ABBIE-Enabled CAR-T Manufacturing: Expanding Toward Neurological Diseases Like Multiple Sclerosis and Alzheimer's

CAR-T cell therapy has already reshaped cancer treatment by enabling a patient's own T cells to recognize and destroy malignant cells. Yet traditional CAR-T manufacturing still relies heavily on viral vectors, random genomic insertion, and complex, costly processes. SOHM Inc.'s ABBIE platform — a programmable integrase-dCas9 genome-editing system — offers a next-generation alternative with the potential not only to improve CAR-T manufacturing for cancer, but also to open new therapeutic doors in neurological diseases such as Multiple Sclerosis (MS) and Alzheimer's disease. (SOHM reference)

What Makes ABBIE Different?

As described by SOHM, ABBIE fuses a viral integrase with a catalytically inactive CRISPR-Cas9 ("dCas9"). The dCas9 component precisely guides the integrase to a predetermined genomic site, enabling controlled integration of therapeutic DNA such as a CAR construct.

(SOHM reference)

This design offers multiple advantages:

- Predictable, safe genomic integration at controlled sites
- Avoidance of double-strand DNA breaks, lowering genotoxic risk
- Non-viral delivery, reducing manufacturing and regulatory hurdles
- Programmability, enabling multiplex engineering for complex or next-gen CAR designs

These improvements could help re-engineer CAR-T manufacturing into a faster, safer, more scalable process — traits that are essential when considering applications beyond oncology.

Extending CAR-T to Neurological Diseases

Why Multiple Sclerosis (MS)?

Multiple Sclerosis (MS) is a chronic autoimmune disease in which the immune system attacks the myelin sheath that insulates neurons in the brain and spinal cord. MS involves autoreactive B cells and T cells as well as neuroinflammation within the central nervous system (CNS). This makes MS one of the most promising neurological targets for next-generation immunotherapies.

Recent studies indicate that CAR-T and CAR-T regulatory (CAR-Treg) approaches could address key immunological drivers of MS:

- Targeting autoreactive B cells. Anti-CD19 CAR-T cells have already demonstrated potent and selective depletion of B cells, outperforming monoclonal antibodies in preclinical models.
- Applying CAR-Tregs to suppress neuroinflammation. MOG-specific CAR-T regulatory cells (targeting Myelin Oligodendrocyte Glycoprotein) reduced inflammation and disease severity in animal models of MS-like disease.
- Long-lasting immune “reset.” CAR-T therapies in autoimmune diseases may offer durable remission without continuous immunosuppressive therapy.

Given that MS lacks a cure and current therapies mainly slow progression, CAR-T — especially ABBIE-enhanced CAR-T — represents a fundamentally new therapeutic direction.

How ABBIE Could Accelerate CAR-T for MS and Neuroimmune Diseases

ABBIE’s design offers several advantages uniquely suited for neurological autoimmune disorders:

1. Increased Safety for Non-Cancer Patients

Patients with MS or other chronic conditions require extremely safe therapies. ABBIE’s controlled insertion lowers risks associated with random viral integration — risks that may be acceptable for life-threatening cancers but not for long-term neurological diseases.

2. Reliable Engineering of CAR-Tregs

CAR-Treg therapies demand high genetic precision. ABBIE’s programmable insertion allows stable engineering of regulatory T cells without genotoxic stress — ideal for therapies intended to restore immune tolerance, not destroy cells.

3. Lower Cost and Greater Scalability

MS affects nearly 3 million people worldwide, far more than the population eligible for cancer CAR-T. ABBIE’s non-viral, streamlined process could make CAR-T viable for large-scale

treatment.

4. Expanded Functionality for CNS-specific CAR-T

Multiplex engineering could allow the addition of:

- CNS-homing receptors
- Microglial-modulating genes
- Inflammation-sensitive “on/off” switches
- Safety circuits to prevent CNS overactivation

These types of advanced modifications become far more feasible with ABBIE’s site-directed integration.

Could ABBIE-Engineered CAR-T Help Alzheimer’s Disease?

Alzheimer’s disease is fundamentally neurodegenerative, but immune dysregulation and inflammation play significant roles. While CAR-T for Alzheimer’s is still highly experimental, researchers have proposed several future strategies:

- CAR-T designed to clear pathological proteins such as amyloid-? or tau
- CAR-T or CAR-Tregs engineered to modulate microglial activation
- Immune cells programmed to deliver neuroprotective factors
- CNS-targeting CAR-T enabling more direct action in brain tissue

ABBIE’s ability to controllably insert large or multi-gene constructs could support these kinds of next-generation cellular therapies, though significant research is still required.

Barriers and Challenges Ahead

Even with ABBIE’s advantages, several hurdles remain before CAR-T reaches neurological clinics:

- CNS access: Engineered cells must safely traverse or act within the CNS.
- Target identification: MS has clearer immune targets than Alzheimer’s, but both need validated, disease-specific markers to avoid off-target damage.

- Long-term safety: CAR-T cells may persist for years; ABBIE must ensure there is no unintended genomic impact over time.
- Manufacturing maturity: ABBIE-based CAR-T will need to be developed for this purpose and must demonstrate consistent safety, precision, and clinical-grade performance.

Conclusion: A Promising Path Forward

ABBIE-enabled CAR-T manufacturing represents an important step toward safer and more scalable cellular immunotherapy. While initially developed to improve CAR-T for cancer, ABBIE's precision and flexibility may make it uniquely suited for future therapies targeting Multiple Sclerosis, autoimmune neuroinflammation, and potentially even Alzheimer's disease.

For MS in particular, CAR-T and CAR-Treg therapies are already supported by growing preclinical evidence. ABBIE could accelerate their translation into patient care by offering a safer, non-viral, and more predictable engineering platform. Although significant scientific and regulatory challenges remain, ABBIE + CAR-T reflects a powerful technological foundation for the next era of neurological therapeutics.