NF2 Compass

A Quarterly Advocure Online Newsletter

Formerly known as "Flutterby"

Advocure NF2 Inc. is a Working Advocacy Group, Liason, and 501 (c)(3) Public Charity for the NF2 International Community and NF2 Crew.

Our Mission ..... pg 1
NF2 in the News ..... pg 1
NF2ers in the News ..... pg 8
NF2 Weblogs ..... pg 9
Advocure advocating for NF2 research funding on CDMRP-NFRP ..... pg 10
Featured Extraordinary NF2er ..... pg 12
Dr. Marco Giovannini at HRI: interview with Advocure ..... pg 13
Fundraising ..... pg 16
NF2 Clinical Trials & Studies ..... pg 17
NF Symposiums or Conferences ..... pg 21
Some Pharmaceuticals of NF2 Interest ..... pg 21

Our Mission:

Advocure NF2 is dedicated to advocacy, and to strengthening efforts that expedite research contributing to systemic therapies to treat and eventually cure NF2.

Email: contact@advocurenf2.org
Web: www.advocurenf2.org

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How To Help

Advocure NF2 Inc. is a 501(c)(3) public charity. All contributions to Advocure NF2 Inc. are tax-deductible.

Thank You For Your Support!

NF2 In The News

Thank you for helping us **raise $100,000 for children's tumor research!**

We have committed the money to two major NF2 research projects this year.

AdvocureNF2 Funds Research - Having raised $100,000 in 2011 (100% of monies raised were directed to NF2 research), AdvocureNF2, Inc will soon be requesting submissions for the next batch of grants in the fall of 2012… Meanwhile, the 2011 awards went to **Dr. Brad Welling**, of Ohio State University (OSU), who is to develop a medical therapy for NF2 utilizing two novel small molecule compounds, AR-12 and AR-42, as well as to screen a library of pure, structurally defined natural compounds for potent growth inhibitory activity in schwannomas and meningioma. The other award was to **Dr. Marco Giovannini** at House Research Institute (HRI), who will be starting a Phase 2 clinical trial of RAD001 for NF2. Clinicaltrials.gov, study #NCT01345136.

NF Coalition lobbies Congress for FY13 NF research funding - AdvocureNF2 members John Manth (and family), as well as Barbara Franklin join forces with the *'NF Coalition'* in lobbying Congress for FY13 NF research funding at CDMRP-NFRP and NIH.

AdvocureNF2 members advocate and help direct NF2 research funding at the CDMRP-NFRP - From FY08 to present, Advocure members Sheila Heal, Barbara Franklin, and Rosemary Lee (among others) have participated as Consumer Reviewers at the CDMRP-NFRP to

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ensure that NF2 interests are represented on the NFRP. We are helping to direct both NF research and research funding, and to raise awareness about the devastation of this disease."

3rd NF2: State of the Art, International Conference - This meeting will focus on Epidemiology, Genetics and Natural History of NF2, NF2 surgery and radiosurgery, Auditory Rehabilitation and Animal models and preclinical and clinical trials…Restricted to doctors and scientists.

2012 NF Forum: June 8-10 in New Orleans - Save the Date! The Children's Tumor Foundation's annual NF Forum (for patients and families) will for the first time be held adjacent to the NF Conference.

2012 NF Conference: Open for Registration and Abstract Submission - The Children's Tumor Foundation's NF Conference will take place June 9-12, 2012 in New Orleans, LA. For more information, to register, or to submit an abstract, please click **here.** Restricted to doctors and scientists only.

Congressional Compromise Provides Funding for NF Research in FY12 - House and Senate negotiators have agreed to include $12.8 million for NF research in the 2012 Department of Defense budget...

Department of Defense Neurofibromatosis Research Program (NFRP); Funding Opportunities for FY12 - The NFRP is providing the information in this pre-announcement to allow investigators time to plan and develop applications. FY12 NFRP program announcements and general application instructions for the following award mechanisms are anticipated to be posted on Grants.gov in February 2012. This pre-announcement should not be construed as an obligation by the government.

Advocure interviews Dr. Marco Giovannini in 2011 on his ongoing NF2 groundbreaking research at HRI. - Last Spring, representatives of Advocure NF2, Inc. visited Dr. Marco Giovannini at the House Research Institute's Center for Neural Tumor Research. A plaque of Appreciation for HRI's continuing NF2 research was presented to Dr. Giovannini and his laboratory colleagues. The following is a summary of the conversation between Dr. Marco Giovannini and Advocure NF2's Roland Thoms and Sheila Heal... (Read the interview below).

Neurofibromatosis Type 2: Clinical Trial now on - A new treatment is currently under investigation for treating VS that result from NF2. Principle Investigator: Dr. M Giovannini is conducting a Phase II clinical trial on RAD001 at HRI; Clinicaltrials.gov study #NCT01345136. The purpose of the study is to determine if RAD001 treatment will shrink or slow the growth of the VSs in NF2 patients. Secondary objectives include determining if RAD001 treatment will improve hearing ability in NF2 patients. *(Editor's note: The other RAD001 trials for NF2 are, PI(s): Dr. M Karajannis at NYU; study #NCT01419639, and Dr. M Kalamarides in Paris; study #NCT01490476).*

Support Federal Funding for FY13 NF Research - Your voice is critical to this effort! Now is the time to contact Congress to request support in FY13 for NF Research. Please take action now to secure this essential funding - The *'Dear Colleague'* letter just went out to all House offices requesting support for $16 million in funding for the Army's NF Research Program (NFRP) in the FY13 Defense Appropriations bill and inclusion of report language on NF research at the National Institutes of Health (NIH) in the FY13 Labor-HHS-Education Appropriations bill. Please contact members of the House and ask them to add their name to these letters! ***The deadline to sign the letters is March 13th.*** For additional guidance, please see NF Inc's new **Advocacy webpage.**

Consensus recommendations for current treatments and accelerating clinical trials for patients with neurofibromatosis type 2 - ... In June 2010, representatives of the international NF2 research and clinical community convened under the leadership of Drs. D. Gareth Evans (University of Manchester) and Marco Giovannini (House Research Institute) to review the state of NF2 treatment and clinical trials. This manuscript summarizes the expert opinions about current treatments for NF2 associated tumors and recommendations for advancing therapies emerging from that meeting. The development of effective therapies for NF2 associated tumors has the potential for significant clinical advancement not only for patients with NF2 but for thousands of neuro-oncology patients afflicted with these tumors…

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Afinitor (RAD001) – Anti-Cancer Therapy - Afinitor (everolimus), formerly known as RAD001, is a macrolide antibiotic derived from rapamycin that is being investigated by Novartis as a potential treatment for various solid tumours, including advanced kidney cancer...

Annette Bakker, Ph.D. Appointed Senior Vice President of Research and Drug Development - The Children's Tumor Foundation has appointed Annette Bakker, Ph.D., to the newly-created position of Senior Vice President of Research and Drug Development...

Children's Tumor Foundation Funds Two New DrugDiscovery Initiative Awards, and Increases DDI Award Levels for 2012! CTF is delighted to announce the recipients of the Drug Discovery Initiative Awards from our fall 2011 round. Dr. Toshifumi Tomoda of the Beckman Research Institute receives a $15,000 in vitro Award to study autophagy-inducing compounds as candidate therapeutics for NF2. Dr. David Little of the University of Sydney receives a $30,000 in vivo Award to study MEK inhibition as a therapeutic approach in mouse models of NF1 related tibial pseudarthrosis... CTF is also pleased to announce that for 2012 we are significantly increasing DDI Award levels! We now offer $25,000 for in vitro DDI Awards, $50,000 for in vivo DDI Awards, and $75,000 for Advanced DDI Awards. There are two DDI Award deadlines in 2012: February 28th and August 31st. No preliminary data is required for DDI Award applications, and cutting-edge ideas are encouraged. If you have any questions about the DDI program, please contact Min Wong at CTF.

2012 Young Investigator Awards is now open! - The application process for the 2012 Young Investigator Award program is NOW OPEN! Please note the deadlines for the pre-application and full application. Please be sure to carefully read the guidelines of the application process...
APPLICATION PROCESS DEADLINES:
January 27, 2012: Pre-Application Due.
February 24, 2012: Invite to submit Full Appl. will sent via email.
April 2, 2012: Full Application Due.

Announcing CTF's 2011 Young Investigator Award Recipients
The Children's Tumor Foundation is delighted to announce the funding of SIX Young Investigator Awardees for the 2011 round. The recipients include three postdoctoral awardees and three graduate students; three focused on aspects of NF1 including tumors, bone dysplasia and learning disabilities; and three focused on NF2 or schwannomatosis. Four awardees are US-based and two are international. Details of the Awards, as well as Past Awardees are listed.... The 2011 Young Investigator Awardees for NF2 are:
1. **Miriam Smith, Ph.D.**, University of Manchester, United Kingdom. Project: Identification of novel genes predisposing to schwannomas and meningiomas by exome.
2. **Jianzhong Yu, Ph.D.**, Johns Hopkins University. Project: Molecular genetic characterization of the Merlin tumor suppressor protein complex.
3. **Alejandra Petrilli Guinart**, University of Central Florida. Project: Investigating a new drug target for NF2.

New procedure repairs severed nerves in minutes, restoring limb use in days or weeks - American scientists believe a new procedure to repair severed nerves could result in patients recovering in days or weeks, rather than months or years. The team used a cellular mechanism similar to that used by many invertebrates to repair damage to nerve axons. Their results are published today in the Journal of Neuroscience Research...

New RNA-Based Therapeutic Strategies for Controlling Gene Expression - Small RNA-based nucleic acid drugs represent a promising new class of therapeutic agents for silencing abnormal or overactive disease-causing genes, and researchers have discovered new mechanisms by which RNA drugs can control gene activity. A comprehensive review article in Nucleic Acid Therapeutics, a peer-reviewed journal published by Mary Ann Liebert, Inc., details these advances...

Researchers follow a path to a potential therapy for NF2, a rare tumor disorder - The proteins that provide cells with a sense of personal space could lead to a therapeutic target for Neurofibromatosis Type 2 (NF2), an inherited cancer disorder, according to researchers at The Wistar Institute. Their findings,

which appear in the April 12 issue of the journal Cancer Cell, could have profound implications for NF2 and related cancers, such as mesothelioma...

Genetic 'green light' could lead to a cure for hundreds of ills - Scientists have altered the 'code of life' in a breakthrough that could lead to cures for hundreds of devastating diseases. The discovery, hailed as 'the new miracle of modern medicine' could lead to ways of ending the symptoms and the pain caused by up to a third of genetic conditions...

Effective neurofibromatosis therapeutics blocking the oncogenic kinase PAK1 - NF1 gene product is a RAS GTPase activating protein (GAP) of 2,818 amino acids, which normally attenuates the GTP-dependent signal transducing activity of the G protein RAS. Dysfunction of this GAP leads to the abnormal activation of RAS, and eventually an oncogenic kinase called PAK1 as well. NF2 gene product is "Merlin" which directly inactivates PAK1. Thus, dysfunction of Merlin causes the abnormal activation of PAK1...

NIH Clinical Collection - The NIH Clinical Collection (NCC), a plated array of approximately 450 clinically tested compounds, is now available for distribution through the above website.

Dry Eye Treatment - ... Which Artificial Tears should you use? We list below guidelines that may be helpful in treating dry eyes. The guidelines listed below are derived from a review of the published literature...

Preparing for Precision Medicine - ... Had Ms. H.'s cancer been diagnosed before 2004, her oncologist might have offered her a treatment to which about 10% of patients have a response, with the remainder gaining a negligible survival benefit and experiencing clinically significant side effects. But her diagnosis was made in 2011, when her biopsy tissue could be analyzed for a panel of genetic variants that can reliably predict whether the disease will respond to treatment. Her tumor was shown to be responsive to a specific targeted agent, whose administration led to a remission lasting almost a year; her only side effect was a rash...

Tailored gene therapy 'could help brain cancer treatment - Personalised gene therapies could significantly increase the survival rate among brain cancer patients, a new study has found... According to Macmillan Cancer Support, a small number of brain tumours are caused by genetic conditions such as neurofibromatosis type 1 and type 2, tuberous sclerosis and syndromes such as Li-Fraumeni and Von Hippel-Lindau.

Commencement Of Patient Enrollment For A Phase 3 Dry Eye Syndrome Study - Denali Concrete Management Inc. (OTCBB: DCMG) announced that it has commenced patient enrollment for a phase 3 clinical study of the safety and efficacy of CF101, daily administered orally, in patients with moderate-to-severe Dry Eye Syndrome. This multi-center clinical trial is conducted in the United States, Europe and Israel. The randomized, double-masked clinical trial will include 231 patients who will be randomized to receive 2 doses of CF101 and Placebo, for a period of 24 weeks. The primary efficacy endpoint will be complete clearing of corneal staining...

IBM Contributes Data to the National Institutes of Health (NIH) to Speed Drug Discovery and Cancer Research Innovation - IBM (NYSE: IBM) today announced it is contributing a massive database of chemical data extracted from millions of patents and scientific literature to the National Institutes of Health. This contribution will allow researchers to more easily visualize important relationships among chemical compounds to aid in drug discovery and support advanced cancer research...

ADA Business BRIEF: Communicating with People Who Are Deaf or Hard of Hearing in Hospital Settings - People who are deaf or hard of hearing use a variety of ways to communicate. Some rely on sign language interpreters or assistive listening devices; some rely primarily on written messages. Many can speak even though they cannot hear. The method of communication and the services or aids the hospital must provide will vary depending upon the abilities of the person who is deaf or hard of hearing and on the complexity and nature of the

communications that are required. Effective communication is particularly critical in health care settings where miscommunication may lead to misdiagnosis and improper or delayed medical treatment.

Hot Pink Tumors - Gliomas glow hot pink after patients take experimental drug 5-Aminolevulinic Acid...

Patient Information, Neurofibromatosis Type 2 (NF2) - This leaflet is for patients and relatives who attend the neurofibromatosis type 2 (NF2) clinic in Cambridge...

Neurofibromatosis Working Group at MD Anderson - The Neurofibromatosis Working Group is a collaborative effort between the departments of Neurosurgery, Investigational Cancer Therapeutics and Neuro-Oncology. Our aim is to provide outstanding care for patients with neurofibromatosis and to perform cutting-edge research leading to new treatments for these disorders...

Watch the NF2 webinar with Scott Plotkin, MD - If you were not able to attend our NF2 webinar with guest presenter Scott Plotkin, MD, you can watch it here! You will need windows media player to view...

Stem Cells and Regeneration of the Auditory Nerve - Overview: Cochlear implants function by electrically stimulating auditory neurons in the absence of hair cells, to enable hearing in severe to profoundly deaf individuals. The efficacy of this device therefore depends on a critical number of surviving auditory neurons. Stem cell transplantation therapy is emerging as a potential strategy for auditory nerve rehabilitation, as differentiated stem cells may provide a source of replacement auditory neurons to the deaf cochlea...

Regeneration of human auditory nerve. In vitro/in video demonstration of neural progenitor cells in adult human and guinea pig spiral ganglion - Abstract: The results suggest that the mammalian auditory nerve has the capability for self-renewal and replacement. Transplantation of progenitor cells together with established means to induce neural differentiation and fiber growth may facilitate strategies for better repair and treatment of auditory neuronal damage...

How to spot bogus research. - The words "clinically proven," loved and abused by infomercials and health-store potions, no longer carry the same weight they once did...

Project Endeavor Provides High-Speed Internet Service for Deaf and Hard Of Hearing - Qualified deaf and hard-of-hearing individuals can connect to the Internet through Project Endeavor's discounted Internet packages, which include discounted service plans and free video communications equipment. Project Endeavor also offers videos that demonstrate the benefits of using the Internet, in both text and American Sign Language (ASL)...

Weight Loss & Cachexia... - ...Cachexia is a clinical wasting syndrome. Symptoms include weakness and a marked and progressive loss of body weight, fat, and muscle. Anorexia and cachexia frequently occur together; however, cachexia can occur in individuals who are ingesting adequate calories and protein but who are not absorbing nutrients well....

Clinical Trials for regenerating muscles in humans are soon to start... - Scientists have regenerated functional muscle tissue in mice, opening the door for a new clinical therapy for major muscle trauma. The team used a novel protocol to coax human muscle cells into a stem cell-like state and grew the reprogrammed cells on biopolymer microthreads. Surprisingly, the micro...

The Inhibitory Effect of Honokiol, a Natural Plant Product, on Vestibular Schwannoma Cells. - ...CONCLUSIONS: Honokiol, a low molecular weight natural product, inhibits cell proliferation and promotes apoptosis in schwannoma cells by targeting the ERK pathway. Our data suggest that honokiol can be evaluated as a chemotherapeutic agent for VS.

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Get up to 75% off on medications you use everyday. - Get your pharmacy card and start saving up to 75% on thousands of prescriptions drugs you use everyday... The Pharmacy Discount Card is a FREE, pre-activated card that offers discounts on prescriptions that range from 0%-75% depending on the drug and location. The use of the discount card, is just like shopping at a discount store. The products are the same, but the pricing is different...

NIH Early Independence Awards - January 30th Deadline! - The National Institutes of Health (NIH) has announced a funding opportunity for the NIH Director's Early Independence Awards for junior investigators wishing to "skip the post-doc" and immediately begin independent research. Budgets may be up to $250,000 in direct costs per year, for up to five years...The deadline for submitting Early Independence Award applications is January 30, 2012 with Letters of Intent due by December 30, 2011.

NF2 mutation screening (NCG referrals) – clinical pro-forma - Central Manchester and Manchester Children's University Hospital (in the UK)... This form should accompany all requests for mutation screening of the NF2 gene. It is not necessary to complete this form for follow on tests where a mutation has already been identified within a family...

Cochlear Implantation in patients with Neurofibromatosis type 2 and patients with vestibular schwannoma in the only hearing ear - …neurofibromatosis type 2 (NF2) and patients with vestibular schwannoma (VS) in the only ... MRI axial and coronal view of neurofibromatosis type 2 patient ...

Lack of Neurofibromatosis Type 2 Gene Promoter Methylation in Sporadic Vestibular Schwannomas - ...Conclusions: Our study suggests that NF2 gene inactivation by promoter hypermethylation is a rare or very uncommon mechanism of NF2 gene inactivation in sporadic VS. Other mechanisms destabilizing the NF2 gene product, yet to be identified, might play a role in the genesis of VS apart from the loss or mutation of the NF2 gene.

AR-42 against Neurofibromatosis Type 2 and HTLV-1 - ...Type 2 Neurofibromatosis is a result of an autosomal-dominant gene mutation. Due to these genes various schwannomas and meningiomas are formed in vestibular parts. AR-42 when used in 500mM concentration causes inhibition of schwannoma cells formation. While at concentration 1.5 µM it causes inhibition of meningioma cells growth...

Avastin for Neurofibromatosis - ...Information is limited and restricted to case reports. VEGF blockade with bevacizumab improved hearing in some, but not all, patients with neurofibromatosis type 2 and was associated with a reduction in the volume of most growing vestibular schwannomas(Plotkin). Mautner reproted 2 cases of schwannoma regression onA vastin. Clearly this is very preliminary. There is an onging study: Bevacizumab for Symptomatic Vestibular Schwannoma in Neurofibromatosis Type 2 (NF2), NCT01207687.

Genetic and Epigenetic Alterations of the NF2 Gene in Sporadic Vestibular Schwannomas - Mutations in the neurofibromatosis type 2 (NF2) tumor-suppressor gene have been identified in not only NF2-related tumors but also sporadic vestibular ...

Team develops tumor destruction method that also creates immunity - Even when surgical tumor removal is combined with a heavy dose of chemotherapy or radiation, there's no guarantee that the cancer will not return. Now researchers at Tel Aviv University are strengthening the odds in favor of permanent tumor destruction — and an immunity to the cancer's return — with a new method of tumor removal...

MRF Announces First Biopharmaceutical Partnership with ENDECE Neural, LLC - We are most pleased to share with you the exciting news that the Myelin Repair Foundation has established an official partnership with ENDECE Neural, LLC, a biopharmaceutical company based in Wisconsin. This is the MRF's first major partnership with a biopharmaceutical company, and has been established to help expedite a myelin repair medicine as a possible clinical trial candidate...

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Roche (RHHBY) Warns of Counterfeit Avastin in the U.S. - The maker of the widely prescribed cancer drug Avastin is warning doctors and patients about counterfeit vials of the product that have been distributed in the U.S. Roche's Genentech unit said Tuesday that the fake products do not contain the key ingredient in Avastin, which is used to treat cancers of the colon, lung, kidney and brain. The drug is a huge money-maker for Roche, generating about $6 billion a year. A spokeswoman said the counterfeit drug has been distributed to health care facilities in the U.S., though it's unclear how many vials are in circulation or where they may be concentrated. The company is working with the Food and Drug Administration to track down the counterfeit vials and analyze their contents.

Neurofibroma Educational Series: Neurofibromatosis type 2: an update - The transcript included here is updated medical information by NYU NF2 Specialists, in regards to NF2 and include descriptions of the clinical features, advances and difficulties in molecular diagnosis, current treatment and controversies, simplified molecular pathways and drug development and the...

A step forward in effort to regenerate damaged nerves - The carnage evident in disasters like car wrecks or wartime battles is oftentimes mirrored within the bodies of the people involved. A severe wound can leave blood vessels and nerves severed, bones broken, and cellular wreckage strewn throughout the body – a debris field within the body itself...

New streamlined Advocacy webpage at NF, Inc- The carnage evident in disasters like car wrecks or wartime battles is oftentimes mirrored within the bodies of the people involved. A severe wound can leave blood vessels and nerves severed, bones broken, and cellular wreckage strewn throughout the body – a debris field within the body itself...

2012 CDMRP-NFRP Research Highlight: Defining Quality of Life in NF2 - Neurofibromatosis Type 2 (NF2) is a genetic disorder characterized by the development of bilateral vestibular schwannomas, benign tumors of the nerve that transmits sensory information from the inner ear to the brain. NF2 patients are also at risk for developing other types of nervous system tumors....

2008 CDMRP-NFRP Research Highlight: Using Modified Oncolytic Herpes Simplex Virus (HSV) to Treat NF2 Tumors - Schwannomas and meningiomas are tumors that form in neurofibromatosis 2 (NF2) patients by overgrowth of cells that support neurons in the nervous system. Such tumors can cause pain, paralysis, seizures, hearing loss, and death. Through his Fiscal Year 2003 Therapeutic Development Award, Dr. Robert Martuza and his colleagues Dr. Xandra Breakefield and Dr. Samuel Rabkin sought to develop safe, targeted gene delivery methods to treat and evaluate responses in Schwannomas and meningiomas...

Arno Therapeutics Receives Two Orphan-Drug Designations for AR-42 in Treatment of Central-Nervous-System Tumors - Arno Therapeutics, Inc. announced today that its investigational compound, AR-42, has been granted orphan-drug designation by the U.S. Food and Drug Administration for the treatment of meningioma and schwannoma of the central nervous system...

NF Scholarship Program; provided by NF Inc, NE - The NF Inc, Northeast Scholarship Program was established with funds raised at the Steps 2 Cure NF road races and walkathons. The scholarships are awarded to assist persons with Neurofibromatosis (NF) to continue their education after high school and pursue undergraduate degrees. Application Deadline is April 14, 2012...

In Reversing Motor Nerve Damage, Time Is of the Essence: 'Wait and See' in Injuries Like Carpal Tunnel Syndrome May Miss a Window for Recovery - When a motor nerve is severely damaged, people rarely recover full muscle strength and function. Neuroscientists from Children's Hospital Boston, combining patient data with observations in a mouse model, now show why. It's not that motor nerve fibers don't re-grow -- they can -- but they don't grow fast enough. By the time they get to the muscle fibers, they can no longer communicate with them...

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NF2ers in the News

Bill Wells, an NF Hero's Hero - On December 17, 2011, Bill Wells ran 31 miles and raised $45,000 in the Seth's Fat Ass 50k race in Springfield, MA, in honor of Celia LaBarbera who lives with **NF2**. Below is Bill's account of this experience...

Monusko shares story to encourage others to be their own health advocate - GAYLORD - Jennifer Monusko, 35, has a medical disorder so rare that most people have never heard of it. Its name is **neurofibromatosis type 2 (NF2),** and it only affects one in about 25,000 people. At this point in time there is no cure...

Can you hear the silence? - Hearing Link - Fred Suter says 'Can you hear the silence? I can. Always. I've been deafened since I was 17 due to the disease **Neurofibromatosis Type 2 (NF2)**, and since then live in complete silence. What proved at first an enormous strike in life, I have now found ways to cope with it…

Rebuilding my life - with NF2 - Hearing Link - My name is Natalie. I'm 24 and I live in Manchester. I have **Neurofibromatosis Type 2 (NF2)**. I became completely deaf two years ago as a result of two brain tumours on the hearing nerves. Although I had always known that it was likely I would become deaf, I put it to the back of my mind. I don't think I actually believed that it would happen...

Challenge USA - Hearing Link - My name is Jessica Cook. I am 21 years old and I live in the UK. This article is about my traveling experience on a six week camping trek around the USA in September/October last year, from the point of view of someone who is hearing impaired... I have a genetic condition called **Neurofibromatosis Type 2 (NF2)**...

Hearing loss doesn't stop FMU grad - FLORENCE - Jonathan Smith is like any early-20s college graduate. He's looking for a job. Smith graduated from Francis Marion University in December with a degree in Management Information Systems. But his path to the diploma nearly stopped before it could begin in the summer before his freshman year. "I noticed my hearing dropped in my left ear," said Smith. His mother recommended they see a specialist, and an MRI revealed he had **neurofibromatosis type II,** or brain tumors on his auditory nerve and pressing against his brain stem. Two of them. Smith said the disease causes tumors to form on any nerve in the body…

NF1 and NF2 - Inspire forum, NF Inc - Hello everyone, I'm new around here - my son, 11yo, has recently been diagnosed with **NF2**. As **NF2** have been put together on this forum. Apparently (from the little I've heard/learned/read) they are two very different conditions and information that applies to one condition is irrelevant to the other. The only reason they've been put together is that they have such a similar name (purely due to the common issue of tumours of the nerves). Does anyone else with **NF2** find it complex reading through posts about NF and then realising it's NF1 that's being discussed, not **NF2**? …

Teen's illness can't stand in the way of music - The State Journal-Register - Eighteen-year-old Andrea Heath is at war. Just three years ago, she decided she would fulfill her young life's goal of writing music to accompany the lyrics she had spent much of high school penning. She wanted to share them with her friends and fans, but most of all she wanted to hear the music, too. Andrea suffers from a disease called **NF2**, which causes multiple tumors to grow inside her body. Diagnosed in 2005, the Springfield High School graduate's condition is characterized by multiple tumors on the cranial and spinal nerves…

Resident anticipates regaining his hearing - Imperial Valley Press - El Centro resident Miguel Duarte's resume says he is tri-lingual: He speaks English, Spanish and American Sign Language. "I am profoundly deaf," Duarte said with his high-pitched voice revealing a slight Mexican accent. Everything started when he was 18, he said, "that's when I started getting sick." Dizziness, headaches, lack of balance and a ringing in the ears forced Duarte to visit a doctor. "I didn't know what was wrong with me," he said, and after several studies he was diagnosed with **neurofibromatosis type 2**...

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Jessica Stone update - MUSKEGON, MI. (WZZM) - … It's been three years since Jessica made the decision to lose her hearing in order to save her life. A tumor caused by her **neurofibromatosis II** was growing on her brain stem removing it would mean silencing her world, a choice she willingly made, but one she knew wouldn't cure her…

A holiday story about the meaning of perseverance, and its role in success - …Elchonon Hellinger, 26, of Miami Beach could easily be the Dickensian subject of a holiday story about someone living with a serious, debilitating illness. Since infancy, he has suffered from **Neurofibromatosis Type 2**, which causes the continuous growth of benign tumors — a malady that affects one in every 60,000 people…

Republican sportswriter to run 50K race as $50,000 fund-raiser for Wilbraham girl with rare form of cancer - MassLive.com - Bill Wells, a sportswriter at The Republican, is running Seth's Fat Ass 50K Dec. 17 in hopes of raising $50,000 for research toward **Neurofibromatosis 2** in honor of Celia LaBarbera.

Running For Celia - SPRINGFIELD, MA. (ABC40) - Celia LaBarbera is just seven years old, but she's endured 17 surgeries so far - removing tumors from her brain, spine and torso… She's been diagnosed with **Neurofibromatosis Type 2** - a rare and deadly type of cancer...

Republican sportswriter runs 50K race as fund-raiser for Wilbraham girl - MassLive.com - We made it. I'm not quite sure how, but we made it. Saturday morning at Forest Park, I entered a 50K race as a $50,000 fund-raiser in honor of Celia LaBarbera, a 7-year-old girl from Wilbraham who has **Neurofibromatosis 2**, which is a rare type of cancer which has no known cure...

All In The Family At Windsor Town Hall - The Hartford Courant - Larry LaBarbera has been the town's assessor only for about six months, but he knows that his fellow employees consider him to be a part of the family — even if some of them haven't even met him yet. That became evident to him late last week when he learned that a number of them had come together on short notice to donate about $1,000 to the Children's Tumor Foundation. The oganization works to fund treatment and research for a rare form of cancer, **neurofibromatosis 2**, which struck his now 7-year-old daughter, Celia, when she was just a few months old.

Counting down to the New Year: 2011 - A year in headlines - Morning Star – July: … Ashley's Ride, an event honoring the memory of local resident Ashley Nicole Sexton featuring a pig roast, auction and six-hour motorcycle ride took place for the fourth year in a row July 23, raising $20,000 toward the research of **Neurofibromatosis type 2**, which Sexton suffered from…

Division Student Fights Neurofibromatosis in Daytona - Bailey Gribben is a 9th grader at Division Ave High School and is out fundraising for the Children's Tumor Foundation (CTF) to help advance research towards a cure for **Neurofibromatosis (NF)**, a disease he knows all too well...

NF2 Weblogs

Amber - *Hope4Life*
Allyson - *Allyson's Hope*
Anne - *One-Hundred-Forty-Point-Six Miles to help cure NF*
Cindy - *Things Fall Apart*
Girish - *Glad to Hear*
Holly - *Never Giving Up Hope*
Jacob - *Learning to make lemonade...*
Jamie - *anomalous adventures, existence in liminal spaces*
Jessica - *Life Inspires Me*
Johnna - *40 and On*
José - *terapia*
Katie - *BionicKatie*
KC - *SO BE IT...*
Leah - *Run4Leah-CureNF*
Olivia - *The Fabulous Running Mommy*
Rebecca - *NF2 Odyssey*
Shanna - *Living a Life Based on Hope & Faith*

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Advocure advocating for NF2 research funding in CDMRP-NFRP

From FY08 to present, **AdvocureNF2** members have participated as Consumer Reviewers at the CDMRP-NFRP to ensure that NF2 interests are represented on the NFRP. Directing both research and research funding, and to raise awareness about the devastation of this disease.

FY11

Sheila Heal – Advocure member who served on the NFRP Consumer Review Panel, and **Catriona Miller** – NF2 community member nominated by Advocure to serve on the NFRP Consumer Review Panel in FY11.

Neurofibromatosis advocates Sheila Heal and Catriona Miller recently participated in the evaluation of research proposals submitted to the Neurofibromatosis Research Program (NFRP) sponsored by the U.S. Department of Defense. Sheila Heal and Catriona Miller were nominated for participation in the program by **Advocure NF2, Inc.** As consumer reviewers, they were full voting members, along with prominent scientists, at meetings to determine how the $16 million appropriated by Congress for Fiscal Year (FY11) will be spent on future Neurofibromatosis research.

Consumer reviewers are asked to represent the collective view of Neurofibromatosis survivors and patients, family members, and persons at risk for the disease, when they prepare comments on the impact of the research on issues such as disease prevention, screening, diagnosis, treatment, and quality of life after treatment. Commenting on serving as a consumer reviewer:

Sheila Heal: *"It's a privilege to serve as a representative for the NF community and work with the impressive assemblage of scientists, doctors, clinicians and administrators. In learning the CDMRP process, I further recognize and appreciate the scientists' and institutional investment required for effective proposal development. This funding and research is critical to the future of NF patients and their families."*

Catriona Miller: *"Participating in the CDMRP-NFRP review panel was an inspiring experience. The review panel was full of energy, enthusiasm, and great ideas. Scientists, clinicians, and family members critiqued each grant as equals. Successes in recent years with growth factor inhibitor drugs have rejuvenated hope and interest in NF2 research."*

Consumer advocates and scientists have worked together in this unique partnership to evaluate the scientific merit of Neurofibromatosis research proposals since 1996. To date, more than 49 consumer reviewers have served on Neurofibromatosis panels alongside scientists in the review process. Colonel Jeffrey C. Leggit, M.D., Director of the Congressionally Directed Medical Research Programs (CDMRP), expressed his appreciation for the consumer advocates' perspective in the scientific review sessions. "The Consumer Reviewers on each panel are instrumental in helping the scientists understand the patient's perspective and provided valuable insight into the potential impact of the proposed project. They bring with them a sense of urgency and remind all of the human element involved in medical research."

There were 83 neurofibromatosis research applications reviewed for 2011 fiscal year funds. Scientists applying propose to conduct innovative neurofibromatosis research aimed at the elimination of neurofibromatosis. The NFRP fills important gaps not addressed by other funding agencies by supporting groundbreaking, high-risk, high-gain research while encouraging out-of-the-box thinking.

FY10

Barbara Franklin – Advocure member who served on the NFRP Consumer Review Panel – *Excerpt from the **FY10 NFRP Program Booklet**, pg 7.*

Barbara Franklin, of **Advocure** - an international grassroots advocacy group seeking treatment options and supporting the NF2 community - has served as a Consumer Peer Reviewer for the NFRP since FY07. When Barbara's son, Adam, was 10 years old, he was diagnosed with NF2, and since then, has undergone a number of brain surgeries that have left him with diminished hearing and vision. He is now 26 and, Barbara reports, doing well. He is still closely monitored for persistent brain and spinal tumors but lives life with a "joie de vivre that is unmatched—and a positive attitude that has helped him achieve great things." Of her experience in working with the NFRP over the years, Barbara reflects, *"This program is one of the most important—if not the—most important aspect of NF2 research. As such, I have committed myself to being a part of it as often as I can. There's no doubt there's work to do, but it is so rewarding to see the incredible breakthrough concepts that researchers propose, as well as the amazing devotion that all participants - consumers and scientists alike - give to this program. I have watched it grow since its inception and it only gets better."*

FY09 & FY08

Rosemary Lee – Advocure member emeritus who served on the NFRP Consumer Review Panel.

Neurofibromatosis advocate Rosemary Lee recently participated in the evaluation of research proposals submitted to the Neurofibromatosis Research Program (NFRP) sponsored by the U.S. Department of Defense. Rosemary Lee was nominated for participation in the program by **Advocure NF2, Inc**. As a consumer reviewer, she was a full voting member, along with prominent scientists, at meetings to determine how Congress' FY08 appropriation of $8 million will be spent on future Neurofibromatosis research.

Consumer reviewers are asked to represent the collective view of Neurofibromatosis survivors and patients, family members, and persons at risk for the disease, when they prepare comments on the impact of the research on issues such as disease prevention, screening, diagnosis, treatment, and quality of life after treatment. Rosemary Lee was one of 7 consumer advocates who participated in the August 2008 peer review meetings and provided comments and scores for research proposals.

Consumer advocates and scientists have worked together in this unique partnership to evaluate the scientific merit of Neurofibromatosis research proposals since 1996. To date, more than 35 consumer reviewers have served on Neurofibromatosis panels alongside scientists in the review process. Captain E. Melissa Kaime, M.D., Director of the Congressionally Directed Medical Research Programs (CDMRP), expressed her appreciation for the consumer advocates' perspective in the scientific review sessions. *"They have provided valuable insight into funding decisions and helped the scientists understand the consumers' perspective of innovative research. Likewise, the consumer advocates have been enriched by learning more about Neurofibromatosis through discussing proposed research with scientists and seeing the future hopes of successful research."*

More than 65 Neurofibromatosis research proposals will be reviewed for FY08 funds. Scientists applying propose to conduct innovative Neurofibromatosis research aimed at the elimination of Neurofibromatosis. Proposals were solicited across all disciplines, including basic, clinical, social, and psychosocial sciences, as well as public health, economics, quality of life, alternative therapies, occupational health, nursing research, and environmental concerns.

More information about the Department of Defense Neurofibromatosis Research Program (NFRP) is available at the Website: **http://cdmrp.army.mil.**

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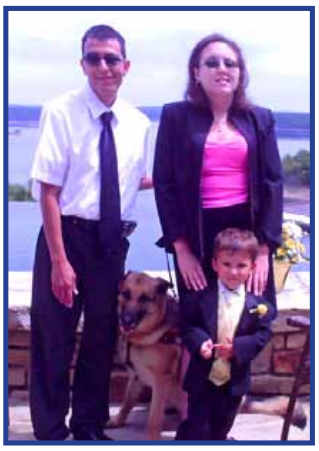
NF2 Compass
A Quarterly Advocure Online Newsletter
Formerly known as "Flutterby"

Extraordinary NF2er — Holly Alonzo

By: Holly Alonzo



Holly's husband Edward, Edward's guide dog Andre, Holly, and their son Isaiah

Two years ago, my already darkened world was plunged into silence. At the age of twenty-five, I am now completely deaf, totally blind, and severely physically impaired. All because of NF2. As a child, neither my parents nor I had heard of the disease. If we had, maybe we would have caught the signs before things got so bad for me.

I was born "normal." I was just another beautiful baby girl with two loving parents. I always had some vision and balance problems as a child. Then my hearing in my right ear started dropping, and tinnitus drove me nuts. When I was thirteen, I was constantly losing my balance and having episodes of blurry vision. Sometimes my vision would even black out. I went to the emergency room and had an MRI performed. A very large tumor was found on my brainstem. Emergency surgery was scheduled, and I was diagnosed with NF2.

After my first brain surgery, I woke up blind. The right side of my face was paralyzed and I wasn't able to swallow. I had extensive therapy to regain the ability to eat solid foods, walk, and regain my smile. I had to learn braille, and how to get around on my own using a white cane. I worked with a mobility instructor twice a month until I learned to be independent again.

I had a few more tumors removed soon after that—some from the brain and some from the cervical spine. Although it was rough, I just tried to stay strong. Thankfully, my loving parents were always there to help me through it. I had lost the hearing in my right ear around the time I was diagnosed with NF2. Despite it all, I lived as normal of a life as possible. When I was twenty years old, I was pregnant with my son. I had no idea that pregnancy could affect my tumor growth. Two weeks after I delivered my son, I found out that my left vestibular schwannoma (VS) had doubled in size during pregnancy. This was not good news since it was my only hearing ear. We held off on surgery and continued to watch and wait. Since I had already lost hearing in my right ear, I had the right VS removed and the surgeons attempted to place an auditory brainstem implant (ABI). Sadly, the ABI placement was unsuccessful during that surgery. I was terrified. I knew then that I would one day be totally deaf and blind, and that was something I couldn't even begin to imagine.

I already knew basic sign language, but I began trying to learn more signs. I just spent as much time as I could with my son enjoying the sounds he made and his first words. Unfortunately, my left VS continued to rapidly grow. I waited as long as I could to have it removed, because I knew that after surgery all of my hearing would be gone forever. I was also trying to find a way that I could try for a second attempt at an ABI. My miracle came, and a lot of people supported me. Just in time, I flew to Los Angeles and had my five centimeter VS removed. I was having symptoms that alerted the doctors that it was a life-threatening situation at that point. By this time, my family had learned to finger spell and could communicate with me by signing into my hand. When I went into surgery, there wasn't much hearing left to lose, but the vertigo was very tough when I woke up. This time, the ABI placement was successful. That gave me comfort and hope. My family and husband were there for me throughout it all.

Since I have no vision, no hearing, and no working vestibular nerves, I have worse than terrible balance. I also have nerve damage in my right leg. The quad muscles are non-existent and it's a wonder I can even walk at all; but I try my best and just take one step at a time. I can't walk unassisted, or I will lose balance and fall.

I can communicate with those who sign to me in my hand and by reading braille using a deaf-blind communicator. My husband and parents help let me know what is going on around me. I can hear a few environmental sounds with my ABI. My son and I communicate absolutely fabulous together. He brings me all the joy in the world. I began showing him signs when I first started losing hearing, when he was an infant. When he learns to spell words and can finger spell to me the signs he doesn't know, communication will be so much easier, but for now he really tries and we are a good team.

Who knows how NF2 will affect me next. I know that even with all I have been through and lost, I am still lucky to be alive and get to enjoy all these blessings. I will just keep living life the best way I can—One day at a time and never giving up hope.

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Dr. Marco Giovannini at HRI:

Interview with AdvocureNF2, Inc.
By: Sheila Heal, AdvocureNF2, Inc

On May 25, 2011, representatives of Advocure NF, Inc. visited Dr. Marco Giovannini at the House Research Institute's Center for Neural Tumor Research. A plaque of Appreciation for HRI's continuing NF2 research was presented to Dr. Giovannini and his laboratory colleagues. The following is a summary of the conversation between Dr. Marco Giovannini and Advocure NF2's Roland Thoms and Sheila Heal.

Advocure: Dr. Giovannini, thank you for inviting us to your beautiful research lab this afternoon and for sharing your time with us. You have been working on NF2 research since 1994, starting at the Curie Institute in Paris. In 1999, the DoD NFRP consortium grant allowed Doctors K. Shannon, T. Jacks, L. Parada, A. McClatchey, and yourself, to develop the mouse models for NF2 and NF1 that exist today. Was that a critical step?

Dr. Giovannini: Absolutely yes. The results of that effort have been exceptionally successful by any measure. The NF Mouse Models Consortium generated accurate models of many NF1- and NF2-associated tumors and provided these mice to over 100 laboratories worldwide. Studies performed in these models by us and by other investigators have contributed fundamental insights into mechanisms of tumor formation and provided preclinical data that have led to novel drug trials. The strains produced through this effort are also the backbone of the Preclinical Consortium developed by the Children's Tumor Foundation. This visionary series of competitive awards by the CDMRP has not only advanced our knowledge of NF1 and NF2 disease pathogenesis but has enabled our consortium to generate novel reagents that will help to advance the field for years to come.

When I moved my lab to the House Ear Institute in 2008, I had the opportunity to access the largest population of NF2 patients in the US and to collaborate with Dr. Derald Brackmann, a leading surgeon for vestibular schwannomas. Our idea was to use the mouse models of NF2 to test drugs, based on the most recent knowledge of the molecular mechanisms of NF2, in order to identify new candidates to test in clinical trials. As a first approach, we focused on drugs that were already in advanced therapy development for other tumors.

On RAD0001:

At one point it became clear that we had one candidate that was outperforming other drugs, so we focused extensively on this drug (RAD001), a derivative of rapamycin, which has been extensively studied clinically and is FDA approved for several oncological indications, including Tuberous Sclerosis, a close relative of NF1 & NF2. We have tested this drug across all of our NF2 models, including the meningioma models that we have developed in collaboration with Dr. Michel Kalamarides in Paris. Based on the promising results, House Research Institute approached Novartis clinical oncology team and they accepted to collaborate with us on a clinical trial with RAD001 for NF2 vestibular schwannoma (**www.clinicaltrials.gov, study #NCT01345136**, Dr. Giovannini, Principal Investigator, Dr. Doherty, Medical Coordinator, Dr. Brackmann, Co-Investigator). **This drug has a good safety profile and excellent oral bioavailability that allows a once-a-day treatment over several months.** We are very excited about this work since it is a unique example of translational research: going directly from basic science research studies to clinical research. At HRI, we are now screening patients for inclusion in the trial by analyzing our NF2 patients' tumor growth over the past 12 months.

On Hsp90 Inhibitors:

Dr. Giovannini: We are also interested in another class of compounds, the inhibitors of Hsp90. The heat shock protein 90 (Hsp90), is necessary for the activity of many of the proteins which regulate several cellular processes and which are often mutated in cancers, as well as in NF2 tumors. Inhibiting the function of Hsp90 results in degradation of the mutated proteins, and prevents growth of cancer cells. The molecular chaperone Hsp90 is a promising new target in cancer therapy and selective Hsp90 inhibitors are currently in clinical trials. Our preliminary observations show that inhibition of Hsp90 blocks the growth of Nf2-deficient cells in culture and in vivo in NF2 mouse models. We are studying this further to provide enough evidence to support the further study of these drugs as therapeutics for NF2-related tumors.

This program was started in collaboration with NexGenix Pharmaceuticals, which is now developing highly potent HSp90 inhibitors in collaboration with the University of Strasbourg in France. Since then we have also tested Hsp90 inhibitors that are already being used in clinical trials to compare their potency in stopping the growth of NF2 tumors.

Advocure: Might you be poised for a clinical trial with an Hsp90 inhibitor within 5 years?

Dr. Giovannini: There are now several HSP90 inhibitors undergoing clinical evaluation, and 31 active HSP90 inhibitor oncology trials. Therefore, if we confirm efficacy in the various NF2 mouse models and if we identify an inhibitor with a good safety profile, we should be able to rapidly start a trial.

On EGF pathway Inhibitors:

Dr. Giovannini: In addition to these targets, several studies have shown that membrane receptors of the EGF family are abnormally activated in NF2 tumors and that pharmacologic inhibition of these receptors has an inhibitory effect in NF2 cells in vitro. These receptors exist on the cell surface and are activated by binding of specific ligands. As a result, downstream signaling proteins initiate several signal transduction cascades leading to DNA synthesis and cell proliferation. Mutations, amplifications or misregulations of EGFR or family members are implicated in about 30% of all epithelial cancers, and it is the target of an expanding class of anticancer therapies. In collaboration with Dr. McClatchey at Harvard, we found that one covalent EGFR inhibitor developed by Avila Therapeutics showed excellent and durable efficacy in cultured Nf2-/- Schwann cells.

We are in the process of analyzing the efficacy of EGFR inhibitors in preclinical studies using our mouse models. A positive outcome from this study will provide the proof-of-concept evidence to support the use of covalent pan-ErbB inhibitors as a therapeutic option for NF2-related tumors.

On Natural compounds:

Advocure: Can natural compounds help people with NF2?

Dr. Giovannini: Today, about 80% of the world population residing in developing countries still rely almost entirely on plant products for their primary health care. The remaining 20% of individuals living in developed countries use, in more than 25% of cases, pharmaceuticals which have been directly derived from plant products. Throughout medical history, plant products have been shown to be valuable sources of novel anti-cancer drugs. The active principle is often present in a mixture of other compounds from a natural source and it has to be isolated and purified. As an example, Rapamycin was first discovered as a product of a bacterium found in a soil sample from Easter Island, also known as Rapa Nui, hence the name. The problem with non-purified natural anti-cancer compounds is that the bioavailability is often poor (Curcumin, Propolis) and multiple approaches including nanoparticles and liposomes are being sought to overcome this important limitation.

On Stem Cells:

Dr. Giovannini: In the case of NF we should not think of Stem Cell therapy as a replacement treatment, like in neurodegenerative diseases, but the notion of "Tumor Initiating Cells" is very important here since these cells are refractory to chemotherapy and radiation treatment and lead to recurrent tumors in patients.

Advocure: What about the articles that report mouse spinal cord injury treatment with stem cell therapy?

Dr. Giovannini: Of course, it is tempting to think that stem cell therapy could be used to repair neurologic deficits resulting from schwannoma growth or facial nerve damage following microsurgery. We will have to follow closely the progress in nerve repair strategies to eventually apply them to NF2.

On Genomics:

Dr. Giovannini: Recent technological advances have made it feasible to sequence DNA on a large scale. The scale necessary for ambitious projects such as sequencing an entire personal or tumor genome is mostly done by high-tech machines, such as those that we have here at HRI. Much as your eye can scan a sequence of letters to read a sentence, these machines "read" a sequence of DNA bases. Each person has their own unique genome, that is, all of our DNA, which is unique to each human being. We have recently completed the first NF2 genome project, the sequencing of a NF2 patient "personal" DNA and one tumor from this patient. The comparison of the sequences of the two genomes will allow us to identify the gene mutations that are present only in tumor cells and that can influence tumor growth. For example, this analysis can shed light on why some NF2 tumors are slow and others are fast growing, and why some NF2 tumors stop growing while others progress and even become malignant. We also hope that studying entire genome sequences will help us understand how the genome as a whole functions, specifically, how genes orchestrate the growth, development and malignant transformation of a tumor. However, sequencing the NF2 patient and related tumor genomes does not immediately reveal their genetic secrets. We still have to translate those strings of letters into an understanding of how the genome works: what the various genes do, how different genes are related, and how the various parts of the genome are coordinated. For this bioinformatic analysis, we collaborate with Dr. Stan Nelson at UCLA's Jonsson Comprehensive Cancer Center.

Dr. Nelson and his team help us to sort out and assemble that huge amount of sequencing data into useful information.

Obviously, these findings are not immediately applicable to people's everyday lives, in terms of developing therapeutic treatments, but most fundamental research isn't. The point here is that the first steps to understanding the genome of a tumor as a whole are being taken, which broadens our understanding of tumor development one step at a time.

Advocure: What is the exome sequencing? How can this be applied to NF2?

Dr. Giovannini: Exome sequencing is a "lite" version of whole genome sequencing. Routine whole genome sequencing of large numbers of individuals is still not feasible partly due to the high cost associated with this technology. Therefore, it is necessary to use an alternative approach, in which only the parts of genome that contain genes (the "exome") are sequenced. The "exome" represents all the exons (i.e., protein coding regions) in the human genome. In total there are about 180,000 exons in the human genome which represents about 3% of the entire genome. It is estimated that the protein coding regions of the human genome constitute about 85% of the disease-causing mutations.

On Gene Therapy:

Advocure: Referring to gene therapy, could you speak about viral vectors? Could we use virus to deliver the "Merlin" protein into the cells of our patients?

Dr. Giovannini: Gene therapy uses viruses or other vectors to introduce new genetic material, such as a functional NF2 gene, or genes that render cells more susceptible to other therapies (drugs or radiation) into tumor cells. The major challenges have been delivery of DNA to a large number of target tumor cells and duration of expression of the gene. In addition, cancer can develop as a result of the insertion of the gene into a cell's genome. As a result, the FDA has not yet approved any human gene therapy product for sale.

In contrast to "somatic" gene therapy, the concept of "germline" gene therapy is highly controversial. While it could spare future generations in a family from having a particular genetic disorder, such as NF2, it might affect embryo development or have long-term side effects that are unpredictable. Moreover, since individuals who would be affected by germline gene therapy are not yet born, they can't choose whether to have the treatment. Because of these ethical concerns, the U.S. Government does not allow federal funds to be used for research on germline gene therapy in people.

On Synthetic NF2 Protein:

Advocure: Can the NF2 protein Merlin, be produced synthetically?

Dr. Giovannini: Yes, it can. Again, the problem is how to get the synthetic protein inside tumor cells. The effectiveness of protein therapy has been limited by its low delivery efficiency and poor stability against proteases in the cell, which digest the protein. New approaches, including those based on nanocapsules, are currently evaluated that would allow proteins to be delivered to cells with high efficiency, while maintaining low toxicity.

On Short-Term and Long-Term Therapies:

Advocure: Is the majority of your lab work at HRI focused on scientific, longer term discoveries, or shorter term therapies?

Dr. Giovannini: My lab's focus in on translational NF2 research. Since we moved to HRI the effort has been equally shared between basic, pre-clinical, and clinical research.

Advocure: You are close to bringing a new therapy if RAD001 performs as you expect it to. Is there more pressure on scientists to deliver short-term therapies?

Dr. Giovannini: There is pressure on scientists is to deliver therapies quickly for every disease for which there are only limited therapeutic options. However, I remain firmly convinced that the basic knowledge of the molecular mechanisms of NF2 tumor suppression will bring us the best treatments. Therefore, in my opinion patient-driven foundations, foundations such as Advocure NF2, should support both short and long term scientific projects.

Advocure: Generally, researchers in basic science search for discoveries and answers to the vast unknown in order to answer the mysteries of NF2 - discoveries and knowledge that will take years to unravel. In doing this work, do we benefit in the short term for treatments and today's quality of life?

Dr. Giovannini: Of course. If you look back even ten years, the clinical management of NF2 has dramatically improved, vastly due to this research. Now we know more about the growth pattern of these tumors, and there is more propensity to wait and see what the disease progression is before attempting any therapeutic intervention. Also, understanding the natural history and angiogenesis of NF2 tumors led to the use of anti-angiogenic drugs, such as Avastin.

So there are always advances along the way. They may not be revolutionary,

but when you put them all together, and look back ten years, it is impressive. And when we look ten years forward, towards even more understanding that translates into better clinical management, it should be even more impressive.

On Information Sharing and Duplication of Efforts:

Advocure: How do you feel about the sharing of information between NF2 doctors around the world? Do doctors duplicate efforts? Is that advantageous or an unwise use of resources?

Dr. Giovannini: In science and medicine, duplication of efforts is not necessarily a negative situation. On the contrary, it expands knowledge and information sharing among scientists is usually good. For example, we heard of some very remarkable successes in Europe with ABI implantation in NF2 patients, and soon after a team of neurosurgeons went to Europe to understand what was done differently. They were very open to learn and towards sharing information.

Sharing of information and knowledge is one reason behind the organization of the NF2: State of the Art meetings. In Paris, in 2006, with Dr. Kalamarides, we felt that it was important to convene with doctors interested in NF2 worldwide. Again, in May 2010, we hosted the NF2: State of the Art meeting, with Dr. Brackmann and Dr. Bob Shannon in Las Vegas followed by a CTF-sponsored workshop on NF2 clinical trials. A paper was just published in the Journal of Medical Genetics summarizing the outcomes of that meeting.

On Funding:

Advocure: In speaking to the NF2 community regarding fundraising, what can we say to give the fundraisers an impetus to act?

Dr. Giovannini: We have seen tremendous progress since the identification of the NF2 gene in 1993. The last ten years have been amazing in terms of advances, discoveries, and potential application. The development of clinical trials, such as the one for Avastin was a big push forward. I would like to tell the community that we are a very dedicated group of people sharing the overarching goal of understanding and fighting NF2. Thus, we share with you the same objective: to find good and better therapies.

Advocure: Does your lab need funding?

Dr. Giovannini: Due to the economic downturn of today, I think that all scientists I know are struggling for funding.

Advocure: Is there one particular area or phase of research that needs funding more, since funding is so limited?

Dr. Giovannini: That is a very hard question. I believe all three of the major phases of therapeutic development for NF2 should be funded: Basic research, preclinical testing, and clinical trials for most promising drugs. In our experience, preclinical testing is by far the most difficult for which to procure funding.

Advocure: How do you think that Advocure can help in getting funding to some of the needed work?

Dr. Giovannini: One way is to put pressure on Federal Granting Agencies to allocate funds to all three areas of NF2 research. We still need basic science to better understand the mechanisms and to identify the drug targets that are

Fundraising:

- **Zazzle™ - Cups & Stuff**
  Let us customize a product for you; T-shirts, cups, hats with logos, family photos, pet photos, etc.

- **Magazine Subscriptions**
  Need to renew a magazine or gift idea for the upcoming holidays?
  An easy way to contribute to NF2 is to purchase a ***magazine subscription***. Forty percent (40%) of the proceeds will be donated to Advocure. For a list of magazines **click here.**

- **Adam Goodkind NF2 Research Fund**
  c/o Children's Tumor Foundation
  95 Pine Street, 16th Floor, New York, N.Y. 10055

- Another easy way to contribute to NF2 is to visit us and donate on **Facebook.**

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NF2 and Other Relevant Clinical Trials and Studies:

NIH STUDIES:

- **Natural History Study of Patients with Neurofibromatosis Type 2 (NF2)**
  ClinicalTrials.gov Identifier: NCT00598351
  This study is currently recruiting participants.
  This study will examine over the long-term the progress of patients with **neurofibromatosis Type 2 (NF2)**, a condition associated with tumors of the nerves, brain and spinal cord. It will study patients' tumors to learn how fast they can grow and if certain factors might affect their growth. It will also examine the effects of the tumors on patients' abilities to carry out activities of daily living. People between 8 and 75 years of age with **NF2** may be eligible for this study, (most expenses are reimbursed).
  Location: National Institutes of Health Clinical Center, Bethesda, MD, USA.

- **Using Positron Emission Tomography (PET) to Predict Intracranial Tumor Growth in Neurofibromatosis Type II (NF2) Patients**
  ClinicalTrials.gov Identifier: NCT01222728
  This study is currently recruiting participants.
  Objectives - To use magnetic resonance imaging and positron emission tomography to better understand the growth of brain tumors in people with **neurofibromatosis type II (NF2)**.
  Location: National Institutes of Health Clinical Center, Bethesda, MD, USA.

RAD001:

- **Efficacy and Safety Study of RAD001 in the Growth of the Vestibular Schwannoma(s) in Neurofibromatosis 2 (NF2) Patients**
  ClinicalTrials.gov Identifier: NCT01490476
  This study is currently recruiting participants.

  The purpose of the study is to determine if RAD001 treatment will shrink or slow the growth of the vestibular schwannoma(s) in Neurofibromatosis 2 (NF2) patients.
  Location: Hôpital Beaujon, Clichy, France

- **Study of RAD001 for Treatment of NF2-related Vestibular Schwannoma**
  ClinicalTrials.gov Identifier: NCT01345136
  This study is not yet open for participant recruitment
  The purpose of the study is to determine if RAD001 treatment will shrink or slow the growth of the vestibular schwannoma(s) in Neurofibromatosis 2 (NF2) patients. Secondary objectives include determining if RAD001 treatment will improve hearing ability in NF2 patients.
  Location: House Research Institute, Los Angeles, CA, USA.

- **Phase II Study of Everolimus (RAD001) in Children and Adults With Neurofibromatosis Type 2**
  ClinicalTrials.gov Identifier: NCT01419639
  This study is currently recruiting participants.
  Primary Outcome Measures - Radiographic Response: To estimate the objective response rates to RAD001 in patients with NF2-related tumors including cranial nerve schwannomas, meningiomas and ependymomas. Radiographic response for study purposes = greater than or equal to 15% reduction in tumor volume in any of the target tumors (partial response). Complete disappearance of any of the target tumors = complete response. MRI of the brain and spine will be performed every 3 months. If an objective response (15% reduction in tumor volume compared to baseline) is observed in any target tumor or stable disease, drug will be continued.
  Location: New York University Medical Center, New York, NY, USA.

- **Everolimus (RAD001) for the Treatment of Malignant Pleural Mesothelioma With Merlin/NF2 Loss as a Biomarker to Predict Sensitivity**
  ClinicalTrials.gov Identifier: NCT01024946
  This study is ongoing, but not recruiting participants.
  For patients with malignant pleural mesothelioma that has grown despite treatment with standard chemotherapy, no treatment has yet proven beneficial. The purpose of this study is to find out what effects, both good and bad, that

everolimus has on the cancer. Everolimus works by blocking a protein that helps the cancer grow. The goal of this clinical research study is to learn if the study drug everolimus can shrink or slow the growth of mesothelioma. The safety of this drug will also be studied. The patients' physical state, changes in the size of the tumor, and laboratory findings taken during the study will help us decide if everolimus is safe and effective.

Locations: Dana Farber Cancer Institute, Boston, MA, USA
Memorial Sloan-Kettering Cancer Center, New York, NY, USA
University of Pennsylvania, Philadelphia, PA, USA.

BEVACIZUMAB (Avastin™):

- **Phase 2 Study of Bevacizumab (Avastin™) in Children and Adults With Neurofibromatosis Type 2 and Symptomatic Vestibular Schwannoma**

ClinicalTrials.gov Identifier: NCT01207687

This study is ongoing, but not recruiting participants.

This study is exploring whether a drug that is approved by the FDA and is currently used to treat other tumors might also work to treat VSs. Based on people who have taken this drug to treat VSs already, there is some reason to think that it might be helpful to certain people with **NF2**. People enrolled in this study will receive the drug one time every three weeks for one year by infusion. This study will follow subjects over the course of the year that the person is taking the drug and for six months after the drug is stopped. This study is recruiting people who have **NF2** and are currently having symptoms of tinnitus, dizziness, and/or hearing loss from their VSs. If you have **NF2** and are currently having symptoms caused by your VSs, you may be eligible to participate.

Locations: Johns Hopkins Comprehensive Neurofibromtosis Center Baltimore, MD, USA.
National Cancer Institute, Bethesda, MD, USA.
Massachusetts General Hospital, Boston, MA, USA.

- **Trial of the Combination of Bevacizumab (Avastin™) and Everolimus (RAD001) in Patients With Refractory, Progressive Intracranial Meningioma**

ClinicalTrials.gov Identifier: NCT00972335

This study is ongoing, but not recruiting participants.

In this multi-center, Phase II trial, the investigators plan to evaluate the activity of the combination of bevacizumab (Avastin™) and everolimus in patients with recurrent, progressive meningioma following maximal treatment with surgical resection and local radiation therapy. Although these patients are relatively rare, there is currently no established standard of treatment for a disease that causes a great deal of morbidity, and that is eventually fatal.

Locations: Florida Hospital Cancer Institute, Orlando, FL, USA
Norton Cancer Institute, Louisville, KY, USA
Nebraska Methodist Cancer Center, Omaha, Nebraska, USA
University of Pittsburgh Medical Center, Pittsburgh, PA, USA
UT Cancer Institute Memphis, Memphis, TN, USA
Tennessee Oncology, PLLC, Nashville, TN, USA
Peninsula Cancer Institute, Newport News, VA, USA

- **Bevacizumab (Avastin™) in Treating Patients With Recurrent or Progressive Meningiomas**

ClinicalTrials.gov Identifier: NCT01125046

This study is currently recruiting participants

RATIONALE: Monoclonal antibodies, such as bevacizumab (Avastin™), can block tumor growth in different ways. Some block the ability of tumor cells to grow and spread. Others find tumor cells and help kill them or carry tumor-killing substances to them. PURPOSE: This phase II trial is studying how well bevacizumab (Avastin™) works in treating patients with recurrent or progression meningiomas.

Location: Northwestern University, Chicago, IL, USA.

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UT Cancer Insititute Memphis, Memphis, TN, USA.
Tennessee Oncology, PLLC, Nashville, TN, USA.
Peninsula Cancer Institute, Newport News, VA, USA.

NILOTINIB:

- **Phase II Study of Nilotinib in Growing Vestibular Schwannomas**

ClinicalTrials.gov Identifier: NCT01201538

This study is currently recruiting participants.

The primary objective of this study is to evaluate the efficacy of Nilotinib in the treatment of patients with progressing sporadic and NF2 VS. Secondary objectives of this study is to evaluate the toxicity profile, quality of life and symptom management of Nilotinib in the treatment of patients with progressing VS.

Location: Toronto Western Hospital, University Health Network, Toronto, ON, Canada.

LAPATINIB:

- **Concentration and Activity of Lapatinib in Vestibular Schwannomas**

ClinicalTrials.gov Identifier: NCT00863122

This study is currently recruiting participants.

This phase 0 study is exploring whether a drug that is approved by the FDA and is currently used to treat breast cancer might also work to treat VS. This study will measure the amount of drug that travels from the bloodstream and arrives at the tumor. This drug is safe and has few side effects. If this drug is shown to reach the tumor, it might be used in the future to treat VS without needing surgery or radiation. This study is recruiting people who are having surgery for VS. If you are going to have surgery to treat a VS, you may be eligible to participate.

Locations: House Ear Institute, Los Angeles, CA, USA.
John Hopkins Hospital, Baltimore, MD, USA.
New York University Medical Center, New York, NY, USA.
Ohio State University Medical Center, Columbus, OH, USA.

- **Phase II Study of Lapatinib Study for Children and Adults With Neurofibromatosis Type 2 (NF2) and NF2-Related Tumors**

ClinicalTrials.gov Identifier: NCT00973739

This study is ongoing, but not recruiting participants.

The purpose of this study is to determine if Lapatinib has any effect on tumors found in patients with Neurofibromatosis 2 (NF2).

Location: New York University School of Medicine, New York, NY, USA.

SORAFENIB:

- **Sorafenib in a NF2 study, in the UK**

Adults who have Neurofibromatosis 2 (NF2) and skin tumours (schwannomas) are invited to participate in a research study being undertaken in Plymouth and Manchester; **Professor C. Oliver Hanemann**, a consultant neurologist at the Peninsula College of Medicine and Dentistry in Plymouth is the Chief Investigator...

SUNITINIB:

- **Sunitinib in Treating Patients with Recurrent or Unresectable Meningioma, Intracranial Hemangiopericytoma, or Intracranial Hemangioblastoma**

ClinicalTrials.gov Identifier: NCT00561665

The recruitment status of this study is unknown because the information has not been verified recently.

This phase II trial is studying sunitinib to see how well it works in treating patients with recurrent or unresectable meningioma, intracranial hemangiopericytoma, or intracranial hemangioblastoma.

Locations: Dana-Farber/Harvard Cancer Center at Dana-Farber Cancer Institute, Boston, MA, USA.
Memorial Sloan-Kettering Cancer Center, New York, NY, USA.
UPMC Cancer Centers, Pittsburgh, PA, USA.
University of Virginia Cancer Center, Charlottesville, VA, USA.

NF2 Compass
A Quarterly Advocure Online Newsletter
Formerly known as "Flutterby"

- **Phase II Trial of Sunitinib (SU011248) in Patients with Recurrent or Inoperable Meningioma**

ClinicalTrials.gov Identifier: NCT00589784

This study is currently recruiting participants.

Sunitinib is a drug approved for advanced kidney cancer. Sunitinib is also being studied for other tumors. It may be useful in the treatment of brain tumors because it can prevent formation of new blood vessels that allow tumor cells to survive and grow.

Locations: Dana-Farber/Harvard Cancer Center at Dana-Farber Cancer Institute, Boston, MA, USA.
Memorial Sloan-Kettering Cancer Center, New York, NY, USA.
UPMC Cancer Centers, Pittsburgh, PA, USA.
University of Virginia Cancer Center, Charlottesville, VA, USA.

PTC299:

- **PTC299 for Treatment of Neurofibromatosis Type 2 (NF2)**

ClinicalTrials.gov Identifier: NCT00911248

This study is ongoing, but not recruiting participants.

PTC299 is an oral drug that has been shown to decrease production of VEGF in animal models of human cancer. In these animal models, oral PTC299 administration decreases VEGF levels in the tumor and in the bloodstream, decreases blood vessel numbers in the tumor, and significantly slows or halts tumor growth. This Phase 2 study is designed to test the hypothesis that PTC299 will be tolerable and will show evidence of VEGF reduction, anti-tumor activity, and hearing improvement when administered orally to patients with **NF2**

- **Oncology – PTC299**

Location: Massachusetts General Hospital, Boston, MA, USA.

SOM230:

- **Phase II Study of SOM230 in Patients With Recurrent or Progressive Meningioma**

ClinicalTrials.gov Identifier: NCT00813592

This study is ongoing, but not recruiting participants.

This is a single-arm, phase II trial of SOM230 in patients with documented recurrent or progressive intracranial meningioma who have failed conventional therapy and are not candidates for complete surgical resection of their tumors and/or radiation at the time of study entry.

Location: Huntsman Cancer Institute. Salt Lake City, UT, USA.

- **Monthly SOM230C for Recurrent or Progressive Meningioma**

ClinicalTrials.gov Identifier: NCT00859040

This study is ongoing, but not recruiting participants.

The purpose of this research study is to evaluate the effectiveness and safety of SOM230C in treating recurrent meningiomas. SOM230C is a newly discovered drug that may stop meningioma cells from growing abnormally. This drug has been used in treatment of other tumors, and information from those other research studies suggests that SOM230C may help to stop the growth of meningiomas.

Locations: Cedars-Sinai Medical Center, Los Angeles, CA, USA.
Northwestern University, Chicago, IL, USA.
Dana-Farber Cancer Institute & Massachusetts General Hospital & Beth Israel Deaconess Medical Center, Boston, MA, USA.
Memorial Sloan-Kettering Cancer Center, New York, NY, USA.
Duke University Medical Center, Preston Robert Tisch Brain Tumor Center, Durham, NC, USA.
Wake Forest University Baptist Medical Center, Winston-Salem, NC, USA.

MISC. STUDIES:

- **Auditory brainstem implant (ABI) patients needed for research study at MEEI and MGH.**

A clinical research study of patients who have an auditory brainstem implant (ABI) is being conducted jointly by researchers. We will use specialized hearing testing to better understand how your brain responds to stimulation from your ABI.

Location: Massachusetts Eye and Ear Infirmary, Boston, MA, USA.

- **Neurofibromatosis Type 2 Associated Color Vision Anomalies and Birth Defects: Incidence and Insights**

What is the purpose of the study?

1. Determine the frequency of birth defects and miscarriages in patients with **NF2**.
2. Determine the frequency of color blindness in NF2 patients

Location: Ohio State University Medical Center, Columbus, OH, USA.

NF2 Compass
A Quarterly Advocure Online Newsletter
Formerly known as "Flutterby"

SOME Pharmaceuticals of NF2 Interest:

**If you have any questions about these, please discuss with your primary caregiver and/or oncologist*.*

• **PTC124 (Ataluren™)**, investigational new drug designed to enable the formation of a functioning protein in patients with genetic disorders due a nonsense mutation. *"…..Though there may be applications in all forms of NF, it is considered that there may be most relevance initially to NF2 where nonsense mutations account for a significant proportion of sporadic cases."*

• Bevacizumab **(Avastin™)** is a biologic antibody designed to specifically inhibit the VEGF protein that plays an important role in development and maintenance of blood vessels, a process known as angiogenesis.

- Sorafenib **(Nexavar™)**
- Erlotinib **(Tarceva™)**
- OSU-HDAC42 **(AR-42™)**
- OSU-03012 **(AR-12™)**
- **PTC299**
- **PTC124** (Ataluren)
- **Nilotinib** (Tasigna™)
- **Curcumin**
- **Dasatinib**
- **BIBF 1120 (Vargatef™)**
- seraphinib
- **Valproic Acid**
- **Rapamycin**
- **Cetuximab**
- **Trastuzumab** (Herceptin™)
- Vandetanib **(Zactima™)**
- **Lapatinib** (Tykerb™)
- Caffeic Acid (**BIO30™**)
- **RAD001** (Everolimus)
- **BEZ-235**
- malatinib

NF Symposiums or Conferences With an NF2 component

- ***May 21-22, 2012 • Manchester Conference Centre, Weston Building, Sackville Street, Manchester, UK***
  Third NF2 State of the Art conference
  Hosted by the Manchester NF2 Multidisciplinary Team

- ***June 8-10, 2012 • New Orleans, LA, USA***
  2012 NF Forum
  Captioned, intended for NF patients & families
  Hosted by the Children's Tumor Foundation (CTF)

- ***June 9-12, 2012 • New Orleans, LA, USA***
  2012 NF Conference
  Intended for the scientific and clinical community only, by invitation.
  Hosted by the Children's Tumor Foundation (CTF)

- ***September 6-9, 2012 • Istanbul, Turkey***
  15th European NF Meeting
  Hosted by the Turkish NF Association

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