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When DNA Meets AI [Entire Talk]

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Midway through a M.D./Ph.D program at UCLA, Alice Zhang made a discovery that she felt could reverberate far beyond the halls of academia. So she shifted directions, leaving her Ph.D program to found Verge Genomics, a biomedical firm that aims to unite genetic research and artificial intelligence in service of drug discovery. She describes how AI can revolutionize the drug discovery process, and reframes risk-taking as a simple series of optimistic next steps.

Transcript

(futuristic music) - [Narrator] Who you are, defines how you build.. - I'm very excited to be here today, partly because I actually started Verge Genomics when I was a student.. So I was originally a grad student at UCLA when I first started becoming interested in the drug discovery process.. And it was in that moment I realized how broken drug discovery is right now.. It's still largely a guessing game, but we're in this really unique moment of time right now where advances in genomics and machine learning are really poising us to re-think the way we do drug discovery and take a lot of the guesswork out of drug discovery.. And so I started Verge really with a vision of creating a scalable drug discovery engine that could be repeated, not just for one disease but across many different diseases.. And eventually apply to even larger human conditions, such as aging, disease prevention and addiction.. So I want to start out with kind of why I went into the field in the first place, which is for the patients.. And at Verge our first disease area that we focused in, is in ALS.. So, ALS is a rapidly degenerating disorder in which patients progressively become paralyzed..

Losing their ability to walk, to eat and eventually to breath.. And unfortunately, because most of these patients die within three years and under our current drug discovery system, it takes over 15 years just to find a single new drug, most of these patients won't get the drugs that they need.. At Verge we've been able to use artificial intelligence to identify over a dozen promising drug candidates that are showing effect in our pre-clinical models.. They're showing effect in mice that we've engineered with ALS in them.. So I'm about to show you a video of three mice that have ALS.. And they're at the kind of initial early stages of ALS where they're starting to lose their ability to walk and their muscles are starting to waste.. And so you can see that these muscles, these mice are already losing their ability to walk and have a hard time staying on this rotating wheel.. But when we give these very same ALS mice injections of a drug discovered entirely by our platform, they recover their ability to walk and stay on this rotating wheel.. And what's so exciting about this drug, is that it's actually just one of many drugs that we've identified showing promising effects in the lab, but also one of many diseases that we're currently pursuing.. And that's really what is so exciting to me about this platform, is the potential to find drugs not just for one disease but to eventually scale across many different diseases..

And at Verge, we're building an engine really with the vision of creating and helping enable a world in which cures exist for every single human disease out there without an available treatment.. Well first I want to start by taking you through kind of my personal story and where it all began.. Because if you had asked me five years ago, or told me five years ago that you would be a CEO of a biotech company, I probably would have laughed.. I would be like, never in a million years.. So I was born in the DC area.. And here are my parents, they're immigrants from China.. This is a picture of me from what my friends called the Bruce Lee era because apparently I look like Bruce Lee with an awesome haircut and monochromatic jumpsuit.. But really it was a unique moment, like shortly thereafter around middle school when I started realizing what death was.. Kind of dark and morbid, but I couldn't stop thinking about it, and I was like, you know, what do I want to be thinking in the very last moment on my death bed? What is the last thought I want to have? And I realized that what I wanted to be thinking was that I have made the maximum amount of impact on the world that I know I could have.. And in fact because I was kind of neurotic, I also had like this formula in my head, where I was like, I will maximize for the greatest Delta per patient, across the greatest number of patients in the shortest period of time..

So that led me to science because I thought at the time, what better way to really impact people than to really change the

way they interact with their bodies and the way they live their lives.. So I actually went to the National Institute of Health and had my first science experience in high school which to be honest I absolutely hated.. I was at the bench, I was pipetting, I was like doing these molecular biology experiments and it was a very classical kind of old-school form of molecular form of biology which teaches us that one gene in your DNA always corresponds to one protein.. And there are scientists that dedicate their entire lives to actually just study one gene in hopes of finding a link to disease.. But this all changed one day when one day during lab meeting this lab member got up and gave a lab meeting.. And his name is Doctor Wuchty, Stefan Wuchty and he was this Austrian biophysicist.. I was kind of like, what is a physicist doing in a cancer biology lab? But then, he showed in his meeting these beautiful network diagrams of hundreds of different genes.. And so it turns out that the story is much more complex.. It turns out there are over 22,500 genes in our genome each of which together incorporate over a 100,000 proteins.. And he asked, "What if instead of studying "one gene at a time, we actually looked at "how all of these genes interact to cause disease." And it was just something that was so obvious to me, I couldn't stop thinking about it the next night..

I was like what can I do to get involved? This makes so much sense that we look at hundreds of genes at a time to study disease.. So the next day, I went up to his door and I knocked on his door.. And I asked, hey, how can I get involved in more projects? And in a very kind of rough European way, he was like, "Well, why don't you just go code up, "like find all 100,000 proteins of the human protein, "put together a map and come back to me when you're done.. "And oh by the way, you'll need to know Python." And being a high school student, I was like oh, okay cool, yeah will do.. And I left his office.. I B-lined straight from my test and I immediately Googled what is Python? And that is legitimately how I learned how to code which was really just driven by this burning desire to really understand how these biological networks worked.. And unbeknownst to me, this was actually part of a larger historical narrative that was happening at the time.. You see in the 1950s, we had the molecular biology revolution which really gave us the tools to study one gene at a time.. And this enabled companies such as Genentech, Biogen and Amgen to start, but in the 2000s we had the Genomics revolution.. The human genome is sequenced which gave us the tools to study tens of thousands of genes at once..

And this meant drug discovery was no longer a biology problem, but it became a data science problem, it became a physics problem, it became a problem of multiple disciplines.. And I believe that the next generation of biotech companies will rely on integrating all of these disciplines together to be successful.. And so this is my kind of second turning point.. So I'm trying to walk through a series of turning points that I felt like set me up for starting the company.. Even though I didn't know it at the time.. And this is a really critical one.. So fast forward, few years later, I'm in college, and I'm studying in the lab of Saeed Tavazoie who is one of the pioneers in genomics in cancer biology.. And so at the time, it was the end of my senior year in college, and I was thinking, you know, the MD/PhD might really be the best way to tackle that life mission of mine which was to make as much impact as possible but I was 20 at the time, the MD/PhD program is like 8 years at minimum, up to 12 to 15 years and I just like, was having this existential crisis.. I could not fathom what 8 years meant.. Nor could I commit to anything..

I was like, do I really want to be a physician scientist? How do I even know? Do I really want to be a doctor? He kind of sat me down and he told me, "Look Alice, there's no way that you know "that you want to become a doctor "unless you just start medical school.. "And you won't know if you want to be a professor "unless you just start graduate school.. "And you don't like it, you can always just leave or pivot.. "You're not committed to it for the rest of your life, "but at least then you will not have left any rock unturned "and you'll just have gotten started." And so that was a really big light bulb moment for me and I think to this day I see so many people get stuck on these paths that they think they've committed to and really have their lives ruled by this kind of sunk cost fallacy.. And in reality, you'll never know.. You'll never know whether or not a path is right for you unless you just take the first step.. Unless you just get started.. And that was just really big for me throughout the rest of my career.. Ironically, it was also a big theme for me when I decided to leave the MD/PhD.. So this is in 2010 when I began my MD/PhD with 11 other colleagues..

Interestingly, actually four of these people did not end up finishing the program and I actually met my co-founder who's that guy right behind me on this very day this picture was taken.. And so when I started medical school, in a lot of ways it was profoundly fulfilling.. I got to see these patients every day, it felt like I was making an impact on individual patients and their families but I couldn't keep this kind of gnawing feeling I was having.. That, you know, that was it.. I could see patients and it would be impactful for them, but there was a limit to how many patients I could see in my lifetime.. And so I transitioned to the PhD, and that's when I started focusing on drug discovery for my thesis and specifically on the very earliest stages of drug discovery.. So right now in even the first phase of drug discovery it takes about five years and over a quarter billion dollars to even just screen through drugs and find drugs that work.. And this is because a lot of pharma companies are paying for failures.. So oftentimes their brute-force screening tens to hundreds of thousands of compounds just to identify one that works in the lab.. And I thought there must be a better way to do this..

And so back in grad school, I started coding up some of the first algorithms to find new drugs for nerve regeneration.. So spinal cord injury, nerve injury.. And quite shockingly the very first drug that was predicted by the algorithm, when we put it into mice, with crushed nerves, helped them recover function of their nerves much faster than even the leading standard.. And this was just the first drug we tested.. And so when compared to the current pharma success rate, I thought wow, this is really a compelling finding.. But when I was writing it up for publication, I was writing up the manuscript, I kind of thought like, do I want to just publish this? And let it sit on a bookshelf somewhere? Or what is the best path to actually getting this

product to patients? And I realized that really if I wasn't going to be the one to push it out, there'd be very few other people that would be as qualified to really advance this to commercialization.. And I think the second thing that was happening for me at the time was I want to do this PhD with really big hopes that I can make a discovery that would impact billions.. But what I realized was the kind of realities of day to day academia were very much still focused on publications first.. And not so much on direct patient translation.. So in many ways, it's ironic because the actual reason I went into the MD/PhD ended up also being the reason I left..

Which was I found that starting a startup was the most direct fulfillment of creating patient impact as quickly as possible.. This is also another reason I ended up leaving my program which was we got into Y Combinator.. And so I actually learned about Y Combinator through two Google searches.. The first was what is an incubator? And then the second one was what is the best incubator in the world? This was the first thing so I clicked on it.. And I realized that the applications are due in about a week.. So my co-founder and I went and we like spent a week writing up this application.. And the day before it was due, I gave it to a friend that had started a startup and he just tells me, "Alice, you're gonna need to forget everything "they taught you in grad school "and write this like you would write it for your mom, "so your mom can understand." And that was another light bulb moment for me which was like, they taught me the specific way to write and the specific jargon in grad school that I had to unlearn, but that was also a huge blessing for me.. In just entrepreneurship, which is the first step is actually learning how to communicate your idea in a way that's as simple as possible and figure out what people you're talking to care about and communicated to why they should actually care about your idea.. So I actually ended up scrapping it and pulling an all nighter.. Rewriting it actually thinking that my mom was gonna read it, and we got in..

And so I kinda wanna end with, at least this section.. A lot of people ask me and they say, "You must have been so brave "to leave the grad school program or to make the leap." But the honest answer is, it never felt like a leap, it always felt like a next step.. It felt like the next step towards answering a long list of questions and I feel like that's a lot of what entrepreneurship is.. So the first question for us was, will anyone even care about this idea? And luckily we found that YC did care.. And then the next question was can we actually get funding to grow our idea? And the question after that was can we build an initial team to actually build the product? And can we actually grow a team to take the product to the next level? So really this was just kind of a cascading journey of individual steps.. But it really taught me that the most important thing is to just stay adaptable and I think that people get so caught up in trying to figure out where do I want to end up? What is the best path there? Is this really where I want to be? When in reality you can never really know and the best thing you can do is just to take the next step to find out more information if that is true or not.. So I'm gonna talk a little bit about some of the challenges that I faced specifically when building an AI and drug discovery company.. And so when I first started, I realized that one of the biggest barriers right now from preventing AI from fully realizing it's potential in drug discovery are these huge silos that exist between different industries.. There's silos that exist between computational teams, biology, chemistry, drug development and even academia and industry.. And the first thing I wanted to do was create a team that broke down some of these silos..

So we really set out from day one to create this truly integrated team that combines top experts in machine learning and statistics with drug developers, neurobiologists and chemists.. And it's been so important to have these people sitting side by side with each other because the computational people really understand what they're making.. They really understand what their product needs to look like and the biologists can design experiments that produce the right types of data for the computational team.. I think another challenge that we faced when we first started was a lot of companies have trouble figuring out how they actually create value from their algorithms.. And so we decided from day one that we didn't want to just be a software company, but we actually wanted to own the products or the potential billion dollar drugs that would come out of our platform.. So what we did from day one was create a vertically integrated company.. What that means is that we have both the front end of a machine learning algorithms as well as our own in house drug discovery and animal facilities and labs.. So this allows us to actually create our own sets of proprietary data by sourcing thousands of different patient brains and sequencing it ourselves.. And mining this data to figure out what are the groups of genes or gene networks that are causing disease.. By looking at these gene networks, we've been able to build a robust first-in-class drug portfolio of over a dozen breakthrough opportunities in six different diseases..

And importantly, because we have our own integrated labs we can quickly turn these predictions into real drugs as well as see if our predictions actually work and feed that data back in to continuously improve the algorithms.. So the second challenge I see facing the field is really a problem of data availability.. So machine learning in tech is fundamentally different from machine learning in biology because most of human biology is still unknown.. That's to say there's a huge missing data problem.. And we encountered this problem when we actually were looking at the data sets available and we saw that these data sets were vastly underpowered and poorly designed and could not be used for machine learning.. And what's important here is that the sophistication of your algorithms is irrelevant if we don't have enough data from which to train and to learn.. So we have embarked on this two year internal data regeneration initiative where we now generate all of our own proprietary patient data sets and we do this by partnering with over a dozen different hospitals, brain banks, and universities to actually source thousands of patient brains after they've died and we sequence that internally to create now one of the largest patient training datasets in the world for ALS and Parkinson's disease.. But while training data is really important for generating predictions, for every AI company you need to have validation data.. So we take all of these predictions, and we actually test them in our biology labs to create a huge body of validation data that feeds back into the algorithms and constantly improves them over time and across diseases as well.. And this is critical for any company in AI and biology because AI cannot be a

black box in biology..

You need to have a way to actually see if the predictions work and to let those predictions guide the improvement of the actual algorithms themselves.. And so the last challenge we have, sounds pretty simple, does it even work? So there's this concept in startups that there are two types of risk.. There's technical risk, can you build a product? And market risk, do people want your product? And so for biotech companies, the market risk is pretty obvious.. If you created an Alzheimer's disease tomorrow that actually worked, you'd immediately have hundreds of millions of people clamoring to get that drug and willing to pay anything.. So the biggest challenge really is technical risk, and that's huge.. Does what you're predicting actually work and will it work in a patient? And that's the biggest challenge and that's another reason why we built out this vertical integration because if you don't have labs, you can't test if your predictions are working.. But you can't just go into humans from day one to test it, and a big challenge in drug discovery that's lead to a lot of failures are that people only test in mice before they go into humans.. And drugs and mice historically haven't translated well in neuroscience.. So what we've done instead at Verge is we've leveraged a new technology using human stem cells.. And what we can do, is we can actually take skin cells from patients with disease such as Alzheimer's disease and we can actually turn those into brain cells in a dish..

And then we combine that with robotic systems internally to be able to test all of our AI predictions at scale in cheap and automated human trials before we even go to clinic.. So here is one of the systems that we used to test our predictions.. We plate the patient brain cells on this dish, and we treat them with the drugs predicted by our platform.. This robotic arm then comes along every day, takes the plate out from the incubator and places it underneath the microscope at the same exact location.. This microscope then moves along and images each well up to multiple times a day, enabling us to recreate the live growth and degeneration of individual living brain cells in real patients with ALS, Parkinson's disease and Alzheimer's disease.. So this is a live, time lapse image from a real.... brain cells from a real patient with ALS.. And you can see here that over time these white lines disintegrate into these tiny white dots.. And that's the process of the cell dying.. This is also the same process that causes ALS in patients..

Now we can actually take these images, and we can algorithmically analyze them and create these types of survival curves.. So on the X-axis, you have time over the course of days and the Y-axis, you have percent of the cells that are still living.. And you can see on the red line, that ALS patient brain cells tend to die off much more quickly than on the black line which are healthy patient brain cells.. Now what's been so exciting for us, over the last year, is that when we took the first drug from our platform and we put it into these very same ALS patient brain cells, we could actually completely rescue them from dying.. In fact, restoring them to the very same levels as healthy patients.. This is the first time that any AI predicted drug has worked not only in mice, but also in human brain cells as well.. So I kind of just want to end with where do I think biotech is going over the next five to 10 years, and really starting with an area that's near and dear to my heart, neurodegeneration.. So I talk about some of the challenges with drug discovery and in no other disease is it as severe as in neurodegeneration.. So Alzheimer's disease, currently is the only disease that has actual growing death rates and it's the only disease of top disease in which there's no drug that can slow, prevent or cure these diseases.. And as we all get older, we'll be increasingly affected by these diseases..

So why can't we figure it out? It's because these diseases are incredibly complex and the traditional drug discovery method isn't sufficient to tackle them.. In fact, in the last year there have been seven billion dollar Alzheimer failures from big pharma and in fact, last year Pfizer announced that it was shuttering its entire neuroscience division, laying off over 300 employees.. But what is less written about is the scientific and technological renaissance that's actually happening in neuroscience right now.. And I think it's super interesting because anytime you have a big income bin that is turning away from a huge untapped market combined with a convergence of technological advances, you create this sort of money ball opportunity for smaller companies to really come along and transform the entire landscape.. And I'll talk about a couple of these advances.. The first of course is genomics.. So in 2000, some of you might have seen this figure, in the 2000s, it cost over 100 million dollars to sequence a single genome.. Today, it costs less than a thousand dollars.. And in fact, this has dropped so quickly that it's even surpassed what's predicted by Moore's law of computing costs.. And so just like the decline in computing costs has fundamentally changed the way we interact with the physical world, I think that this increase in genomic data will change the way we think about disease..

Now, I'm gonna talk about three additional technologies that we use at Verge to get a leg up on drug discovery.. The first, is that we are one of the first to actually be able to collect brain samples and sequence them from live patients with Parkinson's disease.. So this is deep brain stimulation, it's an advance in surgery that allows us to implant a device into a patients brain and turn it on to prevent Parkinson's patients from having tremors.. But there's also a second unexpected advantage here which is that we can actually access patient tissue from a patient while he or she is still living and sequence it to be the first to get an unprecedented glimpse into earlier disease progression.. We've also started single cell sequencing which is a technology I think will revolutionize genomics in the next five years.. So instead of sequencing patients brains at the tissue level, we can actually take individual cells and sequence their nuclei and that for the first time gives us a glimpse into solid type complexity at a resolution we haven't been able to achieve before.. And lastly, using the same technology I showed you earlier in our lab, we're now also able to take patients skin cells and actually turn them into 3D brain organoids in the lab which allow us to model the brain in a degree of complexity we haven't seen before.. So a lot of these technologies like these will also change the type of companies that are coming out.. And I think these advances have already lead to a

proliferation of biotech companies with nontraditional profiles.. So these are companies that have been started by technologists and biologists coming together and are lead by savvy teams that grew up in the genomics and the AI era..

These are teams that recognize the importance of creating multidisciplinary teams that interface between computer science, physics and computational biology.. And I think there'll be an explosion of these types of companies in the next five years.. So I want to end with, while I consider us in this kind of new era of biotech companies, life sciences is still a very traditional field.. For example, it's very rare for there to be a founder who is also a CEO today in biotech and most are really started by a small group of venture capital firms that bring in professional management.. So in the very beginning it was quite challenging for a company like ours to really breakthrough.. And I learned a couple really important lessons in how you can actually create an advantage from scratch.. And the first thing I learned was do things are laborious, especially in the beginning because as a founder, you will need to be the one doing things yourself to really kickstart the company.. As an example, when I first started the company, to hire the team, our initial team, I personally interviewed about 1,200 people myself and I did that by actually going on upwork.com finding some outsourced people on Upwork and actually then going through a decades worth of publications, from nature, cell, science whatever had the word genomics in it.. I found the first three authors, found their emails and I would email out hundreds of people per week.. I like to think every computational biologist has an email from me in their inbox..

But that was really, really critical for me because not only did I understand and learn the field, understand how to hire but I was able to recruit a rockstar team exactly in the mold of what I envisioned for the team.. And it was after building that really stellar team that made recruiting actually so much easier after that.. The next lesson is one I consider really important for myself personally which is that I think it's one of my greatest responsibilities as a CEO to grow faster personally than your company does.. So what do I mean by that? The first thing is that you have to get really comfortable with taking a hard look at yourself and understanding what it is you're bad at, what you don't know, and what you need to learn.. You need to get really okay with that and then you need to be absolutely shameless about learning it, finding advisors, filling the gaps.. And so I always like to say Verge was built on a foundation of cold emails.. Whenever I found I didn't know anything, whether it was business development or drug development I would literally go and put together a list of emails of who I think is the best of the best, and I would just cold email them, actually very surprised by how many people responded, but that's kind of how I started building my foundation of expertise.. And I think the last thing is that you have to stay hungry to find step wise functions for personal growth.. So rather than trying things with trial and error, how can I find things that will really boost my own growth? And so things that worked for me, for example, are executive coaching, reading a ton of books, and finding other founders that have gotten through it.. And so that brings me to my last point, which is that being a founder is a very singular, it's a very challenging and oftentimes it's a really lonely experience..

And so I would not be where I was now, if I did not myself find a group of other founders that would eventually become my best friends with the shared experiences.. So these are people that I would literally text at midnight, and be like crap, I have to fire someone for the first time.. How do I fire someone? And then I would text them and like, I just fired someone, does anyone want to grab a drink? And so these are people that really have seen, we've seen each others companies really from beginning all the way through.. Our friends company was just acquired last week.. So that's a picture taken last week.. And I think this is so important because as a founder it's really, really hard to know where to get good advice.. You're gonna be told what to do by your investors, by your advisors, by your employees, none of which you're sure has the companies best interests at heart.. And so I think the best advice I've always gotten have been from other founders that have gone through the same thing especially founders that are about a year or two ahead of me.. And that's really the best way to kind of anticipate what you don't know.. And lastly, I feel like building an important, a personal support network for yourself is really key to actually building a sustainable business of the prosstime because you will need places to look for advice throughout the whole entire journey..

So I'll start taking questions now.. (audience applauds) - [Audience Member] So in that 15 year model that drug companies are facing with their phase-out drugs, how much of that is taken up by needing to get approvals and going through their drug trials that takes up time for these approvals and that's something you guys are having such challenges facing, I'm a little curious, tell me about that.. - Yeah, so a lot of that time-- - [Audience Member] (speaks faintly) Question.. - So the question was of the 15 years, how much of that is taken up the approval process and does our technology address that component? So of the 15 year and two billion dollar figure, the average it takes to get a drug developed, a vast majority of that time in cause is actually working through the failures, right? So if you just happen to have the magical drug from day one, the process would not be that long, but the challenge is actually okay, I have to test like a million drugs before I even find some viable candidates, then of these viable candidates, 10% of them are actually safe and then of those, 10% actually work in humans.. And so it's the kind of repetition of needing to start over and over again and a lot of failures that contributes to a lot of that time and cost.. - [Audience Member] First of all, thank you so much, this was truly inspiring.. I was wondering if you could share a little bit more about how your prediction technology works? And how you identify drugs for treatments? - Yeah so as I was talking about-- - [Audience Member] Question.. - Oh sorry.. So she asked how does, could you tell us a bit more about how the prediction technology works, how you identify drugs for treatments? So the technology works kind of based on two premises.. The first is that diseases are not caused by one gene, they're caused by hundreds of genes..

The second is that we need to look at human data from day one rather than just making guesses about what we think causes disease.. So the prediction works by actually taking real brains from patients that have died from some of these

diseases, Alzheimer's disease, Parkinson's disease and looking across their entire genome to see what's changing.. So for example, we might see a group of 100 genes that are always going up in Alzheimer patients but not in healthy aged people of the same age and what we want to do is then find drugs that turn off those same hundred genes.. And that's where the machine learning comes in is how do we leverage knowledge about what we know about the interactions between genes to find these key hubs that are in the middle of these networks, and how can we target those to turn off all hundred genes at one time.. Back there - [Audience Member] You getting your focus on being vertically integrated and also considering the fact that Verge is currently is a startup, looking more into the future, what are your plans for handling some of the trials? And is your goal to ultimately partner with some of the big pharma companies or how do you plan on scaling that up within the company? - So her question was given our focus on vertical integration, what are our plans for executing clinical trials? Will we be partnering with other pharma companies or doing it ourselves? So the advantage of having the platform which is unusual for companies that we actually have a wealth of opportunities to go after, so you can think of it as a portfolio, and many different drugs even within each disease.. And so our goal is to not only expand those diseases, but also to show that we can get them further.. So partnering, you know, in biotech it's almost impossible to do the whole thing by yourself for everything so what we'll likely end up doing is we will select a couple of programs that we advanced ourselves and then also partner out other programs so that we can have as many shots on goal as possible.. - [Audience Member] I have a question around just how you think about pricing of your drugs once they're fully developed, given that you're able to bring them to market faster.. One of the big challenges many of these treatment centers make sure that they're very expensive and so will your medicine be more affordable and therefore will (muffled speaking).. - Sure, the question was how do we think about pricing, that a lot of drugs right now, there's a lot of questions around expense and affordability, do we think we can have an impact on pricing..

So right now, if you think of drug development chain as a very long 12 year chain, we're at the very beginning and will likely be partnering with companies as we near the end.. So I think it's really hard to say what effect we'll have directly on pricing because that's really determined by the owners at the very end but I think at a higher level a lot of the arguments for having high drug prices are the cost it takes to get there.. It's very expensive and the companies need to recoup some of those costs.. So the long term hope is that if we can really show that this works even for the first disease, other companies will start adopting it, right? Other companies will say we need to pay for attention to computational approaches to actually predict these drugs in advance.. And across the field, adoption of computational biology will then eventually drive down prices.. So I think focusing in how can we reduce costs and increase efficiency is really a key point in the pricing discussion.. - [Audience Member] Are the drugs that you discover, drugs that are being repurposed that already exist? Are they like new compounds altogether? Are they like gene editing of CRISPR-Cas? - Yeah, great question.. So the question was are the drugs that we're discovering, are they repurposed, so they're taking an old drug for new disease? Are they new drugs? Or are they gene therapies? So the drugs we're developing internally are actually new drugs, so we have a whole medicinal chemistry team that takes drugs and actually tweaks the structures to make them work even better and to remove the toxicities and we also have some gene therapy in house.. So we actually take, we can take a gene, we can package it into a virus, and then inject it into mice that have the disease and this quickly knocks down the gene and it's actually a therapy that's currently being tested in the clinic as well.. Yes..

- [Audience Member] Question I had was, developing the company, did you start first by partnering with the university, and did you figure out why did you choose that? - So the question was about funding and if we partnered with university versus gotten private funding and why did we choose that route.. So we have raised to date, 36 million from venture capital since we started in 2015.. We also partner with universities.. So those two pasts aren't necessarily mutually exclusive but we just felt that private funding would allow us to grow as quickly as possible and I really do think it's a field that's gonna grow rapidly in the next few years so we really want to be first movers on that.. - [Audience Member] Firstly, thanks very much for your talk, and my question has to do with, so you started coming up with the idea while you were a researching grad student, so curious, how exactly does that work when you're able to walk away with what you are working on while supporting an academic environment in order to pursue it on your own? - So the question was, so I was.... I founded the company while I was in university and how it works that I could kind of leave the university and work on it on my own.. So the way we started was a bit different in that the company as it is now, is not actually working on any of the in terms of the drugs and IP itself is not the same as what I did at UCLA.. At UCLA, during my grad school I was really kind of learning about the concepts of neuroscience and systems biology and that's where I really kind of opened my eyes to the concept of taking a network could be used in drug discovery.. When we left UCLA, we actually ended up recoding everything entirely from scratch and working entirely new diseases so that allowed us to have a pretty clean separation.. Back there..

- [Audience Member] So when starting at Y Combinator was a relatively low amount of funding compared to what you raised, how did you set those first few milestones for the company where you need to in order to advance through this (muffled speaking)? - Yeah, so the question was when I first started out Y Combinator was a relatively low amount of funding compared to what we have now, how do we set the milestones in the early days? So it's kind of funny, when you go into Y Combinator, you meet in these groups, and they tell you to set metrics every week and so every week we were going in, other people were like, "Oh, we have like this 30% week over week user growth." And our metric initially was number of drugs discovered which was always zero.. So it was always like, yeah zero drugs discovered this week.. Same last week, and same next week.. And actually that was a really, I feel like, a key lesson for me to understand that actually metrics for all companies are not the same and when to kind of like adopt advice and when to ignore it or when to adopt a different form of advice.. And so for us, the metrics were always around technical risk.. So I think obviously if you can create a drug that works, every pharma company will want it, and every patient will want it.. The kind of question is how do you actually create a case that

your technology works? So a lot of our early milestones were technical.. It was showing, okay we made this prediction, can we put it in some cells and show that it actually works? Which actually innovative itself is a big step because of the silos, computational teams, kind of infrequently actually test their predictions.. And then next was if we put into a living animal, could we actually see an effect? And then could we actually make a drug that was safe and nontoxic? So a lot of our milestones are very much a scientific based and then another big one was the team.. Can we actually recruit a team that really bought into the idea enough to join..

And that's actually a big de-risking factor for people because no one knows the technology more like engineers and scientists so if you have really high quality scientists are coming into your company that are all in, that's also a really positive signal for other folks as well.. Back there in the blue.. - [Audience Member] Your patient library of data is a big competitive advantage for you.. And I'm assuming that those additional like, tissue donations came from patients and their families and you're the one that's gonna work on the competitive advantage.. And so I'm wondering how do you talk with patients and their families, or your nonprofit partners about that data and what it means to be the company that own that database? - Yeah, so the question was it seems like our patient database is a big advantage and so when patients initially donate the tissue, how do we interact with these universities as a for profit company when the universities are initially nonprofit.. So I think the first thing that makes it easier for us is that we are not selling the data.. So we're not actually directly profiting off of that data.. Most of the patients, when they consent actually consent to it being used more widely by the public so usually in either collaborations or universities and brain banks, they don't really exclude for profits companies from using it, but we're also at the same time, we're not selling the data.. So in a lot of sense, we are actually pretty early, we are a research company.. We're doing fundamental research to see if we can learn anything about how the disease works and then we start designing drugs if we do find something, a new discovery about the disease..

We also publish it too.. So for example, we published a manuscript in nature medicine last February, showing a new mechanism of ALS with some collaborators at University of Southern California.. So in that case, it actually did lead to a new discovery that benefited the field.. And that's kind of our perspective that whenever possible, we want to release data information that benefits and moves the field forward.. - [Audience Member] Last question.. - So I'd like to touch up on this, the last element which you mentioned, I understood from your talk that I think personal and professional improvement in people around you helps you when you're making those difficult decisions, it also seems like being out of Y Combinator, it helped you to build the end.. Now my question is what sort of advice could you give to individuals if we don't have that sort of incubator experience to help them? - So the question was, at the end of the presentation I talked about how important it was to have a network, and for me Y Combinator was important source of people in the network.. For those that aren't doing YC, is there any advice I can give for building that network? So I would always think about this kind of like how I think about many other problems in startup, which is first, I think, identifying what are high density sources for finding other founders.. So oftentimes if you go to, like YC actually holds public events.. The Female Founders Conference is an example..

I would focus on what are kind of a list of events where founders will almost certainly be found.. I think venture capital firms, if you have connections there also will be a high density sources.. Or even just cold emailing, honestly I know sounds like, some people have their versions to it, but you'll be surprised.. Like I get cold emails all the time from other founders and I actually view it as my responsibility to help them because I got helped out so much when I was a founder by other founders that did not know me.. Actually when I was applying to YC, I just would randomly email YC founders on Facebook that I didn't know for help and advice and those people actually ended up becoming investors, advisors eventually.. So I think founders are definitely open, I think more open than most to helping out other people at the beginning because oftentimes they're helped out so much themselves.. (audience applauds) (futuristic music)..