



Dec-97

Unexpected to Tricia and Phil the first signs of the nightmare that is yet to come. Tricia took Nathan to a movie and he froze when entering the theatre due to the sudden change of light.

Apr-98

Phil is noticing that Nathan is having trouble tracking a hockey puck moving across the floor and hitting a baseball when pitched.

Jun-98

Nathan's 4 year old check up at his local pediatrician identified developmental delays while performing standardized childhood developmental testing. The doctor was not concerned but Tricia insisted on having a more detailed evaluation performed on Nathan. Nathan tested at a 3 year 9 month level of development. When he was 12 months he tested at a 21 months. When he was 24 months he tested at 31 months. When he was 36 months he tested at 39 months.

Jul-98

Innovative therapy OT, PT, Speech evaluations performed (7/8/98).

Jul-98-Sep-98

Nathan received therapy. Some days good results most days no results. Most difficulty in speech with cognitive ability. Fine motor skills also lacking (cutting, build bridge, draw cross...)

Jul-98

Noticed while in speech therapy session that Nathan was losing track of yellow game pieces on a yellow table. He could not track color objects on like color surfaces. When using scissors Nathan always tried to cut on top of the paper.

Jul-98

Nathan was continually tripping over his 11 month old brother who was crawling on the floor. Nathan would also trip over items out of place in our home. He began to



have trouble with shadows on walking surfaces. He thought that they were steps and tried to step over them many times.

Aug-98

Nathan had his first optometrist appointment with Dr. Fred Hidaji. The doctor said Nathan seem to have good vision 20/40, but was hard to test since Nathan did not cooperate during testing. Tricia and I asked about night blindness and then the doctor threw his toy on the ground and dimmed the lights. Nathan could not locate his toy on the floor. The doctor then referred us to Riley for further optometric evaluations.

Sep-98

Nathan had an optometry appointment at Riley. Doctor said that he had 20/40 vision but did notice some retinal changes and wanted to perform an ERG on him. Come back in 4 months for test. Dr. Dan Neely (9/11/98)

Oct-98

Riley performed full day developmental evaluation. Determined delays. tested 2.5 years of development. Mainly in speech (10/27/98).

Nov-98

EEG performed and results were documented as normal (11/12/98).

Nov-98

ERG was performed and results were non-measurable night vision and low day vision. Suggest RP, Leber congenital amaurosis, congenital night blindness, multi system diseases (NCL is one of the two suggested on 11/12/98).

Nov-98

Nathan has many blood tests performed, lactate, fatty acid pyruvate... Everything turned out normal.

Nov-98

MRI was performed and showed minor abnormalities of the parietal and occipital lobes (11/23/98). Nov-98 Nathan's first visit to Head of Neurology at Riley Hospital, Dr. Garg. Dr. Garg informed us he believed that Nathan had Batten disease. Given the vision problem and the developmental delay (11/30/98).



Dec-98

Dr. Garg ordered a punch biopsy on 12/2/98 to be taken from his Nathan's back for diagnosis of Batten disease.

Dec-98

Nathan's punch biopsy came back negative on 12/23/98. Dr. Garg told us that Nathan did not have batten disease and he would just have to observe him over time to try to find out what was wrong. Come back in 6 months for an evaluation. There was nothing that he could do.

Dec-98

Phil launches the Nathan's Battle website. The website was created initially to house all of Nathan's medical records. Phil spent countless hours researching possible therapies and diagnoses by emailing his records across the world. Phil and Tricia realized the importance to being the focal point for all of Nathan's medical records and began the battle to help Nathan.

Jan-99

Riley's optometry department then said that there was nothing that they could do until Nathan was 8 to do another ERG while awake. Just come back in a year for a check up (7/8/99).

Jan-99

Phil got the name of Dr. Forrest Ellis from an old school friend and scheduled an appointment at the Midwest Eye Institute.

Jan-99

Dr. Ellis examines Nathan. Says he has 20/40 but hard to examine due to his age. Dr. Ellis will consult with other doctors across country to try to determine a potential diagnosis.

Feb-99

Dr. Ellis schedules appointment to get pictures of Nathan's eyes. Nathan does not cooperate so Ellis scheduled an ERG, conjunctive biopsy, and blood drawn for DNA analysis.



Feb-99

Nathan had ERG, conjunctive biopsy, and blood drawn.

Mar-99

Conjunctive biopsy comes back negative for CLN2

Mar-99

DNA diagnosis from Mass General comes back Positive for CLN2 on 3/12/99

May-99

Phil and Tricia want second opinion on blood mapping and get blood drawn to send to Institute for Basic Research in Staten Island NY.

May-99

IBR confirms diagnosis of CLN2. Received on 5/18/99 only one allele found containing the classical late infantile form of this disease.

Jun-99

Tricia and Phil upon getting a diagnosis sought to see one of the world's clinical experts on Batten disease. Dr. Rose-Mary Boustany has seen several hundred cases of batten disease and is a leader in the NCL world. Tricia and Phil want the best for their children and take Nathan to see one of the world leaders on the disease. They still hold on to the hope that he has been mis-diagnosed and hope she will tell them that Nathan does not have Batten's. Dr. Boustany confirms the diagnosis of LINCL on 6/7/99.

Aug-99

Nathan starts school at the Indiana School for the Blind.

Aug-99

Nathan's Battle first annual golf outing was held and raised over 14k with overwhelming support with over 150 golfers. They were told by the golf course that since it was the first outing that they would only have around 30 golfers. The community support for the Milto's is overwhelming. This event marks the beginning of Nathan's Battle.



Sep-99

Phil talks to Ricky Bennett for the first time about the NCLRA. Mr. Bennett is a proactive parent helping lead scientific research to develop therapies for the NCLs. Mr. Bennett has two children with Juvenile Batten's and is mainly focusing on CLN3 therapies. Ricky invites Phil to participate in the NCLRA and help host a conference at the NIH with the leading researchers in the world on the disorders. Mr. Bennett encourages Phil to lead the efforts for the CLN2 cause. Mr. Bennett explains that there seems to be some promising research for CLN2 but someone needs to take a leadership role for this disorder.

Oct-99

Friends of Phil and Tricia hold a tremendously successful Nathan's Battle Benefit Dinner to raise money for research. This event raised over \$85 thousand dollars and was attended by nearly 1000 people. Every local television station was in attendance and ran stories on this wonderful event.

Oct-99

Phil and Tricia take Nathan to NY for two weeks for alternative medicine approach. Alternative treatments included nuero feed back, lymphatic drainage, craniosacral, bioacoustics, and a drastic change in Nathan's diet was prescribed.

Nov-99

Phil attends the NCLRA "Action for Therapy" conference at the NIH in Bethesda Maryland. This conference gathered the countries leading experts on NCLs and potential therapeutic approaches. The FDA and NIH attended and gave input regarding therapy development.

Dec-99

Nathan was taken off extreme diet by Tricia and Phil. After two months, Tricia did not notice any positive changes with Nathan. Nathan was losing weight and not enjoying eating the foods that he was given. The change back seemed to make Nathan much happier.

Jan-00

Phil goes to St. Louis to meet with Dr. Mark Sands from Washington University, Caroline Wright from Australia and Liz Aruleo from California to have a conference call with Cynthia Rask of the FDA. Phil develops first points of Action plan to



develop a CLN2/CLN1 gene transfer therapy. At this point, Phil realized that he needed to attract a sponsor from the private sector. The emotional draw was not going to be enough to convince a company to get involved with rare disease.

Jan-00

Phil writes letter to Senator Lugar to appeal for assistance with Nathan's Battle.

Feb-00

Phil develops business plan to attract biotech companies and other clinical trial partners to work on CLN2. Phil drew upon his business experience and entrepreneurial knowledge to develop a business plan that would get the interest of companies. The premise of Phil's plan is to solve this disease and role out what is learned to the other 40 LSDs and then other metabolic diseases. The business plan outlines a financially rewarding venture to undertake for any company interested.

Feb-00

Phil organizes local meeting with the community. This meeting is designed to give friends and family an update on Nathan and to organize the direction of Nathan's Battle for the future. The local community rallies and joins Nathan's Battle to help form the Awareness committee and the Fund raising committee of the organization. The Nathan's Battle Foundation begins a structured approach on the Scientific, Awareness, and Fundraising fronts of the battle.

Feb-00

Phil gets invited to speak at the Senator Lugar's "Lincoln Day Dinner" where over 400 political constituents attend to hear Nathan's grim fate. Phil pleads for assistance from the political community. The political front of Phil's plan is starting to take shape. Phil also gets to hold a 25 minute one on one meeting with Senator Lugar to discuss the Nathan's Battle cause and get the Senator's insight for assistance.

Mar-00

Phil begins to contact clinical trial partners to create interest in collaborating on a CLN2 gene transfer therapy. Phil and the NCLRA decide to hold a conference for interested parties to attend and learn more about the opportunities of this clinical trial. Phil wants to get every element of a clinical trial to attend this conference so that all questions can be answered. Phil contacts over 65 prospective clinical trial partners to attend the conference from biotech's, clinical centers, researchers, FDA, NIH,



neurosurgeons, clinicians, academics... Phil speaks with leading biotech companies high level executives and leading scientist to explain the business opportunity and the objectives of a CLN2 clinical trial. The "Clinical Trial Initiative Conference" is scheduled for May at the NIH.

Mar-00

Phil goes to Philadelphia to visit Matthew During regarding his clinical trial efforts in canavan disease and gets Dr. During interested in working with him on CLN2. Dr. During is a pioneer in therapy development and has performed a gene therapy clinical trial. He is highly sought after and his time is limited but after meeting with Phil agrees to collaborate on CLN2 projects.

Apr-00

Phil meets with the Indiana University Advanced Research & Technology Institute. He meets with Arun Srivastava a pioneer in AAV development and the board of directors of the institute to discuss the business opportunity with CLN2.

Apr-00

Phil goes to Washington DC to meet with Senator Lugar's administrative assistant. Phil also visits Congressman Dan Burton's office and the FDA oversight committee advisors about the Nathan's Battle's cause.

Apr-00

Phil, Ricky Bennett, Russelle Rankin of the NCLRA meet with Dr. Gerald Fischbach the director of National Institute for Neurological Disorders and Stroke (NINDS) regarding the NCLRAs November "Action For Therapy" conference recommendations and key NCL issues. Dr. Fishbauch is receptive to the recommendations and offers NINDS assistance to the NCLRA.

Apr-00

Nathan seems to be having jerky movements. Tricia and Phil are not sure exactly when these movements started.

May-00

Tricia and Phil take Nathan to the NIH in Bethesda, Maryland to see Dr. Kurt Fishbeck to evaluate a possible drug therapy clinical trial. This drug therapy is being used by other disorders to help increase the enzyme level production of Nathan's cells.



Tricia, Nathan, and Phil visit and discuss possibilities of the use of Gentamycin as a possible therapy. Cell line test on Nathan's fibroblast show only limited gain in function of enzyme production. At this time this project is still under evaluation.

May-00

Phil along with other members of the NCLRA went to the NIH to host the "Clinical Trial Initiative Conference". Phil conducted this conference hosted at the National Institutes of Health, Bethesda, Maryland on May 11, 2000 and May 12, 2000. This conference was tremendously productive in fostering collaboration and propelling research toward a clinical trial for CLN1/CLN2. The "Clinical Trial Initiative Conference" was the first of its kind. Never before had a group been assembled that contained competing biotech companies, research scientist, clinicians, a neurosurgeon, universities, clinical centers, the FDA, the NIH, and a parent group (the NCLRA). The success of the meeting was mainly due to the open collaboration between each party interested in achieving a common goal, a treatment for CLN1/CLN2 children. The NCLRA organized and funded this conference. Each attendee comes to the conference based on Phil's conversations and the business plan he developed.

May-00

One of the biotech companies that attended the "Clinical Trial Initiative" conference, announces that they are committing to pursue a therapy for CLN2.

May-00

Nathan begins to scoot across floor more often instead of walking. He is beginning to lose coordination and balance. Nathan still walks but will often scoot to get from room to room. Tricia believes that he has lost some confidence from falling and bumping into many items during this period of time.

Jun-00

After the conclusion of the "Clinical Trial Initiative" conference, Phil develops a conference summary. The summary gives overviews of the conference, highlighting that the development of a CLN2/AAV gene transfer therapy is an achievable goal. No issues were presented that did not have a working resolution. The conference confirmed that the necessary science is in place to move forward toward a clinical trial for CLN2. The document also lists the tremendous accomplishments from the conference.



Jul-00

Phil networks with industry leaders of therapy development and the concept of a Non-For-Profit therapy development model is developed. Phil quickly takes this concept and develops it to attract partners for implementation of this novel concept.

Jul-00

Phil goes to the University of Iowa to visit one of the worlds experts in gene therapy for lysosomal storage disorders, Dr. Beverly Davidson. Phil meets with Dr. Davidson's leading scientist to review CLN2 data and to discuss their progress and direction.

Aug-00

Phil goes to N.Y. to meet with Cornell University's Institute of Genetic Medicine. Phil meets with the institute members to present the idea of taking on CLN2 as a Non-For-Profit model to develop therapies for rare diseases.

Aug-00

The University submits a proposal to Phil to work with him in developing the Non-For-Profit model for rare diseases and developing a gene transfer therapy for CLN2.

Sep-00

The Nathan's Battle Foundation is nationally recognized by the National Institutes of Health as an authority on Batten disease. The NIH has added the foundation to there website of advisors on this disorder and is viewed as advisors in the research community. See www.ninds.nih.gov/health_and_medical/disorders/batten.htm.

Sep-00

Phil gets invited to attend a "Gene Therapy for Neurological Disorders" workshop at the National Institutes of Health in Bethesda, Maryland. This workshop is organized to shape and design the of future of the gene therapy development process.

Sep-00

The second annual Nathan's Battle Golf outing is held at Valle Vista Country Club. The support from the local community is tremendous.

Sep-00

Phil goes to Oxford, England for the NCL-2000 world conference. This conference is



attended by the world leaders in NCL research. Phil meets with leading scientists from around the world to help advance therapy development for CLN2. Phil presents his ideas on therapy development to the world leaders in the NCLs.

Sep-00

After reviewing the Universities proposal and a conference call to go over key questions, Phil writes a proposal acceptance letter to begin the CLN2 Gene Transfer project on Oct. 1, 2000.

Sep-00

Nathan's Battle Under the Big top is held. Barnum Bailey Circus allows Nathan's Battle to have a fund raising night. This was a large scale event for Nathan's Battle. The foundation sold over 3500 tickets to this event and over 7000 people were in attendance at Conseco Fieldhouse in Indianapolis. There was a tremendous amount of media coverage on this event. Every major news station ran a story on this event. Two of the stations ran the story as the "Top Story" and they had coverage all day.

Oct-00

The Non-For-Profit model for CLN2 gene transfer therapy project begins on October 1, 2000. Phil will play a key role in the project management of this project.

Oct-00

Phil speaks at the Southern Indianapolis Rotary club about Nathan's Battle. This was a luncheon that was attended by the areas leading business leaders.

Oct-00

Phil gets key scientists and doctors aboard with the Non-For-Profit model approach. Industry leading companies are now looking to partner with Phil in this approach. The novel concept of NFP therapy development is getting national attention.

Oct-00

Phil is asked to prepare a presentation for the Society of Neuroscience conference in New Orleans by the Rett syndrome foundation. Phil prepares the presentation to explain rare disease therapy development and how rare diseases should unite to expedite the development process.



Oct-00

Phil attends a clinicians meeting at the University's medical center. Phil schedules the meeting with two of the NCL leading clinicians. Phil is able to get Dr. Rose-Mary Boustany and Dr. Kristina Wisniewski to meet with the project team.

Oct-00

Phil attends a "Gene Therapy for Neurological Disorders" workshop at the National Institutes of Health in Bethesda, Maryland. The workshop's purpose is designed to shape and direct the future of the gene therapy development process for LSDs.

Oct-00

Phil schedules meetings with Mark Sands and Peter Lobel to meet with the gene transfer project team. The close relationships that Phil has developed with these scientist encouraged them to travel to NY and meet with the team.

Oct-00

Nathan had a Grand Mal seizure. Nathan had a seizure that lasted over 4 minutes and he had to be hospitalized over night for observation. An EEG was performed and the results showed that he was having seizures frequently. Nathan was put on an anti-seizure medication called, Depakote.

Nov-00

Phil attends the Society for Neuroscience conference in New Orleans. Phil discusses the Non-For-Profit therapy development model and the rare disease therapy development process with other leading advocacy groups. Phil wants to organize other rare diseases to have a stronger voice when approaching the RAC and the FDA.

Dec-00

Phil attends a meeting at the Cornell Medical Center in New York for discussions of their Genetic Program in Pediatric Neurology. Phil meets with the Medical Center's Chairman, Chairman of Neurology, Vice Chairman of Pediatrics, and Dr. Rose-Mary Boustany.

Dec-00

Phil was invited to and attended a meeting at Rochester University on "Implementing Gene Therapy for Parkinson's Disease: Collaboration, Conservatism and Consensus". This meeting is designed to address gene transfer development issues faced during the



development process. Conflicts of interest, intellectual property, non-disclosure agreements, and other business related issues encountered when developing therapies are discussed. The Non-For-Profit Model that the Nathan's Battle Foundation is using to develop a gene transfer therapy for CLN2 successfully addresses many of these issues.

Dec-00

Phil goes to Boston to meet with lead representatives of Genzyme Corporation. Phil meets with Genzyme's CSO, business development people, neuroscience/ gene therapy directors, and legal council to define Nathan's Battle Foundation's relationship with Genzyme as it relates to the Non-For-Profit therapy development project. The goal is to define legal relationships that create a "win/win/win" situations for Genzyme, Nathan's Battle Foundation, and the academic University performing the clinical study. These negotiations are critical to the successful develop and commercialization of a therapy for CLN2.

Jan-01

The Nathan's Battle Foundation receives commitment from a national prime time television news program to air a story on our efforts. The foundation had offers from two different major prime time television programs to cover Nathan's Battle. The goal for the national attention is to increase awareness to obtain philanthropic support and to ensure regulatory accountability during the RAC and FDA review process.

Jan-01

Cornell University makes an official statement about gene transfer therapy project with the Nathan's Battle Foundation. The official statement is as follows: "The Institute of Genetic Medicine at Weill Medical College of Cornell University is working with Nathan's Battle Foundation to prepare a detailed outline of the steps the Foundation will need to take to move to a clinical program, and what the clinical program would entail."

Feb-01

CBS's "The Early Show" filmed an interview segment with Tricia and Phil. No air date has been given, but will air before the end of March. And the national prime time television news program, "48 Hours", began following Nathan's Battle for their future story to air sometime within the next 5 months.



Mar-01

Cornell University's Institute of Genetic Medicine delivers the Feasibility of Gene Therapy for Late Infantile Neuronal Ceroid Lipofuscinosis to the Nathan's Battle Foundation for review. The document confirms the feasibility of a successful clinical trial for LINCL. The summary of the document states "...assuming the resources are available, and the regulatory climate is supportive, it is the conclusion of this report that it is possible to initiate clinical trial(s) for the CNS and retinal manifestations of LINCL..."

Mar-01

Complete devastation overcomes the Milto family when test results from their youngest son, P.J., comeback positive for Late Infantile Batten disease. The Milto family is attempting to deal with the unbearable diagnosis of their youngest son. Nathan's Battle now becomes a WAR!!! We MUST win both the battle and the war.

Mar-01

Phil goes to New York to meet with the gene transfer project team to plan the next stages of the LINCL clinical trial project. The goal will be to develop a work plan that includes specific tasks, timeframes, milestones, and funding requirements.

April 01

Breaking news that a very similar gene therapy AAV clinical trial has gained approval from the FDA to treat Canavan disease. This approval will help the approval process for Nathan's Battle. Our gene therapy project is using the same vector and delivery methods. The Canavan clinical trial design is very similar to the technology proposed for our CLN2 clinical trial. Both trials will be using inter cranial injections of AAV mediated gene therapy to the Central Nervous System. This should set a precedent for the approval process for our AAV-CLN2 clinical trial. This is great news.

April-01

A Nathan's Battle Foundation Update meeting is held at Perry Meridian High School to inform the community of the latest successes, accomplishments, and challenges that we face. The meeting helped to define specific ways people can help to solve our funding problem. The science is in place, we just have to get the funding. Money is the only thing stopping us from developing a treatment for Nathan and P.J.



April-01

Phil speaks with BBC reporter from the United Kingdom about the Nathan's Battle Foundation and how a UK family is helping support NBF (www.fundraising.freeservers.com) Check out the favorite links section.

May-01

Mark Schultz benefit concert held for Nathan's Battle. The concert was a huge success with over 1000 people in attendance to support our cause.

May-01

Nathan's Battle becomes part of the Indianapolis 500. Walker Racing places the Nathan's Battle logo on the nose cone of Sarah Fisher's race car.

June-01

Nathan's Battle Family Run/Walk was a huge success. Near 1000 Nathan's Battle supporters participated in the event and raised over \$81,000. The MOMs Club put on a top notch event that generated overwhelming support.

June-01

Canavan disease clinical trial performed first AAV2 inter cranial human injections on June 5th. This news is very exciting for Nathan's Battle because it utilizes the same technology proposed for our clinical trial. Our gene therapy project is using the same vector and delivery methods.

June-01

The prestigious Indianapolis Business Journal runs a front page article on Nathan's Battle. The story "In a race for life", discusses the efforts and accomplishments of Nathan's Battle Foundation. Illustrating how Nathan's Battle is "Managing Science" by applying business principles to propel therapy development. A leading Late Infantile Batten disease scientist, Dr. Peter Lobel, and a program director from the National Institutes of Health, Dr. Giovanna Spinnella, are quoted recognizing the efforts accomplished by the organization.

June - 01

Phil attends project status meeting at Cornell University. Project is on schedule.



June - 01

We appreciate the national exposure on 48-Hours and we hope that the story brought much needed awareness to Batten disease. Unfortunately, the story that aired was a small part of Nathan's Battle. Please read the web site to learn more about the focus of our efforts to aid in the development of therapies for this devastating disease

June - 01

Nathan's Battle at the Ritz dinner benefit was a great success. Over 600 tickets were sold for this event and over \$80,000 was raised. The Milto's were presented with the Sagamore of the Wabash award from the Governor of Indiana.

July - 01

MIBOR auction raises near \$8000.

July - 01

GVS - Nathan's Battle Golf outing at Hillview Country Club raises over \$57,000. This was a tremendous event with golfers coming from multiple states. CBS affiliate sports director participated and was a guest speaker during dinner. 37 foursomes over filled the field with corporate sponsors for every hole.

July - 01

Phil attends gene transfer project status meeting in NYC. The project is aggressively progressing by performing multiple tasks in parallel. The project team is taking continue to produce promising data to support a successful clinical trial.

July - 01

Phil receives a "historical" email from a parent of the first child treated in the Canavan AAV2 clinical trial. The mother expresses her praises for the scientist and explains that her child is performing tasks that she has not been able to perform for several years. *"... In one month, regained skills that she lost one year ago. Her physical therapist has seen her demonstrate head control that she hasn't seen in 3 1/2 years. Everyone has noticed a change. Her tone, her responsivity, her awareness, her ability to move, have all improved. After having watched my child deteriorate for 1,1/2 years, dreading the passing of each day, I can now have the joy of watching her improve with time. Her birthday next week will be a happy occasion in which we can look forward to the future..."* Although, they are not out of the woods yet and many



evaluations must be performed, this information is extremely uplifting and demonstrates the reality of such therapies.

July - 01

Max and Erma's dinner benefit raised over \$19,500 for Nathan's Battle. This event was very well attended and covered by many of the local media affiliates.

July - 01

Phil attends the BDSRA national conference in Chicago. Many of the leading Batten scientists presented updates of their latest research. The data that was presented was very promising and continues to support the viability of therapies for LINCL. The scientists' promising data provide the foundations for future therapies. Gene therapy, adult stem cell therapy, and small molecule pharmaceutical therapies all have very encouraging data presented to support potential therapies. Nathan's Battle is currently pursuing therapy projects in all three areas.

July - 01

St. Barnabas's Garage Sale for Nathan's Battle raises over \$14,000. This was a massive one day garage sale supported by hundreds of NB supporters.

July - 01

The Crabbie open golf outing is held to support Nathan's Battle.

July - 01

The NIH gives formal approval to a new funding mechanism to for Gene Therapy for Neurological Disorders ([link](#)). This grant was designed with the work Nathan's Battle has performed to develop a Not-For-Profit therapy development model to develop a platform for therapy technologies to leverage to other diseases. Nathan's Battle's gene transfer project at Cornell has helped mold the future of therapy development for rare diseases by reinforcing the need for such a mechanism.

August - 01

Phil travels to Philadelphia to meet with the country's only scientist to take a therapy for a neurodegenerative disorder of the brain to the clinic. Phil investigates a promising Adult Stem Cell therapy proposal. Adult stem cell therapies can introduce cells into the brain that can produce the missing enzyme and differentiate into neurons to "re-grow" the brain and aid in regaining loss function.



August - 01

Nathan has major surgery performed. Nathan under goes a Nissen Fundoplication (Fundo) and has a G-tube inserted into his stomach. The G-tube was inserted to keep Nathan healthy and strong. The Fundo will prevent reflux from occurring and causing phenomena in the future. These procedures will keep Nathan strong as he waits for a therapy to be developed.

August - 01

Nathan's Battle initiates a small molecule pharmaceutical drug screening project to screen compounds on Nathan's cell lines. Over 700 compounds are being screened by the leading CLN2 laboratory to evaluate therapeutic effects.

August - 01

Cut-A-Thon and carnival raise near \$8,000. This was a great event and fun for all that attended.

August - 01

3rd Annual Nathan's Battle Golf Outing raised over \$8,000. This event continues to be well supported by many close friends of Tricia and Phil.

August - 01

Nathan's Battle at Broadmoor Country Club Golf Tournament was a first class golf outing. This event had many corporate and local sponsors. Four golfers had a chance to win \$1 MILLION and a minimum of 1/2 was to be donated back to the foundation. As local news media watched, one golfer's shot was right on line for the million but ended just 10 feet short of the cup. This event raised over \$46,000.

September - 01

Nathan and P.J.'s Ride and family fun day was held. This was a spin tingling event as you watched the countless motorcycles ride to support Nathan's Battle. These big burly bikers have a huge spot in their hearts for kids and rallied to support the cause. This event raised over \$23,000.

September - 01

Ringling Bros. and Barnum & Bailey Circus held Nathan's Battle Under the Big Top II. Ringling Bros. and Barnum & Bailey graciously approached Nathan's Battle to have a fundraising performance again this year. Ringling Bros. and Barnum & Bailey



Circus donated \$1.00 to the Nathan's Battle Foundation for every ticket sold for the benefit performance at Conseco Field house. Thousands came to enjoy the greatest show on earth and to support Nathan's Battle.

September - 01

Nathan's Battle - An Evening on the Canal Walk black tie dinner benefit was held. This was truly an elegant evening full of fun, food, auctions and entertainment. This event was held at the NCAA headquarters and everyone who attended had a wonderful time. This event raised near \$70,000 for Nathan's Battle. The organizers did a wonderful job.

September - 01

Nathan's Battle - Race For Life 4 mile Run/Walk took place. This event demonstrated the overwhelming support that NB is receiving from the community with the tremendous amount of participants and volunteers. Racing industry experts boasted of this well organized top notch event. The Race for Life raised over \$32,000 for Nathan's Battle.

October - 01

Nathan's Battle Ice Skate-A-Thon was held at Pan Am plaza in downtown Indianapolis. This event may of taken place on ice but it sure warmed the hearts of everyone involved to skate for such a good cause. Nathan's Battle benefited from all the days events, which included skating, door prizes and raffles with professional hockey players from the Indianapolis Ice to help out the boys.

October - 01

Phil attends a project status meeting with the gene transfer therapy project team at Cornell. The project manager presented the status of the each team to Phil. The project team evaluated various strategies and approaches to move the project forward toward the clinic. The project is still on schedule. Many of the project teams are actually a head of schedule. Pre-clinical studies are in progress, vector and analytic development are finished ahead of schedule, clinical protocol development is on schedule, and manufacturing and characterization is ahead of schedule.

November - 01

Kiwanis Battle Run was held to support Nathan's Battle Foundation. Kiwanis



members put forth a herculean effort to make this event a tremendous success. Many sponsors and community volunteers made this a special event.

November - 01

Phil was invited to attend the advocacy breakfast meeting at the Society for Neuroscience conference in San Diego. Phil was asked to share the efforts and accomplishments of NBF with other leading advocacy groups, scientists, and regulatory agencies.

November-01

Phil, along with other NCLRA members hosted a dinner in San Diego with 20 of the world's leading stem cell scientists. Scientists from Sweden, the United Kingdom, and the United States attended to gain a better understanding of the NCLs. Much interest and excitement was generated to apply cell mediated technologies toward the NCLs. The NCLs prove to be a good target disease for these therapies.

December-01

Phil traveled to California to meet with a leading stem cell research company. This company's expertise in stem cell technologies are extremely promising and they are directed by some of the worlds top scientists in the field. The company gained interest in the NCLs by attending the dinner Phil's group hosted in San Diego. Phil met with company leaders to: present background information on CLN2, the benefits of working on CLN2 as a disease target for cell mediated therapies, and NBF's value in facilitating the obtainment of CLN2 reagents, academic collaborations, clinical program experience, and regulatory relationships. The company tentatively agreed to investigate CLN2 using their cell mediated technologies toward the development of therapeutic applications.

December-01

Phil attended a Cornell project status meeting in NYC. The project team updated Phil of each team's current status. The main focus of this meeting was to make strategy decisions on the best possible approaches to move the project forward toward the clinic. Key pre-clinical dosage and distribution studies are being performed. The results to these studies will define the remainder of the project. Clinical protocols and toxicity studies are being developed for early stage regulatory review. The drug manufacturing team has successfully manufactured several batches of vector and are also preparing for the initial regulatory review process.



December-01

The feasibility study that Cornell produced for the Nathan's Battle Foundation is published in the Journal of the American Medical Association (JAMA). This is a major scientific publication. The article abstract can be review by clicking [HERE](#).

Feburary-02

Nathan's Battle Foundation enters into an agreement with a biotech company to greatly expand NBF's high through-put drug screening program. This is a major project to screen several compound libraries (libraries include the FDA-2000 and the GNC libraries). NBF is the first and currently the only organization performing drug screening for CLN2. This screening will actually use Nathan's cells to screen drugs against. This therapy would introduce a drug compound into the body that could cross the blood brain barrier into the Central Nervous System of a patient to either enhance residual enzyme activity or remove the storage material that is harmful to the patient.

Feburary-02

The Indianapolis Ice, CHL professional hockey team, host "Pack The House" night at Conesco Fieldhouse to benefit Nathan's Battle Foundation. Nathan was able to go on the ice and perform a ceremonial "puck drop" to start the game on center ice. A new record of over 14,000 Ice fans were in attendance to support the Ice and local charities.

Feburary-02

Phil attends gene transfer project status meeting at the Weill Medical College of Cornell in NYC. The project update was extremely encouraging. For the first time, pre-clinical data using our specific vector/gene combination (AAV2-CLN2) demonstrate successful gene delivery into models. This data continues to support the hypothesis under which we work. The whole project team was very upbeat with this new data. Now that we have demonstrated gene delivery, the next steps are to perform dosage and distribution studies and scale up to larger models before moving to humans. The project is still on schedule.

Feburary-02

The Nathan' Battle Foundation works with a leading stem cell company and a major west coast University to assist in the coordination of applying new stem cell



technologies to NCL disorders. NBF will be supporting a project to evaluate these technologies on a NCL model.

March-02

Tricia and Phil have an EEG performed on PJ. They have a great deal of concern as PJ is having trouble with his vision, balance, and walking. The EEG was to evaluate potential seizure activity. PJ's EEG was abnormal and he is now placed on seizure mediation to help control this activity. PJ's innocence of the road in front of him give NBF even more power to continue the battle.

March - 02

Phil receives an update from two of the Canavan AAV2 gene therapy patient's mothers on their child's progress. These children were both injected with a similar gene therapy as the Cornell project's proposed therapy. The first mother stated "*...my child's latest report is great. She has new myelin all over her brain. This clearly correlates with clinical improvement. I am convinced that this study will be very positive...*". The second mother exclaimed, "*...my son is really doing well, he is still making gains in all areas. He is eating really well, and moving more, and overall just looks very healthy. His MRI is showing new myelin in 25 places in his brain, the doctor is seeing the same type of medical results for the other two kids as well. Also, his scores on neuro-assessments and neurological exams have improved and are higher than those of an untreated child...*". This data continues to support the realities of gene therapy for Batten disease.

March-02

Tricia and Phil take Nathan and PJ to Duke University to see one of the world's leading clinical experts on Batten disease. This expert will help consult the boys local physicians on the proper care for the boys. Clinically evaluating the children will help her have better insight in determining the proper "cocktail" of medications the boys will need. Getting the children the proper mediation is an ongoing struggle with no clear cut answers. Over the last several months, Nathan has been battling different issues and has been in and out of the hospital. The disease has also been showing it's symptoms in PJ.

March-02

Phil travels to the west coast to aid in the initiation of a new cell mediated therapy project. Phil met with the project teams from the academic group and the biotech



team to walk through the proposed work plan and to review the current progress. The initial data from this project demonstrates promising results in similar disease models. A detailed study of a NCL model is now underway.

April-02

Phil attends a Cornell project status meeting in NYC. The project is still progressing as we continue to demonstrate success of transferring CLN2 gene into the CNS of models. Dosage studies are being performed as the manufacturing team finalizes production techniques. Large model studies are now being initiated.

April-02

Phil visits Dr. Peter Lobel's laboratory at the Robert Wood Johnson Medical Center in N.J. on the Rutgers University campus. Dr. Lobel's lab is the world's leading CLN2/TPP1 enzyme scientific group. Dr. Lobel and Phil met to discuss the latest progress on enzyme delivery, model development, and NBF's therapy development projects. NBF is supporting the Lobel laboratories to further CLN2 protein research.

May-02

Mark Schultz benefit concert held for Nathan's Battle. The concert raised over \$20,000 for NBF. The concert was attended by near 1000 concert goers. Mr. Schultz announced that he will continue to raise funds for NBF throughout his tour and introduce his audiences to Nathan's Battle. NBF has given his song, "He's My Son", new meaning for him.

June-02

Nathan's Battle Family Run/Walk was another success. Supporters from all over attended this years walk to continue their support of NBF. The MOMs Club put on another great event.

July - 02

Max and Erma's held an all day benefit for NBF. This years event was very well attended and beat last years attendance records.

July-02

Phil attends a Cornell project status meeting in NYC. The project continues to progress as we prepare for large model studies to begin. Dosage and distribution



studies are being finalized in small models and the protocol development team will begin drafting the regulatory documentation.

July-02

Phil visited with a leading stem cell scientist to go over his latest finding. This leading scientist is preparing to perform preliminary studies on a NCL model for NBF. NCL studies are scheduled to begin within the next few months.

July- 02

The second Nathan and P.J.'s Ride was another success. The biker community showed their huge hearts as they participated in large numbers and raised near \$30,000. The ride was escorted by the Indianapolis Motor Speedway around the Circle of Downtown Indianapolis to Southside Harley Davidson for auctions, food, and music.

August - 02

Nathan's Battle Race For Life 4 mile Run/Walk was another top notch event. The organizers of this event did a tremendous job orchestrating this large scale event. Near 100 volunteers helped to ensure the success of this event. Over 300 participants pushed themselves to achieve personal best as they continued to show their support for NBF. One of the lead runners actually yelled Nathan's name as he ran the course to help motivate himself. Truly a spine tingling experience to have others draw strength from Nathan's spirit.

August - 02

Another first class golf tournament was held at the Nathan's Battle at Broadmoor Country Club Golf outing. This event had many corporate and local sponsors. Four golfers had a chance to win \$1 MILLION and a minimum of 1/2 was to be donated back to the foundation. Local media were in attendance to cover the event. Unfortunately, the golfers accuracy was not there to cash in on the chances but everyone in attendance had a great time. This event raised over \$31,000.

September - 02

Roche Diagnostics Inc. supports Nathan's Battle's fight against Batten Disease. Roche is a leading healthcare company with a uniquely broad spectrum of innovative solutions. For more than 100 years, Roche has been active in the discovery, development, manufacture and marketing of novel healthcare solutions. Roche



recognizes the importance of the research NBF is developing and as a responsible corporation actively involved in the community has recently supported our locally based international foundation focused on improving society by developing therapies for rare diseases. Roche and NBF will make a great partnership.

September - 02

The 4th Nathan's Battle Golf Outing was held at the Valle Vista Country Club. This event demonstrates the tremendous support the Milto family has from its closest friends and the community. The outing was very well attended with over 130 golfers and many corporate sponsors. The outing raised over \$10,000 for the fight against Batten disease. Just as important as the funds raised, the heartfelt support that the Milto's received helps them continue their fight. This support gives them strength to get through their family's daily struggles and strength to fight the war against Batten disease. Nathan and P.J. attendance at the event left many of the golfers with a sobering understanding of the cruel affects of the disease and the urgency and necessity of the ground breaking work of NBF.

Sep-02

Nathan's Battle Under the Big top 2 took place. Ringling Brothers & Barnum and Bailey Circus partnered with Nathan's Battle Foundation to hold a special benefit performance. This was a spectacular display of entertainment. The world famous circus made Phil and Tricia the honorary ring masters for the night. The Greatest Show on Earth was simply just that as Indianapolis demonstrated its tremendous support for NBF with attendance of over 10,000 at Conseco Fieldhouse.

October - 02

The Cornell CLN2 Gene Transfer project submits for Pre-IND approvals with the FDA. The Cornell project team reached a major milestone this month by submitting for Pre-IND (Investigational New Drug application) review with the Food and Drug Administration. Phil attended the Cornell project team status meeting in NYC to review the detailed Pre-IND design. This is the beginning of the final stages of the drug development process. Large animal studies and toxicity studies are the two major milestones left to accomplish before submitting for final regulatory approvals. If the FDA is supportive of the Pre-IND, the project team's "goal" is to reach human clinical trials by October 2003. Large animal studies begin in the first week of December 2002 with toxicity studies commencing in April 2003. In less than



12 months we could be saving children's lives. Even with this tremendous scientific news, funding is still our biggest obstacle. Cornell informed Phil that they will need \$100K/ month for the next 12 months. NBF's current funding will run out in February 2003 (As of Oct. 2002 NBF's remaining balance is \$400K).

November - 02

Phil was invited to attend his third straight advocacy breakfast meeting at the Society for Neuroscience conference in Orlando. NBF continues to be a cutting edge leader in rare disease therapy development and is sought to share their approach and accomplishments.

November - 02

The second Kiwanis Battle Run was held to support Nathan's Battle Foundation. The Kiwanis continue to show their support for NBF. Many members and volunteers worked hard to hold this event. Sponsors' support and the many participants demonstrated their overwhelming support of NBF. Another great event by the Kiwanis as they continue helping children with their mission and particularly ones in their own community.

November-02

Phil was invited to attend "The Neurobiology of Disease Workshop - Stem cells for Neurodegenerative Diseases" at the Society for Neuroscience conference by the workshop's organizing chairman. Phil participated in the day long cell mediated workshop with many of world's leading stem cell scientists. This workshop set the ground work for future studies of LINCL gaining much interest by scientific groups as LINCL proves to be a great disease target for moving cell mediated research toward clinical applications.

November-02

The Milto family attended a Mark Schultz benefit concert in Columbus Ohio for Nathan's Battle. NBF has expanded across the country in research and with many fundraising events. The concert was organized by NBF supports in Ohio and attended by other LINCL families. NBF is gaining more and more national and international support. Mr. Schultz gave a wonderful performance raising money and awareness for NBF. This concert was a moving experience for all that attended. Check Mark's web site to see his support "[on my heart](#)".



December - 02

The FDA accepts the Cornell CLN2 Gene Transfer project approach and gives the Pre-IND package a favorable review with minor modifications. The Cornell department Chairman stated, "This is a major leap forward". With the FDA's support, the project team can move quickly into the final stages of drug development.

December - 02

On December 2, 2002, the Cornell CLN2 Gene Transfer project begins large model and toxicity studies. This starts the final stages of the drug development process. Large animal studies and toxicity studies are the two major milestones left to accomplish before submitting for final regulatory approvals. The FDA was supportive for us to begin both studies concurrently to expedite the process.

January - 03

NBF receives more national exposure as The Learning Channel airs a story on the Milto's. The Learning Channel aired a version of CBS's Medical Mysteries show containing segments from the 48 Hours story.

January - 03

Phil attends a Cornell project status meeting in NYC. The Cornell team presents more promising data from long-term rat studies and the initial primate studies. The long term rat studies demonstrate exciting news in that the gene is expressing over many months. While the early primate data is even more promising than the team expected. These large animal studies will continue over the next several months with toxicity studies set to begin in March. The project is closing in on clinical trials.

February - 03

A Nathan's Battle dinner benefit was held. This event was another tremendous display of the overwhelming community support. Near 1,200 supporters attended this heartfelt event. The event was an incredible success raising over \$185,000.00 for the foundation. Supporters gave from their hearts knowing that they are making a difference while being inspired by the brave presents of Nathan and innocent smiles of PJ. The Milto's always have dreamed of having a family. Their dream is still about their family but it is now just to keep their family. This community and others around the world now share in the Milto's dream and soon they will be living their dream again.



February - 03

Nathan's Battle receives a letter from Cornell University outlining the projects successes, remaining steps and required funding needed to get to clinical trials. Cornell believes believe that given the over 22 months of data produced from this effort: including rodent distribution and expression studies, long-term rodent studies, initial non-human primate studies, and initial favorable FDA reviews, that if the biology continues to support our theory in the primates and if the regulatory climate is supportive a human clinical can be initiated once the necessary funding is obtained to perform the final few tasks to gain regulatory approvals.

March - 03

The Cornell gene transfer project begins non human primate toxicity studies. This is a major milestone for the project. The large animal toxicity studies are the final step in the drug development process. The results to these studies will help complete our application to the FDA to gain regulatory approvals to move to human clinical trials. Another major project milestone is in process.

March - 03

NBF's drug screening program begins performing PCR studies on the list of previously identified positive enzyme affecting compounds. These studies will definitively analyze the compounds to determine potential therapeutic benefit for CLN2 patients. NBF's earlier drug screening findings identified a group of FDA approved drugs that had an affect on the missing enzyme.

March - 03

The Nathan's Battle "Lift for Life" was held to raise funds for the foundation. This unique event raised funds as contestants competed in a weight lifting competition. Power Clean, Bench Press, Dead lift and 2 Man Dead events were held demonstrating amazing efforts of strength. NBF continues to get "stronger" with community support. One day we will all be as strong as Nathan and P.J.

March - 03

P.J. has surgery performed to have a feeding tube installed. The feeding tube was inserted to keep P.J. healthy and strong. This procedures will keep P.J. strong as he waits for a therapy to be developed



April - 03

NBF projects are featured presentations at the NCL World conference. Phil attends the International Congress on NCLs. The NCL-2003 world conference is attended by the world's leading experts in NCL research. This conference featured presentations on two of NBF's leading projects.

Our gene transfer project at Cornell was presented by Dr. Ron Crystal. The NCL researchers were impressed by the progress and sound data from our research. One of the leading researchers stated that with this type of data the project will definitely go to clinic.

A NBF initiated cell mediated project from Stem Cells Inc. also presented their amazing findings. STI's data is the most promising data ever produced in a NCL model. The data demonstrated the viability for this technology to be used to treat children clinically. STI is now mounting a clinical program to bring this therapy to patients. Formal meetings with the NIH and FDA are scheduled.

May - 03

Phil attends Cornell project status meeting in NYC. The Cornell team presented more promising data from the primate efficacy studies. The primate data meets the "Go" criteria defined with the regulatory agencies to move to humans. The primate toxicology studies began in March (the final major step). All other project tasks continue to move forward on schedule. The project is closing in on clinical trials.

June - 03

Phil is the Key Note Speaker at the Indiana Health Industry conference (www.ihif.org) held in the Indianapolis convention center. This conference was attended by over 600 life science professionals as part of the Indiana Life Sciences Initiative. These life sciences professional heard about the accomplishments of the Nathan's Battle Foundation. NBF is developing therapies as it's own "non-for-profit" biotech company just as the attending parties are hoping to accomplish. Phil shared NBF's approach and business strategies used to enable the drug development process. The underlining message brought to the group was the reason for such an initiative is for the patients that depend on their success. NBF humanizes the industry for what drives our biotech is Nathan and P.J. The presentation was acknowledge by a standing ovation by all who attended.



June - 03

The Cornell gene transfer project performs the final non human primate surgeries for the toxicity studies. These last animals are the final critical path task necessary to complete the large animal toxicity studies. These studies are the final step in the drug development process. The results to these studies will help complete our application to the FDA to gain regulatory approvals to move to human clinical trials. The project continues to progress toward the clinic.

July - 03

The Cornell gene transfer project holds a key CLN2 clinicians meeting to define patient evaluation criteria for the human clinical trial. CLN2 clinical markers and endpoints will continue to be refined for the upcoming human trials.

August - 03

The third Nathan's Battle Family Walk was another success. Supporters from all over attended this years walk to continue their support of NBF.

August-03

Nathan's Battle wins an award from Eli Lilly and Company. Phil received the award from the major pharmaceutical company for the pursuit of health care innovation. Phil was one of 17 winners out of a group of over 6000. Phil was nominated by the global procurement group from Eli Lilly and Comany.

August - 03

The Million Dollar Duck Race was held in downtown Indianapolis on the canal in White River State Park during the Taste of Indiana. This was a spectacular event attended by thousands of duck adopters. Everyone looked on with excitement as the ducks "raced" down the canal where winners won items like a new Saturn car, a hot tub and J.L. Johnson shopping spree. Several television station were in attendance to cover the exciting event.

August - 03

A First class golf tournament was held at the Nathan's Battle at Broadmoor Country Club Golf outing. This event was well supported by many return sponsors. Four golfers had a chance to win \$1 MILLION and a minimum of 1/2 was to be donated back to the foundation. These golfers were all very close to winning the prize. Three of the four were within 12 feet of the cup. One golfer's shot was tracking right toward



the hole but stopped just short. He said it was the ball selection that made it check-up. It was a great effort and all who attended had a great time.

September - 03

The 5th Nathan's Battle Golf Outing was held at the Hickory Stick Golf Course. This event demonstrates the tremendous support the Milto family has from its closest friends and the community. Outback Steakhouse was a major sponsor and catered the events dinner. The outing was very well attended with over 130 golfers and many corporate sponsors. Just as important as the funds raised, the heartfelt support that the Milto's received helps them continue their fight. This support gives them strength to get through their family's daily struggles and strength to fight the war against Batten disease.

September - 03

Ringling Bros. and Barnum & Bailey Circus held Nathan's Battle Under the Big Top. Ringling Bros. and Barnum & Bailey graciously approached Nathan's Battle to have a fundraising performance again this year. Ringling Bros. and Barnum & Bailey Circus donated portions of the proceeds to the Nathan's Battle Foundation for tickets sold during the benefit performance at Conseco Field house. Thousands came to enjoy the greatest show on earth and to support Nathan's Battle.

September- 03

The national award winning Nathan and P.J.'s Ride was held and it was another huge success. The organizing committee did an incredible job with this event. This event had more sponsorship and prizes than any previous event. The biker community showed their huge hearts as they participated in large numbers and raised over \$40,000. The Milto family will forever be indebted to the organizers of this event. An army of bikers spent a year organizing this event lead by Papaw and his right hand Melissa.

September - 03

The final large animal toxicology studies were completed in September. This milestone signifies the end of the drug testing process. The data will now be analyzed and prepared to be included in our submissions to the FDA. The project team will submit for regulatory approvals by December 2003. There are 4 agencies that must approve our trial. If the regulatory approval process goes well we could begin the HUMAN CLINICAL TRIALS in January 2004. The approval process could take



from 1 to 6 months. We are unsure how long the process will take. We are months away from saving lives!

October - 03

Phil attends Cornell project status meeting in NYC. The Cornell team presented recent data from the primate toxicology studies. The data from the toxicology studies demonstrated the drug is safe and can be used in humans. The human protocols and remaining data are being finalized for the regulatory submissions. All regulatory documentation will be submitted BY December 2003. Patient evaluations will start in January 2004. It is unknown how long the FDA and RAC approval process will take (could take from 1-6 months).

October - 03

Cornell agrees to allow Nathan's Battle Foundation to enter into a pledge agreement with the University to fund the actual clinical trial. Normally clinical trials require the funding secured before the work can begin but Cornell aids NBF by letting the Foundation pay the expenses over time based on a milestone driven funding schedule. Cornell demonstrates their continued leading role in genetic medicine by not delaying the trial and partnering with NBF to move forward. Funding is still the main issue and is desperately needed to treat these innocent children.

November - 03

Stem Cells Inc. is moving forward with a clinical program for Batten disease. The [company's](#) cell mediated technology has demonstrated strong efficacy data in INCL mice and they have committed to moving forward to the clinic. Key new leadership has been added to direct the program and significant financing has been raised by investors given the promising in vivo data. NBF continues collaborations with the company to aid in the advancement of their technology.

December - 03

Continued studies on CLN2 knockout mice (mice that have the disease) demonstrate our vectors clear the harmful storage in the mice brains. These studies are being performed by a major biotech company using our vectors in a collaboration with the Cornell team. These ongoing studies provide additional sound scientific data to support the use of our vectors to treat the disease. The vector has "worked" in the over 300 rodents, in the 40+ primates, and in the knockout diseased animals. It has



been tested on all drug development tools with tremendous success. It is now time to move to humans.

December - 03

Cornell's final study data was completed confirming the drug will work. The data demonstrated robust enzyme expression at an 18-month time point in the animals with no negative side effects. This data is extremely promising and is the first of its kind at an 18-month time interval.

December - 03

Phil meets with Cornell's imaging center director to discuss partnering with our clinical trial project. The imaging center at Cornell is a newly built multi-million dollar, state of the art facility with all the latest capabilities in the field (anatomical, functional, and spectroscopic imaging technologies). The director of the facility is excited about the opportunity to partner with the the project to provide imaging needs for patients in the trial. While in NYC, Phil was invited to lecture to medical students in a genetic medicine course at Cornell. The students were able to get real life experience with a rare disease and gain an understanding of NBF's efforts.

December - 03

Phil signs \$2.1 million dollar milestone driven pledge agreement with Cornell University to pay for the human clinical trial. The pledge allows the trial to begin without any delay and is based on Cornell's ability to satisfy treatment milestones. NBF must make quarterly payments of \$177,000 for the next three years starting January 2004. This is great news so that children will be treated immediately following regulatory approvals. Unfortunately, we do not have these funds secured and need to raise the required funds. We need help raising these funds. We have develop a cure and just need to pay to TREAT these innocent children.

January - 04

Gene transfer IND receives approval from RAC (Recombinant Advisory Committee). Receiving formal approval from the RAC is a major milestone and is a testament to the quality of data that has been produced over the last 3 years. The Cornell team has done a tremendous job developing the IND with quality data and an outstanding clinical plan.



January - 04

NBF's Drug Screening program validates three potential compounds that show promise in-vitro to enhance TPP-1 enzyme production. Next step is planning the in-vivo studies in KO animal models.

February - 04

The Indianapolis Business Journal recognizes Nathan's Battle's accomplishments with their prestigious 40 under 40 award.

February - 04

Nathan's Battle Foundation wins the Health Care Heroes Advancements in Health Care Category. This award was given based on the tremendous advancements NBF has made in novel treatment technologies. NBF was honored to be placed in the company of some of the country's leading physicians and medical professionals.

February - 04

The Gene Transfer Clinical Trial at Cornell receives FDA approval to begin treating humans with the new drug.

March - 04

Phil meets with Executive Hospital Director of New York-Presbyterian, The University Hospital of Columbia and Cornell, to discuss arrangements to fund the expenses associated with performing the clinical trial. The Director was supportive of the effort and offered to assist NBF by allowing for the Foundation to pay for the procedures at reduced rates.

March - 04

The Gene Transfer Clinical Trial at Cornell receives formal IBR approvals to begin the "Screening" protocol. Patients begin enrolling in the "Screening Protocol" for ultimately inclusion into the Gene Transfer Clinical Trial.

March - 04

Nathan and P.J. go to New York to participate in the "Screening Protocol". The screening protocol included a battery of tests and evaluations including a MRI. Both boys were in NYC for 3 days to participate with hopes of meeting the Clinical Trials inclusion criteria to be able to participate in the trial.



April - 04

The Gene Transfer Clinical Trial at Cornell receives final formal approvals from all regulatory levels to begin the "Treatment" protocol. Previously approved by the FDA.

May - 04

Phil attended the Lysosomal Diseases and the Brain Conference in Washington D.C. He was invited to help propel LSD's toward therapeutic applications. The focus of the conference was to move research from the bench to the clinic. Something in which NBF has first hand experience.

May - 04

Stem Cells Inc. publicly commits to moving their technology to the clinic for INCL and LINCL. Stem Cells Inc. is well positioned to move to the clinic by Q1 2005. NBF's efforts to get SCI involved with NCLs is producing measurable results. Their data has continued to be extremely promising and they have made some key hires to guide the program to the clinic.

May - 04

Genzyme, a major biotech company who focuses on lysosomal storage diseases, submits an abstract to the Society of Neuroscience demonstrating the use of our vector (AAV2cuCLN2) successfully impacts the disease in CLN2 knockout mice which have the disease. The abstract's title is: *Intracranial Gene Delivery of Human CLN2 Reduces Brain Pathology in a Mouse Model of Late Infantile Neuronal Ceroid Lipofuscinoses (LINCL)*. This abstract is authored by scientists from Genzyme, Cornell, Iowa, Robert Wood Johnson and supported by NBF. Just one of several successful studies being carried out with the CLN2 KO mouse and the above collaborators using our vector.

June - 04

NBF makes HISTORY. The human clinical trial begins. The first ever treatment for LINCL is administered to a child. The first child was treated with AAV2cuCLN2, the drug we have been developing for the last 3.5 years. This is a historical accomplishment which would not of been possible without all the supporters of NBF. Everyone who ever supported NBF in anyway should be proud of this initial accomplishment. This is a major step in winning the war against this disease. We are winning the battles to win the war.



June - 04

Stem Cells Inc. receives \$20 million in new equity financing. This infusion of new capital is one critical factor toward enabling them to initiate their first clinical trial in Batten disease in 2005.

June - 04

NATHAN GETS TREATED! Nathan participates in the human clinical trial at Cornell. Nathan does very well through the procedure. The procedure goes as planned. Nathan is a true Champion in more ways than one. This is a significant accomplishment for everyone involved.

July - 04

Nathan has his 14 day and 30 day check ups and is doing well. Nathan's 14 day check up was performed locally and his 30 day check was done back in NYC. Nathan remains very stable.

July - 04

P.J. GETS TREATED! P.J. participates in the human clinical trial at Cornell. The procedure goes as planned and P.J. does very well. P.J. is a very strong little boy. This is another major accomplishment for NBF. Focusing on winning the battles and the war!!!

August - 04

P.J. has his 14 and 30 day check ups and everything is as planned. The 14 day check was performed locally and the 30 day check up was done in NYC. P.J. is back to his pre-surgery condition, smiling and laughing often. Nathan also had his 60 day check up and everything is fine with him as well.

September - 04

The national award winning Nathan and P.J.'s Ride was held and it was another huge success. The ride committee did an exceptional job. The event was an all day celebration for Nathan's Battle. Over 800 motorcycles participated in the ride and well over 1100 people. This event had more sponsors, activities and prizes than any previous event. The Milto family continues to be forever indebted to the organizers of this event. The organizers were lead again by Papaw and his right hand Melissa. The ride raised over \$78,000 for the Foundation.



September - 04

Nathan had his 90 day check-up and P.J. had his 60 day check-up. Both boys are very stable and doing well!!

September- 04

The Nathan's Battle at Broadmoor Country Club Golf outing was held. This event was well supported by many returning sponsors. This was a great outing for everyone. The organizers did a tremendous job once again.

October- 04

The 4th child participates in the gene transfer clinical trial. The most severely affected child with Late Infantile Batten Disease undergoes the treatment procedure. The project team performs the procedure on this very severely affected LINCL child in hopes to determine the full scope of potential benefit in disease ranges of LINCL children. It is unknown how the child will respond with the treatment and if the disease progression is too far advanced for the "drug" to have time to benefit the child. This is another move forward in research with hopes to fully understand the potential benefits or limits of the treatment.

October- 04

P.J. had his 90 day check-up is still doing well. No change with this treatment is a positive and so far so good.

December- 04

Nathan goes to NYC to have his 6 month evaluation performed. This evaluation includes a MRI and MRS to better help evaluate the effects of the treatment on the CNS. Nathan's MRI shows No Change! Again, given the goals of the treatment to stop the progression of the disease, no change is a POSITIVE result, meaning if the brain doesn't show more degradation then the therapy may be working. MRS results will not be available for several weeks. Nathan continues to be a very happy boy.

January - 05

STEMCELLS, INC. Announces filing of Investigational New Drug (IND) for human neural stem cell transplant treatment for Batten Disease to the U.S. Food and Drug Administration (FDA). This Phase I Clinical Trial at Stanford would Be First-Ever Using Transplantation of Human Neural (Brain) Subject to approval, the Company plans to begin its first clinical investigation of its human neural (brain) stem cells



(HuCNS-SC – StemCells' proprietary neural cell therapy product) in Batten disease. If approved by the FDA, this would mark the first-ever FDA-approved clinical trial to use a purified composition of human neural stem cells as the potential therapeutic agent. On approval of the IND by the FDA, the study will be conducted at Stanford University Medical Center. NBF's efforts to get SCI involved with NCLs has produced another potential treatment for LINCL.

April- 05

The fifth child was treated in the gene transfer clinical trail at Cornell University. This child did very well. She was out of intensive care in a couple of days and was released from the hospital as scheduled, shortly after the procedure. This child completes the Severe rated children and now the team will move to less severely affected children.

June- 05

The sixth child was treated in the gene transfer clinical trail at Cornell University. This child was the first "Moderately" affected child to be treated. This child also did well with the procedure. The team is very excited to follow the progress of this "Moderately" affected child. The belief is the less affected the child is by the disease the more benefit the drug may have for the child.

July- 05

Nathan goes to NYC to have his 12 month evaluation performed. This is a clinical evaluation to monitor his overall condition and neurological status. The 12 month evaluation part of the trial to gather data to better help determine the effects of the treatment. Nathan's overall condition was viewed as no real change. No Change! Again, given the goals of the treatment to slow or stop the progression of the disease, no change is a POSITIVE result.

July- 05

P.J. goes to NYC to have his 12 month evaluation performed. The same clinical evaluations are performed on him as they were on Nathan. As with Nathan, P.J.'s overall condition was viewed as no real change. No Change! Again, given the goals of the treatment to slow or stop the progression of the disease, no change is a POSITIVE result.



August- 05

The Nathan's Battle at Broadmoor Country Club Golf outing was held. This event was well supported by many returning sponsors. This was a great outing for everyone. The organizers did a tremendous job once again.

September- 05

The seventh child was treated in the gene transfer clinical trial at Cornell University. This child was the second "Moderately" affected child to be treated. This child also did well with the procedure. The team continues to be very excited as they treat more "Moderately" affected children. They are very interested in monitoring the effects of the treatments on these children over time. The belief is the less affected the child is by the disease the more benefit the drug may have for the child.

October - 05

Stem Cells Inc. receives FDA approval to begin a Phase I human clinical trial of Neural Stem Cells to Treat Batten Disease. This is the first ever approved trial to transplant human neural stem cells in the brain. No other disease has ever been treated using neural stem cells and the first ever treatment will be attempted in Batten disease. [Click](#) for details.

November- 05

The eighth child was treated in the gene transfer clinical trial at Cornell University. This child was the third "Moderately" affected child to be treated. This child did very well with the procedure. This child was moderately affected but still has many faculties about her and for the most part would be a "normal" little girl. The goal for these treatments is to treat children that have not progressed so treating this little angel has everyone excited about her potential.

December- 05

Nathan goes to NYC for his 18 month follow up visit. The 18 month evaluation is the final short term evaluation point in the clinical trial protocol. The 18 month evaluation was 3 days of testing which included a MRI/MRS study. Nathan did very well with all the test and clinical evaluations. Nathan has thrived over the last 18 months gaining over 16 pounds and growing 4-5 inches. His clinical status remains stable and hopes for the future is that this stable status will continue. We hope and believe that we may have stopped or slowed the disease in the brain and the concern



for the future would be any potential downstream affects from pre-existing damage to his systemic neurological, pulmonary, or renal systems.

March - 06

P.J. goes to NYC for his 18 month follow up visit. The 18 month evaluation is the final short term evaluation point in the clinical trial protocol. The 18 month evaluation was 3 days of testing which included a MRI/MRS study. P.J. did well with all the test and clinical evaluations. His clinical status remains stable and hopes for the future is that this stable status will continue. We hope and believe that we may have stopped or slowed the disease in the brain and the concern for the future would be any potential downstream affects from pre-existing damage to his systemic neurological, pulmonary, or renal systems.

May - 06

Stem Cells Inc. receives hospital IRB approval from the Oregon Health & Science University to begin the trial at OHSU Doernbecher Children's Hospital in Portland, Oregon. Both clearance by the FDA and IRB were necessary to initiate the clinical trial. Subjects are currently being screened for inclusion into the clinical trail. The first patient is scheduled to be treated this Summer. This is the first ever approved trial to transplant human neural stem cells in the brain. No other disease has ever been treated using neural stem cells and the first ever treatment will be attempted in Batten disease.

June - 06

Cornell has developed a new gene therapy vector to treat Late Infantile Batten disease. This new vector, AAVrh10, has for the first time demonstrated in CLN2-KO mice tremendous clinical benefit. Diseased mice treated with this new vector are able to walk up and down a balance beam and hang on a "high wire" and climb across a "hire wire". Non-treated animals can not walk and fall off the balance beam. And non-treated animals can not grip or climb on the wire. Treated animals life span are also greatly increased over non-treated animals. This is the first time such remarkable clinical data has been demonstrated in animal models by any proposed therapy. Cornell has begun an effort to mount a clinical program for this new drug and hope to submit an IND to the FDA within the next 12 months.

November- 07

The initial AAV2-CLN2 gene transfer clinical trial is completed. The trial data



clearly showed that the treatment was effective and was a success. The gene therapy treatment demonstrated clinical improvements in the children based on the LINCL rating scale. Based on the scale, the treatment slowed or stopped the progression of the disease within the CNS. A tremendous amount was learned from the clinical and has positioned us to move the next trial. One main discovery was that we are on the correct tract with introducing the enzyme into the CNS via gene transfer. The new drug AAVrh10-CLN2 will get even more enzyme distribution through out the CNS and allow for more benefit for the patient as also demonstrated in the CLN2 knockout animals.

May - 08

The results to our gene therapy clinical trial were published in the Human Gene Therapy Medical Journal. The trial's data scientifically demonstrates that our gene therapy clinical trial was a success in slowing the progression of the disease as well as being safe. The publication proves our therapeutic approach as a safe and viable platform to treat other neurological diseases. The findings supports our therapy and further gives justification for our new version of the drug as it will be safe and expand upon the successes of our initial trial. As indicated before, our new version of the drug gets tremendous enzyme expression in animal models and demonstrates tremendous clinical benefits in these animals. The new drug has curative properties in the animal models. NIH or private funding is all that the new drug is waiting for in order to move forward to a new clinical trail.

May - 08

Our new drug (AAVhr10-CLN2) is ready and waiting to move forward to clinical trials. All pre-clinical data and toxicology data has been completed. The FDA has given preliminary support of the trial and now funding is the only thing stopping the treatment of children. Cornell has submitted for NIH funding but has been in an holding pattern for some time. Private funding or NIH fund would enable Cornell to move forward with this tremendously promising drug.