Top RNA Biotech Startups To Watch in 2021

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RNA therapeutics at a glance

For many years the focus of therapeutic developments and scientific research was directed at the genome and DNA-related proteins. Yet, there is a completely different level of cell regulation – transcriptome level, presented by RNAs. RNA molecules are not just intermediates between DNA and proteins, in fact, they carry enzymatic functions, control gene expression, and build up proteins from amino acids.

Major breakthroughs in transcriptomics have been made since the beginning of the century: the discovery of RNA interference in 2001 blew up the industry and was awarded the Nobel Prize in 2006. RNA interference is a gene silencing mechanism promoted by small siRNA molecules that are also exploited in patisiran and inotersen – first-in-class RNA therapeutics. Both drugs target transthyretin, a protein involved in the pathogenesis of transthyretin-mediated amyloidosis, and reduce the expression of its mutant version.

Today, RNA therapies can be categorized into 3 broad groups: RNAs that modulate DNA, RNAs that target proteins, RNAs that encode proteins, and hybrids of three listed approaches. Among existing modalities – ASOs, single-stranded antisense oligonucleotides that block mRNA translation, siRNAs and microRNAs that degrade protein-encoding mRNAs, RNA aptamers that tightly bind specific spots on proteins and regulate their functioning. In addition to that, last year showed a real boom in mRNA vaccines, with coronavirus vaccines and cancer vaccines being the most prominent representatives.

While there are numerous companies developing RNA-based therapeutics and vaccines, including major corporations like Pfizer, BioNtech, Moderna, etc, below we decided to list several biotech startups to keep an eye on.

Orna therapeutics

Orna therapeutics is a Cambridge-based biotech startup founded in 2019 whose main focus lies in the novel field of circular RNAs (oRNAs) which is the next step in RNA-based therapies. The company’s
innovation relies on the groundbreaking results of Prof. Daniel Andersson's group (MIT) that investigated oRNAs and found its superiority over linear analogs in terms of stability, protein expression, and synthetic availability. The potential applications of this technology are far-reaching, including Orna's initial focus on developing in situ CAR-T delivery system which avoids costly and complicated procedures of the current immunotherapies. The company already managed to close the Series A round in February 2021 raising $80 million from a group of prominent healthcare investors including F2 Ventures, Taiho Ventures, and MPM Capital.

Tidal therapeutics

Tidal Therapeutics is another Cambridge-based startup from 2019 targeting in vivo reprogramming of immune cells by RNAs. They have developed a technology that enables selective delivery of genetic cargo to specific cells by using proprietary nanoparticles. In contrast to the ex vivo, where cells are taken out of the body for modification, this approach would potentially increase safety, improve the dosing regime and reduce the risk of adverse reactions. Although the company is only in its preclinical stage, it has gained significant attention from big pharma and in April 2021 signed an acquisition agreement with Sanofi with $160 million of upfront payment. Sanofi has seen the potential for this technology to bring the CAR-T treatment to a much broader patient population by greatly reducing the costs and ready to invest an additional $310 million upon reaching the critical milestones in the R&D program.

Korro Bio

A USA-based startup Korro Bio has a smart approach to gene editing that relies on the natural RNA editing system, already present in all human cells. The company utilizes the short synthetic RNA strands to activate the ADAR (Adenosine Deaminases Acting on RNA) and guide it to make a specific fix in the messenger RNA. In comparison to CRISP technology when DNA gene material is altered directly, RNA editing only alters the genetic messenger and could be stopped at any time in case of adverse reactions. It also eliminates the need for an intrusive injection of a third-party enzyme, therefore decreasing the risk and optimizing the safety profile.

Although the company was founded in 2020 it has already raised a Series A in Sep 2020, attracting $91.5 million with Wu Capital as the lead investor.
Shape therapeutics

Shape therapeutics also leverages a natural ADAR RNA editing system and makes use of it in the number of their products, such as the RNA Fix™ system for single-mutation genetic diseases. They have also developed an RNA Skip™ to fix the mutations associated with premature stop codons and enable the production of fully corrected protein. In order to face the delivery challenges, they are developing an AAVid™ capsid delivery platform which through the screening between millions of possible AAV (Adeno Associated Viruses) selects the most suitable for specific disease tissues.

The company was founded in Seattle, USA in 2018 and gained attention from notable investors, including New Enterprise Associates, Tectonic Associates, Mission BioCapital who believed in the company's future and took part in Series A totaling $35.5 million.

Remix Therapeutics

The majority of the diseases are caused by protein malfunction and therefore are the main targets in the current pharmaceutical world. Remix Therapeutics, a company founded by former Atlas Venture Executive in Residence Peter Smith in 2019 in Cambridge USA, decided to get back to the origin of protein expression and alter at the level when the RNA sequences are produced. They are planning to use small molecule therapies which have advantages of simple dosage and increased stability inside the living organism. Their research team has presented a REMaster technology for the development of new therapies which consists of three main parts, such as a database of RNA messengers, screenings techniques to validate the target and a custom library of small molecules.

After an initial seed round when Atlas Ventures and The Column group supported the company with $16 million in Jan 2019, they quickly attracted more investors and held Series A raising an additional $65 million led by Foresite Capital in Dec 2020.
Triplet Therapeutics

There are more than 50 genetic diseases with expanded nucleotide repeats, which is basically a genetic error when some nucleotide sequences are excessively copied onto the new DNA. The target here is the DDR or DNA damage response, which normally should fix the damaged DNA when corrupted is responsible for most of these disorders, including Huntington's disease, myotonic dystrophy and others. Triplet Therapeutics is trying to handle these issues by developing an antisense oligonucleotide (ASO) and small interfering RNAs that can selectively inhibit the DDR-specific proteins thereby halting the onset and progression of diseases connected with expanded repeat.

Being founded in 2019 by Nessan Bermingham, a biotech entrepreneur and venture partner at Atlas Venture, the company already raised $59 million, including $49 million from Series A round led by MPM Capital and Pfizer Venture Investments, the venture capital arm of Pfizer Inc.

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