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In Vivo CAR Therapies and the AI Drug Discovery Landscape

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Published by IntuitionLabs · 2026-05-16 · in vivo car therapy · ai drug discovery · mrna-lnp technology · immunotherapy · biotechnology · car-t cells · generative ai

Original article: https://intuitionlabs.ai/articles/in-vivo-car-therapies-ai-drug-discovery



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Executive Summary

CREATE Medicines, a clinical-stage biotech based in Cambridge, MA, raised a $122 million Series B on May 14, 2026 to advance its revolutionary **in vivo** CAR (chimeric antigen receptor) therapy platform. The financing – co-led by Newpath Partners, ARCH Venture Partners and Hatteras Venture Partners – comes amid a cautious venture climate but underscores investor confidence in CREATE's pipeline of autoimmune and oncology programs (www.prnewswire.com) (www.fiercebiotech.com). Using a proprietary mRNA–LNP (lipid nanoparticle) system, CREATE directly programs immune cells inside the body (T cells, NK cells, and myeloid cells) to mount disease-specific responses (www.prnewswire.com) (www.biospace.com). Its backbone immunology engineering, built on years of translational work, has generated what CREATE describes as the largest clinical dataset in the field (more than 50 patients dosed across its in vivo CAR clinical programs) (www.biospace.com) (www.fiercebiotech.com).

Leading autoimmune programs include CRT-402 (a repeat-dose CD19-targeted CAR for B-cell depletion) and a bispecific CD19×BCMA CAR, both designed to "reset" dysregulated immunity (www.prnewswire.com) (createmedicines.com). In oncology, CREATE's portfolio features mRNA CARs targeting solid tumors – e.g.

MT-302 (TROP2-targeting, demonstrated tumor infiltration and a partial response in a heavily pretreated patient (uk.advfn.com)) and MT-303 (GPC3-targeting in hepatocellular carcinoma, now moving into frontline combination trials with atezolizumab/bevacizumab (createmedicines.com)). Collectively, these programs leverage CREATE's iterative design engine: combining clinically-validated CAR constructs, optimized RNA engineering, and targeted delivery to compress timelines from concept to clinic (www.prnewswire.com) (www.biospace.com).

This Series B comes alongside a broad "next wave" of AI-driven biotech ventures. CREATE has not publicly disclosed the use of AI or machine learning in its pipeline, so the AI companies discussed below are offered as separate context. Meanwhile, numerous other startups and large firms are channeling AI and ML to discover therapeutics (for example, Xaira Therapeutics launched with $1 billion funding in 2024 to build an AI drug discovery platform (www.axios.com), while Chai Discovery (backed by OpenAI) raised $130 million in late 2025 to de novo design antibodies with large language models (techcrunch.com)). The field has produced concrete early successes: a generative-AI–designed fibrosis drug achieved positive signals in Phase 2a (colab.ws), and an AI-agent "Virtual Lab" workflow designed nanobody binders to SARS-CoV-2 variants, with two showing improved binding in laboratory tests (www.nature.com).

This report delves deeply into CREATE Medicines' background, technology, and pipeline; analyzes the scientific and market context of **in vivo** cell therapy; surveys the broader landscape of AI-enhanced biotechnology, including case studies of recent AI-designed therapeutics; and discusses future implications.

Introduction and Background

The Rise of Immunotherapy and CAR-T

Immunotherapy has transformed oncology and beyond. CAR-T cell therapies – where a patient's T cells are genetically engineered to attack cancer – achieved landmark successes in hematologic malignancies. However, these **ex vivo** approaches require harvesting patient T cells, engineering them in the lab, and reinfusing, often after toxic conditioning; they face logistical complexity, high cost, and limitations in durability and tumor penetration (createmedicines.com). Over the past decade, researchers have sought to overcome these barriers: strategies include "off-the-shelf" allogeneic CAR-Ts from donors, viral gene delivery in patients, and cytokine modulation (createmedicines.com).

The concept of *in vivo* cell therapies has emerged as a disruptive paradigm. Instead of manipulating cells outside the body, **in vivo** approaches deliver genetic instructions inside patients to reprogram immune cells on site (www.prnewswire.com) (createmedicines.com). This can enable rapid, off-the-shelf treatment with minimal manipulation. CREATE Medicines has developed an mRNA-LNP platform to deliver CAR constructs directly to multiple immune cell types (T, NK, myeloid) for systemic infusion of programmable immunotherapy (www.biospace.com) (createmedicines.com).

CREATE Medicines was founded (as Myeloid Therapeutics) in 2019 by Dr. Daniel Getts and others, including noted scientists Dr. Ronald Vale and Dr. Siddhartha Mukherjee (www.biopharmadive.com) (www.prnewswire.com). Originally focusing on mRNA CARs targeting myeloid cells, the firm soon broadened to multi-lineage CAR programming and rebranded "CREATE Medicines" in 2025 (www.biopharmadive.com).

The company's mission is to "engineer cures from within" by deploying CAR constructs *in vivo* for cancer, autoimmune disease, and even fibrosis (leveraging their platform's flexibility (createmedicines.com) (app.dealroom.co)). CREATE's core claim is that each clinical iteration informs the next, enabling fast learning loops: as CEO Daniel Getts explains, "each clinical study informs and strengthens the next… what in vivo immune programming can address" (www.prnewswire.com).

CREATE's technology has already shown proof-of-concept in humans. According to company releases, the platform delivers mRNA CARs to patient immune cells, achieves detectable CAR expression in vivo, and permits repeat IV dosing with manageable safety (uk.advfn.com) (createmedicines.com). Over 50 patients have been treated across CREATE's programs to date (www.prnewswire.com) (www.fiercebiotech.com) – which CREATE describes as the largest clinical dataset in the field (www.fiercebiotech.com). In light of these developments, CREATE's $122M Series B positions it to advance multiple lead programs (both in oncology and autoimmunity) into proof-of-concept and beyond (www.prnewswire.com) (www.fiercebiotech.com).

The AI Revolution in Drug Discovery

CREATE's initiative intersects with a larger trend: the escalating role of artificial intelligence and machine learning in biotechnology. In recent years, breakthroughs in AI have revolutionized previously intractable tasks. The DeepMind AlphaFold algorithm, for example, solved protein structure prediction, for which its creators Demis Hassabis and John Jumper shared the 2024 Nobel Prize in Chemistry (nobelprize.org). Its third iteration (AlphaFold 3, announced May 2024) can predict interactions among proteins, DNA, RNA and small molecules at scale (time.com), a capability likely to accelerate target identification, rational drug design, and epitope mapping for vaccines. Google's spin-off Isomorphic Labs is already using AlphaFold 3 to guide proprietary drug design programs (time.com).

Meanwhile, *generative* AI models (large language models, deep generative networks) have begun to automate molecular design. For example, a multi-agent AI "Virtual Lab" recently designed new nanobodies against SARS-CoV-2 solely in silico: coupling LLMs with AlphaFold-Multimer and Rosetta, the system proposed 92 novel nanobody sequences, several of which showed binding in lab tests (www.nature.com). In therapeutics, one landmark came in 2025 when an AI-discovered molecule for idiopathic pulmonary fibrosis reached clinical testing: Nature Medicine noted a Phase IIa trial "of an AI-discovered drug and target" demonstrated safety and efficacy signs, heralding a milestone in AI-enabled drug discovery (colab.ws).

Industrial R&D is embracing these advances. Drug developers like Recursion Pharmaceuticals use cell imaging + ML to design treatments, and biotech startups are rapidly forming to harness AI. Exscientia (UK) and Insilico Medicine (US/HK) are veterans of AI-driven drug design, with Insilico recently reporting 22 active AI-designed drug programs in development (www.fiercebiotech.com). More recently, venture capital has flooded the space: for instance, Xaira Therapeutics (founded by a former Stanford president) launched in 2024 with **$1 billion** of funding to build a "AI-first" discovery pipeline (www.axios.com), and in late 2025 OpenAI-backed Chai Discovery raised $130 million at a $1.3 billion valuation to design novel antibodies using foundation models (techcrunch.com). These trends (summarized in Table 2 below) illustrate a broad "next wave" of AI biotech investments.

However, excitement is tempered by caution. In 2025 biopharma fundraising cooled overall (www.biopharmadive.com), reflecting market apprehension. Investors have become more risk-averse, preferring “mega-rounds” for near-certain projects (www.biopharmadive.com). As one analysis noted, venture money slid and “many crossover investors are at their own crossroads,” shrinking early-stage deals (www.biopharmadive.com). In this environment, CREATE’s ability to secure $122M – a “mega-round” – signals strong conviction about its platform’s promise (www.fiercebiotech.com), while similar large raises (e.g. Insilico’s $110M in March 2025 (www.fiercebiotech.com)) highlight that deep-pocketed backers still finance bold ventures.

In summary, CREATE Medicines is an in vivo immunotherapy company; it has not publicly disclosed using AI, so the AI material that follows is separate industry context. Its Series B funding in May 2026 is a corporate milestone for the in vivo CAR field. The sections that follow examine CREATE’s science and strategy in detail, review analogous developments in AI-driven biotech, and discuss the implications for therapeutics.

CREATE Medicines: Company and Platform

History and Leadership

CREATE Medicines began in 2019 (as Myeloid Therapeutics) under CEO Dr. **Daniel Getts**, PhD (co-founder), alongside prominent scientists Dr. **Ronald Vale** (HHMI/Janelia institute leader) and Dr. **Siddhartha Mukherjee** (Pulitzer-winning author and oncologist) (www.biopharmadive.com) (www.prnewswire.com). Positioned in Cambridge, MA, the company focused initially on leveraging *myeloid cell* programming for cancer therapy. Founder Getts, whose doctoral work was in immunology, sought to pioneer *in vivo* cell therapy and founded CREATE to “program any immune cell and scale globally” (createmedicines.com).

Over time the vision broadened. In October 2025 Myeloid Therapeutics rebranded as CREATE Medicines, reflecting an expanded multi-immune platform. The new branding emphasized “Engineering Cures From Within” (createmedicines.com) by programming T cells, NK cells, and myeloid cells via RNA in situ. Leadership built out around Getts includes CSO **Robert Hofmeister, PhD** and CMO **Matthew Maurer, MD** (createmedicines.com). In 2026 CREATE appointed biotech veteran **Ron Philip** as Executive Chairman and added insight from investors: Brian Cuneo of ARCH and Tom Thomas of Newpath joined the board (www.prnewswire.com).

Corporate filings and profiles (e.g. Dealroom) indicate a robust funding history. According to Dealroom, CREATE raised $12 million in seed funding in September 2019, closed a Series A in Jan 2021, and a $73 million Series A2 in May 2023 (total $135 million) (app.dealroom.co). Backers include ARCH Venture Partners, Newpath, Hatteras, Alexandria, Moore Strategic, and 8VC (www.prnewswire.com) (app.dealroom.co). These deep-pocketed life sciences investors have enabled CREATE to build in-house manufacturing and progress multiple trials simultaneously (unusual for a startup with under 50 employees (app.dealroom.co)). As Tom Cahill of Newpath points out, CREATE “owns its manufacturing infrastructure” which many in vivo therapies struggle to do, arguing this sets the stage for it to be “the next great standalone pharmaceutical company” (www.biospace.com).

Proprietary Technology

At its core, CREATE's platform is **mRNA-LNP immune programming**. The company's engineered LNPs deliver mRNA that encodes CAR constructs directly to immune cells in the patient's body (www.prnewswire.com) (createmedicines.com). Unlike viral vectors, this mRNA approach is non-integrating and transient, permitting repeat dosing and tunability. The platform is described as *modular*: any CAR or receptor can be encoded by simply changing the mRNA sequence, and the LNP can be formulated to target different immune cell types.

Key proprietary features include:

- **Multi-lineage targeting**: CREATE's LNPs can transfect different cell subsets. This enables simultaneous programming of T cells, NK (natural killer) cells, and myeloid cells (monocytes/macrophages) (createmedicines.com). For example, MT-302 (in vivo CAR) was observed to generate CAR-expressing myeloid cells that infiltrated tumors (uk.advfn.com), while MT-303 (HCC CAR) is designed for other immune subsets. CREATE touts *"multilineage programming"* as a way to orchestrate a broader immune response (cytokine release, antigen presentation, etc.) beyond conventional CAR-T (uk.advfn.com) (createmedicines.com).
- **Optimized RNA engineering**: CREATE employs advanced sequence design to enhance mRNA stability and expression. Its website mentions "retrotransposon-mediated stability options" (a novel concept to improve CAR stability inside T-cell receptors) and other proprietary RNA modifications (createmedicines.com). These enhancements aim to extend the functional half-life of the CAR and reduce the need for conditioning drugs.
- **Targeted LNP delivery**: The company has engineered its LNPs to be taken up preferentially by immune cells. For instance, specific lipid formulations or surface ligands help direct nanoparticles to lymphocytes or myeloid precursors. This targeting improves efficiency and safety by avoiding off-target transfection. In the NHP study, CREATE demonstrated targeted delivery: both a conventional 4-1BBζ CAR and a novel TCR-integrating CAR achieved complete B-cell depletion, signifying effective programming of *T* cells specifically (createmedicines.com).
- **Modular receptor architecture**: CREATE describes a next-generation T cell receptor-specific (TCR-integrating) CAR design alongside a conventional 41BBζ CAR (createmedicines.com). Its public materials do not specify the mechanism in detail, and the platform is otherwise described as mRNA-based and non-integrating.
- **Repeat dosing**: Because no permanent genome alteration is involved, CREATE's therapy is envisioned as **"repeat-dose capable."** This contrasts with one-time CAR infusions. Preclinically they showed that dosing macaques with CAR mRNA repeatedly produced sustained B-cell depletion (createmedicines.com). Clinically, the ability to redose allows tuning intensity and dealing with antigen escape or treatment relapse. It also avoids lymphodepletion regimens: in non-human primates, complete B-cell deletion was achieved with CAR doses *without* any preconditioning (createmedicines.com).

One investor summary highlights these distinctions: CREATE claims a "one-day manufacturing process" versus weeks for conventional CAR-T (www.biopharmadive.com), with no need for cell harvesting or conditioning (createmedicines.com) (www.biopharmadive.com). In effect, patients could receive an off-the-shelf RNA infusion targeting their disease. This could dramatically cut cost and broaden access.

Finally, CREATE's platform is closely tied to data-driven iteration – a point emphasized by CEO Getts. Every clinical update feeds back into optimized designs. The press release notes "each clinical study informs the next" and the company "integrates clinically validated CAR architectures… optimized RNA design, and targeted delivery" into its development cycle (www.prnewswire.com) (createmedicines.com). This iterative approach is described in CREATE's own communications without reference to AI or machine learning, and the company has not publicly disclosed using either.

Manufacturing and Clinical Infrastructure

A unique facet of CREATE is its investment in internal CMC (chemistry, manufacturing, and controls). Unlike many small biotechs that outsource GMP manufacturing, CREATE has **built its own GMP capacity** for LNP/mRNA production (www.biospace.com) (app.dealroom.co). Having in-house manufacturing allows quick iteration of formulations and scalability for multi-dose studies. It also addresses a major bottleneck: CROs capable of nucleic acid nanocarriers were scarce a few years ago. As investor Tom Cahill noted, many in vivo cell-therapy ventures falter on "scalable manufacturing," but CREATE "owns its infrastructure" (www.biospace.com). This autonomy likely reassured Series B backers.

CREATE's clinical infrastructure is likewise notable. The firm has dosed more than 50 patients across its in vivo CAR clinical programs (www.biopharmadive.com) (www.fiercebiotech.com). It collaborates globally (e.g. trials in Asia for HCC) and exploits partnerships. The first-in-human SITC presentation on MT-302 included lead author Rasha Cosman from Australia's Kinghorn Cancer Centre (uk.advfn.com). Such international sites broaden patient access and data diversity. For the $122M round, Alexandria Venture Investments (which often backs clinical-stage cos) also participated (www.prnewswire.com).

In summary, CREATE has assembled from 2019 to 2026 a coherent enterprise: world-class scientific founders, a dedicated platform technology with multiple unique features, a track record of early clinical data, and robust backing from leading biotech investors (app.dealroom.co) (www.prnewswire.com). According to the company's release, the Series B funding will support advancement of its clinical pipeline across autoimmune disease and oncology.

CREATE Medicines Pipeline: Autoimmune Programs

CREATE views autoimmune diseases as a major target for its **in vivo** CAR platform. The rationale is straightforward: many autoimmune disorders involve rogue B cells or plasma cells producing pathogenic antibodies, or self-reactive T cells. CAR-T therapies targeting B cells (for example, anti-CD19 CAR-T) have

shown promise in lupus, rheumatoid arthritis, and other conditions (www.prnewswire.com) (createmedicines.com). However, ex vivo CAR-T for autoimmunity would face the same manufacturing hurdles. An **in vivo** approach could reset the immune system by depleting B cells more simply and repetitively.

According to CREATE's disclosures, its autoimmune pipeline is currently **all preclinical** (no human patients dosed yet) (www.fiercebiotech.com). The lead autoimmunity program is **CRT-402**, an *in vivo* CD19-targeted CAR-T therapy. In animal models (non-human primates), a single systemic dose of CRT-402 produced **"deep and durable B cell depletion,"** and crucially, this effect was shown to be redosable (www.prnewswire.com) (createmedicines.com). This suggests that a patient could receive multiple doses of CRT-402 to fine-tune B-cell recovery, effectively inducing immune "reset." The February 2026 press release stated that complete B-cell deletion was achieved via both a novel T-cell-receptor-integrating CAR and a conventional 4-1BBζ CAR, with no lymphodepletion needed (createmedicines.com). These NHP results are being presented at Keystone Symposia and underpin plans to enter the clinic in **H2 2026** (createmedicines.com).

In parallel, CREATE is developing a **dual CAR CD19 × BCMA** construct for autoimmunity (www.prnewswire.com). The idea is to broaden efficacy: while CD19 ablation can treat diseases like lupus or multiple sclerosis, combining CD19 with BCMA (typically a plasma cell target) could address conditions where long-lived plasma cells drive pathology (such as refractory lupus, Sjögren's syndrome, etc.). Although specifics are scant, the company notes this program is designed to "broaden therapeutic reach across refractory autoimmune indications" (www.prnewswire.com). Both CRT-402 and the dual CAR are enhanced by CREATE's platform features (e.g. the ability to redose until B cells repopulate at a controlled rate, and to choose CAR architectures optimal for autoimmune use).

CREATE has not yet cited specific disease indications in press releases, but external analyses suggest targets. For example, one FierceBiotech tracker notes Create's focus on B-cell depletion "immune reset," implying diseases such as systemic lupus erythematosus or refractory ANCA-associated vasculitis. The emphasis on **repeat dosing** indicates a different paradigm than one-shot CAR-T; it may allow periodic immune suppression followed by observation, akin to chronic therapy. This could be transformative for autoimmunity.

Context and Comparisons

CREATE is not the only company pursuing **in vivo** CAR-T for autoimmunity: in 2025 AbbVie agreed to acquire Capstan Therapeutics, whose CPTX2309 is an in vivo anti-CD19 CAR-T candidate for B cell-mediated autoimmune diseases that is in Phase 1. Ex vivo CAR-T companies (Cellectis, Allogene, others) generally target oncology. Tolerance induction in autoimmunity has largely relied on biologics (e.g. rituximab) or stem cell transplants.

Competitor activity in in vivo engineering for immune modulation is evolving, and specific competitor programs are not detailed here. CREATE has not publicly detailed any use of AI or machine learning in designing its pipeline.

Preclinical Data

The core preclinical evidence for CREATE's autoimmune strategy comes from the **NHP B-cell depletion study** (createmedicines.com). Key points:

- **Efficacy**: Both a conventional 4-1BBζ CAR and a novel TCR-integrating CAR achieved complete depletion of peripheral B cells in macaques (createmedicines.com). This shows the platform can robustly generate functional CAR-T cells *in vivo* at therapeutic levels.
- **Safety**: In the reported NHP data, repeated dosing did not cause overt toxicity (the emphasis was on "clinically de-risked" by enabling redosing) (createmedicines.com).
- **Repeat dosing**: The NHPs tolerated multiple rounds of RNA LNP infusion, which re-depleted B cells after they began to return (createmedicines.com). This is a unique capability; ex vivo CAR-T is a single infusion, often with potentially irreversible lymphodepletion.
- **Mechanism**: The CAR constructs delivered presumably included either a classical CD19 CAR or one integrating into the TCR α/β locus (to mimic normal antigen rescanning) (createmedicines.com). The fact that both designs worked gives CREATE flexibility to choose architectures.

These data support use in human autoimmune disease; hence CREATE plans to file an IND (Investigational New Drug) for CRT-402. The press release explicitly states "clinical entry planned H2 2026" (createmedicines.com). Once in clinic, CREATE's iterative model will apply: human safety and pharmacodynamics will be studied, then used to refine dosing and design.

Opportunities and Challenges

If successful, in vivo CAR-T for autoimmunity could become a first-line or rescue therapy in diseases like lupus or myositis. The advantages include: no need for apheresis or complicated manufacturing, possibility of outpatient infusion, and controllable dosing. CREATE's CEO envisions enabling an "immune reset" via flexible repeat dosing (www.prnewswire.com).

However, challenges remain. Autoimmune patients often require long-term management; it is unknown how patients will respond to repeated CAR infusions (e.g. antibody development against CAR components). Furthermore, autoimmunity trials can be slow and require careful endpoints. CREATE will need to demonstrate not just biological activity (B cell clearance) but actual improvement in disease markers/symptoms. They also must monitor for immunogenicity of CAR mRNA (though LNP tech is improving). Regulatory pathways for this novel modality are still being established; they may partly follow precedents from ex vivo CAR-T approvals, but bridging T cell engraftment data will be needed.

Nonetheless, investors clearly see potential: CREATE's Series B specifically highlighted "advancement of [the] CD19-targeted in vivo CAR-T therapy for autoimmune disease into the clinic" (www.prnewswire.com). The substantial funding should allow them to move quickly through toxicology and towards first-in-human trials (potentially in diseases of high unmet need with well-known autoantibody profiles).

CREATE Medicines Pipeline: Oncology Programs

In oncology, CREATE is pursuing **in vivo CAR therapies for solid tumors**. Several programs are in human trials, underlining the company's claim of having "the largest clinical dataset in the field" of in vivo CARs (www.prnewswire.com) (www.fiercebiotech.com).

MT-302: TROP2-targeting CAR for Solid Tumors

Program: *MT-302*. **Target:** TROP2 (a cell surface glycoprotein overexpressed in many epithelial cancers). **Indication:** Advanced, TROP2-positive solid tumors (initially Phase 1/2 in heavily pretreated patients; now also exploring frontline setting). **Modality:** In vivo LNP-encoded CAR, designed primarily to program myeloid cells (monocytes/macrophages) with an anti-TROP2 receptor (uk.advfn.com). TROP2 is chosen for broad applicability (e.g. breast, lung, urothelial cancers).

Clinical Status: The first-in-human dose-escalation was completed with promising results, reported at SITC 2025 (uk.advfn.com). In that Phase 1 trial (the “MYE Symphony” study), 27 patients with advanced TROP2+ cancers received MT-302 across 7 dose cohorts (uk.advfn.com). Key findings:

- **Safety:** The safety profile was *manageable*. Safety results are as reported by the company in a press release and have not been independently verified here; readers should consult the company’s full disclosures and any peer-reviewed publication.
- **Pharmacodynamics:** CAR^+ myeloid cells were detected infiltrating tumors (uk.advfn.com). The presence of CAR-myeloid cells in tumor biopsies confirmed *in vivo* transfection and redistribution of programmed cells. In addition, patients showed increased intratumoral T-cell infiltration and cytokine release (IFNγ, CXCL9/10), indicating a broader immune activation cascade (uk.advfn.com).
- **Preliminary Efficacy:** Among heavily pretreated patients, one confirmed partial response (PR) was observed in a patient with HR+ breast cancer on study for 16 months (uk.advfn.com). While a single PR in Phase 1 isn’t definitive, in this context it is notable (heavily pretreated, modest activity from monotherapy). The investigators reported “signs of anti-tumor activity” correlated with the biological markers (uk.advfn.com).
- **Dose:** The maximum tolerated dose (MTD) was 0.10 mg/kg without steroids. Some seemingly therapeutic activity was seen at even very low doses (0.015 mg/kg) (uk.advfn.com), suggesting a potent modality.
- **Platform Validation:** CREATE noted that this is the first *in vivo* CAR therapy to show direct tumor penetration and biochemical activity in solid tumors (uk.advfn.com). CEO Getts called it a “foundational moment” proving that CAR-modified immune cells can reprogram themselves in situ to attack tumors (uk.advfn.com).

Based on these results, CREATE is advancing MT-302 aggressively. A new investigator-initiated Phase 1/2 trial (“SPaCE-MT”) led by Amsterdam UMC is evaluating MT-302 in combination with CAPOX with or without nivolumab or trastuzumab in patients with advanced gastroesophageal cancer (www.biospace.com) (uk.advfn.com). The idea is that MT-302’s immune activation may synergize with other therapies.

Implications: MT-302 demonstrates the promise of targeted myeloid reprogramming. Unlike conventional CAR-T (which generally programs T cells), MT-302 seems to hinge on converting macrophages into tumor destroyers. Early data showed these CAR-myeloid cells remodeling the tumor microenvironment (e.g. upregulating chemokines that recruit T cells) (uk.advfn.com). If further trials validate this, MT-302 could pioneer a new class of solid tumor therapy, potentially addressing “immune cold” tumors that T cells alone struggle to penetrate.

MT-303: GPC3-targeting CAR for Liver Cancer

Program: *MT-303*. **Target:** Glypican-3 (GPC3), a cell surface proteoglycan overexpressed in hepatocellular carcinoma (HCC) and some other tumors. **Indication:** Initially metastatic HCC (liver cancer); now testing in frontline setting. **Modality:** In vivo CAR delivered via LNP, presumably also to program innate cells (myeloid), although specifics aren't fully disclosed.

Clinical Status: MT-303 advanced rapidly from single-agent trial to a combination trial. CREATE announced in December 2025 that it had **dosed the first patient** in a new Phase 1/2 trial of MT-303 combined with the standard-of-care immunotherapy (atezolizumab + bevacizumab) in frontline HCC (createmedicines.com). This is noteworthy: mostly, novel agents start in refractory populations. That CREATE is moving MT-303 into newly diagnosed patients suggests confidence in its safety and potential additive benefit.

Prior to that, the company reported correlative data from its MT-302 and MT-303 monotherapy programs across more than 40 treated patients (createmedicines.com). In practice, first-line HCC has shifted to atezolizumab/bevacizumab; by co-administering MT-303 in this setting, CREATE aims to deepen responses. The published rationale is that monotherapy data showed *in vivo* CAR expression, immune activation, and tumor infiltration in these patients (createmedicines.com). The trial description notes that monotherapy-created markers "provide strong rationale for combination" (createmedicines.com).

Key points from the Dec 2025 announcement:

- **Monotherapy Data:** Across >40 treated patients (with MT-303 or MT-302), correlative biopsies confirmed CAR expression in tumors, cytokine/chemokine changes (elevated IFNγ and CXCL9/10), and increased immune cell infiltration (createmedicines.com) (uk.advfn.com). These confirm the drug hits its target in human subjects.
- **Safety:** MT-303 alone was reportedly well-tolerated; the press emphasized "manageable and differentiated safety profile" (createmedicines.com). For MT-302, safety data are company-reported and early; whether combination with other immunotherapies is feasible remains to be shown.
- **Strategic Positioning:** For HCC, where immune fitness is better in treatment-naïve patients, CREATE expects more potent tumor control when adding MT-303. Dr. Maurer (CMO) noted that early data (immune activation signals) and safety "support our confidence" in moving to combination frontline trials (createmedicines.com).
- **Trial Design:** The frontline HCC study (NCT06478693) is a multi-center, open-label, dose-escalation and expansion trial of MT-303 in combination with atezolizumab and bevacizumab, designed to investigate safety, tolerability, pharmacokinetics, pharmacodynamics, and preliminary antitumor activity; the company's release does not describe a randomized comparison against standard of care alone.

If MT-303 proves effective, it could fill a major need. HCC is a global killer with limited options; immune-based combos have improved survival but many patients do not respond fully. An agent that recruits innate immunity (like MT-303) could convert nonresponders. Off-tumor safety remains a key consideration for potent therapies and has not been established for MT-303 here.

MT-304: HER2-targeting CAR for Breast and Other Cancers

Program: *MT-304*. **Target:** HER2 (ERBB2), a well-known oncogenic receptor in breast, gastric, and other tumors. **Indication:** HER2-positive solid tumors (breast, gastric, others), multi-arm Phase 1/2. **Modality:** In vivo CAR delivered by LNP; designed to trigger both innate and adaptive immune responses.

Clinical Status: According to press, MT-304 entered first-in-human trials by May 2026. Create's statement indicated the first patient was dosed in early Phase 1/2 for MT-304 (www.biopharmadive.com). Additional details (Aug 2025) clarify:

- MT-304 encodes a CAR against the HER2 protein and is intended to **"trigger multiple arms of the immune system to attack at the same time."** (www.biopharmadive.com)
- The trial includes HER2+ metastatic breast cancer as well as other HER2+ tumors (e.g. gastric) (www.biopharmadive.com).
- The LNP formulation may target both T cells and innate cells, to maximize anti-HER2 effects.
- As a HER2 program, it leverages extensive oncology biology knowledge (HER2 signaling, patient stratification) and potentially benefits from combination with HER2-targeted drugs or checkpoint inhibitors later on.

No efficacy or safety data have been reported yet. However, choosing HER2 (a well-validated target of approved drugs and even biparatopic antibodies) as a platform target is a strategic move: it de-risks the biology. If the RNA CAR can bind HER2, it may induce tumor kill through multiple mechanisms (phagocytosis, ADCC-like effects, etc). Because many breast and gastric cancers remain uncontrolled even after multiple lines (as seen with trastuzumab resistance), an entirely new modality approach could capture a niche.

Pipeline Summary and Table

Together, CREATE's pipeline spans solid tumors and autoimmune disease (See Table 1). All oncology programs exploit the same underlying delivery and cell-targeting platform but differ in antigen and immune focus. At writing, MT-302 and MT-303 are in clinical trials (Phase 1 monotherapy and Phase 1/2 combo respectively), MT-304 is beginning Phase 1/2, and CRT-402, a preclinical CAR construct, targets B cells (CRT-401, listed on the company's pipeline page as a separate multi-immune program, is not described further here) (createmedicines.com) (www.prnewswire.com).

> **Table 1: CREATE Medicines Pipeline (Programs and Status)** (Note: Create's internal names and last-checked status; sources in various releases.)

Program	Target / Mechanism	Indication / Use	Immune Cells Targeted	Development Status (Year)	Key Data / Notes
MT-302	TROP2 (tumor antigen)	Advanced solid tumors (e.g. breast, lung); investigator-initiated combination trial (SPaCE-MT) in advanced gastroesophageal cancer initiated	Primarily myeloid cells (macrophages)	Phase 1 completed (2025); frontline combination Phase 1/2 (2025–26)	**First-in-human results**: CAR⁺ myeloid cells infiltrated tumors; immune activation and 1 partial response observed in refractory patients (uk.advfn.com). Proof-of-mechanism achieved for in vivo CAR in solid tumor.
MT-303	GPC3 (glypican-3)	Hepatocellular carcinoma (liver cancer)	Myeloid cells	Phase 1 monotherapy (2025); frontline combo Phase 1/2 (2026)	First patient dosed in combination trial (atezo/bev) in Dec 2025 (createmedicines.com). Monotherapy: *In vivo* CAR expression and tumor infiltration reported across >40 treated patients in the combined MT-302 and MT-303 monotherapy programs; company describes MT-303 safety as manageable (createmedicines.com).
MT-304	HER2 (ERBB2)	HER2+ breast cancer; HER2+ gastric cancer	Undisclosed (likely multi-immune)	Phase 1/2 (2026)	Dosed first patient in Phase 1/2 (breast and other HER2+ tumors) (www.biopharmadive.com). Preclinical: targets multiple immune arms. >50 patients treated overall across programs (as of May 2026) (www.prnewswire.com).
CRT-402	CD19 (B-cell marker)	Autoimmune (B-cell–mediated diseases)	T cells	Preclinical (NHP efficacy, IND planned H2 2026)	NHPs: deep, durable B-cell depletion achieved, redosable (complete depletion with novel CAR designs) (createmedicines.com). Clinical IND expected 2026 (createmedicines.com). Enables controlled immune reset.
Dual CAR (CD19×BCMA)	CD19 × BCMA (bispecific)	Broad spectrum B-cell/plasma autoimmune	T cells	Preclinical	Designed to target both B cells and long-lived plasma cells “to broaden therapeutic reach” in refractory autoimmunity (www.prnewswire.com). Development stage unspecified.
CRT-401	Not confirmed in this article	Not confirmed in this article	Multi-immune	See company pipeline page	(Limited public info; company pipeline page lists CRT-401 among its multi-immune programs (createmedicines.com).) Target and stage should be checked against the company’s pipeline page.

Sources: Company press releases and website (www.prnewswire.com) (uk.advfn.com) (createmedicines.com); pipeline slide (createmedicines.com); BioPharma Dive report (www.biopharmadive.com).

Table 1 illustrates CREATE's strategy: leveraging the same platform across diverse diseases. This breadth is attractive to investors ("multiple immune cell populations in vivo" (www.prnewswire.com)) but also challenging. The oncology programs require demonstrating anti-tumor efficacy beyond correlative markers, while the autoimmune programs must confirm durable immune reset. Overall, the evidence to date is early and company-reported: the human data come from oncology programs, while the autoimmune programs have preclinical (non-human primate) data only.

Series B Funding and Market Context

On May 14, 2026, CREATE announced closing a **$122 million Series B** round co-led by Newpath Partners, ARCH Venture Partners, and Hatteras Venture Partners (www.prnewswire.com) (www.fiercebiotech.com). Alexandria Venture Investments (Alexandria Real Estate's VC arm) also participated, along with existing syndicate members. This infusion brings CREATE's total raised to ≈$257 M (when combined with the prior $135 M (app.dealroom.co)) and, per the company release, will support advancement of its clinical pipeline across autoimmune disease and oncology.

The press release cited two main aims for the funds: (1) advance CRT-402 (CD19 CAR) for autoimmune into the clinic, and expand the dual CAR program; (2) continue clinical progress in oncology (notably first-line HCC and others) (www.prnewswire.com). Implicitly, R&D and manufacturing capacity also get bolstered. Included in the announcement were three new executive appointments: Ron Philip as Executive Chair, and Brian Cuneo (ARCH) and Tom Thomas (Newpath) to the board (www.prnewswire.com) (www.biospace.com). These moves signal readiness for the complex path ahead.

Investor Confidence in the Platform

It is instructive to view CREATE's raise in the context of 2026 biotech financing. According to **Fierce Biotech's Fundraising Tracker** for 2026, CREATE's $122M was among the largest in Q2-May 2026 (www.fiercebiotech.com). Interestingly, Fierce noted that "as the wave of in vivo CAR-T hype crests, Create is catching the swell with a $122M Series B" (www.fiercebiotech.com). In their eyes, CREATE is surf-riding a trending technology. The article emphasized that CREATE's autoimmune pipeline is still preclinical, but the oncology side already had the "largest clinical dataset in the field" (www.fiercebiotech.com) (a point drawn directly from CREATE's releases). Essentially, Fierce contextualizes the round as propping up both early (autoimmunity) and late (cancer) bets.

This was a noticeably large raise for a private biotech in 2026. Venture funding in biotech had cooled: a mid-2025 report found overall biotech venture funding fell from $7B in Q1 to $4.8B in Q2, with first financings at their lowest total in five quarters (www.biopharmadive.com). Many investors were only writing big checks to "sure bets," leaving seed and A rounds scarce (www.biopharmadive.com). Against that backdrop, a $122M deal suggests CREATE is considered close to a de-risked category: a bridge or mezzanine round to push major programs to readouts. Notably, HSBC's analysis of biotech VC noted a shift toward mega-rounds ($100M+) that can substitute for multiple earlier financings (www.biopharmadive.com). HSBC's Norris said

such megarounds let companies “get almost three traditional rounds” through one financing; a $122M raise may play a similar role for Create, though that is our inference rather than an HSBC statement about Create (www.biopharmadive.com), letting the company rapidly advance multiple assets without interim financing.

While overall deal counts fell, the biggest deals still were hitting biotech, especially AI-enabled platforms. For comparison, Fierce’s tracker shows other 2026 mega-rounds: Alphabet’s Isomorphic Labs ($2.1B Series B in May 2026) (www.fiercebiotech.com), Cytospire ($83M) and Tortugas ($106M) in April, etc. In AI drug discovery specifically, numerous startups raised large rounds (e.g. Insilico’s $110M in funding round, Chai’s $130M). Table 2 (below) lists select “AI biotech” companies with recent financings. These are shown for context only; CREATE has not disclosed using AI.

Importantly, not all big rounds welcome equal risk. Some were in diagnostic or research tools, others (like CREATE) in therapeutics. The inclusion of Alexandria (specializing in life science real estate and biotech venture) also indicates confidence in the science and facilities. Quotes from investors in the PR reflect high expectations: Newpath’s Tom Cahill said CREATE “can become the next great standalone pharmaceutical company” (www.biospace.com), referencing its “science ahead of the field.” ARCH’s Brian Cuneo emphasized CREATE’s differentiated platform and position to “play an important role in the future of autoimmune disease and oncology” (www.biospace.com).

Thus, the Series B serves multiple purposes: validating CREATE’s progress, fueling critical clinical trials, and strengthening the team/board. In the company's own words, the funding is intended to support advancement of its clinical pipeline across autoimmune disease and oncology; the autoimmune programs remain preclinical. In a landscape where biotech startups often struggle to raise money (www.biopharmadive.com), it’s a vote of investor confidence in CREATE’s in vivo CAR platform.

The Next Wave of AI-Driven Biotech

Separately from CREATE, which has not disclosed using AI, the infusion of artificial intelligence into biotech R&D is a larger phenomenon. Beyond CREATE, numerous **biotech startups and partnerships** are leveraging AI to accelerate drug discovery, optimize molecules, and design novel therapies. Below we highlight several notable examples and trends, supplementing with case studies where available.

Examples of AI-Driven Biotech Ventures

- **Xaira Therapeutics**: Launched April 2024 by former Genentech CSO Marc Tessier-Lavigne, this startup aims to integrate ML, lab automation, and therapeutics. It debuted with an eye-popping **$1 billion** of funding co-led by Arch Venture Partners and Foresite Capital (www.axios.com). Xaira’s approach is to build an “AI-assisted drug discovery platform” combining generative models with wet-lab systems. Its advisory board includes industry luminaries (Scott Gottlieb, Carolyn Bertozzi) (www.axios.com). Though no products are public yet, Xaira exemplifies “big play” bets: deploying huge capital on the hypothesis that integrated AI can dramatically shorten drug pipelines.

- **Chai Discovery**: Co-founded by AI researchers (with OpenAI connections), Chai raised $70 M in Series A (Aug 2025) and $130 M in Series B (Dec 2025) (techcrunch.com). It uses large language models tuned for proteins to design **de novo antibodies**. (Technically, Chai's models can predict interactions between molecules and generate sequences with desired binding properties (techcrunch.com).) Chai incorporates new "foundation models" to create custom antibody candidates from scratch, not just modifying existing ones. After its Series B, total funding was over $225M (techcrunch.com). According to CEO Josh Meier, their models are now designing molecules "that have properties we'd want from actual drugs" – a claim backed by reports of improved success rates in early experiments (techcrunch.com). Thus, Chai is a prime example of bleeding-edge AI (LLMs) applied directly to biologic therapeutics, with high-profile backing and fast fundraising.
- **Insilico Medicine**: A pioneer in AI for small-molecule discovery, Insilico (co-founded 2014 by Alex Zhavoronkov) listed on the Hong Kong Stock Exchange (stock code 3696) in December 2025. It combines generative networks with robotics for end-to-end drug design. In March 2025, Insilico secured **$110 M** in Series E financing (www.fiercebiotech.com). Its lead candidate, *rentosertib* (originally ISM001-055), targets idiopathic pulmonary fibrosis; notably, both the molecule and its biological target were discovered by Insilico's AI algorithms (www.fiercebiotech.com). Rentosertib delivered "positive topline results" in a Phase 2a trial in China, confirming a dose-dependent lung capacity improvement (www.fiercebiotech.com). In July 2026 the company announced the initiation of a Phase III trial of rentosertib in idiopathic pulmonary fibrosis, expected to enroll 320 participants across 47 centers in China. Insilico reports having mapped 22 AI-designed programs through candidate nomination (www.fiercebiotech.com). This case shows AI's tangible output: an AI-derived drug actually working in humans. The recent fundraising will support pivotal trials and further AI/platform development (www.fiercebiotech.com).
- **AbCellera**: This antibody discovery company (IPO 2020, ticker ABCL) identifies therapeutic antibodies from single B-cell data and partnered on bamlanivimab for COVID-19. It is included as an antibody-discovery comparator rather than as an AI drug designer.
- **Recursion Pharmaceuticals**: Another public company (ticker RXRX, IPO 2021), Recursion uses AI to interpret massive cellular image datasets. It screens hundreds of millions of cell images with deep learning, linking phenotypes to chemical structures to find leads. Recursion priced its April 2021 IPO at $18.00 per share, with expected gross proceeds of $436.4 million before any exercise of the underwriters' option. It's a leading example of high-throughput data + AI in biotech. While Recursion is more a platform than pipeline, it won't need to raise new VC (it's public) but it illustrates how AI platforms can underpin pharmaceutical pipelines.
- **Exscientia**: UK company (founded 2012) focused on small-molecule design via AI. Went public on Nasdaq in 2021. Had partnerships with pharma and even had an AI-generated molecule (DSP-1181) enter Phase 1 in 2020 (discovered via Exscientia's algorithms for OCD). Its October 2021 Nasdaq IPO was priced at $22.00 per ADS. In November 2024 Exscientia was acquired by Recursion and became its wholly owned subsidiary.

- **Other $$$ Rounds**: The newmarketpitch funding data (Table below) shows many AI-driven series in 2025. For instance, TandemAI ($22M in Series A, Nov 2025 (newmarketpitch.com)), etc. Insilico's $110M (growth equity) and others like Pharmaceutical Robotics (Lab automation) show diversity of AI bets.

The above examples demonstrate a few threads:

- **Generative AI**: Companies like Insilico, Chai, funded heavily to use generative ML models (GANs, LLMs, diffusion) to design either small molecules or biologics from first principles.
- **AI + Robotics**: Many blend AI with automated labs . Investors like Flagship, Orogen, Founders Fund are active.
- **AI Internals**: Beyond discovery, some use AI to optimize trials (AI Ventures, Unlearn.ai working on synthetic cohorts).
- **Big Tech Involvement**: Google/Alphabet's Isomorphic Labs ($2.1B Series B May 2026 (www.fiercebiotech.com)), Microsoft's various health projects, Amazon/AWS providing compute, show tech giants backing this trend.

Table 2: Select Recent AI-driven Biotech Companies and Funding (2024–2026)

Company	Focus/Approach	Notable Funding (Date)	Investors/Valuation	Key Achievements / Notes
Xaira Therapeutics	AI-powered drug discovery platform	$1.0B Seed (Apr 2024)	Arch, Foresite, Sequoia, etc (all big names) (www.axios.com)	Founded by ex-Stanford president; aims to develop mfg + ML pipeline.
Chai Discovery	LLM-based antibody/biologics design	$70M Series A (Aug 2025); $130M Series B (Dec 2025)	General Catalyst, Oak HC/FT, OpenAI, etc (techcrunch.com) (post-money $1.3B)	"Computer-aided design suite" for custom antibodies (techcrunch.com). Has in-house AI models (Chai 2.0) improving design success rates.
Insilico Medicine	Generative AI small-molecule platform + robotics	$110M Series E (Mar 2025) (www.fiercebiotech.com)	Value Partners (lead, HK); listed on HKEX (3696.HK) since Dec 2025	AI-designed fibrosis drug (rentosertib) in Phase 3; positive Phase 2a results (www.fiercebiotech.com). 22 AI-designed programs accelerated (www.fiercebiotech.com).
Recursion Pharma	Phenotypic screen imaging + AI (drug discovery)	$436M IPO (Apr 2021, before underwriters' option);	Public (Nasdaq: RXRX)	Built vast image libraries, AI models to link genes, images, molecules. Robust partnerships (Boehringer, Takeda).
Exscientia	AI for small-molecule drug design (ML/algorithmic)	~$305M upsized IPO (Oct 2021, before underwriters' option)	Acquired by Recursion (Nov 2024); formerly Nasdaq: EXAI	First AI-designed drug in clinic (Phase 1), various pharma collabs.

** represents older rounds for context.*

Sources: Axios/TechCrunch news and industry reports (www.axios.com) (techcrunch.com) (www.fiercebiotech.com); industry trackers (newmarketpitch.com).

This non-exhaustive list underscores how venture funds remain willing to back bold “AI + biology” plays. In context, **CREATE Medicines** is not itself described as an AI-driven discovery company: it has not publicly disclosed the use of AI or machine learning in its pipeline, and it is discussed alongside these companies only as another well-funded biotech financing in the same period. For scale only, the $122M Series B is of similar size to Insilico’s $110M Series E and Chai’s $130M Series B.

Case Study: Computational Nanobodies (Nature, 2025)

Beyond corporate examples, recent academic work demonstrates AI’s power in therapeutic design. In a July 2025 Nature article (Swanson *et al.*), researchers created a completely *in silico* pipeline (the “Virtual Lab”) to design nanobody binders to SARS-CoV-2 variants (www.nature.com). They used an ensemble of AI tools – a language model (ESM), AlphaFold-Multimer, and Rosetta – orchestrated by a team of LLM “agents” that proposed experiments and analyzed outcomes (www.nature.com). The highlight: the AI system designed **92 new nanobody sequences**, some with predicted high-affinity to variants; subsequent lab validation confirmed several candidates (www.nature.com).

This study is paradigm-shifting: it shows an autonomous AI pipeline (with human oversight) can go from problem statement to actual therapeutic candidates. It does not target human cells per se, but the approach could be adapted to anything from enzyme design to immune receptor optimization. CREATE has not publicly detailed any use of AI algorithms, so this study is not evidence about CREATE's methods. Swanson *et al.* describe “the protein language model ESM… the protein folding model AlphaFold-Multimer… and Rosetta” working together (www.nature.com). CREATE describes its “optimized RNA design” and “differentiated receptor design” (createmedicines.com) without specifying whether computational techniques are involved.

Challenges and Realism

Despite optimism, many AI-focused biotech bets have stumbled. In drug discovery, some experiments fail to generalize beyond initial models: not every AI-proposed molecule is actually synthesizable or effective. Biopharma Dive noted a specialized survey showing venture capital had retracted from less-certain bets by mid-2025 (www.biopharmadive.com). Pipelines in AI-enabled drug discovery face the same clinical attrition as any other research.

Moreover, deploying AI in cell therapies has unique hurdles. AI models trained on small-molecule data may not directly apply to designing CARs or LNPs. The algorithms must be integrated with complex immunology knowledge. CREATE has not disclosed whether or how it uses AI, so these hurdles are general industry context rather than a description of its methods.

Implications and Future Directions

CREATE Medicines stands at a confluence of cutting-edge trends: **in vivo** immunotherapy and AI-enabled drug design. If its trials succeed, it could pioneer a new therapeutic modality. The implications are multi-fold:

- **Clinical Impact:** Successfully reprogramming immune cells inside patients could expand CAR-T therapy beyond rare cancers into common autoimmune diseases, and make powerful treatments accessible in low-resource settings. The repeat-dosing capability and off-the-shelf nature mean even chronic diseases might be managed with periodic infusions, unlike one-off gene therapies.
- **Industrial Change:** This could shift how biotech pipelines are built. Instead of focusing on small molecules or monoclonal antibodies, we might see more investment in “code therapies” – using RNA as a generic delivery format. Startups will hold libraries of CAR designs, LNP formulations, etc. Bioreactors for LNP production may become standard infrastructure. Partnerships may form between computational groups (who design the NP and payload) and immunotherapy groups (who run trials).
- **Partnering:** If CREATE's clinical data continue to be positive, larger pharmaceutical companies might show interest in in vivo CAR programs, for example through licensing or acquisition. This is speculation, not a reported development. CREATE has not disclosed using AI, so its results should not be read as validating AI-driven pipeline design.
- **Regulatory Landscape:** CREATE and similar firms will face novel regulatory scrutiny. The FDA and EMA may develop new guidelines for in vivo cell therapies. Questions about long-term safety of repeated mRNA CAR dosing, immunogenicity, biodistribution, etc., will need answering. The AI aspect (e.g. if data-driven predictions were used to design the CAR sequences) could factor into regulatory discussions about transparency and validation of algorithms. The community may push for standards (cf. FDA’s recent AI/ML in medical devices guidelines).
- **Next Biotech Wave:** CREATE has not disclosed using AI, so it should not be read as part of this AI trend. More broadly, emerging areas of AI-enabled biotech include: AI for cell therapy manufacturing (automated CAR-T production), AI-driven microbiome therapeutics (e.g. generating consortia to recalibrate gut immunity), and personalized neoantigen vaccines (AI predicting epitopes). Another frontier is **AI-guided CRISPR in vivo** (such as base editing for genetic diseases); tech giants like Vertex and Beam are doing CRISPR ex vivo, but in vivo editing with AI-designed guides could be next.
- **Global and Ethical Considerations:** Biotech innovation like this raises societal questions. If autoimmune diseases can be “reset” with CARs, we might see therapy guidelines akin to vaccination schedules (e.g. “CAR booster shots”). Affordability will be critical – on one hand, lack of cell harvesting should cut costs; on the other, developing and manufacturing RNA can be expensive. Equity of access and long-term follow-up (for safety of new modalities) will require policy planning.

We should note historical context: breakthroughs in biotechnology often went through hype cycles. mRNA vaccines, for example, had decades of development quietly before COVID-19. AI in biotech might similarly seem dreamlike now, but it will likely be integrated stepwise. CREATE’s Series B is one milestone – not the end. Each upcoming trial (e.g. CRT-402’s first human, MT-302 phase 2) will be a test of whether the hype translates to patients. Industry watchers will scrutinize both positive and negative data to adjust their bets.

Case Studies and Real-World Examples

To provide concrete context, we examine a few relevant case studies of AI in therapy development and in vivo cell programming.

Case Study 1: AI-Designed Nanobodies (Nature 2025)

As discussed, **Swanson *et al.* (Nature 7/29/25)** created a fully AI-guided workflow to design nanobody (camelid antibody fragment) therapies to SARS-CoV-2. The researchers assembled multiple neural networks: a principal investigator LLM that coordinated the search, a team of “scientist agents,” and integration of models like ESM and AlphaFold-Multimer (www.nature.com). They produced 92 candidate nanobody sequences **entirely in silico**, then some of these showed promising binding in bench experiments. This illustrates that:

- The Virtual Lab designed 92 candidate nanobody binders to SARS-CoV-2 variants; experimental validation found two with improved binding to the recent JN.1 or KP.3 variants while maintaining strong binding to the ancestral spike protein. These are research binders, not approved or clinical-stage therapies.
- The loop between AI prediction and lab testing can be short: the designed sequences were experimentally tested within the study.

This study is a research demonstration in a different field from CREATE's CAR programs, and CREATE has not disclosed using similar methods. The Nature example is a research demonstration; separately, Insilico reports 22 AI-designed programs (www.fiercebiotech.com).

Case Study 2: AI-Discovered Drug in Clinic (Nature Medicine 2025)

In 2025 Nature Medicine published the results of a randomized, double-blind, placebo-controlled Phase 2a trial of rentosertib (formerly ISM001-055), a generative-AI-designed small-molecule inhibitor of TNIK, in **IPF (idiopathic pulmonary fibrosis)** (Xu *et al.*). In the 12-week trial, 71 patients were randomized to one of three rentosertib dose regimens or placebo; treatment-emergent adverse event rates were similar across arms, and the 60 mg once-daily group showed a mean forced vital capacity change of +98.4 ml versus -20.3 ml for placebo (PubMed). The trial was small and short, and the authors conclude that it warrants further investigation in larger, longer trials.

The significance for our discussion is limited but real: this is an early clinical test of a drug whose molecule and target were both identified using generative AI, developed by Insilico (discussed above). CREATE has not disclosed using AI, so this case is separate industry context and says nothing about CREATE's own methods.

Case Study 3: In Vivo CAR-T in Humans

Though still emerging, some in vivo CAR-T efforts outside CREATE can be mentioned. One Chinese startup, **Vivacta Bio** (Shanghai), reported first-in-human results at the 2025 ASH Annual Meeting for GT801, an in vivo CAR-T product candidate being evaluated in a Phase 1 investigator-initiated study in non-Hodgkin’s lymphoma

(www.prnewswire.com). Another, **Myeloid Therapeutics (now CREATE)** had earlier phase work. Off the shelf, academic groups have performed limited in vivo CAR via viral injection in mice, but no approved therapies yet. CREATE reports having dosed more than 50 patients and describes this as the largest clinical dataset in the field; Fierce Biotech relays that claim (www.fiercebiotech.com). Other developers, such as those named above, are also reporting human data, and the article offers no independent comparison.

Nonetheless, this entire approach is extremely early. If CREATE or others fails in trials (e.g. no improvement vs control, or safety issues), it would set the field back. Conversely, a major positive signal (e.g. a high complete remission rate in a solid tumor trial) would catalyze rapid adoption. History shows biotech pivots on such results. Thus, observationally, series B money likely flows heavily once initial safety is established; the true test will be efficacy outcomes in later, larger clinical studies, which the company has not yet announced.

Discussion and Future Outlook

Looking ahead, several considerations shape the trajectory of CREATE and the AI-biotech paradigm:

- **Further Clinical Readouts**: CREATE's upcoming milestones include first-in-human for CRT-402 (autoimmune CAR) and combination trials for MT-303. The success of MT-302's combination trial in solid tumors will be watched closely. Regulatory filings (IND applications) and poster presentations will reveal secrets of their science.
- **Competition and Collaboration**: If in vivo CAR-T proves feasible, we may see big mergers or collaborations. Traditional pharma might acquire or partner. CREATE's approach differs from ex vivo CAR-T, but partnerships with companies lacking strong mRNA tech could make sense.
- **AI Ecosystem Growth**: The broader AI tools will mature. Large protein databases (immunome data, single-cell atlases) can be fused with ML to find new immunotherapy targets. Create could incorporate those data to identify next-generation CAR targets (beyond CD19/BCMA/HER2). Also, generative AI (e.g. Diffusion models for peptides) will improve LNP components or delivery sequences.
- **Monetization and Business Model**: For investors, a key question is: will CREATE remain independent or become an acquisition target? Board composition hints at building a standalone pharma brand ("next great standalone" as Tom Cahill said (www.biospace.com)). But also, in vivo CAR manufacturing and regulatory risk mean partnerships with pharma giants (e.g. Novartis or BMS) could accelerate commercialization.
- **Societal Impact**: If CREATE's in vivo CARs succeed, how will healthcare adapt? Chronic autoimmune diseases might be treated with periodic gene-therapy-like infusions; oncology regimens could include at-need "immune boosters". There will be challenges in roll-out (e.g. controlling therapy intensity, handling off-target autoimmune side-effects, etc.). Biotech innovation often has ripple effects: for example, FDA expedited pathways might expand to these modalities, insurance coverage frameworks evolve.

Critically, **CREATE's story is also a caution**: as with any new tech, there will be failures. In-cell programming has open questions: will patients lose engineered CAR cells to immune clearance (anti-CAR immunity)? Will repeated dosing eventually trigger tolerance (like anti-PEG antibodies to LNP formulations)? The company's own claim of iterative learning suggests they expect to refine these issues trial by trial.

Finally, while we emphasize AI, it is worth remembering biology's complexity. No AI model can today guarantee a safe, effective CAR-T drug. Nonetheless, the nanobody and IPF cases show how AI-generated designs can be paired with rigorous wet-lab and clinical validation. Those cases are separate from CREATE, which has not disclosed using AI.

Conclusion

CREATE Medicines' $122M Series B is a notable financing for the in vivo CAR field. Over its first few years, CREATE has reported, in company releases, what it describes as the "largest clinical dataset" for **in vivo** CAR therapies (www.fiercebiotech.com), and developed an mRNA-LNP platform; the human data reported so far are early and company-reported, from oncology programs, while the autoimmune programs are preclinical (non-human primate) only. Its lead programs – from the CD19 CAR for autoimmune (CRT-402) to the TROP2 CAR for solid tumors (MT-302) – demonstrate the breadth of its pipeline and the radical potential of direct immune reprogramming (uk.advfn.com) (createmedicines.com).

The timing of this raise – mid-2026 – is significant. The biotech investment climate is selective: general venture funding had slowed (www.biopharmadive.com), yet megafunds are flowing to AI-focused platforms. Separately from CREATE, which has not disclosed using AI, companies such as Insilico, Chai and Xaira have convinced investors that their data-centric approaches are worth funding at scale (www.axios.com) (techcrunch.com) (www.fiercebiotech.com). The company's leaders and backers articulate high expectations: they see a path to reshape treatment paradigms in diseases from SLE to HCC (www.prnewswire.com) (www.biospace.com).

This report has charted CREATE's journey with depth: its origin, technology innovation, detailed program status, and the evidence supporting its strategies. We also examined the broader context of AI in biotech – from breathtaking lab demonstrations (AI-designed nanobodies) to nascent clinical successes (AI-discovered IPF drug) – providing context for the in vivo CAR field. CREATE itself has not publicly described using AI in its pipeline, so the AI-biotech material is separate context. We have included tables summarizing its pipeline and peer companies, with sources cited inline (www.prnewswire.com) (uk.advfn.com) (www.axios.com) (time.com).

In the coming years, CREATE Medicines will face crucial tests. Clinical outcomes from its ongoing oncology trials, first-in-human data for its autoimmune programs, safety data from new indications, and the competitive responses of larger pharmas will all shape its fate. For the field at large, the success or failure of CREATE's approach will inform the viability of **in vivo** CAR-T and the role of AI in immunotherapy. For now, the convergence of science, capital, and ambition makes this a watershed moment: CREATE's Series B closing on May 14, 2026 is a notable financing for the in vivo CAR field, separate from the AI-biotech context discussed above.

Source links

Links cited in this article, in order of first appearance. Full addresses are provided for readers using extracted text.

1. https://www.prnewswire.com/news-releases/create-medicines-announces-122-million-series-b-financing-to-advance-in-vivo-car-pipeline-in-autoimmune-disease-and-oncology-302771778.html
2. https://www.fiercebiotech.com/biotech/fierce-biotech-fundraising-tracker-26

3. https://www.biospace.com/press-releases/create-medicines-announces-122-million-series-b-financing-to-advance-in-vivo-car-pipeline-in-autoimmune-disease-and-oncology
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About IntuitionLabs

IntuitionLabs is an AI consulting, custom software development and data engineering firm serving pharmaceutical, biotechnology, medical-device and other life-science organizations. We work with clinical, regulatory, medical-affairs, commercial, quality and IT teams to connect technology decisions with the work people need to accomplish.

AI consulting and adoption

Our AI enablement services cover readiness assessments, use-case selection, governance and policies, team workshops, adoption measurement and ongoing advisory support. We help organizations structure the information layer behind AI: source material, context, permissions and maintained knowledge that make generated answers useful and reviewable. Private LLM inference and hosted AI options support teams evaluating how to operate AI with appropriate control over their data and infrastructure.

Software, data and life-science workflows

IntuitionLabs develops custom software for pharma and biotech, integrates enterprise systems, and builds data engineering and business intelligence solutions. Areas of focus include AI agents, regulatory research, medical writing, medical affairs, CMC information, competitive intelligence and clinical-document workflows. Our eTMF intelligence work includes cross-system reconciliation and inspection-readiness support.

Enterprise platforms and regulated delivery

We provide Veeva services, application support, managed services, integrations and custom applications, alongside enterprise content work involving platforms such as Egnyte. For regulated workflows, our services include GxP enablement, computer-system validation and software development addressing 21 CFR Part 11 requirements. The applicable controls, validation responsibilities and acceptance criteria are defined for each engagement.

Work with IntuitionLabs

Explore AI enablement, pharma and biotech software development, data engineering and BI, and Veeva services. Contact IntuitionLabs to discuss your workflow, information sources and implementation needs.

IntuitionLabs publishes educational research to help life-science teams make informed technology decisions. Coverage of a product or organization does not imply a client relationship, endorsement or partnership.

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