



Noah Siedman's NewYorkBIO Presentation

Good afternoon, everyone, thank you to the NewYorkBIO folks for putting on this event and inviting me to speak & thank you to Mr. Surrey for the generous introduction, I am excited to be here and to have a chance to share some of my experience.

To that end I'll say a little about myself and what has brought me here to speak with you all today; My name is Noah Siedman, my younger brother, Benjamin had a rare genetic disorder called Sanfilippo Syndrome or MPS type III B which is in order of increasing specificity and difficulty to pronounce an enzyme deficiency disorder, a lysosomal storage disorder and a form of mucopolysaccharidosis (that's the MPS part). Sanfilippo is incurable, untreatable, and inevitably fatal, including for Benjamin who passed away 10 years ago this February at the age of 17. Since his diagnosis at 2.5 (I was four) I have organized fundraisers, spoken publicly to raise awareness, advocated and helped others to understand what my brother was going through, and now, as an adult work as an advocate in another rare disease community. My life has nearly always intersected with the world of rare disease and as a result, I have grappled with some of the questions I see asked by families I work with today, when I was five trying to sell lemonade at the end of my driveway & when I was 11 sitting at the dinner table helping to figure out a way for Ben to swallow his medication without choking, when I was 15 talking to classmates about being a carrier as we started our unit on genetics in bio class.

I have spent a lot of time introspecting, distilling, and then sharing my experiences in the 25 years since Ben's diagnosis and I have come up with a lot of different answers, I've highlighted different parts of that experience and I have tried desperately to find some perfect lesson or revelation to hand out to others based on all that my family and I went through. And for all of that, I am pretty confident that there isn't one thing or rather that this is another of those simultaneously frustrating and comforting moments where the process is the thing.

Hopefully, this serves as a bit of an introduction to who I am, to how much I love big words, but also as of a preface to how I think about my experiences.

Today, I'd like to dig into something that has been bugging me, hope. No, I'm not bothered by hope itself, more the increasing trepidation around invoking hope when we talk about the rare experience.

I get the hesitation, hope is incredibly, inextricably personal. Hope is risky, it's committal, it isn't always productive and it can, in the context of rare disease feel like a luxury we can't afford. I don't know that I disagree with any of that nor do I precisely fault anyone who stays away from using the word when talking to the families and patients they support or in their own internal dialogue.

I don't imagine that I can or even should change how we as a community interface with hope, but I'd like very much to show you how I look at it, through the lens of my own journey.

I think that perhaps the best way is to simplify before inviting in all of the complexity so here is a very simple hope, one that most everyone has entertained at some point:

I hope I win the lottery: it was what \$900 so odd million dollars when I bought my ticket on the way to the train, an incredible amount of money. The hope of Noah, today on his way into the city.

Nothing problematic there right, I paid my \$20 bucks for some quick play numbers and pocketed the ticket till the drawing on Friday. I spent a few idle minutes on the Amtrak imagining how nice it would be to have a gas range with 6 burners and a vent hood that actually worked and then I opened my email and got on with my life. In a few days, when I almost assuredly don't win, I'll shake my head, chuck the ticket in the trash, and return to whatever I've got planned for the weekend.

I like this one as a starting point because there is a good chance that I'm not the only one in this room who is going through this exact process, I mean maybe you all have higher aspirations than a nice stove, but the broad strokes are the same.

Now for the fun bit: The way I see it, this hope has four parts, something out of my control (that's the lottery drawing), a commitment on my part (\$20 dollars which could have been the first decent slices of pizza I've had in months), a vision of success (being able to cook on high heat without apologizing to my neighbors about the fire alarm) and a confrontation (probably losing and moving on). In the context of the lottery, none of those

things are tough to engage with, we are not challenged by any of them. So let's try another one!

This was a common refrain in my house growing up: I hope Ben poops today. The hope of a college-age Noah, who had taken an active role in caring for his brother.

Anyone who is or has cared for someone can relate to this one I'm sure, motility rules our day-to-day lives, poop is no joke in the rare disease world. A different hope, sure, but the elements are the same, there is a very different kind of lottery drawing, a vision of success - an early afternoon walk with a happy and calm Ben instead of a grumpy, disgruntled one - a confrontation likely in the form of this prune, pear juice and glucosamine concoction that I can still smell ten years later, despite how well it got things moving. This hope too feels safe, to talk about, to joke about. This too can't be the kind of hope that we are afraid of.

I hope Dr. Fu's research is approved for a clinical trial. The hope of a teenage Noah who knew that research was the best pathway to helping his brother.

This one is a little harder - messier, a little more vulnerable, and maybe a little more hopeful - whatever that means.

I suppose the FDA approval process can feel a lot like the lottery these days, so there is the thing out of my control, as far as commitment well my family and I had been fundraising for nearly two years to pay for the preceding animal trials, vector production

and all of the other things that go hand in hand with a clinical trial proposal. So that takes care of the first two parts.

What did success look like, while it's harder for me to write from the mindset of my teenage self now that I am on the wrong side of 30, I know that I had read every paper on the research, and I knew about the improved brain function in the rodent models, the reduced muscular deterioration in the large animal studies, I also knew that even were it delivered the same day I gave thought to that hope it would be too late for Ben.

So, the truth is that I don't know exactly what my vision for success was, it might have been knowing that other siblings would not go through the same thing that I did, it might have been no longer fearing the implications that my carrier status had on my future or none of those things. Finally, what did the confrontation look like?

We succeeded, the drug went to clinical trials, two cohorts were dosed and now almost 15 years later the results are in: not a miracle cure nor a complete flop. I guess that at face value this might not seem like much of a confrontation, but I think that success and failure; realizing our hopes or being forced to give them up. Both hold an element of confrontation. Because in hoping we set an expectation, we make a commitment to what our world will look like if that hope prevails even though we know that reality can never be exactly as we imagine it.

I think that this would be a fine place to stop the ride, to clean things up and finally get to my point, but I have one more hope, so stick with me a little longer.

I hope that Ben will be cured. The hope of five-year-old Noah clutching a jar of not very much change from his dubious lemonade stand venture.

This is the obvious one, the simplest, broadest, most hope-iest hope of the bunch and I'd bet everyone saw it coming. It's the one that sits at the heart of all the others, the one that only a child could be brave enough to voice. So, let's put it to the same test as all the others: First off something out of my control, well at 5 and shooting for the moon pretty much everything was, so that is check 1 out of 4. Commitment? Sure \$6.75 in small change from the handful of neighbors I'd been able to guilt into a somewhat warm cup of lemonade takes care of that one.

Confrontation, no deviation from the pattern there, I lived most of my life watching Ben's disease progress, and I held his hand until it went cold the day he died, almost 15 years of confrontation.

Last we come to the hope part, what did 5-year-old Noah imagine the world would be like if his brother was cured? Well, he would have had a friend and partner, someone to mentor and to order around, someone to take the blame, and someone to grow up with. Five-year-olds don't know much about anything beyond their own noses, so I imagined he would be like me. And to tell you the truth, to this day I still imagine life with my brother where he was miraculously cured, I still think about his personality, what he loved, and how he laughed. In a different speech, this might be where I tell you how 5-year-old Noah's hope is still going strong, and it is, and it's a good speech but I've got to stick to my plan.

And fortunately for you all, I think I'm running out of time, so I'll be concise. The problem with talking about hopes in the rare disease world is that alongside each of those four parts in a hope there is the opportunity for support – a need for support.

There are advocates here who are working to turn that FDA approval process from a lottery into something agile, transparent, and efficient and I am sure many who would have happily explained to my younger self how it will all work.

There are friends, family, who can join you in a vision for hope realized, who can remind you why to risk hoping.

There are medical professionals, palliative care experts, and specialists in every rare disease who can help prepare you for the confrontation, to spread it out over time, and arm you for it when it does come.

There are researchers, scientists, and industry professionals who can commit alongside you so that we don't hope alone.

Here it is, the straightforward actionable item at the end of all my talking:

When hope comes up in your lives, personal or professional, break it down into those four parts (the uncontrolled element, the commitment, the vision and, the confrontation), figure out where you can give support or where you might need it. It will make all the difference.

Thank you all once again for taking the time to listen, and for the opportunity to speak!

Have a great afternoon!