

Science Will Win S1E4

Nikhil: I would love for my future to be where my three-year-old's never know that I have hemophilia because they don't see their dad, going away to infuse himself. If their dad falls down while playing with them, he doesn't suddenly end up on the couch with a swollen ankle or a bruised knee that keeps him in bed for two or three days. I would love for there to be a reality where my kids are told that their dad has hemophilia, but this doesn't impact their relationship with their dad or what they can do with their dad.

Adam: That's Nikhil Gadre. He's the hemophilia gene therapy commercial lead at Pfizer. Nikhil's professional aspirations have always been motivated by his personal ones and his strong connection to the hemophilia community. We heard from Nikhil in the last episode - he suffers from the rare bleeding disorder, Hemophilia A.

As someone who is so closely connected to the impact of rare diseases, Nikhil is acutely aware of the potential of gene therapy, and what it could mean if it's approved.

Nikhil: The way I describe what I do is I work with colleagues all over the world to help bring gene therapies to patients

Adam: To do that, Nikhil works hard to educate patients, physicians and society at large on gene therapy's potential.

Nikhil: Gene therapy has the ability to truly turn science fiction into science fact. It has the ability to change the lives of patients like me. And if we do our duty to be open, to be transparent, to be courageous, and to ensure that there is no stone left unturned to bring these therapies to patients' lives.

Adam: Welcome to Science Will Win, a miniseries exploring the future of gene therapies. I'm Adam Rutherford.

Just a reminder before we get started: Gene Therapy is a promising area but it's investigational in nature for many diseases. There is so much research to be done to understand the safety and efficacy of these potential therapies. Remember that you should always discuss treatment options with your healthcare provider.

Now, over the last three episodes, we've talked to experts from around the world. They've shed light on the history of gene therapy, the state that we're in today, and some of the obstacles that we'll need to face. The common thread amongst it all is hope for the future and the potential of using genes as medicine to transform lives.

In this final episode, we're going to explore what this future could look like. This is gonna require an enormous effort over the next few years, and it means re-imagining how we think about healthcare provision.

This is a huge task. But there are glimmers of what the future may hold.

Let's start by looking at a report from Europe, specifically. The European Organization for Rare Diseases, or EURORDIS has created what they call the Rare 2030 Foresight Study.

Simone: The foresight study called 2030 basically pulled together the community on rare diseases from the patients to the clinicians, to the academics, to the industry, to the policy makers, to come up and

Science Will Win S1E4

understand what the current situation is, what are the shortcomings, what are the trends, and ultimately what kind of scenarios that we are likely to see in Europe.

Adam: EURORDIS's public affairs director, Simone Boselli. In previous episodes, he's walked us through European health care policy. But he's also really focused on what future policy could look like in the EU.

The Foresight Study found four different possible scenarios for what the world may look like for people living with rare disease in 2030. These scenarios are based on 10 trends that will affect rare disease policy: they include healthcare budgets, patient empowerment and engagement, and multistakeholder cooperation. The goal is to use these scenarios to create a shared vision for a new and improved policy framework in Europe.

Now the four scenarios they modeled have got super snappy names: Fast over Fair, It's Up to You to Get What You Want, Technology Alone Will Save You, and Investment for Social Justice.

So first, Fast over Fair occurs when stakeholders only collaborate when they share the same interest. The challenges of creating fast and fair innovation have the potential to lead to frustration and distrust in healthcare, science, and their governing bodies.

It's Up to You to Get What You Want happens when this distrust persists. A two-tiered healthcare system forms where basic care is provided by the government and the second tier is reserved for those who can pay for faster access and higher quality care.

Innovation slows because the tiered system means a lack of investment in data collection and sharing platforms. The innovation that does arise is very expensive and excludes many patients. The patient pool becomes so small that investment in research and development seems impractical.

Now the third scenario, Technology Alone Will Save You means that private companies, instead of the government, are managing rare disease patients' health. The privatization of healthcare systems and innovation means that patients are responsible for managing their own health and there is very little patient organization support.

And then there's the fourth scenario, which is EURORDIS's recommended path: Investment for Social Justice.

Simone: What we landed on, and not surprisingly so, is on investment for social justice. We start from a deeper understanding of the needs at the starting point of the innovation process, the unmet needs that we are talking about of the people living with rare diseases, but it's based on a collective accountability, solidarity, a greater degree of solidarity among citizens, countries, as well as diseases as a political priority in the sense that we all very well know that we cannot achieve any meaningful improvement in rare diseases if we don't work together. And this is our vision from the very beginning between diseases, between associations, between countries, because alone, we wouldn't be able to go anywhere and therefore creating the condition for greater solidarity amongst diseases, countries, diseases and countries it's of utmost importance.

Adam: I think it's significant to really think about this final scenario. In so many ways, this focus on social justice could re-organize policy, health systems, and this ultimately, benefit patients. And not just in the

Science Will Win S1E4

EU. While the policy and systems may vary, the focus on social justice could benefit patients around the world.

At the center is the all-important idea of inclusion, recognition, and equitable access.

Reda: I don't think that I'm exaggerating when I say that equitable access is critical, not just for patients, but for humanity

Adam: That is Reda Guiha. Now Reda is the Regional President for International Developed Markets at Pfizer Rare Disease. He and his team focus on access to gene therapy and raising awareness of rare diseases.

And like so many people involved with rare diseases, his motivation comes from his own life experiences.

Reda: Throughout my life, I had the opportunity to live and study and work in many different countries. And these countries had different healthcare systems, which allowed me to witness firsthand the impact of equitable access to healthcare on patients, their families, and their communities and their societies. So, I think equitable access to healthcare is crucial. It is crucial in achieving, social justice, as well as economic development. This is why, I think this should be always a priority for governments, governments across the globe.

Adam: Now we've talked a lot about gene therapy's life-changing potential - it's what motivates everyone who's working in the field. We have the motivation, we have the demand, the determination, but if this potential is to become a reality in the near future, there are some serious challenges we need to address first.

This vision for the future – for social justice for people living with rare diseases – isn't just going to happen, of course. In the EU, the U.S., and around the world, we'll need to rethink healthcare in order to get there.

Paolo: These therapies are actually, you know, a revolution also for healthcare systems in the way they are administered the way healthcare systems are regulated, how payers work. So, there was, and there still is a need to change the way we are doing things, you know, if you look at, from the healthcare system and perspective.

There's always a way in this case, it's for society and for stakeholders to rethink how they have been doing things until now and how they could do better in the future.

Adam: That is Paolo Morgese, the European director of market access and member relations for the Alliance for Regenerative Medicine, also known as ARM.

He was previously working for an investment and venture capital firm that focused on cell and gene therapies. He's been working in this space for more than a decade now, and he's seen how things are beginning to change:

Science Will Win S1E4

Paolo: So I would say that there has been in the last years, a genuine will to adapt, a recognition that there is a need to adapt or to change, some things so processes, approaches, methods, payment models.

Adam: But this change is incremental, and it happens on smaller scales in each country, or region. For the future, Durhane Wong-Rieger -- chair at Rare Disease International who we've heard from in previous episodes -- well, she wants to think bigger:

Durhane: So I'm hoping that on a global scale, as we think for the right thing farther and further ahead, you know, if we can apply the same kind of thinking as we would to electric cars, you know, as we talk about climate change, right? This, the same opportunity that we got, this is the most important thing that is happening, you know, in our lifetimes, we had nuclear energy, we've had the digital revolution, we now had the genetic genomic revolution. This is transformative and we need to address it in exactly that same way.

Adam: These therapies genuinely have the potential to transform patients' lives, but also society in terms of how we think about healthcare. And so, we're all going to have to start thinking differently. For Durhane, and lots of rare disease advocates, the way forward requires new solutions.

To start, we need to think about how we encourage and continue innovation in this space.

Erik: I think it's widely recognized that the United States is a leading innovator

Adam: That's Erik Paulsen, a former congressman and chair of the Institute for Gene Therapies.

Erik: You know, the challenge today is that there's not one simple solution on how to make these more accessible. And that's why I think it's so important that all these different stakeholders and policymakers, you know, are working together to address some barriers that are out there.

Adam: One early example of this is the Orphan Drug Act of 1983.

Now Orphan Drugs are generally medicines for rare diseases -- the FDA defines diseases as rare when they affect fewer than 200,000 people in the U.S. Because these medicines will be used by so few people, the Orphan Drug Act provides incentives for industry to invest and develop treatments through things like tax credits and grants.

This is a policy that was implemented in the U.S., but also provided something of a roadmap for other countries to follow.

In fact, the EU adopted its own Orphan Medicinal Products or OMP regulation in the year 2000.

MEP Sokol: European Union made the real breakthrough when it's adopted the orphan medicinal products regulation more than 20 years ago. So this was a big change. This was a big change in paradigm because it really created the concrete incentives for the private sector, for the companies to really invest into these orphan drugs. And without these incentives, this would not have been possible.

Adam: That's Professor Tomislav Sokol, a member of the European Parliament.

Science Will Win S1E4

In the EU, orphan medicinal products are defined slightly differently: They are drugs and therapies that are designed to treat life-threatening or very serious conditions that affect fewer than 5 in 10,000 people in the European Union.

These regulations have had a sizable impact. Since their introduction, there has been a huge increase in the number of orphan drug approvals in both the US and Europe. Just a few decades ago, there was a handful. Today, there are hundreds. And a recent study found that in Europe over half of these medicines would not have been economically viable without the EU's OMP Regulation.

Now that is a really big deal. It shows that innovation cannot exist in a vacuum. There is a whole ecosystem that makes these potential breakthroughs possible. But with every new discovery comes a new challenge -- how do we demonstrate value and ensure access to these new potential medicines, like cell and gene therapies? And what happens if we really do see between 10 and 20 cell and gene therapies approved per year in the not-so-distant future?

So, in the years to come, there could be more and more advanced medicines, like gene therapy, getting approval. And, if we are to achieve equitable access, that means having an adequate system in place beforehand becomes all the more important. Now is the time to figure this out. And there's a lot of work to do. Here's Paolo Morgese again:

Paolo: These are systems that are based mainly on traditional randomized clinical trials and cell and gene therapies and gene therapies specifically are, you know, are developing in a different way. Clinical trials are done differently. Also the long term effect is something that is not necessarily known at the beginning.

Adam: As we've explored before, clinical trials for rare diseases are smaller. The patient populations just aren't as big and there are many unknowns, particularly with potential new ways of treating disease such as with gene therapy medicines. That presents a challenge because, as you might remember from previous episodes – data is an important part of assessing value and helping to ensure patient access

Paolo: So you need to collect data over time. And this links to real world evidence, methods and infrastructure. So the way these drugs are assessed, it's very different from traditional drugs, and there's a whole set of changes that need to happen to make this possible. And actually, many countries are making these changes, are adapting, are really investing in new approaches and new technology and infrastructure and methods to, to better assess gene therapies.

Adam: And I want to remind you that data is central to all of this, but it's really important to remember that these data come from real people making difficult and sometimes life-changing decisions.

And herein lies yet another challenge and that is data privacy and security. So how do we go about collecting data and what could it mean for patient access?

That is something Paolo has been thinking a lot about. Again, it comes down to collaboration.

Paolo: So the European union has the ambition to develop pan European infrastructure for collecting data. So that would be really something that will help the sector to advance because having a system to collect data and infrastructure, to collect data real time, and that is generally accepted and is considered

Science Will Win S1E4

objective by all stakeholders will help a lot. So when we talk about innovative payment models, the outcome measure part is it's a critical component of that. So only when you have a way to measure outcomes that is generally recognized as reliable, robust, you know, not bias, transparent, data can be interchangeable, you know, across the board between different players. So that type of situation really, you can leverage that tool and you can implement innovative payment models. So that will be for Europe actually a major change and something important for moving forward for granting access to gene therapies.

Adam: Collecting data is an important piece of the puzzle. Sharing data though is equally important:

Karolina: In the area of rare diseases where we have probably, you know, three patients in the Netherlands, two in Spain, the European collaboration and exchange of data - it's key. It's really key, not only for the patient, not only for the payers, but especially that I think for the clinicians, because thanks to this data, the clinicians, you know, will have also will trust that these treatments, you know, work well and that, you know, that they have the follow-up data they have done. With this data they will have like longer history that they could look back. And I think this, the collaboration about the registry infrastructure for this advanced therapies in is key for the success of access to the therapies.

Adam: That's Karolina Hanslik. Karolina worked on the Rare Impact Project at EURORDIS. Part of that work involved facilitating conversation among different groups, such as regulatory bodies, patient groups, and clinicians. The goal is to increase access to gene therapies through greater collaboration across Europe.

The Rare Impact team advocates for centralized data registries. A registry is an interactive database that organizes, stores, and presents healthcare information. They're set up to collect data about treatment and outcomes for a patient population with a specific disease. And since this centralized registry data is all in one spot, there can be broad analyses to find trends, and ultimately, help doctors improve health outcomes for patients.

Because these disorders are so rare and complex, data registries are critical for tracking progress in gene therapy development and treatment. These systems allow for benchmarking, for treatment surveillance, for tracking durability of treatment, potential side effects over time, and much more.

Karolina: There are many registries, disease registries, patient registries, there're also registries that are organized within the manufacturers. There are also some registries that are set up at the national level. And I think in the future all these registries should, you know, start collaborating.

And in the future, it would be really important to have like the concept of the Federation of data. So the European countries collaborate and then internally they exchange the data about these patients. And, we will have the data in the future and the follow-up data, which will also inform the value of the treatment.

Adam: When you think back to this issue of cross border health care – we talked about this in Episode 3; patients getting treated all around the EU – this secure data sharing becomes all the more important.

But let's take this a step further. Data registries are also an integral part of success for what's known as European Reference Networks, or ERNs.

Science Will Win S1E4

These networks are an important resource, especially when it comes to improving care of rare disease patients in Europe. They're virtual and they aim to connect healthcare providers across Europe with the intent to help European rare disease patients get better access to high quality healthcare. So that way, this specialized knowledge isn't just consolidated in one country, or region.

Clinicians and healthcare professionals throughout Europe can connect and organize patient information through a secure online platform. And it facilitates more collaborative conversation and effort surrounding diagnosis and treating patients.

ERNs also provide a structure – a path to healthcare – for rare disease patients. Here's Simone Boselli again:

Simone: The knowledge can travel through the European reference network and therefore specialists throughout Europe can provide someone in any corner of Europe with the right diagnosis, with the right and appropriate care pathway.

Adam: Patients can't access ERNs directly. But, with consent and in accordance with all the rules and regulations, their information can be transferred to the ERN member from their respective country. Therefore, making the path to care in their country more directed and more personal.

Simone: If those European reference networks are properly embedded in the national healthcare and even regional healthcare pathways. And therefore, that's how I see it is when a therapy is made available because of the regulation, we have a structured pathway to access at European level where we know when the assessment will be done. Where we know when the discussion around the value will take place, according to what criteria. And I think that's really represents equity and transparency of the process that is so necessary to make sure that the decisions are understood not only by the patient community, but by the civil society at large.

Adam: There are just so many ripple effects when it comes to rare diseases. A rare disease has an effect on your health, of course. But it also can affect what career you pursue, your aspirations, where you live, your family life and their lives, especially if someone in the family is a caregiver.

All of these things are certainly important to the individual, but also to society as a whole.

And that's what's so important to remember when we're thinking about gene therapy. If eligible patients who want it can get access, that potential one-time treatment could replace years or even a lifetime of managing an illness.

Erik: We have an opportunity to make a difference if we can align the different resources together, and then advocate for some solutions that we know policymakers, ultimately will care about if they're educated on the opportunities to make a difference in this space.

Adam: That's Erik Paulsen again. Although we have this big opportunity, when it comes to the big changes needed to pave the way for gene therapies, Erik has also seen a healthy dose of skepticism.

Erik: A lot of that is I think for the lack of understanding of how to really help patients or modify the healthcare system and society that can benefit from these incredible medical advances that are offered

by gene therapies.

And so rather than pumping the brakes on this new technology, we should be advancing the opportunities as quickly as possible. And that includes addressing, again, the regulatory and the reimbursement hurdles that will speed the near-term access to gene therapies, and then look at how do we advocate for more sustainable long-term solutions.

Adam: As these therapies become part of the political conversation, Erik has also watched the tenor change.

Erik: The good news is that there are more policymakers that are meeting with these folks. There's rare disease days and months, and focuses by policymakers where there's more of an emphasis now on what can be done to help, you know, reduce some of the regulatory barriers, making sure that there's accessibility for these treatments, for people of all backgrounds. And so policymakers are digging in and caring more about this as well.

Adam: It's important to remember how huge that difference could be. But it can also feel like the challenges ahead are insurmountable. Patients have no time to lose. And, it's imperative to get this right – to ensure these treatments are safe and effective. But I want to step back a bit and think about these challenges a little differently.

Over the course of the pandemic, we've seen how governments, industry, and healthcare providers can come together efficiently to solve an urgent medical need.

Collaboration was the key there. And the same goes for gene therapy. Many different groups will need to come together to solve problems and enact systemic changes to facilitate access.

The regulatory framework that affected COVID vaccines' development surprisingly also connects to gene therapy. Here's Paige Bischoff, the senior vice president of global public affairs at the Alliance for Regenerative Medicine.

Paige: We were really happy to see during the COVID pandemic that the European commission granted a temporary derogation or exemption of the GMO legislation in order for vaccines to be developed.

However, it still applies to gene therapies right now.

Adam: GMOs – genetically modified organisms. What do vaccines have to do with GMOs? Well, some COVID-19 vaccines use mRNA, a small piece of genetic material that teaches the body how to build immunity. By European standards, that means it's classified as a GMO.

In Europe, the GMO status would have slowed or even halted mRNA vaccine development. But, because of the pandemic, the EU decided to make vaccines and treatments for COVID-19 exempt from some of the GMO restrictions.

Gene therapies have also found themselves under the GMO designation in the EU. That's because -- as we've learned throughout this podcast series -- gene therapy is the introduction, removal or change in genetic material into the cells of a patient to treat a specific disease.

Science Will Win S1E4

Paige: The GMO legislation is problematic because it's an unintended consequence for gene therapy and for gene therapy trials. It was put into place to protect crops and to protect agriculture. But now it's really creating a barrier for European developers and it's delaying patient access.

Adam: Alongside two other trade associations, the Alliance for Regenerative Medicine has called for the permanent exemption of GMO requirement for gene therapies. They're urging policymakers to grant this exemption because unlike crops and agriculture, gene therapies do not result in significant environmental risk. Advocates say that if this push is successful, clinical trials investigating gene therapies in Europe will accelerate, meaning data will be available earlier and ultimately this could help expedite access for patients.

This is something we've seen bear out in other regions around the world, like in the US or Asia, where GMO legislation is far less complex and cumbersome.

Finally, I want to return to one more important lesson from the pandemic. And that is the importance of health and equitable access to healthcare.

There is a lot riding on the potential for gene therapy. And this potential to transform lives – for patients, for families, for physicians, and for society – all of this can only be realized when it's accessible to appropriate patients who want to pursue it.

It's a long road, full of challenges. But it's also full of inspiration. Innovation. Solutions. Change. And a real drive to get there as quickly and safely as possible.

In our interviews over the course of this miniseries, we asked people to envision what a future with a successful, accessible gene therapy might look like. And I want to leave you with some of their answers.

First, here's Paolo Morgese:

Paolo: We will have a certain number of patients, their families, we will have an impact on our society. Change the way healthcare is, you know, is done, is managed. We will also bring resources and investment to other treatments that will come that, you know, there are areas where we are working are, let's say not me, but, let's say as humanity or, you know, our research is, is working hard to find gene therapies and treatments for many other diseases.

Adam: Now Paige Bischoff:

Paige: I think the most exciting thing is that we've kind of just cracked the door, open a hair, and it is going to at some point in the not-too-distant future really swing wide open because we do believe this is the future of medicine. And just think of how many patients around the globe, these types of therapies are going to be able to help in the future. It's just amazing. It's exciting.

Adam: This one from Reda Guiha:

Reda: It's a noble cause. It's really a noble cause. And imagine if we can reach every eligible patient out there, you know, imagine the impact on humanity.

Adam: Now Karolina Hanslik:

Science Will Win S1E4

Karolina: My hope for the future and advanced therapies, cell and gene therapies is that, you know, once a child is born, that the child will get immediate treatment. And, this is I think the hope of all parents that have children that were born with a genetic disease.

Adam: And finally, Nikhil Gadre, who comes to this on a personal level. What could an approved gene therapy for hemophilia mean to him, and others like him living with severe hemophilia?

Nikhil: That ability to not have hemophilia be a part of their decision-making, of their limitations or of their definitions of what is, and what's not possible.

Adam: Science Will Win was hosted by me, Adam Rutherford.

That was the last episode in this mini-series, but we hope you'll join us for future seasons.

Please do take a minute to rate, review and follow Science Will Win on Apple Podcasts, Spotify or wherever you listen to podcasts. It really helps new listeners to find the show. Special thanks to our guests, to the Rare Disease team at Pfizer and Wonder Media Network.

Thank you so much for listening!