

# Seismic Therapeutic

## Category:

Best Startup

## Company Name:

Seismic Therapeutic

## Turnover and/or Funding:

This was not included on the list of questions. Please let us know if we need to add additional information here.

## Sub-Category:

Biotechnology

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

Seismic Therapeutic, Inc. is a biotechnology company shifting how immunology therapies are discovered and developed by integrating machine learning. Seismic was founded in 2021 by a team of leading immunology drug developers, machine learning innovators and company builders. The spark of the idea for Seismic happened when its world-renowned scientific founders, including Timothy A. Springer (Harvard Medical School and Boston Children's Hospital), a protein scientist and early builder of biotech companies, and Debora Marks (Harvard Medical School), a trailblazer in machine learning, came together with cutting-edge insights for applying machine learning to components protein structure and design. By October 2021, Seismic was ready to accelerate forward with the CEO appointment of Jo Viney, an immunology leader that has taken 13 drugs to the clinic at Biogen, Amgen, Genentech; most recently as President and CEO of Pandion Therapeutics, she led the company's \$1.85 billion acquisition by Merck. Under Dr. Viney's leadership, Seismic has raised \$247 million from blue chip life sciences and technology investors, and built a drug platform and team to usher in a new era of immunology drug development integrating machine learning to impact the lives of patients.

While there are wide-ranging ideas for how machine learning (ML) can revolutionize the drug industry, the veteran team at Seismic has carved out a clear direction for applying ML to create biologic medicines. Biologics are complex because they are derived from

living cells; they are also the predominant class of drugs to successfully target the immune system. Yet, their complexity makes them challenging to design into safe and effective medicines, because optimizing them involves inefficient, independent, sequential iteration and a protracted combination of steps that are time-consuming and expensive. Using the company's proprietary IMPACT platform, it is now possible to optimize the drug-like properties of a biologic in parallel - what Seismic calls "parallelization" - to accelerate the development of novel treatments for immunologic diseases.

Immunologic diseases, commonly classified as autoimmune or allergic, chronically affect patients throughout their lifetime and are steadily increasing in prevalence, with approximately 50 million Americans diagnosed with one of 100+ autoimmune diseases, including rheumatoid arthritis, lupus and myasthenia gravis. Despite the introduction of new therapies, systemic immunosuppression (steroids) is still the backbone of treating autoimmune diseases, leaving unmet needs for new therapies. Similarly, allergic diseases are common and growing in prevalence with approximately 20 million Americans suffering from food allergies. New therapeutic strategies are sought after that can treat allergies to multiple foods simultaneously to address the needs of patients.

Seismic is on a course to expedite and improve the creation of biologic medicines by applying ML. Now, only three years since its Series A financing, Seismic's first two drug candidates have begun human clinical trials, a third is in IND-enabling studies for allergic diseases, and a robust pipeline is behind. The Seismic team is forging a path to show the power of machine learning to accelerate the immunology biologics drug discovery process and doing it on an unprecedented scale, for better medicines for patients.

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

Seismic views itself as a new breed of drug developer, applying machine learning technologies for a specific drug modality - biologics - in a dedicated therapeutic area - immunology. Seismic's pioneering innovations using ML have resulted in its broad, wholly-owned pipeline and patent estate for immunology drug programs, including three issued patents and more applications on file. Based on these innovations, Seismic's two lead drug programs are in clinical trials, including a novel enzyme and a novel antibody therapy, to make a difference for patients with autoimmune and allergic diseases.

S-1117: S-1117 is a novel pan-IgG protease that can cleave all IgG subtypes thought to be responsible for autoantibody-mediated diseases. Overcoming the short half-life and immunogenicity of non-engineered bacterial protease therapies used in acute

conditions, S-1117 has been designed to drive durable IgG reduction with the potential for repeat dosing and a longer half-life in the body for more convenient dosing.

Preclinical results have shown that S-1117:

- addressed multiple, clinically-validated, orthogonal pathogenic mechanisms in autoimmunity within a single molecule.[1]
- directly cleaved circulating, immune-complexed, membrane-bound, and B-cell receptor IgG without affecting other Ig isotypes.[1]
- demonstrated superior efficacy in therapeutic models of ITP compared to a benchmark FcRn inhibitor.[1]

With its multi-mechanism approach, S-1117 aims to target a greater proportion of patients and achieve minimal symptoms/remission in a greater number of diseases than other emerging therapies, to address diseases such as myasthenia gravis, chronic inflammatory demyelinating polyneuropathy, and immune thrombocytopenia. On its path to patients, S-1117 entered Phase 1 clinical study in March 2025.

**S-4321:** S-4321 is a novel bifunctional antibody that agonizes PD 1 and Fc-gamma receptor IIb (FcγRIIb), two critically important inhibitory receptors expressed on different immune cell types. Specifically, S-4321 binds PD 1 with low affinity to optimally agonize the inhibitory receptor on T cells and binds FcγRIIb selectively (thereby avoiding the activation of other FcγRs) to agonize the inhibitory FcγRIIb receptor on antigen presenting cells. Unlike first generation PD 1 agonists, S-4321 is designed to target PD 1 without cell depletion, thus preserving regulatory T cells (Tregs), a cell type that is essential for maintaining normal immune homeostasis.

Preclinical results have shown these attributes for S-4321:

- The Fab domain of S-4321 demonstrated low affinity for PD-1 and achieved PD-1 agonism without causing target depletion or IL-2 production.[2]
- The Fc domain of S-4321 selectively engaged the inhibitory FcγRIIb receptor, preventing the depletion of PD-1 expressing T cells, such as Tregs, and avoiding the production of proinflammatory cytokines.[2]
- Furthermore, S-4321 promoted the induction of Tregs and prevented GvHD progression in a murine model.[2]
- Non-human primate studies demonstrated dose-proportional exposure and ~70% bioavailability of S-4321 with subcutaneous dosing.[2]

By engaging inhibitory receptors on both sides of the T cell/antigen presenting cell synapse, S-4321's unique dual-cell activity has the potential for clinical benefit in diseases driven by dysregulated cell-mediated immunity, including rheumatoid arthritis, inflammatory bowel disease, lupus, Sjogren's syndrome, dermatomyositis, psoriatic arthritis, and giant cell arthritis. S-4321 entered Phase 1 clinical study in April 2025.

**Why this drug or device is innovative, the broad implications for future research, and/or how it will improve the human condition:**

In designing novel treatments for immune-driven diseases, Seismic had developed novel, customized ML tools within its IMPACT platform. Overall, the ML tools have enabled parallelization, thereby eliminating numerous cycles of iteration and mutation combinations and shortening design test cycles for Seismic to rapidly identify its drug candidates that have moved quickly into clinical trials. Seismic's R&D approach identified previously unexplored sequences for designing biologic medicines with optimal drug-like properties.

Seismic believes that machine learning (ML) does not operate best in a silo within the complex process of making a new drug. Rather, Seismic predicts that near-term opportunities will be realized when the power of advanced ML technologies are guided by experienced drug hunters, like Seismic's experts in the field of biologics drugs for immunologic diseases.

Seismic's immunology drug developers guide the application of ML and work seamlessly and side-by-side with machine learning experts. The unique way that Seismic has integrated ML into drug discovery is embodied in the company's IMPACT platform which seeks to improve efficiency and scale over conventional therapeutics discovery. Machine learning is one of four key components within this platform - along with structural biology, protein engineering and translational immunology - and everything is guided by Seismic's experienced drug hunters.

By integrating the power of ML learning with a 'surgical strike' to address the challenges of biologic drugs, Seismic is showing that a quantum leap is possible for improved medicines for immunologic diseases. Seismic's new biologics are designed to target the underlying drivers of immune-driven diseases, improving on most current treatments that only manage symptoms and prevent further damage. The company's two drug candidates in clinical trials could deliver differentiated disease-modifying therapies which significantly improve morbidity and quality of life for patients suffering from a range of autoimmune and allergic diseases.

Seismic's proprietary IMPACT platform was instrumental in advancing S-1117 and S-4321 from hit identification to development candidate in about 18 months, in contrast to the industry average of 36 months. The IMPACT platform enabled Seismic to optimize multiple properties of biologics simultaneously, thereby reducing the number of design and test cycles to identify top candidates. The company built several proprietary ML algorithms to improve developability, tune function, and reduce immunogenicity.

Seismic has an extra ingredient at the heart of the company that drives its success: a very tangible company culture of inclusiveness and commitment to community impact. An employee-led IMPACTor team is empowered to initiate cultural awareness, philanthropic and volunteer activities that are an essential part of the Seismic culture that binds its team together. They are constantly challenging themselves to think about how to give back and create change and impact in their communities.

In an equally united and focused way, the Seismic team is driving toward making an impact on drug discovery by creating a major shift in immunology drug discovery by integrating machine learning for better biologic medicines. A decade from now, Seismic hopes to look back and see that this was a major turning point for incorporating ML to biologics drugs development.

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

Website: <https://seismictx.com/>

Press Release: Seismic Therapeutic Doses First Cohort in Phase 1 Clinical Trial of S-1117, a Novel Pan IgG Protease Therapy for Antibody-Mediated Diseases, <https://seismictx.com/seismic-therapeutic-doses-first-cohort-in-phase-1-clinical-trial-of-s-1117-a-novel-pan-igg-protease-therapy-for-antibody-mediated-diseases/>

(Cited as reference [1] in Development & Clinical Or Preclinical Evidence section)  
Poster: Preclinical pharmacology of S-1117, a novel engineered Fc-fused IgG degrading enzyme, for chronic treatment of autoantibody-mediated diseases, [https://seismictx.com/wp-content/uploads/2024/12/Seismic-ASH-poster\\_S-1117\\_FINAL\\_120924.pdf](https://seismictx.com/wp-content/uploads/2024/12/Seismic-ASH-poster_S-1117_FINAL_120924.pdf)

Press Release: Seismic Therapeutic Doses First Cohort in Phase 1 Clinical Trial of S-4321, a Novel Bifunctional Antibody that Agonizes PD-1 and FcγRIIb Inhibitory Receptors for the Treatment of Autoimmune Disease, <https://seismictx.com/seismic-therapeutic-doses-first-cohort-in-phase-1-clinical-trial-of-s-4321-a-novel-bifunctional-antibody-that-agonizes-pd-1-and-fc%ce%b3riib-inhibitory-receptors-for-the-treatment-of-autoimmune-disea/>

(Cited as reference [2] in Development & Clinical Or Preclinical Evidence section)  
Poster: S-4321, a novel dual-cell bidirectional PD-1:FcγRIIb selective agonist antibody for the treatment of autoimmune disease, [https://seismictx.com/wp-content/uploads/2024/11/Seismic-ACR-poster\\_S-4321\\_FINAL\\_111024.pdf](https://seismictx.com/wp-content/uploads/2024/11/Seismic-ACR-poster_S-4321_FINAL_111024.pdf)

**References File Document upload:**

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