

Medical Progress in Pompe Disease

In 1932, JC Pompe, a Dutch pathologist, described a 7-month-old infant with a greatly enlarged heart who had died shortly after being admitted to the hospital. This was the first mention of the disorder that later became known as Pompe disease (more on the history of Dr Pompe, refer to Attach 1). Thirty years later, a scientist in Belgium discovered that people with Pompe disease were missing an enzyme called **acid alpha-glucosidase**, or **acid maltase**. This enzyme is normally found inside a compartment of the cell called the **lysosome**. Like all enzymes, acid alpha-glucosidase has a specific job to do. It helps break down glycogen, a form of sugar that is stored in muscle cells and released when the body needs energy. Without the enzyme, glycogen builds up in the cells and weakens muscles throughout the body. Ever since the link between acid alpha-glucosidase and Pompe disease was discovered, researchers around the world have been searching for ways to replace the missing enzyme. Though we do not yet have a cure for Pompe disease, Myozyme is an enzyme replacement therapy (ERT) that provides patients with the enzyme (alpha-glucosidase) they are lacking. The active substance in Myozyme, alglucosidase alfa, is a copy of human alpha-glucosidase, which is produced by a method known as 'recombinant DNA technology'. The replacement enzyme helps to break down glycogen and stops it building up abnormally in the cells. The European Commission granted a marketing authorization for Myozyme valid throughout the European Union on 29 March 2006. The Food and Drug Administration (FDA) granted marketing approval for Myozyme (alglucosidase alfa) in the United States on April 28, 2006.



Myozyme is a medication intended to replace an enzyme that is missing or markedly deficient in people diagnosed with Pompe disease. This type of medication is known as an enzyme replacement therapy (or ERT). Treatment with Myozyme is not a cure for Pompe disease; that is, it does not correct the underlying genetic defect.¹

¹ http://www.myozyme.com/patients/what_is_myozyme.aspx

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This handout describes the medical advances that are moving us closer to possibly other approved treatments that could also be offered to everyone with Pompe disease.

Q: What is enzyme replacement therapy? How can it help people with Pompe disease?

A: People who have Pompe disease have little or none of a lysosomal enzyme known as acid alpha-glucosidase (GAA). Enzyme replacement therapy (ERT) with Myozyme (alglucosidase alfa) works by replacing the missing or deficient GAA enzyme. Enzyme replacement has been a treatment approach used with other lysosomal storage disorders such as Type 1 Gaucher disease and Fabry disease²

Myozyme is made using recombinant genetic technology, a process that allows scientists to alter the genetic make-up of an organism to produce human proteins, including enzymes. This process, which takes place at Genzyme facilities, occurs in three stages:

Stage 1 - Growing Cells to Produce Human Enzyme:

Making Myozyme begins by inserting the human gene for the acid alpha-glucosidase (GAA) enzyme (the enzyme that is deficient in people with Pompe disease) into CHO (Chinese hamster ovary) cells.

Once the CHO cells have the gene, they will begin to manufacture the human GAA enzyme. For this to happen, the cells are kept under special conditions in large tanks called bioreactors. Each day, liquid is removed from the bioreactor, and the enzyme those cells have produced is collected for purification.

Stage 2- Enzyme Purification:

Myozyme must meet very high standards for purity and safety. The enzyme is purified using a process called column chromatography. Chromatography is a method of separating and isolating the parts of a mixture to remove the unwanted substances. As the enzyme moves through multiple chromatography columns, it becomes more purified.

Stage 3 - Filling and Finishing:

After purification, the enzyme is put into sterile glass vials. After the vials are filled, they are placed into a freeze dryer for about 48 hours. In the freeze dryer, water evaporates off the enzyme and leaves a cake-like dry substance. In this form, the enzyme is more stable. Multiple tests are conducted through the manufacturing process to help ensure Myozyme meets the highest standards. Each vial is inspected before it is released and made available to patients.

² http://www.myozyme.com/patients/what_is_myozyme.aspx

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Making Myozyme is a complex process that takes several months and could only be accomplished after many years of development and testing.³

Myozyme is given **intravenously** (injected directly into the bloodstream) so that it can reach the muscles and break down the glycogen that causes damage when it builds up in the cells. While ERT is not a cure for Pompe disease, it may slow the progression of muscle weakness and improve muscle function. ERT is a long-term treatment that is given at regular intervals (i.e. once a week or twice a month). The dose is based on the patient's weight.

Myozyme is now approved for treatment and commercially available in many countries worldwide.

FOR USA PATIENTS ONLY:

Myozyme is marketed inside the United States (US) as both Myozyme (160L) and Lumizyme (4000L).

The name change from Myozyme to Lumizyme was based on the US Food and Drug Administration (FDA) determination that the Myozyme produced in the larger scale (4000L) bioreactor possessed slightly different biochemical characteristics than the original Myozyme produced in the smaller scale (160L), and should therefore be classified as a different drug with a different name.

The brochure will refer to both Myozyme / Lumizyme as just Myozyme

The following information in this brochure is about the medical progress being made in Pompe disease. This information was provided by the biotech companies and reflect the company's philosophy.

Q: What is NeoGAA and how does it work?

A: NeoGAA, a research molecule is the internal name of Genzyme's recombinant enzyme replacement therapy candidate in development for the treatment of Pompe disease. NeoGAA has been designed to improve the delivery of recombinant human acid alpha glucosidase (rhGAA) to the lysosomes of muscle cells by increasing mannose-6-phosphate carbohydrates on the surface of the protein molecule to target the mannose-6-phosphate receptors responsible for cellular uptake.

³ http://www.myozyme.com/patients/what_is_myozyme/enzyme_replacement_therapy_and_myozyme.aspx

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Genzyme has conducted extensive research over several years with the goal of enhancing the targeting of rhGAA to muscle cells with greater efficiency. Several scientific papers have been published on studies using neoGAA in the Pompe mouse model that demonstrate its ability to clear glycogen in muscle tissues to a greater extent than Myozyme (alglucosidase alfa). Additional findings from the Pompe mouse model demonstrated that neoGAA improved muscle strength and function to a significantly greater extent than Myozyme⁴. Genzyme is actively working on completing the data package necessary to file an IND (investigational new drug application) for neoGAA in order to initiate clinical trials to evaluate the safety and efficacy of neoGAA in humans.

Q: What is the EMBASSY study?

A: EMBASSY is a Genzyme study using alglucosidase alfa in adults with Pompe disease and stands for Exploratory Muscle Biopsy and Biomarker Assessment Study. The study's objective is to evaluate the clearance of glycogen in muscle tissue in adults with Pompe disease through tissue analysis, imaging and biochemical markers. This study is designed to understand more about the disease relative to a patient's response to enzyme replacement therapy, and may help to inform the clinical trial design for future research in Pompe disease. For more information please see Clinicaltrials.gov or [EU Clinical Trials Register](http://EU_Clinical_Trials_Register)⁵

Q: What is BMN 701? How does this treatment work?

A: On August 17, 2010 BioMarin Pharmaceutical Inc. (BioMarin) acquired ZyStor Therapeutics, Inc. (ZyStor) a privately-held biotechnology company developing ERT for the treatment of lysosomal storage disorders. ZC-701 became known as BMN 701 at this time. On August 30, 2010 BioMarin received orphan drug designation from the FDA for BMN 701, a novel fusion of insulin-like growth factor 2 and alpha glucosidase (IGF2-GAA) in development for the treatment of Pompe disease.

As part of their assessment for Orphan Drug designation, the FDA determined that BMN-701 is sufficiently different from alglucosidase alfa (Myozyme) to allow for a unique orphan designation. For this reason, clinical superiority over alglucosidase alfa was not necessary to secure orphan exclusivity for BMN 701.⁶

BMN-701 has the potential to possibly deliver more enzymes to lysosomes compared to traditional mannose-6-phosphate targeted approaches using the GILT technology.

Glycosylation Independent Lysosomal Targeting (GILT) technology is the first peptide-based targeting technology that enables efficient targeting of enzyme replacement the-

⁴ Zhu et al., Mol Ther, 2009, 17, 954-963

⁵ <http://clinicaltrials.gov/ct2/show/NCT01288027?term=Myozyme&rank=12>

⁶ <http://www.pharmpro.com/news/2010/08/agencies-and-organizations-BioMarin-Receives-Orphan-Drug-Designation/>

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therapeutics to the lysosomal compartment of cells in a variety of tissues. BMN 701 is a recombinant protein containing GILT tag fused to GAA, thereby allowing more efficient delivery of GAA to the lysosome of muscle cells. In preclinical research, BMN 701 was found to be both safe and highly efficacious in well studied animal models. In animal models, preclinical efficacy was seen at doses much lower than those reported for the currently approved drug for the treatment of Pompe disease. It is anticipated that the first in-human trial of BMN 701 will be conducted in late-onset Pompe patients.⁷

The FDA approval of the BMN 701 IND represents an important step in developing an improved treatment for Pompe patients. Clinical studies will show whether this new therapeutic approach provides the same benefit in humans as in preclinical testing.⁸

If you are interested in learning more about the Orphan Drug Act:

<http://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/TherapeuticBiologicApplications/ucm094512.pdf>

What does Pharmacological Chaperone Therapy mean?

A: Amicus Therapeutics is developing orally administered, small molecule drugs called pharmacological chaperones.

Pharmacological chaperone technology involves the use of small molecules that selectively bind to and stabilize proteins in cells, leading to improved protein folding and trafficking, and increased activity. In their Pompe program, Amicus has been investigating the use of the pharmacological chaperone AT2220 to bind to destabilized GAA enzyme (acid alpha glucosidase or acid α -glucosidase) and thereby restore its intended biological function of degrading glycogen substrate in lysosomes. Amicus continues to advance its program evaluating the use of pharmacological chaperones in combination with enzyme replacement therapy (ERT) as an expansion of the chaperone technology platform⁹.

Pharmacological chaperone technology addresses human genetic diseases resulting from misfolded proteins. Amicus uses the small molecule drugs, or “chaperones”, to selectively bind to a target protein and increase its stability. The binding of the chaperone molecule helps the protein fold into its correct three-dimensional shape. This allows the protein to be trafficked from the ER (endoplasmic reticulum) to the appropriate location in the cell, thereby increasing protein activity and cellular function and reducing stress on cells.¹⁰

⁷ <http://www.apjohnventures.com/documents/ZyStorPR3Q09.pdf>

⁸ <http://www.pharmpro.com/news/2010/08/agencies-and-organizations-BioMarin-Receives-Orphan-Drug-Designation/>

⁹ <http://www.amicustherapeutics.com/about/profile.asp>

¹⁰ <http://www.amicustherapeutics.com/technology/pharmacologicalchaperones.asp>

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Certain human diseases result from mutations in specific genes that, in many cases, lead to the production of proteins with reduced stability. Proteins with these mutations may not achieve their correct three-dimensional shape and are generally referred to as misfolded proteins. Misfolded proteins are often recognized by cells as having defects and, as a result, are eliminated prior to reaching their intended location in the cell. The reduced or completely absent biological activity of these proteins leads to impaired cellular function and, ultimately, to disease.

Lysosomal storage disorders, such as Fabry disease, Gaucher disease, and Pompe disease, are just a few examples of diseases in which a protein-folding defect is the primary cause of the pathology.

In addition to a monotherapy approach for Fabry disease, Amicus also is evaluating the use of pharmacological chaperones in combination with enzyme replacement therapy (ERT) as an expansion of the chaperone technology platform for lysosomal storage disorders.

Co-administration of Pharmacological Chaperones with ERT:

Amicus previously reported promising preclinical data demonstrating that the co-administration of a pharmacological chaperone with ERT has the potential to address key limitations of ERT. The addition of a pharmacological chaperone has been shown to prevent the loss of activity of ERT in the circulation, increase tissue uptake, and increase substrate reduction in multiple disease-relevant tissues of animal models of Pompe disease. Preclinical proof of concept has been established for Fabry disease and Pompe disease. The company currently is sponsoring a Phase 2A clinical study of the co-administration of AT1001 and ERT for the treatment of Fabry disease.

About AT2220:

Data from Phase 1 studies in 72 healthy volunteers demonstrated that AT2220 was generally safe and well tolerated at all doses evaluated, with no drug-related serious adverse events. Based on these data and encouraging safety data from preclinical studies, Amicus initiated a Phase 2 clinical trial of AT2220 as a monotherapy treatment in adults with Pompe disease. The protocol involved initial treatment with a high dose of AT2220. Two patients enrolled in the trial experienced adverse events categorized as serious and probably related to treatment with AT2220, and as a result the IND was placed on clinical hold in February 2009. The patients subsequently returned to baseline.

Amicus completed a thorough investigation of the events, including the completion of additional preclinical and Phase 1 studies. As a result the Company decided to continue development of AT2220 co-administered with ERT but not as a monotherapy.¹¹ In-

¹¹ <http://ir.amicustherapeutics.com/releasedetail.cfm?ReleaseID=555245>

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formation from the company's multiple studies and discussions with the FDA lead to removal of the clinical hold on AT2220 in March of 2011. Amicus' Pompe program continues to advance and a Phase 2A clinical trial of the pharmacological chaperone and Myozyme is expected to begin during the second half of 2011.

Q: What is gene therapy? How can it help people with Pompe disease?

A: The concept of Gene Therapy was introduced in the late 1970s after the development of recombinant DNA technology. At this time, many approaches for Gene Therapy are being evaluated in animal models of human diseases and in clinical trials. While there have been no completely successful applications of Gene Therapy for human disease, considerable progress has been made.

Genes are the building blocks of inheritance. Passed from parent to child, they contain specific sequences of bases (adenine [A], thymine [T], cytosine [C], and guanine [G]) that encode instructions on how to make proteins. Although genes get a lot of attention, it's the proteins that perform most life functions and even make up the majority of cellular structures. When genes are altered so that the encoded proteins are unable to carry out their normal functions, genetic disorders can result.

Gene therapy is a technique for correcting defective genes responsible for disease development.

Some of the different types of viruses used as gene therapy vectors:

- **Retroviruses** - A class of viruses that can create double-stranded DNA copies of their RNA genomes. These copies of its genome can be integrated into the chromosomes of host cells. Human immunodeficiency virus (HIV) is a retrovirus.
- **Adenoviruses** - A class of viruses with double-stranded DNA genomes that cause respiratory, intestinal, and eye infections in humans. The virus that causes the common cold is an adenovirus.
- **Adeno-associated viruses** - A class of small, single-stranded DNA viruses that can insert their genetic material at a specific site on chromosome 19.

Q: What factors have kept gene therapy from becoming an effective treatment for genetic disease?

A: The following factors have kept gene therapy from becoming an effective treatment for genetic disease:

- **Short-lived nature of gene therapy** - Before gene therapy can become a permanent cure for any condition, the therapeutic DNA introduced into target cells must remain functional and the cells containing the therapeutic DNA must be

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long-lived and stable. Problems with integrating therapeutic DNA into the genome and the rapidly dividing nature of many cells prevent gene therapy from achieving any long-term benefits. Patients will have to undergo multiple rounds of gene therapy.

- **Immune response** - Anytime a foreign object is introduced into human tissues, the immune system is designed to attack the invader. The risk of stimulating the immune system in a way that reduces gene therapy effectiveness is always a potential risk. Furthermore, the immune system's enhanced response to invaders it has seen before makes it difficult for gene therapy to be repeated in patients.
- **Problems with viral vectors** - Viruses, while the carrier of choice in most gene therapy studies, present a variety of potential problems to the patient --toxicity, immune and inflammatory responses, and gene control and targeting issues. In addition, there is always the fear that the viral vector, once inside the patient, may recover its ability to cause disease.
- **Multigene disorders** - Conditions or disorders that arise from mutations in a single gene are the best candidates for gene therapy. Unfortunately, some the most commonly occurring disorders, such as heart disease, high blood pressure, Alzheimer's disease, arthritis, and diabetes, are caused by the combined effects of variations in many genes. Multigene or multifactorial disorders such as these would be especially difficult to treat effectively using gene therapy.¹²

Q: How Can Gene Therapy Help People Diagnosed with Lysosomal Storage Diseases:

A: The concept of gene therapy for lysosomal storage disease was borne out of finding that this category of genetic disease is exclusively due to recessive inheritance, and that a single gene is responsible for all primary disease manifestations. Of course, there are many secondary abnormalities that are associated with the main pathophysiology and would not contribute to the disease in the absence of the primary causative mutations.

An important aspect of the decision to pursue gene therapy for any condition is that the pathophysiology (the functional changes associated with or resulting from disease or injury) related to gene function is fully understood, specifically: Is the condition due solely to the target gene? Is the therapeutic range large enough to allow for unregulated gene expression? Is tissue-restricted expression required and what are the immunological consequences of transgene expression? The approach of gene augmentation or

¹² Human Genome Project (HGP) http://www.ornl.gov/sci/techresources/Human_Genome/home.shtml

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replacement therapy is likely to fit best with these criteria and therefore appropriate for a recessive condition like Pompe disease.

Q: If Pompe disease is being treated with ERT, why do we need Gene Therapy?

A: Myozyme has been shown to improve ventilator-free survival rates in patients with infantile-onset disease, however long-term follow-up of subjects showed a progressive loss of independent ventilation with 22 of the original 38 subjects. Furthermore, all subjects have demonstrated functional deficits in respiratory function and disease progression has not been eliminated. Given these findings in the treated patient population, further understanding of the incomplete response to ERT and identify additional therapeutic or adjunct therapy is being researched.¹³

A successful gene therapy strategy for the treatment of Pompe disease would address many of the disease manifestations, which are defined by a new natural history with the regulatory approval of ERT. Although the ultimate goal is to simultaneously correct all affected tissues, initial clinical trial efforts will focus on establishing the safe and effective delivery of AAV vectors to dystrophic muscle using an approach that is clinically relevant. To this end, an open label, phase I/II study administering rAAV2/1-CMV-hGAA by direct intramuscular injection to the diaphragm of Pompe human subjects has been initiated.

This study is designed to target respiratory insufficiency which is the most life-threatening manifestation of Pompe disease. The target population for this study is children aged 3-14 who are dependent on mechanical ventilation despite ERT. The subject population for this study is well defined because of disease progression to the point of ventilatory failure. These children represent the more severely affected spectrum of Pompe patients and the population most in need of improved therapeutic strategies.

In the coming gene therapy trial, scientists will incorporate the correct gene to produce GAA into an adeno-associated virus, which already exists in most people, and inject it into each patient's diaphragm. The intent is to "infect" cells of Pompe patients with the genetic machinery they have been missing since birth.¹⁴

It is being researched that gene therapy is a way to augment the current treatment for Pompe patients, which involves intravenous infusions to replace the missing GAA enzyme.¹⁵

¹³ Pompe Disease Gene Therapy: Human Molecular Genetics, 2011 (Apr16, 2011)

¹⁴ Science Daily <http://www.sciencedaily.com/releases/2010/01/100126101409.htm>

¹⁵ Science Daily <http://www.sciencedaily.com/releases/2010/01/100126101409.htm>

Q: Is bone marrow transplantation an option for treating Pompe disease?

A: Bone marrow is the soft tissue inside the bones where new stem cells are produced. Stem cells are immature cells in the bone marrow that give rise to all of your blood cells. Your blood is made of:

- Red blood cells (which carry oxygen to your tissues)
- White blood cells (which fight infection)
- Platelets (which help your blood clot)

Normal stem cells are capable of creating new cells that contain the enzyme missing in people with Pompe disease. Bone marrow transplantation, or BMT, is a way to replace bone marrow stem cells that do not have enough of the enzyme with normal stem cells that will supply acid alpha-glucosidase to the muscles. This approach has been tried but has not yet been successful.

Q: What is the process for developing new treatments?

A: The process of developing, testing and gaining approval for new treatments involves many critical steps and typically can take approximately ten years from preclinical development to drug approval. The following is a general description of the stages of drug development in the United States.

Preclinical Testing:

Preclinical testing is conducted to evaluate the safety of an investigational treatment before administration to humans and to assess the treatment's potential to impact a disease. In this stage, scientists test the treatment in a laboratory and through animal experiments in order to collect safety data and to evaluate biological activity against the targeted disease.

Clinical Trials:

Clinical trials are research studies that test how well new medical approaches work in people. Each study answers scientific questions and tries to find better ways to prevent, screen for, diagnose or treat a disease. Clinical trials may also compare a new treatment to a treatment that is already available.

Every clinical trial has a protocol, or action plan, for conducting the trial. The plan describes what will be done in the study, how it will be conducted, and why each part of the study is necessary. Each study has its own rules about who can participate. Some studies need volunteers with a certain disease. Some need healthy people. Others want just men or just women.

In the United States, an independent committee of physicians, statisticians and members of the community must approve and monitor the protocol. They make sure that the risks are small and are worth the potential benefits.

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Clinical trials are done in 4 phases:

- **Phase 1 Clinical Trial:** The investigational treatment is tested for the first time in humans. Phase 1 studies are most often conducted in healthy volunteers (about 20-80). The purpose of Phase 1 trials is to evaluate safety in humans at a range of doses. Phase 1 studies also provide pharmacokinetic (how the body affects the drug) and pharmacodynamic (how the drug affects the body) data.
- **Phase 2 Clinical Trials:** Phase 2 trials include more participants (about 100-300) who have the disease being studied. In Phase 2 trials, researchers seek to gather further safety data and preliminary evidence of the drug's beneficial effects (efficacy), and they develop and refine research methods for future trials with the drug. If the Phase 2 trials indicate that the drug may be effective--and the risks are considered acceptable, given the observed efficacy and the severity of the disease--the drug moves to Phase 3.
- **Phase 3 Clinical Trials:** In Phase 3 trials, the drug is studied in a larger number of people with the disease and provides the information necessary to evaluate use of the treatment in the general patient population. This phase further tests the product's effectiveness, and monitors side effects. As more and more participants are tested over longer periods of time, the less common side effects are more likely to be revealed.
- **Phase 4 Clinical Trials:** In the United States, once clinical trials are completed, a New Drug Application (NDA) is submitted to the Food and Drug Administration (FDA) for review. The NDA contains all the scientific data that a company has gathered regarding the safety and effectiveness of an investigational treatment. The FDA reviews the NDA and if approved, the new treatment can be marketed and distributed.

Once the treatment is on the market, additional studies may be performed to evaluate treatment effectiveness and safety during routine use or to assess the treatment in new segments of the patient population.¹⁶

Q: What are the benefits and risks of participating in a clinical trial?

A: For rare disorders like Pompe disease, taking part in a research study may give patients access to experimental treatments that could improve, save, or extend their lives. Expanded access programs could provide treatment to patients with more severe disease who might not otherwise qualify for a clinical trial. Randomized studies that enroll larger numbers of patients (but assign them to different groups to compare treatments)

¹⁶ Understanding Clinical Trials: <http://clinicaltrials.gov/ct2/info/understand>

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could give people with less severe disease the chance to begin treatment before muscle weakness has progressed beyond mild disability. Because your health is closely monitored, enrolling in a clinical trial also gives you access to medical care from experts in Pompe disease.

Before deciding to participate in a clinical trial, it is important to weigh the possible risks as well as the benefits. Read the protocol and talk with your healthcare provider (or your child's healthcare provider) to get a better idea of your chances for being accepted into the clinical trial and how long it might be before you could start treatment. Think about how taking part in the trial could affect your health, your family, your job, and anything else that may matter to you. Be sure to ask what kind of support would be available to you if you decide to enroll. Also be sure to ask if any of your expenses would be covered if you have to travel any distance to the study site.

Q: How can I find out about clinical trials that are going on in my area?

A: To learn more about clinical trials worldwide that are now recruiting patients with Pompe disease, go to the following websites:

- [ClinicalTrials.gov](http://www.clinicaltrials.gov): This is a registry and results database of federally and privately supported clinical trials conducted in the United States and around the world. ClinicalTrials.gov gives you information about a trial's purpose, who may participate, locations, and phone numbers for more details. This information should be used in conjunction with advice from health care professionals. www.clinicaltrials.gov
- [EU Clinical Trials Register](https://www.clinicaltrialsregister.eu): This Register allows you to search for information on clinical trials in European Union (EU) member states and the European Economic Area (EEA) and clinical trials which are conducted outside the EU/EEA if they form part of a pediatric investigation plan (PIP). This information should be used in conjunction with advice from health care professionals. <https://www.clinicaltrialsregister.eu>

Where to Learn More

These sources can help you keep up with the research developments and treatment advances for Pompe disease:

- For more information on animal models:
 - Understanding **Animal Research**
http://www.understandinganimalresearch.org.uk/your_health/pompe_disease?print=true

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- Pompe disease – A starring role for animal research
<http://speakingofresearch.com/2010/01/25/pompe-disease-%E2%80%93-a-starring-role-for-animal-research/>
- For more information on the **clinical trial process**, visit www.clinicaltrials.gov or <https://www.clinicaltrialsregister.eu>
- The **International Pompe Association IPA** is a federation of Pompe disease patient groups around the world. To find the contact for your country, visit the IPA Web site at www.worldpompe.org. The IPA publishes updates on clinical trials and treatment studies for Pompe disease.
- **ClinicalTrials.gov**: The ClinicalTrial.gov is a registry and results database of federally and privately supported clinical trials conducted in the United States and around the world. ClinicalTrials.gov gives you information about a trial's purpose, who may participate, locations, and phone numbers for more details. This information should be used in conjunction with advice from health care professionals.
<http://clinicaltrials.gov/>
- **EU Clinical Trials Register**: The EU Clinical Trials Register website allows a person to search for information on clinical trials in European Union (EU) member states and the European Economic Area (EEA) and clinical trials which are conducted outside the EU/EEA if they form part of a paediatric investigation plan (PIP).
<https://www.clinicaltrialsregister.eu/>
- **Pompe Center Erasmus MC Rotterdam**: The Pompe Center is an initiative of researchers and clinicians of the Erasmus University, the Sophia Children's Hospital, and the Academic Hospital, united in the Erasmus MC, Rotterdam. The Pompe Center is aimed to function as a center of expertise in the field of Pompe disease. In this role the Center will be active in generating, collecting and forwarding of information that it considers important for the well-being of patients and for the understanding of Pompe disease in all its molecular, clinical and therapeutic aspects. <http://www.pompecenter.nl/en/?Home>
- **Pompe Community website**: The Genzyme Corporation's Pompe Community website www.pompe.com: offers the Pompe community comprehensive information on the disease, as well as resources and support to help manage the challenges it may bring.
- **American College of Medical Genetics (ACMG) Practical Guideline**: Pompe Disease Diagnosis and Management Guideline 2006. Vol. 8. No. 5. The *ACMG guidelines were designed as an educational resource for physicians and other health care providers.*

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- **BioMarin:** BioMarin develops and commercializes innovative biopharmaceuticals for serious diseases and medical conditions. <http://www.bmrn.com/about-us/index.php>
- **The Powell Gene Therapy Center:** The primary mission of the Gene Therapy Center at the University of Florida is to merge molecular genetics research and health care delivery by developing new therapeutic strategies for the treatment of human diseases that involve gene transfer. The idea of gene therapy is a logical and natural progression of the last 20 years of research in medical genetics and molecular biology.
- **Amicus Therapeutics:** Is a biopharmaceutical company focused on the discovery, development and commercialization of novel small molecule, orally administered drugs known as pharmacological chaperones, for the treatment of a range of human genetic diseases. <http://www.amicustherapeutics.com/default.asp>

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