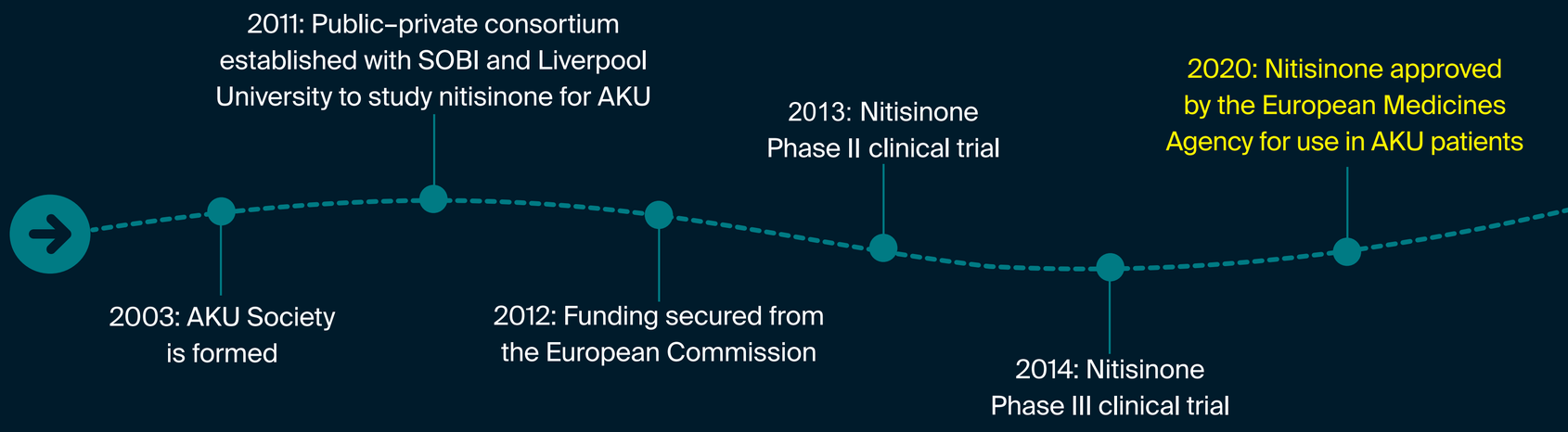
Rare disease partnership pathways; is the road only paved with good intentions?

Nick Sireau, PhD

CEO and Chair of Trustees at the AKU Society
Co-founder and Chair of Beacon
Lumanity Expert Patient Council

We sat down with Nick Sireau – CEO of the AKU Society, a rare disease advocacy group, and a member of the Lumanity Expert Patient Council – to talk about the challenges facing the rare disease community. This included the impact of the pandemic on patients with rare disease and their families, and also the need for better partnerships with stakeholders to accelerate and broaden access to life-saving treatments for the rare disease community. Here we share his incredible personal journey in advocacy, and his insights for meaningful change.

The long road to approval for drug repurposing



Hear my Voice

Q&A

Please introduce yourself and give us a brief history of your organization?

I am Nick Sireau, the Chair and CEO of a patient advocacy group called the Alkaptonuria Society. Alkaptonuria – or AKU for short – is also known as "black bone disease", and is an ultra-rare genetic disease that affects two of my boys. It is characterized by a single gene defect, which means they can't produce a specific enzyme, leading to an accumulation of an acid called homogentisic acid at 2000 times the normal rate. This acid binds to cartilage and bone, turning them black in a process called ochronosis. As the joints deteriorate, the spine deteriorates; my boys also have problems with their heart, eyes, ears and other different parts of the body. So as life develops, it becomes severely disabling.

We set up the AKU Society 19 years ago, in 2003, and over the past 19 years we have been focused on developing treatments for this disease. We have been particularly successfully with one treatment, a drug called nitisinone, and over the past ten years we have taken it through a Phase II and a Phase III study, and it was approved by the European Medicines Agency a year and a half ago for the treatment of AKU. Both my boys are now under treatment and it seems to be going very well.

I have also set up a charity called FindaCure, which is being rebranded to the name Beacon. This is an advocacy group for all rare diseases. At Beacon we provide training and support to people who want to set up their own rare disease patient groups. So a lot of what we learned from the AKU journey we've put into Beacon.

How would you define your organization's purpose?

At AKU, our main objective is to develop treatments and ultimately a cure. We also provide practical support for patients in the UK, and around the world, to help them live with the disease and to access those treatments. The charity is based in the UK, but we do help patients around the world; we have set up sister societies in many different countries – such as Italy, Germany, The Netherlands, Slovakia, Jordan, India, Brazil, USA, and Canada. My parents have also set up a French AKU society called ALCAP in France.

At Beacon, we are working with numerous rare disease patient groups in the UK, but also more broadly on what we call 'drug repurposing' – basically using drugs that have already been approved for one indication and redeveloping them for other indications – which is a much faster process than developing a drug from scratch. However, it's a very difficult process.

The first problem you face is that many drugs which are used for other conditions will be off patent, so there are no intellectual property rights, meaning that pharmaceutical companies are not really interested in developing them because they won't be able to protect it and won't be able to charge a price high enough to then get a return on their investment. So you have to find other ways of doing it. In the case of nitisinone for AKU, it was a drug which was coming off patent in 2017, and we managed to work very closely with the company that owned the drug – Swedish Orphan Biovitrum (SOBI) – and convinced them to take this on as a philanthropic project, which they did. And we also managed to get funding from the European Commission, so it was very much a public–private partnership which was critical to the success of the project. SOBI may break even with this project; they are not going to make significant profits, but on the other hand owned the rights to this drug. We believe it can work for AKU and they believed it was the right thing to do.

So we set up a consortium, which was led by Dr Lakshminarayan Ranganath at the Royal Liverpool University Hospital, the AKU Society, the University of Liverpool and SOBI. We received €6 million from the European Commission, which allowed us to implement and establish the clinical trials. Because they were successful, SOBI then went to the European Medicines Agency to apply for a marketing authorization, which was granted.

The other problem with drug repurposing is that fundraising really takes a long time because there aren't many pots of funding for this kind of work. The European Commission does a call for proposals every two or three years for rare diseases, but that is heavily oversubscribed: when we applied ten years ago, I think there were 600 or 700 applicants. We've tried many times since then to apply to the European Commission, and it's become so competitive.

Even though I accept it is really tough to do drug repurposing, particularly when your drug is off patent, the example of this public–private partnership demonstrates there is a way to make it work.

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What are the biggest challenges your members face?

One of the biggest challenges we face as a rare disease advocacy group, is identification of patients. When you work with an ultra-rare disease, it very much is like looking for the needle in the haystack. We have to do patient identification campaigns. Fifteen years ago, we did a mailing to all 11,000 GP surgeries in the UK highlighting the symptoms of AKU and included a survey. That helped us to identify around 70 or 80 patients. But it isn't practical to do that globally: we can't do mailings around the world. And in developing countries, it's very difficult. You often just have to rely on a doctor who might have a personal interest in the disease.

A second challenge is funding, which is really tough and it's getting tougher post COVID-19, and with the increasingly challenging economic situation. Additionally, there's so much good science and projects out there at the moment from so many universities, which makes it very difficult, I think, for the funders and reviewers to actually decide which proposal to go with and share limited funding.

The third challenge is the complexity of the science. For advocacy groups, setting up and running a clinical trial, for instance, is very difficult. Increasingly, new therapies such as the one we're looking at with gene therapy are challenging. People have worked on gene therapy for 40 years now, yet there are still only a handful that have been approved and there are still many outstanding questions. It is often hard for advocacy groups to know where to go for this type of information for their members.

How well does the pharmaceutical industry understand the challenges your patients face?

I think it depends. For instance, I think what SOBI did with our advocacy group – setting up and funding a public private–partnership to repurpose nitisinone – was absolutely exemplary. I think it's a really good model of a patient group, pharma company, academic institution and hospital collaboration, which worked really well. Other companies might not have the same philanthropic approach. We also have the situation where companies tend to go for the same rare diseases, because those are diseases that are much better understood and for which there's a regulatory route and a clear return on their investment.

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Is the pharmaceutical industry helping you address your challenges?

You have to 'de-risk' it for the companies. They have investors and the investors want to go to the places with the least risk. Having a center of excellence that brings together the patients, a multidisciplinary team, the university and hopefully a research team for a disease makes a massive difference. For AKU, we set up the Center of Excellence in Liverpool ten years ago at the Royal Liverpool University Hospital, which is also the National AKU Center, where we had access to research labs, animal models and other facilities. And then if the research is successful, we can then take it straight into the clinic to do clinical trials at the center.

Generally, I think pharmaceutical companies should be doing more pro bono work and providing more funding to patient groups. They could be offering resources and expertise to support with pharmacovigilance and the regulatory details for clinical trials, for example. I use the example of the legal industry: for AKU we get pro bono work from UK firms such as White & Case and Hogan Lovells, who put a certain percentage of their profits into providing pro bono services. Another example is a company in Cambridge, UK called Costello Medical, who are involved in many fields, including health and economics. They have a pro bono division and have provided us with tens of thousands of pounds worth of support.
I think if the pharma industry had a pro bono department with people with regulatory expertise, clinical trial expertise, and other specialized skills, then a patient group could approach them and say "I'm working on this rare disease and I really need help developing a clinical trial protocol because we just can't afford it". I think that would be awesome.

What more could be done for patients in your view?

Support for mental health. Many patients with rare diseases, and especially those with chronic conditions, tend to suffer from poor mental health. It's compounded for rare diseases because of the rarity of their condition, so they will not necessarily meet anybody else with the condition. For many, there is no patient group to join, and they might not have a center of excellence nearby. So they'll be very much lost in the healthcare system and in the wider world. I think a lot of work needs to be done to support their mental health, particularly post-pandemic. What the pandemic showed is that mental health is a huge problem, particularly for people being locked at home with chronic and rare conditions who can't get treatments and support. It's a massive issue, especially for patients with rare diseases.

If you could change one thing to benefit your membership and reflect their needs, what would it be?

So much of it really comes back to funding. As a patient group, we spend so much time completing very large funding applications from a number of sources – from pharma, to large European grant programs for millions, to tiny applications to trusts and foundations for a few hundred pounds. It's very time consuming and it's getting more competitive. So, there is definitely a need for more money, and more partnerships, for rare disease patient groups.

Nick Sireau, PhD, is the CEO and Chair of Trustees at the AKU Society, a patient group that helps people with AKU, a rare genetic disease affecting both of his children. The AKU Society and Nick are the winners of the 2021 Members Award by EURORDIS (the European Organisation of Rare Diseases) because of their work on successfully developing a new treatment for AKU. Nick is co-founder and Chair of Beacon, an organization that helps all rare disease patient groups. He is the editor of *Rare Diseases: Challenges and Opportunities for Social Entrepreneurs* (Greenleaf 2013) and of the *Patient Group Handbook: A Practical Guide for Research and Drug Development* (Beacon 2016). Nick is co-founder and Chair of Beacon, a medical charity that funds research into obsessive-compulsive disorder (OCD), a common yet debilitating mental health condition. He is also co-founder of Sirgartan Therapeutics, a biotech that focuses on new treatments for OCD. Nick has a BA from Oxford University, an MSc in management studies from the Lyon Graduate School of Business and a PhD in social psychology from City University.
He is a fellow of the Ashoka Fellowship of Social Entrepreneurs.