Transcript Webinar

Clare Goddard >> Okay. Welcome, everybody. Just letting everyone settle in. And make sure that the captions are on, et cetera. Just give you a few seconds just to make sure you're set up.

>> Okay. So welcome, everyone. Thank you to our panelists today. Welcome to everybody joining. This is our first NF2 BioSolutions webinar from the UK team. It's great to have you here and thank you all very much for joining. This is being recorded, and it's going out live as well. You'll be able to capture anything you've missed as we go through.

My name is Clare Goddard. I'm a wife and mother of two with neurofibromatosis type 2. That's my most important role. I'm also the CEO of NF2 BioSolutions UK and very proud to be too. We're a registered charity in the UK, and through NF2 BioSolutions, we are advancing bacteriotherapy, immunotherapies as treatments for NF2.

As a global entity in the UK, the charity is formed of patients and family all with a link to neurofibromatosis type 2. We all volunteer our time and skills to seek solutions to the condition, and all the money raised goes directly to our projects.

So in the next hour, we'll hear about the work that the UK arm of NF2 BioSolutions is currently supporting. We'll hear direct from the research lab in Manchester. We'll hear from an inspirational fund-raiser, and we'll also hear from our charity trustee, Professor Gareth Evans, who I'm sure lots of you are familiar with.

You've all been sending in some questions, so thank you for that. We'll be answering them as we go through. So we're very lucky to have support from -- we have lots and lots of support with the charity, and we have clinicians and medical professionals that are helping us all the time and supporting our work.

It's my pleasure to kick off this hour and introduce you to Tony Jones, who is CEO at One Nucleus, one of the organizations supporting us. Over to you, Tony, to give a bit of background as to why you're here. Thank you.

Tony Jones >> Thanks very much, Clare. Welcome, everybody. I'll echo those warm remarks. I guess for One Nucleus, we're a life science membership group for companies all active in researching, discovering, supporting new medicine discoveries. We're headquartered in Cambridge. A big role, we support companies in seeking finance and operational support and insight and connections.

Actually, a key part of what we do is about provoking good questions within the community. Can we collectively do better? What's the best way to do things? And as much as we're funded by description from our 400-plus company members, actually, there really is no more important question than have we got patients at the center of everything we're thinking about and doing?

So we tend to offer complimentary membership to patient groups and the research charities because that keeps the sanity check of what we're doing as an industry. We all have Monday morning issues to deal with, but actually there's patients on the end of this process every time. Whether it's a funding round for development to go forward, whether it's funding into a research lab to identify new ways of treatment.

So if those things don't work, then we don't actually benefit the people who we're here for. So I was delighted to be asked to get involved in the Find a Cure mentoring program and linked up with Joanne Ward, and one of the early discussions was how do we engage the audience more? How do we get the profile up? How do we raise the awareness of NF2 and how people can help?

I think there's nothing -- no better way of doing that than actually engaging with people to see what their questions are and have experts like Gareth and the researchers, as

well as supporters like andy, on the call, to say this is how collectively we can all get around this.

So get the insight, it's often best done in a conversation between experts, and that brings me to who I'll be handing on to in the form of Mike Ward as one of the best commentators and experienced commentators in the life science industry and has been for a good while now.

Mike has seen trends, patterns of deal making and research come and go, but actually he does a lot to engage companies in, well, are you focused and what this patient centricity actually means and headlines put up. But how do you walk that talk?

So it was an honor for me really to be able to reach out to Mike and say, look, would you do this conversation with the NF2 guys? To bring some of that to life not just for the biopharma industry and the research industry but bring it to the patients as well. With that from me, I'll be happy to answer any questions about One Nucleus and getting involved, but I'll leave it to Mike.

Mike Ward >> Thanks very much, Tony. It's a pleasure being here. My name is Mike Ward. I'm the global head of Life Sciences and health care thought leadership at Clarivate, which is a company that helps academic and industry researchers accelerate their efforts. We do this by tracking the most impactful scientific papers, providing up to date information around patents and trademarks, tracking clinical trial activity. Highlighting which companies are actually interested in particular diseases, for example, the deal making that Tony was referring to there. But really importantly, ensuring that the voice of the patient is actually heard and that their needs are focused all along that sort of discovery, development, and delivery timeline, as well as actually also helping companies understand sort of the latest regulatory policies or also how they might evolve.

In the past two decades, since the completion of the human genome project, we've seen a massive increase in interest in developing treatments for rare diseases. And much of this research is actually conducted in university laboratories, often funded by medical charities like NF2 BioSolutions.

So I'm delighted to be joined today by Grace Gregory and Adam Jones, two Ph.D. researchers at the Geoffrey Jefferson Brain Research Center in Manchester, whose research is actually being backed by NF2 BioSolutions.

Adam Jones Hi, everyone. I'm Adam, one of the Ph.D. students here in Manchester backed by NF2 BioSolutions. My background is strongly grounded in immunology, having worked on the developmental origin, as well as malaria here in Manchester.

So my current work focuses on neurofibromatosis type 2 associated with vestibular schwannoma, which is a tumor that focuses on the cochlear nerve of the ear. I'm interested how inflammation can drive tumor growth. We're using advanced technologies to create a deep facial map of the tumor tissue so that we're able to look at different interactions between cancer cells and interactions targetable with drugs to stop the tumors from growing and hopefully shrink them to improve the hearing of people with neurofibromatosis type 2.

My research partner is the lovely grace, whose work is on meningioma.

Grace Gregory >> Hi, everyone. Thank you so much for having me today. I'm the other NF2 BioSolutions funded Ph.D. student here at Manchester. So I work very closely with Adam, and our projects kind of run in parallel to each other.

I actually come from a drug discovery background because previously I worked on developing new drugs for Alzheimer's disease at the University of Oxford, but now I'm in Manchester, and I'm really focused on working on neurofibromatosis type 2 associated meningioma.

So meningioma are tumors that grow on the membranes that surround the brain and are the second most common tumor type to neurofibromatosis patients after vestibular schwannoma.

So I'm currently looking at how we can target the inflammatory pathways within these tumors with drugs that have been repurposed and validated in other diseases. So our aim really is to shed a light on the inner workings of these tumors and to investigate potential drug targets that could be taken further as new treatments for those with neurofibromatosis type 2.

Mike Ward >> Great. Thanks, Adam and Grace, for joining me. We've only got time for two or three questions from the audience. So I'm going to jump straight in.

So the first question relates to the role of inflammation. Do you think spine tumors like schwannomas and ependymomas grow due to inflammation? And if so, would actually anti-inflammatory drugs treat those as well?

Adam Jones >> So almost all tumors have an inflammatory component to them, so it's very likely that spinal schwannomas and ependymomas will actually benefit from targeting inflammation. However, this has to be validated in the lab by methods we're using now for vestibular schwannoma meningioma. But the simple answer is most likely, yes.

Mike Ward >> And with regards to inflammation in vestibular schwannomas or meningioma, what percentage of tumor is actually inflammation only? How is this sort of your best assessed and monitored? Is it through MRI?

Grace Gregory >> Yeah, that's a good question. So as far as inflammation in the tumors go, it really varies between tumors. It varies between meningioma and vestibular schwannoma, and it varies between each person too. So are very

inflammatory and others not so much, but it is likely that these inflammatory components within these tumors have an impact on growth of these tumors.
And as far as how to measure this inflammatory component, it is possible with MRI, but only with a specific type of MRI called DCE MRI, which is unlikely to be the form of MRI that is used to regularly monitor the tumors that grow in neurofibromatosis type 2 patients.
Mike Ward >> Right, right. Okay. Now I guess the $64,000 question. If drug candidates are identified from sort of the current inflammation research that you guys are doing at Manchester, how soon might these be available to people with NF2?
Adam Jones >> So this will be highly dependent on how well the drugs work in our preclinical studies within the lab, as well as how they actually work within people with neurofibromatosis type 2. But if we are able to find a drug that is effective, very importantly safe, and readily available, hopefully over the next few years there might be a drug available for neurofibromatosis type 2 patients, all going well.
Mike ward >> Sure. We didn't have too much time. It's a shame we couldn't talk for too much longer. I'd like to thank you both for sharing the insights of what you're focusing on. Obviously, we wish you all the best in your efforts. Clearly, it's worth emphasizing that such research is, in fact, an expensive exercise, and therefore it clearly highlights the importance of financial support from medical charities such as NF2 BioSolutions. Of course, that's only possible by the fundraising activity and efforts of volunteers.
So on that important note, I'm going to hand the baton back to Clare.
Clare Goddard >> Thank you, Mike. Thank you, Grace and Adam very much indeed. Very important work you're doing for us. Thank you for being so communicative with us as well. Grace has a blog on her website, and she's inviting patients to come along and put their stories in there. She really wants to open up these links between patients and

research labs. So we really want you to get involved and chat to us, so do look at the website for that. I think Joe will put the link in the chat for me.

It's my absolute pleasure to introduce Andy White, who is one of our fundraisers, an absolute inspiration to us. I'm not going to say too much, Andy, and let you do the talking. Tell us about your fundraiser, please.

Andy white >> Thank you very much indeed, Clare. It's an absolute pleasure to be here. Thank you so much for inviting me. Maybe first of all start with how I got involved myself. As with everyone, there's a personal connection. In my case, my eldest daughter, Rebecca, was diagnosed with NF2 in mid-2019. She's 34 now. So a late diagnosis. And it was a bit of a bolt out of the blue for all of us. We'd never heard of NF2. It was not in our family. It doesn't run in the family at all. So it looks like it was a spontaneous mutation, in Becca's case, a de novo case of NF2. That was how we started to get involved.

Now, Becca's been on Avastin since shortly after her diagnosis, which has been fantastic. She's been lucky enough to be getting that. She's got bilateral vestibular schwannomas. The Avastin has been more or less keeping those in check. Her left hearing is a bit challenging at the moment. We're looking into cochlear implants for that and a hearing aid and a pen microphone. She's a teacher, so she needs to operate in a classroom environment. So it's very important the hearing is augmented as much as we possibly can.

That's how I got introduced to this world, and it's sort of coinciding --

Clare Goddard >> How much did you raise?

Andy White >> How much have we raised? Well, we raised 14,000 pounds in the event that I've just done. So what happened was this diagnosis and Rebecca being diagnosed coincided with my 60th birthday. So a friend of mine, a lifelong friend. We're

both turning 60 at the same time, more or less. We decided to do a fundraising event. We did the coast to coast, the Alfred wane Wright coast-to-coast to Robin hood's bay, and we raised that 14,000 pounds. That was last September/October.

It was great. We know that that money. We know exactly where it's going, so that's great. I think Adam and Grace are getting some of that in their research, if I understand correctly. So it's great to know the money is going to something very, very concrete. Yeah, it's been a great ride so far.

Clare Goddard >> Brilliant. Yeah, that money's gone directly to the lab in Manchester, every single penny. So what was the most -- people may be looking at us and thinking, I'd like to get involved and do some fundraising myself. Have you got any good tips on what things work well with your fund-raising? Was there a particular thing that was quite easy to do that just raised money well? I know you got involved with a band as well to help raise money. You did all sorts of different things.

Tell us the bit about how we can raise money easily, what you found worked well, and what was fun as well? What were the fun bits?

Andy White >> I think, first of all, a good idea and an important thing is to have a narrative, to have a story. I think that's something that really helped us. Mike and I -- my friend Mike Whitehouse, my co-walker. We had a narrative. We had a story. It was visceral. It was personal. Two friends coming together. He's known Rebecca all his life. So it was a very personal thing, and I think we were able to leverage that narrative and also amplify it through social media. I'm not a great lover of social media sometimes, but it's very, very important for getting messages out there. Not having heard of NF2 myself, something that was very important to me was awareness, was really getting that awareness across. I think the narrative in the story is very important.

So have something that's personal, have something that engages other people in a story.

The second thing, I think, for me certainly, corporate sponsorship is important. Don't be scared to approach organizations. Something that Mike himself said was that people want to have the chance to do good, and that applies to companies as well as to individuals. So don't be afraid to approach corporate sponsors. We wouldn't have got anywhere near 14,000 without Hudson, our corporate sponsor, who was so generous, so supportive of the whole thing. So corporate sponsorship, I think, is a great way to go.

Maybe a few techniques as well. One thing that we found worked very well was that, when someone made a donation, we always thanked everyone personally, individually. But when we did thank them, we -- not everyone, but a lot of them, we challenged them to identify two friends or two colleagues that weren't in our networks, so completely new to the story. Challenge them to find two people to pass on the story to.

Whether that was for a donation for just the story, sending them to the giving page to read the story and raise awareness, and that sort of multiplies the whole thing, which I thought was really, really great.

When we were on the walk, we had these postcards. So we had these postcards printed with the whole story on the back and our sponsors as well, and everyone we met on the walk, whether it's just walking past them on the walk -- the coast-to-coast is quite -- it's a famous walk. Lots of people do it. Every time we passed someone, they got a postcard. Everyone in the evening in the bed and breakfast, they got a postcard. That brought lots of money, and that was amazing. Not just the money, the awareness as well, people reading this postcard and saying, never heard of this. This is amazing.

Clare Goddard >> What you touched on there with the awareness is a huge piece of people with NF2 because some people with NF2 present and they look like they may have a difficulty, but you can't always tell with the hearing impairment what people are going through. It's those hidden disabilities as well. It's so important to raise awareness and to get neurofibromatosis type 2 out there.

Andy White >> It's very important, yes. It's very important to Mike and I it's about awareness as well as raising the money.

Clare Goddard >> Thank you very much for your efforts. It was a massive personal achievement for you as well. You're training hard, and we were comparing training notes, weren't we? Well, your training notes. So thank you very much for doing all that for us. It's a fantastic amount. Thank you very much to Hudson's.

Andy white >> You're welcome. More to come.

Clare Goddard >> Fantastic. On that note, we have the 28th of February, it's Rare Diseases Day, and on the 22nd of May, that's NF2 Day. So if anybody's thinking, wants an inspiration for fundraisers towards those events, we'll be having our own fundraisers and doing lots of different things. So get in touch with us if you'd like to get involved. Thank you, andy.

Now I'll pass over to Professor Gareth Evans, who is a medical geneticist and NF2 expert. Back over to you, Mike.

Mike Ward >> Thank you so much, Clare. What an inspiring story, Andy. Congratulations on those efforts. Earlier on, I spoke to Grace and Adam, two Ph.D. students at the start of their research careers, but now it's my pleasure to introduce professor Gareth Evans.

Gareth Evans >> Someone at the end of their career.

Mike Ward >> I wouldn't say that. For those who don't know you, you're chair of genetics and cancer epidemiology. In the past 30 years, you've established a national and an international reputation in clinical research aspects of cancer genetics, particularly in neurofibromatosis and breast cancer.

Namely, you have that successful bid for 7.5 million for the NF2 service in 2010. And also, as Clare said, you're a trustee of the charity. It's great that you've agreed to join me and agreed to answer questions that have been provided by NF2 patients and their careers.

The first question relates to the drug that Andy's daughter is on, monoclonal antibody, also known as Avastin. It's given to people to slow the growth or shrink schwannomas. The question people ask, is there an alternative to Avastin?

Gareth Evans >> So at the moment, Avastin is the only proven drug that can treat NF2 related tumors. It's still not licensed for use, so the drug company have not made any efforts to license the drug, so we're only able to give it in the UK because we have essentially equivalent to approval because the social services have approved it for use but with very specific criteria, which we have to get ratified by a partner center.

Typically, we're talking about a rapidly growing schwannoma, which would otherwise result in patient deficit, loss of hearing, if you had to do surgery, or a spinal tumor that would cause potentially loss of function if you took it out.

So we are still having to give it within a relatively strict protocol, but it is extremely effective in schwannomas. The problem is it doesn't really work in meningiomas. We often have to stop treatment to treat meningiomas.

Ependymomas, there's some evidence it worked in cystic ependymomas.

Ependymomas are the tumors within the spinal cord itself. Sometimes we can get

some really good responses if there's a cystic component to those tumors. No other therapies have passed any sort of reasonable bar for saying that they are effective.

Mike Ward >> Right, right. Are there any news or candidate drugs that are being tested in trial? You have particularly ones people with NF2 could actually join?

Gareth Evans >> Well, at the moment in the UK, there is no open trial. There is a trial of what's called an hDak inhibitor, set up at the moment, a histone inhibitor. They've gotten approval from the FDA, the Food and Drug Administration in the states, so that's a huge step. I've been involved in setting up the protocol for it. It's a drug that's pretty tolerable, not bad side effects. They are the drug company are very enthusiastic it's likely to have effect on meningiomas and schwannomas, so to be more targeted to both the main NF2 tumor types.

Hopefully, that trial will start later this year. In terms of other promising candidates out there, Brigatinib, which has been, I've seen in the chat, that's in a trial called Intuit in the United States. There's a lot of buzz about Brigatinib. It was the top candidate of all of the pipeline drugs that have been looked at. We're very, very hopeful that will have an effect, particularly on meningiomas, but it is not available off -- it's not licensed yet because it's not been proven to be effective. So we are anxiously awaiting the results of the American studies led from Scott Plotkin in Boston.

Mike ward >> And when do you expect to get that readout?

Gareth Evans >> I've been trying to get an early read on these things. Drug trials, they have to be quite rigorous. They're only really allowed to uncover, particularly in randomized trials, when they reach a particular point in terms of number of patients that have shown any effect. So I've not been given a definite on when we'll be told, but I imagine it will be in the next six to eight months.

Mike ward >> Right, right, okay. That's something to look out for. Is there -- this is a question from the audience, very specific. Is there anything in the research pipeline for effective treatments for children affected by NF2?

Gareth Evans >> So all of these treatments potentially can be given to children. I mean, there is usually a higher bar that's required, but a lot of these drugs are repurposed drugs. So they've already been shown to be tolerable in adults and children.

The likelihood is most of these drugs will be approved for treatment over the age of 6. Essentially, it's very rare we have to treat anyone with NF2 before 6. So children will be eligible for most of these trials going forward. After all, probably 30, 40 percent of NF2 present symptomatically in childhood. We're missing a huge chunk of who we want to treat. If we want to prevent longer term Harms of treating so many tumors with NF2, then we need to get in with a treatment earlier.

Mike ward >> Is there any specific work in hand sort of finding a cure for schwannomatosis, in particular?

Gareth Evans >> Schwannomatosis, the feeling is that what works for NF2 will work for schwannomatosis. Because the schwannoma tumors that occur in schwannomatosis effectively have both copies of the NF2 gene aberrant. They've been damaged. What schwannomatosis does, it accelerates that process but for whatever reason it does not do that on the vestibular nerve to the same extent, and it doesn't seem to give you the meningiomas and some of the other picture of NF2.

There is pretty good evidence that Avastin works fairly similar in schwannomatosis, although mostly anecdotal. I think most of the thought is what works in NF2 will work in schwannomatosis, particularly if it's schwannoma driven therapy.

There is an initiative in Europe where we are lumping together NF2 and schwannomatosis. You've heard it here first, but we've talked about neurofibromatosis.

That is a misnomer because NF2 patients do not develop neurofibromas. There is a process going through to change the name. The NF2 will almost certainly stick because the gene symbol is pretty much indelible now because it's been out there for so long, but it will be likely to be NF2 related schwannomatosis seems to be what we're going with.

So neurofibromatosis will disappear, hopefully, because it's wrong. It should never have been called neurofibromatosis. So NF2 and schwannomatosis are going to be bed fellows going forward. And that's right because they are essentially the reason the tumors occur is because the NF2 gene is made aberrant.

Mike ward >> As a follow on, constant pain is sort of a major issue with anyone suffering from schwannomatosis. What advice would you have in that context?

Gareth Evans >> The main advice is to get to a specialist center, get to a good pain clinic. The thing with schwannomatosis pain is it's neuropathic pain, so it's really only neuropathic drugs at the moment that are likely to work, the sort of Gabapentin type drugs, some of the antidepressant drugs work quite well, the tricyclics, and Tegretol works to some extent.

Many NF2 patients find they don't work and stop taking them because they simply don't work. Again, there are projects in the United States with trying to develop pain medication. Scott Plotkin, again, has a promising candidate in Boston, and the EU-PEARL initiative is specifically developing a basket protocol to develop drugs specifically for pain in schwannomatosis.

It is really remarkable how schwannomas in schwannomatosis cause pain when they're very, very small, almost sometimes excruciating pain, whereas in NF2, it's relatively uncommon for schwannomas to cause significant pain.

That really does, even though the NF2 gene is the gene that is targeted, there is something about what happens in schwannomatosis that is different in that it targets the sensory nerves. In NF2, it seems that schwannomas target the motor nerve roots. So you end up more with loss of muscle function when the schwannomas cause problems. You actually rarely see motor deficits, people using functional weakness in schwannomatosis unless the surgeon's gone in and pranged the motor part of the nerve.

Mike ward >> How can the work of NF2 BioSolutions UK support Manchester, help someone with NF2? I think actually hearing what Grace and Adam actually said and what they're doing, that's probably answered that question.

The next one for you, Gareth, is one member of the audience has noted that a number of NF2 patients in the same family seem to suffer with peripheral nerve neuropathy. Is this linked with the NF2?

Gareth Evans >> Yes, so there is evidence that you get a peripheral neuropathy in NF2. It seems to be sometimes linked to the tumors but also not linked to tumors. A peripheral neuropathy is where you get sort of glove and stocking loss of sensation, so you lose sensation in the fingers. You start losing muscle function in the fingers and the toes. So that does appear to be a feature.

And it does seem to be a feature in those with the more severe types of genetic mutation, pathogenetic variants in the NF2 gene. You do also get something called mononeuropathies, where a specific nerve root is targeted, and you see that much more in children.

So you see a child develops what is thought to be a bell's palsy, and it's actually a facial weakness that never fully recovers or a wrist drop or a foot drop. So we have a number

of NF2 patients who thought they had polio in childhood, but they never had polio. They had a mononeuropathy associated with their NF2.

You sometimes get the eyes affecting, particularly the third cranial nerve can cause the eye to go out and the eyelid to come down a little bit. So there are a number of these mononeuropathies, which, again, are more common in childhood. Peripheral neuropathies tend to happen more in adulthood.

Mike ward >> Another question from the audience. To what extent do hormones affect the tumor growth?

Gareth Evans >> The hormones that -- the most work has been done on is really estrogen and progesterone and the feeling the women may have more problems than men. However, there is slim evidence it has any impact on schwannomas. In fact, men have a higher incidence of vestibular schwannoma early in life, and there's no evidence that there's any difference in severity of schwannomas between men and women.

For meningiomas, it is a little bit different. In fact, it's odd that boys have a higher risk of meningiomas than girls, but once you hit puberty and progesterone starts to go up, then that causes more meningiomas in girls, and women sort of overtake men at around 20 years of age, and they're more likely to develop multiple meningiomas, and the meningiomas can be a bit more problematic.

So progesterone, definitely for meningiomas, it has been a target of anti-progestin therapy, again, not particular ly good results, but some patients remain on anti-progestin medication, and that seems to have some benefit. After menopause, meningiomas tend to progress less in women. So, again, that would be a hormonal element to it.

The other sort of unexplained thing is why puberty seems to be quite a big trigger for growth. We know that vestibular schwannomas that are identified in very young children rarely grow very fast. They're tiny tumors -- now, there are exceptions, but

most young children that are followed up, they do not really start to pick up their growth until puberty.

Something about puberty triggers growth, so the most rapid growth we see with vestibular schwannomas in NF2 is in children from about 13, 14 years of age up to about 25. Then the vestibular schwannomas tend to grow less fast. We do not know what it is, but it is likely to be something hormonal -- growth hormone, no real evidence for that, but something hormonal around puberty that Triggers particularly vestibular schwannomas to grow more rapidly.

Nobel prize if you find out, Grace or Adam, what it is.

Mike ward >> In the past decade, the harnessing of the immune system to target and suppress tumors has come on leaps and bounds. Do you think such immunotherapy approaches could actually have a role in treating or even curing NF2?

Gareth Evans >> So there has been some work done on this, Matthias Karajannis' group published about eight or nine years ago a paper looking at immune modulation in schwannomas and meningiomas and found that actually there was a high portion of NF2 related schwannomas that tended to be targets for these checkpoint inhibitor drugs.

That really fits, again, with the work that Grace and Adam are doing. These tumors, the growing schwannomas are packed with macrophages, so these are tumors that are potentially targets for the immune system. Definitely there is thought that that could be something that might be effective. These are very expensive drugs, though, checkpoint inhibitor drugs, and they're not without side effects. So there might be more straightforward, simple ways of approaching the inflammation that Adam and Grace are really looking at.

Can we actually find an inexpensive drug that's got lots of evidence behind it and lots of safety behind it that we can use to target that particular aspect?

The only other area where NF2 related is there is a small number of mesotheliomas, which are the asbestos driven lung cancers are driven by NF2 related diseases. You'll be pleased to learn that mesothelioma and NF2 is not a particular issue, but don't go around exposing yourself to asbestos.

Mike ward >> You wouldn't want to do that anyway.

Gareth Evans >> I was very silly when I was a boy. I used to play on these asbestos roofs. So I'm not sure how much asbestos I exposed myself to. It wasn't really known then.

Mike ward >> Just talking about the sort of use of checkpoint inhibitors, so do NF tumors, are they expressing PD-1, or is it other --

Gareth Evans >> That is what Matthias showed, that they appeared to be overexpressing PD-1. The majority of schwannomas from that study were overexpressing PD-1, whereas meningiomas, it was much less clear. So that's why. But there's really been very little work since, and I'm not aware of any study where checkpoint inhibitors have been used as a treatment in NF2.

Mike ward >> Right. I guess you're right to point out these checkpoint inhibitors, at the moment they're expensive.

Gareth Evans >> They will come down, prices will come down.

Mike ward >> Within ten years --

Gareth Evans >> When Avastin came off patent, the price dropped by 75 percent. So it was hugely less expensive to treat with Avastin.

Mike ward >> So all this work that's been done elsewhere, there will be a benefit.

Gareth Evans >> Yes, there will be a benefit from that.

Mike ward >> So another sort of scientific breakthrough in the past decade has been the advent of gene editing technique, such as CRISPR/Cas9. To what extent do you think such approaches might benefit people with NF2?

Gareth Evans >> Obviously, the underlying problem is a gene mutation, and if you can correct that gene mutation in the appropriate cells in the body, then potentially that's a cure. So absolutely that is something that could be really, really helpful, but it's making sure you correct it in the right cells in the body, in enough cells in the body to make a difference.

So it's not like hearing cystic fibrosis, where just getting enough of the cells fixed that you produce the right protein is good enough to help someone. You need to be correcting the mistake probably in over 90 percent of the cells to really make a difference in terms of preventing the formation of schwannomas, meningiomas, ependymomas, et cetera.

So that's the bar. The bar is very high in preventing tumors because you have -- it's not good enough to get 10 percent of cells corrected. It needs to be 90 percent-plus cells where you correct the genetic fold.

Mike ward >> Right. One of our audience has picked up on the news that drugs developed through AIDS and HIV might offer help to patients with meningioma and schwannoma. How quickly do you think this observation could be translated into a possible treatment for NF2 patients? Could it actually be a possible treatment for children affected by NF2?

Gareth Evans >> Yeah, I mean, the anti-retrovirals, really the HIV treatments, are very tolerable, very few side effects. People take them for life. So potentially, it's a promising target. I mean, this is preclinical work that suggested that these drugs may be effective.

We've been trying to go around the world asking people, is there anyone out there with NF2 who's been on these drugs so we can actually see if there's been an effect, and we would need to build up enough patients to give at least some clinical outcomes.
We're now asking, is there anyone out there with meningiomas or just isolated meningiomas or schwannomas, and we picked up a few, but not a vast number. So the next step would be to do -- if you've got enough clinical information, you could go straight into a sort of phase 2 trial.
Otherwise, probably what you're going to need to do is something called a phase 0 trial or window trial, where you treat with a drug, and then ideally, if you've got a tumor under the skin that you can take before and after treatment to see if the drug is getting into the schwannomas is having an effect on the schwannomas.
So you treat for maybe three months and then harvest a tumor before and after treatment. So those sort of window trials are a quite quick way of finding out whether the drug is effective and would then be -- then you could maybe go into a phase 2, phase 3 trial.
But if we have no human data out there and it's just test tubes, then really we need to have some solid human data before going into a bigger study because these are expensive trials. We need a bit more than a cellular model to tell us whether or not it's going to work.
Mike ward >> Sure. Obviously, that's a challenge in a lot of drug discovery, drug development. This is something you kind of alluded to a little earlier in our conversation, the challenge in getting access to sort of exciting and new effective medicines is potentially the high cost. So I just wanted to ask, how confident are you that the new NF2 treatments, based on gene therapy or immunotherapy, would be available through the NHS?

I'm just thinking because you were once associated with NICE, and they're kind of the arbiters of what is cost effective. Just to get your perspective.

Gareth Evans >> The NHS is not as miserly at some people think. Just today there's been a splash about the NHS approving the most expensive drug of all, which is a gene therapy for monochromatic leukodystrophy, which costs 3.5 million. Obviously, the NHS does look at orphan diseases, and NF2 is an orphan disease. And will definitely be open if there's good evidence a drug is effective.

We've been able to do that with Avastin. There was enough evidence from Scott Plotkin's work in Boston that we were able to get that approved. So if the Brigatinib trial is effective, I am very confident we will get Brigatinib into the NHS relatively quickly.

We do have an advantage in highly specialized services that it doesn't necessarily have to go through a full nice appraisal. The bar is a little bit lower in materials of cost effectiveness than the bar is for standard things like breast cancer treatment. For orphan diseases, the bar is -- you don't have to jump quite as high to get a drug into the NHS.

Mike ward >> I'm sure that's sort of comforting news, be reassuring to the audience. I know sort of your question, which clearly is front of mind for a lot of the audience is what is the current status of research associated with deafness and NF2?

Gareth Evans >> So obviously, most of the research in the last sort of 20, 30 years has been trying to rehabilitate people with auditory brain stem implants, cochlear implants. We're finding that, if the cochlear nerve is preserved, that cochlear implants are really a very good option. You get very good ability to interpret sound with cochlear implants. ABIs are much less clear because ideally you want to be going to the cochlear and passing the information down the nerve through established pathways to the brain rather than sticking electrodes into the brain itself, the brain stem itself.

But there are some people with really quite good results from ABIs. In terms of nerve regeneration, that is certainly something that's been -- that has been studied. Is it possible to regenerate the cochlear nerve? If nerve regeneration studies become more promising, then absolutely, regenerating the cochlear nerve would be something that would be looked at. But if it's not there, then that's a problem.

It's more -- now, we know, for instance, that -- and I think there were some other questions here -- that deafness is not just simply squashing the nerve. It might be secretions that are caused from the tumor that actually damage the cochlear itself, and it might be affecting the blood supply to the cochlear. So the cochlear is damaged because the blood supply is damaged, and the nerve is still fine. The nerve is still functioning fine.

That's why a lot of deafness can be managed with a cochlear implant. There are a number of NF2 patients around the country who do really, really well with cochlear implants, but that can only work if the cochlear nerve is intact.

Mike ward >> Right. There's also been a lot of talk about the gut microbiome and its influence on inflammation. I wonder if this has prompted, the next question, to what extent do you think diet plays a role in the growth of NF2 tumors? And if it does, is there anything that people should either stop eating or start eating to slow down that growth?

Gareth Evans >> Well, there are these sort of motions to have anti-inflammatory diets. Some people are moving in that direction. Is that a way to go? I think we need to see some evidence that that is effective. As long as the anti-inflammatory diet doesn't do you any harm, the concern is people taking medications that have anecdotal inflammation that potentially are harmful. Obviously, people talk about tumor, Curcumin has been mentioned by a lot of people, but there's no evidence that Curcumin works. However, I don't think there's any harm by taking Curcumin in your diet.

By the way, putting extra Turmeric on your food is not the amount you need to have an effect. It's certainly possible. Grace and Adam are working on the whole inflammation story that diet may be part of the trigger, but I think we need more evidence. That means you're going to have to go chasing food samples, I think, Adam. He's not smiling. With gut microbiome, you have to look at the gut microbiome, don't you?

Mike ward >> Clearly, that question around diet, et cetera, it's around, okay, so in terms of quality of life and longevity, what advice, or what are the best ways for people with NF2 to achieve the quality of life and longevity?

Gareth Evans >> I think the UK model is the best we have. The strongest evidence is going to -- going and getting your NF2 managed by an expert center is the best way of prolonging your life. Avastin, I think, is already having an effect at prolonging life with NF2.

The worst thing to do is to go to some gung ho surgeon who just goes in and operates on everything or you get blasted with radiation when you're a child. Radiation has long-term issues and hitting 12, 13-year-old children while everything is growing with radiation is not a particularly good idea.

All of the evidence about radiation from Hiroshima to children getting radiation for head lice let alone vestibular schwannomas, it's not necessarily a good idea. So radiation should not be the first call. That's why we need drugs. We need drugs that mean that ideally we're not Chucking things at people.

So the real important thing in NF2 is to preserve function for as long as they can. There's precious little evidence that going in gung ho early does any good and may do a lot of harm.

I think what we hope for is drugs that are going to make -- you know, safer drugs that are going to make a big difference in holding off on the necessity to do surgery or radiation treatment.

Mike ward >> Okay. So we're almost at the end of time. Finally, I guess the question sort of, if you're on that looking at drugs, how optimistic are you that we might find a cure for NF2?

Gareth Evans >> Cure is a hard one because I think, to cure NF2 you need to be able to correct the gene fault. I think much more likely we are going to have drugs that can halt the progress of NF2 at a stage where someone hasn't lost any function, and that is as close to and as good of a cure as you can get.

So I think that's where we'll get. Hopefully, we will have treatments that will stop NF2 patients going deaf, stop NF2 patients losing muscular function, ending up in a wheelchair, et cetera. That is my hope. Yes, gene therapy is the ultimate if we can correct the fault, if we can do that. If gene editing gets us that far, that is the ultimate. I would be hopeful, but I think we have a lot more hoops to jump through, and I think drugs will be there before gene therapy will get us there.

Mike ward >> Thank you, Gareth, for this fascinating conversation. The insights you've shared clearly highlight sort of the efforts being made by the research community and organizations such as NF2 BioSolutions. So thanks very much.

I'm now going to hand back over to Clare for some closing remarks.

Clare Goddard >> Thank you, everyone. Thank you, Mike, Grace, Adam, Andy, Gareth, and Tony, and Gilles, who's been my tech support here. That was an incredible hour. Lots of information. We appreciate everything you're doing and the time that you've given to go through that. As I say, as a wife and mom of two with NF2, this kind of chat is invaluable. So thank you very much. For the hope.

We're going to be putting a poll up for you to answer questions. Please answer that poll before you leave. And I want to also get a feedback form because, if we can, I'd like to do this again and see how we can learn from this one and make it bigger and better. So

Gareth Evans >> There are many, many questions that haven't been answered, and people are asking if we can answer those questions. I don't know if anyone wants to collate the ones that haven't been answered, and I can have a go at some of them.

Clare Goddard >> That's okay, Gareth. We'll collect all of them together.

Gareth Evans >> Some of them were answered, at least partly answered. There are things like proton beam radiation effective on peripheral nerve tumors.

Clare Goddard >> Yeah, absolutely. We don't want to be cheeky and go over the hour of your time. So what we could do is we could collate those and get them to you, if that's okay, and then we'll send them out in a different way, if that's all right with you.