

Ascidian Therapeutics

Category:

Best Startup

Company Name:

Ascidian Therapeutics

Turnover and/or Funding:

\$50 million Series A funding from ATP - Announced October 12, 2022

\$40 million Series A extension (ATP) - Announced November 8, 2023

\$1.8B partnership with Roche targeting neurological diseases - Announced June 18, 2024

Sub-Category:

Biotechnology

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

Ascidian Therapeutics is rewriting the future of genetic medicine-literally.

Rather than correcting single base pairs like traditional gene editors, Ascidian's RNA exon editors rewrite entire chapters of the transcriptome in vivo-whole exons at the kilobase scale-to repair the genetic instructions behind complex diseases. This approach opens new therapeutic possibilities for conditions that are out of reach for DNA-based gene editing or traditional gene therapy.

Founded by life sciences venture capital firm ATP and led by renowned neuroscientist and former pharma R&D executive Michael Ehlers, M.D., Ph.D., Ascidian launched in 2022 with a bold mission: to precisely and safely correct genetic mutations at scale, using the cell's natural RNA splicing machinery-without altering the genome and without using foreign enzymes.

In just two years, the company moved from stealth to the clinic, raising significant private funding and securing a \$1.8 billion collaboration with Roche for the discovery and development of RNA exon editing therapeutics targeting neurological diseases.

Breakthrough milestones achieved to date:

- FDA clearance and Fast Track designation for ACDN-01, the first-ever RNA exon editor to enter human trials, targeting Stargardt disease-the most common inherited macular degeneration (~30,000 patients in the U.S.), for which there are currently no approved treatments.
- Only RNA editor of any kind whose IND cleared with U.S. FDA as first regulator.
- Entered clinic faster and more efficiently than any prior gene editing platform.
- \$1.8 billion Roche partnership, validating potential of treating complex neurological diseases by large-scale exon editing of RNA.

What sets RNA exon editing apart:

- Works fully in vivo: Operates entirely within the patient's cells, eliminating the need for ex vivo cell manipulation or transplantation.
- Edits RNA, not DNA: Reduces risks associated with genomic modifications.
- Edits multiple whole exons at the kilobase scale, not only single bases: Precisely corrects multiple whole exons, which can address more mutations for more patients than current gene editing or base editing approaches.
- Uses no exogenous/foreign enzymes: Does not require foreign enzymes (e.g., bacterial enzymes), which can pose immunological risks or require delivery with dual AAV vectors.
- Maintains native gene expression: Ensures target gene expression is precisely controlled by the cell.
- Is agnostic to delivery vehicle: Is small enough to fit in delivery vectors such as AAV, and can be used with multiple, clinically validated delivery vehicles tailored appropriately for each program.
- Harnesses the splicing machinery present in every human cell: Enables precise correction of genetic mutations with broad applicability across a wide range of diseases.

This approach directly addresses a major unmet need. Many devastating inherited diseases-such as Stargardt disease, and many neuromuscular and neurological disorders-are caused by mutations in genes too large or complex for existing technologies. Ascidian's RNA exon editing therapeutics have the potential to reach these patients.

Ascidian is not just editing RNA-it's rewriting the blueprint of therapeutic development, offering a powerful new way to correct genetic disease at its source, with the precision, scalability, and safety profile needed to transform lives at scale.

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

Ascidian Therapeutics is redefining what's possible in RNA medicine through the development of novel, in vivo RNA exon editors-capable of replacing multiple contiguous exons with a single therapeutic agent.

This breakthrough technology was engineered by integrating high-throughput molecular biology with deep sequencing, machine learning, and advanced computational design to enable targeted, efficient, and durable RNA editing at the kilobase scale. The result: a powerful, first-in-class modality that leverages the body's own splicing machinery to repair faulty RNA transcripts-with no need for foreign enzymes, DNA editing, or ex vivo manipulation.

Inspired by ascidians (sea squirts)-marine organisms that naturally rewire their transcriptome through RNA trans-splicing-Ascidian has built RNA exon editing therapeutics that work with the body, not against it, offering the potential for a fundamentally safer and more scalable approach to correcting the genetic root cause of disease.

Lead Program: ACDN-01 for Stargardt Disease

Ascidian's lead program, ACDN-01, targets Stargardt disease, the most common form of inherited macular degeneration. This blinding condition-caused by diverse mutations in the large, complex ABCA4 gene-leads to progressive vision loss, typically beginning in childhood or young adulthood. Despite the severity and prevalence (~30,000 affected in the U.S.), there are no FDA-approved treatments.

Conventional gene therapy approaches are not suitable due to AAV vector size limitations, and DNA base editing lacks the breadth to address the mutational heterogeneity of ABCA4. In contrast, ACDN-01 has the potential to treat over 70% of people with Stargardt disease with a single dose, delivered with a single AAV vector.

Compelling Preclinical Evidence

As presented at multiple medical meetings, ACDN-01 has demonstrated efficient and specific ABCA4 exon editing across multiple models:

- Human cell lines harboring ABCA4 mutations
- Human retinal explants, cultured after organ donation, enabling measurement of editing in human photoreceptors
- Non-human primates, demonstrating durable, functional protein expression at time points extending to six months

The non-human primate data are the first to show therapeutically relevant levels of functional ABCA4 protein across any genetic strategy for treating Stargardt disease - and demonstrate the most efficient and durable RNA exon editing via trans-splicing in large animals ever reported.

This robust translational package laid the foundation for the ongoing Phase 1/2

STELLAR clinical trial, currently evaluating ACDN-01's safety and efficacy in humans.

Strategic Partnership: Roche & Neurology

In 2024, Ascidian entered a \$42M upfront, \$1.8 billion total value global R&D collaboration with Roche for the discovery and development of RNA exon editing therapeutics for neurological diseases. This collaboration reflects strong industry validation and positions Ascidian to bring first-in-class RNA exon editing medicines to some of the most intractable disorders of the central nervous system.

Together, Ascidian and Roche aim to unlock the therapeutic potential of RNA exon editing across multiple neurological diseases-and deliver a new class of precision medicines to patients who currently have few or no options.

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

Ascidian's RNA exon editing therapeutics offer a novel and highly differentiated approach to correcting the genetic basis of disease - with far-reaching potential to save and improve lives.

While existing approaches focus on editing single base pairs or delivering replacement genes, Ascidian has developed first-in-class RNA exon editors that can precisely replace multiple contiguous exons-at the kilobase scale, in vivo, and without introducing foreign enzymes or modifying the genome.

This breakthrough approach opens the door to a completely new category of RNA therapeutics that meet genetic disease head on-therapies that can restore normal protein expression by correcting large, disease-causing mutations at the transcript level. Ascidian's RNA exon editors are uniquely suited to treat diseases driven by mutations in large, complex, or highly variable genes-conditions that are often out of reach for gene therapy, gene or base editing, or modalities which don't address the root cause of disease.

Because Ascidian's RNA exon editors work entirely within a patient's own cells-harnessing the cell's native splicing machinery-they offer the potential for exceptional specificity, safety, and scalability. There are no foreign enzymes to trigger immune responses, no irreversible DNA edits, and no ex vivo manipulation or cumbersome cell therapy procedures required.

Far-reaching implications

Ascidian is currently advancing a focused pipeline of programs in high-unmet need areas across retinal, neurological, neuromuscular, and other genetically defined diseases.

Beyond correcting disease, RNA exon editing may also one day allow scientists to enhance biological resilience, insert protective gene variants, or rewire cellular pathways in real time. Hypomorphic transcripts, controlled feedback loops, or inducible splicing patterns could all be designed into future therapeutics-enabling transcriptome engineering that can match the complexity of the mechanisms driving disease.

As Mariano Garcia-Blanco, M.D., Ph.D., a pioneer in RNA trans-splicing, put it:
\"When we first began to elucidate RNA trans-splicing in the 1990s, my hope was such research would be taken forward to help patients with intractable genetic diseases. Ascidian is bringing that vision to fruition-and with efficiencies even more than I dared to imagine. I'm optimistic about Ascidian's potential to translate decades of effort in the lab into meaningful treatments in the clinic. Doing so could bring the RNA therapeutics revolution to the treatment of many more human diseases.\"

Ascidian is not simply advancing RNA therapeutics-it's expanding what's possible. By turning the cell's own machinery into a precise tool for transcript rewriting, Ascidian has created a new foundation for treating-and potentially eventually preventing-some of the most complex and devastating human diseases of our time.

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

1. Ascidian Therapeutics Launches to Rewrite RNA, October 12, 2022. Press release: https://ascidian-tx.com/media/Ascidian%20Therapeutics%20PR_12%20October%202022.pdf
2. Ascidian Therapeutics Raises \$40 Million in Series A Extension Financing, November 8, 2023. Press release: https://ascidian-tx.com/wp-content/uploads/2023/11/Ascidian-Series-A-extension-and-CEO-appointment-press-release-Nov-8-2023_final.pdf
3. Ascidian Therapeutics Announces First-Ever IND for an RNA Exon Editor as FDA Approves Trial Plan and Fast Tracks ACDN-01 in Stargardt Disease and Other ABCA4 Retinopathies, January 29, 2024. Press release: https://ascidian-tx.com/wp-content/uploads/2024/01/Ascidian-IND-Acceptance-Release_FINAL.1.29.24.pdf
4. Ascidian Therapeutics Enters Collaboration with Roche for Discovery and Development of RNA Exon Editing Therapeutics Targeting Neurological Diseases, June 18, 2024. Press release: https://ascidian-tx.com/wp-content/uploads/2024/06/Ascidian-Roche-Partnership-Press-Release_06.18.24.pdf

5. RNA exon editing: Splicing the way to treat human diseases, Molecular Therapy Nucleic Acids, September 10, 2024. Published article:
<https://www.sciencedirect.com/science/article/pii/S2162253124001987>

References File Document upload:

N/A