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 improvements to the clinical care of affected people.

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LDNZ’s Charities Commission
Registration number
CC24962
Hello to our Lysosomal Community

The past few years certainly seem like a constant stream of two-steps-forward-and-three-steps-back episodes, when it comes to our efforts to secure funded access to therapies for patients with a lysosomal disease.

Some good things did happen, and some bad.

- **A big positive** – The special fund for rare diseases resulted in 4 enzyme replacement therapies for Lysosomal diseases being listed on the Pharmaceutical schedule, meaning all patients with those diseases who fit treatment criteria, will get automatic access to treatment. The 4 funded treatments are Naglazyme for Maroteaux-Lamy disease, Aldurazyme for infants with Hurler disease prior to a transplant, Elaprase for infants with Hunter disease, also prior to a transplant, and Myozyme for infants with Pompe disease. We are very pleased with the progress made in getting these treatments listed on the schedule and automatically funded.

- **A big negative** – a combination of government stealing funds out of the medicine budget, and Pharmac having no sense of urgency about rare diseases, meant it was very close to 3 years between the announcement of the special fund, and the final decisions from that funding round.

- **Another big negative** – when we review the process followed in the rare disease drug fund, we estimated that of more than 100 patients with the diseases that were indicated as likely candidates under this fund, by the close of the fund there will be fewer than 5 of those patients getting new access to treatments that were not previously funded through any government source. **Explanation** – for several years any very young patients with Hurler or Hunter disease having a transplant were given access to enzyme treatment via Pharmac’s exceptional circumstances scheme. This means the decision for those 2 diseases was a shift between funds rather than new access for previously unfunded therapies.

- **And adding insult to injury** – an application for Myozyme to be listed on the schedule for adults with Pompe disease, hit a brick wall at Pharmac’s advisory committee (PTAC), which recommended that funding of Myozyme be declined. Though that is not a definitive end to that application, it is such an obstacle that this disease, which seemed a prime example of a treatment that should have received a positive decision under the rare diseases fund, seems doomed in Pharmac’s process. This highlights an apparent failure of Pharmac’s new decision process, their “factors for consideration” to have little or no practical effect at all.

- And during all of this some more good things happened with 4 or our adult Pompe patients gaining access to a clinical trial of a new treatment, and 4 others winning access to compassionate access to Myozyme from Sanofi-Genzyme. This positive outcome, no thanks to Pharmac at all, is in the shadow of the very sad news that Laurie Hill, one of our adults with Pompe disease, died at the end of 2016. Laurie would certainly still be with us and facing many more good years, if restricted medicine funding had not been applied in such a discriminatory and inequitable manner by Pharmac.
More details on these points about medicine access are in this edition of the newsletter. We are very conscious that this issue is a very high-profile and time-consuming issue for LDNZ. It tends to overshadow other things we do, including assisting with information, contacts, research support, and getting the right clinical care for Lysosomal families. We plan to feature more of these other activities in our next newsletter.

Best wishes to you all,

John Forman  
Chair of LDNZ

PTAC Review of Myozyme and the review of the special fund for rare diseases

In 2016 Sanofi-Genzyme submitted an application for listing of Myozyme on the Pharmaceutical schedule, to treat adults with Pompe disease. LDNZ understands there were discussions between the company and Pharmac when the tender call went out for the rare disease fund in late 2014, with Pharmac encouraging the company to make a regular schedule application, rather than channel it through the rare disease fund.

LDNZ found out about this in 2016 when the application had been submitted and was going through Pharmac’s internal process, following a staff change in the company where a new rep was not aware of Pharmac’s insistence “that LDNZ should not be informed about it”. We followed the PTAC review closely as it was the first occasion when the new “factors for consideration” were being applied in Pharmac’s decision-making process. These new aspects to their decision criteria seemed a possible channel through which a broader and more inclusive set of factors could influence decision, hopefully to balance out the disadvantage inherent in rarity.

Our long-standing frustration with medicine funding decisions has turned to renewed cynicism and some degree of anger, when it has become apparent that their factors for consideration have apparently had no effect whatsoever at the PTAC level. That committee gave scant attention to the new decision-making guidance and made it recommendation based on evidence and costs only. No focus went on to the right of patients to be treated, the need for equity in decision-making, nor any reference to fairness in how this disadvantaged group could possible get a fair go in the medicines system.

We think Pharmac has been in a significant bind in recent years. They appeared to want to do something positive to improve access to medicines for rare diseases, and their special fund seemed a positive start, despite the woefully inadequate amount of money to progress that new policy. Their difficulties showed up starkly when government and
DHBs stripped most surplus cash out of the medicines budget, leaving them with very little discretionary spending power. That, perhaps, is the central reason for a lot of smoke and mirrors about shifting expenditure between budgets as a pretense about the amount of money allocated to funding treatments for rare diseases. It is difficult to escape the conclusion that the PTAC recommendation on Myozyme starkly highlights a lack of any intent to make a real and substantial difference to medicine access for rare diseases, either on the part of government or Pharmac.

LDNZ restates its view that a separate fund, adequately resourced, with more appropriate criteria, and managed away from Pharmac, is the most practical way of making real progress on medicine access for rare diseases. This is the position supported by most political parties prior to the 2014 election, and one we are keen to see restated by them in this election year.

Much-loved teacher and counsellor, Laurie Hill, loses battle with Pompe Disease

On 30\textsuperscript{th} December Laurie Hill lost his battle with Pompe Disease. Fellow sufferers and LDNZ were heart broken to hear this news. Laurie was a strong campaigner with us as we tried to get policy shifted so rare disease could get funded treatment in New Zealand. He was such a wonderful man and is sadly missed by all who knew him.

Read the press release here
Samantha's petition on funding of Myozyme, and other rare diseases.

Our November 2016 newsletter reported on Samantha's petition being presented at Parliament. Since then we have received a request for a written submission from the Health select committee. This has been submitted and we expect we will soon hear from them with a date to be heard in person by the committee.

This is an important part of the process of keeping officials accountable for their actions, and pointing out to Parliament the problems that occur with existing legislation and policy. We will draw their attention to the almost impossible dilemmas of trying to get fair treatment for rare diseases through the system as it is set up, and how Pharmac applies it.

The most fundamental problem is the lack of recognition of the built-in disadvantage that applies to novel treatments for rare diseases. When the emphasis is on evidence and cost-effectiveness, there is an almost automatic fail for most new treatments for rare diseases because of the uncertainty of evidence that invariably comes with such small patient numbers, and the higher unit costs of producing them.

LDNZ believes the fixing of these problems will likely come only via a change to the legislation governing medicine access, and/or a significant new policy direction from government about how a special fund for rare diseases is set up and operated, to ensure equity for those with rare diseases.

LDNZ Press Release: Pharma Company gives up on Pharmac

Sanofi Genzyme developed Myozyme, a complex biological treatment for Pompe disease, a lysosomal disease, over ten years ago. Since that time funded treatment of affected patients has spread to 76 countries. Over that decade, NZ’s drug purchasing agency Pharmac has consistently refused to fund it, leaving the 10 patients here abandoned and facing relentless decline in their health and quality of life.

After substantial renewed efforts to negotiate with Pharmac, and with a recent recommendation from Pharmac’s PTAC committee, released early February, that funding should be declined, the company has decided to provide the treatment free to for NZ patients. Read more: http://www.ldnz.org.nz/__data/assets/pdf_file/0011/57782/Press-release-28-February-2017.pdf
Sanofi Genzyme Fund Myozyme for 4 NZ Patients.

Four Pompe patients in New Zealand have been accepted into Sanofi Genzyme’s global humanitarian program. This means that Sanofi Genzyme will provide them with enzyme replacement therapy at no cost.

Patients are considered for Sanofi Genzyme’s humanitarian program when all other treatment options have been exhausted. In this case - the Pharmacology Therapeutics Advisory Committee of New Zealand’s recent decision not to offer reimbursement for these patients, combined with each person’s individual health circumstances, meant that other treatment options weren’t available to them.

Pompe is a progressive and debilitating disease. In lieu of reimbursement, we could see that our humanitarian program was their only hope for treatment. We are now working with their New Zealand based physician to ensure that treatment is delivered as quickly as possible.

We are still focused on delivering long-term, sustainable access to treatment via reimbursement in New Zealand. We have responded to PTAC and hope they will review their recommendation. Myozyme is already reimbursed in 76 countries. New Zealand is now one of only three OECD countries without reimbursement.

Oliver Lodewyk – Had surgery at Starship and is now home
Hollie Forman – was in hospital having Investigative Tests
Hayden Noble – was in hospital with an unexplained infection
The ISMRD Board of Directors are thrilled to bring our 5th International Conference for Glycoprotein Storage Diseases to Rome!

- Registrations and accommodation bookings are now open.

The Scientific Committee’s vision for the meeting is: In November 2017, the 5th International Conference on Glycoproteinoses will be held in Rome, Italy. We believe that moving this conference from the United States to Europe will raise awareness of these rare lysosomal disorders and increase the global visibility of ISMRD as a family-centric organization that funds scientific research and meetings.

Like earlier ISMRD gatherings, the conference will bring together basic scientists and clinicians from around the world to share with patient families and colleagues their latest discoveries in the areas of glycoproteinoses pathophysiology, investigational and preclinical therapy development, and clinical trials for these rare disorders.

The intent of the conference is 4-fold:

1. to stimulate the exchange of ideas,
2. to form new collaborations among investigators and clinicians with different expertise,
3. to spark interest in these complex diseases among postdoctoral research fellows and graduate students, and
4. to strengthen connections among affected families around the world, so they are better informed and supported.

The ultimate goal of the ISMRD is to foster national and international partnerships to efficiently advance therapies for children and adolescents who suffer from these rare and currently incurable diseases.

We look forward to welcoming you all to Rome, Italy.

For more information about this exciting meeting please go to www.ismrd.org
Aiming High for MPS
MPS and Related Diseases Society 15th National Conference
7-9 July 2017, Gold Coast QLD

The Australian MPS Society announces its 15th National Conference. The line-up for the weekend will provide the latest information in clinical management and treatment, research and most importantly opportunities to network with experts in the MPS community, including clinicians, scientists, health care professionals and researchers. As well as professional presentations there will be a variety of talks reflecting personal experiences, workshops and opportunities for participants to reflect and share knowledge in a casual and supportive environment. The venue may have changed but Sea World Resort is sure to offer a fun and interactive conference for everyone. We look forward to seeing you there!

Vanessa Ede-Scott Operations Manager
For more information please see our information and registration pack (PDF)

In the past LDNZ has supported families to attend this meeting. If there is anyone who is interested in attending please let us know. Contact Jenny at jenny.noble@xtra.co.nz

Amicus Therapeutics Presents Important New Scientific Findings and Preclinical Data for Pompe Program at WORLD Symposium™ 2017

Scientific Findings Reveal that Cellular Damage Alters Trafficking for Key Proteins Involved in Muscle Membrane Integrity and Muscle Repair

Preclinical Studies Demonstrate Reversal of Cellular Damage and Significant Improvements in Muscle Strength in GAA Knock-out Mice After Treatment with Amicus Novel Pompe Treatment Paradigm

Feb. 15, 2017 - Amicus Therapeutics, a global biotechnology company at the forefront of rare and orphan diseases, presented new scientific findings and preclinical data on functional outcomes stating that ATB200/AT2221 is a novel treatment paradigm that consists of ATB200, a unique recombinant human acid alpha-glucosidase (rhGAA) enzyme with optimized carbohydrate structures, particularly mannose-6 phosphate (M6P), to enhance uptake in muscles, co-administered with AT2221, a pharmacological chaperone designed to stabilize ERT in circulation. Read More
**Abeona says it will start Sanfilippo B gene therapy trial**

Abeona Therapeutics announced it is just weeks away from enrolling the first patients in a trial of its gene therapy for the lysosomal storage disease Sanfilippo B.

The news comes as the gene therapy candidate—called ABO-101—has just been awarded orphan status in Europe to go alongside the FDA’s orphan designation which was granted last year.

Sanfilippo B syndrome, or mucopolysaccharidosis IIIB (MPS IIIB), is triggered by genetic mutations that shutter N-acetyl-α-D-glucosaminidase (NAGLU) enzyme activity and cause a substance called heparan sulfate to accumulate and cause damage to cells, particularly in the central nervous system. Read more

**Study suggests new therapy for Gaucher disease**

February 22, 2017

Scientists propose that blocking a molecule that drives inflammation and organ damage in Gaucher, and maybe other lysosomal storage diseases, as a possible treatment with fewer risks and lower costs than current therapies. The team conducted the study in mouse models of lysosomal storage disease and in cells from blood samples donated by people with Gaucher disease. Read more

**ArmaGen reports preliminary evidence of cognitive improvement in children with MPS I treated with AGT-181**

*Findings Demonstrate Ability of ArmaGen’s Proprietary Drug Delivery Technology to Transport Biopharmaceuticals Across the Blood-Brain Barrier*

Calabasas, Calif., February 16, 2017 – ArmaGen, Inc., a privately held biotechnology company focused on developing ground-breaking therapies to treat severe neurological disorders, today reported preliminary evidence of cognitive improvement in children treated with AGT-181, the company’s investigational therapy for the treatment of Hurler and Hurler-Scheie syndrome (also known as mucopolysaccharidosis type I, or MPS I). The initial results from an ongoing Phase 2 proof-of-concept (POC) study, presented today at the 13th annual WORLDsymposium in San Diego, California, suggest that AGT-181 may improve
cognitive function in patients with MPS I, demonstrating the ability of ArmaGen’s proprietary drug delivery technology to transport biopharmaceuticals across the blood-brain barrier. Read more

### FDA permits marketing of first newborn screening system for detection of four, rare metabolic disorders

The U.S. Food and Drug Administration today permitted marketing of the Seeker System for the screening of four, rare Lysosomal Storage Disorders (LSDs) in newborns. The Seeker system is designed to detect Mucopolysaccharidosis Type I (MPS I), Pompe, Gaucher and Fabry. It is the first newborn screening test permitted to be marketed by the FDA for these disorders. Read more

### Shire to Highlight Advancements in Rare Genetic Diseases at WORLDSymposium

CAMBRIDGE, Massachusetts, USA – Shire plc (LSE: SHP, NASDAQ: SHPG), the global leader in rare diseases, presented 14 posters, including two late-breaking abstracts, at the 13th annual WORLDSymposium™ 2017 in San Diego, Calif., (February 13-17). Presentations are focused on data in lysosomal storage diseases (LSDs), including Hunter syndrome (also known as Mucopolysaccharidosis type II or MPS II), type 1 Gaucher disease, and Fabry disease, and highlight Shire's commitment to innovative research in genetic diseases. Read More

### ISMRD and their Partners fund two Mucolipidosis Research Projects.

ISMRD is delighted to announce on behalf of all our funding partners in the ML Research initiative, the approval of a proposal to begin research on Gene Therapy in ML II.

**Project 1:** To evaluate AAV Gene Therapy in the feline model of ML II.

*The aims of the project are:* Feline mucolipidosis II (ML II) is a model of human ML II, a devastating and incurable disorder that is often fatal in childhood. ML II is an inherited disorder in which one copy of a faulty gene is inherited...
from each parent. Gene therapy utilizes a virus as a vehicle to deliver a healthy, functional copy of the defective gene.

One specific type of virus, adeno-associated virus (AAV), has been engineered to act as a safe and efficient gene delivery system. Systemic, or intravenous, delivery of AAV has been evaluated in animal models of numerous diseases related to ML II and has recently been approved for a human clinical trial.

**Project 2: Osteoporosis in Mucolipidosis II - A Potential Corrective approach.**

Skeletal alterations are common symptoms in mucolipidosis (ML) II and III patients leading to progressive decline of mobility, stiffness and chronic joint pain, strongly reducing the quality of life. In bone cells of patients the targeting of multiple lysosomal enzymes is disturbed. Consequently, the accumulation of nondegraded storage material in lysosomes impairs the function of bone-forming osteoblasts, osteocytes and chondrocytes of the cartilage. We found that the progressive bone loss in MLII mice is caused by the presence of dysfunctional osteoblasts combined with an increased number of bone-resorbing osteoclasts, which is most likely induced by the strongly elevated expression of the osteoclastogenic cytokine interleukin-6 (II-6), that could be shown also in MLIII cultured osteoblasts.

Read more

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**CTD Holdings Receives FDA Fast Track Designation for Development of Trappsol® Cyclo™ to Treat Niemann-Pick Disease Type C**

17th January 2017  CTD Holdings, Inc. a clinical-stage biotechnology company that develops cyclodextrin-based products for the treatment of disease, today announced that the U.S. Food and Drug Administration (FDA) has granted Fast Track designation to Trappsol® Cyclo™ for the treatment of systemic Niemann-Pick Disease Type C (NPC), a rare and fatal genetic disease. Trappsol® Cyclo™ is the Company’s proprietary formulation of hydroxypropyl beta cyclodextrin in development for the treatment of NPC; it has previously been designated an Orphan Drug by the FDA and the European Medicines Agency. Read More
Lysogene Announces Baseline Data from First International Pivotal Observational Study in MPS IIIA

Wednesday, March 29, 2017

PARIS, France, and CAMBRIDGE, Massachusetts, USA - Lysogene, a leading, biopharmaceutical company pioneering in gene therapy technology applied to central nervous system diseases, announced baseline data from its Sanfilippo A Multi-national Observational Study (SAMOS). Data from this first international pivotal observational study was the topic of a poster presentation made at the 13th Annual WORLDSymposium™ in San Diego, Calif. Sanfilippo A is also known as Mucopolysaccharidosis Type IIIA (MPS IIIA).

SAMOS has been designed to evaluate the clinical progression in untreated MPS IIIA patients. As agreed with the regulatory authorities, this study is to function as a non-concurrent control for the upcoming Lysogene phase II/III pivotal gene therapy trial.

Toward refinement of the study design, including selection of appropriate clinical endpoints and assessment tools, Lysogene formed a clinical expert panel and established the first international neurologist and neuropsychologist expert group.

As a result of this advisory meeting, the most relevant primary endpoint was determined to be cognitive assessment using the Bayley Scales of Infant and Toddler Development, 3rd edition (BSID-III), and the Vineland Adaptive Behaviour Scale, 2nd edition was defined as a useful secondary endpoint measure. The cognitive assessment is particularly important in MPS IIIA in the absence of a validated biomarker that correlates with CNS disease progression and clinical response to future therapy.

Cognitive age assessed on the first 15 patients, aged between 3 and 8 years old, using the BSID-III confirms the progressive intellectual decline, hyperactivity and behaviour changes in these individuals. Lysogene’s collaborative approach has allowed for meta-analysis with a natural history study performed at the University of Minnesota (Shapiro et al., 2015). Read more

Uk Government Announces Plans to Implement the UK Strategy for Rare Diseases with NHS England

Wednesday, March 29, 2017

LONDON, UK - Philip Dunne MP, Minister of State for Health has announced that the National Health Service England will develop an implementation plan for the commitments outlined in the UK Strategy for Rare Diseases that it can influence by the end of the year. For those commitments that are outside of the scope of NHS England, the Department of Health will support its arm’s length bodies to coordinate plans for implementation.
This is a fantastic result for patients and families affected by rare, genetic and undiagnosed conditions in England and across the UK, and will provide the rare disease community with an effective tool to hold the Government to account to improve services and care for patients.

The announcement came during a debate on the implementation of the UK Strategy for Rare Diseases, which was held yesterday (28 March 2017) in Westminster Hall, House of Commons. A number of MPs, representing patients from across the UK, took part in the debate, tabled by Ben Howlett MP who chairs the All Party Parliamentary Group (APPG) on Rare, Genetic and Undiagnosed Conditions. They included Jim Shannon MP, Chi Onwurah MP, Greg Mulholland MP, Andrew Bingham MP, Ms Margaret Ritchie MP, Daniel Zeichner MP, Martyn Day MP, Stuart Blair Donaldson MP, Mrs Sharon Hodgson MP and Mr George Howarth MP.

A STRATEGY WITHOUT A Plan
Ben Howlett MP introduced the debate, explaining the enormity of the situation facing the 3.5 million people in the UK who will be affected by a rare disease at some point in their life. Ben Howlett MP discussed the publication of the UK Strategy for Rare Diseases and its progress to date in the four nations of the UK, explaining that while implementation plans have been developed in Scotland, Wales and Northern Ireland, England has not yet developed a plan.

Parliamentarians went on to discuss a number of issues facing rare disease patients in their constituencies, and highlighted problems with the delivery of services across the four nations of the UK. The proposed changes to the NICE’s Highly Specialised Technologies (HST) evaluation programme was also discussed.

This is wonderful news for the UK. If only our own government here in New Zealand would do the same. How much easier it would be for all those with Rare Diseases to access medicines and Health Care.