



# Lysosomal Grape Vine

Newsletter

May 2010



## Our Mission

To improve contacts, information, sharing and support among affected people and their families within New Zealand and Internationally.

To advocate for and support accelerated research into the causes and treatment of Lysosomal Storage Diseases.

To advocate for and support, and improvements to the clinical care of affected people.

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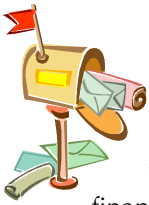
Global Genes Project

Latest Clinical Trials and Research updates.



**Happy Jack Cops all his  
wishes**

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## Hello to our Lysosomal family network.

Here is a copy of the report prepared for the LDNZ trustees meeting held in March 2010, sent out to all of you so you can see what has been going on behind the scenes over the past year. This report covers the financial year July 2008 – June 2009, and includes some commentary up to the date of our meeting in March 2010.

### Overview:

2009 was a particularly difficult year for LDNZ, due to the world financial crisis, which in turn affected our ability to secure a good level of grant funding to run our organisation. Lottery community who has been one of our main sources of funding granted just \$4,000, however JR McKenzie increased their support to \$10,000. A number of grant funders who have funded us in the past did not do so during 2009. In contrast to the difficulty getting core funds for LDNZ operations, we had a large inflow of funds for special projects held during this time.

Our viability and continued survival as an organisation was maintained by two key fundraisers: Ra Timms held a very successful Charity golf tournament raising approx \$20,000. We held our 3<sup>rd</sup> Annual Charity dinner in September 2009 and again this was another successful event raising \$28,000. These events are a good fundraiser for LDNZ but are not on the agenda for 2010 or 2011. Organising such event is becoming more difficult, and we feel we are unable to sustain the effort required to keep those special fundraisers going. The ability of the community to support them is also restrained by the economic environment.

We had great success in 2009 with Pharmac agreeing to fund Elapraxe for Hunter Syndrome, and although this was a good break through it will be more difficult to achieve funding for Pompe, Fabry and MPS6 as we don't have the impact on young children that we can push forward as an example of urgent need to access these therapies. Pursuing approval for ERT funding is high on LDNZ's priority list, and we have plans to continue our lobbying about that.

### Finances:

During the 2008 – 2009 financial year we had quite a lot going on which saw a large amount of funds go through our accounts.

- November 2008 we held our 1<sup>st</sup> Asia Pacific Lysosomal Conference which saw delegates attend from all over the world.
- Jenny Noble won a scholarship from the AMP foundation worth \$60,000. This scholarship came in 3 parts.  
\$10,000 to support the 1<sup>st</sup> International Bone Consensus meeting.  
\$20,000 to support families to the 2008 conference  
\$30,000 for New Zealand and Australian families with Glycoprotein Storage diseases to be included in a Natural History Study.
- In February 2009 we took 15 Lysosomal families to Wellington to meet all the political parties to outline the issues they faced in not being able to access specialised medicines.
- In March 2009 Jenny and I travelled to Massey University to meet the research team there, learn about their plans, and to present a cheque to Bob Jolly to help support his research project for Sanfilippo Disease.

These activities resulted in income for the year ended 30<sup>th</sup> June 2009 of \$242,475 but with expenditure exceeding \$286,000 our funds were considerably depleted down to \$113,862. A good portion of the remaining funds are tagged for supporting families to attend the Batten and 2010 MPS meetings in Adelaide, Targeted research projects, and work on our Managed clinical networks project, the re-branding of LDNZ's publicity materials and our special family support grant.

So in spite of the bank balance at the end of the year, we have a significant challenge in maintaining enough income to keep our organisation running.

**Managed Clinical Networks:**

NZORD held a special workshop in Wellington in November with patient support groups and the National Health Board. There were several presentations by patient groups outlining the issues they face in trying to access appropriate specialist services. LDNZ was able to outline the extreme issues our families faced with getting appropriate access, and we were able to provide the meeting with the very helpful comments of the Health & Disability Commissioner advising the Director General of Health that current arrangements were not acceptable, and asking him to give some urgency to resolving these issues.

Especially pleasing was a commitment made by the chair of the National Health Board, Murray Horn, that he would consider two proposals for networks for rare diseases. NZORD has decided to submit proposals for Lysosomal/Metabolic Diseases and Epidermolysis Bullosa, and a lot of work will be required in preparation of those cases during the year ahead.

**Genetic Services:**

LDNZ is concerned that diagnosis of our diseases is difficult and perhaps not getting done due to cost. Getting improvements to Genetic services is difficult as many reports on the need to improve these services have been shelved over the years. In 2009 the review of genetic services was finally revived and the case for a single national service, with secured funding, is now under consideration by the National Health Board.

**Family Support:**

Family support for Lysosomal families continues on a case by case basis, and is driven by the need of the families. Referral of new families to LDNZ continues to be a problem. We are still not sure how well our organisation's details are being given to new families on diagnosis. We often don't get direct contact about newly diagnosed families, and learn about them sometimes when they are in crisis and need help. LDNZ needs to look at how we can raise our profile and improve the way information about LDNZ is supplied to new families.

**Publicity Materials:**

The re-branding of LDNZ began in 2009 with a new banner, business cards and letterhead. We still need to revamp our brochures and A4 handouts but this will now be dependent on finding appropriate funding to complete this task. The website has had its makeover and is in a new content management system, and we are working on a project to update the content on the website. Jenny will be working on this with Ben who manages the NZORD websites, through which the LDNZ site is provided.

**Medicines Strategy:**

After many years of lobbying on improved access to medicines, and high cost, highly specialised medicines in particular, there is now some real progress happening with a significant boost to medicine funding in the 2009 budget, and a Ministerial panel set up to review access to high cost and specialist medicines. It is hoped that new funding will be available for these drugs.

At the date of our meeting in March 2010, the panel has produced an interim report in response to the Minister's request for a mechanism on how to get high cost medicines funded. There is concern that the panel has taken an approach of trying to fix the whole of the medicine system in the hope that some efficiencies might release funding for high cost medicines, and that this approach will not produce real changes in the short term. We have suggested that a more practical approach is needed with specific funds allocated. This should make some real difference if the panel's proposal to use the exceptional circumstances scheme is used, but will not provide a solution if the existing EC criteria and budget are relied on.

The Minister is due to get his report soon and his response to that will tell us how it is going to work. If the proposed mechanism does not solve the problem of medicine access for our families, we will still have our strong moral arguments to use in promoting access, but getting a good mechanism in place will make it much easier for us to achieve our aims.

### Carers Strategy:

This strategy says good things about government recognition and support for carers, but is a high level document that needs some serious work to implement the principles in it. Although the new Government supports the strategy they have taken few initiatives to move forward with any of the main objectives in the strategy. In fact, the Social Development Minister has instructed officials to cease work on scoping a payment for carers. In addition, the government has appealed against the Human Rights Review Tribunal decision that the Ministry of Health had unlawfully discriminated on the basis of family status, and that family carers should be paid for the care they provide, in circumstances where the government would otherwise have to pay for that care. The decision to appeal is a serious blow to the interests of carers and the disabled people they support.

### Trust Accountability:

The trustees met in February 2009 for the Annual Meeting and to plan activities for the year ahead. Activities based on that plan have been carried out mainly by Jenny with regular reporting to the chair of the Trust, with additional issues being referred to the trustees by e-mail for decisions. This continues the pattern from past years where we meet face-to-face once a year for a full day of review and planning, and deal with all matters in between times by phone and email.

Keeping our books in order is very ably supported by Tim Hannagan through his accounting firm and this help is much appreciated, especially as the volume and complexity of transactions has grown in recent years,

Much of Jenny's time throughout 2009 and the early part of 2010 has been taken up with planning for the 2010 International MPS symposium which takes place in June this year in Adelaide. LDNZ is an equal partner with the Australian MPS society and the Adelaide Lysosomal Research Unit, in hosting and organising the meeting. My grateful thanks to trustees Dianne Webster, Dave Palmer, and Philip McKinstry for their support throughout this time, and in particular to Jenny for the significant commitment she makes to ensure the success of LDNZ's day-to-day operations.

**John Forman**  
Chairperson  
LDNZ



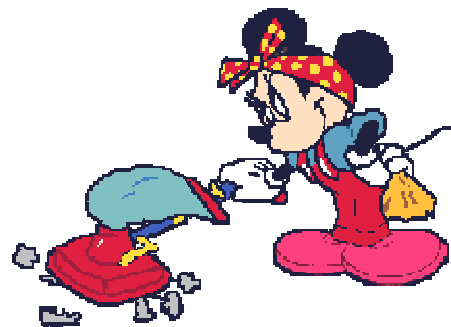
Behind every successful man is a surprised woman!

~Maryon Pearson~

I'm not going to vacuum until

Comet makes one you can ride on!

~Roseanne Barr~



## Report on National Tay-Sach and Allied organisations

Boston – April 2009

By Joanne Labeledzki

*LDNZ were thrilled to be able to send Joanne to the National Tay-Sach meeting in Boston. Joanne lost her beautiful daughter in 2008 and had never met another family who had the same lysosomal disease as Brooke. This was an opportunity for Joanne to heal and learn more about Sandhoff disease.*

In April last year I was lucky enough to meet some amazing families who helped me through the devastating journey that Sandhoff disease took us on. With help from Lysosomal Diseases New Zealand and the National Tay-Sachs and Allied Diseases organisation, my mother, son and I flew to Boston and spent 4 days talking, listening, learning, grieving and healing with others who knew what it was like.

Brooke was born in March 2006 and appeared healthy until her 9 month Plunket check. It was then that the decline started becoming obvious and by 14months she was diagnosed with Sandhoff Disease. Less than a year later she passed away in March 2008 three days before her second birthday.

During the year this disease slowly took our daughter, I found great comfort in the journals of other families, most of whom meet yearly at the NTSAD conference in the United States. It was my dream to attend this as soon as I heard about it as I didn't know of anyone else in New Zealand at the time.

The conference was the best thing I could have done. Straight away we were given our supplies and Riorden was whisked off to enjoy children's activities for the whole 4 days including a sibling session where he got to talk about his sister.

Mum and I went to the grief session first where I finally met my special friend I found on the internet; her daughter lived to be 6 with Infantile Sandhoff disease. There were sessions aimed at just grandparents & friends, there were sessions for just women, men and siblings. They broke the diseases down into Infantile, Juvenile and Adult forms, along with Leukodystrophies and Canavan.

Those sessions where we got to talk in a relaxed atmosphere were the best. We discovered we were all the same, even though we came from different parts of the world, different levels of society and different beliefs. We were all comfortable and enjoyed talking together which is something families with rare diseases are lucky if they get to do. There is just nothing like a conversation with other mothers about the ever changing seizures or the benefits of a big comfy pushchair over a wheelchair. Likewise with the men, they seemed to have quite a few impromptu sessions in the hospitality suite (bar), but whenever we found them they were always firmly engrossed in serious conversations about their child and how they were dealing with things. It was the best therapy for everyone!

There were children attending with Tay-Sachs, Sandhoff disease, GM1 and Metachromatic Leukodystrophy, it was hard seeing them as I really wanted Brooke to be there with me, to park pushchairs next to another affected child's, to touch the hand of another little angel. But on the other hand I was sad to see them, knowing what they were going through and what lay ahead. My goal was to hold another child and I did, ironically her name was also Brooke, she had GM1.

I found one of the sessions quite hard; it compared philosophies of care from one extreme to the other. One was all about equipment, feeding tubes and 24hr nursing care. The other was natural with no tubes or needles. I have brought home with me a copy of a DVD I found helpful when Brooke was first diagnosed. I have passed it on to LDNZ as I think it would be helpful for newly diagnosed families and it is called 'Cameron's Arc'. It follows a family's journey with their doctors and how they decided on her care plan. Copies can be obtained from NTSAD also.

The Scientific session was parent focused, we sat at tables according to our understanding of the therapies and medical advances while the Scientists moved around at set intervals and explained things to us (I was a beginner and honestly it still went right over my head). What sunk in though is that there is a lot going on that you don't realise, and I am really glad they are on our side.

The 'Action' session was aimed at giving us ideas to raise awareness and fundraise to help find cures for all these diseases. It was empowering to see the enthusiasm some of the parents have, even though their children might have died ten years ago they are still going strong.

After all the talking, we were exhausted but a huge weight had been lifted. Riorden was sad to leave, he had a ball and I'm glad he has had this opportunity and knows he's not the only one who's lost a brother or sister to Sandhoff disease. A Remembrance Ceremony and a Gala Dinner ended the conference, goodbyes till next time and a long trip home brought us back to reality.

I will go again one day and hopefully I'll be one of those empowering parents from 10yrs ago. Thank you so much LDNZ!

### ***Joanne Labedzki***

*I made this picture of all the children I came to know before the conference and got to meet a few of them and many of their parents in Boston. I was surprised to arrive and find they had used it for the back cover of the conference booklet!*



## It's hard work being Fabry-affected.

*By Anna Percy*

***Anna attended the International Fabry meeting in Amsterdam on 5<sup>th</sup> Feb. Below is her report.***

Thanks to a series of prior engagements affecting Jenny, John, and the other board members of LDNZ, I found myself representing our association at the Fabry International Network (FIN) conference in Amsterdam on February 5 & 6 2010. Because my son is affected by Fabry disease I jumped at the chance to attend - also because I lived in Amsterdam for two years in the 1980's and I still have many friends there.

Anyone jealous of me for the opportunity to travel so far will be pleased to know that the conference was hard work. This wasn't a talkfest but a high powered planning session. Building on the excellent work of the FIN board before the meeting, we had to finalise the vision, purpose, values, collaborative guidelines, aims and objectives of FIN and to develop a two-year action plan with dates and names – all in two days. There was quite a lot of eating but not much sleep and certainly no chance to doze off at the back of the hall. We spent most of the time working in small groups haggling over details of wording and giving shape to the emerging international consensus on how best to support Fabry-affected people, their families and communities.

We also heard from the three industry partners of FIN – Genzyme, Shire and Amicus – about new developments. This was quite unique really, given that these three companies are competitors. FIN has indeed done a stunning job of creating a single Fabry “hub” to which many organisations willingly contribute. Briefly, the overview given by the organisations was:

- Genzyme is still in real trouble with many of their biological reactors out of action and only 30% of normal output. This is affecting many patients around the world, with access to Fabrazyme rationed and most people on less than their recommended dose. FIN is assisting with the distribution of information and updates to the Fabry community, both directly and through medical channels. There really wasn't any news about when this situation will end.
- Amicus's update won't be news to those NZ patients on the trial of small molecule (chaperone) therapy. They simply said where the trials were up to and that so far things were going well.
- Shire is a company I hadn't heard from directly. They make Replagal which is a very similar product to Fabrazyme but the microbiology of how the two products are manufactured differs significantly. Shire has a proprietary piece of genetic technology which has the effect of putting a neighbouring gene into “overdrive”, so they can produce more of a specific protein. This is at the core of how they produce Replagal and is something they will be applying to other genetic products in future.

FIN also has a medical reference group, and doctors from the UK, France and Israel were there to assist us and also to give their own view of new developments. Of these presentations, the one from Dr Stephen Waldeck in the United Kingdom was the most relevant. Drawing on a mixture of published and yet-to-be published data from UK records of Fabry-affected patients, he gave an overview of some emerging findings. Without placing too much emphasis on the unpublished component, the key messages are:

- Doctors are looking for relatively subtle drug impacts, in a disease which not only affects a very small number of people but which even then follows a very different course from patient to patient. The “gold standard” of proof, involving scientific trials across hundreds or even thousands of patients, isn’t achievable. The science of Fabry disease is a mix of the “silver standard” of multi-patient clinical data, some “bronze standard” research based on the Fabry registries, and a lot of relatively worthless single-patient observations.
- Based on “silver standard” UK clinical data across a range of measurable indicators of heart and kidney function, ERT appears to be holding Fabry-affected people who are not yet showing damage within the healthy range, and stabilising the condition of people who already have measurable damage. This isn’t as much as people originally hoped that the drugs would achieve; in particular, the evidence for reversal of existing damage isn’t stunning.
- For kidney disease specifically, biopsies seem to show more damage than is evident from blood or urine testing.

But enough science; what about action? The Fabry International Network now has a complete action plan, but it’s still in the form of many large, scribbled-on pieces of paper. These are in the hands of Louise O’Mara, who did an outstanding job of facilitating the meeting, and will be transforming our work into a written document shortly. So watch the website ([www.fin.org](http://www.fin.org)) and hopefully it won’t contradict my memory too much.

My own, rather selective, memory is that assisting countries like NZ which don’t have access to appropriate treatment is a very high priority indeed in FIN’s action plan. They can’t do it for us, but being part of an international network gives us access to industry and medical advice, and even better to the people in other countries who have fought this battle themselves and won. Two relevant steps in FIN’s action plan are:

1. Developing a “Fabry road map” setting out the steps taken in countries which have secured access to treatment. Did they achieve this through bureaucratic or political channels? Was the media involved? The courts?? In the end, what tipped the balance and got them access to treatment?
2. Consolidating the rules around access to ERT treatment in countries that do have it. Do they treat everyone, or just those with major symptoms, and at what level of symptoms does ERT treatment begin in Australia, the UK, Canada, Brazil, Israel and the other countries which fund it for their citizens?

Both these pieces of work will be outstanding lobbying tools for NZ and for other countries with no access to appropriate treatment.

Finally, it was an honour to meet people from 23 Fabry organisations in 21 countries, many of whom are themselves affected with Fabry disease, and to represent our own LDNZ at this important meeting.

*Thank you Anna for such a wonderful report and ensuring that LDNZ can play a role in the International Fabry group. We look forward to working with them for the good of all those affected by Fabry disease.*



*Early this year LDNZ was invited to become a partner in the global genes project celebrating world rare disease day. We think this is an exciting project which will work well in New Zealand.*

*LDNZ will be working with NZORD to develop a rare disease awareness program for New Zealand. Check out the website and think about how you can encourage your work place to wear jeans on or around 28<sup>th</sup> February 2011 with donations going to LDNZ.*

#### HOW DID THE GLOBAL GENES PROJECT COME ABOUT?

As part of World Rare Disease Day 2009, a video began circulating on You Tube that was developed by a rare disease parent advocate. The video showed the natural connection between jeans and genes.

Using that video as inspiration, a group of individuals and rare disease organizations decided to take this connection to the next level by creating the Global Genes Project, a grassroots effort to use jeans to raise awareness for rare genetic disorders.

This group has grown and continues to add individuals and organizations that want to be involved. Our hope is that the rare disease community as a whole will view this initiative as an opportunity to build unity around this important cause. Creating a platform for collaboration, while building awareness, educating and engaging support from the general public.

To learn more about this new group visit: <http://www.globalgenesproject.org/>



## Happy Jack Cops All his wishes – as printed in the Palmerston North community paper 10/3/2010



Jack Peacock has a wish to become a policeman and to holiday on the Gold Coast – and yesterday it all came true.

The seven-year-old Whakarongo pupil has a life threatening illness called Hunter Syndrome, a terminal and debilitating genetic disease, and the Make-A-Wish foundation organised for police to turn up to his school and award him his wish.

Jack's morning began with the news he was taking a trip with his family to the Gold Coast on Friday. The foundation has organised for Jack's dad, Kendall, who is in the army and serving in East Timor, to meet the rest of the family in Brisbane. This will be the first time Jack has seen his dad in six months.

After arriving in style to school in foundation volunteer Michael Earley's Corvette, the whole school and police met him on the school's tennis court.

Senior sergeant Brett Amas and dog handler Lance Kennedy presented Jack with a tiny tailored-to-fit police uniform. Grinning from ear to ear, Jack said he was extremely excited about his new uniform and trip.

His mother, Kirsty Peacock, applied to the Make-A-Wish foundation four years ago, when Jack was three. His wish was accepted then, but it has taken this long to do the holiday because he's been through quite a bit of treatment.



## The successful effort to develop Myozyme<sup>®</sup>, and bring new hope to families affected by Pompe disease.

The release of a new movie, *Extraordinary Measures*, is about a family affected by Pompe disease, and is raising new levels of interest about Pompe and the amazing effort over more than 10 years to develop Myozyme, the first therapy to treat this devastating illness. The movie *Extraordinary Measures*, featuring actors Harrison Ford and Brendan Fraser, is based on the work of a man named John Crowley, who has two children with Pompe disease.

### *The Path to Myozyme*

Beginning in the 1960s and fuelled by the biotechnology revolution in 1980s, researchers at academic centers around the world initiated work to identify a treatment for Pompe – including therapies that could replace the missing GAA enzyme in patients.

Based on these early efforts, from 1998-2002 Genzyme worked to advance promising research involving four different drug candidates to treat Pompe:

- a transgenic enzyme developed in a joint venture with Pharming Group N.V, a company in The Netherlands
- An enzyme that was developed by Synpac (North Carolina), Inc., a company in the U.S.
- an enzyme that was developed internally at Genzyme in conjunction with researchers at Duke University in the U.S. and Erasmus Medical Center in The Netherlands
- an enzyme with chemical modifications that was developed by a company called Novazyme Pharmaceuticals, Inc., which was acquired by Genzyme in 2001

### *The Mother of All Experiments*

In 2002, researchers initiated a major effort to study and compare these four drugs to determine which candidates offered the best chance of success in treating Pompe disease. This effort involved extensive research and analysis – the undertaking was so large and so important that it was nicknamed “The Mother of All Experiments” by the research team leaders.

### *The Bravery and Heroism of Families Affected by Pompe*

There are many stories of extraordinary effort and sacrifice among the families who joined in the effort to develop Myozyme:

- In 2003 in Naples, Italy, parents of a young girl with Pompe chained themselves to a fence outside the ministry of health and initiated a hunger strike in a desperate effort to draw attention to their daughter, who was facing serious health problems because of Pompe disease.
- During the same time period, news outlets in Spain were running a series of stories about a young boy in Madrid who was affected by Pompe and whose parents were working to get him enrolled in the clinical trial for Myozyme.

- A mother of a baby with Pompe in the U.S. had to act alone to take part in this research effort while her husband was on military duty overseas. On her own, she relocated her baby and two older children to a new city while her husband was away.
- One family had a daughter diagnosed with Pompe at six weeks old. The family was familiar with the disease; their oldest daughter died from severe medical complications associated with Pompe in 2002. The parents were desperate for their daughter to receive treatment: "I feel like we are racing against a clock...we are determined, we will save her."

Based on these and so many other stories of sacrifice and hope, the final clinical trial for Myozyme was fully enrolled with patients in 2004.

*To read more about this amazing journey go to: <http://www.genzyme.com/pompemovie>*



## StemCells, Inc. Plans to Advance to Second Clinical Trial in Batten Disease

**PALO ALTO, Calif., April 21, 2010** – StemCells, Inc. (NASDAQ: STEM) announced today that it has submitted a protocol to the FDA for initiation of a second clinical trial of its proprietary HuCNS-SC® human neural stem cells in neuronal ceroid lipofuscinosis (NCL), which is also often referred to as Batten disease. NCL is a genetic disorder characterized by the absence of a critical enzyme, which leads to the loss of neurons and the eventual death of the patient. The Company completed a Phase I clinical trial in NCL in January 2009 and reported the results to the FDA in September 2009.

"Our first NCL trial was focused primarily on safety, and our data showed that the cells, the immunosuppression regimen and the procedure were all well tolerated," stated Stephen Huhn, MD, FACS, FAAP, Vice President and Head of the CNS program at StemCells, Inc. "This positive safety profile encourages us to advance our clinical program in NCL, and this second trial will place an increased emphasis on the measurement of clinical benefit. We have shown that our HuCNS-SC cells produce the enzyme missing in NCL, so our strategy is to transplant our cells and have them provide enough enzyme to keep the patient's own neurons intact and functioning. We believe that demonstrating benefit will depend on how many neurons are alive at the time of the transplant, so unlike our first trial, which enrolled patients with few neurons left to protect, this second trial is designed to enroll patients who have less neuronal degeneration and cognitive impairment."

The proposed new trial is designed to further assess the safety of HuCNS-SC cells in NCL, while also examining the ability of the cells to affect the progression of the disease. The Company plans to enroll six patients with infantile and late infantile NCL. Because intervention prior to the final stages of the disease will likely be key to providing a therapeutic benefit, the Company plans to enroll patients with less brain atrophy than those enrolled in its first trial. Under the proposed protocol, all patients would be transplanted with HuCNS-SC cells and immunosuppressed for nine months. The patients would also be evaluated and assessed at regular intervals over the course of 12 months following transplantation. As the Company intends to follow the effects of this therapy long-term, a separate four-year observational study would be initiated at the conclusion of this trial. Upon FDA authorization of the trial protocol, the Company will proceed with site selection and seek the necessary Institutional Review Board approval to initiate the trial. **To read more go to <http://www.stemcellsinc.com/news/100421.html>**

## BioMarin Reports Encouraging Preliminary Data on BMN 110 for MPS IVA Phase III Trial expected to start by late 2010 or early 2011

**February 4, 2010** – BioMarin Pharmaceutical Inc. (Nasdaq: BMRN) today announced an update on the Phase I/II trial for BMN 110 or N-acetylgalactosamine 6-sulfatase (GALNS), intended for the treatment of the lysosomal storage disorder Mucopolysaccharidosis Type IVA (MPS IVA), or Morquio A Syndrome. Preliminary clinical data from the first 24 weeks of the study (12 weeks at 0.1mg/kg and 12 weeks at 1.0 mg/kg) have been evaluated, and BioMarin plans to announce top-line results for the full 36- week study after completion of dosing at 2.0 mg/kg in the second quarter of 2010.

### Key Observations:

- Keratan sulfate (KS) levels fall within a few weeks after the start of therapy.
- Improvements in 6-minute walk distance and 3-minute stair climb at 24 weeks are consistent with those observed with clinical studies for MPS I, MPS II, and MPS VI.
- The frequency and severity of infusion reactions appear comparable to those observed with Naglazyme and Aldurazyme. "Although still early, they are encouraged by these initial signals of efficacy of GALNS enzyme replacement therapy for Morquio disease. Additional results will become available following the 2.0 mg/kg dose phase, but compared to other studies conducted in MPS diseases, they are encouraged by the reduction in KS and improvements in walk distance and stair climb. Based on these results, they feel more confident about endurance as a primary endpoint for a Phase III trial and that a Phase III trial can be conducted as expeditiously as previous trials of enzyme replacement therapy,"

For more information please go to: <http://www.bmrn.com>

## Zavesca® (miglustat) receives positive vote from the FDA's Endocrinologic and Metabolic Drugs Advisory Committee for the treatment of Niemann-Pick type C disease

**ALLSCHWIL/BASEL, SWITZERLAND - 12 January 2010** - Actelion Ltd (SIX: ATLN) announced today that United States (US) Food and Drug Administration's (FDA) Endocrinologic and Metabolic Drugs Advisory Committee voted (10 yes to 3 no) in its final vote in question that the benefit/risk profile of Zavesca® (miglustat) supports its approval for the treatment of progressive neurological manifestations in adult patients and paediatric patients with Niemann-Pick type C (NP-C) disease. NP-C disease is a very rare, relentlessly progressive and eventually fatal neurodegenerative genetic disorder for which no specific treatment is currently approved in the US.

The decision was based on results from the clinical trial OGT 918-007 and two multi-centre NP-C disease cohort studies as well as other clinical trials in related lysosomal storage disorders for the safety and tolerability evaluation.

Zavesca® is the only specific treatment available for patients with NP-C disease. It received approval in the European Union (EU) and other countries in 2009. Zavesca® is also indicated in the US, the EU and other countries for the oral treatment of adult patients with mild to moderate type 1 Gaucher disease for whom enzyme replacement therapy is unsuitable or is not a therapeutic option. The use of Zavesca® is supported by over 10 years of clinical trials and post-marketing experience across indications...

*For more information:* <http://podcasts.mayoclinic.org/2008/07/11/niemann-pick-disease-type-c/>

## NZ Research updates for Sanfilippo Disease

*Last year LDNZ sponsored further research for Sanfilippo disease under the care of Prof. Bob Jolly from Massey University, Palmerston North. Below is a small article on their research project. Prof Jolly will be presenting the full findings at the 11<sup>th</sup> International MPS and Related Diseases symposium in Adelaide June 2010.*

### **Anatomical and physiological principles underlying intra-cisternal enzyme replacement therapy in lysosomal storage diseases.** R.D. Jolly, Massey University.

Research with the group at Adelaide Women and Children's hospital has shown that in mucopolysaccharidosis IIIA (MPSIIIA) in mice and dogs, direct injection of replacement enzyme into the cerebrospinal fluid (CSF) is a potential therapy for human patients. Recent research at Massey University has involved routes of dispersal of enzyme within the subarachnoid space of the meninges and the way it gets into the brain.

Time/lapse computerised tomography (CT) with contrast media, injections of India ink or enzyme; have shown well defined routes of dispersion in the meninges involving the basal cisterns, brain sulci and fissures that explain distribution patterns in the early enzyme replacement experiments in dogs. They also show that posture after injection may be important in distribution of enzyme. The motive force for mixing and moving CSF in the meninges is likely brain pulsation associated with arterial pulse.

Immunocytochemistry with traditional light or confocal microscopy has shown that enzyme mainly enters the brain by a perivascular route that extends down onto capillaries as well as superficial diffusion through the meninges. From blood vessels it diffuses paravascularly to be taken up by neurons and other brain cells. Distribution of enzyme is variable within the brain, but an understanding of the underlying anatomical and physiological principles involved should help optimize therapeutic protocols.



## Clinical Trials and Studies

### **Surrogate Endpoint Trial (SET) for Individuals with MPS IIIA**

Sponsored by Shire Human Genetic Therapies

SET is a one-year, multi-center study designed to study the natural progression of Sanfilippo A syndrome, or MPS IIIA, in approximately 20 patients. During a period of 12 months participants in the study will be evaluated to assess the severity and progression of MPS IIIA, as measured by developmental age and milestones, central nervous system function (including cognition, speech and motor skills) and biochemical markers of the condition (levels of heparin sulfate and its breakdown products in blood, urine and cerebrospinal fluid). Additional information can be found at [www.clinicaltrials.gov](http://www.clinicaltrials.gov) (identifier NCT01047306)



### MPS II Intrathecal Enzyme Replacement Clinical Trial

Shire Human Genetic Therapies is sponsoring a clinical trial at the University of North Carolina at Chapel Hill to learn if direct administration of recombinant enzyme into the fluid around the brain and spinal cord is safe and a possible treatment for children with MPS II with developmental delays. "A phase I/II safety and ascending dose ranging study of idursulfase administration via an intrathecal drug delivery device in pediatric patients with MPS II who demonstrate evidence of central nervous system involvement and who are receiving treatment with Elapraise™," said Joseph Muenzer, MD, PhD, principal investigator for the clinical trial.

Currently there is no approved therapy for treating the brain and spinal cord in patients with the severe form of MPS II. The goal of this study is to give a new preparation of iduronate-2-sulfatase (idursulfase-IT) directly into the fluid surrounding the brain and spinal cord (intrathecal administration). The new form of iduronate-2-sulfatase has not been used before in patients with MPS II and is considered investigational. It has not been approved by the FDA or any other regulatory agency. To read more go to: <http://www.mppsociety.org>



### MPS III

Shire Pharmaceuticals Group, as part of its research to evaluate new approaches to the problem of treatment of the central nervous system, is hoping to move its MPS III A program forward. If the trial to directly administer the enzyme into the central nervous system of individuals with MPS III A is successful, Shire hopes to expand its research initiatives to include MPS III A. The Shire Web site is [www.shire.com](http://www.shire.com). For more information regarding clinical trials visit: [www.clinicaltrials.gov](http://www.clinicaltrials.gov) and search "mucopolysaccharidosis".



### The Natural History of Metachromatic Leukodystrophy (rhASA-NH-US)

Sponsored by: Shire Human Genetic Therapies, Inc

There have not been longitudinal studies which track patients' neurologically or developmentally in a systematic manner. By simultaneously tracking patients' neurodevelopment along with neuroimaging and neurophysiologic studies it becomes much easier to draw conclusions on the differential effects of the disease process and any available treatments that patients might receive. In addition, many of the gene mutations, which cause MLD have not been linked to the age of onset or the expected disease course. [www.clinicaltrials.gov](http://www.clinicaltrials.gov) (identifier NCT00639132)

*Anything for a better  
View !!!*



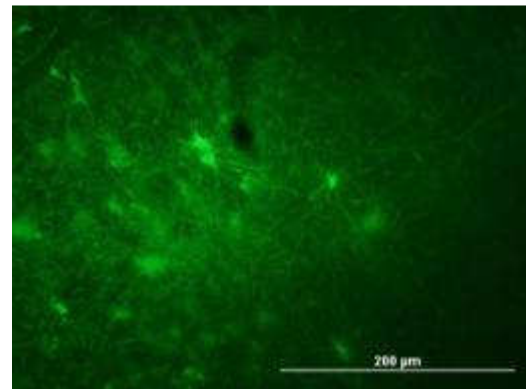
The Batten disease research group in New Zealand have teamed up with Imke Tammen's group in Australia and Jon Cooper in London into a network, BARN, which stands for Batten disease animal research network, and we even have a logo. Current research efforts are focused towards treatments, and our two flocks of sheep with different forms of Batten disease (CLN5 and CLN6) are ideal for studying this.



**Batten Animal Research Network**

**Gene therapy.** The sheep are an ideal model for working out methods, logistics and prognosis for gene therapy because they have large complex human-like brains. In collaboration with Stephanie Hughes and Kate Linterman at Otago we have found that we can inject a gene transfer vector carrying a gene into the sheep brain and the gene is expressed with no harm to the sheep over 80 days. This is exciting. Currently we are exploring modifications to target different cell types and surgical techniques to target different regions of the brain, aiming to trial the injection of a Batten gene into the affected sheep and see if we can ameliorate the disease this way. In collaboration with Jon Cooper in London we also intend to explore a greater range of vectors to see which is best for this purpose.

**Anti-inflammatory therapy.** The discovery that neuroinflammation is an early part of the disease cascade led us to trial an easily available anti-inflammatory drug, minocycline, in lambs after weaning to see if this would slow or stop the development of disease. Chronic oral administration of the drug in food led to pharmacological concentrations in the brain and did no harm, but it did not change the courses of the disease. We chose this drug because it was readily available and we wanted an example to set up the facilities and methods. Work continues to map the inflammation cascade, so that we can identify critical points and test drugs aimed at them.



**Left** Brain surgery on a sheep to trial gene transfer. **Right** Microscope picture of gene transfer to cells in the brain, shown by the glowing green fluorescent marker

*Please help the work of Lysosomal Diseases  
New Zealand*

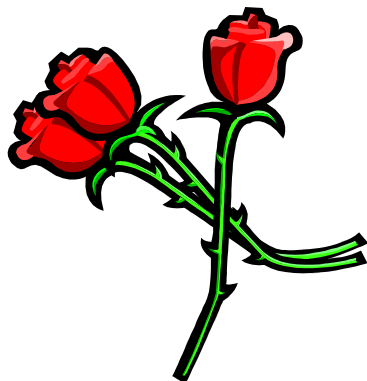
Donations over \$5.00 made to Lysosomal Diseases New Zealand are Tax deductible.

**Funds raised by LDNZ cover the following areas**

Funding of all administration expenses for our group.

- Supporting families wishing to attend Conferences.
- Lobbying the Ministry for improvements to diagnosis, screening and care.
- Keeping in touch with researchers and biotech companies on research progress.
- Supporting some research efforts here in New Zealand.
- Keeping you informed of progress with our mission.
- Advocating for families for disability support, health services and access to therapies.

We gratefully accept donations that will enable us to continue toward our goal of a future free of the tragic consequences of Lysosomal Storage Diseases.



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