NF2 Compass

A Quarterly Advocure Online-Newsletter

Formerly known as 'Flutterby'

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

Issue 7, page 1; autumn 2010.

In this Issue:

Our Mission:

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

Advocure Inc
advocates for a cure

Email: contact@advocurenf2.org

Web: www.advocurenf2.org

RSS Feeds

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

PayPal NF2 Donate

NF2 donations, and in memory for those we lost:

- *Jaime Cirillo*
- *Cindy Henrion*
- *Mischelle Johnson Sturm*
- *Barbara Howell Weaver*
- *Beth Catharine*
- *Jennifer S Schwartz*
- *Julie Pittman Bogard*

Thank you for your support!

NF2 in the News:

- CONFERENCE 2010 ***Advocure Attends the 2010 NF Conference*** - An Advocure representative attended the recent 2010 NF Conference in Baltimore, held in June 2010.

- ***Advocure Participated in the Recent CDMRP-NFRP Peer Review Panel, 2010*** - An Advocure representative participated at the recent CDMRP-NFRP peer review panel on behalf on the NF2 community and Crew in July 2010, Washington D.C. Thus, ensuring the needs of NF2 are fairly represented and that essential NF2 research is funded.

- Find us on Facebook **Advocure is now on Facebook!** Help support our Cause.

- ***'Help Stop NF2'*** is a new 501(c)(3) NF2 public charity, founded in 2009 by Harley and Rebecca Dufek.

- **NF2 Biology and Drug Targets** - The principle behind the recently reported promising trial of *bevacizumab* (Avastin) in NF2, where the drug was seen to reduce tumor volume and restore hearing in a small number of patients …….. *Wong et al.* review the rationale for VEGF-targeted drug therapies in NF2 in mouse models, examining the underlying biological changes of the tumors in response to this therapy…….. In a CTF funded research study, *Ammoun et al.* report

a study that examines the rationale for testing drugs that target receptor tyrosine kinases (RTKs) as candidate NF2 therapies. The drug Lapatinib which inhibits this signaling was then tested on human VS explants and found to quiet these pathways and reduce cell proliferation……. *Bensenor et al.* examine the question of how the NF2 protein merlin functions inside the cell to control growth…….. *Stamenkovic and Yuprovide* a review merlin function.

- ***NF2 Clinical Management*** - *Neary et al.* have developed a questionnaire for the purposes of measuring the primary and secondary quality of life impacts of NF2……*Lim et al.* report on a case of tanycytic ependymoma, a rare subtype of ependymoma rarely seen in NF2, in a 16 year old girl…….. *Sisk et al*. review the clinical feature of epiretinal membranes (lesions in the eye that cause reduced visual acuity) and from a study of 4 patients propose these as a novel predictor of NF2 severe phenotype in otherwise asymptomatic children. ……A controversial area in NF2 clinical management, radiosurgery was a focus of the NF2 meetings in Las Vegas, with a conclusion that there is a place for radiosurgery in NF2 under certain circumstances such as small and difficult to reach tumors (to be detailed in the forthcoming recommendations paper from that meeting). *Sharma et al*. present a review of the use of Gamma Knife radiosurgery on tumor control and hearing preservation in NF2. A tumor control rate of 87.5% is reported with 33.3% tumor regression. Hearing preservation of in 66.7% was seen but the group acknowledges that long term follow up is key to fully evaluate the application and outcome of this technology……. *Colletti et al.* do a retrospective analysis of 114 individual ABI surgeries (83 adults and 31 children) performed between 1997 and 2008 and find that overall ABI has a low rate of complications, especially in NF2. …… *Schwartz et al.* report the first case of trigeminal neuralgia resulting from an ABI cable's nonvascular compression in an NF2 patient.

- ***Novartis Shifts Focus to Rare Diseases****, CEO Vasella Sees Value in Niche Drugs That Can Have Broader Uses. - Like most pharmaceutical companies' CEOs, Daniel Vasella, chairman and chief executive of Switzerland's Novartis AG, is facing a large cocktail of problems. Insurers, governments and others who pay for health care—called "payers" in the industry lingo—are increasingly refusing to cover expensive new drugs that aren't substantially better than older, cheaper treatments. Regulators have become more safety conscious and less willing to approve new products for sale. And through a series of large mergers, pharmaceuticals giants have found bureaucracy creeping in and hampering their development of new drugs.....*

- ***Pfizer Deal Signals Move Into Rare Diseases***

  The world's largest drug company is thinking small. Pfizer said Tuesday that it had licensed the worldwide rights to a treatment for *Gaucher disease*, a rare genetic disorder, from Protalix Biotherapeutics, an Israeli biotechnology company, The New York Times's Andrew Pollack writes.....

- "…***Dr. Cristina Fernandez-Valle***, an associate professor of molecular biology and microbiology at UCF has landed $2 million in federal grants to research proteins that could help treat tumors associated with NF2, a disease that can leave children and young adults deaf, partially paralyzed or brain damaged…."

- ***NF2 Cell and Molecular Biology – Insights from the Lens*** - Over half of individuals with NF2 will develop cataracts in the lens of the eye called PSCs. *Wiley et al.* present some ideas for the biological basis of these cataracts. The NF2 gene was inactivated in a genetic mouse model only in the developing cells that will give rise to the lens, called fiber cells. Unlike normal fiber cells, the NF2 inactivated fiber cells were unable to stop dividing at the correct time in development, and also continued to express genes associate with their immature stage. These fiber cells failed to take on their usual elongated shape in the lens and do not form appropriate connections and associations with neighboring cells. Overall the lens failed to detach from other tissues as it should but continued to grow into a tumor-like mass. These findings highlight the molecular events underpinning NF2 related cataracts and this new mouse model will be helpful for screening candidate NF2 drug therapies.

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- **Dr. Marco Giovannini**, director of the CTF's NF Preclinical Consortium Center at House Ear Institute (HEI), talks about NF2 and the Foundation sponsored research being advanced in his lab.

- NF2 Cell and Molecular Biology – Signaling -A study with first author Children's Tumor Foundation Young Investigator Awardee *Geoffrey Kilili* has uncovered novel ideas about merlin signaling. In the fruit fly, merlin protein function acts by promoting Hippo. The mammalian Hippo homolog is Mst2 and, as in flies, it mediates merlin tumor suppressor function/prevention of excess cell proliferation. Meanwhile Mst2 itself is negatively regulated by Raf-1. *Kilili* found that merlin did not necessarily promote Mst2 signaling in mammalian cells; and, inhibiting Mst2 impairs Raf-1 signaling, after which cell proliferation ceases. This research reveals a potentially more complex role for Mst2 than previously thought, perhaps dual roles for Mst2 as a tumor suppressor and as a cell growth promoter. *Yu et al.* shed light on mechanisms of Merlin function and identify Kibra, another upstream component of the Hippo signaling pathway that functions together with Mer and Ex in a protein complex localized to the apical domain of epithelial cells, and that this protein complex regulates the Hippo kinase cascade and implicate Kibra as a potential tumor suppressor with relevance to neurofibromatosis. *Bosco et al*. endeavor to shed light on the mechanism through which merlin normally exerts its tumor-suppressive function, and thereby, on how this is disrupted in NF2 tumors. Through a series of elegant experiments using NF2 knockout mouse embryonic fibroblasts the group proposes an essential role for Rac1-mediated canonical Wnt signaling in the loss of contact inhibition in NF2-deficient cells. In one third of glioblastomas NF2 gene function is inactivated. *Morales et al*. report that this inactivation can happen in 2 ways: decreased NF2 protein expression, or, due to increased levels of related protein ezrin, which disables NF2 function by intermolecular association and aberrant intracellular recruitment. *Yi et al.* describe efforts to optimize drugs that target the p21-activated kinases (PAKs), candidate drug targets in NF2. This is also the focus of current CTF Drug Discovery Initiative Award recipient *Dr. Joe Kissil* (The Wistar Institute).

- Massachusetts Eye and Ear Infirmary ***NF2 Patients Needed for New Vestibular Study at MEEI*** – *"Harvard Medical School / Massachusetts Eye and Ear Infirmary Boston MA. Adrian Priesol, M.D. at (617) 573-4148. The general clinical goal for our study is to quantify motion perception for a range of vestibular disorders. A long-term goal is to develop new clinical tests to provide early diagnosis for vestibular disorders. These clinical research efforts are part of a broader basic science investigation of vestibular thresholds. At this time, we are seeking NF2 patients who have complete loss of vestibular (i.e., "balance/equilibrium organ") function in both ears following surgical removal of tumors from both ears. Travel reimbursement would be paid for all qualifying volunteers."*

- **Rare Diseases Patient Registry Survey** – "*As a stakeholder in the rare disease community, your opinions are needed regarding patient registry business models and the functions needed to support a global rare disease registry program. Please complete a short anonymous survey (approximately 3 minutes) to be sure your interests are represented. This is not an NIH ORDR sponsored survey - all responses will be held in confidence and only aggregated survey results will be shared. Your input is critial to understand the current needs of stakeholders and to deliver the best possible registry solutions for the rare disease community. If you have any questions or concerns, or would like to learn more about our registry programs please contact me directly at kyle@innolyst.com."*

- **NFA News: July 2010** - Newsletter by the Neurofibromatosis Association of the UK. Article by Dr. Evans: *'The New Nationally Commissioned NF2 Service'*, listed the four NF2 centers in the UK.

- **Proposed Sorafenib Trial in the UK for NF2 is Canceled** - *excerpt from the summer 2010 issue of 'NF2 News' - "We recently heard from Dr. Hanemann that his grant application for a trial of sorafenib has not been funded. This is disappointing BUT be reassured that Dr. Hanemann will continue to seek funding ….."*

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- ***Climb Kilimanjaro to STOP NF2*** *– "On 10-10-10 we will summit the highest peak in Africa and raise awareness for NF2! Join us on our high-altitude, luxury trek to Tanzania's crown jewel, Kilimanjaro, the "Roof of Africa" at 19,340 feet. No previous climbing experience is necessary."*

- ***Bittersweet symphony: Before deafness, she's going to hear her favorite sounds****; Philadelphia Daily News - Kristen D'Antonio, a 20-year old from Norristown, PA, is featured in a News Story about her life since being diagnosed with NF2 at the age of 17…*

- ***Girl Organizes Family Fun Day****; Northamptonshire Evening Telegraph - Savannah Hobbs, 11, who suffers from Neurofibromatosis type 2 (NF2) which causes benign tumours to grow on her nerves, has appealed to the public to support ...*

- ***Son's Illness Alters Dad's, Family's View of How to Live****; Sheboygan Press - Jackson is one of only three 8-year-olds in a 300-patient national study centered on a life-threatening condition known as neurofibromatosis type 2, or NF2, ...*

- ***Life is the Reason****; Manila Bulletin - Kcat Can says, "God didn't give me NF2 without any reason…..*

- ***Benefit Set for Man Battling Rare Disorder****; Gadsden Times - Tim Richardson has been diagnosed with Type 2 neurofibromatosis, a condition that consists of many nerve tumors, his wife, Zerlene Richardson, said. ...*

- ***Woman with Genetic Disorder Needs Help****; Malaysia Star - Foong, 24, has been suffering from Neurofibromatosis Type 2 (NFII), an illness of the nervous system that causes benign tumours to grow in the body,....*

- CDMRP Congressionally Directed Medical Programs (CDMRP)'s **NF Research Program booklet.**

- FDA New FDA Funds Could Support Neurofibromatosis Clinical Trials - Phase 1 clinical trials are eligible for grants of up to $200,000 per year for up to 3 years. Phase 2 and 3 clinical trials are eligible for grants up to $400,000 per year for 4 years.

- NF ***If you would like to join NF California's NF2 Committee, Please Let Us Know!*** *– "We understand that those with NF2 have unique needs and hope for specialized topics during educational meetings and symposiums. To better help us serve our members with NF2, NFC is looking for additional members for our NF2 committee. By email events@nfcalifornia.org or by phone: 707-469-0467". Thank you.*

- EurekAlert! ***Merlin Protein Found to Control Liver Stem Cells, Prevent Tumor****, EurekAlert - "We found that mutation of the NF2 tumor suppressor gene in the mouse liver ... The current study was designed to investigate the role of NF2 and merlin in ...*

- Children's Tumor Foundation **NEW! $100K Clinical Research Awards Available - Deadline 9/15** – The Children's Tumor Foundation (CTF) announces a call for Letters of Intent for Clinical Research Awards of up to $100,000. Clinical Research Awards seeks broad-thinking novel ideas to conduct pilot clinical trials of candidate therapeutics for the treatment of tumors and other manifestations of NF1, NF2 and schwannomatosis; OR innovative studies ancillary or adjunct to clinical trials that - if successful - will contribute to the advancement of effective clinical therapies for neurofibromatosis.

- Children's Tumor Foundation CTF Announces the 2010 YIA Recipients – The Children's Tumor Foundation (CTF) announced the 2010 YIA Recipients, 2 out of the 6 awardees were for NF2.

- FDA *Database Aims to Spark Orphan-Disease Drug Development - For months now, the Food and Drug Administration has been trying novel ways of encouraging drug makers to develop drugs for rare diseases.....*

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- ***National Cancer Institute (NIH NCI)- Complementary and Alternative Medicine***

"We are learning about CAM therapies every day, but there is still more to learn. Consumers may use the terms "natural," "holistic," "home remedy," or "Eastern medicine" to refer to CAM. However, experts use five categories to describe it. These are listed below with a few examples for each. (For a complete list of therapies, go to the National Center for Complementary and Alternative Medicine, (NCCAM), http://nccam.nih.gov/health)."

1/ ***MIND-BODY MEDICINES:*** *These are based on the belief that your mind is able to affect your body. Some examples are:* ***Meditation:*** *Focused breathing or repetition of words or phrases to quiet the mind;* ***Biofeedback:*** *Using simple machines, the patient learns how to affect certain body functions that are normally out of one's awareness (such as heart rate);* ***Hypnosis:*** *A state of relaxed and focused attention in which the patient concentrates on a certain feeling, idea, or suggestion to aid in healing;* ***Yoga:*** *Systems of stretches and poses, with special attention given to breathing;* ***Imagery:*** *Imagining scenes, pictures, or experiences to help the body heal;* ***Creative outlets:*** *Such as art, music, or dance.*

2/ ***BIOLOGICALLY BASED PRACTICES:*** *This type of CAM uses things found in nature. This includes dietary supplements and herbal products. Some examples are:* ***Vitamins, Herbs, Foods, Special diets.*** *A note about nutrition: It's common for people with cancer to have questions about different foods to eat during treatment. Yet it's important to know that there is no one food or special diet that has been proven to control cancer. Too much of any one food is not helpful, and may even be harmful. Because of nutrition needs you may have, it's best to talk with the doctor in charge of your treatment about the foods you should be eating.*

3/ ***MANIPULATIVE AND BODY-BASED PRACTICES:*** *These are based on working with one or more parts of the body. Some examples are:* ***Massage:*** *Manipulation of tissues with hands or special tools.* ***Chiropractic care:*** *A type of manipulation of the joints and skeletal system.* ***Reflexology:*** *Using pressure points in the hands or feet to affect other parts of the body.*

4/ ***ENERGY MEDICINE:*** *Energy medicine involves the belief that the body has energy fields that can be used for healing and wellness. Therapists use pressure or move the body by placing their hands in or through these fields. Some examples are:* ***Tai Chi:*** *involves slow, gentle movements with a focus on the breath and concentration.* ***Reiki:*** *Balancing energy either from a distance or by placing hands on or near the patient.* ***Therapeutic touch:*** *Moving hands over energy fields of the body.*

5. ***WHOLE MEDICAL SYSTEMS:*** *These are healing systems and beliefs that have evolved over time in different cultures and parts of the world. Some examples are:* ***Ayurvedic medicine:*** *A system from India emphasizing balance among body, mind, and spirit.* ***Chinese medicine:*** *Based on the view that health is a balance in the body of two forces called yin and yang.* ***Acupuncture:*** *is a common practice in Chinese medicine that involves stimulating specific points on the body to promote health, or to lessen disease symptoms and treatment side effects.* ***Homeopathy:*** *Uses very small doses of substances to trigger the body to heal itself.* ***Naturopathic medicine:*** *Uses different methods that help the body naturally heal itself.*

- ***Olivia Hernandez's Fundraising Page - Never Give Up!*** *– "It's that time of year again, time for the NF Endurance Team to hit the Long Beach Marathon! I am back this year as a Team Captain, and need your help to reach my goal of raising $5000 for CTF! .... All donations to the NF Endurance Team are restricted for use in the CTF science and research programs for NF."*

- **NF2's *Merlin* Protein Finds a New Role - in the Liver** A new study reveals that *merlin* also plays an important role in activating and regulating cell growth … in the liver.

- **Senate Bill Encourages Companies to Develop Rare Disease Drugs**- The senate introduced the *Creating Hope Act*: legislation to encourage pharmaceutical and biotechnology companies to focus more intently on cures for rare diseases that affect children and which today have no treatments…..

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- Children's Tumor Foundation ***Presents Neurofibromatosis Experts On Video from the 2010 NF Conference*** - Short videos from the 2010 NF Conference featuring such luminaries as Dr. Gareth Evans, Dr. Bruce Korf, Dr. Sue Huson, Dr. Vic Riccardi and Dr. Jaishri Blakeley. Captioned.

- YouTube ***Dr. Jaishri Blakely Speaks on NF***

  Dr. Jaishri Blakely speaks on Neurofibromatosis. Captioned.

- YouTube ***Dr. Gareth Evans Speaks on NF***

  Dr. Gareth Evans speaks on Neurofibromatosis. Captioned.

- YouTube ***Dr. Sue Huson Speaks on NF***

  Dr. Sue Huson speaks on Neurofibromatosis. Captioned.

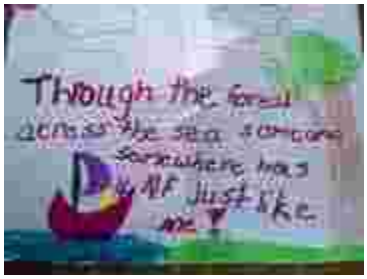
- YouTube ***Drs. Tom Roland & John Golfinos of NYU Medical Center*** - The Children's Tumor Foundation was pleased to honor Dr. Roland and Dr. Golfinos at the 2008 Annual Benefit Dinner with the Children's Humanitarian Award. Together the doctors established one of the world's leading centers for treatment of NF2-related vestibular schwannoma surgery and clinical management at New York University. Captioned.

- NCAM National Center for Complementary and Alternative Medicine - There are many terms used to describe approaches to health care that are outside the realm of conventional medicine as practiced in the United States. This fact sheet explains how the National Center for Complementary and Alternative Medicine (NCCAM), a component of the National Institutes of Health (NIH), defines some of the key terms used in the field of complementary and alternative medicine (CAM).

- First Annual South Jersey RIDE4NF 2010

Thank you!

To everyone who donated their time and money to help make the First Annual South Jersey RIDE4NF 2010 Poker Run/Benefit a success Sunday, July 11th. With your help we raised over $5,200 in order to fund research to find a cure to Neurofibromatosis (a central nervous system that causes tumors to grow on the brain and spine and any nerve in the body).



Thank you all!
Jaime Cirillo,
Family & Friends

To make a donation visit:
http://www.firstgiving.com/jaimecirillo

All of the people in the above two photos have been affected by NF, and have joined together Sunday, July 11th 2010 to meet for the first time after years of feeling alone - because the disorder is so rare.

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Fundraising:

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

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, please click here.

Avastin NF2 Survey Appeal

Dear NF2 Crew Community:

Thank you for your efforts in pushing out the *Avastin* Survey that CTF is conducting. Unfortunately despite all ofour combined efforts I have received only TWELVE responses.

The problem is a dozen cases is not much to go on. It is hard to believe that a community as far reaching as the *Crew* has only a dozen folks in its network that have taken *Avastin*. We really need to hear from EVERYONE with NF2 who has taken *Avastin* so we can fill out the picture as much as we can. I see a glimmer of interesting data from these surveys, but the participant count is so few.
Trust me - there is no reason that I or CTF will benefit from doing this that will take away from the fine work that your group and other groups are doing to end NF2. We are all in this with the same goals. And believe me I have plenty of other projects that need attention - but I think this is such an important project which is why I keep pushing it and pushing it until I am sure you are tired of me.

Let me share with you what drives me - the written responses I have received. These range from someone feeling that taking *Avastin* is pointless and only delaying the inevitable surgery and deafness; to those who say, '*Avastin* has changed my life' restoring some auditory capability and getting someone out of a wheelchair and shrinking tumors. With more participants in this survey, we strengthen this picture of who is responding, when, and at what doses and regime, and give it heft. This is why it actually breaks my heart that there might be folks out there taking *Avastin* that have opted for whatever reason not to complete the survey.

I hope to go back every few months to the dozen respondents and see if we can keep tracking their responses to *Avastin* over time. If this is the full extent of those on *Avastin* then it will still be very informative and I am tremendously grateful for everyone's participation. But we do need more participants if you are out there. Not only could your data help shape this picture, with enough data maybe it even gives us ammunition with which to help shape the way that doctors and even industry think about developing treatments for NF2.

You can download the survey right from our home page www.ctf.org or email me and I will send it to you. You can provide as much or as little info as you want and can stay anonymous if you wish.

Thank you!
KIM

Kim Hunter-Schaedle, Ph.D.
Chief Scientific Officer
Children's Tumor Foundation

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Advocating for NF Federal Research Funding

by: John and Linda Manth
Advocure NF2, Inc.

How is NF Federally Funded?

Since 1996, NF research has been funded by Congress through the Congressionally Directed Medical Research Programs (CDMRP-NFRP) (from the Department of Defense (DOD)), and through the National Institutes of Health (NIH).

Government 101

United States Congress

The United States Congress is the bicameral legislature of the federal government of the United States of America, consisting of the *Senate* and the *House of Representatives.* The Congress meets in the United States Capitol in Washington, D.C. Both *Senators* and *Representatives* are chosen through direct election. Each of the 435 members of the *House of Representatives (*Congressmen) represents a district and serves a two-year term. House seats are apportioned among the states by population. Meanwhile, the 100 *Senators* serve staggered six-year terms. Each state has two senators, regardless of population.

These are the links to finding your *senator* and/or *representative:*

• ***U.S. Senate:*** http://www.senate.gov/

• ***U.S. House of Representatives:*** http://www.house.gov/

Current US Federal legislative Information. Bills, Laws, Congressional Record, reports, and links to further information can be found at: http://thomas.loc.gov/

Committees

Both the House of Representatives and the Senate have committees that draft laws and determine funding levels for various appropriations. The following are the committees which are most important for NF federal funding.

Senate Committee on Appropriations

- Labor, Health and Human Services, Education Subcommittee
- Defense Subcommittee

House Appropriations Committee

- Labor, Health and Human Services, Education Subcommittee
- Defense Subcommittee

Why do We Need to Advocate

Advocacy is an area that many NF2 patients and families are unfamiliar with and as a result may or may not be interested in participating in. The United States Government funds research for NF1, NF2 and Schwannamatosis through the Congressional Directed Medical Research Program (CDMRP=NFRP) and the National Institutes of Health (NIH).

These two agencies currently fund millions of dollars toward research. We need to advocate for not only the continuation of this funding, but for funding to increase, specifically in the area of NF2 research.

How to Advocate

At Your Home District:

Everyone in the United States has a local *Congressman* from their district and two *Senators* from their state. You can make an appointment and meet with one of their staffers anytime you would like to. It is more difficult to get a face-to- face meeting with the actual *Senator* or *Congressman,* but it can be done if you are flexible and persistent. Both your local *Congressman* and State *Senators* will have offices within a close proximity to your home town or city. Meeting at your home district is definitely easier than traveling to Washington, DC and can be equally effective if you meet with a staffer that relays your

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message to *the Congressman/Senator* if a face-to-face cannot be arranged.

Going to Washington DC:

Going to DC to lobby is a much more extensive effort. Appointments have to be made ahead of time and it can have more impact if it is timed correctly. The following year's appropriations begin getting discussed in February of the current year (eg. in Feb. 2010 fiscal year 2011's appropriations begin to be discussed) with negotiations usually lasting into August/September. Those discussions all begin with a *'Dear Colleague Letter'* that must be circulated in February and needs enough signatures on it. A *'Dear Colleague Letter'* is a letter written by one *Congressman/Senator* asking a committee to consider a certain level of funding. The more signatures on a letter, the more influence it is likely to have. While meeting with *Congressmen/Senators* at anytime is valuable, it definitely has more impact when your cause is fresh in the minds of the people who are actually signing on.

Letter Writing:

Writing letters can also be effective. It takes approximately 30 letters about the same subject to have an impact on a *Congressman/Senator.* This is best done with a concerted effort through NF organizations like *NF Inc.* and *CTF* who each have lobbyists assisting their organizations and supplying them with up-to-date information. *ADVOCURE* will supply links to those organizations along with sample letters, which again may have more of an effect at certain times of the year. Letters are sent by e-mailing not postal service because of security screening. Here are the links for *NF Inc* and *CTF's* advocacy information and sample letters:

- http://nfnetwork.org/get_involved/advocacy/ *(NF Inc)*
- http://www.ctf.org/How-You-Can-Help/advocacy.html *(CTF)*

How to Lobby Your Legislator - Even as a single person, you can have an impact on how your legislator votes, and what bills he or she decides to sponsor:
http://www.ehow.com/how_4783812_lobby-your-legislator.html

Tell Your Personal Story:

To leave a positive impression on a *Congressman/Senator* you should think about leaving something with them to help make a personal connection. Some people have photos, picture books made up, wrist bands related to fundraising they do. Think of something that the staffer you are most likely meeting with can take to the *Congressman/Senator* and really relay your story and why funding for NF is so important.

What to Ask for:

If you are going to meet with a staffer the first thing they will ask you is "What can we do for you?" You want to have an answer, and a specific one would be best. The reason why timing is more important here is because of the *'Dear Colleague Letter'.* Asking for the *Congressman/Senator's* signature on that letter is a great achievement.

If the *Congressman/Senator* you are meeting with is on one of the above mentioned committees, they are NOT allowed to sign a *'Dear Colleague'* Letter, since they are a member of the committee determining the appropriations. By meeting with an actual committee member, you may actually yield more power. You simply need to ask them to not only continue NF funding, but increase NF's allocation. These members change each year and again *ADVOCURE* can post links to sites where this information is available. Keep in mind members of both branches of government and committee members have all been contacted by an NF representative, the "squeaky wheel gets the oil!"

How Can *ADVOCURE NF2* Assist?

ADVOCURE would like to be the coordinators and assist NF2 patients and families with their advocacy efforts. If we are going to have a voice, having a unified voice would be best Consider donating or directing your fundraising efforts to advocacy. This is where thousands of dollars in supporting lobbying can turn into millions of dollars of federal research funding. Money donated to *ADVOCURE* could be used to assist in the cost of lobbyists associated with NF groups. For further information and assistance, please contact us at: contact@advocurenf2.org

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The *CDMRP-NFRP* and NF2

Recently, Advocure NF2 Inc wrote to and asked the Congressionally Directed Research Programs (CDMRP NFRP) director, Dr. Naba Bora for clarification on CDMRP's grant funding mechanism, as well as to explain its present NF Consortium centers lack of 'NF2 expertise'.

Q. *Can you please tell us if the Consortium grant funding is up for renewal in 2011? If so what, if anything, can ADVOCURE, as well as the NF2 community, do to enable renewed funding that includes an NF2 center or two?*

A. The CDMRP NFRP does not offer renewals for grants. With appropriate justification for continued support of an existing initiative such as a Consortium, a competition based process would be implemented to allow submission of a new proposal. This process would allow applications from any organization so it would not be restricted to the existing grantee. Because of acquisition regulations, we cannot release any information about future initiatives until funding has been appropriated and recommendations have been made by the Integration Panel. Information will be made available to the public through the release of a Program Announcement.

The Consortium was developed to address several problems that NF investigators were facing in conducting clinical trials. To address these problems it was determined that there was a lack of adequate infrastructure which is needed to support such trials and that a consortium would be better able to do so. It was also felt that such an initiative would be complicated to establish and more so if it was initially required to address two distinct disorders, NF1 and NF2. Another consideration was the current state of the science. Because NFRP funding is not guaranteed from year to year it is difficult to plan for more than one year at a time. When the NF Consortium was developed we were fortunate enough to have received $25M which enabled us to commit the extensive resources needed to support such a large undertaking.

With the advances in NF2 research there are greater opportunities to purse NF2 trials so the NF Consortium has set up a NF2 Committee and representatives have been in discussions with the NF2 scientific community about conducting NF2 clinical trials. The NFRP truly appreciates the dedication of Advocure and its representatives.

Q. *It is our understanding the present plan is to utilize the centers that were originally chosen for their NF1 expertise. While there is currently an "NF2 Committee" within the Consortium, there is no plan to expand or change the original structure of the Consortium. This seems like fitting a square peg into a round hole?*

A. Since the intent of the NF consortium was first to conduct NF1 studies before expanding, only sites with the capability to recruit sufficient numbers of NF1 patients were selected. **It would not be possible to conduct NF2 trials without including additional NF2 specific sites. The operating procedures of the consortium include the ability to add sites as needed for specific studies and the consortium is aware of the need for NF2 sites to support a trial.**

We are confident that the leaders in the NF field will work together to advance NF2 research and to find effective treatments.

Sincerely,
Naba Bora, Ph.D.
CDMRP NFRP, U.S. Department of Defense (DOD)

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NF Consortium and NF2: A Summary

by: R Silva
Advocure NF2, Inc.

In 2004, the Congressionally Directed Medical Research Programs (CDMRP)'s Neurofibromatosis Research Program (NFRP), took the controversial step of announcing a new *NF Consortium Award*, to develop the infrastructure and resources for investigators to conceive, develop, and conduct collaborative clinical trials - **but for NF1 only.**

And therein lies the reason Advocure NF2 Inc was formed.

Despite the fact that the NF2 gene was identified in 1993 and much has been learned about how the gene works, there is still no systemic drug therapy for NF2.

Recently, Advocure followed up if this situation has improved.

The *NF Consortium's* program manager, Karen Cole – Plourde, replied that a newly formed *'NF2 Committee'* within the *NF Consortium* was initiated in 2009, for the purpose of expanding its activities to include NF2:

> *"The NF2 committee has been charged with identification of candidate clinical trials for patients with NF2 and developing protocols for future implementation by the NF Consortium."*

The co-chairs of the newly formed *NF2 Committee* are Dr. James Tonsgard of Chicago's Children, and Dr. Nichole Ullrich of Boston's Children. In July 2010, Dr. Elizabeth Schorry of Cincinnati's Children, and Dr. Scott Plotkin of Boston (MGH) were added also as members of this committee.

In addition, the *NF Consortium* is to begin:

> "Collaborations with Dr. Scott Plotkin on an NF2 grant titled, ***A Phase II Trial of Bevacizumab in Treatment of Symptomatic Vestibular Schwannoma.*** Dr. Scott Plotkin has obtained funding from *Genentech* to support this study and will utilize the *NF Consortium* to include patient recruitment from participating sites."

However, currently (as noted by Advocure), all ten *NF Consortium* sites are 'appropriate' for NF1 patients only. Thus, adequate NF2 patient recruitment numbers from this arrangement may not be feasible, as recently pointed out by Dr. Naba Bora of the CDMRP NFRP :

> *"It would not be possible to conduct NF2 trials without including additional NF2 specific sites* [Advocure note: such as NYU, OSU, HEI, etc, where adequate NF2 patient numbers exist]. *The operating procedures of the consortium include the ability to add sites as needed for specific studies and the consortium is aware of the need for NF2 sites to support a trial."*

On August 23 2010, Advocure NF2 was invited to participate in a conference call with both Dr. Bruce Korf (Principal Investigator of the Consortium) and Dr. Roger Packer (Chair of the Consortium), in order to clarify the NF Consortium's timeline on NF2's inclusion for trials.

Issues/Responses, by: Barbara Franklin, Advocure NF2:

1. The *NF Consortium* was formed following a meeting jointly sponsored by the *DOD* and *NIH*. The main impetus was recognition that clinical trials were difficult to conduct in any single institution, and the complexities of regulatory requirements make it desirable to have a central operations center to facilitate these issues. At the time of the original meeting, the NF2 researchers present encouraged the group to focus first on NF1, in part because at the time there were no drugs available to test in NF2 patients and in part because they recognized the complexity in establishing the *consortium*.

2. It was very complicated to get up and running, including getting significant funding. It has required several years to get the infrastructure up and running smoothly.

3. The centers were chosen by *DOD* following an open competitive process - they made a significant contribution of funding.

4. Most of the *consortium* sites have their greatest expertise with children with NF1, as the original protocols were mainly tailored to this group (see point #1).

5. Dr. Scott Plotkin's proposed trial fits well as he wants it to initially be focused on 12-30 year olds. *Genentech* is financing some of this and wants as few sites as possible, to be able to adequately audit these sites. This effort has been between Scott and *Genentech*.

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6. If Dr. Scott Plotkin can get *Genentech* to agree to other additional sites, its fine with them. But again, there would need to be significant funding and coordination to get them up to speed.

7. A site also must be prepared to cover some of the shared expenses not covered by the grant.

8. They guesstimate that each hospital pays more than $100,000 for this operations support.

9. Any center that participates has to pledge that *consortium* protocols will be given priority, so as to avoid biases, e.g., keeping out the most difficult cases, to avoid artificial positive or negative results.

10. Some centers more "appropriate" for NF2 declined to be part of this, as they have other drugs they're testing and don't necessarily want to prioritize the *Consortium* drugs.

11. Because of the orphan drug status, it is an easier step for a pharma company to stop/pull out of the trial if it becomes problematic.

12. The way the *consortium* works is that the centers that are part of it must be included in the study, they can't be cut out. Other sites can be added on a case-by-case basis according to their ability to participate and the need to include them to achieve the aims of a particular study.

13. In terms of a timetable, under normal circumstances this might be 6 months, but due to the complexity including contract negotiations that haven't even begun yet between *Genentec* and *DOD*, this will be 8-9 months' away at the earliest.

14. *DOD* has been great – and actually is helping streamline the process going forward.

15. It is believed that centers will work with other hospitals nearby to advise NF2 patients of this trial. An example of this would be *Cincinnati* working with *Ohio State.*

The following are answers to questions that Ms. Barbara Franklin asked Dr. Bruce Korf to answer after the conference call:

1. **Q**: How will patient care be monitored during this trial if a patient from *Ohio State* participates with *Cincinnati,* for instance (or a patient from *House* participates with *Utah?)*

   A: *There are strict requirements for monitoring patients stipulated in the protocol. Some of these can be done at a remote site (like MRIs or blood tests); others require travel to the consortium site.*

2. ***Q:*** Will travel to a consortium center be required? If so, who pays for the travel?

   A: *It is necessary to travel to the consortium site to get access to medication and for some evaluations. Funds are not available to support travel. In some cases for other protocols we've been able to get free flights, etc., but otherwise the patients pay for this.*

3. **Q:** Going forward, are there NF2 sites slated for inclusion, e.g., *MGH, HEI, NYU, OSU?*

   A: *It is my hope that we'll be able to submit a proposal in 2011-2012 to renew the consortium and in that process it will be possible to add new sites. I'd strongly favor including major NF2 sites in that proposal.*

4. **Q:** Is there a patient database that will be available for other drugs/centers in the future?

   A: *There is no central patient database associated with the consortium – the funding is related to specific trials, not to creation of such resources. Each site tends to have its own database of patients whom they can call on.*

5. **Q:** Is there collaboration with *NIH, CTF, NF Inc?*

   A: *NIH is one of the sites involved in the consortium. CTF and NF, Inc are familiar with the consortium and tend to refer patients to us if they inquire. I believe that they link to our website as well.*

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Neurofibromatosis Networking – How Can Consortia Advance Research Progress to the Clinic?

Recently, Advocure NF2 Inc wrote CTF to ask for clarification and for explanation of differences between the CDMRP's NF Consortium, CTF's NF Preclinical Consortium, and CTF's NF Clinic Network.

by: Dr. Kim Hunter-Schaedle
Chief Scientific Officer
Children's Tumor Foundation

Neurofibromatosis (NF) research has advanced rapidly in the past five years due in part to the three major initiatives that support multi site clinical trials, collaborative preclinical drug screening and a national network of NF clinics, respectively. Though established independently, these initiatives are anticipated to become further interlinked and be major drivers toward finding effective treatments for NF2.

Phase II NF Clinical Trials Consortium: Prior to the mid-2000's, only a handful of small NF clinical trials had been initiated. This was due in part to the fact that NF biology had not yet ripened to a point where there were obvious drug therapies to test; and in part because recruiting sufficient patients for an NF clinical trial is daunting, even for large NF clinics. To accelerate this, in 2005 the Congressionally Directed Medical Research Program for Neurofibromatosis Research (CDMRP NFRP) funded a multi site Phase II NF Clinical Trials Consortium. The initial focus was on NF1, since NF1 biology was at that time somewhat further advanced than NF2, providing some rationale for selecting drugs to be tested. Nine participating sites were selected by CDMRP through a competitive process. The Phase II Consortium has since commenced trials of Lovastatin for cognitive defects; Sirolimus for plexiform neurofibromas; and Everolimus for optic pathway glioma. A management infrastructure has been established with a coordinating center at University of Alabama. At the recent Children's Tumor Foundation Workshop 'NF2: State of the Trial', the NF2 researchers considered the opportunity to utilize the Phase II group's infrastructure to conduct NF2 clinical trials. The current participating centers are enthusiastic about this, and it will require adding consortium sites with significant NF2 expertise. Discussions are now underway to conduct the first NF2 clinical trial within the Phase II Consortium. For more information and updates on this initiative visit: http://nfconsortium.org/

Advocure Note: As of summer 2010, CDMRP's ten NF Consortium centers are:

1. *Children's Hospital, Boston*
2. *Children's Hospital at Westmead, University of Sydney*
3. *Children's National Medical Center (Washington, D.C.)*
4. *Cincinnati Children's Hospital Medical Center*
5. *National Cancer Institute (Bethesda, MD)*
6. *University of Alabama at Birmingham*
7. *University of Chicago*
8. *University of Pennsylvania*
9. *University of Utah*
10. *Washington University (St. Louis)*

NF Preclinical Consortium and Clinical Trial Awards: In 2006 the Children's Tumor Foundation (CTF) developed a Strategic Plan for NF Research, identifying areas that needed funding in order to advance more rapidly toward identifying effective NF drug treatments. The top area of need identified was for coordinated preclinical drug testing – i.e. assessing candidate NF drugs in cells or in mouse models to see what drugs might be worth advancing to clinical trials. NF preclinical drug screening is significantly aided by the fact that there are a number of outstanding genetic mouse models of individual NF tumor types. In 2007 CTF assembled an NF Preclinical Consortium (NFPC) of 6 sites – these included mouse models of both NF1 and NF2 tumors. NFPC has tested a series of promising drugs in collaboration with pharmaceutical and biotechnology companies. The companies provide the drug as well as technical support and……

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guidance. Industry partners to date have included Novartis, Genentech and Avila Therapeutics. This has been CTFs largest funded program ever -a total cost of just over $4M. In conjunction with NFPC, CTF also set up a Clinical Trial Awards program offering $125,000 to support pilot clinical trials, setting aside a total of $1M for this program over 3 years. To date two trials have been funded including one NF2 (Lapatinib, phase zero) which is ongoing. Looking ahead, CTF will work closely with the Phase II Trials Consortium sites so that emerging promising drugs can quickly go forward into pilot trials then Phase II studies. For more information and updates on this initiative visit: http://www.ctf.org/For-Scientists/ddi-nf-preclinical-consortium.html

***Advocure Note*: As of summer 2010, CTF's six NF Preclinical Consortium centers are:**

1. *University of California, San Francisco (NF1)*
2. *Washington University School of Medicine (NF1)*
3. *Cincinnati Children's Hospital Medical Center (NF1)*
4. *House Ear Institute (NF2)*
5. *Harvard Med School/Mass General Hospital (NF2)*
6. *Harvard Medical School/Brigham & Women's Hospital (NF1)*

NF Clinic Network, Patient Registry and BioBank:

Recommendations of the CTF 2006 Strategic Plan for NF Research was to establish a national NF Clinic Network; and an NF Patient Registry and BioBank. At that time, though a number of websites (including CTF) listed clinics that saw NF patients there was no readily available detailed information about individual clinics, nor any standard measures by which these clinics could be compared. In 2007 the CTF Clinical Care Advisory Board launched the NF Clinic Network and developed 'Principles of Operation of an NF Clinic' making these publicly available. Any clinic was eligible to apply for membership of the NF Clinic Network (NFCN) and those clinics considered to be meeting the 'Principles' became 'NFCN Affiliate Clinics'. To date NFCN has 45 member sites seeing a reported total of 8,000 NF patients (350 of these NF2 patients) in 2009. Each site is evaluated annually through a reporting system. Between 2008 and 2010, CTF has provided various amounts of funding to NFCN, initially to support clinic coordinator positions, but more recently to encourage clinics to host family and education symposia and to improve clinic interactions with the local NF patients and families. Clinic coordinators from NFCN and non-network clinics gathered at the NF Conference, to exchange ideas and network; a 2011 gathering is planned at the American College of Medical Genetics. To maintain communication throughout the year, in 2010 CTF is introducing a ListServ for clinic staff to exchange questions and thoughts. In late 2010 CTF will launch the long anticipated NF Patient Registry and BioBank. It is anticipated this resource will not only enhance collaboration between NFCN clinics, but will be a major driver in connecting the clinics more closely with NF research and clinical trials. For more information and updates on this initiative visit: http://www.ctf.org/For-Scientists/nf-clinic-network.html

Advocure Note:
As of summer 2010, the 44 U.S. hospitals or sites that make up CTF's NF Clinic Network (in alphabetical order by State) are:

1. *Neurocutaneous Clinic, Arkansas Children's Hospital (Little Rock, AR)*
2. *University of Alabama at Birmingham, Neurofibromatosis Clinic (Birmingham, AL)*
3. *Neurofibromatosis Planning Clinic, St. Joseph's Hospital and Medical Center (Phoenix, AZ)*
4. *Neurocutaneous Disorders Program, Children's Hospital Los Angeles (Los Angeles, CA)*
5. *UCSF NF/Ras Pathway Clinic, UCSF Children's Hospital (San Francisco, CA)*
6. *Comprehensive Neurofibromatosis Program, South Bay Regional Genetics Center, Santa Clara Valley (San Jose, CA)*
7. *Neurocutaneous Clinic, The Children's Hospital (Aurora, CO)*
8. *Neurofibromatosis Clinic, Children's National Medical Center (Washington, DC)*

continued on the next page……

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9. *The Neurofibromatosis Clinic, Disney Children's Hospital (Orlando, FL)*
10. *Miami Children's Hospital Neurofibromatosis Center (Miami, FL)*
11. *Neurofibromatosis Clinic, Tampa General Hospital (Tampa, FL)*
12. *Neurofibromatosis Clinic, Children's Memorial Hospital (Chicago, IL)*
13. *The University of Chicago NF Program, the University of Chicago Medical Center (Chicago, IL)*
14. *Indiana University Neurofibromatosis Clinic, Riley Hospital for Children (Indianapolis, IN)*
15. *Neurofibromatosis Clinic, University of Iowa Hospitals and Clinics (Iowa City, IA)*
16. *LSUHSC/Children's Hospital Neurofibromatosis Clinic of New Orleans, Children's Hospital of New Orleans (New Orleans, LA)*
17. *The Comprehensive Neurofibromatosis Center, Johns Hopkins (Baltimore, MD)*
18. *Trans-NIH Intramural NF Clinic, NIH/NHGRI (Bethesda, MD)*
19. *MGH Neurofibromatosis Clinic, Massachusetts General Hospital (Boston, MA)*
20. *Neurofibromatosis Center, Children's Hospital Boston (Boston, MA)*
21. *Henry Ford Neurofibromatosis Clinic, Henry Ford Hospital (Detroit, MI)*
22. *Mayo Clinic, Mayo College of Medicine (Rochester, MN)*
23. *The Minnesota Neurofibromatosis Clinic without Walls (Minneapolis, MN)*
24. *Washington University NF Clinic, (St. Louis Children's Hospital (St. Louis, MO)*
25. *Neurofibromatosis Clinic, Cardinal Glennon Children's Medical Center (St. Louis, MO)*
26. *The Neurofibromatosis Center of New Jersey, UMDNJ-University Hospital (Newark, NJ)*
27. *The Neurofibromatosis Center at Montifiore (Bronx, NY)*
28. *Neurofibromatosis clinic, New York Presbyterian-Columbia University Medical Center (New York, NY)*
29. *The Comprehensive Neurofibromatosis Clinic, New York Presbyterian- Weill Cornell Medical Center, Division of Child Neurology (New York, NY)*
30. *NYU Langone Medical Center NF Clinic, Hassenfeld Clinic (New York, NY)*
31. *Neurofibromatosis Clinic, University of North Carolina Hospitals (Chapel Hill, NC)*
32. *NF Program at Duke University Medical Center, Duke University Medical Center (Durham, NC)*
33. *Neurofibromatosis Clinic, Nationwide Children's Hospital (Columbus, OH)*
34. *Ohio State University Medical Center (Columbus, OH)*
35. *Cincinnati Neurofibromatosis Center, CCHMC, Div. of Human Genetics (Cincinnati, OH)*
36. *Comprehensive Neurofibromatosis Program, Cleveland Clinic Foundation (Cleveland, OH)*
37. *University of Oklahoma NF Clinic, OU Children's Physicians Building (Oklahoma City, OK)*
38. *Neurofibromatosis Clinic, Children's Hospital of Philadelphia (Philadelphia, PA)*
39. *Neurofibromatosis Clinic, Children's Hospital of Pittsburgh (Pittsburgh, PA)*
40. *Neurofibromatosis Clinic, Texas Children's Hospital Clinical (Houston, TX)*
41. *Comprehensive Neurofibromatosis Clinic, Children's Medical Center of Dallas, University of Texas Southwestern Medical Center (Dallas, Texas)*
42. *University of Utah NF Clinic (Salt Lake City, UT)*
43. *Neurofibromatosis Clinic, Children's Hospital and Regional Medical Center (Seattle, WA)*
44. *Neurofibromatosis Clinic, Children's Hospital of Wisconsin (Milwaukee, WI)*

Symposia of NF2 Interest

- Sept 9-12, 2010 in Oslo, Norway, 14th European NF-Meeting, 2010 Oslo, Hosted by The Norwegian NF Association and Frambu.
- Oct 16, 2010 in Chicago, IL, USA, NF Midwest 2010 Symposium. Hosted by Neurofibromatosis Midwest – NF Inc.
- Oct 24, 2010 in Boston, MA, USA, NF Symposium. Sponsored by the Center for Neurofibromatosis and Allied Disorders (CNfAD).
- June 11-14, 2011 in Jackson Hole, WY, USA. **2011 NF Conference**. Hosted by the Children's Tumor Foundation (CTF).

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Proposed *Nilotinib* Trials Announced for NF2

Recently, Advocure NF2 Inc spoke with both Dr. Abhijit Guha of UHN TWH in Toronto and Novartis regarding proposed clinical trials of Nilotinib on Adult and Pediatric NF2. Set to begin in spring of 2011 in Canada.

by: Barbara Franklin
Advocure NF2, Inc.

A new ***NF2 Phase 2*** clinical trial has been announced using *Nilotinib,* the second generation of *Gleevec* (which has been used for decades in a variety of other human tumors). This trial will be through the University Health Network (UHN), in Toronto Canada.

Dr. Abhijit Guha, Professor of Neurosurgery will conduct and is the Primary Investigator of this trial. Dr. Guha studied sporadic and NF2 schwannomas cell lines provided by House Ear Institute (HEI) and found that they over expressed *PDGF* and *c-Kit Receptors,* which are inhibited by *Gleevec.* He then tested *Gleevec* on these cell lines. It inhibited schwannoma viability, proliferation and growth, as well as induced apoptosis or cell death. He reported these findings in Cancer Research, in 2009.

Novartis has developed *Nilotinib,* by slightly modifying the structure of *Gleevec,* to address the problem of tumors which become resistance to *Gleevec* after a period of treatment. This targeted biologic also offers lower toxicity and increased tissue penetration - thus potentially having even better results with less side effects. To date, *Nilotinib* only has been given to adults who have developed a resistance to *Gleevec*, with very satisfactory results. There have been no similar studies in children, and its potential use in schwannomas has not been tested. This trial will consist of 45 adult patients with growing vestibular schwannomas, i.e., as seen in serial MRIs showing volumetric growth greater than 15%. *Nilotinib* is an oral drug, and in the trial, will be taken twice a day. The cohort will include both sporadic and NF2 patients. The drug will be administered for 12 months, with follow up for another two years. The key exclusions will be vestibular schwannomas which due to compression of the brainstem or hydrocephalus is already causing symptoms such as ataxia and headache. The objectives are to determine if the drug can stabilize the growth of the vestibular schwannomas or cause shrinkage of the tumors as defined by 20% or more reduction by MRI volumetric measurement. In addition to tumor growth, other parameters related to hearing, quality of life will also be measured and compared to historical and concurrent patient groups who are managed with current standard treatment strategies which include observation, surgery or radiosurgery.

It is Dr. Guha's intention to also track other NF2 associated tumors, such as meningiomas and other schwannomas during the trial. They are using a consortium of hospitals throughout Canada to recruit patients, majority of whom will have NF2.

A ***pediatric Phase 1*** dose escalation trial is planned for the near future through Hospital for Sick Children in Toronto, the largest pediatric hospital in Canada.

While Dr. Guha is excited about the potential of this drug, he, like many others believe that NF2 may have to be treated with a combination of current treatment strategies (surgery, radiosurgery) and likely multiple biological therapies aimed at different biological properties of the tumor cells such as increased proliferation, vascularization etc. The treatment strategies will likely not be the same for all patients, but must be individualized and altered as the tumor and patient characteristics change with time. He pointed out that schwannomas are not driven by just one genetic alteration, but rather multiple pathways and thus, monotherapy will not be the 'Holy Grail'.

RESEARCH
at University Health Network

Abhijit Guha, FACS, FRCSC, MD, MSc, is co-director of the Arthur & Sonia Labbatt Brain Tumour Research Centre at the Hospital for Sick Children's Research Institute and holds the Alan & Susan Hudson Chair in Neuro-oncology at the University of Toronto. Dr. Guha also undertakes clinical trials in surgical neuro-oncology as a neurosurgeon-scientist based at UHN's Toronto Western Hospital. He is a past president of the Society of Neuro-oncology and serves as medical advisor to Acoustic Neuroma Society of Canada and Neurfibromatosis Society of Ontario.

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NF2 Clinical Trials & 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****).*

- ***Concentration and Activity of Lapatinib in Vestibular Schwannomas***
  ClinicalTrials.gov Identifier: NCT00863122
  This study is currently recruiting participants.
  This 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

- **Neurofibromatosis Type 2 Associated Color Vision Anomalies and Birth Defects: Incidence and Insights**
  This study is currently recruiting participants
  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

- ***PTC299 for Treatment of Neurofibromatosis Type 2 (NF2)***
  ClinicalTrials.gov Identifier: NCT00911248
  This study is currently 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. Safety studies in research animals indicate good tolerability at doses and drug levels that are higher than those planned for the clinical studies. Results from Phase 1a studies in healthy volunteers indicate that PTC299 achieves levels of PTC299 in the bloodstream that are known to be active in animal models of human tumor. This Phase 2 study is designed to test the hypothesis that PTC299 will be tolerable and will show evidence of VEGF reduction, antitumor activity, and hearing improvement when administered orally to patients with NF2.
  • Oncology – PTC299
  • Neurofibromatosis Type 2 Clinical Trial Overview
  • Neurofibromatosis Type 2 Trial FAQ

- ***Phase II Trial of Bevacizumab in Patients With Recurrent or Progressive Meningiomas***
  ClinicalTrials.gov Identifier: NCT01125046
  This study is not yet open for participant recruitment.
  RATIONALE: Monoclonal antibodies, such as bevacizumab, 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 works in treating patients with recurrent or progression meningiomas.

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NF2 Clinical Trials & Studies, cont.

- ***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.
  Lapatinib is an oral drug that is approved by Food and Drug Administration (FDA) for other types of tumors, it is not approved by the FDA for treatment of NF2 related tumors. The investigators know a lot about how well it is tolerated, but the investigators do not know if it is effective in treating your condition, therefore it is considered to be an investigational medication. This study will test whether Lapatinib may shrink tumors commonly found in patients with NF2 or stop them from growing. This will help us to decide if Lapatinib should be used to treat NF2 patients in future. Lapatinib is a drug that has been used for over 10 years to treat various forms of cancer. It has not been studied for the treatment of tumors in NF2 patients.

- ***Sunitinib in Treating Patients with Recurrent or Unresectable Meningioma, Intracranial Hemangiopericytoma, or Intracranial Hemangioblastoma***
  ClinicalTrials.gov Identifier: NCT00561665
  This study is currently recruiting participants.
  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

- ***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.

- ***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 currently 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.

- ***Monthly SOM230C for Recurrent or Progressive Meningioma***
  ClinicalTrials.gov Identifier: NCT00859040
  This study is currently 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.

- ***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.

NF2 Compass
A Quarterly Advocure Online-Newsletter
Formerly Known as Flutterby
Advocure NF2 Inc. is a Working Advocacy Group, Liaison, and 501(c)(3) Public Charity for the NF2 International Community & NF2 Crew.
Issue 7, page 19; autumn 2010

NF2 Clinical Trials & Studies, cont.

- ***Corticosteroids in Prevention of Facial Palsy after Cranial Base Surgery***
  ClinicalTrials.gov Identifier: NCT00438087
  This study is currently recruiting participants.
  Facial palsy after surgical removal of cranial base tumors adherent to the nerve can partly be explained by inflammation.

- ***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.

- ***Safety and Efficacy Study of BrainPort® Balance Device in Peripheral Vestibular Dysfunction.***
  ClinicalTrials.gov Identifier: NCT00768378
  This study has been completed.
  The purpose of this study is to assess the safety and efficacy of the BrainPort balance device in improving balance and gait as measured by clinically accepted standardized balance assessments in subjects with peripheral vestibular dysfunction.
  • Wicab is sponsoring clinical studies to evaluate the effectiveness of the BrainPort® balance device for improving balance in people with balance difficulties.

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
- **lapatinib**
- propolis (**BIO30**™ propolis)
- valproic acid
- rapamycin
- cetuximab
- trastuzumab
- vandetanib (Zactima™)
- **nilotinib**
- **curcumin**

If there is any other information about NF2 drugs or drug trials that you wish to bring to our attention, please contact us at: contact@advocurenf2.org

For more trials and/or studies, please see: *www.clinicaltrials.gov/ct2/results?term=nf2*

When there, please try inputting "neurofibromatosis type 2", or a NF2 tissue type, such as; "Vestibular Schwannoma", "Schwannoma", "Meningioma", "Glioma", "Ependymoma", or "Astrocytoma", within the relevant search field.

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Why not forward it to them? Thanks.

http://www.advocurenf2.org/newsletter/NF2-compass_2010fall.pdf