

John F. Crowley: What we saw with people with Pompe when they switched from the existing standard of care medicine, from almost every patient we could make them stronger. If they could walk, they could walk further. If they could breathe, they could breathe a little bit better.

[MUSIC INTRO]

Jerry Lee: Hi everyone. And welcome to Talks at GS. I'm excited to be joined today by John F. Crowley, Chairman and CEO of Amicus Therapeutics.

John's involvement with biotechnology started in 1998 with the diagnosis of two of his children with Pompe Disease, a rare, severe, and often fatal neuromuscular disorder. He left his role at Bristol-Myers Squibb to join and found Novazyme Therapeutics. And since 2005, he's been chairman and CEO of Amicus Therapeutics.

John, thank you so much for joining us.

John F. Crowley: Yeah, Jerry, it's such a pleasure to see you again in person. So, this is terrific.

Jerry Lee: Where I'd like to start is really with your involvement in biotechnology. As I mentioned before, it started with this 1998 diagnosis. And with that, your, candidly, your dive into biotechnology, to the science. And so, I'd love to start the story there, with that diagnosis and with your role at Bristol-Myers Squibb, how did you think about prosecuting this problem?

John F. Crowley: Yeah Jerry, you know, that takes us back to 1998. And at the time it seemed to be an extraordinary experience and set of events for our family.

As we've learned now in this 23 plus year journey, it really isn't, coming into the world of science and medicine, for people who didn't know anything about it. You know, my dad was a cop in North Jersey. Growing up, I really didn't like science. I wasn't very good at it, which is probably why I went to law school and picked more of a liberal arts background.

But you know, we had at that point in March of 1998, we had three children. We had our son John, who was just over three years old. We had Megan, who was 15 months old. And we had Patrick, who was seven days old.

And I still remember it well. It was a Friday the 13th, March 13th, 1998. I was just out of business school and we had started working at a consulting firm. And you know, like many people in banking and other careers, working around the clock.

And by about a year of age we had realized that our Megan wasn't doing the things that a year old should do. Otherwise perfectly healthy, alert, remarkably precocious even as a young, young child. But wasn't pulling up in the crib. Wasn't taking those first steps. And we went from pediatrician to neurologist to expert. From blood tests to muscle biopsy. And on that Friday the 13th we got the diagnosis.

We were actually called the day before to come see the doctor. It wasn't a clinic day, so it was quiet. It was at Oakland Children's Hospital. And the doctor very nervously with a social worker said they had the test results and that they were seeing something called glycogen. So, a stored form of sugar building up on the pathology slides and in Megan's muscles. And I remember the doctor saying it looked like it was a disease called Pompe Disease. And I remember asking him, "Is it serious?" And he said, "Yes, it's very serious."

You know, our fear up to that point in those couple of weeks or month or two before was that maybe Megan wouldn't walk. And it was way worse than that. The doc said that she had this rare form of muscular dystrophy. There was no treatment. And she would live to be but a couple of years old. That she'd get very weak and very sick very quickly. And you talk about just a punch to the gut for Aileen and I, my wife and I.

And then he looked, and we didn't have Megan with us, but we had Patrick, seven days old in a car carrier. And the doctor looked at Patrick and said that there is a 25 percent chance that he would have the disease and need to be tested.

And we went through, really that day of the long ride back to Walnut Creek in California, we went through a lot of emotions. We went through the shock, the grief, the denial, the anger. And by late that night, I was online trying to do some research and I don't think Google was even started yet, but there were some older search engines, and I got into the world of science and medicine and papers.

And I remember waking Aileen up in the middle of the night and rattling off this paper I had found from Duke University about a

test in an animal model of Pompe Disease and that they had an enzyme therapy in development. And I'm rattling all this off. I didn't understand what it meant. And Aileen asked me, "What does it mean?" And I remember telling her, "I think it just means that there's some hope."

Jerry Lee: It's an amazing start to the story. When you think about where you are today as Chairman and CEO of Amicus Therapeutics, a commercial biotech, when you rewind to those moments in Walnut Creek, when you think about leaving that job at Bristol-Myers Squibb, how did you actually think about that departure or that transition, that transition into, not just biotech and science, as you say, but to entrepreneurship?

John F. Crowley: You know, Jerry, it was a long two years going from March of '98 to March of 2000 where I left the consulting firm. We moved back east. I worked for Bristol-Myers. Just a wonderful company. Incredible people. Incredibly supportive of our family.

You know, I remember walking into Bristol and seeing on the wall, you know, the mission statement "to extend and enhance human life." And you know, for us with children with, you know, this devastating disease, that kind of hit home, that mission aspect of it.

And you know, for us going through all of that, and in that really 12 month period after the diagnosis, Megan did get profoundly weak and needed a feeding tube to eat. Needed a ventilator to breathe. She was in the ICU by September of '98. She almost died three times in a week. Her heart stopped. Pretty devastating. And then six months later, we went through it all again with Patrick. So, within a year we had two kids on ventilators.

I was at Bristol. It was a great experience. But I never went there to kind of go through a boot camp to learn how to run a biopharma company. I did it because it was a good job. It paid well. Good health insurance. Good people. And in my nights and weekends, researched everything I could and traveled to the conferences and met doctors and finally got to the point by March of 2000 where time was our greatest challenge. You know? We had to beat this mistake of nature. But we also had to beat time, that sense of urgency. And that's really what caused me to leave Bristol to partner with this researcher at the University of Oklahoma to launch us into this world of medicine.

I think, Jerry, more than anything, we didn't want to look back years later if the kids' lives had been very short and wish that we had done something else. We didn't want to have any regrets.

So, for us to just, you know, find something that would buy more time. That would, you know, extend the kids' life, to give them better quality of life. I remember, taking it back to the night Megan was diagnosed, I thought, prayed. And I just prayed that she'd get to her second birthday. Just to be two. Something we take for granted with kids these days. But just to get there.

And then we got there. And then it was, okay, can we get her to her third and so on? And we'll come to where Megan is today, which is in a beautiful place with her success in life and the inspiration she's provided us and so many. But that's really what we wanted to do, was to just try to move the ball forward.

But becoming an entrepreneur was more that I did it because we had to. Nobody else was really doing research in a biotech in Pompe Disease at the time. And we just wanted to catalyze the field. And I wanted to be all in.

And so, I left that job at Bristol and went to help start that small little company.

Jerry Lee: As you thought about starting that company, you've referred to laboratories where you've kind of considered various technologies. You ended up going with the University of Oklahoma. How did you think about prosecuting that specific lab, that specific PhD, that specific team?

John F. Crowley: Took me about a year or two to really understand the science and the field and the medicine. And I had a lot to learn. And I met some great researchers in Europe, in the Netherlands, at Duke University. Now, there weren't a lot of people working on Pompe, but there were a few.

And the last that I met was a brilliant glycobiochemist out of the University of Oklahoma. And he had an idea that, you know, what you need to do is to think about an enzyme replacement therapy. That was state of the art technology then. And to make an enzyme therapy that has these sugars, these carbohydrates attached to it.

So, the kids are missing a protein. But you've got to make sure that if you're infusing it into their blood, that it's getting to their muscles, all muscles of their body. And he had an idea

and a technology to manipulate the carbohydrates to allow greater absorption and uptake of the enzyme, which should make for a better drug.

But frankly then, we didn't have any drug. So, any drug would have been a step ahead. Just something, again, to buy time and quality of life.

And candidly, I remember he was frustrated one night on the phone. I was frustrated because of this race against time. And finally, I kind of volunteered, I said, you know, "Heck Bill, maybe I should just come out and run it." And there was this kind of awkward pause. And then I did. I was on a plane the next day. We spent all day together. And I came home that weekend and Aileen and I talked about it.

You know, I tend to be a little more analytical and structured. And weighed the pros and cons. And Aileen just said, "You know what, if it's what you think we have to do and it's in your head and your heart, just go ahead and do it." And it was tough because not only would I be giving up, you know, the job at Bristol, I'd be coming into something that was about as risky as you can get.

Jerry Lee: Let's zoom back out to COVID. What's been your reaction to the way in which we've galvanized the biotech and pharmaceutical industry to really fight the COVID pandemic?

John F. Crowley: I mean, the world was rocked for all of us. Immediately we went into crisis mode at Amicus. I had learned in my military days, you know, working in a high temp organization, particularly in the global war on terror around the world, we managed a good part, in our part of the world, the war on terror by video conference. And we took some of those principles of leadership. So, we managed that. Every company did that.

But to see the extraordinary response. To go from sequencing the gene for COVID-19 in January of 2020, to into clinical studies a couple of months after, to where we are today? You know, the biopharmaceutical industrial has saved the world. We knew we'd develop a vaccine. Everybody said it would take three, five, seven years. And those of us close to it, who believed in the science, believed in the leadership, thought if we could break down barriers, we actually could do it a lot faster than that and alleviate an enormous amount of human suffering, medical suffering, life suffering, economic suffering.

But we had to beat time. So, that sense of urgency, that working 24/7. But it wasn't just the companies in development. It was the entire ecosystems: the systems around the manufacturing, the clinical trials that were stood up, incredible efforts, the regulatory response at the FDA. You know? This was around the clock with Peter Marks' leadership and others, Janet Woodcock at FDA. This was priority number one. And they, too, made it happen. It was a change of mindset.

And I actually think, you know, as we think about as we develop medicines in rare diseases, those are things we think about all the time. Great medicines that have to profoundly change people's lives. We have to beat time. It has to meet a regulatory gold standard.

And the fourth part for us and for COVID was access. 100 percent access. And those, I think, are themes and lessons in drug development that we could take to accelerate research and development, clinical research, break down regulatory barriers and move technologies in a safe, effective way to patients faster. If we could do that and take that as lessons from COVID, I think we'll be in a much better place across the board as a society.

Jerry Lee: You're making me verklempt. Never were truer words said, John. I feel like one of the biggest thrills of my career at Goldman Sachs has been serving you, has been serving Amicus, has been serving Patrick, has been serving Megan, has been serving patients with Pompe, with Fabry, and hopefully, at one point, gene therapy.

I will say, the words you just used really resonate with me. Over the last year, we as a firm, we as a team, we may play a very small role in that ecosystem. But that very small role is still a thrill. It's a thrill to us in healthcare. It's a thrill to our analysts, our associates. It shows that, you know, every little piece of the system came together last year to the point where many of our colleagues, our family members, people in New York City now have all been jabbed twice. And it's just extraordinary how the system came together. So, I thank you for that.

Going back to COVID, I'd love to hear a little bit more about your leadership during COVID. So, you're commercial with Galafold. You're working through the FDA with AT-GAA. You're engineering partnerships left and right trying to push the envelope on new science like gene therapy. What was the biggest

challenge that you as a leader encountered during COVID last year?

John F. Crowley: People were scared. Uncertainty brings anxiety. They were scared for their physical health, their economic wellbeing. Are they going to have a job? Are we going to be able to deliver on our clinical trials, our commercial? All of it? You know, would the company fall apart?

And so, we needed to reassure our team. So, we put in place a program called Amicus Cares from day one. In fact, the very first thing I did day one, I gave every nonexecutive in the company a \$1,000 one-time bonus. And I said, "You know what, you're going to have expenses you don't know. I know many of you have good careers. Just take it. Use it for whatever." And it was meaningful for many people. But it was also a sign, a sign that we care. A sign of our financial strength. And that we would, you know, go over and above without anybody ever asking. So, we put a lot of programs in place.

And I learned from my time in the military as well, when you're managing a crisis and you're doing it remotely, you've got to be a very visible leader. So, one of the things I undertook was, I said within the first 30 days I want to see on a Zoom screen every Amicus employee. So, within 30 days, we did it in small groups. So, a country may have five employees. I don't think any group was more than a dozen or so, we broke some of our larger teams up. And these are people who I typically wouldn't be in meetings with as part of the normal flow of business. But it was important that I hear from them, but that they see me, and you convey a measured confidence.

The other part of it is, in addition to being visible, you've got to be honest. You've got to be transparent.

Jerry Lee: Let's talk a little bit about the military. You were a US Naval officer, commissioned officer. You were part of JSOC, Joint Special Operations Command. You are a veteran of Afghanistan. I've been on board calls with you where you've been on sat phone from Afghanistan. Tim Ferriss, a very well known podcaster called you a modern day Captain America.

John F. Crowley: Tim needs to meet more people. But that was very, very kind.

Jerry Lee: He also said you've got the biggest shoulders in business. And so, I guess my question is, we focused a lot on

entrepreneurship, on leadership in biotech, what lessons do you take from your military experiences into the leader that you are today?

John F. Crowley: You know, I think, Jerry, what the military will do will prepare you, give you leadership responsibilities at a very early stage in your career, that you otherwise wouldn't typically get. And in time of conflict, do it in a way that's incredibly intense and, you know, in many cases entrust you, in wartime for sure, but in peacetime as well, you're in training, with the lives of the people that you work with. So, I think you could take some basic, I don't want to say basic, but important lessons about being a leader in the military. And you know, lessons around the principles of leadership, around integrity leadership, around servant leadership, teamwork, all of that, taught extraordinarily well in our armed services.

I think maybe more than anything though, you learn that sense of why you're doing what you're doing. You're doing it for the people around you. And you're doing it for your country. You're doing it for a greater sense. And so, ultimately, you learn about mission. You learn about purpose. And you learn about sacrifice.

In one of my rotations out of Afghanistan, I remember it was we were in Bagram Airfield and we were waiting for then Air Force rotator. And it was like seven hours delayed. So, if you think, you know, commercial airlines are tough sometimes, you know, you just sit there and you wait. Just you want to get home. We'd been in a pretty intense time there. And I looked up at a poster on the wall and it had a silhouette of US troops. And beneath it, it just had the words "Live of life worthy of their sacrifice." And I looked at it. And I found meaning and inspiration in it. But then I kind of went back to, you know, I'm kind of hot, where can I get a bottle of water? And I just want to go. It's going to be three days, four days to get home.

I got home. And a couple of days later I got a call from one of the very senior officers, actually senior enlisted at our command. I was an intelligence officer working for a particular Navy SEAL team. And I got a call from a senior enlisted. And he said, "Sir, I just want to let you know you're going to see something on the news shortly. They're gone." I'm going, "Chief, master chief, what are you talking about?" He said, "Sir, the team, they're all gone. There was a helo shot down, helicopter shot down." It was the guys I worked with. It was my team. 31 guys. Shot down and killed. Who I had just left a few days

before who we had served with, worked with, sacrificed. You know? And to see their sacrifice. To two days later go to Dover and to be there to receive their remains, Dover Air Force Base. To see their families. You know? I think to see that raw emotion. And you see the true face of sacrifice.

You can see all the bumper stickers and "thank you for your service" and the parades and the warm embraces and sometimes the very sad returns. But for me, to have seen-- and we had lost other folks, you know, in the journey. But to see it on that scale and to see it so real, and to see that raw emotion on those families' faces is something I'll never forget. And certainly, paints for me the notion of what true heroes and true sacrifice are all about.

Jerry Lee: I appreciate you sharing that with us John. I think that you honor your team the way you carry yourself, the way you lead Amicus everyday.

John F. Crowley: Yeah, just like the poster said, just live a life worthy of their sacrifice.

Jerry Lee: Let's take a turn back into biotech. Let's talk a little bit about Amicus. This morning, congratulations, you announced the successful pre-BLA meeting with the FDA for AT-GAA for Pompe. How has that adventure been? And what are you looking forward to on AT-GAA?

John F. Crowley: Yeah. So, with Pompe Disease, when we founded Amicus, Jerry, we had a big vision. We wanted to become one of the world's leading global biotech companies. Novazyme was a marathon. Or it was a sprint, rather. It wasn't a marathon. It was 18 months, start to finish, to go from a couple of us forming that company to the sale to Genzyme. And then Genzyme took it on them to develop that first generation medicine. And it was important. And it saved a lot of people's lives living with Pompe, including Megan and Patrick's.

But we knew by 2004/2005, we needed a better approach, a step forward. And that's oftentimes what we see in biotech. You know? It's these incremental steps forward. Two steps forward, one step back usually. And sometimes we get that backwards.

Look, we really wanted to build this significant biotech company. We had an original technology that became our now approved medicine for a rare disease called Fabry disease. It's been, as you know, a very, very successful product for patients

for Amicus.

In Pompe we struggled for a number of years finding the right technology. We actually had a clinical program that failed. Stopping that program after four years of investment was really difficult. We went back to the drawing board and we thought what other way could we make a technology, use a technology to make a medicine in Pompe?

And our now brilliant, he's always been brilliant, but our now Chief Science Officer Hung Do, who was with me as Novazyme, he had the idea that he could make an enzyme therapy that would be better targeted, similar to the idea that we had at Novazyme. But he had a different way to do it. A way that could be more effective, potentially, and that could also be much more manufacturable.

That was in 2010. It took six years to go from that idea to a molecule to put it into the clinic. And now we've been doing this for five years in clinical studies. We've had great success in our phase I/II studies.

What we saw with people with Pompe when they switched from the existing standard of care medicine, from almost every patient we could make them stronger. If they could walk, they could walk further. If they could breathe, they could breathe a little bit better. Quality of measures, you know, for people like my Megan in a wheelchair on a ventilator, you know, can she move her arms better? Type better? You know, personal hygiene?

When we went into that study, Megan participated in a patient symposium where we asked, "What's meaningful for you?" And some patients were talking about, you know, going back to work and walking further and lifting weights again, the things that were meaningful for them. What Megan said, she was a senior in high school, she said, "I want two things I would like." And she was nervous. And she's not a nervous type. She said, "Number one, I'd like to be able to breathe for one minute without my ventilator," because she knows it's an accident with her trach that could be life threatening. So yes, while she'd love to breathe without a ventilator, just one minute off would be hugely impactful for her.

And then she said, "The second thing is, if I could speak more clearly so that when I go to college, I could make more friends." You know, you can take all our clinical researchers and doctors and experts in the room, just to hear that very,

very human aspect of what's meaningful in making the medicine. It really shaped how we think about the development.

And you know, fast forward to where we are. We've just completed the pivotal phase III study. And yes, this morning, we don't always get good news in biotech, but it's nice on a Monday morning to put out a good press release.

We had a meeting a short while ago in April with the US FDA. Presented those results from our phase III, our plan for now moving to the regulatory submissions for approval. The FDA is aligned with our plan to move forward. They provided very helpful feedback that will make, I think, a very strong submission.

I know the drug works. I know it helps people. We're preparing for a global launch to get it to as many patients as quickly as possible. And that's all we ever want, whether it's us or another company, patients and doctors to have choices of medicine and let them individually decide.

Jerry Lee: Thanks very much John. I know you've talked about Megan a couple of times. And I'd love to spend just a minute on Megan.

When you think back to those moments, you know, 20 plus years ago to where she was walking across a stage, graduating from Notre Dame to now being a graduate student, an adult woman graduate student at the University of North Carolina, what reflections do you have on that experience?

John F. Crowley: You know, again Jerry, I think what we all want for our children, and I told this to my daughter as she was making her decision for college, we want them to be happy, safe, and fulfilled. And for Megan, she lives life in a way that we just can't appreciate. And she knows that she wasn't supposed to be two years old. And now that she's 24 years old and, you know, still in a wheelchair on a ventilator, you know, what she's taught us in life, and Patrick as well, is they, I think, taught us more about life and love and living than we've ever taught them. And when they were younger, at least, without their ever knowing that they were teaching us. And so many others.

You know, people say, always tell Megan, "Oh, you're such an inspiration." And she's got a wickedly dry good sense of humor. She goes, "Oh, thank you. Thank you." And then I'll pull her aside, say, "Yes Megan, you're such an inspiration. Especially

every month when I get your credit card bill in the first of every month. Such an inspiration."

But, you know, just this resiliency that she's got. She wants to live a full, meaningful life. A happy life. And she wants to participate in society and to give back. She's passionate about the Make A Wish Foundation that's been an important part of our lives. When she was a Wish kid in 2001, it was just such a wonderful experience at Disney World for Megan, for our family to not have to worry about doctors and nurses and just be a kid. And she wants to give back.

She was president of the Make A Wish club at Notre Dame. You know, from our home at the time in New Jersey to Notre Dame, it's 600 miles. 12 hours. And for her to go away with a team of nurses, the students in her dorm at Ryan Hall who surrounded her with support and love and lifelong friendships was an incredible experience. So, I'm very proud of Megan. I'm very proud of the community at Notre Dame that embraced her and her differences. And she got through four years at Notre Dame with a double major.

Physically it just takes her two or three times as long to do everything that it takes us. Almost never complained. And sometimes the weather got a little chilly out there. But she was able to get through. Spending every single night in her dorm at Ryan Hall. And to graduate on time. And upon graduation to determine that she wanted to be a social worker. And to go down to Chapel Hill to UNC and, you know, one of the best social work programs in the country. And now we're going to go down to Chapel Hill next week and she's going to get her Master's in Social Work. And she wants to be a social worker with children with rare diseases. And so, we're incredibly proud.

Jerry Lee: You've obviously been in the spotlight quite a bit over the last 20 years. What would you say is the message-- what message would you leave for your audiences here today about your role, your legacy in biotech and healthcare and the ecosystem?

John F. Crowley: You know, I think for we as leaders in biotechnology, and Goldman Sachs as important partners, as are many of our key advisors and partners, to realize, you know, that sense of purpose. Everybody in their job needs to have a sense of purpose. For us, it's pretty straightforward what we do. Maybe an extreme sense of purpose. But every organization has or should have it, whether you're making a widget and

building a team to serve somebody building a vibrant business that, you know, economic success helps build families, families build communities, all those concepts. You could find great meaning in everything you do. But you've got to have that purpose and meaning. It's just so incredibly important.

And I think that's a lesson that we live. Sometimes it gets lost in the minutia of running a public company and the challenges of science and medicine, regulatory. But having that sense of purpose. In my Tim Ferriss interview, Tim asked at the end, he asks everybody he interviews, you know, "What's your line or whatever you want to leave people with?" And I hadn't prepared at all. I've known Tim for years. I hadn't prepared for that interview. But I just said, and one of my mentors in the Navy actually always lead with this line, "It's bigger than you." It's bigger than you.

Jerry Lee: John, thank you again. As you know, it's an honor to speak with you, as it always is, over the last decade plus. And on behalf of Goldman Sachs, thank you for spending the time with us today.

John F. Crowley: Thank you, it's an honor.

Jerry Lee: Thank you.

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