



Gateway

News from Huntington's NSW & ACT

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Success! ASO drug reduces levels of mutant protein in Huntington's disease patients

Amazing news from Ionis and Roche! HTRx drug successfully lowers harmful huntingtin protein in spinal fluid.

By Dr Jeff Carroll Edited by Dr Tamara Maiuri

In an announcement likely to stand as one of the biggest breakthroughs in Huntington's disease since the discovery of the HD gene in 1993, Ionis and Roche today announced that the first human trial of a huntingtin-lowering drug, IONIS-HTRx, demonstrates that it reduces mutant huntingtin in the nervous system, and is safe and well-tolerated.



What's this huntingtin-lowering stuff all about?

The therapy we're most excited about for Huntington's disease is called huntingtin-lowering. You might also hear this approach called gene silencing, but huntingtin-lowering is more accurate, as we'll explain.

Everyone has two copies of the HD gene - one they inherited from their mom, and the other from dad. In people destined to develop HD, one of these copies of the HD gene is changed, or mutated in a very specific way.

Right near the beginning of the HD gene is a repetitive sequence that reads, in the code used by scientists to describe DNA, C-A-G. People who won't develop Huntington's Disease have around 20 repetitions of this sequence, while in people destined to develop HD, it's longer, most commonly 40 CAG repeats or more.

Our cells use genes as recipes to build proteins - little molecular machines that do useful stuff in cells. When a cell needs to make more of a certain protein, copies of the instructions are made in a chemical closely related to DNA, called RNA. Scientists call this scratch copy of a gene the messenger RNA because it carries each gene's information from the DNA to the cells

protein building machines.

This means there's more than one place in the cell where we can find the information in the HD mutation - the abnormally long repeat found in peoples' DNA is also copied into the messenger, RNA. Ultimately, cells use this RNA message as instructions for constructing a protein - the huntingtin protein.

Most research in HD suggests it's the huntingtin protein, not its gene or messenger, that causes brain cells to malfunction and die in people with HD. But what we know for sure is that every single person with HD has a mutated copy of the HD gene, which acts as the blueprint for the toxic protein. This makes the mutant HD gene enemy number one for those of us working to develop new therapies.

The rapid advancement of science over the last few decades has given scientists a big toolbox for selectively shutting down specific genes. Some techniques, like antisense oligonucleotides have been around for decades. Newer techniques, notably genome editing tools like CRISPR/Cas9 have only been discovered and developed over the last few years.

While the details of the technologies differ, in

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the HD world, they all have an exciting potential application - to reduce the amount of the huntingtin protein. In numerous animal trials, using a wide range of these silencing tools, when researchers shut down the abnormal huntingtin gene, animal models of HD get better, or never get sick in the first place.

That's cool science, but nobody really cares about curing Huntington's disease in a mouse, or a fruit fly or a worm. We want to cure HD in the species that matters most to us – humans with HD.

Reminder: what's the history of this drug and trial?

Amongst all the huntingtin-lowering technologies that exist, the most developed approach is called antisense oligonucleotides or ASOs. These are short, custom-built, chemically-modified pieces of DNA that can freely enter cells. Once inside, they locate and help destroy a specific messenger RNA - in this case, the one instructing cells how to make the huntingtin protein.

Ionis Pharmaceuticals, in Carlsbad California, has been developing ASOs for a range of diseases for decades. Years ago, they realized that HD was a perfect fit for their technology, because we know that if, in animals, we reduce the levels of the huntingtin protein in the brain, we improve their HD-like symptoms.

Last year Ionis had a massive success with an ASO for another brain disease called spinal muscular atrophy (SMA). Those trials tested whether an ASO delivered to the spinal fluid could help improve the condition of babies born with this horrible fatal illness. Same basic technology, but targeting a different gene.

Kids in the Ionis SMA trial did so well that regulators asked them to halt the trial early, so that every kid in the study, including those getting the placebo, could receive the drug. Basically, if the disease had taken its normal course, the kids would have gotten progressively weaker and died. But many of the kids treated with the drug were getting stronger and living much longer.

Ionis' SMA drug was subsequently approved in the US, EU and many other countries, and is now being given to children with SMA around the world.

So, what about HD?

Ionis has been working on antisense oligonucleotides (ASOs) for HD since the early 2000s, first in simple cells and then moving into several different animal species. The effects they were seeing were promising, and testing in humans became a real possibility. Anticipation

built in 2013 when pharmaceutical giant Roche announced a partnership with Ionis to develop the ASO drug for HD, which they call *IONIS-HTT Rx *. This brought huge resources and experience at Roche to bear on the problem of Huntington's disease.

In July 2015, the most exciting drug trial so far in Huntington's disease began - one in which an ASO designed to reduce production of huntingtin protein was actually delivered to people with HD. The trial was designed to test the safety of the drug and whether or not the drug could do what it was designed to do - reduce the production of the huntingtin protein. We were really excited about this trial starting, and wrote about the trial launch here.

In any drug development effort, the first goal has to be ensuring the drug doesn't have toxic side effects. History provides us with many examples of drugs that seemed like a good idea, but had unexpected side effects when given to people.

With this in mind, Ionis and Roche designed a study whose main aim was determining whether the drug is safe when administered to people, which has to be the first step in the drug development process.

This first study enrolled 46 people with early HD symptoms in Germany, Canada and the UK. The trial began in July 2015 and was planned to end in November, 2017. As you'll see, the whole trial happened right on schedule, which doesn't always happen!

Before we talk about results, there are a few important details for people to keep in mind. First, ASO drugs do not get into the brain if swallowed in a pill form. As a consequence, ASO drugs for brain diseases are delivered by injecting them at the base of the spine, using a technique called lumbar puncture. It sounds a little scary, but it's actually a very common procedure, done thousands of times per day in hospitals around the world.

Second, this study included a placebo arm. That means that some of the participants went through all the steps, but received injections without drugs. This is an absolutely critical component of trials - if we don't have a group of people without drug, how can we be sure that changes we observe are due to the drug, and not some other factor?

Finally, dose. Any time researchers give a drug to people for the first time, they start with a very low dose. In a trial like this, formally called a multiple ascending dose study, the first participants receive a low dose and then

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We have a new name

Huntington's NSW & ACT

Since 1975 when the Association was first formed our membership and contacts have always included families, supporters and health professionals from the ACT. For some years now we have had an authority to fundraise in the ACT. So it only seemed fitting, that while we were in the process of updating our Constitution, we take the opportunity to change our name.

At the Annual General Meeting held on 18th November, those present voted unanimously to adopt both the new Constitution and our new name "Huntington's NSW & ACT Inc."

In due course we will be changing the website, our letterhead and logo, publications and other collateral.

This change will better reflect the reality that the Association has always included serving and representing the HD community in the ACT as well as NSW.

Successful Grants Received

We were one of five charities to receive a \$10,000 grant from Grace Gives.

Grace acknowledge that the reason they have grown as a company over the years is due to their local communities. So, each year, Grace undertakes a range of initiatives to support the communities throughout Australia and New Zealand in which it operates. We are most grateful to Grace for the opportunity to participate and for choosing us as one of the recipients this year.



Special thanks also to all those who voted for us which ensured we were in the top 10 list of finalists.



A grant of \$2,000 has been received from Pfizer. Pfizer CARES Community Collaboration Grants provide an opportunity for Pfizer staff to apply for funding to support their favourite local charity. Through a competitive internal process, grants are awarded to the selected charities of Pfizer teams and individuals.

We extend our appreciation to Christine Sharp, a member of the Association, for submitting an application on our behalf.

The Board & Staff of Huntington's NSW & ACT would like to thank our members, supporters, funders and everyone who contributed in any way to make 2017 a fantastic year. We wish you and your families a very happy Christmas and a peaceful 2018.



The Year in Review...

At the Annual General Meeting held in November, the following were elected to the Board -

President: Brian Rumbold

Vice President: Deborah Cockrell

Secretary: Therese Alting

Treasurer: Stephen Guthrie

Members: Katy Clymo and Alison Hill

Here are the main reports from our 2016-2017 Annual Report presented at the AGM. The full report, including the audited financial report can be found on our website. www.huntingtonsnsw.org.au. If you would like a printed copy, please contact us.

President's Report

The Board thanks the staff for its commitment over the last year. First, thank you to Robyn, our Executive Officer, who, week after week, goes above and beyond what is strictly necessary to serve and represent the HD community. She has displayed remarkable dedication to furthering the awareness of HD, advocating for services and championing the HD Service at Westmead, and encouraging the staff in serving clients and the community.

As we look across the activities and events we are running, sponsoring or supporting, there's evidence that we are finding ways to engage more people than in the recent past in social clubs and support groups. Thanks to Amanda for the work she has been putting in to build our activities and encourage more people to take part. I know many people are really thankful that these group activities are available and we want to build on this area.

We began our Youth Program at the start of 2017 – HD Youth Connection. We've welcomed Amy as our Youth Worker, and she has done an amazing job designing the service, and getting it up-and-running as she has become involved with families and young people wanting support. We started the service on the back of fundraising in the last couple of years. This year's fundraising has helped secure the service for the next couple of years—we get no special funding for HDYC, so the support of the community has been vital in making this happen.

In the background, Stewart has kept our administrative systems ticking over. However, his volunteering and the extra contributions he has made to Association events—particularly fundraising activities—has been phenomenal.

Fundraising has been amazing over the last three months. Pauline put an incredible amount of work into the preparations for Walk4Hope in September. It's getting harder and harder to raise charity funds today, but the HD community—including family and friends, plus

many professionals and workers from the Health sector—gave great support. Highlights included the Redhead Challenge in Orange and the Australian Doctors Orchestra concert—in which the HD Service's Associate Professor Clement Loy added style and finesse to the oboes.

Year-to-date we have a combination of donations and fundraising of around \$179,000. The ADO concert has contributed around \$60,000 to this—a quite remarkable result from a remarkable event.

We face challenges in the coming year. Our grant from the NSW Government for the Rural Carers Support Program will end on June 30. We are in a competitive tendering process to gain further funding so we can keep supporting people in regional and rural areas, but the nature of what we are able to do will change—and what that service will look like will depend on the funding we can secure—if not from the Government then from other sources. In the meantime, Julie continues to provide support to many rural families who, I know, depend on this service when dealing with their challenging—and often changing—circumstances.

I want to acknowledge retiring Board member, Richard Bobbitt. Richard has been on the Board for over twenty years and has served as both President and Treasurer. He has been committed to the Association and, as a Board member, has advocated passionately for the needs of the HD community. We will miss his wisdom on the Board. Thank you also to Felicity O'Neil who has strongly represented the ACT HD community on the Board over the past three years.

The Board again thanks the Association's members for their support, and we look forward to serving the HD community in the coming year.



Brian Rumbold
President

Social and Support Programs

Social club

Our Social club welcomed another new member into their fortnightly hang-out. This program is for adults in the early stages of HD, and is designed to alleviate the social isolation that is experienced with having HD. In a social setting our people enjoy a friendly meal, card and board games, trivia, footy tipping, indoor games like: bowls, quoits, darts, bowling; and creative arts. Unfortunately, at the end of December, the Heartmoves exercise program ceased as the YMCA found it unsustainable. We are exploring new avenues of partnership to re-establish an exercise program tailored to our community.



A brief partnership was formed with the S.E.A.T Project, which is the construction of an ordinary stool

to encourage teamwork, problem solving, and connection. The build was a mix of confusion, frustration, laughter and satisfaction all rolled into one. Working with the bamboo SEAT itself allowed each person the opportunity to realise they can still create something with their own hands... an art that is often lost due to HD. In designing the SEAT decoration, we had the privilege of listening to their stories of life, family, travel, likes, dislikes, talents, and memories; revealing their true personalities. The decoration saw all this represented on the SEATs and then the SEAT was gifted to family members to be celebrated and displayed in their homes.

Holiday camp - Cars, Dogs & Drumming

A small group of campers, in the early stages of HD, tripped away with us to meet and enjoy the company of people like themselves; while their families appreciated a well-earned rest. This year we also offered HD families the opportunity to try out the camp. Locals dropped in for the day to join in with the activities or took time to visit a relative.

So what did our campers do? Well, they devoured yummy home-styled cooking and relaxed in the tranquil bush setting, but they were keener to have some fun! Even when the weather turned dark our daily activities did not disappoint; there was something for everybody! We warmed up with lake-side walks, porcelain painting, Easter egg making, croquet, card and board games, tenpin bowling, trivia, quoits, and

lots of laughs.

Our car enthusiasts loved venturing out to the car museum, where hours were spent drooling over and posing with some classics. Our masterminds even planned on ways to liberate these beauties into the hands of more worthy owners; us J! These gangster dreams were toned down with a visit from some special guests Bella and Gracie, therapy dogs from Delta Society. Their gentle nature allowed for petting, patting and cuddling at will, which then prompted our campers to smile and share stories about their own furry friends.

On the flip-side, our primal beings were unleashed through Craig's DrumAbility program (Kids on Congas). Drumming is a wonderful experience that everyone can and should attempt! It transformed our quiet campers into animated musicians and conductors, for that moment they lost any personal hang-ups; it was jaw dropping.

'MyVoice' art fellowship

Creative beings inhabit Elsie Court Cottage. Every fortnight a wonderful group of people come together in a social setting to discover their inner creative artist. Yes, people share in their common HD experiences, but here they are able to safely explore the person that they are through drawing, painting, poetry, storytelling, laughter and play. Our people have not only crafted beautiful artworks, they have found a fresh way to communicate and formed new friendships and support. Their motto is "Don't worry we are here!"

and this represents this unique experience. Thanks to Stephen Dernocoure, our art facilitator, for making every meeting an adventure into remembering whom we truly are.



Central Coast Support (self-managed)

This tight-knit group embarked on a new direction this year. They decided to trial coffee chats, have more social gatherings and meet formally every 3 months. It's been quite evident over the years, how helpful carers and family members find talking to and sharing with others who have had similar experiences.

Coffee chats (Visiting program)

'Coffee chats' were borne from the want to get

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together at more convenient times. The group have been successful in reconnecting with members who were feeling isolated.

Social gatherings

After a successful picnic with family and friends, came their inaugural Barefoot Bowls day.

The group would like to thank management, staff and bowling club members, of Davidson RSL. They researched HD, provided a luncheon room and bowling lessons and went out of their way to help the group have a great afternoon.



Carer's Support Group

This group meet over coffee and cake to share invaluable knowledge from their experiences. Though members have lost loved ones they choose to stay connected to support those who are now struggling and to gain strength as they prepare to care for the next generation.

Family Support Group

The group met quarterly and welcomed a new family. Outside of the meetings they pass on valuable information and updates through email and phone.

Fundraising and awareness continue to be high priorities. Their affiliated social golf club hosted another fun-filled *Huntington's day*, raising vital funds. While their social connections assisted in securing radio advertising to promoting our Walks 4 Hope.

We are very grateful to this group for their unwavering support of Huntington's NSW.

West Ryde Carers Support Group

The attendance at this well-established support group averages 12 each month and continues to be hosted by Huntington's NSW. The group is guided through current concerns and requests topical presentations to aid their carer education. It is facilitated by the NSW HD Service Social Workers with some input from our Executive Officer.

Living Well with HD education seminars

Two information sessions for people and families of those who were newly diagnosed were facilitated by the HD Outreach Service staff, one hosted at Elsie Cottage. The seminars were

created after receiving feedback that families wanted early information and tips on social services, exercise; diet; memory and planning aids; planning ahead and research updates. Both sessions were well attended, and we look forward to hosting them again next year.

NDIS

This year we have seen the National Disability Insurance Scheme (NDIS) fully roll out in NSW and ACT. We have been busy investigating how our community needs us to be involved within the NDIS and how we can make the transition and pathways easier for HD families. The outcomes of these investigations will become apparent in the coming year.

Volunteers

Regular assistance

Thanks to Stewart who is now in his 4th year of being a Social club assistant and driver. The club would not run as smoothly without him and would lack the banter element.

Thanks also to Robyn for the lovely home cooked meals she prepares for our Social club members.

Special thanks to Masumi for the careful effort she provides as our Office Assistant.

Student placement program

We partnered again with the Sydney Medical School's Master of Genetic Counselling program, at the University of Sydney. Our part is to provide student placement opportunities to Post Graduate students who are interested in experiencing the "lived" experiences of those with a neuro degenerative disease. This year's cohort assisted with our Social club and Art fellowship as well as researching ideas for a community engagement initiative.

*Amanda Dickey
Programs Officer*

Rural and Regional Support Program

Regional Trips

During the past year the program has provided information, support and referrals to family members, people with HD or at risk for HD, health professionals and community organisations. The Rural Social Worked has worked collaboratively with the HD Clinic at Westmead to provide holistic care for families in rural and regional areas whilst on regional and rural visits and as a support when families attend the HD Clinic. A working relationship has been

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established with Sibling Care at Westmead Children's Hospital and Huntington's NSW to allow the children of families that travel from rural and regional areas to have their children looked after while they attend appointments at the HD Clinic at Westmead Hospital.

Partnerships

Partnerships have been formed with Carers NSW and Ability Links. The partnership with Ability Links, which is a local government initiative as a fore-runner to the National Disability Insurance Scheme (NDIS), has been in various geographical areas, including the Mid North Coast, Far North Coast, South Coast and Newcastle. This partnership has allowed us to form support groups at Port Macquarie and the forward planning for another group in the Illawarra. The partnership with Carers NSW was to provide a six-week therapeutic group for carers of people with Huntington's disease.

Talk-Link

Talk-Link was developed in conjunction with Carers NSW. The group is conducted via phone and is designed to reach carers who may not have the opportunity to participate in a face-to-face support group or in some cases have never been able to be a part of a support group. It was collaboratively agreed that the facilitators of the group would be from Carers NSW and Huntington's NSW, utilising knowledge and understanding of carers and Huntington's disease. The process of establishing and conducting a group via a telephone allowed us to reach carers from the north, south and west of NSW.

Key elements important to each person were discussed prior to agreeing to participate and enrolling for the group. Participants of the group have formed rapport with each other after discussing topics that can be emotive and difficult. The group started was nine participants but reduced to six due to unforeseen circumstances. The topics covered included coping with stress, communication, boundaries, grief and loss and self-care with a focus on participants gathering knowledge and skills on how to deal with each topic that was discussed. Considerable peer education took place within the group with significant interactions and discussions between participants and the facilitators. The program was well received by all participants and it is anticipated that further Talk-Link groups will be held in the near future.

Support Groups

The Port Macquarie support group which was established in May meets monthly with an

average attendance of eight at each meeting. Huntington's NSW negotiated with Ability Links in Coffs Harbour to transport carers from the far north coast to the group in Port Macquarie, such is the need for support groups for families.

The Inheritance movie was screened in Port Macquarie in September with support from Ability Links. The movie was well attended by families and members of the local community attended. Contact was also made with a number of new families from the area some of whom now attend the support group.

The Wollongong group is in its infancy however it has attracted around 10 people at its initial meetings.

Newcastle Carers' Group

The support group in Newcastle, established more than 20 years ago, meets monthly with a steady attendance of between 6 and 9. Since the establishment of a small Huntington's NSW office at Jesmond Neighbourhood Centre, the group have been meeting at the centre. The group have commented on the convenience of meeting at the centre, the disability access and parking at the door. The focus of the group has been growing the number of people attend the group. One group member has also produced a flyer to be distributed to doctor's surgeries, community centers, hospitals and services who work with people effected by HD. This flyer was designed with the focus of growing the number of people attending the Newcastle carers group. The support group elected to have a screening of The Inheritance movie at the hall in the Neighbourhood Centre in September and it was attended by twenty people.

ACT Support Group

This group meets bi-monthly, usually for Saturday lunch and is attended by families from Canberra and surrounding areas. It is facilitated by Felicity O'Neil and when possible a staff member from the Association has also attended.

Julie Leto
Rural Social Worker

Youth Liaison Program

In February this year, Huntington's NSW Youth Connection Program (HDYC) was launched. The primary goal of this program is to promote and increase the psychological and emotional wellbeing of children and young people impacted by Huntington's Disease through the delivery of a youth focussed service.

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It has been identified that there are over 400 children and young people from NSW and the ACT impacted by HD. Through providing effective, long term engagement and early intervention, the program aims to foster resilience and strength in these young people to improve their quality of life and prepare them for potential crises that being impacted by HD will most likely bring.

To facilitate this program, HNSW employed the world's 8th Huntington's specific youth worker. There was a great response to the launch of this program from the international HD youth worker community and the Huntington's Disease Youth Organisation (HDYO) upon learning that HNSW had started this youth program.

All the international youth workers have been in contact to offer their support and share their information and advice on starting similar youth programs in their areas. This collaboration and shared information in relation to program design has been and will continue to be an invaluable resource for the NSW Youth Connection Program. All workers have been communicating on telephone and by email, and also meeting periodically throughout the year on skype for an international HD worker support meeting where they are able to share ideas, case studies and offer each other much needed support.

Another encouraging response has been from the Huntington's professionals in NSW. The first part of this program involved meeting with these professionals to inform them of the program's launch and prepare them for referring to the service. All the Huntington's professionals have responded with understanding and enthusiasm and are making some great referrals to the service on behalf of the HD families in their care, resulting in these families being able to access a more holistic care that includes a service with a focus on the emotional wellbeing of children and young people impacted by HD.

As part of the commitment to collaboration with these HD professionals, HDYC was asked to present a session at September's NSW Health Huntington's Disease Seminar for Family Carers. This was positively received and will hopefully be the start of many such collaborative interagency events for HDYC. This continued work together is the key to this program being ongoing and successful and has, so far been a very positive experience.

During these first few months, the program has been able to connect with a number of children and young people. These engagements have been varied in their approach and purpose. Some have been individual engagements with



young people, some have been with children, their parents and their extended families, and others have been solely with parents.

The work with individual young people has been predominately counselling and referrals. Some of this counselling has been focussed around a family's transition from having a relatively 'well' parent to that parent's needs changing considerably with the advancement of HD. HDYC has engaged and helped these young people navigate their way through these crisis situations whilst maintaining relatively 'normal' lives, attending school, continuing to be involved in sport, creative pursuits and social commitments.

Other engagements with individual young people have been around the complexities that surround the decision to test or not to test for HD, whilst some have been around supporting the young person who has already made the decision to test and is awaiting results, as this can be a potentially volatile time for a young person.

The other part of this program's work so far has been family work with a child/young person focus. This has included engagement with parents in order to guide them to best understand and support their own children in relation to HD and give them the tools to utilise and the confidence in their ability to communicate effectively with their children in relation to the impacts HD is having and will potentially have in the future.

To support and encourage this youth engagement a strong identity has been created for the program over these initial months both visually and conceptually, with youth focussed flyers, business cards and a Facebook page for people to both interact with and utilise as a platform for engaging with the youth worker directly.

The aim of this promotional aspect of the program was to appeal to young people and reiterate that this is a youth focussed service specifically for them, differentiating it from the other available HD services that are being utilised by their parents/carers. The flyers and

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business cards have been made available to all staff at the HD outreach service, Westmead Hospital and they are currently giving these out to families that they feel would benefit from engagement with the service.

This is an exciting time for this new program as it grows and evolves to meet the needs of the young people in our HD community and we thank the HD community and HD professionals for their enthusiasm, fundraising and support for this new service.

*Amy Hale
Youth Liaison Worker*

Fundraising Highlights

Darwin to Perth

The year kicked off early in February with a golf day at Blackheath in the Blue Mountains. This was the second fundraising event organised by Bob Montgomery, Bill Pixton and the Sunrise Rotary Club in anticipation of Bob's cycle from Darwin to Perth. They were a passionate bunch of people all doing their very best to help someone else and really were 'on board' for Bob's marathon cycle. We loved all the photos and updates on the cycle from Darwin which resulted in an incredible \$52,715 for Huntington's NSW and Motor Neurone NSW. *We don't believe Bob has finished yet, look out for the next adventure in 2018!*

Hunter Bikers

The Hunter Bikers is a group of people who have dedicated their year to selling raffle tickets to raise funds for Huntington's NSW. They have been amazing, giving up weekends and any opportunity they can find to sell raffle tickets, race days, pubs, fairs... you name it they are there. The raffle will be drawn in 2018. Apart from selling raffle tickets they have created so much awareness for HD in the Hunter district. We are so proud and grateful to them, particularly Michael Curtis, Stephen Meek, Kelly and Brittani Faulkner.

High Teas

Kumar Periera, former Master Chef contestant, hosted a very elegant high tea in Pyrmont. This was lots of fun, hats, makeup 'touch up' bar and lots of prosecco with yummy treats. We are looking forward to Kumar joining us again in 2018 for something different.

Kerrie Fitzpatrick pulled off a fantastic High Tea at the 'Bowlo' in Windsor, she is always committed to raising funds and even managed

to get Susan Templeman, Federal MP for Macquarie as her guest speaker.

Rachael Brooking was busy in Orange in September and once again organised a high tea on the same day as the Walk 4 Hope!

Denman Devils Old Boys

Robyn and I travelled to Denman in May to meet the Denman Devils Old Boys. There we met up with Jodie and Barry Sowter. Not quite knowing what to expect, we found ourselves in the middle of a football field in Denman (upper Hunter) being presented with a cheque for \$4,000.

Huntington's Awareness Month - September

What a month that was across the state, with so many things happening:

The Inheritance Screening in Orange and Port Macquarie
Trivia at the Lady Hampshire in Camperdown
Walk 4 Hope – Croudace Bay, Canberra, Parramatta and Orange
High Tea in Orange
Guinness Book of Records attempt 'Hunt for Red Head' in Orange
Westmead Hospital Stall
St Joseph's Hospital Stall
Hunter Valley Extravaganza Raffle
Settler's Tavern Golf Day and Trivia
Jasmin from the International Grammar School

At all the walks, we met new families and caught up with old families. Although every walk is the 'Walk 4



Hope' they are all different and each year changes. This year we raised around \$80,000 across all four walks. Congratulations and thank you to all our fundraisers for their support and generosity. We look forward to the 5th anniversary of Walk 4 Hope in 2018!

Australian Doctors Orchestra

Earlier in the year we were invited to meet with Drs Cathy Fraser and Clement Loy who are members of the Australian Doctors Orchestra (ADO) organising committee. This resulted in Huntington's NSW being the chosen charity to benefit from the ADO's 25th anniversary concert. Many months of hard work culminated in a fantastic concert entitled "Bolero" held at The

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participants who join later receive higher doses of the drug. This enables doctors to carefully monitor people on each new dose, so any negative effects of treatment are caught early.

What has happened now?

On Monday, December 11th, Ionis put out a press release describing the main results of the first study of IONIS-HTTRx. The headline was: "Ionis pharmaceuticals licenses IONIS-HTTRx to partner following SUCCESSFUL Phase 1/2a Study in patients with Huntington's Disease". It also said: "Dose-dependent Reductions of Mutant Huntingtin Protein Observed".

If you're wondering how excited you should be about this - both HDBuzz editors indulged in a little bit of happy dancing when they saw the press release. It's really big news!

We'll explain why this is so exciting soon, but there's a few things to keep in mind.

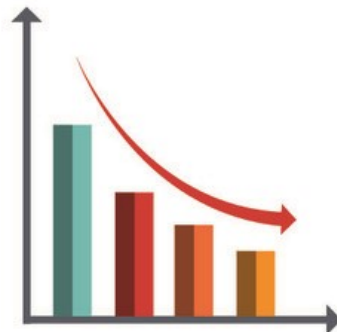
First - safety. Ionis and Roche very carefully monitored the subjects in the trial to look for any signs that the drug is not safe. In the press release, Ionis reports: "the safety and tolerability profile of IONIS-HTTRx observed in the Phase 1/2a study supports continued development". That means there were no significant safety issues observed in the participants, so the first hurdle for this drug in HD has been cleared and we can move on to the next steps.

Remember - this trial was not designed to prove that IONIS-HTTRx helps with HD symptoms or progression. The primary goal of this study was to establish that the drug is safe. The first time you put a new drug into someone's body, you want to expose as few people as possible, in case there are unexpected safety problems.

Also, remember that this study was short - each patient only received 4 months of injections. This is too short a time to look for changes in the rate of HD progression. Even if IONIS-HTTRx turns out to be a wonder drug, the impact on symptoms after only 4 months of treatment could be tiny, and we would not expect to detect them in such a small trial.

So - and this is a really important message - we won't know yet whether the drug made peoples' HD symptoms better.

However, the trial was able to go beyond safety in one important way. Every time the volunteers



Dose-dependent reductions of mutant huntingtin protein were seen in the spinal fluid from patients who received the drug

in the trial were given a dose of the drug, a sample of their cerebrospinal fluid - which bathes the brain and spinal cord - was collected.

Previous work had demonstrated that the levels of the huntingtin protein can be measured in the cerebrospinal fluid. It seems that, as cells are becoming sick during the course of HD, some of their contents are spilled into this fluid, which circulates around the brain.

Since the goal of huntingtin lowering therapies like IONIS-HTTRx is to reduce the amount of the huntingtin protein in vulnerable brain cells, in theory this gives us a great way to tell whether the drug is doing what it's meant to do. We simply measure levels of huntingtin protein in the cerebrospinal fluid before and after drug treatment.

We think the most exciting news in today's press release from Ionis is this: "In the Phase 1/2a study, dose-dependent reductions of mutant huntingtin were observed among patients treated with IONIS-HTTRx". Frank Bennett, Ionis' chief scientist, went as far as to state that the reductions seen "substantially exceeded our expectations".

This means that patients treated with IONIS-HTTRx have reductions in the huntingtin protein in their cerebrospinal fluid. Based on this result, it looks like the drug is doing what it's meant to do, and that huntingtin lowering has been achieved!

The dose-dependent bit means that higher doses of the drug lead to lower levels of huntingtin in their spinal fluid. That's really nice evidence that the effect observed is really due to the drug, and not some other aspect of the treatment.

Now what?

This is big, and everyone in the HD community should be thankful to the brave volunteers who signed up for a demanding trial, as well as their families and caregivers. We should also be thankful to Roche, and particularly Ionis, who believed in this approach and worked for many years to get to this point.

But we're not done yet! What's next?

First, we have to conduct a trial with sufficient numbers of people, and a long enough treatment, to impact the course of HD

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symptoms. The success of this first trial sets the stage for a larger study in hundreds of HD patients, as soon as possible.

The researchers involved in this study know how urgent the need for the next trial is. In the press release, the primary investigator of the study, Professor Sarah Tabrizi, said: "the key now is to move quickly to a larger trial to test whether IONIS-HTTRx slows disease progression". Roche's firm opt-in, announced today, is a great sign that such a trial can be expected soon. As soon as details are released, you'll read about them on HDBuzz.

This is a great day in the HD community, and it sets us on the path to even more exciting work in 2018. For the first time in history, HD patients are being treated with drugs known to reduce the amount of huntingtin protein in their brain. Until we conduct the next trial, we won't know if this reduces the impact of HD. And while we know the drug is safe in the short term, we will also have to watch carefully for any long-term adverse effects. But we're facing this problem with renewed excitement and hope. It's the best early Christmas present we could have hoped for.

Acknowledgement: hdbuzz.net



Editor's Note:

This is very exciting news and we have every reason to be optimistic. However there is still much work to be done in the research process.

You can keep yourself informed about current research by following our Facebook page, our website and the HDBuzz website.

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Concourse in Chatswood. We are extremely grateful to the ADO committee, particularly Cathy and Clement who worked tirelessly to obtain



meaningful sponsorship for the event. It was a huge 'win win' for HNSW – the concert was attended by over 900 people and a complete sell-out concert with major drawcard classical guitarist, Slava Grigoryan.

Each and every one of these events had many volunteers – too many to name all and we could not have done it without them – they made it all possible.

Media

Media coverage included The Project Channel 10, ABC Central West, Talking Lifestyle with Tim Webster, Win TV, NOVA Radio network.

Thank You

Thanks to the following organisations and people for raising both funds and awareness for Huntington's NSW throughout the year.

Veronica Ali, Rachael Brooking, Rachel Cook, Michael Curtis, Brittani Faulkner, Kelly Faulkner, Mark Faulkner, Kerrie Fitzpatrick, Cathy Fraser, Julie George, Alex Gualtieri, Angela and Dennis Hiscock, Glenette Jeffrey-Konig, Jasmin Kohl, Stephen Meek, Bob and Jenny Montgomery, Clement Loy, Kumar Pereira, Bill Pixton, Aiden Roberts, Barry Sowter, Garry Wrench. Active Locums, Australian Chamber Orchestra, Australian Doctors Orchestra, Captain Cook Cruises, Device Technologies, Douglass Hanly Moir Pathology, Hunter Biker's Inc, Lions, Parramatta and Elmore Vale, Loviz Arts, Maui Jim, Meriton, Neilson Foundation, Omega Ensemble, Parramatta Cheerleaders, Pfizer, Selby and Friends, Settler's Tavern Social Golf Club, Suncorp, Taylored Images, The Lady Hampshire Hotel, The Springs, The Star, Vittoria Coffee, Western Sydney University.

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Huntington's NSW & ACT Inc.

The Association is a not-for-profit organisation established in 1975.

Our Mission

The energies and resources of Huntington's NSW & ACT are directed towards satisfying the needs of people with or at risk for Huntington's Disease and their families in NSW and the ACT by providing and/or facilitating delivery of a range of quality services.

Our Philosophy

People with Huntington's Disease and their families are individuals with equal value to all other members of Australian society, with the right to treatment and care by knowledgeable professionals and care givers, the right to appropriate support services and the right to have the best quality of life possible.

Our Services

These include education and information; advocacy; counselling and referral; holiday programs; family support; rural outreach and client services.

Our Board

President: Brian Rumbold
Vice President: Deb Cockrell
Treasurer: Stephen Guthrie
Secretary: Therese Alting
Members: Katy Clymo
Alison Hill

Association and Other Useful Contacts

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Predictive Testing

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