ENDPOINTSNEWS

July 29, 2020 08:03 AM EDT *Updated 08:16 AM*

Financing | Startups | Cell/Gene Tx

# 'Exquisite control': Flagship pulls off $85M rally around Omega Therapeutics' clinical push for epigenetic programming tech

Amber Tong
***Senior Editor***

Omega Therapeutics began, as all biotech fledglings incubated at Flagship Labs do, with an off-the-wall question: Can one control gene expression but not create the massive nucleic acid sequence changes that are created by gene therapy and gene editing?

Not long after the internal team began ruminating on the idea, as chief Mahesh Karande explained at the official launch last September, they found an answer in a seminal paper published by Rick Young's group at the Whitehead Institute. Genes and their regulatory elements, he found, generally reside in loops closed off by a pair of CTCF proteins — neighborhoods that were later named "insulated genomic domains," or IGDs. By sending regulator or effector proteins to dysregulated IGDs (there are more than 15,000 of them in total), Omega's pitch was to create a controlled epigenetic programming platform for what Karande calls the "control room of human biology."

ENDPOINTSNEWS

Thomas McCauley

"It wasn't at all clear 20 years when the genome was sequenced which regulatory elements affected which genes," CSO Thomas McCauley tells *Endpoints News*. "And the recognition that the 3-dimensional structure was the key to that puzzle was really what the company was founded on."

What the startup was able to also tap into was a way to formulate and deliver their new invention — a DNA binding domain liganded to an epigenetic regulator protein — with existing methods. Through connections to their Flagship kin who have broken ground in mRNA and lipid nanoparticle (LNP) technologies, Karande says even GMP manufacturing wouldn't be a problem.

In Karande's telling, it is the combination of the new biology and the "exquisite control" they can achieve with an "elegantly simple" approach that enticed yet unnamed investors to join Flagship for the long haul in a $85 million financing round.

"$85 million is better in our hands than in the hands of many other modalities," he says.

With five programs lined up in cancer, inflammation, autoimmune, metabolic and rare genetic diseases, the company expects to start its first clinical trial in 2021. The Cambridge, MA-based team of 45 will likely grow to somewhere between 50 and 60 before then.

Because the drug substance they are directing to specific, insulated sites is essentially naturally occurring and easily-degraded proteins used by the human body to tune genes up or down, Karande expects few hurdles on the safety front. Leveraging mRNA and LNP as delivery vehicles also lends itself to modular design, a key draw for the software analogy-inclined crowd.

"Even over the last year, year and a half, our cycle time in terms of concept to initial testing to really development-ready composition has shortened dramatically and really will support a very steady cadence of programs toward the clinic," McCauley says.

Once Omega proves its platform, he suggests, they might consider swapping out the time-tested LNP for other delivery methods.The same goes for targets: You want to start out with oncogenes, growth factors and other known but previously undruggable genetic elements before moving into uncharted territory.

Karande, who ran Novartis' Africa division and headed up a cancer franchise before jumping to biotech, isn't shy about reimagining medicine with this new class of epigenetic drugs. On top of all the potential for specific targeting and fine-tuning, Omega can select for the durability of the effector proteins that form their controllers, ranging from acute application to chronic use of up to two months.

"We are in unprecedented times when it comes to control of biology," he says.

AUTHOR
Amber Tong
***Senior Editor***
amber@endpointsnews.com@AmberTongPW