ThermoFisher SCIENTIFIC

Insider insights:

Tom Holmes, Global Head of Supply Chain
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Can a small start-up count on a global CDMO to help them change the world?

When two young innovators, Justin Klee and Joshua Cohen, Co-Founders and Co-CEOs of Amylyx Pharmaceuticals, discovered a potentially life-changing molecule in their dorm room at Brown University, they embarked on a journey to clinical trials to help treat people living with ALS. Amylyx' Global Head of Supply Chain, Tom Holmes, shares more about their experience teaming up with Thermo Fisher Scientific to manufacture their product.

How did you come to hear about Amylyx and meet Justin and Josh?

I met Justin and Josh through a mutual friend that worked at Vertex Pharmaceuticals for several years. He was doing contract work for them and thought that I would be a good fit for Amylyx as they were growing the company.

Had you ever worked at a startup like Amylyx before in your career?

No. Prior to Amylyx I had never worked at a startup. I spent 24 years at Biogen in Cambridge, MA before meeting Justin and Josh and joining Amylyx. Even in the very early pre-commercial days at Biogen, we had multiple drugs being sold through licensing partnerships with big pharmaceutical companies. I was intrigued by Amylyx' vision and mission to address ALS and the tenacity of the young, entrepreneurial co-founders. They were just very refreshing and sparked my energy and interest immediately.

What drew you to them? What was interesting about working with them?

There are a number of things that drew me to Amylyx. One was the indication of an illness that has been left with unanswered questions for too long. The second was the opportunity to work at a small company and be on the front lines of making a real difference. And the third – and not in this order – was the connection I felt with Justin and Josh.

Justin, Josh and I had several appointments early on to discuss the challenges they faced in their supply chain and manufacturing operations. It was at that point that I thought I was probably going to join them in a consulting role. But these discussions further underlined the need for someone to own supply and CMC full-time.

At that time, did they already have a manufacturing partner?

When I met Justin and Josh, they were just moving from another rather small manufacturing CDMO to Thermo Fisher Scientific's facility in Whitby, Ontario. The conversations were around technical transfer, scale up, and going from clinical phase manufacturing up to commercial manufacturing.

They were spending a lot of time in the area of managing supplies and general CMC issues, mostly because they had not yet really focused on that area in their careers. They were novices, I would say, in making supply decisions and overseeing manufacturing operations.

You heard that they were moving to Thermo Fisher as their partner. How did how did that make you feel?

Once I found out that they were working with a company like Thermo Fisher, I knew that they would be working with a reputable, high-quality enterprise. It made me more interested in the role and in the future of their supply chain.

What were the first challenges when you came on board at Amylyx?

Going from being at a company of approximately one thousand employees to becoming employee number four was definitely a challenge. The other challenge in a small company is there is nobody to delegate work to so you have to be very judicious with your time and energy. You have approach every day with a view of what must be done and what would be nice to get done. The company that I worked at before was primarily focused on biologics and large-molecule manufacturing. Amylyx is focused on small molecule manufacturing, so there are some differences in approach. I would also say the fact we really only had one shot on goal with this single asset was very different from where I had previously worked.

In your eyes, was it "all or nothing" if you were going to work for Amylyx?

Yes, and I knew that going in, which was worth the bet for several reasons. ALS is one of these unique diseases where, even though it's a very small patient population, everyone seems to know someone who has ALS or has had it. That was a big draw for me. I was also attracted to the chance to build something from the ground up. I've never had that opportunity before.

With regard to manufacturing, were you concerned that you would get lost in the shuffle as a small company?

I never felt that way. I have always believed that with CDMOs – while they are cognizant of the money you spend with them – what really drives the business is the relationship, the transparency, and the working agreement that you have with their senior management and project teams.

We always say this – and it is very much something that we believe in– that the Thermo Fisher manufacturing site in Whitby is an extension of Amylyx. They are Amylyx' eyes and ears in making the product. It's really important that we have that connection with our project, technical, quality, and regulatory teams. We feel it's a partnership and that the employees of Thermo Fisher are extensions of the Amylyx family.

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What are some of the obstacles and challenges you face? Have you gotten past them?

One of the challenges for any project – and we're no different – is the timeline pressure. You set up a timeline that has some dependencies and as things move forward, especially in manufacturing, some of those dependencies don't go as planned, such as additional testing or documentation. But, we understand that the ALS community is counting on us to deliver a new, effective therapy. Every day or week that we can shave off the timeline is extremely important for us.

Where do you stand currently and what are you looking forward to?

Right now, we're actively engaged in regulatory agency discussions in the US, Canada, and Europe. In terms of where we are with Thermo Fisher relative to commercializing this product, we have completed scale-up and validation, which is demonstrating process control through three consecutive batches. We are now preparing product for further clinical work and our commercialization plans.

That must be pretty exciting after all this work?

It's exciting and it's rewarding. When I started, I think Amylyx had done approximately five batches for two distinct clinical trials. We're now up to 17. After the validation batches, the three consecutive batches that I mentioned will be well into the twenty-batch range. It's extremely rewarding to be at the point when you feel like you've got process, consistency, and control.

What has Thermo Fisher's role been with helping you ramp up production to that level?

We ran different models of forecasts and provided the Thermo Fisher team with the patient numbers for the US and internationally. Based on the forecast of what we thought our product would likely consume in the marketplace, the Thermo Fisher team at the Whitby site had to ensure they had enough capacity. They determined, and we agreed, that they indeed would need a second machine. As part of our discussions on going from development to commercialization, Thermo Fisher factored the cost of a new proprietary machine into their capital budget and purchased it. This is the key piece of equipment in our manufacturing process. In our partnership, transparency is extremely important.

As you're working with Amylyx and taking this process forward, what concerns keep you up at night?

The biggest concern that I have – and I think it's consistent with any new product introduction – is the variability of the uptake and how fast adoption and reimbursement of the product might be. We know inherently that forecasts are wrong, but we don't know by what percentage or in what direction. What keeps me up at night a bit – especially in a launch scenario for a drug with this impact – is how we maintain agility in responding to what actually happens in the commercial marketplace. Because in the end, people living with ALS and other neurodegenerative diseases have no time to wait.

In the very early launch days, a company like Thermo Fisher knows that there is going to be volatility in the uptake of any new product, and that we may need to come back with revised production numbers, total quantity, and batch quantity numbers. It's important we maintain strong communication through the launch period.

When you look down the road one, three, or five years from now, what do you see in Amylyx' future?

It's my hope that we will change the paradigm in terms of what people with ALS believe their life expectancy will be, and that we will extend the opportunity for us, and other companies, to further develop therapies that could be delivered in combination with our medicine or improve medical options. We've had the privilege to talk to many people living with ALS, and consistently we hear that they're looking for something that will allow them to retain their function, prolong their life, and give them time – time with their families, time to enjoy life, and time to hopefully discover additional treatment options to keep them healthy. I believe this is just the beginning of potentially changing the life expectancy for all those with ALS.

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What's your favorite memory of working with the team?

About two weeks after I joined Amylyx, we went to Manhattan, New York, for DCAT, a convention of contract manufacturers and chemical API suppliers. During that week, I set up business connections with all the suppliers in the Amylyx supply chain. Taking Justin and Josh through each of those meetings, talking to the top-tier management of each of our suppliers, and letting them know the importance of what we were doing at Amylyx, was a great experience. We also got to go out and enjoy ourselves a couple of evenings, which broke the ice and made me feel like I was part of something special. I think people who break bread together, travel together, and spend time together have a better working relationship.

Given your experience at Amylyx and partnering with Thermo Fisher, what is your advice to other companies like Amylyx?

More and more smaller companies need to think about innovating continuously as they grow. At times, patient communities don't get enough attention from larger drug developers because the size and depth of resources that make them successful in terms of innovation, speed and decision making also mean that they are more compartmentalized, complex, and slower to respond. Smaller companies with more accessible leadership can communicate more directly with less layers of review and they have a better chance of tackling unmet "orphan indications".

One of the things that a contract manufacturing enterprise - Thermo Fisher in particular - provides companies with is end-to end-capability. As a small company, you can have a novel, innovative idea, as Justin and Josh did, and bring it all the way from early toxicology studies, animal studies, first in human studies, multicenter placebo-controlled studies, and to regulatory agencies for a potential approval without having any brick and mortar, testing labs, or distribution capabilities.

The world we live in today has highly experienced, dedicated, professional sites like Thermo Fisher that can partner with you as a virtual, small company, and give you access to patients who need medicine.

What is your advice to young innovators like Justin and Josh?

My son is a third-year university student. What I tell him is to dream big, don't be afraid to ask questions, and don't sell yourself short in terms of your ambition. What Justin and Josh have shown me is that they don't have all the answers, but they have the tenacity to find out the answers to questions that lead them to really big ideas. They were bold, innovative, and creative and did a lot themselves just by asking experts in the field the right questions and going from there. That's an important aspect of the story: be curious and bold enough to go out and find the answers you're seeking, find people who have the answers, and don't give up.

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