synexa | Life Sciences

Translating Oncology Innovation into Autoimmune Disease

Contents

Translating Oncology Innovation into Autoimmune Disease

How the oncology toolkit is crossing therapeutic borders, and what drug developers must understand to navigate the immunological shift.

Executive Summary

Over the past five years, one of the clearest shifts in biopharmaceutical R&D has been the movement of oncology-born technologies (most prominently CAR-T cell therapy, but also antibody-drug conjugates (ADCs) and bispecific T-cell engagers) into the treatment of autoimmune and rheumatic diseases.

What began as experimental crossover is becoming a broader rethinking of immune intervention itself. Yet autoimmune disease is not oncology with a different endpoint. The biology is more heterogeneous, the therapeutic window narrower, and the definition of success far less binary than tumour eradication. The autoimmune disease space presents a fundamentally different immunological context: patient heterogeneity, biomarker strategy, treatment timelines, and even the definition of clinical success.

The challenge now is not whether these therapies can work in autoimmune disease, but how to translate them safely into a fundamentally different biological and clinical setting.

1. Why Now? The Convergence Points

For decades, oncology and rheumatology have existed as largely parallel therapeutic disciplines. Of course, they share immunological vocabulary - T-cells, B-cells, cytokines, checkpoint pathways - but the drug development logic was almost entirely separate.

Oncology pursues tumour eradication; rheumatology pursues symptom suppression and disease modification. The former is driven by objective response rates and survival curves, the latter by composite clinical scores, quality of life measures and the management of lifelong, relapsing-remitting conditions.

So, what has changed?

Firstly, we must acknowledge oncology's success with immune-based therapies, revealing the extraordinary plasticity of immune cell engineering. Chimeric antigen receptor T-cell (CAR-T) therapy, developed to destroy malignant B-cells in haematological cancers, demonstrated that targeted, deep B-cell depletion was achievable and durable. The key insight (and the hinge on which the autoimmune pivot turns) is that autoreactive B-cells and malignant B-cells share surface markers: CD19 and BCMA are expressed on the same pathogenic B-cells that drive many autoimmune conditions.

Secondly, the limitations of current rheumatology therapies have left substantial unmet need, particularly in achieving durable, mechanism-based control of disease. Despite the progress of biologics, TNF inhibitors, IL-6 blockade, JAK inhibitors, most patients with systemic autoimmune conditions face a lifelong journey of immunosuppression, incomplete disease control, continued organ damage and the very real challenge of treatment fatigue. The concept of sustained, drug-free remission has never entered the autoimmune lexicon, until now.

Our third convergence point relates to commercial pressure. Immuno-oncology is a crowded space, with hundreds of competing programmes, and differentiation becoming increasingly difficult. The autoimmune landscape offers a large, underserved patient population, cleaner competitive landscape in novel modalities and, critically, regulatory pathways that are beginning to mature.

2. The Landmark Studies that Accelerated the Field

It would be hard to argue that any single piece of data did more to legitimise the autoimmune CAR-T pivot than the case series published in the *New England Journal of Medicine* in February 2024.

Müller et al. CD19 CAR-T Cell Therapy in Autoimmune Disease: A Case Series with Follow-up.

Fifteen patients with severe, treatment-refractory systemic autoimmune diseases: eight with systemic lupus erythematosus (SLE), three with idiopathic inflammatory myositis, and four with systemic sclerosis, received a single infusion of CD19-targeting CAR-T-cells following lymphodepleting preconditioning with fludarabine and cyclophosphamide.

At a median follow-up of 15 months (range 4-29 months), all 15 patients were in remission or had achieved major clinical responses. Autoantibodies disappeared. All patients had discontinued immunosuppressive therapy entirely. In the SLE cohort, all eight patients achieved DORIS remission criteria, with SLEDAI-2K scores of zero at six months, and disease activity remained absent through 24 months of follow-up.

The accompanying NEJM editorial posed the question that has animated the field ever since: "CAR T-cells- a new horizon for autoimmunity?"

What followed was a series of companion studies that suggested these findings were reproducible across multiple autoimmune indications. A study published in Cell (2024) demonstrated that allogeneic CD19-targeting CAR-T therapy in patients with severe myositis and systemic sclerosis produced comparable results, opening the door to off-the-shelf approaches that could improve scalability and manufacturing logistics. Case series in antisynthetase syndrome, juvenile dermatomyositis, immune-mediated necrotising myopathy, and even myasthenia gravis have followed in rapid succession.

25
CAR-T trials in autoimmune diseases registered in 2024 - the highest single year peak to date

50+
Active clinical trials for advanced medicinal therapeutic products in autoimmune indications as of mid-2024

64-70%
Proportion of autoimmune CAR-T trials currently in Phase I indicating a field in rapid expansion

At ACR Convergence 2025, two studies presented preliminary results from dual-targeted CAR-T approaches, targeting both CD19 and BCMA simultaneously in SLE, showing encouraging safety, efficacy, and B-cell kinetics that suggest the field is already iterating beyond first-generation constructs.

These studies suggest that autoimmune therapy may be shifting from continuous suppression toward finite, potentially disease-modifying intervention.

3. Who is Pivoting, and Why

The industry response has been equally interesting to watch. What began as a small number of exploratory academic programmes has rapidly evolved into a broader commercial shift, with both large pharmaceutical companies and emerging biotechs repositioning oncology-derived immune engineering platforms for autoimmune disease.

Infrastructure originally built for haematological malignancies, including CAR-T manufacturing, lymphodepletion protocols, specialist treatment centres, and B-cell targeting expertise, is now being redirected toward diseases such as lupus, myositis, and systemic sclerosis.

Among large pharmaceutical companies, Bristol Myers Squibb has emerged as one of the clearest examples of this transition. Its investments in in vivo cell therapy and antigen-specific immune tolerance suggest a strategy that extends beyond chronic immunosuppression toward scalable immune reprogramming approaches.

Similarly, AstraZeneca has expanded aggressively into autoimmune cell therapy through its acquisition of Gracell Biotechnologies, gaining access to dual-targeting CD19 / BCMA CAR-T programmes and accelerated manufacturing platforms. These programmes sit alongside an already established immunology portfolio, reflecting how oncology and autoimmune development are beginning to converge operationally as well as scientifically.

Roche and Genentech have also positioned autoimmune disease as a logical extension of their long-standing expertise in B-cell biology and haematological oncology.

At the same time, a new generation of autoimmune-focused biotechnology companies has emerged. Kyverna Therapeutics has built its pipeline almost entirely around CAR-T therapy for autoimmune disease, with programmes spanning lupus and neurological autoimmunity. Artiva Biotherapeutics has shifted its focus toward NK-cell therapies for autoimmune indications, while Allogene Therapeutics is extending off-the-shelf allogeneic CAR-T approaches beyond oncology.

Taken together, these programmes suggest that the field is no longer treating autoimmune CAR-T as a niche field. The industry is building the manufacturing, regulatory, and clinical infrastructure required to make immune-reset strategies scalable beyond highly specialised academic centres.

4. The Translation: What Oncology Developers Must Understand About Autoimmune Disease

One of the easiest mistakes a developer can make is to assume that an oncology programme can simply be adapted for autoimmune diseases. The biology is not interchangeable. Below are the critical translational dimensions that must be addressed.

1. The immune milieu is reversed, and actively hostile

In oncology, CAR-T therapies are deployed into immunosuppressed tumour microenvironments where the central challenge is sustaining T-cell activity despite immune evasion. Autoimmune disease presents the opposite problem: a chronically activated and dysregulated immune system, often in the context of established tissue injury and systemic inflammation.

This altered immune context changes both efficacy and safety dynamics. Cytokine release syndrome (CRS), immune effector cell-associated neurotoxicity syndrome (ICANS), and haemophagocytic lymphohistiocytosis (HLH) remain important risks, but their presentation and management may differ substantially in patients with autoimmune disease.

An additional complexity emerging from early autoimmune CAR-T studies is the recognition of local immune effector cell-associated toxicity syndrome (LICATS), described by the Erlangen group as a localised inflammatory phenomenon occurring in affected tissues following CAR-T infusion. Unlike CRS or ICANS, LICATS is currently thought to reflect local immune engagement within diseased tissue rather than uncontrolled systemic hyperinflammation.

This distinction becomes clinically important. Aggressive immunosuppression strategies adapted directly from oncology could potentially compromise CAR-T persistence or blunt therapeutic efficacy if localised inflammatory responses are misinterpreted as severe systemic toxicity.

As autoimmune CAR-T programmes expand, developers will likely need safety frameworks designed specifically for autoimmune disease rather than relying entirely on oncology-derived grading systems. Biomarkers, imaging approaches, and tissue-specific monitoring strategies may all become increasingly important for distinguishing harmful systemic inflammation from localised therapeutic immune activity.

Table 1: Comparative overview of toxicities

To help differentiate how these toxicities fit together clinically, they can be grouped by their mechanism and severity:

Toxicity	Scope	Clinical Presentation	Relationship to Autoimmunity
CRS	Systemic	High fever, hypotension, hypoxia, capillary leak	Driven by immediate systemic cytokine storm post-infusion
ICANS	Central Nervous System	Confusion, aphasia, cognitive deficits, seizures.	Neurotoxicity often following or overlapping with severe CRS
HLH / IEC-HS	Systemic / Hematologic	Hyperferritinemia (>10,000 ng / mL), cytopenias, hepatosplenomegaly	Delayed, severe macrophage hyperactivation triggered by dysregulated immune response
LICATS	Local / Organ-Specific	Transient skin rashes, joint pain, or temporary renal impairment	Directly mirrors prior autoimmune organ involvement; benign tissue-level immune reset

2. The biomarker plan must be rebuilt for autoimmune disease

Biomarker frameworks developed in oncology do not transfer cleanly into autoimmune disease. In cancer, response markers are often directly linked to tumour burden or target engagement: circulating tumour DNA (ctDNA), PSA, CA-125, or RECIST-defined radiographic response. While imperfect, these markers are generally measurable against a relatively discrete pathological process.

Autoimmune disease is fundamentally different. Disease activity in conditions such as systemic lupus erythematosus (SLE) or rheumatoid arthritis (RA) is heterogeneous, dynamic, and often biologically fragmented across patients. Clinical response is still largely assessed through composite scoring systems such as DAS28, SLEDAI-2K, or the EUSTAR Activity Index, but these tools were designed primarily for clinical assessment and trial standardisation rather than mechanistic monitoring of immune reset therapies.

Cytokines and chemokines remain among the most intensively studied biomarker candidates, although there are limitations. In RA, IL-17A has shown moderate correlation with disease activity indices including DAS28 and CDAI. In SLE, the 2024 PRECISESADS study identified markers such as CCL8, CXCL13, and IL-1RA as correlating with SLEDAI-2K scores across a large multicentre cohort. However, the study also highlighted a central problem facing the field: many inflammatory biomarkers lack disease specificity and are heavily influenced by treatment itself.

This becomes particularly important in the context of cell therapy. CAR-T mediated immune depletion and reconstitution fundamentally reshape cytokine networks, immune cell populations, and inflammatory signalling over time. Static biomarkers measured at isolated timepoints are therefore unlikely to capture the biological complexity of response or relapse. The field is moving toward multidimensional biomarker strategies that integrate longitudinal proteomics, immune cell phenotyping, autoantibody kinetics, and potentially tissue-level or spatial profiling approaches.

The challenge is determining which immune circuits are being durably reset, which are re-emerging, and which patients are most likely to sustain treatment-free remission.

3. Endpoint definition: What does success look like?

Tied to the previous point, a critical challenge for autoimmune disease is defining what constitutes a meaningful endpoint: Complete clinical remission? Drug-free remission maintained at 12 months? Absence of organ damage accrual? Resolution of autoantibodies?

In oncology, regulatory endpoints carry decades of validation: overall survival and progression-free survival anchor most approvals. In autoimmune disease, equivalent clarity does not yet exist for newer modalities. The field is still learning how to define, measure, and present to regulators. Developers must engage early with FDA and EMA on acceptable endpoint frameworks for immune reset therapies.

4. The autoimmune patient is not the oncology patient

The clinical context of autoimmune disease changes the therapeutic calculus substantially. In haematological oncology, CAR-T therapies are often used in patients with life-threatening disease and limited remaining treatment options. Significant toxicity may be considered acceptable in exchange for the possibility of durable remission.

Autoimmune disease presents a different scenario. Patients are frequently younger, may live with their disease for decades, and are comparing investigational therapies against established standards of care that can still provide meaningful disease control. As a result, the tolerance for severe toxicity is considerably lower.

Many patients are also already immunologically vulnerable due to chronic corticosteroids, biologics, or other immunosuppressive therapies. Lymphodepleting regimens administered prior to CAR-T infusion, for example, occur on top of an already compromised immune system, creating infection risks that differ meaningfully from those seen in oncology populations.

Early autoimmune CAR-T studies have already highlighted some of these challenges. The Erlangen series reported respiratory infections and CMV reactivation during periods of maximal immunosuppression, underscoring the need for dedicated infection monitoring and supportive care strategies as these therapies expand into broader patient populations.

5. Disease heterogeneity and the problem of patient selection

One of oncology's most important translational advances was the recognition that patient selection determines therapeutic success. Biomarkers such as HER2 amplification, EGFR mutation status, MSI-H, and PD-L1 expression transformed clinical trial design by identifying the patients most likely to respond.

Autoimmune disease presents a similar challenge, although the stratification frameworks remain far less developed.

Conditions such as systemic lupus erythematosus (SLE) are clinically grouped under a single diagnosis despite representing multiple underlying immunological states. In some patients, disease appears predominantly interferon-driven; in others, complement dysregulation, plasma cell biology, or distinct autoreactive B-cell programmes may play a larger role. A therapy is unlikely to behave identically across these biological subtypes.

Early signals supporting this idea are already emerging. In the Erlangen cohort, serological remission appeared less complete in Scl70-positive systemic sclerosis patients, suggesting that underlying disease biology may influence both depth and durability of response.

As autoimmune cell therapy programmes mature, deep immunological profiling at baseline will likely become increasingly important, not only for patient selection, but also for understanding resistance, relapse, and long-term remission biology.

6. The broader technology transfer

CAR-T therapy may be the clearest example of oncology technology migrating into autoimmune disease, but the same translational movement is now visible across multiple therapeutic platforms.

Antibody-drug conjugates (ADCs), originally engineered for targeted cytotoxic delivery in cancer, are beginning to enter autoimmune development programmes. As highlighted previously, the autoimmune setting changes the safety equation substantially. In oncology, off-target toxicity may be acceptable in the context of aggressive malignancy. In chronic autoimmune disease, long-term exposure, linker stability, and bystander effects require much closer scrutiny, particularly in younger patients expected to live for decades after treatment.

Bispecific antibodies and T-cell engagers are following a similar trajectory. Constructs initially designed to redirect cytotoxic T-cells toward tumour antigens are now being explored as tools for selective immune-cell depletion in diseases such as lupus and rheumatoid arthritis. Approaches such as IGM Biosciences' IgM-based bispecific platform illustrate how engineering strategies developed for oncology are being repurposed to modulate autoreactive immune networks.

Even more established rheumatology mechanisms are being revisited through an oncology lens. Anti-CD20 therapy has been used in autoimmune disease for years through rituximab, but newer oncology-derived antibodies such as obinutuzumab, engineered for enhanced antibody-dependent cellular cytotoxicity (ADCC), are now advancing into lupus programmes. The underlying logic is increasingly consistent across the field: technologies developed to eliminate malignant immune cells may also be effective in selectively eliminating pathogenic immune populations.

Taken together, these programmes suggest that autoimmune disease is not simply adopting individual oncology drugs. It is inheriting an entire generation of immune-engineering technologies, along with the translational challenges that accompany them.

Closing Perspective

The migration of oncology-derived immune engineering into autoimmune disease is becoming a broader reorganisation of how immune-mediated disease is approached therapeutically.

What makes this transition particularly compelling is that the underlying biology was never entirely separate. The same immune pathways, cell populations, and signalling networks that drive malignant disease also underpin many forms of pathological autoimmunity. Oncology provided the technological acceleration; autoimmune disease is now testing how far those technologies can be translated beyond cancer.

But successful translation will require more than transferring platforms from one indication to another. Autoimmune programmes demand their own biomarker strategies, safety frameworks, patient stratification approaches, and clinical endpoints. Developers entering this space will need to combine the engineering capabilities developed in oncology with a much deeper understanding of immune heterogeneity and chronic inflammatory disease biology. This is likely where the next phase of the field will be defined, by the ability to understand, monitor, and interpret complex immune responses longitudinally across diverse patient populations.

As these programmes mature, translational expertise in autoimmune disease, particularly in biomarker development, immune profiling, and longitudinal clinical monitoring, will become increasingly central to successful development strategies.

Synexa Life Sciences supports the development of next-generation autoimmune therapies with integrated biomarker, bioanalytical and immune profiling solutions designed to characterise mechanism of action, monitor safety and efficacy, identify responsive patient populations, and generate the translational insights needed to accelerate programmes from early research through clinical development. As oncology-derived technologies such as CAR-T-cells, bispecific antibodies and other immune-engineering approaches continue to reshape the autoimmune landscape, Synexa helps developers navigate the biological complexity behind successful clinical translation.

To discuss how Synexa can support your programme, contact our team at ContactUs@synexagroup.com or visit www.synexagroup.com.

Caroline Beltran, PhD

Scientific Director
Synexa Life Sciences

ContactUs@synexagroup.com

References

Landmark clinical studies

1. Müller F, Taubmann J, Bucci L, Wilhelm A, Bergmann C, Völkl S, et al. CD19 CAR T-cell therapy in autoimmune disease- a case series with follow-up. *N Engl J Med.* 2024;390(8):687-700. doi: 10.1056 / NEJMoa2308917
2. Isaacs JD. CAR T-cells - a new horizon for autoimmunity? [editorial]. *N Engl J* Med. 2024;390(8): 758-759. doi: 10.1056 / NEJMe2400203
3. Mackensen A, Müller F, Mougiakakos D, Böltz S, Wilhelm A, Aigner M, et al. Anti-CD19 CAR T cell therapy for refractory systemic lupus erythematosus. *Nat Med.* 2022;28(10):2124-2132. doi: 10.1038 / s41591-022-02017-5
4. Wang X, Wu X, Tan B, Zhu L, Zhang Y, Lin L, et al. Allogeneic CD19-targeted CAR-T therapy in patients with severe myositis and systemic sclerosis. *Cell.* 2024;187(18):4890-4904.e9. doi: 10.1016 / j.cell.2024.06.027
5. Mougiakakos D, Krönke G, Völkl S, et al. CD19-targeted CAR T-cells in refractory systemic lupus erythematosus. *N Engl J Med.* 2021;385(6):567-569. doi: 10.1056 / NEJMc2107725

Key reviews

6. Schett G, Mackensen A, Mougiakakos D. CAR T-cell therapy in autoimmune diseases. *Lancet.* 2023;402(10416):2034-2044. doi: 10.1016 / S0140-6736(23)01126-1
7. Schett G, Müller F, Taubmann J, Mackensen A, Wang W, Furie RA, et al. Advancements and challenges in CAR T cell therapy in autoimmune diseases. *Nat Rev Rheumatol.* 2024;20(9):531-544. doi: 10.1038 / s41584-024-01139-z
8. Taubmann J, Müller F, Yalcin Mutlu M, Völkl S, Aigner M, Bozec A, et al. CD19 chimeric antigen receptor T cell treatment: Unraveling the role of B-cells in systemic lupus erythematosus. *Arthritis Rheumatol.* 2024;76(4):497-504. doi: 10.1002 / art.42784
9. Xu X, Su SH. CAR-T cell therapies in autoimmune rheumatic diseases: a brief report on the clinical trial landscape, current status, and future perspectives. *Front Immunol*. 2025;16:1630569. doi: 10.3389 / fimmu.2025.1630569

Tissue depletion, toxicity and extended case data

10. Tur C, Eckstein M, Velden J, Rauber S, Bergmann C, Auth J, et al. CD19-CAR T-cell therapy induces deep tissue depletion of B-cells. *Ann Rheum Dis*. 2025;84(1):106-114. doi: 10.1136 / ard-2024-226142
11. Hagen M, Müller F, Wirsching A, Kharboutli S, Spoerl S, Düsing C, et al. Local immune effector cell-associated toxicity syndrome in CAR T-cell treated patients with autoimmune disease: an observational study. *Lancet Rheumatol.* 2025;7(6):e424-e433. doi: 10.1016 / S2665-9913(25)00091-8
12. Müller F, Boeltz S, Knitza J, et al. CD19-targeted CAR T-cells in refractory antisynthetase syndrome. *Lancet.* 2023;401(10380):815-818. doi: 10.1016 / S0140-6736(23)00023-5
13. Bergmann C, Müller F, Distler JHW, et al. Treatment of a patient with severe systemic sclerosis (SSc) using CD19-targeted CAR T-cells. *Ann Rheum Dis*. 2023;82(8):1117-1120. doi: 10.1136 / ard-2023-224019
14. Pecher A-C, Hensen L, Klein R, et al. CD19-targeting CAR T-cells for myositis and interstitial lung disease associated with antisynthetase syndrome. *JAMA*. 2023;329(24):2154-2162. doi: 10.1001 / jama.2023.8753

Biomarkers in autoimmune disease

15. Kaptoge S, Cairns BJ, Pennells L, et al. Serum profiling identifies CCL8, CXCL13, and IL-1RA as markers of active disease in patients with systemic lupus erythematosus. *Front Immunol.* 2023;14:1245346. doi: 10.3389 / fimmu.2023.1245346
16. van Baarsen LGM, Vosslamber S, Tijssen M, et al. Validity of clinical associations of biomarkers in translational research studies: the case of systemic autoimmune diseases. *Arthritis Care Res (Hoboken)*. 2010;62(4):465-472. doi: 10.1002 / acr.20123
17. Smolen JS, Aletaha D, McInnes IB. Rheumatoid arthritis. *Lancet.* 2016;388(10055):2023-2038. doi: 10.1016 / S0140-6736(16)30173-8

Industry pivots and pipeline data

18. IGM Biosciences. IGM Biosciences announces strategic pivot to focus exclusively on autoimmunity [press release]. September 30, 2024. Available at: https://ir.igmbio.com
19. Hagen M, Müller F, Wirsching A, Tur C, Krickau T, Metzler M, et al. Safety and long-term efficacy of CD19-CAR T-cell therapy in 30 patients with autoimmune disease [abstract]. *Arthritis Rheumatol.* 2024;76(suppl 9). Available at: https://acrabstracts.org/abstract/safety-and-long-term-efficacy-of-cd19-car-t-cell-therapy-in-30-patients-with-autoimmune-disease
20. ACR Convergence 2025. CAR-T cell therapies show promise for autoimmune disease [press release]. American College of Rheumatology. October 2025. Available at: https://rheumatology.org/press-releases/car-t-cell-therapies-show-promise-for-autoimmune-disease-at-acr-convergence-2025

Endpoints, trial design and regulatory context

21. Franklyn K, Lau CS, Navarra SV, et al. Definition and initial validation of a lupus low disease activity state (LLDAS). *Ann Rheum Dis.* 2016;75(9):1615-1621. doi: 10.1136 / annrheumdis-2015-207726
22. Valentini G, Iudici M, Walker UA, et al. The European Scleroderma Trials and Research group (EUSTAR) task force for the development of revised activity criteria for systemic sclerosis: derivation and validation of a preliminary revised EUSTAR activity index. *Ann Rheum Dis.* 2017;76(1):270-276. doi: 10.1136 / annrheumdis-2016-209768
23. Golder V, Kandane-Rathnayake R, Huq M, et al. Evaluation of remission definitions for systemic lupus erythematosus: a prospective cohort study. *Lancet Rheumatol.* 2019;1(2):e103-e110. doi: 10.1016 / S2665-9913(19)30048-4
24. Lee DW, Santomasso BD, Locke FL, et al. ASTCT consensus grading for cytokine release syndrome and neurologic toxicity associated with immune effector cells. *Biol Blood Marrow Transplant.* 2019;25(4):625-638. doi: 10.1016 / j.bbmt.2018.12.758

synexa | Life Sciences

Get in Touch

ContactUs@synexagroup.com

synexagroup.com