Sanguine

Extinguishing the Flares

A Patient-Powered Path Forward in Lupus Research

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Introduction

The diversity of genetic factors and variability in symptomatology complicates translational and clinical studies related to systemic lupus erythematosus (SLE, or lupus). As an autoimmune disease, SLE has been linked to de novo or inherited mutations in various immune-related genes, as well as environmental triggers.[3] Moreover, innate and adaptive immune dysfunction cause chronic multisystemic inflammation that progressively worsens over time. The manifestation of symptoms is often unpredictable and increasingly debilitating, with inflammatory flare episodes that have variable recurrence. Although some have chronic disease, most people suffering from SLE experience a recurring and remitting disease phenotype based on flare periods that range in severity and time.

The hallmark of SLE diagnosis is the detection of key autoantibodies, such as anti-nuclear antibodies that bind to DNA and RNA primarily. These autoantibodies, in addition to T cell and B cell dysregulation, have key roles in cytokine induction and type I interferon stimulation, which drive inflammation.

Impressive scientific advances have extended SLE lifespan from a 4-year survival rate of ~50% in 1950 to a 15-year survival rate of ~85% as of 2013.[4] Even though the disease landscape continues to improve, SLE continues to take lives prematurely as a result of the morbidities that arise through disease progression. To that end, lupus nephritis, which is present in 40% to 70% of SLE patients, represents the most harmful and difficult-to-treat clinical feature that can lead to chronic renal failure.[5]

Although SLE therapeutic development lags when compared with other rheumatic diseases, the elucidation of new molecular pathways and potential therapeutic targets provides great hope to the future of SLE treatment options.

In this eBook, we rethink the well-known challenges for advancing SLE research by providing innovative solutions to patient reach, recruitment, and biospecimen and data collection. You'll learn how Sanguine's patient-powered approach provides the pharmaceutical industry with an enhanced ability to recruit study participants and collect biospecimens and data through a mobile workforce across the United States. Our leading advantage – a mobile direct-to-patient approach – brings research participation into the patient's home with a primary focus on establishing trusting relationships.

SLE Quick Facts[1,2]

- United States: up to 1.5 million patients
- 90% of SLE patients are women
- 2 to 3 times more prevalent in women of color
- Typical onset: 15–44 years of age
- Annual incidence: ~16,000 new cases per year (U.S.)
- 1 in 3 lupus patients have multiple autoimmune diseases

CHAPTER 1

Reach, Recruit, Retain

>80% Research studies in the United States experience delays due to recruitment problems

>50% Investigative studies fail to meet enrollment requirements

~30% Average participant drop-out rate across clinical trials[5]

Participation burden represents a critical challenge in retaining SLE patients through study completion. Moreover, the added burden of coping with an incurable chronic disease that often takes a long time to diagnose and disproportionately affects marginalized, minority women complicates patient engagement in biomedical research. In comparison to other rheumatic diseases, limited treatment options exist and most randomized controlled trails have failed to achieve primary endpoints, due to a myriad of limitations, one of which stems from enrolling less-than-ideal patient subpopulations.[6]

Taking a Lean, Virtual Approach

With a mobile workforce of more than 135 phlebotomists nationwide **(Figure 1)**, our virtual recruitment and direct-to-patient biospecimen and data collection capabilities are designed to be minimally disruptive to patients' everyday lives. As a result, patient retention is consistently high (93%) across each study we support. Moreover, a high proportion of patients are eager to participate again and over long study periods, meaning the high scientific value of completing longitudinal studies can be realized. By working with researchers to improve study completion rates, we help minimize inconclusive findings and wasted funding, which further motivates patients to embark on the quest toward improved outcomes for SLE.

FIGURE 1. Mobile phlebotomy: U.S. Geographic Distribution. The Sanguine mobile workforce reaches 70% of the population nationwide. Our fleet consists of more than 135 phlebotomists, with 80% of patients having had the same phlebotomist throughout the duration of their participation.

As a mobile direct-to-patient research services company, we access hard-to-reach SLE patients who may otherwise be far from research sites to participate **(Figure 2)**. Our close relationships with the Lupus Foundation of New England and Southern California, in addition to the Lupus Chick and other autoimmune disease non-profit and patient advocacy group partnerships further supports our ability to increasingly be contracted for translational and clinical studies across the autoimmune disease group. In turn, investigators benefit from expanded study recruitment reach and sample collection, ensuring continuity in research and study completion. By substantially reducing the workload on site staff and the number of sites required, researchers can expect rapid enrollment and mobilization from a leaner, virtual approach

Sanguine Stats

93%
Patient retention rate

>2,700
SLE patient members

>85
SLE studies completed

Geographic Distribution of the Sanguine Systemic Lupus Erythematosus Patient Member Community

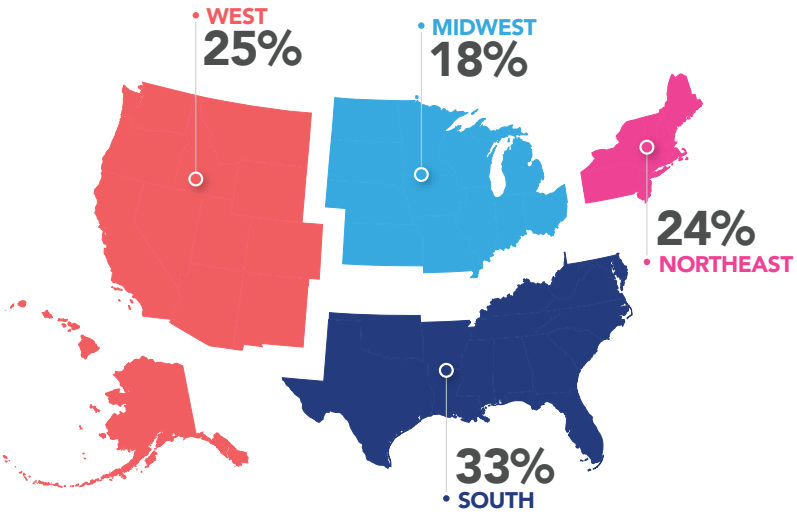


FIGURE 2. A mobile specimen collection approach means streamlined access to increased patient populations. The current Sanguine SLE patient community is made up of >2700 members, roughly equally distributed across the four geographic regions of the U.S. Through strategic online and social media recruitment campaigns, and partnerships with patient advocacy groups, this network is always growing.

Compliance and Quality Assured

Our model is centered around valuing our patient community's autonomy and privacy, and we focus extensively on protecting and enhancing their health. All Sanguine practices and protocols are HIPAA-compliant and IRB-approved. Our informed consent protocol is 21 CFR 11-compliant; our organization maintains the gold standard AAHRPP accreditation for protecting research participants, and we exceed standards set by GCP guidelines.

HIPAA compliant | **IRB approved** | **AAHRPP accredited** | **21 CFR 11 compliant**

Let's Talk

CHAPTER 2

Emerging Therapeutics and Study Criteria

SLE treatment often involves a dynamic approach that is focused on reducing flare episode intensity and maintaining low levels of disease. Hydroxychloroquine and corticosteroids are considered traditional therapies for a wide range of autoimmune diseases, with many SLE patients responding well initially. Though, even as the first line of treatment, adjustment of dose and duration based on disease activity and treatment-associated long-term harm is a constant.

While other autoimmune diseases have seen success with novel therapeutics, SLE has proven more difficult to develop effective targeted treatments against. A substantial number of promising early-phase agents have failed to meet primary end points in large clinical trials, leaving a limited therapeutic landscape for when conventional therapies fail.[7,8]

A New Wave: Immune-modulating Biologics

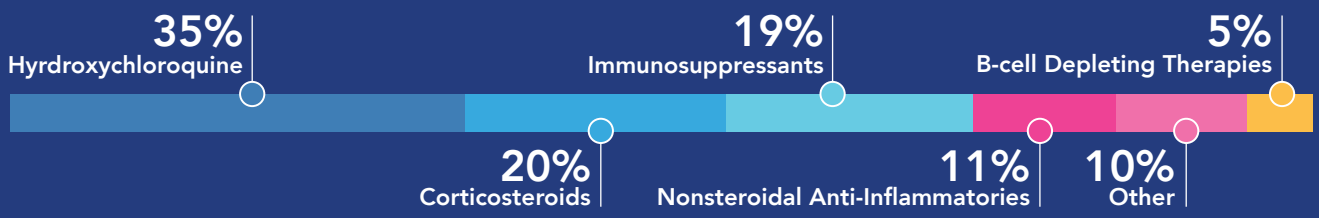
Leading biologics-based therapeutics target either the B cell or T cell-related pathogenic pathways in SLE. Rituximab (Rituxan®, an anti-CD20 monoclonal antibody) and belimumab (Benlysta®, an anti-BAFF monoclonal antibody) are the leading SLE biologics, however there is still a sizeable proportion of patients in which these therapeutics cannot control their disease.[9] Balancing treatment benefit and the risk of adverse events, particularly related to the immunosuppressive aspects of many SLE therapeutics is an ongoing challenge for treatment. As SLE molecular disease pathways continue to be further elucidated, new avenues for therapeutic development are emerging.

BOX.1 SANGUINE SPOTLIGHT

How Do Patients in our Community Manage Their Disease and Symptoms?

Of the more than 2,700 SLE patients in our community, most rely on hydroxychloroquine (35%) and corticosteroid (20%) medications—with many taking combination therapies to treat active lupus symptoms. Of note, our SLE patient community consists of greater than 75 members who utilize belimumab, the first treatment developed and approved specifically for SLE, and has shown promising success in improving disease and reducing dependence on corticosteroids.[10,11]

Although many treatments reduce symptoms, disease management is complex and often limited, highlighting the strong unmet need to improve therapeutics and quality of life.



Start Recruiting Participants for My Study

Increasingly Complex Inclusion and Exclusion Criteria

Specific exclusion and inclusion criteria (e.g., medication profiles, treatment histories) often reduce the number of eligible patients for a study, which hinders progress and statistical power. Our thoroughly curated SLE patient community is highly motivated to participate and understand scientific research. Through a patient-led approach, we drastically improve participant retention (93% compared with the 65% industry average).[12] Moreover, we pre-screen and medical record-verify patients for quick recruitment of the most eligible participants. **Table 1** highlights the common inclusion and exclusion criteria we support in SLE research.

INCLUSION CRITERIA	EXCLUSION CRITERIA
Confirmed clinical diagnosis based on medical record review	Nursing or pregnant females
Moderate to severe disease activity	Serious complications related to SLE (e.g., central nervous system involvement, anti-phospholipid syndrome)
Adapted SLEDAI score	History of particular autoimmune comorbidities
Historical positive antinuclear antibody test result	Known history of HIV, viral hepatitis, and other bloodborne infectious diseases
Historical positive anti-double-stranded DNA test result	Viral infection within the last month
Experiencing a flare	Excessive blood loss, including blood donation
Exhibiting at least one of the following symptoms in the last 10 days during screening: skin rash, arthritis, renal symptoms including active kidney disease, nephritis, pink/cola-colored or foamy urine, high blood pressure, unusual fatigue, swelling evident in the face, hands, or abdomen	Previously received a bone marrow transplant
	Previously taken rituximab (Rituxan®) in the last 2 years
	Previously taken belimumab (Benlysta®) in the last 2 years
	Currently taking and investigational biologic product
	Currently taking high-dose corticosteroids
	Currently taking cyclophosphamide
	Currently taking an anti-TNF-α agent
	Currently taking an anti-CD38 antibody therapy
	Currently taking a B-cell depleting therapy

TABLE 1. Typical inclusion and exclusion criteria supported for SLE studies. All participants enrolled in a research study are medical record-verified for their diagnosis and medical history before in-home sample and data collection.

Setting Meaningful Endpoints

Determining efficacy endpoints for investigational SLE therapeutic studies that are optimized for clinical success is considerably challenging. In general, most pharmaceutical companies now either engage in renal or non-renal focused studies for SLE.[9] Concentrating on renal-related endpoints allows for easily quantifiable laboratory-based hard endpoints such as serum creatinine, glomerular filtration rates, or protein-to-creatine ratio measurements. Non-renal studies, however, require subjective clinical assessments based on one of many SLE disease indices, which each have their advantages and disadvantages when applied in a research setting.

Changes in certain biomarkers, such as a reduction in anti-nuclear antibodies, can also often be correlated to clinical improvement.[13] As novel biomarkers related to SLE disease continue to be identified, developing treatments for particular patient subgroups could be the most reliable path forward.

Make My Study Criteria Feasible >

Sanguine Speaker Series

Steps to Reduce Missed Deadlines & Unnecessary Costs in Research Studies & Trials

Check out our webinar for an in-depth look at how our innovative approach is revolutionizing clinical research–accelerating timelines, increasing patient reach and retention, reducing study costs, and maximizing success.

Integrated recruitment approach: multi-pronged patient recruitment strategies with patient advocacy groups, social media, and community outreach.

Flexible study design: adaptable in-home collections of minimally invasive sample types, expedited sample processing, and central lab coordination to reduce study timelines and cost.

99% PATIENT RECALL RATE

93% STUDY RETENTION RATE

9.6 PATIENT SATISFACTION SCORE

Watch Now >

Stratify to Simplify

Patient stratification based on disease activity may be a key factor in study design for developing effective therapeutics. As a heterogeneous disease, some therapeutics may have greater efficacy at different disease stages and not stratifying in the optimal manner could dilute the treatment effect. Using the appropriate validated disease index to monitor disease state changes over the course of the study is a reliable approach to maximize success. Performing these assessments can be time-consuming, requires clinical training, and can be subjective.

Leverage our direct-to-patient approach and experienced team to deliver accurate, consistent disease index classification that will meet your study demands and maximize success.

Read Case Study >

Partnering with Sanguine means overcoming hurdles in study design, recruitment, retention, and completion through an innovative virtual model that is patient-driven to energize and engage a home-grown SLE patient community to participate. Equipped with a mobile workforce capable of in-home biospecimen and data collection, our patient community members develop trusting relationships with their phlebotomist, allowing for repeat, longitudinal collection. We reduce the burden on patients to increase recruitment capacity and improve study completion rates so that you can make clinically relevant conclusions that will move SLE research forward.

CHAPTER 3

Expect the Unexpected: Flare Events in SLE

SLE translational and clinical studies face substantial hurdles in developing meaningful study designs for assessing novel therapeutics. The unpredictable and highly variable nature of the disease—with variability in severity, progression, and unexpected symptom flare events further complicate individual clinical assessments.

"Flare" Defined

Flare events represent an increase in disease activity, inducing symptoms such as fatigue, skin rash, fever, and pain or swelling of the joints. Flare frequency and severity can vary dramatically from person to person, with remission even lasting years. Controlling and reducing flares is paramount for disease management, as increased flare activity accelerates permanent organ damage and decreases quality of life.

Longitudinal Event-based Sampling: Going Direct-to-Patient

The pivotal role of unexpected flares in SLE disease progression highlights the importance of integrating sample and data collection during such events into research study designs. In general, the ideal endpoint for a study focusing on treatment efficacy should include long-term sampling and comparisons normalized against each patient's baseline assessments. Capturing valuable disease-relevant samples linked to symptomatic flare-up episodes as they onset compared with non-symptomatic periods can yield useful biomarkers to evaluate for efficacy. In addition to evaluating therapeutics, collecting samples longitudinally to evaluate how biomarkers change with shifting disease symptoms is critical to further our understanding of the disease. For example, alterations in key pro-inflammatory blood biomarkers have been associated with changes in disease activity and can be predictive of imminent flare episodes.[14]

For many biomarkers, detecting or predicting changes is contingent on knowledge of individual baseline measurements. As such, biomarkers can be harnessed to support efficacy studies of novel therapeutics to improve disease management both symptomatically and long-term.

Read Case Study >

By adopting our direct-to-patient workflow for event-based sample collection **(Figure 2)**, researchers gain increased reach for recruitment and convenient in-home sample collection for study retention. By enabling longitudinal sampling, our remote model provides researchers with valuable benchmarks for comparing individual baseline phenotypes and flare events within translational, and therapeutic interventional or observational studies. Moreover, integrating electronic surveys and questionnaires or technology-based patient-reported outcome data to supplement biological samples is entirely feasible to provide an all-inclusive view of study participants.

Event-Based In-Home Specimen Collection Workflow

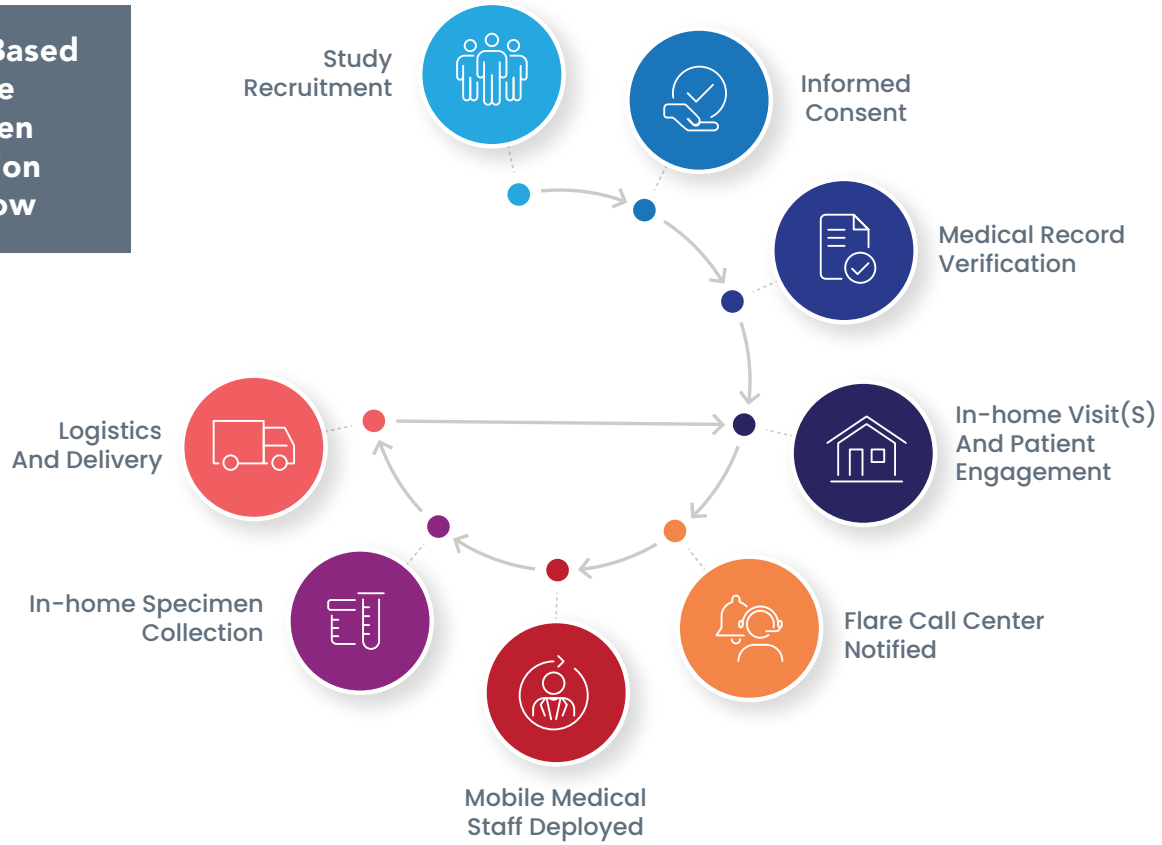


FIGURE 2. A direct-to-patient approach means access to patient samples during a flare event. Collect samples and patient-reported outcome data during or after an acute pain episode, monitor the response or nonresponse to treatment, obtain trough and peak level biospecimens, or other event-based sample collection specific to your study.

Overall, the underlying immune dysregulation and pathogenesis can differ substantially amongst SLE patients—demanding a more focused approach that addresses different subgroups of SLE patients. The chronic impact of symptomatic flares and ongoing inflammation leads to systemic complications that ultimately reduce life expectancy. Therefore, understanding flare pathophysiology is critical to developing therapeutic interventions that reduce severity and frequency to improve quality of life. Taking a direct-to-patient approach allows for the collection of comprehensive data related to constantly changing disease states and unexpected flare events, which can be individualized and channeled to yield more reliable clinical endpoints that can be incredibly difficult to capture by way of conventional study designs.

Gaining Power Over Peril in SLE Research Study Designs

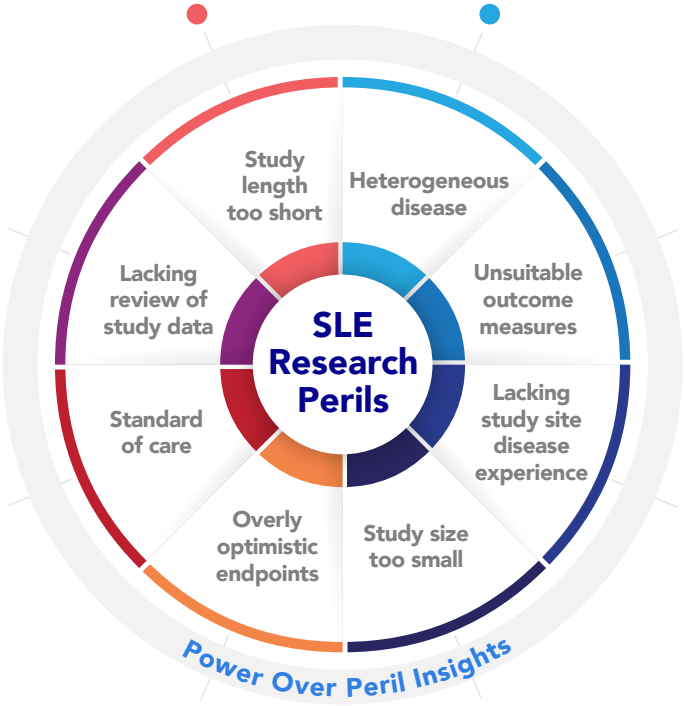
Common challenges in SLE research that can lead to study failures (inner circle) and important considerations for maximizing success (outer circle) are represented below.[8]

Balancing the chronic and unpredictable nature of SLE demands longer observation. Some endpoints may require longer study designs to make meaningful conclusions.

Consider stratifying participants based on disease severity/activity or serological activity with well-defined criteria. But avoid treatment effect dilution or underpowered studies through careful consideration of I/E criteria that are also not too restrictive.

Continuous and timely review of data and safety measures are required to identify gaps in data collection or site training, which can cause study failure.

- Choose parameters that are sensitive to change, can be reliably measured, and are validated.
- Assess pros/cons of disease indices and choose measures based on study goals.
- Molecular biomarkers as outcome measures can help yield quantifiable laboratory data to supplement analyses.
- A focus on organ-specific measures may be preferred, current treatment(s) should not negatively affect overall disease activity.
- Supplement with validated patient-reported outcome data.



Standard of care treatments may confound endpoint analyses. Consider the role of particularly corticosteroids in your study design and criteria.

Disease index subjectivity means investigator consistency during evaluation is imperative. Ensure inclusion criteria are well-defined and the study protocol effectively communicated.

- Properly consider disease activity index to avoid the chance of an artifactual reduction in disease activity.
- Consider the importance of assessing for sustained clinical benefit over a set timeframe.
- Use validated patient-reported outcome measures as secondary endpoints.

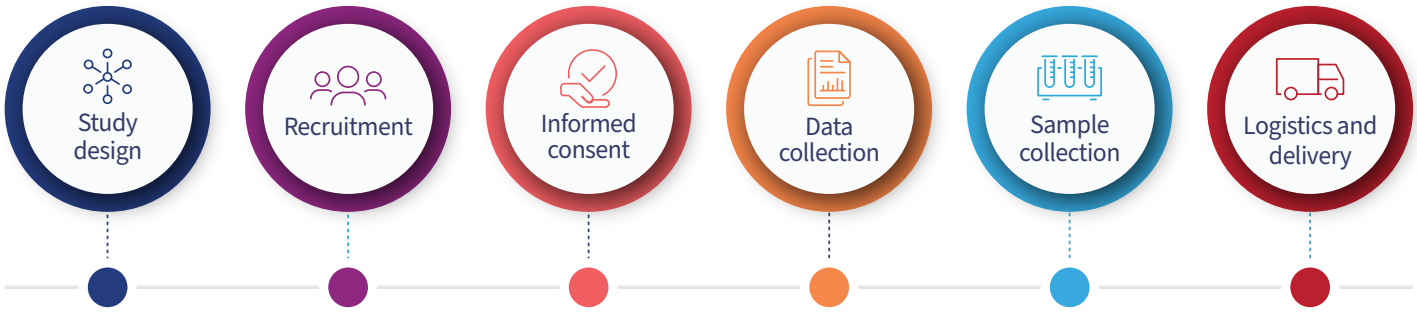
Adequate sample size is necessary to power the study and ensure the conclusions are real.

Get Started Today

Conclusion

Conducting clinical research comes with a high cost and a high study drop-out rate but working with Sanguine sets your study up for the greatest chance of success. The complexities of SLE disease manifestation and their incorporation into study designs and achievable endpoints requires a partner who offers a tailored approach. Working together, we can ensure efficient recruitment, retention, and engagement coupled with high-quality longitudinal sample collection during key physiological disease events. We bridge researchers with patients—giving you access to a powerful platform for advancing biomedical research and having a tangible effect on patients' lives.

Get to market faster with a fully integrated services solution



About Us

Sanguine is a pioneer of in-home biospecimen collection and a leader in direct-to-patient recruitment and digital health innovation. We partner with researchers to expedite and complete studies across various conditions, supporting complex inclusion/exclusion sample and data collection criteria for longitudinal and cross-sectional study designs. Our growing community is made up of more than 30,000 highly engaged patient members, and more than 100 advocacy groups, allowing us to seamlessly work with the pharmaceutical industry on more than 600 pre-clinical and clinical condition-specific research studies to date.

Sanguine

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