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Alkeus, a Bootstrap Success Story, Grows Up With \$150M Series B

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Thirteen years ago, Leonide Saad set out to do something meaningful with his life. He wanted to develop a drug that would make a big difference for patients who have no treatment options.

He combed through 250 different options until he found a candidate that obsessed him. It had potential to treat a leading cause of blindness in children and young adults. No big-name venture capital syndicate lined up. It was hard, and lonely. He couchsurfed at the scientific founder's house countless times to save on hotel bills. He thought about quitting many times. He scraped by for years on the relatively paltry sum of \$2.1 million in angel investment.

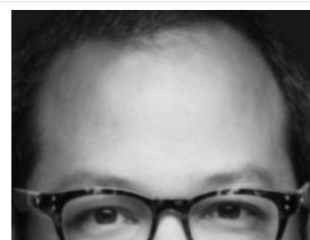
All of that is changing today. That company, Cambridge, Mass.-based Alkeus Pharmaceuticals, is being transformed from one man's obsession into a company with \$150 million in a Series B financing and a plan to seek FDA approval for a first-in-class drug in 2024. The aim is to treat Stargardt's disease, a leading cause of blindness in young people, and a disease which currently has no treatment.

Bain Capital Life Sciences led the financing after 14 months of rigorous due diligence, Saad said. The round also includes TCGX (a crossover fund that's part of The Column Group), Wellington Management and Sofinnova Investments. Joshua Boger, the founder of Vertex Pharmaceuticals, took an early interest in the company and Saad, and has now joined the company as executive chairman. Boger will now get to work with Saad to hire the team and build up the departments and processes necessary for Alkeus to file a New Drug Application in 2024.

If they do this right over the next year or two, they could be in position to manufacture and market a drug that could someday reach up to 150,000 patients worldwide.

"Leonide is the only person on the planet who could have done this," Boger said.

"As soon as I saw this molecule, I said 'it just has to be tested. It just has to be tested,'" Saad said.



The disease biology is straightforward. Stargardt's disease is usually caused by a mutation to the ABCA4 gene. When that gene doesn't work, accelerated dimerization of vitamin A occurs in the eye, creating clumps that damage the retina over time and cause vision loss. More than 30,000 people in the US are thought to have Stargardt's, and while some suffer from progressive vision loss starting around age 5, others begin to lose their vision in their teen years and through young adulthood.



Leonide Saad, Founder and CEO, Alkeus Pharmaceuticals

The idea for Alkeus originates from the lab of Ilyas Washington at Columbia University. His lab tested a deuterated form of Vitamin A. The drug, gileuretinol (ALK-001), is a modified version of regular Vitamin A, except with a stable, heavier isotope of hydrogen at the carbon 20 position. That modification is intended to slow down the dimerization rate of Vitamin A so that it doesn't go so fast as to create the clumps. The drug essentially replaces the normal Vitamin A that the body obtains through diet. The work was **published**, based on animal models, in the Journal of Biological Chemistry in 2011.

In theory, if you can stop the formation of clumps, you can stop damaging the retina.

Over the past decade, Alkeus showed that the deuterated form of Vitamin A could be given safely with a side effect profile in line with placebo. It can be delivered in a once-daily oral capsule. In vitro studies show it slows down dimerization by 4-5 fold, and in vivo mouse studies showed the drug could reduce dimer formation by 80 percent.

The key clinical trial delivered results in 2020. Alkeus randomized 50 late-stage Stargardt's patients — 30 on drug and 20 on placebo — and followed them over 24 months. Researchers found that the Alkeus drug was able to slow the growth rate of lesions in the eye by 21 percent. It was a statistically significant result, and one that appeared to become more clinically meaningful over time.

Those study results have been presented at meetings of the American Society of Retina Specialists, the American Academy of Ophthalmology, and the Association for Research in Vision and Ophthalmology. The data haven't yet been published in a peer-reviewed medical journal, Saad said. Alkeus also isn't yet disclosing the dose — a fact that will have to come out eventually.

Questions certainly do remain, but the clinical results were the basis for Alkeus receiving Breakthrough Therapy Designation from the FDA, and they were enough to secure a significant Series B from a syndicate of investors who know what they're doing. This single randomized trial, for a rare disease such as Stargardt's, should be enough evidence to seek FDA approval, in combination with other studies that make up a safety database with 150 trial participants.

"We're ready to go to the next step," Boger said.

The plan is to get GMP manufacturing that can meet NDA requirements and be ready to scale. There will be considerable work to do in medical education and patient outreach. Today, patients often go on a diagnostic odyssey, seeing 5-6 different doctors and taking 2-3 years on average before they get a diagnosis. By then, vision loss has usually occurred, and it's too late.

Others are **testing** gene therapies for Stargardt's, and even metformin, the diabetes medicine is being tried. Saad and Boger said they see ALK-001 becoming a baseline of therapy for Stargardt's that could be combined with other therapies.



Joshua Boger, executive chairman, Alkeus Pharmaceuticals; founder, Vertex Pharmaceuticals

While the first step in building the company will be seeking FDA approval for the late-stage Stargardt's population based on Phase II results, there will be much more work to do. The company has a safety database of 150 people that will be part of its application to the FDA, and some of them are younger patients who haven't suffered so much progressive damage to their eyes and would like to prevent it.

Given the mechanism of action, and the drug's ability to slow down the growth rate of lesions, it stands to reason that the drug could be more effective in helping people retain their vision if they can start getting it before going to elementary school. The key will be in getting a genetic diagnosis that would give physicians and families a reason to start giving a once-daily pill to a kid who doesn't yet show any signs of vision loss.

Alkeus is also testing another hypothesis with ALK-001 as a treatment for geographic atrophy that results from age-related macular degeneration. That additional indication is being **studied** in a 300-patient, randomized Phase III.

It's been quite a journey for a company that only had one employee for most of its history. The clinical data suggest it has a first-in-class, disease-modifying therapy for a form of blindness that afflicts more people in the US than cystic fibrosis.

Boger was back in his element and displaying the gift of gab I remember from covering him during his Vertex days in the 2000s. He sat shoulder-to-shoulder with Saad in an interview that ran long. I kept wondering about how cheap and easy such a drug might be to manufacture, and how practical it might be to distribute to Stargardt's patients in the US and around the world (especially in comparison to a far more complex biological modality like gene therapy). This is a simple drug that could have a big effect on patients' lives.

Questions about pricing, access, and global scale will go a long way toward determining how big an impact Alkeus might be able to make. Those are questions for another day. For now, it's worth marveling at how far Alkeus has come against the odds.

"The impossible has been done now," Boger said.

Saad was reflective toward the end of our conversation, when I asked him about how he did it. He went so far as to travel personally to all of the clinical sites to make sure the protocol was understood and followed correctly – normally the work of an expensive Contract Research Organization.

"You only live once," said Saad, 45. "How can I have a life that is meaningful and have an impact? I thought it would be a 5-year adventure. I put my personal life on hold. Made lots of sacrifices...I wanted to give up almost every day. It's hard. I thought about getting a cushy job. What kept me going were the patients and physicians I'm working with. I can't abandon them. That's what kept me going 13 years."

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