

Strand Therapeutics

Category:

Best Startup

Company Name:

Strand Therapeutics

Turnover and/or Funding:

The company has raised over \$200 million in funding, including from investors such as Eli Lilly, Amgen, Regeneron Ventures, Redmile Group, Kinnevik, ICONIQ, FPV, and Playground Global.

Sub-Category:

Biotechnology

Corporate history (creation, key milestones, main funding,...)Information on Condition / Disease and need for solution / product (prevalence, existing treatments / solutions):

Strand Therapeutics was founded by MIT scientists to pioneer programmable mRNA therapies that overcome the challenges of conventional gene- and immuno-therapy. Established in Boston, the company has raised over \$200 million in funding, including from investors such as Eli Lilly, Amgen, Regeneron Ventures, Redmile Group, Kinnevik, ICONIQ, FPV, and Playground Global. The team has grown to approximately 100 employees, combining expertise in synthetic biology, mRNA engineering, LNP mRNA manufacturing, immuno-oncology, and clinical development.

Strand's platform emerged from foundational work published in Nature Biotechnology, Nature Chemical Biology, Nature Cancer, and Science, demonstrating that mRNA could be engineered with sophisticated genetic circuits to control when and where therapeutic proteins are expressed. This innovation enables therapies to be active only in specific cell types (such as tumors) while sparing off-target organs (such as healthy tissues), addressing critical safety limitations seen in prior gene therapies and potent protein payloads. Unlike DNA-based gene therapy, which can integrate into the genome unpredictably, Strand's mRNA approach remains transient and non-integrating, reducing long-term risks.

The company's lead program, STX-001, targets advanced solid tumors. These cancers

account for roughly 90% of adult malignancies and are often resistant to standard treatments. Although immune checkpoint inhibitors have revolutionized care for subsets of patients, many individuals with \"cold\" tumors or heavily pretreated disease see limited benefit and have few therapeutic options. Cytokines such as interleukin-12 (IL-12) have long been recognized as potent immune activators capable of inducing tumor regression and durable immunological memory. However, systemic IL-12 delivery has historically led to severe toxicities, including life-threatening inflammation and multi-organ damage, which has prevented the successful development of IL-12 as a drug despite promising efficacy signals.

Strand's approach aims to resolve this unmet need by deploying self-replicating mRNA encoding IL-12 directly into tumors. This strategy activates the tumor microenvironment, eliciting immune responses that can convert \"cold\" tumors into \"hot,\" immunologically active sites. Importantly, it can stimulate systemic antitumor responses, including regression of non-injected lesions, while minimizing systemic cytokine exposure and associated toxicities. The self-replicating mRNA architecture adds a further layer of control and durability, ensuring IL-12 is expressed only in the desired context over sustained periods.

The follow-on product, STX-003, builds on this vision by incorporating next-generation genetic circuits that enable safe intravenous administration, expanding access to patients with inaccessible or metastatic lesions where local injection is not feasible. In preclinical studies, these circuits have demonstrated remarkable selectivity, producing IL-12 within tumors while shutting down expression in healthy tissues such as the liver and spleen. With STX-001 in clinical trials and STX-003 planned to enter the clinic in 2026, Strand Therapeutics aims to transform cancer treatment by creating programmable mRNA immunotherapies capable of delivering potent, precise immune activation and curing cancer patients with no treatment options remaining. Through this work, the company seeks to establish a new paradigm in oncology - therapies that are as programmable as software and as potent as the immune system itself.

History of the development of the solution/product (Intellectual Property, preclinical and clinical datas, development collaborations):

Strand's approach is grounded in robust preclinical evidence showing that IL-12 can eradicate tumors if delivered precisely. Self-replicating mRNA was selected as the therapeutic vehicle because it produces sustained protein expression and inherently stimulates innate immunity, acting as its own adjuvant to rally the immune system against cancer. IL-12 is produced only in tumor cells or the tumor microenvironment, sparing healthy tissues.

STX-001, Strand's lead program, is an LNP-encapsulated self-replicating mRNA encoding IL-12, administered via intratumoral injection. Interim results from the

first-in-human Phase I dose-escalation trial were presented at ASCO 2025. The study enrolled 22 patients with advanced solid tumors who had progressed despite exhausting prior standard-of-care therapies. All patients received STX-001 monotherapy on the trial. The findings were encouraging across safety, activity, and biomarker endpoints. STX-001 was well-tolerated up to 300 micrograms, with most treatment-related adverse events limited to mild or moderate inflammation. There were no Grade 3 treatment-related adverse events up to 100 micrograms, confirming that STX-001 avoided the severe systemic toxicities associated with previous IL-12 therapies. Encouraging monotherapy anti-tumor activity was observed. Multiple patients (refractory melanoma and sarcoma) achieved objective tumor responses, including at least one confirmed complete response (CR) and three partial responses (including a metabolic CR and a pathologic/molecular CR, respectively), along with prolonged stable disease in others. These responses in heavily pretreated cancers suggested that STX-001 could reinitiate immune activity where other therapies (including anti-PD-1, CTLA-4, or LAG-3) had failed. Biomarker analyses demonstrated dose-dependent increases in IL-12 and downstream interferon-gamma induction in plasma, confirming expression from the self-replicating mRNA. Biopsies from treated tumors showed increased infiltration of T cells and other immune cells, indicating that the tumor microenvironment was effectively reprogrammed. Many patients experienced regression of non-injected tumors (abscopal effect), an outcome that has remained elusive for many intratumoral therapies and provides early validation of the platform's potential to drive systemic immunity. These interim results established the first clinical proof-of-concept for Strand's programmable mRNA technology. Based on these data, the company has initiated dose-expansion cohorts and plans combination studies with anti-PD-1 therapy to further improve efficacy. Preparation is underway for Phase II development.

Building on STX-001, Strand is advancing STX-003 as a follow-on product designed for intravenous delivery. STX-003 uses a next-generation LNP formulation optimized for intravenous delivery and a self-replicating IL-12 mRNA backbone which incorporates advanced microRNA-regulated tumor-selective genetic circuitry. Preclinical studies presented at ASGCT 2025 demonstrated that intravenous STX-003 induced potent anti-tumor effects comparable to "uncircuited" IL-12 mRNA but with markedly improved tolerability. Treated tumors had high IL-12 expression, while the spleen and other off-target tissues showed minimal levels. Mice avoided systemic inflammation and weight loss even as tumors regressed. In non-human primates, genetic circuitry reduced off-target IL-12 expression from STX-003 by approximately 90% versus "uncircuited" controls, supporting the safety mechanisms' translational potential. With these promising data, STX-003 is planned for first-in-human trials in 2026 and will extend programmable mRNA immunotherapy to patients whose tumors are not amenable to direct injection.

Why this drug or device is innovative, the broad implications for

future research, and/or how it will improve the human condition:

Strand Therapeutics' self-replicating mRNA programs, STX-001 and STX-003, illustrate how programmable mRNA can redefine cancer immunotherapy. STX-001 is a best-in-class self-replicating mRNA immunotherapy encoding IL-12 that is engineered to express only within injected tumors, enabling potent systemic immune activation with minimal systemic toxicity. Interim clinical data have already shown encouraging evidence of tumor regression/systemic immune responses (abscopal effects) and a favorable safety profile in patients with advanced solid tumors refractory to checkpoint inhibitors. Building on this success, STX-003 is designed to extend treatment to patients whose tumors cannot be directly injected. By incorporating genetic circuits, STX-003 enables intravenous delivery of IL-12 mRNA that selectively activates only in tumor tissues while remaining inert in healthy organs.

Beyond oncology, Strand's platform holds promise for a broad range of diseases. The same principles (programmable regulation with synthetic genetic circuits) can be applied to build treatments targeting diverse indications. For example, STX-005 is an in vivo CAR-T cell therapy, using engineered circular RNA (circRNA) to reprogram T cells inside the body without requiring ex vivo manufacturing. This approach has the potential to democratize cell therapy by eliminating complex logistics and cost barriers. Preclinical results shared at ASGCT 2025 showed that Strand's integration of engineered IRES elements and proprietary sequence design led to strong, long-lasting CAR expression from synthetic circRNA. In preclinical models, this platform enabled efficient T cell reprogramming and potent tumor clearance, pointing to a future where off-the-shelf in vivo engineered CAR-T treatments could be accessible to far more patients.

More broadly, Strand's platform represents a paradigm shift in nucleic acid therapeutics. Classical gene and cell therapies rely on viral vectors or plasmid DNA, which can integrate into the genome and offer limited control over protein expression. In contrast, Strand's mRNA therapies remain transient, do not alter genomic DNA, and are fully programmable. Therapeutic mRNA functions in the cytoplasm, producing proteins before naturally degrading, which allows repeat dosing without accumulating genetic risks. Embedded circuits act like biological software, sensing cellular signals, such as cell type-specific microRNAs, and executing controlled therapeutic programs. For example, our research published in *Nature Biotechnology* and *Nature Chemical Biology* showed that mRNA circuits can behave like logic gates, activating treatment only in disease-relevant contexts while remaining silent in healthy tissues.

The use of self-replicating mRNA and circRNA extends the potency and duration of our drugs. The combination of durable expression and genetic circuitry creates therapies akin to precision-guided biologics: highly active where needed and inactive where not. In oncology, this capability helps overcome the long-standing toxicity challenges of cytokine therapies like IL-12. In immunology, it opens the possibility of in vivo

reprogramming of immune cells to tackle autoimmune diseases.

In summary, Strand Therapeutics is pioneering a new generation of programmable RNA medicines. From tumor-selective IL-12 immunotherapies to in vivo CAR-T therapies using engineered circRNA, Strand is translating years of synthetic biology innovation into tangible clinical impact for safer and more effective treatments across oncology, autoimmune and beyond.

Please provide appropriate references (PubMed, Abstract, Website):

Peer-Reviewed Publications

Wroblewska et al. Nature Biotechnol. 2015. <https://pubmed.ncbi.nlm.nih.gov/26237515/>
Wagner, Becraft et al. Nat Chem Biol. 2018.
<https://pubmed.ncbi.nlm.nih.gov/30327560/>
Li et al. Nature Cancer. 2020. <https://pubmed.ncbi.nlm.nih.gov/34447945/>
Kitada et al. Science. 2018. <https://pubmed.ncbi.nlm.nih.gov/29439214/>

Conference Presentations

AACR 2023 - STX-001 preclinical data.
https://aacrjournals.org/cancerres/article/83/7_Supplement/2731/721561/Abstract-2731-STX-001-a-locally-administered-LNP
ASCO 2024 - STX-001 Phase I design.
https://ascopubs.org/doi/10.1200/JCO.2024.42.16_suppl.TPS2696
ASCO 2025 - STX-001 Phase I results.
https://ascopubs.org/doi/10.1200/JCO.2025.43.16_suppl.9556
SITC 2024 Poster - STX-003 preclinical data.
https://jitc.bmj.com/content/12/Suppl_2/A1487
AACR 2025 - STX-003 preclinical data.
https://aacrjournals.org/cancerres/article/85/8_Supplement_1/3472/757217/Abstract-3472-STX-003-cancer-immunotherapy-with
ASGCT 2025 - STX-003 preclinical data.
<https://www.asgct.org/publications/news/april-2025/28th-annual-meeting-abstracts>
AACR 2024 - STX-005 preclinical data.
<https://www.asgct.org/publications/news/april-2024/now-available-27th-annual-meeting-abstracts>
ASGCT 2025 - STX-005 preclinical data.
<https://www.asgct.org/publications/news/april-2025/28th-annual-meeting-abstracts>

References File Document upload:

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