilizing the **FSR's registry** and database of patients and clinicians, FSR has successfully helped to enroll both academic and industry sponsored clinical trials. In 2024 and 2025, FSR has been able to assist in the successful enrollment of 4 clinical trials.

In addition, FSR has remained committed to building trials that are reflective of the community impacted by the disease. In 2022, FSR conducted a **survey of the black community** to identify barriers related to their access to clinical trials. FSR then conducted a Key Opinion Thought Workshop and a patient focus group to identify potential strategies to improve access. These efforts culminated in a 62-page white paper and FSR hosting a **Congressional Briefing on Capitol Hill**, where we proposed a number of practical solutions.

Challenges for Sarcoidosis Clinical Trials and FSR's Strategic Solutions

Barriers to Randomized Clinical Trials	FSR Strategic Solutions
Clinical perception that sarcoidosis mostly remits	Engage Patient Community
Disproportionate impact to under-represented, under-resourced patients facing known medical bias	Spread Awareness
Belief that current therapies are "good enough"	Collaborate with FSR Volunteers
Limited understanding of sarcoidosis disease mechanisms	Education for Patients & Clinicians
Unclear regulatory approval pathway	Synthesize Industry Perspectives
Sarcoidosis is vastly complex and heterogenic	Provide Clinical Trial Support
Clinical trial enrollment proves challenging	Foster Institutional Collaboration
	Advocate for Regulatory Changes

Randomized clinical trials for sarcoidosis continue to trail behind sister diseases with similar prevalence due to several key problematic barriers. In November 2023, FSR hosted a focused workshop with leading experts in sarcoidosis with the goal of identifying innovative, directed solutions for overcoming these barriers. This session culminated in a white paper on Advancing Clinical Trials and Research.

One of the legislative priorities was to seek clarity from the Department of Labor (DOL) to ensure those eligible for Family Medical Leave would maintain job security when participating in clinical trials through the Family Medical Leave Act (FMLA) protections. FSR, in collaboration with lawyers, identified that these barriers stemmed from the lack of clarity on whether the concept of "therapeutic benefit and treatment" extends to clinical access and clinical trials. On November 8, 2024, the **DOL issued a letter in direct response to FSR** ensuring that both patients and family member caregivers' job security is guaranteed under the FMLA law.

As a means of building on these efforts, in 2024, FSR built a coalition of like-minded organizations, institutions, and leading bioethicists to expand the efforts in knocking down barriers to clinical trials across all chronic diseases.

With the successful creation of disease models, of functional strategies to expedite clinical trial enrollment, and the improvement of pathways to clinical trial participation for all, FSR is poised to work with our researchers, clinicians, and industry partners to take our next bold step to addressing gaps in research and clinical practice in order to improve the care and outcomes for all impacted by sarcoidosis.

A New Approach: Advancing Innovation Through Strategic Evolution

The evolving research landscape presents both new opportunities and challenges that must be addressed in the next phase of FSR's strategic development. The advancement of precision medicine and artificial intelligence (AI), emergence of novel therapeutic modalities, and growing understanding of immune system complexity necessitate a refined approach to research investment. Furthermore, the increasing role of patient engagement in research design and the potential of real-world evidence have created new avenues for investigation that were not fully explored in the previous agenda.

To address these emerging opportunities, FSR initiated the development of a comprehensive new Research Agenda that builds upon established successes while adapting to the changing scientific landscape. This strategic evolution emphasizes two key components:

- **Community-Informed Strategic Planning** – The process has been designed to be transparent, collaborative, and encompassing of broad stakeholder input from patients, researchers, clinicians, and industry partners. This inclusive approach ensures research priorities align with the most pressing needs of the sarcoidosis community while leveraging diverse expertise to identify promising research directions.

- **Addressing Critical Gaps that are Limiting Sarcoidosis Research Advancements** – FSR aims to implement a more sophisticated framework for evaluating and prioritizing FSR's research investments. This framework seeks to optimize the impact of allocated funds while maintaining the organization's commitment to supporting innovative, high-potential research that might not receive traditional funding.

Through this refined approach, FSR sought to catalyze the next generation of breakthroughs in sarcoidosis research while ensuring that investments directly advance the organization's mission of finding a cure and improving patient care. The strategy is guided by a transparent, community-informed process that establishes clear priorities and creates a robust framework for decision-making in research funding.

03

Objectives

Key objectives in creating our new Research Agenda were to:

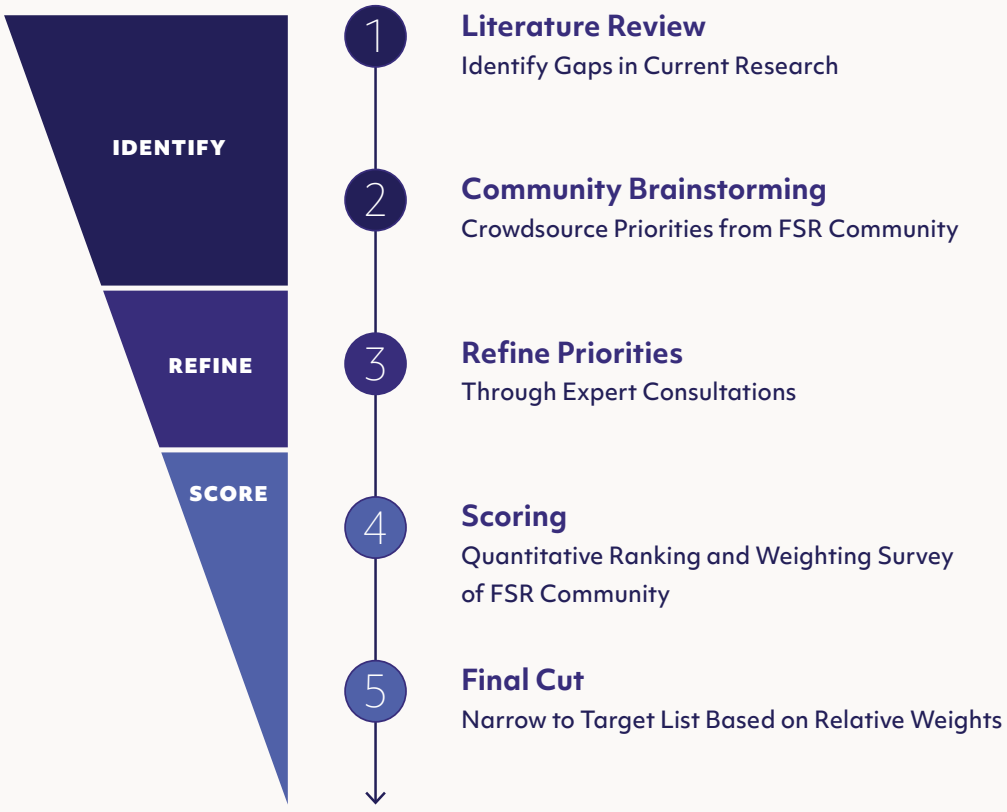
- Confirm topics representing gaps in sarcoidosis research
- Incorporate FSR leadership, patient, and key opinion leader input to develop prioritization criteria
- Establish future funding priorities for FSR
- Develop a process and revised scorecard to inform FSR funding decision-making
- Provide the research community with clear direction and targets to increase the return on investment from FSR's grants

04

Methodology

FSR worked with leading experts in academic research, strategic prioritization, patient engagement and medicine to implement a three-phase/five-step process designed to identify, rank, refine and prioritize FSR's research objectives:

FSR Research Prioritization Process



1. Literature Review

FSR began with a literature review to assess gaps in the current body of evidence. From the 2,048 peer-reviewed articles retrieved, FSR reviewed 743 titles, 109 abstracts and 55 full texts. In-depth analysis revealed a set of potential priorities or characteristics of research that could help fill gaps in the existing body of research.

Knowledge Gaps for Future Research

Patient Experience

Assessing the impact of sarcoidosis on patient quality of life (QoL) and developing interventions that address psychological, social, and physical aspects of the disease is critical. QoL should be considered in clinical trial design.

Novel Treatment Strategies

While corticosteroids are the primary treatment, there is a need for more targeted and effective therapeutic options with fewer side effects. Overall, stronger research methods (randomized trials) and needed in thise space.

Biomarkers

There is a need for the identification of reliable biomarkers for early diagnosis, disease management, prediction of disease course, and drug development. Diagnostic and prognostic biomarkers would inform personalized treatment decisions.

Patient Phenotyping

Research that determines which clinical presentations result from a distinct combination of genetic variants, phenotypic traits and/or environmental factors would improve the ability to predict outcomes and treatment response.

Data Development

More data, better data, and better methods are needed to understand the natural course of sarcoidosis, facts influencing disease progression, the risk of complications over time, mortality, and drug effectiveness.

Etiology and Pathogenesis

The exact cause of sarcoidosis is unknown. Understanding the etiology and pathogenesis of a disease is fundamental in devising effective treatments, preventing its occurence, early diagnosis, and predicting prognosis.

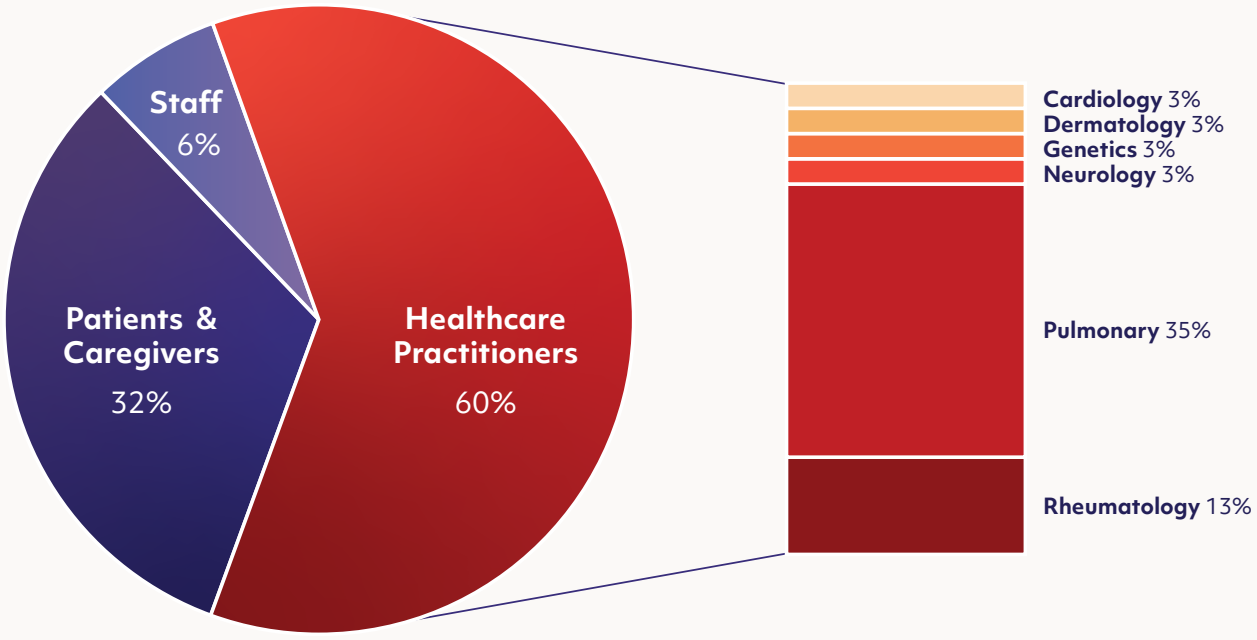
Genetic Studies

More extensive genetic studies and use of cutting-edge methods are needed to understand the genetic basis of sarcoidosis, including the identification of susceptibility genes and the role of genetic variants in disease progress and treatment response.

2. Brainstorming Workshop

FSR convened a workshop of representatives of its staff leadership, Governing Board of Directors, Scientific Advisory Board, Clinical Studies Network, Global Sarcoidosis Clinical Alliance, and the sarcoidosis patient community. Twenty-nine of the 45 invitees participated, including physicians (11 pulmonologists, 4 rheumatologists, and one each of specialists in cardiology, dermatology, genetics, and neurology), patients (4), and board members (3 patients and 3 caregivers). Six FSR staff and consultants also joined the discussion.

Breakdown of Brainstorming Workshop Participation



In the 90-minute recorded Zoom meeting, FSR briefly presented the results of its literature review and engaged workshop participants in a brainstorming exercise designed to generate ideas on where FSR should focus its research. FSR used an online tool (**GroupMap.com**) to collect input and feedback from participants.

Participants were asked to rate each priority from low to high on each of three domains (ease of measurement, connectivity to FSR's mission, and feasibility) and to provide relevant comments. Those scores were translated into numeric scores (low = 0, high = 1). Mean averages for each quality and an average rating for each priority were calculated. From these scores, a "consensus" percentage was calculated (indicating how closely agreement was reached). Participants also rated and generated comments on the priorities identified, based on their connection to FSR's mission, feasibility, and ease of measurement. Quantitative rankings and qualitative comments were analyzed to filter and refine the list of priorities for further evaluation and weighting.

3. Stakeholder 1:1 Interviews to Refine the Priorities

More than 18 hours of semi-structured interviews were conducted with nine stakeholders representing clinical/academic experts, patients and FSR leadership. Interview protocols addressed key questions designed to refine the list of criteria, including: how to refine some of the more broadly-defined priorities, how to resolve overlapping or potentially conflicting priorities, whether and how to separate priorities that are more "traits" or values, and which priorities could be merged or eliminated due to their potential redundancy. Insights were cross-referenced between questions and interviewees to identify recurring themes and relationships. A formal analytical framework was applied to examine consensus areas, differences, and implementation implications.

4. Quantitative Prioritization

Finally, FSR conducted a quantitative survey of key stakeholders in the FSR community to rank and establish weights for each of the proposed priorities and values developed from the first three phases of the process. Thirty-five of the 45 invited stakeholders participated, representing healthcare practitioners (20), patients (7), board members (3 patients and 3 caregivers), and FSR staff (2).

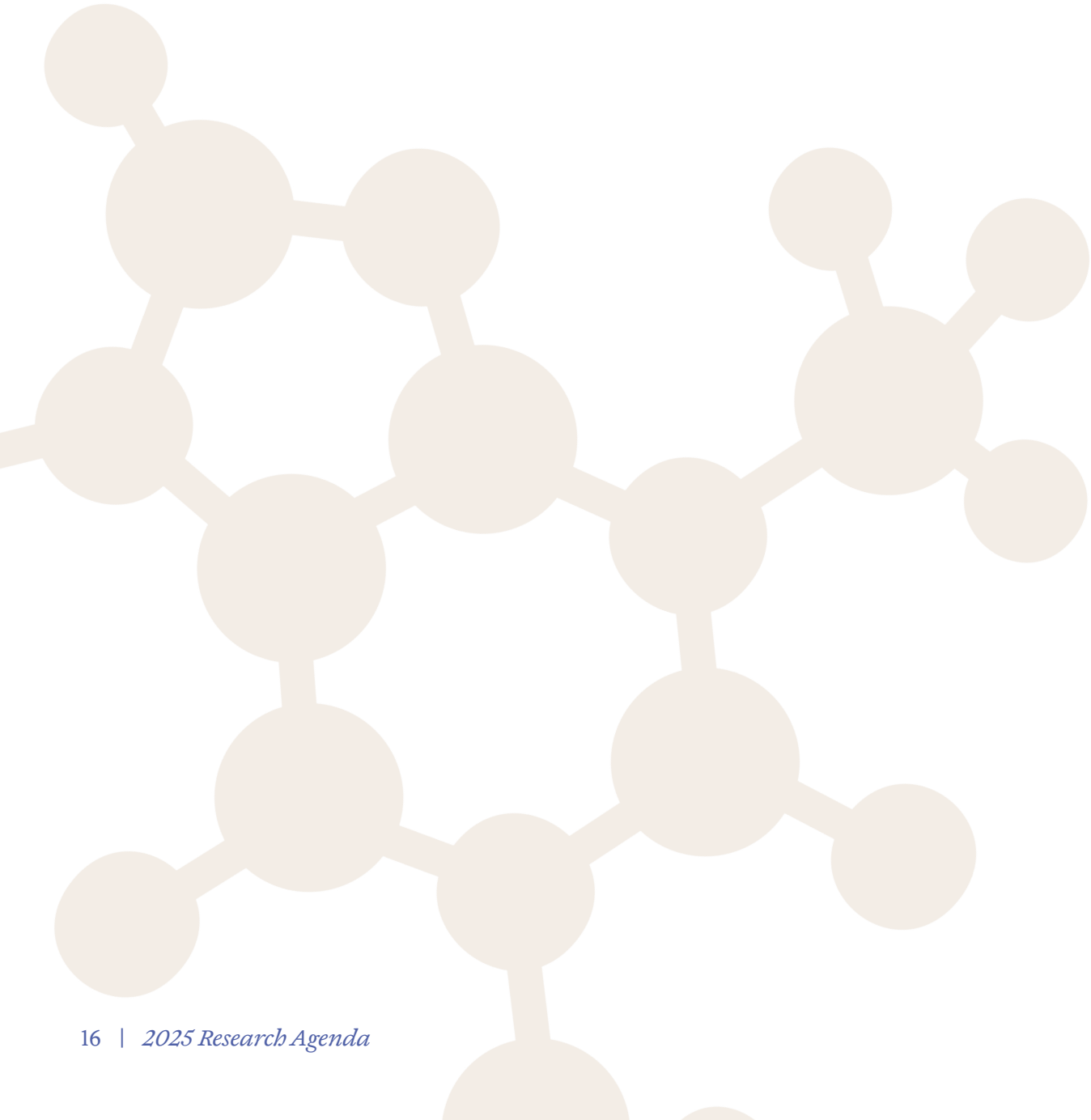
FSR used a scientifically rigorous method to develop a ranking and weights (or "preference shares") using an online tradeoff survey (see **Appendix B**: Prioritization Survey Experimentation Method: Best/Worst Scaling). Survey respondents were given a series of 20-24 tasks in which they were to choose the most and least "important" priorities or values among three options.

Applying Scientific Rigor to the Scoring Process

The Best-Worst Scaling (Object Case, or Case 1) method was chosen to maximize the scientific rigor of the exercise while minimizing cognitive burden on respondents. Best-worst scaling (BWS) represents a sophisticated methodological technique in choice modeling and preference elicitation. This approach, grounded in random utility theory, requires respondents to select both the most and least preferred options from systematically varied choice sets. By forcing discriminating choices between alternatives, BWS overcomes many limitations of traditional rating scales, such as response style bias and scale use heterogeneity. The method is particularly powerful because each choice provides information about both extremes of the preference spectrum, effectively doubling the amount of preference data collected compared to traditional "pick one" approaches.

The scientific validity of BWS stems from its theoretical foundation in discrete choice theory and its empirical demonstration of superior predictive validity compared to alternative methods.[13] The balanced incomplete block design typically employed in BWS ensures that each item appears an equal number of times and is compared against every other item, enabling robust statistical estimation of relative preference weights. BWS specifically

addresses common response biases that plague traditional Likert-type scales: central tendency bias (where respondents avoid extreme responses), acquiescence bias (the tendency to agree with statements regardless of content), and cultural response patterns (such as certain cultures' tendency toward moderate responses compared to Western respondents' greater use of extremes). Additionally, BWS mitigates the impact of social desirability bias by forcing trade-offs between options that might all be considered socially desirable. This systematic approach, combined with the relative cognitive simplicity of identifying extremes, makes BWS particularly effective at quantifying the relative importance of multiple attributes while minimizing the cognitive burden on respondents.



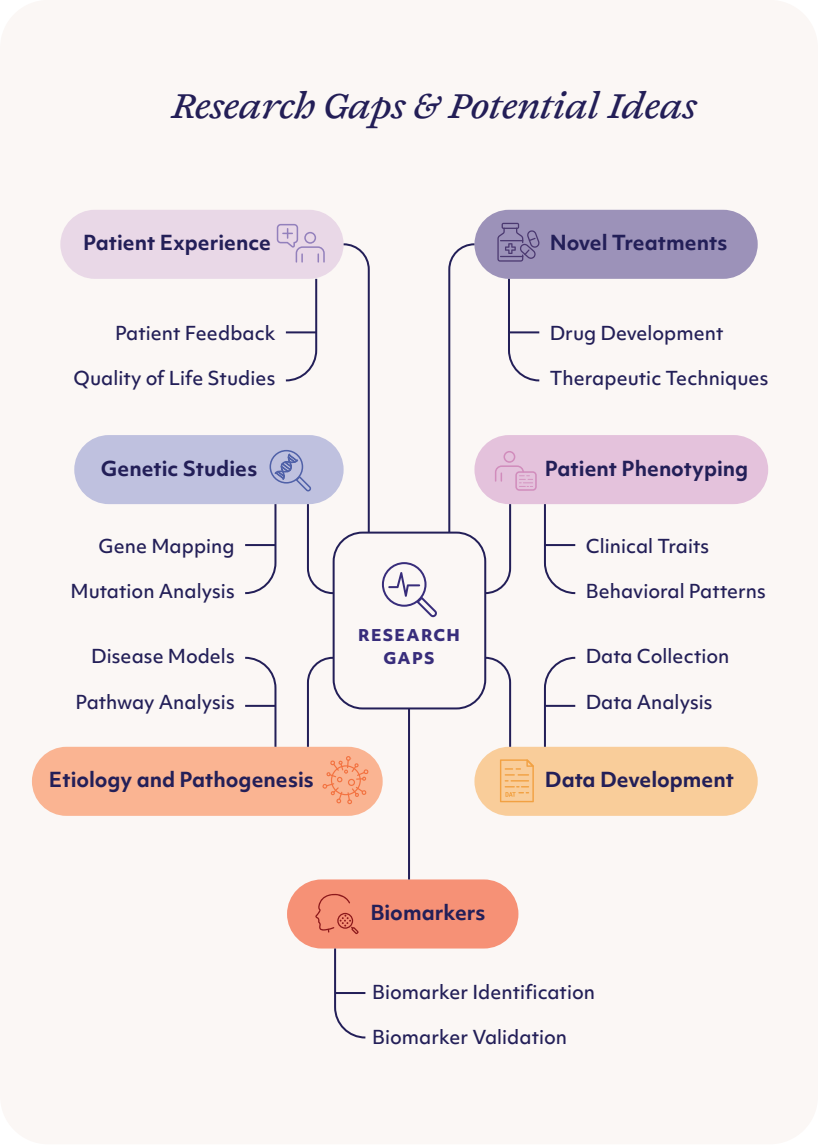
05

Results

The literature review revealed themes in the existing literature. Importantly, sarcoidosis is difficult to diagnose. Because sarcoidosis can mimic other diseases, doctors must carefully consider and rule out conditions like tuberculosis, fungal infections, and other granulomatous diseases.[14] Sarcoidosis, is often referred to as a snowflake disease because no two patients experience the same symptoms and no two patients' diseases progress in the same way.

There are few treatments, which are largely guided by small, uncontrolled trials and expert consensus. There are very few FDA approved therapies in sarcoidosis.[15] Although there is some consensus around treatment of inflammation, treatment strategies still differ institution to institution.

There are some risk factors (some organ systems with high external exposure are most affected) and significant patient and symptom heterogeneity. Given the heterogeneity of the disease, research efforts should move toward a precision medicine approach to define specific "molecular phenotypes."



There are significant data limitations in randomized trial development including lack of established clinical endpoints. Although this has improved greatly over the last five years, there is still limited investment in clinical trials.

Furthermore, there is a need for more and better data and data sharing. Separate from this Research Agenda, FSR is aiming to address this gap through the expansion of FSR's **Patient Registry** and the creation of multi-site clinician input data registry.

Finally, emerging literature suggests a shift toward more integrated and patient-centric care with patient-desired outcomes centered on complex issues like fatigue, although there is limited literature on patient perspectives.

Analysis of the literature review revealed seven general areas where knowledge gaps exist for future research, including: genetic studies, patient phenotyping, data development etiology and pathogenesis, patient experience, novel treatments and biomarkers.

From that research, FSR identified 17 potential ideas for types or characters of research:

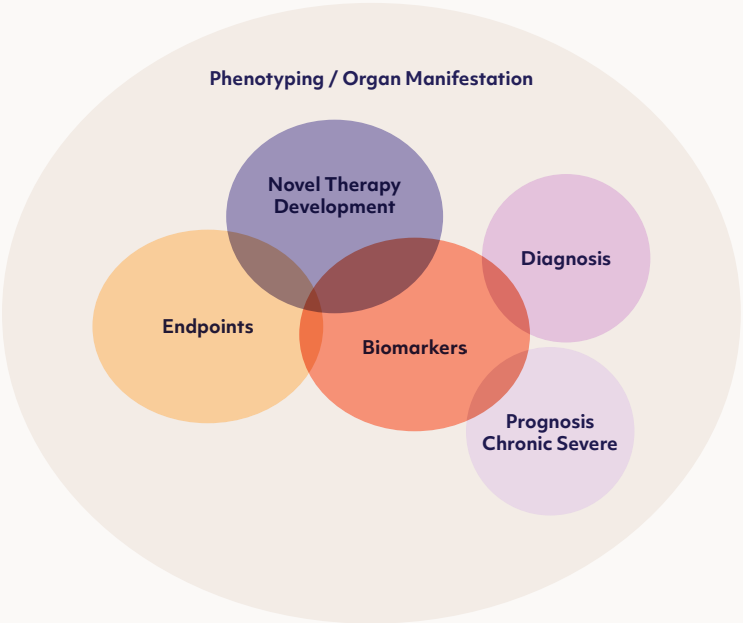
1. **Identifies or defines biomarkers**
2. **Addresses underserved, younger, vulnerable population**
3. **Helps to improve the patient experience**
4. **Supported by high quality data (RCT, sufficiently powered)**
5. **Supports standardization of outcome measures**
6. **Leverages real world evidence**
7. **Supports development of novel treatments**
8. **Supports management of disease (not treatments)**
9. **Addresses large(r) population of patients**
10. **Identifies or defines molecular phenotyping**
11. **Helps improve diagnosis**
12. **Ability to leverage other disease research**
13. **Identifies genetic basis of disease**
14. **Identifies or defines prevention or risk factors**
15. **Immediacy of impact/applicability (vs delayed)**
16. **Identifies causes**
17. **Foundational (can help enable other areas of research)**

THE BRAINSTORMING WORKSHOP was an hour-long zoom meeting with the stakeholder's noted above. Beyond refining the list of priorities listed above, this meeting generated an additional seven priorities to consider use in evaluating future research proposals/opportunities:

1. Identifies or defines biomarkers
2. Addresses underserved, younger, vulnerable population
3. Helps to improve the patient experience
4. Supported by high quality data (RCT, sufficiently powered)
5. Supports standardization of outcome measures
6. Leverages real world evidence
7. Supports development of novel treatments
8. Support the management of disease (not treatments)
9. Addresses large(r) population of patients
10. Identifies or defines molecular phenotyping
11. Helps improve diagnosis
12. Ability to leverage other disease research
13. Identifies genetic basis of disease
14. Identifies or defines prevention or risk factors
15. Immediacy of impact/ applicability (vs delayed)
16. Identifies causes
17. Foundational (can help enable other areas of research)
18. **Outcome measures and/or endpoints for clinical trials**
19. **Provide robust basic science data to serve as pilot data for "definitive" grant applications**
20. **Phenotyping and understanding severity**
21. **Understanding heterogeneity of disease**
22. **Important for the field**
23. **Important for the field and for FSR to support**
24. **Define natural history of disease and risk factors**

THE STAKEHOLDER 1:1 INTERVIEWS helped FSR validate the observations made from the Workshop results. These interviews took place over zoom and lasted approximately 1.5 hour per interviewee. The discussion resulted in the elimination or merger of several priorities as being low in priority or redundant and the refining of definitions of other priorities for greater clarity. The result was a list of nine preliminary research priorities and six research values (as opposed to traits), designed to be as mutually exclusive and completely exhaustive as possible.

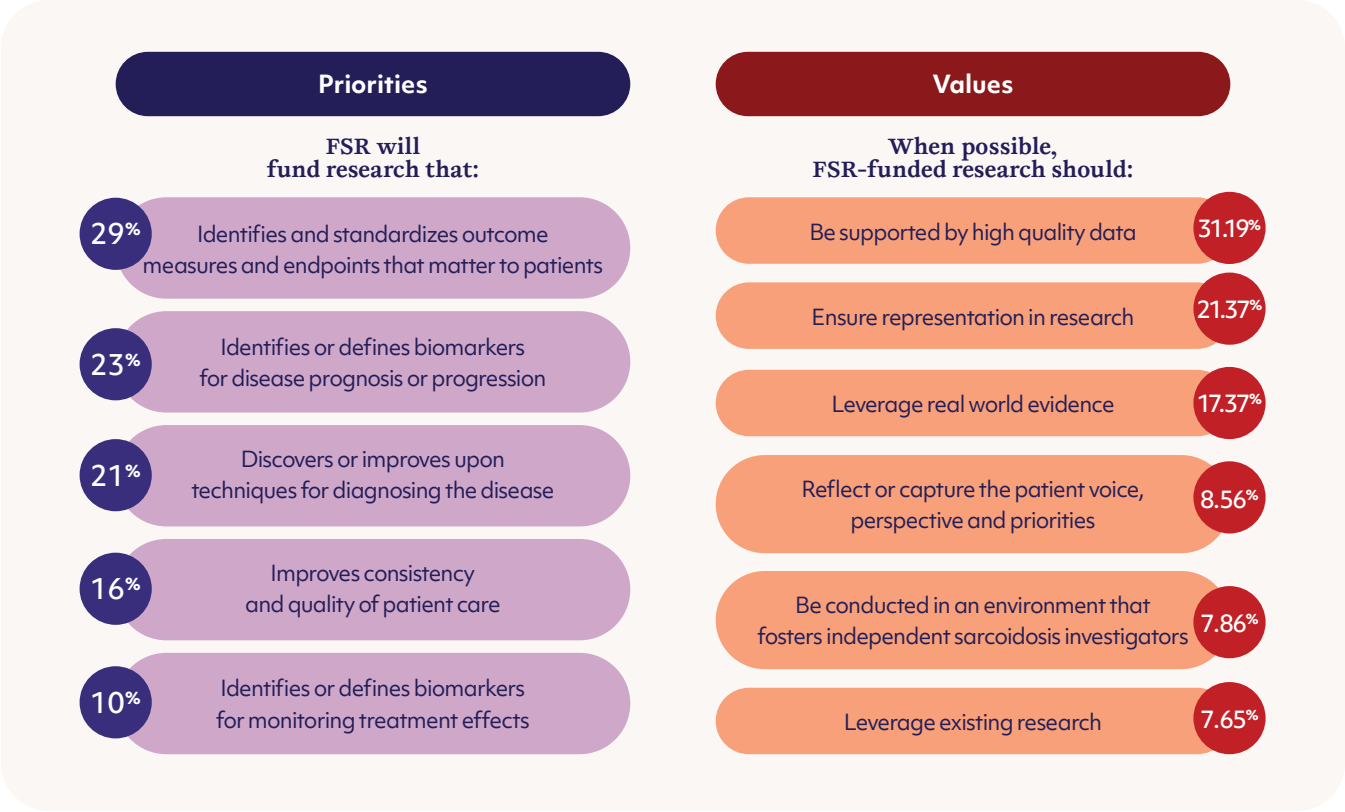
Interrelationships of Priorities



Final Prioritization Results

The results of the Quantitative Prioritization survey revealed that the four lowest ranked research priorities each only generated between 3.7% and 6.77% of the community's preference shares. These priorities were either merged into other priorities or eliminated, and weights were redistributed amongst the final five priorities.

The extensive process to identify, refine, rank and weigh FSR's research priorities amongst the sarcoidosis community reveals a clear set of priorities and values for FSR researchers:



The percentage is the relative weight or importance of each priority and represents the relative focus and energy FSR's community wants research to place on each.

06

Discussion

The process employed by FSR attempted to maximize transparency and collaboration across its community stakeholders using novel techniques to identify, rank, refine and prioritize the organization's research objectives. By working collaboratively with the FSR community to generate 24 "criteria" and honing them down to eleven priorities and values, force-ranked with relative weights, FSR arguably achieved some of the project's objectives, most notably confirming topics representing gaps in sarcoidosis research, incorporating FSR leadership, patient, and key opinion leader input to develop prioritization criteria, values and relative weights for each, and establishing future funding priorities for FSR.

This comprehensive approach revealed a few challenges which will continue to be considered and explored as FSR's new Research Agenda is implemented.

1. Biomarkers vs. Endpoints or "bench" science vs. translational research

There exists an inherent conflict between demonstrating short-term progress and effectiveness for those impacted by sarcoidosis versus the more expensive and long-term process of working in the "harder" discovery of root biological causes and potential cures for future generations.

FSR proposes to address this dilemma by investing additional advocacy resources to increase funding through federal grants or other sources to create the funding mechanisms to support and sustain this type of research. FSR will continue establishing communications systems and collaboration around the FSR community's priorities to improve alignment between the three types of organizations (NIH, FSR and industry).

Furthermore, FSR will focus the efforts from our Research Agenda on demonstrating near-term ROI of research to generate momentum and attract private funding from large organizations to support the long-term science.

Finally, FSR will work with the FSR SAB to develop a long-term scientific strategic plan which will be initiated by a "Biomarker Summit" in 2025, to help the scientific community achieve consensus in the definition and categorization of biomarkers in such a way that will allow us to generate key performance measurement standards.

2. Evaluating Research Proposals: Balancing Focused Excellence and Competing Priorities in Multi-Criteria Decision Analysis

The originally-proposed approach to evaluating research proposals using the weights generated through the prioritization process was to use a multi-criteria decision analysis framework. In it, each application would be evaluated on how well it performed against each priority (high, medium, low) and whether it met FSR values (yes, no); those scores would be adjusted based on the weights created in the prioritization process. For example, a research project that scored high on some of the lower-weighted priorities may not score as well as another project that scored "medium" on the highest weighted priorities.

However, there was some concern that proposals that were "excellent" in one priority could get beaten by projects that were lower quality but hit multiple priorities. To address this concern, an adjusted weighting framework has been proposed that would apply enhanced weight to a proposal's self-designated primary objective while maintaining the value of meeting multiple priorities. This modification aims to preserve the benefits of multi-criteria evaluation while ensuring that breakthrough potential in specific priority areas is not inadvertently undervalued by the scoring system.

In addition, a revised research proposal review process (See **Appendix A**: Research Proposal Review Process) was developed to ensure that:

a) Scientific review remains a primary decision factor for consideration of research funding, and
b) FSR's new priorities and values are effectively incorporated into the process.

This ensures that FSR leadership and Board of Directors will be presented with a variety of insightful recommendations with which to weigh funding decisions that both have a high scientific merit and fulfill the spirit of FSR's priorities and values.

3. Aligning Funding with Achieving Research Priorities

FSR recognizes that achieving its research priorities requires a strategic approach to funding allocation that considers both the relative importance of each priority and the practical costs of conducting the associated research.

To ensure FSR achieves its priority goals, researchers will be encouraged to clearly articulate how their proposals align with FSR's stated priorities and to provide detailed metrics in how they will accomplish their goals. Applicants that demonstrate accomplishment of key objectives in their research may be encouraged to apply for follow-up funding opportunities to help further the development of proposals.

This approach will enable FSR to make more strategic funding decisions that maximize the impact of available resources while advancing the most critical areas of sarcoidosis research.

07

Conclusion

The Research Agenda process revealed the sarcoidosis community's strong preference for identifying and standardizing outcome measures that matter to patients, followed by biomarker development and improved diagnostics. Through extensive stakeholder engagement, including literature review, workshops, interviews, and quantitative prioritization, FSR has established clear research priorities and values that reflect the needs of the entire sarcoidosis community. When implemented, this Research Agenda will represent a significant evolution in FSR's approach, establishing clear priorities while maintaining flexibility to adapt to emerging opportunities. Researchers are advised to refer to the Research Applications Guidelines (**Appendix C**) for examples and further guidance.

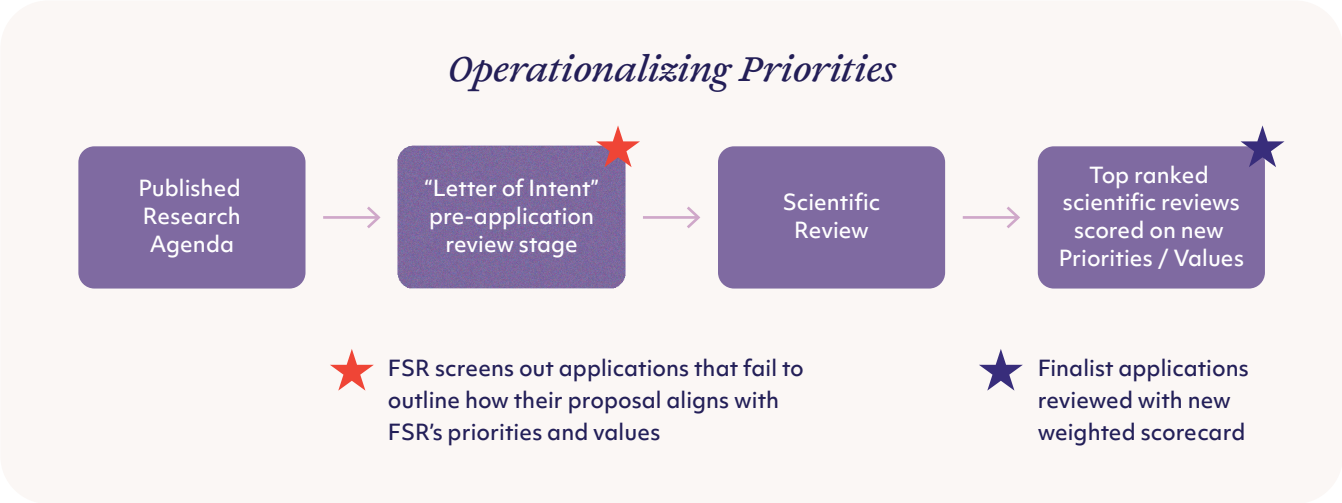
As FSR moves into this next phase, maintaining the balance between short-term clinical impact and long-term scientific discovery will be crucial. The organization's commitment to both rigorous scientific standards and addressing immediate patient needs, as reflected in its prioritization of outcome measures and biomarker research, provides a strong foundation for advancing toward improved treatments and ultimately a cure for sarcoidosis.

Through continued collaboration with its stakeholder community and strategic implementation of its Research Agenda, FSR is well-positioned to accelerate progress in sarcoidosis research while ensuring that investments remain aligned with the most pressing needs of patients and the scientific community. This balanced approach, supported by clear metrics and accountability measures, offers a promising path forward in the organization's mission to improve patient care and find a cure for sarcoidosis. FSR will use the following metrics to evaluate the success and effectiveness of this Research Agenda:

- Increasing grant application average "Priority Alignment" score year-over-year
- Improved alignment of total funding amounts with Research Agenda priorities
- Achievement of each priority's metrics/goals within five years

Appendix A

Research Proposal Review Process



STEPS:

1. FSR publishes its Research Agenda, with clear guidance to research applicants on FSR's strategic priorities and values, including examples

2. Applicants submit a short "Letter of Intent," outlining a brief description of their proposal and how it will align with FSR's values and which priorities

3. A limited number of applicants will be invited to submit a full proposal based on scientific approach and significance, as well as alignment with FSR's priorities and values

4. The Scientific Review Committee will score each application using the standard review scoring process

STEPS (CONT):

5. FSR will train a patient stakeholder committee to further score the top scientifically ranked applications based on the following criteria:

    a. How well does the proposal align to the primary priority as identified by the applicant?
        i. Exceptional
        ii. Good
        iii. Satisfactory
        iv. Marginal
        v. N/A

    b. How well does the proposal align with each of the other FSR priorities?
        i. Exceptional
        ii. Good
        iii. Satisfactory
        iv. Marginal
        v. N/A

    c. Does the proposal meet each of FSR's values?
        i. Yes
        ii. No

6. The Board will finalize award decisions based on a review of the proposals' relative scores.

Sample Review Prioritization for Board Approval

Scientific Review Committee Rank	Investigator Name	Proposal Title	Average Reviewer Total Score	Average Reviewer Total Score	Patient Review Committee Priority Score	Key Considerations
1	Researcher 1	Proposal A	1.94	2.00	75%	scored high on two priorities
2	Researcher 2	Proposal B	2.61	2.67	70%	biomarker project
3	Researcher 3	Proposal C	2.94	3.33	63%	scored highest on values
	Researcher 4	Proposal D	3.06	3.33	70%	scored high on two priorities, including FSR's #1
	Researcher 5	Proposal E	3.17	3.33	60%	diagnostic project *(currently none in portfolio)*
	Researcher 6	Proposal F	3.56	3.67		
	Researcher 7	Proposal G	3.11	3.67		
	Researcher 8	Proposal H	3.50	3.67		
	Researcher 9	Proposal I	3.61	4.33		

Priority scores and key considerations may inform BOD change of ranked order from Grant Review Committee

Appendix B

Prioritization Survey Experiment Method: Best/Worst Scaling

Designed and tested by psychologists and behavioral economists, best/worst scaling is used to assess priorities and creates "preference shares."

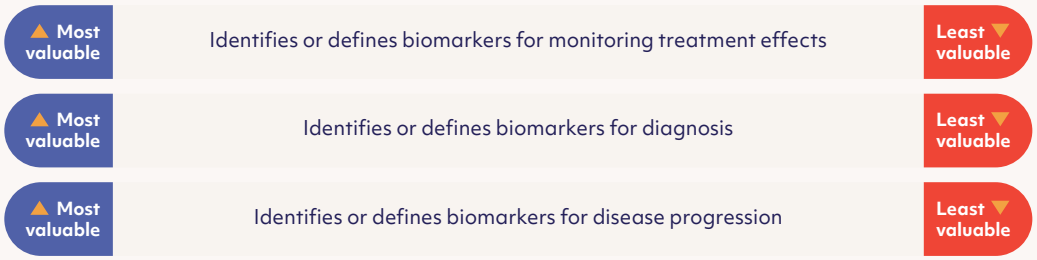
Best/Worse scaling is a strong method to use in identifying priorities because it is designed to reduce biases. Respondents to standard Likert scale prioritization models often interpret and use the rating scales differently. Additionally, Best/Worse Scaling can help to address "end-aversion," where respondents avoid using the extreme ends of scales. Finally, Best/Worse Scaling can help to reduce "order effect bias," to prevent respondents from inferring erroneous information about which items the researchers prioritize based on how the information is listed.

There are several reasons why this strategy is most advantageous in prioritizing. First, it forces respondents to make trade-offs and discriminate between options. Second, it provides cognitive simplicity compared to more complex choice experiments because it only requires the respondent to compare two attributes at a time as opposed to several (e.g., comparing A versus Z as opposed to A+B versus Y+Z).

Below are the instructions that were provided for those who participated in the Best/Worse Survey Instructions:

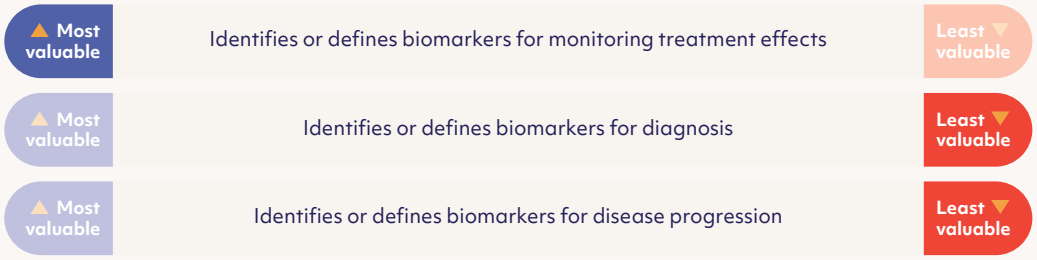
You will be provided a question that will look like this:

FSR seeks to fund research that:



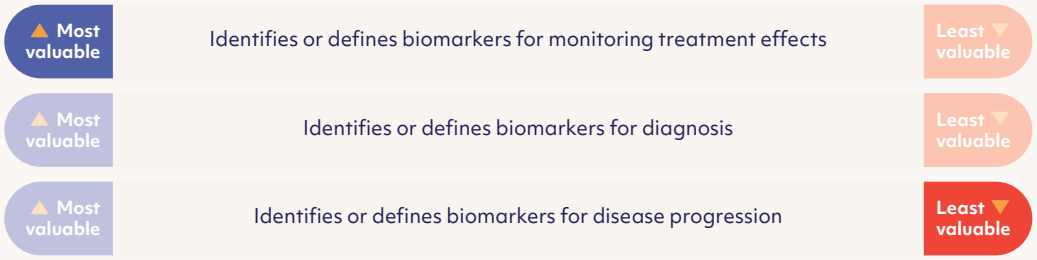
Pick the **one** item among the three that you think is MOST valuable by clicking on one (you can choose only **one**) of the buttons on the left, like this:

FSR seeks to fund research that:



Then choose the **one** item among the three that you think is the LEAST valuable (that doesn't mean it's not valuable, just that compared to the other items, it is LESS valuable), by clicking one (you can only choose **one**) of the buttons on the right, like this:

FSR seeks to fund research that:



This test will be repeated 10-14 times for the priorities section and 10-14 times for the values section.

Appendix C

Research Application Guidelines

FSR RESEARCH APPLICATIONS

The Foundation for Sarcoidosis Research (FSR) leads the charge in advancing scientific understanding of sarcoidosis through strategic research funding. To help the sarcoidosis research community focus their efforts on the needs and priorities of sarcoidosis patients, FSR has developed a process for ensuring research proposals are aligned with those priorities.

Our research funding strategy balances the immediate needs of patients with long-term scientific discovery, supporting both clinical advancements and foundational research. We particularly emphasize innovation in underexplored areas of sarcoidosis research.

SUCCESSFUL RESEARCH GRANT PROPOSAL DEVELOPMENT

Under the leadership of our Board of Directors and Scientific Advisory Board, FSR has developed research priorities in collaboration with the greater sarcoidosis patient and research community. Research proposals will have a greater likelihood of securing an award if they:

- Outline how their research objectives meet one or more of FSR's priorities with greater weight given to priorities in their order listed below
- Identify how the proposal will provide measurements of successful performance against the project's research objectives (see examples of performance and measurements of success for each priority below)
- Iterate how the project will be in alignment with FSR's values (listed below)
- Secure a favorable score for aligning with FSR's priorities and values

Version date April 11, 2025. Guidance for research funding applications will likely evolve.
Please see the **FSR website** for the most up to date guidance.

RESEARCH PRIORITIES

Successful research proposals will need to be aligned with one or more of the following priorities. The key performance measures listed below are tentative. FSR will be working with the FSR Scientific Advisory Board to create measures that will be used to establish progress towards these goals.

1. Standardization of Patient-Centered Outcomes:

Research that identifies and standardizes outcome measures and endpoints that matter to patients.

Examples of Performance:

- Development of validated outcome measures that reflect patient priorities (including clinical outcomes as well as functional or patient reported outcomes like fatigue, quality of life, and other key symptoms)
- Creation of standardized clinical trial endpoints that reflect meaningful improvements in patient function and well-being
- Establishment of consensus definitions for symptom improvement tracking

Tentative Measurements of FSR's Success:

- Number of validated outcome measures developed and adopted
- Publication of consensus guidelines for outcome measurements
- Integration of patient-centered endpoints in clinical trials
- Increased use of outcome measures in clinical and/or patient registries

2. Biomarkers for Disease Prognosis/Progression:

Research that identifies or defines biomarkers for disease prognosis or progression.

Examples of Performance:

- Identification of molecular signatures that predict disease course
- Development of biomarkers that can identify likelihood of progression (e.g., from chronic to acute/severe)

Tentative Measurements of FSR's Success:

- Number of new biomarkers identified
- Number of clinical validation studies completed
- Increase in treatments/therapies that leverage biomarkers to monitor treatment effects
- Implementation of biomarker testing in clinical practice (diagnosis, access to therapies in an expedited way)

3. Diagnostic Innovation:

Research that discovers or improves upon techniques for diagnosing the disease.

Examples of Performance:

- Development of novel diagnostic algorithms
- Validation of new imaging techniques for early detection
- Creation of diagnostic tools for specific organ involvement
- Identification and validation of a reliable biomarker to facilitate accurate diagnosis

Tentative Measurements of FSR's Success:

- Number of new diagnostic tools developed
- Number of diagnostic tools validated
- Reduction in time to diagnosis or specialist referral
- Improved diagnostic accuracy rates
- Reduction in severity of disease at presentation

4. Quality of Patient Care:

Research that contributes to the improvement of consistency and quality of patient care.

Examples of Performance:

- Development of evidence-based treatment guidelines
- Creation of care coordination protocols
- Implementation of standardized assessment tools
- Development of mechanisms of measurement of high quality care clinic to clinic (i.e. quality measures, improvement assessment scales)

Tentative Measurements of FSR's Success:

- Development of standardized protocols that are highly likely to be implemented (e.g., tied with Shared Decision Making)
- Implementation of standardized care protocols
- Reduction in care variability
- Improvement in patient outcomes

5. **Treatment Monitoring:** Research that identifies or defines biomarkers for monitoring treatment effects.

Examples of Performance:

- Development of imaging biomarkers that track disease progression
- Validation of blood-based markers for monitoring disease activity
- Tracking of likelihood to be responsive particular therapy(ies)

Tentative Measurements of FSR's Success:

- Number of validated treatment response markers
- Use in clinical trial design
- Implementation in clinical practice
- Improvement in treatment optimization

RESEARCH VALUES

Where appropriate and/or possible, all FSR-funded research should demonstrate the following characteristics:

- **High-Quality Data -** Research must be supported by robust methodology and data collection, including well-designed study protocols, appropriate statistical power and rigorous data collection and analysis methods.
- **Representation Focus -** Research should address the expanding access to all patients through recruitment strategies, analysis of disparities in care, or targeted interventions.
- **Real-World Evidence -** Research should leverage real-world data and evidence when appropriate, including integration of registry data, real-world effectiveness studies, and/or leveraging practice-based research networks.
- **Patient Voice Integration -** Research should reflect and capture patient perspectives and priorities by engaging patients in study design, through the collection of patient experience data and/or development of patient-driven research questions.
- **Investigator Development -** Research should foster the growth of independent sarcoidosis investigators including mentorship components, career development opportunities and research capacity building.
- **Research Leverage -** Research should build upon and connect with existing research efforts through cross-institutional collaborations, by building on previous findings, or through shared resources and data.

APPLICATION PROCESS

1. Researchers must review the available grant programs and determine which they wish to pursue. Researchers may apply for any grant for which they are eligible.

2. Researchers must submit a letter of intent, indicating which of the FSR's grant programs they will be pursuing, providing a general overview of the proposed project and how it will meet the priorities and values of FSR.

3. FSR's Patient Advisory Committee will review letters of intent to verify that the proposal will align with FSR's priorities and values, while FSR's Scientific Advisory Committee will conduct a parallel review for scientific approach and significance.

4. Applications with a promising scientific approach that best align with FSR's priorities and values will be invited to submit a full grant application.

5. Proposals will be peer reviewed by the Scientific Review Committee made up of internal and external experts. Each proposal will be scored utilizing a standard scoring rubric. Reviewer comments will be made available to each applicant.

6. The top proposals will be further reviewed by the Patient Advisory Committee utilizing a priority/value scoring rubric, basing a higher weight on the priority that is the primary purpose of the grant application.

7. FSR's Board of Directors will finalize the review and recommendations for grants. Applicants will be offered a grant agreement, which will include requirements to provide documentation and reports of progress and measurements of success.

ADDITIONAL TIPS

Researchers interested in applying for FSR funding should carefully review these priorities and values when preparing their proposals. All applications should clearly articulate how the proposed research aligns with FSR's priorities and demonstrate commitment to our research values. Researchers may wish to refer to the FSR Research Agenda Report for more details.

FSR will be holding its research programs accountable to the strategic priorities and goals outlined in its Research Agenda. To do so, FSR will be measuring:

- Increasing grant application average "Priority Alignment" score year-over-year
- Improved alignment of total funding amounts with Research Agenda priorities
- Progress towards each priority's metrics/goals within five years

Anything grant applicants can do to demonstrate how their project fulfilled these goals will increase the likelihood of support. FSR will provide all grant applicants with feedback to improve their proposals for both current and future funding opportunities as appropriate.

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FSR

FSR funds research grants to advance scientific understanding, improve diagnosis and treatment, and ultimately find a cure for sarcoidosis.

LEARN MORE HERE

THESE GRANTS SUPPORT:

- Early-stage investigators in developing specialized skills and conducting innovative research likely to add significant knowledge to the field
- Small-scale or early-stage projects in both clinical and basic science settings
- Targeted grants such as those focused on cardiac sarcoidosis

Since its inception, FSR has awarded over $7 million in research funding and continues to foster collaborations to accelerate research discoveries.