

## Global Organisation for Lysosomal Diseases

### Chairman's Letter

September 2008

Dear members,

Following a consultation exercise with you all - which will be summarised in this newsletter - GOLD's Management Council undertook a strategic review and identified the critical objectives for the future.

The feedback we received confirmed that the membership think that GOLD is an important organisation and best placed to address issues affecting all the LSD community. Despite this, GOLD has lost funding from two of our previous corporate supporters, which leaves us with a deficit in our projected budget to meet these strategic priorities. As a result of this, we have decided to restructure GOLD which will continue to operate, but will no longer employ an Executive Director. However, we have invited Ann Hale to be co-opted onto the Management Council, thus ensuring continuity of the ongoing program.

It is important to stress that as a result of this restructure, the GOLD website



will be maintained and we will continue to build the membership network, whilst we seek alternative funding for specific projects.

As chair of the Management Council since GOLD's inception, and having worked closely with Annie, I wish to acknowledge the enormous commitment, dedication and professionalism which she has always given to our endeavours and I welcome her to the Management Council.

It is important that GOLD develops alternative funding streams. We have so far not had membership fees, but we may have to introduce these in the future. In the meantime, if anyone would like to assist with GOLD's fundraising efforts, or has any other comments or suggestions, please contact [enquiries@goldinfo.org](mailto:enquiries@goldinfo.org)

Best wishes

Chairman, GOLD

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## Welcome to New Members

The following groups have recently joined GOLD, bringing the membership up to 156 groups representing 38 countries. Welcome to all our new members.

#### Clinical/Scientific Groups

Matrix Biology Unit, CYWHS, Australia

Research Institute at Nationwide Children's Hospital, Department of Pediatrics, College of Medicine, Ohio State University, USA

Institut für Physiologische Chemie, Universität Bonn, Germany

Department of Medical Genetics, Yerevan State Medical University, Albania

Metabolic Division at University Children's Hospital in Zurich, Switzerland

Ambulatório de Genética Clínica do Hospital Universitário Alcides Carneiro, Brazil

MPS/ML Treatment Program, Children's Memorial Hospital Division of Genetics, Chicago, USA

#### Patient Organisations

Espoir Vaincre les Maladies Lysosomales au Maroc, Morocco

Taiwan MPS Society, Taiwan

Australian Fabry's Support Group Inc, Australia

## GOLD STRATEGIC REVIEW

Last year we sent out questionnaires to all our member organisations asking for your feedback about GOLD's activities. Thanks to all those who replied. GOLD's Management Council used this information along with a review of GOLD's progress, mission statement, values and objectives and the current business environment to develop a strategic plan for the organisation.

The membership survey indicated that most members think GOLD is doing a good job of fulfilling its mission so far. It was the belief of the membership and the Management Council that the mission statement is strong and encompasses all the keywords integral to the mission and objectives and should not be changed.

The uniqueness of GOLD was seen as:

- GOLD is truly international
- It encompasses all LSD
- It includes all stakeholders – scientists, clinicians, patient organisations and commercial organisations.
- Is patient focussed
- Is not defined by availability of primary treatment

### Accomplishments to Date

#### Organisation Development

- Incorporated as a company.
- Achieved Charitable registration.
- Infrastructure established per UK Company and Charity Law.
- Management Council (elected by membership) established.
- Management Council elections held annually

#### Membership

- 156 member organisations (September 2008)
- Grown over 900% since January 2004.
- 38 countries represented

### Mission Statement:

**GOLD, the Global Organisation for Lysosomal Diseases will foster international collaboration to improve the lives of individuals with lysosomal storage diseases through education, advocacy and research into all aspects of the diseases.**

#### Communication

- Conducted 3 annual General Membership meetings (4 as of October 2007)
- Provide regular updates to membership and website
- Participate and present at conferences
- Annual General Membership meetings.

#### Website

- Website launched March 31<sup>st</sup> 2005, featuring:
  - Public access and member-only areas (registration required)
  - A searchable database of LSDs.
  - The GOLD membership directory.
  - Discussion forums.
  - Information about GOLD's Management Council.
  - Calendar of events.
  - Online membership information & form.
  - Members' News page
  - Notifications of research grants available from member organisations
  - Video streamed Presentations
  - Access to Scriver's OMMBID
  - Links to other sites of general interest, specific patient groups, member organisations etc.
  - Donations facility

#### Educational Programmes & Events

##### Meetings & Lectures

- A UK Membership meeting, with invited guests and family members. Lecture by Professor John Hopwood and question and answer session.

- The Annual Membership meeting  
Guest lectures:

- ◆ 2005 Dr Charles Scriver
- ◆ 2006 Professor Tim Cox.
- ◆ 2007 Dr William Gahl
- ◆ 2008 Dr William Sly

#### Professional Education:

Video-streamed lectures & conferences available on the GOLD website

- NTSAD Medical Research update and Summary of NIH workshop "Glycosphingolipids in Health and Disease"
- Professor Hopwood's UK Lecture
- 2<sup>nd</sup> Lysosomal Storage Diseases and the Brain conference, Sacramento.
- Prof Tim Cox's Guest lecture at GOLD's AGM 2006
- UK Gaucher Association 15th anniversary conference
- International Society for Mucopolysaccharidosis and Related Disorders Scientific and Family Conference
- 10th International MPS and Related Diseases conference
- Scriver's Online Molecular & Metabolic Basis of Inherited Disease (LSD section)

#### Constituent feedback

A questionnaire was issued to all GOLD's member organisations, and available on the GOLD website, prior to the meeting.

Response rate to the questionnaire was 23%, and represented responses from 16 countries.

Clinical and scientific responses came from specialist centres treating single LSD alone to those who researched/diagnosed/treated all

# GOLD STRATEGIC REVIEW

LSD. The numbers of patients seen/ diagnosed in the responding organisations ranged from 30 to over 1000.

Patient Organisation responses came from organisations that represented between 15 to over 1200 patients. The Patient Organisations responded delivered support, advocacy and/or fundraising either alone or in combination. Patient organisations were, on average mature organisations, with length of existence from 1-over 26 years.

Members were asked to rate the importance of GOLD's current and proposed services and suggest additional services which would be beneficial to the membership.

Lobbying to impact legislation	78
GOLD conference	75
Establishing practice guidelines	75
Database: animal models	69
Database; cell lines	69
Registry	66
Patient Education	63
Professional Education	63
Webcasts	60
Member Profiles	50

portunities and threats, the Management Council reviewed the new services proposed by and for GOLD, considered other potential services and set major priorities which they thought were achievable over a 3-5 year timescale and best served the needs of the LSD community.

Table 1 summarises the priorities set and identifies the fit with the challenges/opportunities for the LSD community and how these align with GOLD's objectives.

**GOAL 1:** Build the infrastructure needed to ensure GOLD's efficient operation

**GOAL 2:** Foster the growth and development of LSD patient registries

**GOAL 3:** Increase professional and public understanding of LSD and their unique challenges

**GOAL 4:** Expand the professional response to the challenge of LSD through mutually beneficial partnerships

Rating for GOLD's current Services	% rating important/very
Overall Website	82
Member Directory	75
Member News	75
Disease database	72
Events Calendar	72
OMMBID	68
Video Presentations	66
Forums	53

## Strategic Priorities

Based on the feedback from the membership consultation, the review of challenges/opportunities facing the LSD community and GOLD's strengths, weaknesses op-

Rating for GOLD's proposed Services	% rating important/very important
Clinical Trials list	87
Establishing diagnostic standards	85
Summaries of publications	82
Newsletter: emailed	78
Newsletter: website	69
Newsletter: Paper	25
Consensus/policy statements	78

Strategic Priority:	Addressing challenges:	Meeting Goals:
Newsletter.	Awareness of LSD. Primary healthcare & Diagnostics. Laboratory diagnosis. The blood brain barrier. When to treat? Access to treatment. Natural History studies & Patient registries. Gene therapy.	1,3,5
Website development and Video Presentations	Awareness of LSD. Primary healthcare & Diagnostics. Laboratory diagnosis. The blood brain barrier. When to treat? Access to treatment. Natural History studies & Patient registries. Gene therapy.	1,3,5
Development of Consensus statements	Awareness of LSD. Primary healthcare & Diagnostics. Laboratory diagnosis. When to treat? Access to treatment.	3,4,5
International LSD conference	Will address topical scientific, clinical and patient organisation leadership issues.	3,4,5
Registries	Foster Natural History studies & Patient registries.	2
Diagnostic standards	Primary healthcare & Diagnostics. Laboratory diagnosis.	3
Continued development of membership Network	Awareness of LSD. Primary healthcare & Diagnostics. Laboratory diagnosis. The blood brain barrier. When to treat? Access to treatment. Natural History studies & Patient registries. Gene therapy.	1,3,4,5

## **GOLD Annual General Meeting, 2008**

GOLD's Annual General Meeting was held on Saturday June 29<sup>th</sup> at the International Symposium on MPS and Related Diseases, Vancouver, Canada. The Annual Report and accounts were issued to all member organisations.

Two special resolutions were passed at the AGM. These change the constitution of the organisation so that Management Council members who have served 2 terms of three years may be allowed to stand again. Without this change, any member who had served 2 terms would not be eligible to stand again, and would have to wait for another year before they could be re-nominated. The second resolution applied the same condition to co-opted members of the Management Council. Passing these resolutions does not mean that members of the Management Council will be automatically re-elected, as an election process is held every year, and all members can nominate people for the council.

### **Management Council Elections**

Four members (Ms Rhonda Buyers, Professor Timothy Cox, Dr Roberto Giugliani and Dr Maurizio Scarpa) retired by rotation from the management council

All were nominated and as 4 places were vacant, all were deemed re-elected to the Management Council. Each will serve a term of 3 years.

### **Management Council's report**

Ann Hale presented the annual report on behalf of the Management Council. Membership of GOLD continues to grow steadily – a list of recent members is given on the front page of this newsletter, and a summary of the membership on the back page.

Last year's AGM was held on October 25<sup>th</sup>, during the American Society of Human Genetics Conference, San Diego, CA, USA. Dr William Gahl's impassioned and moving guest lecture on "Advocating for



Dr William Sly, Dr Ann Hale & Professor John Hopwood at the GOLD AGM 2008  
Photo: Dr Joe Clarke

Rare Diseases".has been added to the Video Presentations section of the website.

The website was regularly updated fulfilling key objectives of GOLD to improve education and knowledge about LSD and provide a portal to GOLD's member organisations to help promote collaboration between all stakeholder groups. The site has received over 800,000 hits.

Two updates to Member Organisations were issued during the year, with a number of articles written, by request, for member groups' own newsletters.

The International Society for Mucopolysaccharidosis and Related Diseases 2nd International Conference on Glycoproteinoses was held in Ann Arbor, Michigan. Presentations from this meeting are available on the GOLD website.

A questionnaire was sent out to all member groups, and results were used by the Management Council for a strategic planning exercise, described elsewhere in this newsletter.

John Hopwood explained that the Management Council reviewed our financial position as a result of 2

companies withdrawing funding and decided to restructure GOLD which will continue to operate, but will no longer employ an Executive Director. The Management Council members have invited Ann Hale to be co-opted onto the Management Council, thus ensuring continuity of the ongoing program. It is important to stress that as a result of this restructure, the GOLD website will be maintained and we will continue to operate and expand the GOLD network but need to restructure and refocus our strategic priorities.

### **Annual Guest Lecture**

Our Guest Speaker was Dr William Sly, MD, James B & Joan C Peter Endowed Chair, Alice A. Doisy Department of Biochemistry and Molecular Biology, St Louis University School of medicine. Bill gave us a comprehensive and entertaining historical review of the development of enzyme replacement therapies for LSD. He kindly allowed us to film his Guest Lecture, which is now available on the GOLD website under the Member area video presentations, under the GOLD tab. Full instructions of how to access the video presentations can be found on p 5, along with information about the presentations from the Scientific sessions at the 10th International MPS Symposium.

## 10th International MPS Symposium



The 10th International Symposium on Mucopolysaccharide and Related Diseases was held in Vancouver, Canada from 26 -29<sup>th</sup> June. Presentations from the scientific conference are now available on the GOLD website. More presentations will become available as previously unpublished work, presented by a number of the speakers, is in press, so check back regularly for updates to the presentations.

Go to the GOLD website  
[www.goldinfo.org](http://www.goldinfo.org)

Select> Education and Information> Video Presentations

Log in with your user name (email address) and password

When the Video Presenter loads, select the tab in the right hand column – MPS Symposium and day.

Select the title of the talk you want to view

Select "Play" in either windows media or real player.

The presentation will load. Depending on the speed of your connection, this may take a couple of minutes.

*Please note, if you have problems loading the presentations, this may be due to your firewall blocking access. This is a particular problem with some versions of Norton Internet Security, and you may need to disable your firewall, or designate the website as a trusted site.*

GOLD thanks all the speakers who have consented to have their presentations recorded. Some of the speakers were presenting unpub-

lished material; in those cases, we will hold back the video from the website until their work is in press.

We have had very positive feedback for the presentations on the GOLD website, and know that many people who are unable to attend conferences derive great benefit from being able to catch up with the presentations after the event.

\*If you are not yet registered as a member user of the website: Go to [www.goldinfo.org/forums/register.aspx](http://www.goldinfo.org/forums/register.aspx)  
Enter your email address as user name and choose a password. Select the organisation of which you are a member. You can then access the Video presentations  
You only need to register once

### **Presentations immediately available on the website:**

**Dr. Lorne Clarke:** Welcoming Address:

**Dr. John Hopwood:** Opening Address: Overview of key scientific advancements in the LSDs and hurdles ahead

**Dr. Gregory Pastores:** The Importance of evidence based medicine. Capturing clinical outcome data in the LSDs:

**Dr. Joe Clarke:** Alternative treatment strategies for the LSDS

**Kirsten Harkins:** The importance of MPS Societies

**Dr. Peter Roughley:** Proteoglycans and the joint

**Dr. Jeff Esko:** Glycosaminoglycans and Proteoglycans in disease

**Dr. Lorne Clarke:** Heparin Cofactor II- Thrombin Complex: A Possible Biomarker for the Mucopolysaccharidoses

**Dr. Hugh Perry:** The role of macrophage activation in disease

**Dr. David Begley:** Understanding the Blood-Brain Barrier: A Central Role in Treating Neuronopathic Lysosomal Storage Diseases

**Dr. Haiyan Fu:** Profound CNS Immunity and Functional Benefits of Immunosuppression with Prednisolone for Treating Neurological Disease in MPS IIIB Mice

**Dr. Sharon Byers:** The degradation of aggrecan in MPS VI cartilage.

**Dr. Mark Haskins:** Key insights from animal models of the MPSs

**Dr Josh Woloszynek:** Lysosomal storage results in altered energy balance

**Dr. Alexey Pshezhetsky:** Lysosomal Sialidase Neu4 as a modifier gene for the mouse Tay-Sachs disease

**Dr John Hopwood:** Injection, survival and quantification of sulphamidase-over-expressing glial precursor cells into the MPS-IIIA mouse brain

**Dr. William Sly:** Enzyme replacement therapy for the MPSs, old concepts new tricks

**Dr. Anna Tylki:** Management of MPS III: Natural history and clinical outcomes

**Jeffrey Grubb:** Enzyme chemically modified by periodate oxidation shows enhanced delivery across the Blood Brain Barrier and neuronal correction in murine MPS VII

**Dr Grzegorz Wegrzyn:** The use of genistein-rich isoflavone extract in substrate reduction therapy for Sanfilippo disease: one-year open-label pilot study in 10 patients and follow-up

**Dr. John Hopwood:** Current approaches in Newborn Screening

**Dr. Michael Gelb:** Screening for the MPSs

**Dr John Hopwood:** Newborn screening for lysosomal storage disorders using protein profiling of dried blood-spots

*More presentations will be added as speakers' work is in press. Check back for updates.*

## Tay-Sachs Gene Therapy Consortium

*Sue Kahn, Executive Director of the National Tay Sachs and Allied Diseases Association (NTSAD) tells us about an International Consortium initiating gene therapy for GM2 gangliosidosis.*

The Tay-Sachs Gene Therapy (TSGT) Consortium was formed in the summer of 2007 with the goal of initiating a state of the art clinical trial for Tay-Sachs disease (and possibly Sandhoff disease) in the next 3 - 4 years. The TSGT consortium is composed of scientists from four institutions (Auburn University, Boston College, Cambridge University-UK, and Massachusetts General Hospital) that have been working on experimental gene therapy approaches to treat LSDs.

In recent years, laboratories in the TSGT Consortium, and others, have obtained exceptional therapeutic results with AAV vectors in many animal models of LSDs, including GM2-gangliosidosis. The TSGT Consortium is organized to foster efficient optimization of vectors and delivery strategies condu-

cive to the rapid development of the most effective gene therapy approach to go into the clinical trial. To accomplish this goal they will pool their resources and extensive experience in experimental gene therapy to devise the most effective AAV-based gene therapy approach to treat Tay-Sachs disease and bring it into simultaneous clinical trials in the US and UK.

The most recent research report shows progress on a number of fronts:

- The Tay-Sachs and Sandhoff Natural History Study questionnaires will be mailed in August to all NTSAD GM-2 members and inquiries with addresses in English speaking countries. The results will be the benchmark for the gene therapy and other future clinical trials to determine effectiveness of therapies.
- Distribution of Hex A enzyme throughout the entire mouse brain after injection of a mixture of two AAV vectors into a single

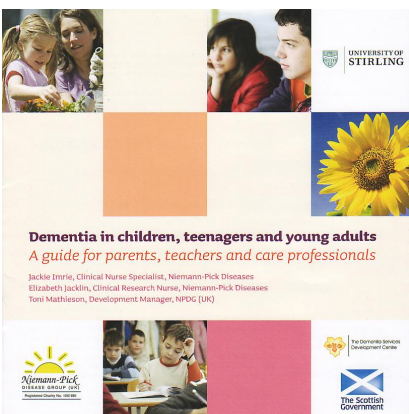
structure on both sides of the brain has been demonstrated.

- Long-term studies of AAV-treated GM2 mice continue, with treated mice at 20-21 months of age, compared to untreated mice that die at 4 months.
- Gene therapy in two GM2 cats with the existing AAV vector system by two direct injections into the brain lived almost twice as long untreated cats.

### Save The Date:

*April 2-5, 2009: NTSAD's 31st Annual Family Conference in Quincy, MA – Just minutes from historic Boston and home of World Series Champions the Boston Red Sox!*

## Niemann Pick Disease Group, UK – Children Teenage & Young Adult Dementia Book



The Niemann Pick Disease Group, UK (NPDG-UK) has published a booklet, "Dementia in Children, Teenagers and Young Adults" in association with the University of Sterling and The Scottish Govern-

ment.

The book, written by Jackie Imrie, Elizabeth Jacklin and Toni Mathieson is a guide for parents, teachers and care professionals. Dementia is usually associated with older people, but children, teens and young adults can experience dementia as a result of certain LSD such as Niemann Pick type C.

This excellent and clearly written reference book is available free of charge from the NPDG-UK. Contact Jackie Imrie, Niemann-Pick Clinical Nurse Specialist ([Jackie.Imrie@CMMC.nhs.uk](mailto:Jackie.Imrie@CMMC.nhs.uk)) or Toni Mathieson, Executive Director, NPDG-UK ([niemannpick@zetnet.co.uk](mailto:niemannpick@zetnet.co.uk))

The group also has a new website, developed by the parents of Hollie, who has NP-C. The website, "Hope for Hollie" raises awareness of NP-C and helps to fundraise for research into Niemann Pick Disease.

HOPE  
FOR  
HOLLIE



[www.hopeforhollie.co.uk](http://www.hopeforhollie.co.uk)

## Batten Disease News

Jan Sablitzky, BDFA Development Officer, updates GOLD's members on the activities of this group:

### Small patient organisations can act as a catalyst for research

On 28<sup>th</sup> March 2008 the UK Batten Disease Family Association hosted a multidisciplinary workshop at University College London entitled *Bringing Therapy to Batten Disease*. This was a great success with over 40 scientists and clinicians and the patient organisation coming together for the first time in the UK to discuss how to facilitate bringing therapy to Batten's. From it, the Organizing Committee have identified the top 10 priorities to deliver and other initiatives in order for the BDFA to be as successful and efficient as possible in creating a pathway to move towards therapies for all types of Batten Disease. As, Prof Robin Ali from Moorfields said to the BDFA, it was like creating a 'virtual institute' – proving that is a very effective way for the BDFA as small charity to use its resources through acting as a catalyst to widen the scientific community's awareness and participation in Batten Disease-related research and the implications for progress in other associated diseases. The BDFA report that new collabora-

tions and research pathways are already emerging from this networking opportunity and another Workshop is planned for 2010.

For further information see the BDFA website at [www.bdfa-uk.org.uk](http://www.bdfa-uk.org.uk) or contact Jan Sablitzky, BDFA Development Officer (0115 965 4815

[bdfa.info@btinternet.com](mailto:bdfa.info@btinternet.com) who would be interested in discussing your organisation's experiences in effective 'research towards therapies' strategy.

On 17th June 2008, a group of more than 40 family members, scientists, clinicians and professionals met at King's College London for a discussion meeting entitled: *"Where are we now and where are we going?"* co-hosted by the UK Batten Disease Family Association (BDFA) - and the Pediatric Storage Disorders Lab, Institute of Psychiatry. The day included scientific updates from Dr Jon Cooper from King's, a tour of the PSDL's labs and discussions on experimental therapies being developed for Batten Disease. Julie Pickering, Chair of the BDFA also outlined the role of the BDFA in the 'Batten Disease UK jigsaw' in how we can significantly improve support and facilitating research and reported on the BDFA's recent

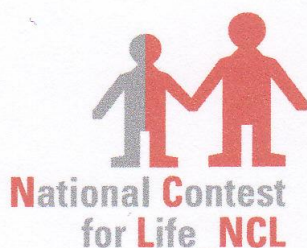
successful scientist-clinician meeting which took place at UCL in March 2008. Dr Sasha Scambler, a medical sociologist from King's College London and a founding member of the BDFA, presented the BDFA-commissioned report findings on 'The Support Needs of Families of Children with Batten Disease'.

The day was designed to update on what is being done towards finding therapies and what we can do to provide a better quality of life for our children. As the feedback from the day has been excellent – everyone found it very interesting and supportive – all agreed that another one should be organised in 2009 so the next one will be held on Tuesday 16th June 2009, again at Dr Cooper's lab in London. If you are interested, please contact Jan Sablitzky, BDFA Development Officer 0115 965 4815 or email: [bdfa.info@btinternet.com](mailto:bdfa.info@btinternet.com) for further information.



**Save The Date:**  
**4th-5th October 2008,**  
**Hampshire, UK**  
**Batten Disease Family**  
**Association Celebrates 10**  
**year anniversary**

## NCL Foundation Postgraduate Fellowship Award



The NCL Foundation aims to find a cure against Neuronal Ceroid Lipofuscinosis (NCL; Batten disease) an LSDs which is the most common neurodegenerative disease of childhood.

The NCL Foundation invites medical and basic science researchers worldwide to submit innovative clinical oriented or translational basic science projects, which can contribute to finding a cure for juvenile NCL. Scientists from related areas of science including Alzheimer's disease, aging, and other lysosomal storage disorders, are particularly encouraged to apply with the aim to extend the NCL research community in move more efficiently towards a cure for NCL.

Grant monies (50,000 euros) are to be used for a postgraduate fellowship in order to undertake the research project. The Foundation's aim is to promote the next generation of young NCL re-search scientists. The official award ceremony will take place as part of a charity event at the end of 2008.

The deadline for applications is October 31, 2008. An application form can be downloaded from the foundation homepage: [www.ncl-foundation.com](http://www.ncl-foundation.com) Please send your application solely via email to: [Research@ncl-foundation.com](mailto:Research@ncl-foundation.com) For further information, please contact: Dr. Frank Stehr, Head of Research and Marketing, NCL-Foundation, Holstenwall 10, 20355 Hamburg, Germany Tel: +49-40-350044-91

## Amicus Therapeutics: Chaperone therapy for LSDs

Amicus Therapeutics is a clinical-stage biopharmaceutical company developing a new class of orally administered drugs called pharmacological chaperones. Amicus' three most advanced product candidates are experimental treatments for Fabry disease, Gaucher disease, and Pompe disease. A brief overview of the current status of these three programs is as follows:

### **AT1001 for Fabry Disease:**

Results from the initial treatment phase of four Phase 2 studies of AT1001, a pharmacological chaperone under investigation for Fabry disease, have been presented at scientific meetings. A fifth extension study is ongoing. Amicus, along with its partner Shire Human Genetic Therapies, Inc., is engaged in ongoing discussions with regulatory agencies regarding plans for a global Phase 3 clinical development program for AT1001. This process is expected to be complete in the second half of 2008, and, subject to the outcome of the dis-

cussions, Amicus plans to initiate a Phase 3 program in the first half of 2009.

### **AT2101 for Gaucher Disease:**

Earlier this year, preliminary results from a Phase 2 clinical study of AT2101, a pharmacological chaperone under investigation for Gaucher disease, were presented at scientific meetings. During this study, subjects were temporarily discontinued from enzyme replacement therapy (ERT) to receive AT2101 for the 4-week treatment phase of the study. A second Phase 2 study currently is enrolling worldwide. This is a 6-month study in individuals who are naïve to ERT or substrate reduction therapy (SRT), or who have not received either ERT or SRT for at least 12 months. Additional information can be found at <http://clinicaltrials.gov/ct2/show/NCT00446550>.

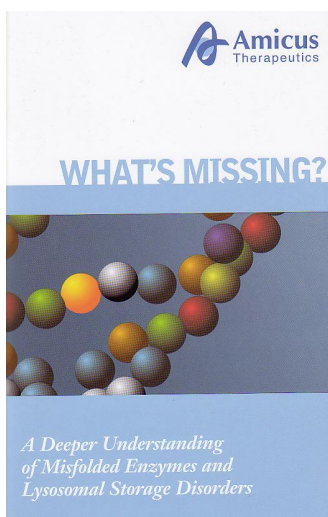
### **AT2220 for Pompe Disease:**

Phase 1 studies of AT2220, a pharmacological chaperone un-

der investigation for Pompe disease, have been completed. An ex vivo response study also has been completed and results of this study, along with Phase 1 data, have been presented at scientific meetings. The purpose of the ex vivo study was to assess the effects of AT2220 on blood and skin samples derived from individuals with Pompe disease who have a variety of different mutations. A Phase 2 study of AT2220 in individuals who are naïve to ERT, or who have not received ERT for at least 3 months, has been initiated in locations worldwide. Additional information can be found at <http://clinicaltrials.gov/ct2/show/NCT00688597>.

If you would like more information about Amicus or the three clinical programs described above, please see [www.amicustherapeutics.com](http://www.amicustherapeutics.com) or contact [patientadvocacy@amicustherapeutics.com](mailto:patientadvocacy@amicustherapeutics.com).

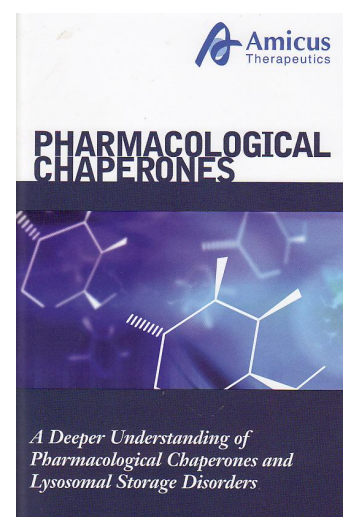
## Informational Booklets - Chaperone therapy for LSDs



Amicus Therapeutics has produced two booklets, *What's Missing?*, with information about Lysosomal Diseases caused by protein misfolding and *Pharmacological Chaperones*, explaining the principles of chaperone therapy with particular reference to lysosomal diseases.

For copies of these books, contact:

[patientadvocacy@amicustherapeutics.com](mailto:patientadvocacy@amicustherapeutics.com)



## USA LEGISLATIVE UPDATES

*Rhonda Buyers, Executive Director of the National Gaucher Foundation provides an update on current USA legislation affecting patients and families with rare diseases.*

Current legislation in the House and Senate has enormous implications for the rare disease community. I would like to thank all those who responded to the NGF "Call to Action", which gives an opportunity to make a difference in not only the Gaucher community, but also the rare disease community as a whole. Please continue to call, write, fax or email your legislators. WE CAN MAKE A DIFFERENCE!

Following are updates of current legislation for which we must continue to advocate:

**HR 5748 - The Ryan Dant Health-care Opportunity Act** - continues to move along well gaining bi-partisan support as it moves through the House of Representatives. Currently, the Bill, which is sponsored by Texas Congressman Kenny Marchant, has 14 co-sponsors; seven each from both sides of the aisle.

HR 5748 is designed to allow a Medicaid state option that would permit individuals who will be forced on to Medicaid because of high drug costs, to be released from qualifying earnings restrictions. The Bill is designed to assist those with extremely high lifelong prescription drug costs and if passed would allow those with ultra rare diseases such as the Lysosomal Disease community to qualify for Medicaid and enter the workforce so that they may become a contributor to their communities.

Ryan Dant and his father Mark returned to Washington on September 15th and 16th to meet with several Representatives from across the US to discuss the importance of this legislation to all those with extremely high prescription drug costs. For a list of the Representatives who have demonstrated their support for the ultra orphan disease community through their co-sponsorship of HR 5748, visit the NGF website at [www.gaucherdisease.org](http://www.gaucherdisease.org).

### **Lifetime Insurance Caps Bill Introduced In U.S. House of Representatives**

Glenn Mones, Vice President for Public Policy, National Hemophilia Foundation

On Thursday, July 17, 2008, Congresswoman Anna Eshoo (CA) along with Representatives Betty Sutton (OH), Jason Altmire (PA) and James Langevin

(RI) introduced **H.R. 6528, the Health Insurance Coverage Protection Act**, which raises the minimum lifetime cap for private health insurance to \$10 million. This bill is identical to the Senate bill (S. 2706) that was introduced by Senator Byron Dorgan in March during NHF's Washington Days.

H.R. 6528:

- \* Sets the minimum level of a lifetime cap placed on a group health plan at \$5 million for the first two years and \$10 million in years three and four.
- \* Provides for an annual inflationary adjustment to a group insurance plan's lifetime cap based on the consumer price index in subsequent years.
- \* Exempts health plans offered to businesses with fewer than 20 employees, but would require that health plans meeting the parameters of the bill be offered to a small business at the employer's request
- \* Calls for an Institute of Medicine Study to determine the number of individuals who reach their lifetime caps.

Introduction of the House bill is a result of the cumulative efforts of the bleeding disorders community. Special recognition goes out to the members of the California chapters who contacted Congresswoman Eshoo and to the Northern Ohio Hemophilia Foundation, the Western Pennsylvania Chapter of NHF, and New England Hemophilia Association who visited with Representatives Sutton, Altmire and Langevin during NHF's Washington Days.

If you haven't already done so, please contact your U.S. senators and representative to urge them to co-sponsor these important bills, there is still time.

The NGF, together with the National Hemophilia Foundation and other organizations, will continue to work on this legislation. As you may recall, in 1996, Senator Jim Jeffords offered an amendment on the Senate floor to the "Kassebaum health reform bill". This amendment was defeated; however, in 1997 Senator Jeffords introduced legislation setting a minimum lifetime cap at \$10 million. Congresswoman Anna Eshoo, in 1996, also introduced legislation setting lifetime caps at \$10 million. The Jeffords and Eshoo bills provided an annual update indexed to the rate of inflation.

### **President Bush Signs Genetic Information Non-discrimination Act into Law**

Glenn Mones, Vice President for Public Policy, National Hemophilia Foundation

On Wednesday, May 21, 2008, President Bush signed the Genetic Information Non-discrimination Act (GINA), historic legislation protecting Americans from discrimination based on the results of genetic testing. The bill was recently passed by Congress with strong bipartisan support after a 13-year struggle and dedicated efforts by a coalition of healthcare and other advocacy organizations, including the National Hemophilia Foundation (NHF).

The new law prevents employers and insurance companies from either requiring genetic test results or from using genetic information as the basis for decisions concerning employment or insurance coverage. The health insurance protections afforded by GINA are expected to roll out in one year. The employment protections will be in place within 18 months.

The legislation protects against genetic discrimination by health insurers or employers by prohibiting:

- \* Group health insurance plans and issuers offering coverage on the group or individual market from basing eligibility determinations or adjusting premiums or contributions on the basis of an individual's genetic information. Insurance companies cannot request, require or purchase the results of genetic tests, or disclose personal genetic information.
- \* Issuers of Medigap policies from adjusting pricing or conditioning eligibility on the basis of genetic information. They cannot request, require or purchase the results of genetic tests, or disclose personal genetic information.
- \* Employers from firing, refusing to hire, or otherwise discriminating with respect to compensation, terms, conditions or privileges of employment. Employers may not request, require or purchase genetic information or disclose personal genetic information. Similar provisions apply to employment agencies and labor organizations.

For additional information or answers to questions about GINA and how it impacts individuals, please go to <http://www.geneticalliance.org/ginaresource> and you will see a very well written, informational guide to the Genetic Information Non-discrimination Act called "What does GINA mean to me?"

*This is a revised version of an article which originally appeared in the National Gaucher Foundation Newsletter.*

## BioMarin Announces Morquio Syndrome Clinical Studies

### *BioMarin Announces Two Clinical Studies for Morquio Patients*

BioMarin Pharmaceutical is investigating a potential treatment that may benefit patients diagnosed with the lysosomal storage disease, mucopolysaccharidosis IVA (MPS IVA; Morquio syndrome.) Morquio syndrome, estimated to occur in 1 in 200,000 to 300,000 live births is caused by the lack of the enzyme galactose 6-sulfatase, essential in breaking down the glycosaminoglycans keratan sulphate.

BioMarin plans to initiate two clinical studies: MorCAP (a clinical assessment program) and a Phase 1/2 clinical trial. Individuals who have participated in the International Morquio Organization (IMO) survey are welcome and encouraged to participate in MorCAP and/or BioMarin's Phase 1 clinical trial.

MorCAP, the Morquio Clinical Assessment Program, has been designed to provide a fuller understanding of Morquio syndrome by

measuring endurance and respiratory function in affected patients among other important aspects of Morquio syndrome. These insights will help BioMarin design future clinical trials as well as understand the medical needs of Morquio patients. Participation in MorCAP will require one or more visits to a clinic or hospital. This study is scheduled to begin in September 2008. Dr. Emil Kakkis, Chief Medical Officer, and Senior Vice President of BioMarin hopes to learn more about the extent and depth of disease in this program and to include as many patients as possible.

In early 2009, BioMarin plans to begin enrolling a small number of patients in a Phase 1/2 clinical trial investigating a potential treatment for Morquio syndrome. The objective of this clinical study is to establish dose response to an enzyme replacement therapy for Morquio syndrome based on pharmacokinetic and pharmacodynamic parameters. Pending results of the

Phase 1/2 study, BioMarin expects to conduct a Phase 3 double-blind, placebo-controlled study enrolling up to 100 patients. This study will likely be conducted in many centres.

Preliminary experiments were designed to demonstrate that the native enzyme being investigated by BioMarin can reach the bones and other tissues that are affected in Morquio patients, says Dr. Kakkis. "We have verified that it is taken up well and that it can penetrate growth cartilage in animal models. It appears to naturally bind bone in *in vitro* studies. Data published to date suggest the native enzyme can clear storage in many cells types including bone cells."

To learn more about participating in MorCAP or the Phase 1/2 study, visit [www.morquioBMRN.com](http://www.morquioBMRN.com). Individuals may also register at the website to receive updates on trial developments.

## Update on Genistein as substrate reduction therapy for LSD.

*Professor Grzegorz Wegrzyn summarises two recent publications from his group:*

### **The use of genistein-rich isoflavone extract in substrate reduction therapy for Sanfilippo disease: open-label, pilot study in 10 pediatric patients.**

*Ewa Piotrowska, Joanna Jakobkiewicz-Banecka, Anna Tyłki-Szymanska, Anna Liberek, Agnieszka Maryniak, Marcelina Malinowska, Barbara Czartoryska, Ewa Puk, Anna Kloska, Tomasz Liberek, Sylwia Baranska, Alicja Wegrzyn and Grzegorz Wegrzyn*

**SUMMARY:** Background: Mucopolysaccharidoses (MPS) are severe disorders caused by deficiencies in enzymes involved in degradation of glycosaminoglycans (GAGs). Although enzyme replacement therapy has become available for some MPS types, treatment of neurodegenerative forms of MPS is an unsolved problem. Recently it has

been demonstrated that genistein (4', 5, 7-trihydroxyisoflavone) inhibits synthesis and reduces levels of GAGs in cultures of fibroblasts of MPS patients, and a potential substrate reduction therapy has been proposed.

**Objective:** This work concerned a pilot clinical study with patients suffering from Sanfilippo disease (MPS type III), in which mental and neurological deterioration is especially severe.

**Methods:** The design of this study was to preliminary estimate of effects of substrate deprivation therapy in treatment of MPS III patients. 10 patients (5 suffering from MPS IIIA and 5 suffering from MPS IIIB) were enrolled into the study. The inclusion criteria were biochemically-confirmed diagnosis and age between 3 and 15 years.

Genistein-rich soy isoflavone ex-

tract was administered orally for 12 months at the dose corresponding to 5 mg genistein per 1 kg of body weight daily.

Urinary GAG levels, hair morphology and cognitive abilities were measured at baseline and after 12 months of the treatment.

**Results:** 10 Caucasian patients (4 males and 6 females; average age: 8 years, range: 3-14 years; average weight: 28 kg, range: 17-43 kg) were treated. After one year of the treatment, statistically significant improvement in all tested parameters was demonstrated (urinary GAG levels,  $p = 0.028$ ; hair morphology,  $p = 0.012$ ), including marked improvement of cognitive functions in eight patients and stabilization in two patients ( $p = 0.012$ ). No significant side effects were observed.

..... continued on p 11

## UK National Longitudinal study for LSD

*Sheena Oxe*, Study co-ordinator, describes the national study being undertaken at the designated LSD treatment centres in England

The National Collaborative Study of Lysosomal storage Disorders is a National Coordinating Centre for Health Technology Assessment funded study and is a collaboration between the Peninsula College of Medicine and Dentistry, clinicians from the seven English treating hospitals and LSD patient support groups. This national study aims to recruit everyone diagnosed with a lysosomal storage disorder in England to understand the natural history of these disorders with and without treatment and to estimate the effectiveness and cost effectiveness of enzyme replacement therapy. Other aims are to estimate the life-time health care cost and other economic impacts on people with LSD and their families; to provide the basis for future research to develop treatment-responsive measures in adults and children and to compare the effectiveness of *Replagal* and *Fabryzyme* in children and adults with Fabry disease. This study is led by Professor Stuart Logan, Paediatric Epidemiologist and Director of the In-

stitute for Health Service Research. The study is overseen by a Trial Steering Committee comprising an independent statistician, three LSD specialist clinicians and Dr Ann Hale from GOLD. The study has strong links with LSD patient support groups, representatives of which sit on the Project Management Team.

By following people with these conditions over a period of time we hope to get a better understanding of how effective treatments are, when the best time to start giving these treatments is, what the appropriate dosing schedules are, and which symptoms led to the diagnosis of the disorder. Another aspect of the study will be to estimate the value for money of these treatments. In order to do this we will look at how frequently people use the NHS, the cost of their treatment, related costs to their family, and compare these for people who are receiving treatment with those people who are not, or for whom treatment is currently unavailable.

The Project Management Team has agreed that initially we will collect

data on Pompe, MPS1 and Gauchers. It was felt that these conditions would allow the work to build on existing data collection for MPS-I and Gauchers as these conditions are already treated as well as begin to look at a system to capture information for a condition where a treatment is just becoming available. In addition these three conditions would allow the systems created to be tested in both adults (Gauchers and Pompe) and children (MPS-I and Pompe). The next conditions are Fabry, MPS II, IV and VI and Niemann Pick C. Although we are only recruiting people who attend one of the seven English treating hospitals in the first instance, we hope that if we can get the right structure and processes in place, then other countries will consider using a similar system. The study is for three years in the first instance and we are hoping to recruit our first Pompe patients in August/September 2008, followed by MPS1 patients in October and Gaucher patients in November.

If you would like to know any more about this study please contact the Study co-ordinator Sheena Oxe: 01392 262924 [sheena.oxer@pms.ac.uk](mailto:sheena.oxer@pms.ac.uk).

## Update on Genistein as substrate reduction therapy for LSD.

(Continued from P 10)

Conclusions: To our knowledge, this is the first report demonstrating improvement of MPS III patients after pharmacological treatment. Thus, substrate deprivation therapy may be considered a promising therapeutic option for patients suffering from Sanfilippo disease.

**Substrate deprivation therapy: a new hope for patients suffering from neuronopathic forms of inherited lysosomal storage diseases.** *Joanna Jakobkiewicz-Banecka, Alicja Wegrzyn and Grzegorz Wegrzyn*

SUMMARY

Lysosomal storage diseases is a group of disorders caused by defects in enzymes responsible for degradation of particular compounds in lysosomes. In most cases, these diseases are fatal, and until recently no treatment was available. Introduction of enzyme replacement therapy was a breakthrough in treatment of some of these diseases. However, while this therapy is effective in reduction of many somatic symptoms, its efficacy in treatment of central nervous system is negligible, if any, mainly because of problems with crossing the blood-brain-barrier by intravenously administered enzyme molecules. On the other hand, there are many lysosomal storage diseases in which central nervous

system is affected. Results of very recent studies indicated that in at least some cases, another type of therapy, called substrate deprivation therapy (or substrate reduction therapy) may be effective in treatment of neuronopathic forms of lysosomal storage diseases. This therapy, based on inhibition of synthesis of compounds which cannot be degraded in cells of patients, has been shown to be effective in several animal models of various diseases, and recent reports demonstrated its efficacy in treatment of patients suffering from Niemann-Pick C disease and Sanfilippo disease.

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**MISSION STATEMENT**

*GOLD, the Global Organisation for Lysosomal Diseases will foster international collaboration to improve the lives of individuals with lysosomal storage diseases through education, advocacy and research into all aspects of the diseases.*

*If you would like to receive a copy of GOLD Update by email, please contact [enquiries@goldinfo.org](mailto:enquiries@goldinfo.org).*

**GOLD's Membership**

Membership of GOLD has expanded significantly since the organisation's inception. The table below shows the breakdown of the member organisations. 38 countries are now represented in the membership network, and this continues to grow. A full membership directory is available on the GOLD website.

ORGANISATION TYPE	TOTAL	NORTH AMERICA		EUROPE		REST OF WORLD
		USA	CANADA	UK	Mainland EUROPE	
Academic, Research or Treatment Centres	97	36	4	14	19	24
Commercial Organisation	5	3		1	1	
Patient Organisation	54	15	2	6	19	12
<b>TOTAL</b>	<b>156</b>	<b>60</b>		<b>60</b>		<b>36</b>

**Upcoming Events**

**2008**

**October 4 - 5th, Hampshire, England**  
 10th Anniversary Conference/AGM  
 Batten Disease Family Association

**November 12 - 15th Philadelphia, PA, USA**  
 American Society of Human Genetics

**November 20 - 23rd Christchurch, New Zealand**  
 Australasian MPS/LSD Conference  
 Australian MPS Society & Lysosomal Diseases New Zealand

**2009**

**April 2 - 5th, Quincy, MA, USA**  
 31st Annual Family Conference.  
 National Tay Sachs and Allied Diseases Association

**June 19 - 21st, Telford, UK**  
 Annual Family/Scientific Conference  
 Niemann-Pick Disease Group

**October 20 -24th Honolulu, Hawaii,**  
 American Society of Human Genetics

**2010**

**June 23-27th 2010, Adelaide, Australia**  
 11th International Symposium on MPS and Related Diseases.  
 Australian MPS Society and Lysosomal Diseases, New Zealand

**November 2 - 6th, Washington, DC, USA**  
 American Society of Human Genetics

*For further details, please see the Calendar of Events page on the GOLD website. If you are organising a meeting, which is not yet listed, and would like to have it listed on GOLD's website or in the next Update, please contact [enquiries@goldinfo.org](mailto:enquiries@goldinfo.org)*

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For information about joining GOLD, email [enquiries@goldinfo.org](mailto:enquiries@goldinfo.org), join online at [www.goldinfo.org](http://www.goldinfo.org) or send in this form. Membership is for organisations with an interest in any aspect of LSD research, clinical practice or patient support & advocacy. Membership is by approval of GOLD's Management Council.

Name \_\_\_\_\_

Organisation \_\_\_\_\_

E-mail \_\_\_\_\_

Phone \_\_\_\_\_ Fax \_\_\_\_\_

Please mail or fax this form to: Dr A Hale, GOLD, PO Box 609, Chalfont St Giles, HP8 4WU, UK. Phone/Fax: +44 (0) 1494 870708

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