Timmerman Report

CAMP4 Raises $100M to Drug 'the Dark Side of the Genome'

By Jingyi Liu and Eric Dai, July 20, 2022

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Venture financing news has slowed down this summer, especially in the megadeal category of $100 million+ rounds.

Cambridge, Mass.-based CAMP4 Therapeutics is the latest to defy the trend.

CAMP4, a company targeting non-coding RNA to restore healthy protein expression, is today announcing a $100 million Series B led by Enavate Sciences, a portfolio company created by Jim Momtazee's Patient Square Capital. Other participants included Gaingels, an LGBTQIA+/Allies investment syndicate, and existing investors 5AM Ventures, Polaris Partners, Northpond Ventures, Andreessen Horowitz, and The Kraft Group.

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The company is developing antisense oligonucleotide therapies that seek to target regulatory sections of RNA to increase the production of certain proteins when the body isn't getting enough. David Bumcrot, the company's chief scientific officer, said that the targets are part of "a subset of long non-coding RNA that arise from regulatory regions of the genome".

Initially referred to as 'junk DNA' and 'the Dark Side of the Genome' at the heels of the Human Genome Project in the late 1990s, noncoding RNAs (ncRNAs) account for the majority of the human transcriptome. As ncRNAs do not encode for protein, they were mostly ignored by scientists and drug developers at first.

It was the pioneering work of researchers like Karen Adelman and Leonard Zon, at Harvard Medical School and Rick Young, at MIT; that showed that a subset of ncRNAs played a direct role in regulating gene expression. These studies revealed a key translational insight that launched CAMP4: tunable mRNA regulation by way of antisense oligonucleotide-regRNA interaction. Young and Zon are co-founders of CAMP4, while Adelman serves on the company's scientific advisory board.

David Bumcrot, chief scientific officer, CAMP4 Therapeutics

CAMP4's approach to drug discovery starts with mapping the regRNAs for a particular gene of interest.

"Our platform is the one that I think is the best in the world at showing you the regRNAs that are likely regulating genes of interest. If we want to regulate a gene through regulatory RNAs, we can tell you what your targets are," said CSO David Bumcrot. Following this, CAMP4 combines its experimental platform with computational modeling to identify and test drug candidates.

CAMP4 is prioritizing its development work on a pair of rare diseases caused by insufficient protein production – Dravet Syndrome and Ornithine transcarbamylase deficiency (OTC deficiency). Most approved and pipeline RNA-targeting therapeutics work through RNA downregulation. Gene therapy and mRNA approaches can drive protein

production through exogenous delivery of protein-encoding genetic material. However, these approaches are also limited by cargo size and immunogenicity.

“Regulatory RNAs have a unique feature where depending on where you put the oligonucleotide can allow for different changes in gene expression, meaning you can both up or down regulate genes. We became particularly interested in the upregulation element, because there are literally hundreds, maybe if not thousands, of diseases where you're just missing a little bit of healthy protein,” CEO Josh Mandel-Brehm said.

CAMP4’s lead indication in Dravet Syndrome is a good example of where targeting regRNA could circumvent traditional gene therapy limitations. Dravet Syndrome is a epileptic encephalopathy caused by haploinsufficiency of SCN1a. At about 6,000 base pairs, the SCN1a gene is too large for AAV gene therapy approaches and lentiviral approaches have limited tropism to the central nervous system.

CAMP4’s RNA Actuating Platform uses next generation sequencing to identify regRNA hotspots that upregulate SCN1a transcription. These hotspots are then matched to ASO drug candidates. Other non-SCN1a gene therapy approaches to treating Dravet Syndrome include degrading non-productive mRNA (Stoke Therapeutics), encoding a transcription factor to SCN1a to upregulate its expression (Encoded Therapeutics) or targeting suppressive and enhancer tRNAs (Tevard Biosciences).

CAMP4 is part of a growing number of biotechs developing drugs that seek to upregulate gene expression. Cambridge, UK-based Transine Therapeutics is a seed-stage company that is developing synthetic lncRNAs to upregulate mRNA in neurology and other indications. Seattle, Wash.-based Tune Therapeutics (which launched with $40M in December 2021) and Cambridge, MA-based Chroma Medicine (which launched with $125M in November 2021) employ epigenetic editing to tune gene expression.

CAMP4 seeks to differentiate itself with its concentration on antisense oligonucleotide interactions with regRNA. Bumcrot, the CSO, notes that one advantage of this approach is the ability to titrate doses to get to healthy protein expression.

Josh Mandel-Brehm, CEO, CAMP4 Therapeutics

“Regulatory RNAs act as rheostats, we're not talking about 10-fold changes, at least not today – we're talking about changes that are within a physiological range that we think makes sense for how the cell wants them to be used,” Bumcrot said.

Mandel-Brehm sees a future for both traditional and regRNA gene therapies. “When you start getting to broader populations the question is: what is the risk you want to take on? Can we get to a place where ASO is given once every six months, or once a year? Is that as good as once and done? Do you need once and done? When you start using these medicines in broader populations, you start getting into some of these questions about those risks versus advantages. I think there's a place for all these modalities that are really important and exciting.”