“When we were introduced to the AKU Society, we had a huge weight lifted off our shoulders. It’s not just a charity, it’s a community, where people can reach out to each other.”
Our Mission

Transforming the lives of AKU patients through patient support, community building and medical research.

The AKU Society is a patient-led support group. We work to improve the lives of those with AKU and those who support them while researching for a cure.

On the cover: An AKU patient asks a question at our Patient workshop
We exist to find a cure for AKU

2019 was a big year for the AKU community. January was the last visit for our AKU patients enrolled in the SONIA 2 (Suitability of Nitisinone in Alkaptonuria 2) clinical trial of nitisinone for AKU. This was the largest ever trial conducted in AKU, with 138 patients from across Europe and the Middle East participating. All of this was coordinated by Prof Ranganath at the Royal Liverpool University Hospital with 12 other hospitals, universities, AKU patient groups and industry in a consortium called DevelopAKUre.

In June, Prof Ranganath went to Stockholm for a meeting with pharma company Sobi, which produces nitisinone and is part of DevelopAKUre. With a mixture of excitement “We’re also working on a complete cure. Gene therapy is the ultimate way forward for genetic disorders such as AKU”
and trepidation, they pored over the enormous amount of data produced by the SONIA 2 study.

After the meeting, they announced to the rest of the consortium that the data was statistically significant, which was excellent news. Sobi's senior management agreed to submit a request to the European Medicines Agency (EMA) for a marketing authorization for nitisinone for AKU.

Putting together the file for the EMA was no easy task. The final version came to thousands of pages of data and text and was submitted in February 2020. The EMA now has 12 months to go over it and get back to us.

This is the culmination of 17 years of work by the AKU Society, the Royal Liverpool University Hospital and the University of Liverpool. When we started in 2003, having an approved treatment for AKU was simply a dream. Through years of hard work, of successes and disappointments, with tens of millions of pounds raised for AKU research, we're now on the verge of that.

But the fight is far from over. Nitisinone has side effects caused by an increase in the amino acid tyrosine. That's why we've started a programme of research into a plant enzyme that could break down tyrosine in the gut and avoid the side effects.

We're also working on a complete cure. Gene therapy is the ultimate way forward for genetic disorders such as AKU. If done correctly, it can repair the faulty gene and restore a normal metabolism for AKU patients. In 2019 we started working on funding applications to test gene therapy in our lab models at the University of Liverpool.

We're still working on this and hope to secure funding later in 2020.

As you'll see in the rest of this impact report for 2019, the AKU Society carried out many other activities too. The National AKU Centre in Liverpool continued to thrive, with patients pleased with the service provided. The Breaking Down Barriers project continued to work with ethnic communities to raise awareness about the risk of genetic diseases. We also launched a new website, a community fundraising drive and much more.

Thank you for all your support. It means a lot to us.

Nick Sireau, Chair and CEO

"Through years of hard work, we're now on the verge of an approved treatment for AKU."

£9,777.60

Parent of a child with AKU and all-round superstar Jess Barnes raised a staggering £9,777 over Christmas. Jess plunged into the English Channel 12 times, risking ice-cold conditions. Jess couldn’t have done it without the support of her friends the Salty Seabirds and from the AKU community. All the money she raised will go towards the upcoming SOFIA paediatric study. We want to thank Jess from the bottom of our hearts. Jess’s dedication and hard work mean we are ever closer to finding out when the damage done by AKU starts.

New website

We are happy to announce that we launched the AKU Society’s new website. The site was redesigned to make it much more accessible and easier to navigate. It features clearer menus, a cleaner design and looks much better on your smartphone. Browser aloud returns and makes the website even more accessible. Let us know what you think.

99%

We saw the end of DevelopAKUre in 2019. Ten years of hard work, planning, examinations, patient visits and trips across Europe finally came to an end. Three clinical sites in Europe saw 138 patients from numerous countries take part in our three clinical trials to prove once and for all that nitisinone reduces homogentisic acid (HGA) in AKU. We did it. We now know the drug lowers HGA in the body by 99%. SOBI, who make the drug, is now taking it to the European Medicines Agency (EMA) for potential licensing for use in AKU.
Ann Kerrigan

2019 also brought very sad news. A long time AKU advocate and dear friend of the AKU Society passed away at the end of summer. Ann will be remembered as always being the first person to volunteer to talk about AKU and our work; she even gave lectures to student doctors about AKU.

We miss you Ann.

8th Patient Workshop

At the end of the year we hosted another successful patient workshop. Held on the 25th November, it celebrated Garrod Day and had a very interesting talk from Prof Ranganath about the end of the SONIA 2 clinical trials. We also enjoyed some chair-based Pilates.

“When we were founded way back in 2003, we would never have dreamt in our wildest dreams that we would be as close as we are now to stopping the burden of AKU once and for all.”

2019 was a hectic year for the AKU Society and we are sure that we will look back on it and realise just how historic it was. The dedication of our team, clinicians, academics and patients has led to AKU patients everywhere being more supported, more knowledgeable and now with an effective treatment. When we were founded way back in 2003, we would never have dreamt in our wildest dreams that we would be as close as we are now to stopping the burden of AKU once and for all. A huge thank you to everyone who has made this new reality possible.
Meet Tony

“In July 2011, at the age of 53, I was diagnosed with alkaptonuria. Prior to this, I had been treated for severe osteoarthritis. This first came to light when I was treated for a problem with a disc in my lumbar spine in 1987. This got progressively worse until I had to retire from the health service where I had been identified as a future leader of NHS Wales. I was told I wouldn’t work again and that I could end up in a wheelchair by the time I was 50.

Having to finish work at the age of 40 was quite a shock and was one that I didn’t really accept. After coming to terms with this and not working for 18 months, with the support of my GP I went to university, qualified as a primary school teacher gaining a first class honours degree. Whilst working as a teacher my physical health continued to deteriorate with the main issues being decreased mobility, pain, breathing and lifting issues.
Prior to being diagnosed with Alkaptonuria I also cared for my wife who was terminally ill and my sister who had Down’s syndrome and dementia.

Living with AKU has been a challenge, but from the time of my diagnosis I was put in touch with the AKU Society and eventually, once agreed with the Welsh Assembly Government, started to attend the National Alkaptonuria Centre in Liverpool. From this I was able to get a better understanding of the condition and what physical conditions I was dealing with. It helped us to plan what needed to be put in place for me to continue in work. I was fortunate to have a supportive head teacher and occupational health team. Eventually, however, I had to finish work on ill health as I physically was unable to function in my teaching role.

Since finishing work I still keep as active as I can, maintaining links with the education system through being a school governor in two primary schools, I am also chairperson for a local choir and in respect to the AKU Society I became a patient trustee, attend conferences to help educate health professionals on the condition, speak at public events, take part in trials and help to give support/advice to fellow AKU patients.”

‘I was able to get a better understanding of the condition and what physical conditions I was dealing with. It helped us to plan what needed to be put in place for me to continue in work.’
Sian Williams hosts a Pilates session at our patient workshop

AKU Society Patient Workshop

3rd November 2019

The Bluecoat
Patient Support

The National AKU Centre (NAC), based at The Royal Liverpool University Hospital, first opened in 2012. Until then anyone diagnosed with AKU relied on the support of their GP and local health care services. Because AKU is so rare, it's hard for doctors to give patients the treatment they deserve. This is due to lack of information, knowledge, delays in diagnoses and lack of treatment options.

The opening of the NAC helped bridge that gap by bringing together expert health professionals to provide the best care and treatment for people affected by AKU.

The NAC is an adult service providing ‘one-stop’ care for patients with a confirmed diagnosis of AKU and plays a vital role in enhancing the quality of life for AKU patients and their families. The AKU Society works in partnership with the NAC helping to coordinate care and assisting patients in obtaining the proper support and improving the patient experience.

The NAC has come on in leaps and bounds and is continually striving to ensure it meets the needs of the patient group. Feedback from patients is collated by the AKU Society and jointly reviewed with the NAC team and used to develop and improve the service for the future. We are strong believers that our patients are the experts in AKU and are at the heart of any changes and decisions in their healthcare and ongoing support.

In 2019, 53 patients attended the NAC, 12 were returning for their 8th annual visit. Every year we see new referrals and need to add more NAC weeks. We added one in June 2019, and we need to add another week in September 2020.

As a patient support organisation, we fulfil many functions: educating patients/carers/families, sharing the AKU experience, providing strength to our service users by helping them manage their condition on a daily basis, raising public awareness, and fundraising.

Lesley with an AKU patient at the NAC
Breaking Down Barriers

Over the past 12 months our involvement with the Breaking Down Barriers Project (BDB) has continued and we have been fortunate enough to receive funding for a third year. This will be used to offer genetic testing to the extended families of NAC patients considered at a higher risk of carrying the AKU gene. We identified the need for this project during discussions with AKU patients who attend the NAC, several of whom asked about genetic testing for partners and family members. The Breaking Down Barriers Project enables us to work with other organisations and patient groups to come together and address the challenge of supporting diverse communities. Working in collaboration with the laboratory team at The Royal Liverpool University Hospital we have been able to identify a suitable sampling system using a simple finger-prick tool that can be used at home and returned for testing. We hope to roll this project out during 2020 incorporating education on genetics and inheritance. Our long-term plan will be to offer such testing to the extended families of all our NAC families.

AKU Health Passport

Many AKU patients find it hard to explain to doctors the impact AKU has on their lives. It was agreed with the group that the best way forward to improve the understanding of AKU was to develop a resource tool that can be used for any healthcare appointment or pre-admission or during a hospital stay outside of the NAC.

In 2019 we were successful in our funding application to develop an AKU health passport. The passport sized document is intended to help staff from health care services to be able to offer the right help at the point of contact with the services and provide the necessary care and treatment needed during the person’s hospital stay or clinic appointment. We held the first consultation session with the patient group during a workshop in November 2019. Here they identified what information they wanted in the passport and came up with some ideas on its design.

We have also approached several healthcare professionals who have no previous experience of working with AKU or knowledge of the condition. This group of professionals are the people who are most likely to make use of and benefit from the passport. We are currently liaising with these health professionals to understand what information they feel should be in the passport to help them to plan the care/treatment for anyone with AKU who is referred to them.

Opposite: An NAC patient takes part in a measured walk assessment
‘I do not feel isolated anymore. It is also good to be on the drug nitisinone. I have more energy since starting it and don’t have to worry about my AKU getting much worse’
Community Building

We have a strong and active patient group who are keen to better understand and manage their disease. By holding and facilitating annual patient workshops we offer the patient group a secure and supportive environment to share experiences, learn practical skills to cope with their disease and gain confidence to continue building a stronger, more united community.

In 2019 we held a patient workshop for our UK patients. Like previous workshops, we held 2019’s at the Bluecoat Centre in the heart of Liverpool. We had several interesting and enjoyable talks, including from the NAC dietician Shirley Judd about the role of diet and exercise in patients’ lives and from NAC clinical lead and Chief Investigator of DevelopAKUre Prof Ranganath Ranga talked about the end of the SONIA 2 clinical trials and what the next steps will be for nitisinone. By far the most popular session was a Pilates session, hosted by Sian Williams. This was chair-based exercises specifically for patients with AKU.

We are now planning our 3rd international patient workshop for Spring 2021. These workshops offer a variety of sessions addressing both the physical and psychological impact of having AKU. We will be offering sessions looking at both mind and body to help widen the focus from physical symptoms and a medical diagnosis to a concern for the patient’s overall quality of life.

Many of our patient group have never met anyone else with the same condition until attending one of these workshops. Many of our patients tell us the best and most important part of the workshop is meeting other patients with the same condition as them as well as meeting staff and professionals who understand AKU. This demonstrates the power of shared experiences and the positive effect they can have on a person’s well-being. Our aim is to empower our patient group, so they feel less isolated and learn how to advocate for their condition.
‘It’s fantastic, I love meeting and talking to other patients because they’re the only people that absolutely understand what I’m going through and how I feel. Just sharing and chatting, that means everything’
At the end of 2019 we launched our newly designed website. Our new site has been designed to be much more user-friendly, accessible and easier to navigate while allowing the most important content to be front and centre.

Earlier last year we were informed that the software we use to host and edit our website would be shut down in March 2020. This meant if we wanted a website at all, we would have to move to a new system called WordPress. This gave us a brilliant opportunity to tweak and change our website so that everyone can use the site and so that it is accessible to as many people as possible.

It now features a redesigned menu anchored around our key aims: Information and Support, Get Involved (fundraising), Research and About Us. Each page has a dedicated landing page with easy to follow links and engaging pictures.

One of the major criticisms of our old website was that it was difficult to find where you can download all our leaflets and newsletters. This has now been redesigned completely. At the top of each page above the menu, you can see the link to ‘Download Resource’ and each resource is now much clearer to find.

As you may have noticed, our blogs have also changed. It’s now clearer to see when blogs were published and allows us to design them how we want. This will mean we can change how they look based on their content. We also increased the font size so that people who struggle to read small text can now hopefully read them.

We have also continued using the innovative Browsealoud plugin. Browsealoud is designed to make websites even more accessible by translating content more faithfully than Google and helps people with learning difficulties and mild visual impairment by reading text aloud and with text masks. To learn more about Browsealoud and how to use it head to the blog on the website or email ciaran@akuociety.org.

We are on the lookout for patients and users of our website to join our team of expert reviewers. If you would like to get involved, we will send you a form to fill in which will ask you what you think of the site, if you feel it is useful for you or newly diagnosed patients and what you think we can improve. Your help is crucial for our new website; without the patient input, we won’t be able to judge if we are helping the community.
High Frequency of AKU in Slovakia

- AKU prevalence in general (1:100,000 to 1:250,000)
- In Slovakia prevalence 1:19,000
- The common European AKU chromosome have had marginal contributions to the AKU gene pool
- Most of the AKU chromosomes have origins in a single small region in the Carpathian mountains.

In 2019 we successfully concluded the largest research project ever to take place in AKU. This was called DevelopAKUre and was a series of three major international clinical trials into the efficacy of nitisinone as a treatment for AKU. In partnership with 12 other organisations made up of pharmaceutical, clinical and patient support organisations, the trials tested whether the drug nitisinone is effective in reducing the acid which causes the damage in AKU and whether it leads to clinical benefit. The AKU Society supported the trials, leading on patient recruitment, patient retention, management and dissemination.

We worked closely with the other members of the DevelopAKUre consortium. These included the Royal Liverpool and Broadgreen University Hospital Trust (UK) as the coordinator, the ALCAP (France) patient group for communications/dissemination and patient support; two small companies Nordic Biosciences (Denmark) for biomarker analysis, PSR (Netherlands) for clinical trial coordination and medical monitoring; pharma company Sobi (Sweden) supplying the drug and regulatory advice; three universities (Liverpool (UK), Siena (Italy) and the Institute of Molecular Physiology Genetics (Slovakia)) for the analysis and interpretation of data; and three clinical trial centres: the Royal Liverpool University Hospital (UK), Hopital Necker (France), and the National Institute of Rheumatic Diseases (Slovakia).

Funding for the trials came from the European Commission. The last patient was seen in January 2019 and the consortium then analysed all the data from the trials. In November 2019, the consortium held an investigator’s meeting at the offices of Sobi in Sweden, where conclusions were drawn up about the data, which was shown to be statistically significant. This led Sobi to file an application for marketing approval with the European Medicines Agency in February 2020. We should hear by early 2021 whether this has been successful.
Nitisinone reduces the levels of homogentisic acid in AKU. However, as this acid lowers, another substance, called tyrosine, increases in patients’ bodies and cannot be excreted normally. High levels of tyrosine are dangerous as this can lead to eye problems including dryness, itching, pain and ultimately blindness if nothing is done to correct this.

Currently, the only way to combat this rise in tyrosine is for patients to strictly adhere to a low tyrosine diet. This diet is restrictive and adds to the daily anxiety AKU patients face. The tyrosine side effect also means we cannot give this life-changing drug to children who have AKU, as high levels of tyrosine could lead to children developing cognitive issues.

To stop this, we need to supply a co-therapy to take alongside nitisinone that will stop the high levels of tyrosine accumulating. We have developed a plant enzyme that breaks down the tyrosine in the gut and excretes it naturally before it can cause any issues. We must prove this enzyme reduces tyrosine in our mice models so we can move forward and begin to explore administering this therapy in AKU patients alongside nitisinone.

Our first two AKU mouse models will be given nitisinone and Dr Juliette Hughes, our post-doctorate researcher, will record tyrosine levels. They will then be given the enzyme to show how it reduces the level of tyrosine. This will hopefully prove that the enzyme works.

Our third mouse model project will use a method to edit the mice’s genes. It will delete the AKU gene from the mice and insert a corrected gene, effectively curing AKU and producing a healthy mouse. This project is vital as we must prove the safety and efficacy of the method on the AKU mice before we can trial this gene therapy on humans.

We also want to find out at what age the damage starts in AKU as this will help us inform when nitisinone should be administered. Previous research has found that the damage to joints caused by AKU could start in children young as 16. However, we do not know if this damage happens even earlier. This is why we are launching a study called SOFIA-Paediatric (Subclinical Ochronosis Features in Alkaptonuria in paediatric age) to study children under 16 who have AKU.

Opposite: Prof Ranaganth, Chief Investigator of the DevelopAKUre clinical trials, gives a talk at our Patient Workshop in 2019.

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**DevelopAKUre Trial Sites**

- **Royal Liverpool University Hospital, Liverpool, UK**
- **Hôpital Necker, Paris, France**
- **National Institute of Rheumatic Diseases, Piešťany, Slovakia.**
“Nitisinone, if it stops the damage, is exactly what all of us need. I want it for all of us; for the children with AKU and the adults who battle with it every day. Nitisinone could stop progression of the disease. It is our miracle.”
“When I found out that the AKU Society needed support in funding the first-ever paediatric study into alkaptonuria, I knew I needed to help.”
Fundraising

What a fantastic year it has been for fundraising. We have had continuous support from trusts and foundations that are funding various projects that are vital in supporting AKU patients and running medical research, including the SOFIA-Paediatric study, which is due to take place end of 2020. This will be to study children who have AKU, to see at what age the debilitating symptoms start. The continuous funding of the NAC has had an enormous impact on patients, who can receive treatment and health assessments for AKU. We have also received funding from the Sylvia Adams Charitable Trust to continue the third year of the ‘Breaking Down Barriers’ project, where we support patients from ethnic minorities and family members with AKU.

Not only have we raised funds for vital projects, but our supporters have also gotten involved! We have had a busy year in terms of community fundraising. During the cold winter months, two brave runners faced the mean Cambridge streets for the Cambridge Half Marathon. Our annual Garrod Day Coffee Morning was held on November 25th, the same day as our UK patient workshop! Coffee mornings were held at the Raremark and Costello Medical offices. Our Patient Support Manager, Lesley, held one in her home and we even had one in California. We held an early cake sale at our office in Cambridge and celebrated Garrod Day with a cake and raffle during our UK patient workshop. So many cakes! To top it off our Christmas appeal for funds for our upcoming SOFIA-Paediatric study was a success, with Jess Barnes inspired to do 12 days of Christmas swims. She raised an astonishing amount, a lovely Christmas present for the AKU Society.

We are excited to see what fundraising events are planned and what funds are raised in 2020.
The AKU Society would like to say a big thank you to our funders, fundraisers, volunteers and supporters. Trusts and foundations have had a huge impact on our ability to run successful projects to help AKU patients and fund vital medical research. Below is a list of funders who have supported us this year and what their grant was used for:

**Childwick Trust** - SOFIA-Paediatric Study

**Anonymous Trust** - SOFIA-Paediatric Study

**Genetic Disorders** - Jeans for Genes Grant for the SOFIA-Paediatric Study

**National AKU Centre** – Patient Support before, during, and after NAC clinics

**European Commission** – FP7 DevelopAKUre project. Our clinical trials into the drug nitisinone

We also want to thank our wonderful community fundraisers this year; Ana and Katja, who ran the Cambridge Half Marathon raising £651.82, everyone who participated in Garrod Day this year where we raised £730, Jess Barnes for raising an amazing amount of £9,777.76 for her 12 days of Christmas Swim and everyone who donated to our Christmas appeal, raising £1,550 in total. Well done!

A massive thank you to everyone who has dedicated their time to raising money, volunteering and supporting the AKU Society. We are extremely grateful for your help.
### Income

- **£266,546**
  - Research and Support: **£261,807**
  - Voluntary: **£4,739**

### Expenditure

- **£251,705**
  - Research and Support: **£222,577**
  - Cost of Generating Income: **£23,620**
  - Governance: **£5,508**

### Funds Summary

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**Resources Expended**

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