Pathways

The Newsletter for Glycoprotein & Related Storage Diseases

A publication of ISMRD

International Rare Disease Day 2013

What went on?

See page 3

HIGHLIGHTS IN THIS EDITION

The International Advocates for Glycoprotein Storage Diseases

3921 Country Club Drive
Lakewood, CA 90712

info@ismrd.org
www.ismrd.org

501 (c) 3 nonprofit organization
FEIN #52-2164838

Our Mission:

ISMRD is the leading advocate for families worldwide affected by a Glycoprotein & Related Storage Disease. Through partnerships built with medicine, science and industry, we seek to detect and cure these diseases, and to enable a network of support and information.

From the President's Desk

By Mark Stark
ISMRD

Welcome to the June edition of the ISRMD newsletter. As you will see as you read through this edition's articles, there are many new efforts by researchers to find therapies and ultimately cures for the rare diseases that affect our children. We are very fortunate to be in an era where the rapidly-evolving understanding of human genetics is creating new pathways for scientists to address devastating congenital diseases. This year, ISMRD is focused on enabling this progress. Our approach to facilitating research falls into three broad categories:

- First, we are raising awareness about our diseases among researchers and public policy decision-makers. We are engaging at the leading scientific conferences, helping sponsor new researchers, and partnering with organizations like the EveryLife Foundation that is discussed on page 7.

- Secondly, we are reaching out to families and helping enable their participation in studies aimed at understanding and developing therapies for rare diseases.

- Thirdly, we are raising funds for research. Given the very high cost of this research, we are working to develop partnerships with industry, government, and other non-profit organizations to direct the funding where it will be most effective.

I very much appreciate your support towards our efforts. I would like to ask that you help our children in any way that you can. ISRMD greatly appreciates your participation, so please let us know how we can do a better job for your family's needs. Please do step forward to participate in research studies; and also please help ISRMD raise funds for research. If you can contribute, or if you can help in other ways, please consider how you may be helping a child somewhere in the world live a better life.

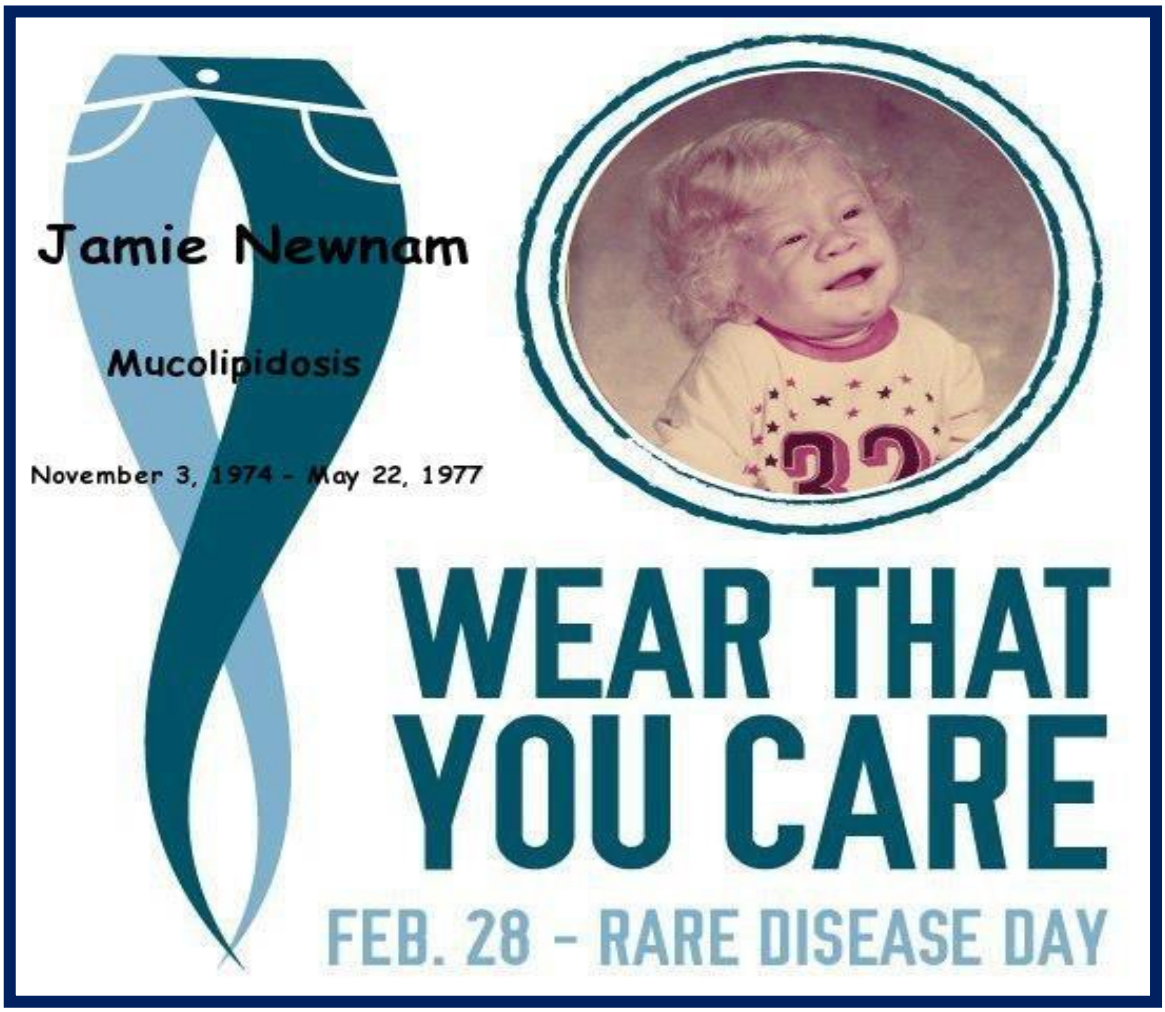
Thank you,

Mark Stark
President
ISMRD

What Went On?

Virginia, USA

ISMRD board member Tish Adkins posted "Wear That You Care" posters on Facebook for other parents and grandparents to use.



Australia

ISMRD board member Carolyn Paisley-Dew held a cinema night on Rare Disease Day. Not only did the event help raise awareness of rare diseases, but it also raised over $1100 for the ISMRD.

Dominic Paisley-Dew, Bella Paisley-Dew, Marie Joly (who has a rare disease called Pemphigus Vulgaris) and Carolyn Paisley-Dew at the Cinema Night in Canberra, Australia on Rare Disease Day

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The newly-formed Rare Voices Australia held an awareness-raising Barbeque Luncheon Event for Members of Parliament at Parliament House. More than 40 Senators and Ministers participated.

ISMRD board members Carolyn Paisley-Dew and John Forman (New Zealand) attended the Rare Voices Australia Parliamentary event

France - Lysogene launches its website for patients

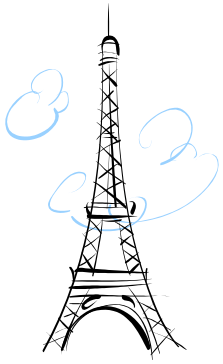
LYSOGENE announced the launch of its website-section entirely dedicated to Patients and Patient Organizations (POs) as a sign of its endeavour to value all those living with an MPS III condition and those who incarnate their voices. With this new action, LYSOGENE reaffirmed its passionate commitment to fight against heavy-debilitating and life-threatening rare diseases with high unmet medical needs and to bring valuable treatments to s and families in high demand.

"LYSOGENE aims at being at the forefront of health improvement for Patients living with Rare Diseases and their families. Our company is dedicated to expanding access to high quality healthcare for those in needs. On this World Rare Disease Day 2013, we stand ready to continue contributing to the fight against MPS IIIA in 2013 and beyond. This new website-section is deemed to become a new arena of exchange with and contribution to the rare diseases community towards our common goal of an enhanced quality of life", LYSOGENE CEO Karen Aiach said.

"We value the knowledge and perspectives from Patients and Patient Organisations (POs) as well as their role in various healthcare decision-making processes. A sound and deep understanding of Patients' and family members' needs and concerns is an absolute prerequisite to plan projects as efficiently as possible and consequently to enhance the ability to fulfil the expectations for an improved health", Vanessa Ferreira PhD, LYSOGENE's Patient Affairs Director continued.

The new website-section is a major step forward targeted to Patients and POs aiming at enhancing visibility about the disease. The website's patient-friendly nature is aimed at a wide audience: Patients, families, POs, medical and scientific staff and all those interested in receiving information on the initiatives promoted by the company. It offers two special features: Educational resources including a LYSOGENE Youtube channel (http://www.youtube.com/user/LYSOGENEchannel) and information about the LYSOGENE Observer-Reported Outcomes Research Program that was implemented in 2012. In addition, POs can explore opportunities for potential collaborative projects with our company. The website also includes information about the team, its core values and its corporate governance guiding principles.

Read more: http://www.lysogene.com/en/patient-area/mission



China's first national organization for rare diseases

Seventeen medical institutions launched China's first national organization against rare diseases on the eve of World Rare Disease Day, in Jinan of east China's Shandong Province.

China Rare Diseases Prevention and Treatment Alliance is committed to the establishment of rare disease treatment centers across the country, research on the cure of such conditions, publicity and medical education of rare diseases, said Han Jinxiang, Communist Party of China secretary of the Shandong Academy of Medical Sciences.

The academy is a founding member of the alliance, and the 17 medical institutions are from 13 provinces.

The alliance will assist in data collection of rare diseases, carry out epidemiological studies and improve treatment, said Han.

World Developments

Emil Kakkis works to lure big-market drugs toward rare diseases

Emil Kakkis, the president and CEO of Ultragenyx Pharmaceutical Inc. and former chief medical officer at BioMarin Pharmaceutical Inc. plans to get more drugs into children with rare diseases. Under the banner of the EveryLife Foundation for Rare Diseases, which Kakkis founded and has largely bankrolled, he is proposing that companies with already-approved, big-market drugs be rewarded with a two-month extension of that drug's patent life if it wins a new Food and Drug Administration-approved label in an orphan disease.

"What if every, single blockbuster cancer drug had three or four pediatric indications in development to gain patent extensions for the whole franchise?" Kakkis wrote in an email.
It isn't just random wondering for Kakkis, who at UCLA co-discovered a treatment for the lysosomal storage disease MPS and followed the drug to San Rafael-based BioMarin (NASDAQ: BMRN). He left BioMarin a dozen years later to start Ultragenyx, which has raised more than $120 million over the past two years and will complete three Phase II studies in rare diseases this year.

Kakkis' plan makes sense for drug makers, he said, because those companies already have expertise in the drugs, can move development along quickly and can be rewarded with an important extra few months of no-competition sales of the drug for its main use.

"It's so easy for them to do, and the value is so significant," Kakkis said in an interview. "It's an efficient way to generate real improvement. There's no new manufacturing process or toxicology process or trying to figure out the indication."

EURORDIS PHARMACOVIGIL WEBPAGE

"Pharmacovigilance" refers to the monitoring of medicines, particularly in the area of safety and side effects. New treatments are becoming increasingly available for rare diseases, and many of these may be tested on smaller patient cohorts than treatments for more common illnesses. Thus, even after a treatment has been tested and approved, it is crucial to continue tracking the benefits and risks patients experience while taking it and to be especially vigilant for side-effects that patients might experience. Here's where you can help.

EURORDIS' new Pharmacovigilance website section (http://www.eurordis.org/pharmacovigilance), available in seven languages, emphasises the importance of reporting any problems a patient experiences with their medicine – whether a prescription drug or an over-the-counter treatment. Sharing experiences with the medicines taken to treat a rare disease is a way of showing solidarity. Letting other members of the community, including the manufacturers of treatments and the agencies responsible for regulating their use, know when an undesired side-effect is experienced helps to improve the medicines available. The new Pharmacovigilance section offers guidance on how to report an adverse effect. Members of the public can report a side effect themselves or ask their health professional to do so. Many patient organisations also offer assistance on reporting side effects. The new section provides a list of available rare disease help lines in Europe, where assistance with reporting an adverse effect can be found. See: http://www.eurordis.org/content/links-help-lines-i-find-it-complex-report-adverse-drug-effect-can-anyone-help

The new Pharmacovigilance section also explains how to check if other patients have reported a similar event. In April 2012, the European Medicines Agency starting making public the suspected adverse drug reaction reports filed by patients, consumers, health professionals or members of the biopharmaceutical industry and stored in the EudraVigilance database. The European Database of Suspected Adverse Drug Reaction Reports (http://www.adrreports.eu/) extracts data from EudraVigilance, allowing the public to view the adverse effects reported for different medicines. One can search for a specific medicine, and sort any existing data on reported side effects by type of reaction reported, age, gender, or geographic location.

The new section has already received praise from the European Medicines Agency. Dr Peter Arlett, Head of Pharmacovigilance and Risk Management, commented that, "Patients organisations have collaborated from the very beginning in the design, planning and implementation of this important piece of legislation. … This EURORDIS initiative will definitely help achieve the goals of the legislation by bringing it closer to patients. It will make it easier for patients to participate in activities which will improve the health of millions of people in Europe."

Orphan drug report forecasts worldwide orphan drug sales to double by 2018

An optimistic future for orphan drugs is predicted by a study conducted by EvaluatePharma. The laws adopted in the US, EU and Japan to encourage research and development of orphan drugs provided significant incentives to pharmaceutical companies developing orphan drugs. These incentives included fee reductions, reduced R&D costs and most notably market exclusivity for a significant period of time (7 years for the US, 10 for EU). Since then orphan drug production has been considered lucrative by many biotechnology companies. The EvaluatePharma report shows a steady increase in orphan drug sales over the years and has forecasted that the worldwide orphan drug sales will double to 15.9% by 2018.

The report has envisaged the return on investment (ROI) for orphan drugs is to be considerably higher than that of non-orphan drugs- 10.3 times and 6 times greater than the investment respectively - which makes orphan drugs a more lucrative option for research and development. This increase in ROI is because of several reasons including the reduced number of patients for an average clinical trial for orphan drugs, the expected increase in worldwide drug sales as well as shorter approval times due to priority review provided to orphan drugs in the US. This increase in ROI does not take into account the tax credits that are provided to orphan drug development in the US. It should be noted that the time taken for Phase III trials does not differ between orphan and non-orphan drugs.

The report also highlights the strong increase in the number of orphan designations provided by US, EU and Japan cumulatively, especially from the year 2003. The report shows that in EU 18.5% of the designations are for ultra rare diseases (prevalence of 10,000 or less), while *"acute myeloid leukaemia is the indication with the most orphan designations"*, blood malignancies come next and the others are for historically well-defined populations like cystic fibrosis and Duchenne muscular dystrophy. This report is rich with information on the potential of orphan drugs in the market and provides an impetus to pharmaceutical companies to go forward with the research and development for orphan drugs and medicinal products.

Read more: http://www.orpha.net/actor/EuropaNews/2013/130606.html

Research Corner

Enzyme replacement therapy for alpha-mannosidosis: 12 months follow-up of a single centre, randomised, multiple dose study

Line Borgwardt (Denmark) gave a presentation at the ISMRD meeting in South Carolina in July last year on the clinical trial on ert for Aplha-Mannosidosis. The following article was published in the March 2013 edition of the Journal of Inherited Metabolic Diseases. The phase 3 trial, which started in December 2012, may have results on the first six months around October 2013.
For more information, go to http://link.springer.com/content/pdf/10.1007%2Fs10545-013-9595-1.pdf

Zymenex in Phase 3 clinical trial in patients with the rare disease Alpha-Mannosidosis

Phase 2 trials demonstrated that the enzyme is clinically effective, safe and well tolerated and a placebo-controlled Phase 3 clinical trial is now underway.

Use of the biotechnologically derived human enzyme product rhLAMAN (Lamazym^{TM}), produced by the Danish biotech company Zymenex and developed for the treatment of patients suffering from alpha-Mannosidosis, has been successfully evaluated in a 12 month dose/response Phase 2a clinical trial and a 6 month follow-up Phase 2b clinical trial in 9 patients. The aim of the trials, which took place at the Department of Clinical Genetics, Copenhagen University Hospital, Denmark, was to confirm the chosen weekly minimum effective dose of 1 mg/kg and to validate the clinical effect of repeated i.v dosing.

Positive changes from baseline after 18 months of dosing have been demonstrated in the primary measured clinical and biochemical endpoints.

Read more: **http://www.zymenex.com/composite-84.htm**

NEW MEMBERS

If you know of any one who has recently joined the Penguin family, please tell us at cdew1@dodo.com.au

We warmly welcome to our Penguin Family

- Mark Van Dam (Australia)
- Rachel Buckamneer (Georgetown, Ohio)
- Patty Wise and grandson Jake (ML ll)
- Liesbeth Blok-Potkamp and her daughter Myrthe Blok (10 years old, ML lll, Netherlands)
- Selma Bonfim De Oliveira Costa
- Felicity McManus

Get Well Soon

If you know of any one who has recently been ill or had surgery or is about to have surgery, please tell us at cdew1@dodo.com.au

Some of our Penguin children and young adults have recently been in hospital, had surgery or are awaiting surgery

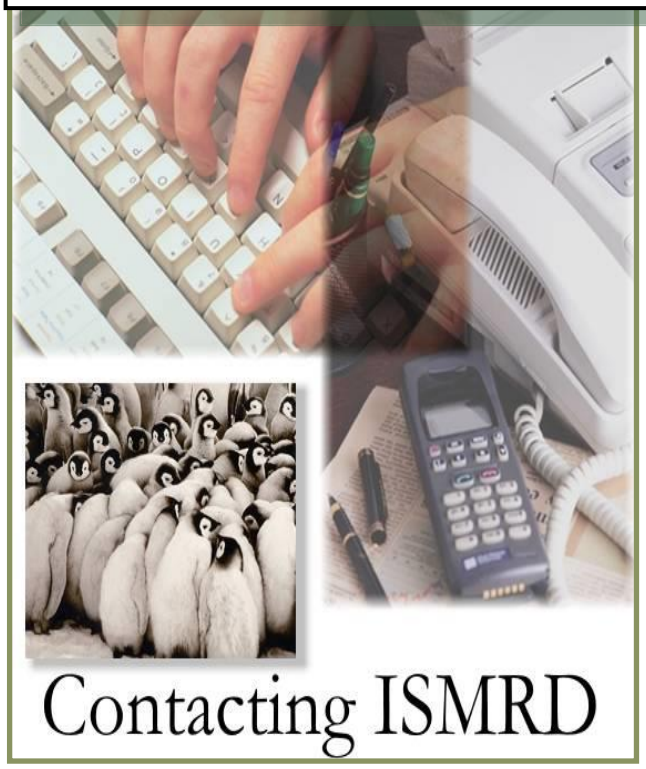
Your Penguin family are thinking of you and praying for a good outcome

- Damian and Jesse-Rose Van Dam (ML lll, Australia) had Carpel Tunnel surgery on 18 April
- Meg Rust (US) is having heel cord lengthening surgery
- Grace Webb (ML ll-lll, Australia) had spinal fusion on 21 May
- Alli Patricia Dennis (ML lll, Australia), pain pump on 18 July
- Lucia Kesner
- Autumn Tobey
- Dale Skipper
- Bianca Adina
- Alli Giunta
- Winnie Johnson
- Dorian Johnson

The Penguin Family extends its deepest condolences to the families and friends of:

- *Selma Nicoly, who passed away on March 20*
- *Kayla Martin, who passed away on May 17*
- *Amber Amick who passed away on May 19*
- *Gabrielle Mae Ross, who passed away on June 7*

ISMRD are the International Advocates for the following disorders: ***Alpha Mannosidosis, Aspartylglucosaminuria, Beta Mannosidosis, Fucosidosis, Galactosialidosis, Mucolipidosis II (I-Cell Disease), Mucolipidosis III (Pseudo-Hurler Polydystrophy), Schindler Diseases and Sialidosis***



ISMRD Board of Directors

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Directors

United States: Jackie James| Andrea Gates | Susan Kester | Melissa Rust | Tish Adkins

Australia: Carolyn Paisley-Dew

Founded in March 1999

Postal Details 3921 Country Club Drive
Lakewood,
CA 90712,
United States

E-mail: info@ismrd.org
Website: www.ismrd.org | FEIN: 52-2164838

ISMRD'S SUNSHINE CARE Committee

ISMRD has a group of parent volunteers called the **"Sunshine Committee"**. Our purpose is to coordinate support for families in need. The type of support varies on the circumstance -- from birthday and weddings, an illness or death in the family, or a family experiencing surgery or a medical crisis. In any case, we provide a little "sunshine" for the family by providing flowers, encouraging messages via email, cards or a phone call -- -whatever we think the family would find most helpful. In order to help others, our group relies on the support of all families because, in essence, we are all part of the ISMRD "Sunshine Committee".

If you are in need of assistance or know someone in our Penguin community who is in need, **please contact Susan Kester**. She will coordinate with the appropriate parties to determine how we can best help.

Feedback Form | Donation

ISMRD would like to hear from you! Send us your feedback, your request for further information or make a donation. Just fill out the appropriate boxes below, cut out this page and then return.

Donations: contributions to ISMRD are tax-deductible in many countries. Consult your nation's local or central tax-collection agency. A copy of our current financial statement is available upon request by contacting ISMRD at our address at. **3921 Country Club Drive, Lakewood, CA 90712, USA**. Documents and information submitted to the State of Maryland are available from the Office of the Secretary of State or the State Licensing Department. Please contact us for further information.

Tell us how you can help!

We would like to hear from you and offer you a part in our vision to link families, support research, develop therapies and find cures.

- Send us names and e-mail addresses of family, friends, and professionals who would be interested in receiving our newsletter or who want to know more about our mission.
- Tell us what you can help us with

☐ Fundraising
☐ Publicity and communication
☐ Do you have any other ideas or other ways that you can help ISMRD?

Name: _____

E-Mail: _____

Please help our Cause

ISMRD is a 501(c) charitable organisation based in the United States serving a global constituency. We provide our services, which include our newsletter, website, outreach activities and support of research, without requesting monthly dues or any other financial restrictions. We gratefully accept donations that will enable us to continue toward our goal of a future free of the tragic consequences of Glycoprotein Storage Diseases.

Yes I would like to Contribute the following (check one)

____ $100
____ $75
____ $50
____ $25

Please Make Your cheque payable to **ISMRD** Thank you

Please give us your name & how to contact

Name: _____

Street: _____

Street 2: _____

City/State/ Province: _____

Country/Postal: _____

E-mail: _____