



# 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  |
| NF2 research Progress Report at OSU .....                        | pg 5  |
| Featured Extraordinary NF2er .....                               | pg 7  |
| Fundraising .....  | pg 8  |
| NF Symposiums or Conferences, etc<br>With an NF2 component ..... | pg 8  |
| NF2 Clinical Trials & Studies.....                               | pg 9  |
| Some Pharmaceuticals of NF2 Interest .....                       | pg 12 |

## 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](mailto:contact@advocurenf2.org)  
Web: [www.advocurenf2.org](http://www.advocurenf2.org)

[Advocure Brochure](#) [RSS Feeds](#)



## 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

*Young "NF2er" Devon Payette shares an awesome message while on vacation at an Ocean City, NJ beach.*



**July 25, 2011** - Kim Underwood Gillet's son Devon Payette, at a beach in Ocean City, NJ! It was his first time at a boardwalk. He had a BLAST! Devon came all the way from Canada to attend the Ride4NF fundraiser hosted by Jaime L. Cirillo on July 23. Awesome message and photo, thank you!

## A benefit through Advocure NF2 Inc. to fund Children's Tumor Research - August 31, 2011



**Saturday, October 22nd, 2011** will be the 7th annual Halloween Bash and our goal is to raise \$100,000. **All donations sent between September 1, 2011 and October 31, 2011 will be matched by the Thoms family**, so we could conceivably raise a total of \$200,000. Please visit the [website](#) for more information or [click here](#) to **donate instantly with PayPal!**

CTF BLOG Update - Call for NIH Bench-To-Bedside Award Apps: Letter of Intent Sept 28th Deadline - August 25, 2011



Do you have a basic discovery that you think you can translate to the clinic for the benefit of patients? The National Institutes of Health (NIH) Clinical Center has announced availability of funds for the 2012 Bench to Bedside Awards Program...

## Rebuilding my life - with NF2 - August 25, 2011

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....





# NF2 Compass

## A QUARTERLY ADVOCURE ONLINE NEWSLETTER



Formerly known as "Flutterby"

### [Various NF video interviews at CTF - August 21, 2011](#)

According to CTF: "all videos ARE captioned". Dr. Scott Plotkin - Progress of **NF2** clinical trials, Gareth Evans - Link Between **NF2** and Schwannomatosis, Dr. Jaishri Blakely - Schwannomatosis or **NF2**, Dr. Gareth Evans - Background - **NF2** & Schwannomatosis, Dr. Gareth Evans - Visual Traits to **NF2**?, Matthias Karajannis - What's happening with **NF** Clinical Trials, etc.

### [Five New Neurofibromatosis Drug Discovery Initiative Awards - August 20, 2011](#)

The Children's Tumor Foundation (CTF) is delighted to announce the funding of five new Drug Discovery Initiative (DDI) Awards totaling \$125,000, from applications received for our spring 2011 deadline.

### [2011 NF Conference Abstract Now Available! - August 20, 2011](#)



The **NF** Conference is the largest annual gathering of researchers and clinicians focused on neurofibromatosis and has been convened by the Children's Tumor Foundation (CTF) for more than 20 years.

### [Phase II Study of Everolimus \(RAD001\) in Children and Adults With Neurofibromatosis Type 2 - August 19, 2011](#)

This trial studies whether Everolimus is efficacious in treating **Neurofibromatosis Type 2**...

### [Study of RAD001 for Treatment of NF2-related Vestibular Schwannoma - August 15, 2011](#)

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. ClinicalTrials.gov Identifier: NCT01345136.

### [New clues to fighting genetic disease - August 12, 2011](#)

"Scientists have hit on a genetic trick that opens up fresh avenues for the treatment of devastating diseases, such as cystic fibrosis, muscular dystrophy and certain forms of cancer," reported The Guardian.....

### [Gene Therapy Cures Adult Leukemia - August 11, 2011](#)



Two of three patients dying of chronic lymphocytic leukemia (CLL) appear cured and a third is in partial remission after infusions of genetically engineered T cells..... (now it's **NF2** and solid tumors' turn)....

### [NFRP Funding Opportunities - August 9, 2011](#)



The Neurofibromatosis Research Program (NFRP) has announced the funding mechanisms for the FY11 appropriation of \$16M.....

### [CTF Funds SIX Neurofibromatosis Young Investigator Awards - August 8, 2011](#)

The Children's Tumor Foundation (CTF) is delighted to announce the funding of SIX Young Investigator Awardees from application received for our 2011 program. 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...

### [NF2 research Progress Report at OSU - August 2011](#)



Our research at OSU (partially funded by Advocure **NF2** Inc) focuses on the generation of mouse models for **NF2**-associated schwannoma and meningioma and the identification of novel therapeutics for these tumors. We have made the following progress in the past year...

### [Middle fossa decompression for hearing preservation: a review of institutional results and indications - August, 2011](#)

A total of 49 patients underwent middle fossa decompression of vestibular schwannoma. Approximately 90% of patients had documented hearing loss before surgery, and more than 50% of patients exhibited significant tumor growth before surgery...

### [Investigation of the intra-tumoural concentration and activity of Nilotinib in cutaneous schwannomas - July 28, 2011](#)

This research study will look at the way in which Nilotinib is taken up into the skin tumours of patients who have **NF2** mutation. The information obtained will be used to decide whether Nilotinib should be investigated further as a treatment for skin tumours caused by **NF2** mutation...





# NF2 Compass

## A QUARTERLY ADVOCURE ONLINE NEWSLETTER



Formerly known as "Flutterby"


### Jessica Stone update - July 25, 2011

...It has 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 (NF2)** 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...

### Beet juice: It does a body very good - July 20, 2011

Beets offer more than just nitrite. Beet juice is packed with Vitamin A, Vitamin B-6, iron and calcium. They have antioxidant and anti-inflammatory benefits. Beet fibre is good for digestive health. An Italian study linked the carotenoids found in beets - lutein and zeaxanthin - as unique support to eye health...

### Proposed Trial for NF2 in the UK - July 13, 2011

 In a human cell culture model, Professor Oliver Hanemann showed that this new target can be effectively inhibited with a drug that leads to the reduction of the tumour's growth. Many **NF2** sufferers have multiple tumours, including schwannomas, at nerve endings in the skin. These 'nerve tumours in the skin' allow an innovative clinical trial design in which one can directly test if the drug gets into the tumour and affects the tumour...

### Nilotinib alone or in combination with Selumetinib is a drug candidate for Neurofibromatosis type 2 - July 13, 2011

Loss of the tumor suppressor merlin is a cause of frequent tumors of the nervous system, such as schwannomas, meningiomas, and ependymomas, which occur spontaneously or as part of **Neurofibromatosis type 2 (NF2)**. Because there is medical need for drug therapies for these tumors, our aim is to find therapeutic targets. We have studied the pathobiology of schwannomas, because they are the most common merlin-deficient tumors and are a model for all merlin-deficient tumors. With use of a human schwannoma in vitro model, we previously described strong overexpression/activation of platelet-derived growth factor receptor- $\beta$  (PDGFR- $\beta$ ) leading to strong, long-lasting activation of extracellular-signal-regulated kinase (ERK1/2) and AKT and increased schwannoma growth, which we successfully inhibited using the PDGFR/Raf inhibitor sorafenib.

### Cranial meningiomas in 411 NF2 patients with proven gene mutations - June 28, 2011

Meningiomas have been reported to occur in approximately 50% of **neurofibromatosis type 2 (NF2)** patients. The **NF2** gene is commonly biallelically inactivated in both schwannomas and meningiomas...

### The Neurofibromatosis Conference: Tumor Targets, Drug Trials and a Schwannomatosis Database - June 15, 2011



"The **2011 NF Conference** kicked off this weekend with some interesting and exciting presentations. On Saturday, Dr.

Filippo Giancotti (MSKCC) provided an update on his novel research first reported in 2010 that described for the first time a role for **NF2** merlin protein in the cell's nucleus. Dr. Giancotti has continued to unravel the signaling activities of merlin in the nucleus, and interestingly also showed that in sections of human meningioma tissue, merlin protein is not present in the nucleus. This would provide support for Dr. Giancotti's unique idea that merlin controls normal cell division and that lack of its nuclear function might be a factor in promoting **NF2** tumor growth...

### Emerging therapeutic targets in schwannomas and other merlin-deficient tumors - June 7, 2011

Deficiency of the tumor suppressor protein merlin leads to the development of benign tumors of the nervous system such as schwannomas, ependymomas and meningiomas. These tumors can occur spontaneously or as part of a tumor predisposition syndrome called **neurofibromatosis type 2 (NF2)**...

### Neck Surgery Eases Facial Paralysis - July 20, 2011

Cutting a strip of platysma muscle from the neck can relieve chronic rigidity and involuntary movement in patients with facial paralysis, according to a small study...

### The Magic of Merlin Antibodies - July 20, 2011

Merlin is an imaginatively-named tumor suppressor encoded by the tumor suppressor gene **NF2**, a member of the Neurofibromin family. It is mainly expressed in nervous tissue. Merlin antibodies have shown **NF2** mutations can cause **Type 2 Neurofibromatosis**...





# NF2 Compass

A QUARTERLY ADVOCURE ONLINE NEWSLETTER



Formerly known as "Flutterby"

### [Knox filmmaker's ET/Russia documentary nearing](#)

[a wrap - July 16, 2011](#) Knoxville News Sentinel

While working on "Nuke Bonds," Beth Humpert was diagnosed with **neurofibromatosis type-2**, a disease that causes tumors generally in the brain....

### [Hang in there, Four Turtles - July 4, 2011](#)

Manila Bulletin

Like me, they are afflicted with **Neurofibromatosis Type 2 (NF2)**. I met the Remigio family in 2007 after they saw me in a TV interview where I mentioned....

### [AstraZeneca and PTC Ally On Small Molecule Drugs against](#)

[Cancer - June 29, 2011](#) Genetic Engineering News

**GEN** ...And a Phase II trial in **Neurofibromatosis Type 2**. The firm's early-stage pipeline includes an HCV program focused on inhibiting HCV replication....

### [Rushing Windsor retiree cries foul over police takedown: 'I'm](#)

[an old man' - June 29, 2011](#) Windsor Star

"I was surprised, because I thought something was wrong with my dad," said Rita, who suffers from **Neurofibromatosis Type 2**, a disorder in which nerve tissue grow tumours that can damage the nerves..."

### [Ed Port is 'up and around,' hospital spokeswoman](#)

[says - June 24, 2011](#) Youngstown Vindicator

Port, 41, suffers from **neurofibromatosis type 2**, a genetic disorder that causes tumors. Port's tumor obscured the left side of his face...

### [Running with a Purpose: Fighting NF - June 16, 2011](#)

**NF** It has been over ten years that my niece, Jessica Stone, was diagnosed with **Neurofibromatosis Type 2 (NF2)**, a benign genetic disorder that causes tumors to grow throughout the central nervous system...

### [Naperville walk combats neurofibromatosis - June 1, 2011](#)

Chicago Daily Herald - My name is Katie Shepard and it was 20 days after my 18th birthday when I was rocked with the diagnosis of **neurofibromatosis type II**...

### [Ride for a cause: Ashley's Ride returns to Mancelona](#)

[for 4th year - July 29, 2011](#) Morning Star

Hundreds gathered on Saturday in Mancelona for the fourth annual "Ashley's Ride," a benefit pig roast, six hour motorcycle ride, and auction in memory of local resident Ashley Nicole Sexton, who passed away from **Neurofibromatosis type 2 (NF2)** at the age of 21...

### [Fortunan receives critical surgery; confident that procedures](#)

[will help - July 28, 2011](#) Humboldt Beacon - Twenty-year old

Wilmot is a native of Humboldt County and was recently diagnosed with **neurofibromatosis (type NF-2)**, a debilitating disease that disrupts...

### [Treatment of patients with advanced neurofibromatosis type 2 \(NF2\) with novel molecularly targeted therapies](#)

There are minimal treatment options for advanced inoperable **neurofibromatosis type 2 (NF2)**, a rare and debilitating disorder presenting with multiple vestibular schwannomas, meningiomas, and ependymomas...

### [An anchor between two worlds](#)



Steve Silverman earlier this week sat at the front of his fourth-grade classroom during a reading exercise, pulled out a crumpled ball of paper and lobbed it at a student. With their hands stretched...

### [Emerging therapeutic targets in schwannomas and other merlin-deficient tumors - June 7, 2011](#)

**PubMed** Deficiency of the tumor suppressor protein merlin leads to the development of benign tumors of the nervous system such as schwannomas, ependymomas and meningiomas. These tumors can occur spontaneously or as part of a tumor predisposition syndrome called **neurofibromatosis type 2 (NF2)**...





# NF2 Compass

## A QUARTERLY ADVOCURE ONLINE NEWSLETTER

Formerly known as "Flutterby"



### NF2 research Progress Report at Ohio State University - August 2011

For a transcript of Dr. Brad Welling's interview with Advocure on March 30, 2011 [click here](#).



Our research focuses on the generation of mouse models for NF2-associated schwannoma and meningioma and the identification of novel therapeutics for these tumors. We have made the following progress in the past year.

#### Research Progress:

##### **(1) Small-molecule inhibitors, AR-12 (formerly named OSU-03012) and AR-42 (previous (S)-HDAC-42):**

AR-12 is a derivative of Celecoxib (Celebrex<sup>TM</sup>) developed by Dr. Ching-Shih Chen at the OSU CCC and licensed to Arno Therapeutics. It is a potent inhibitor of phosphoinositide-dependent kinase 1 (PDK1), an upstream kinase that phosphorylates and activates AKT. We previously showed that AR-12 effectively inhibited both benign and malignant schwannoma cells in vitro and in vivo. We have assessed the pharmacokinetics and pharmacodynamics (PK/PD) of AR-12 and found that it is orally bioavailable and well-tolerated, crosses the blood-brain barrier, and shows little or mild toxicity in mice. AR-12 is currently in Phase I trial for advanced or recurrent solid tumors and lymphoma at multiple participating sites, including OSU.

AR-42 was also developed by Dr. Ching-Shih Chen at OSU. It is a novel hydroxamate-tethered phenylbutyrate derivative and belongs to a class of anti-tumor drugs that act by inhibiting histone deacetylases (HDACs). In addition, AR-42 could down-regulate AKT. We have found that AR-42 inhibited the growth of human vestibular schwannoma and Nf2-deficient mouse schwannoma cells with an IC<sub>50</sub> of 500 nM and 250-350 nM, respectively. AR-42 also inhibited primary meningioma cells and benign meningioma Ben-Men-1 cells with IC<sub>50</sub> values of 1.5 M and 1.0 M, respectively. AR-42 treatment induced cell cycle arrest at G<sub>2</sub> and apoptosis and decreased p-AKT in both vestibular schwannoma and meningioma cells. In vivo

treatment with AR-42 inhibited the growth of schwannoma xenografts, induced apoptosis, and decreased AKT activation (Bush et al., 2011). In addition, AR-42 is also bioavailable and the first-in-human study for relapsed or refractory multiple myeloma, chronic lymphocytic leukemia, and lymphoma is currently in progress within the OSUCCC James Cancer Hospital. Preclinical PK/PD studies show that AR-42 is also well-tolerated with mild toxicity in mice.

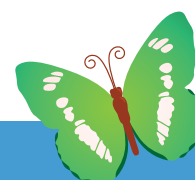
##### **(2) Natural compounds screening:**

Natural products of microbe, plant, or marine origin, either in their naturally-occurring or synthetically-modified forms, have played an important role as established cancer therapeutic agents. In collaboration with Dr. A. Douglas Kinghorn at the OSU College of Pharmacy, we have begun to screen a library of pure, structurally-defined natural products, of which many were found to be highly cytotoxic for one or more cancer cells. From a screen of 19 plant-derived natural compounds, we found that silvestrol potentially inhibit the growth of vestibular schwannoma and meningioma cells with an IC<sub>50</sub> of about 5-10 nM. Silvestrol is a potent anticancer rocaglate derivative from *Aglaia foveolata*. It has potent in vitro and in vivo activities in multiple cancer models including acute lymphoblastic leukemia (ALL) and is currently under pre-clinical development by NCI.

In addition, we are presently testing the efficacy of several commonly-found natural compounds, such as caffeic acid, resveratrol, and curcumin, using various cell culture and animal models for schwannoma and meningioma.

##### **(3) An intracranial luciferase-expressing, merlin-deficient benign meningioma mouse model for therapeutic testing:**

We have shown that Ben-Men-1, a telomerase-immortalized benign human meningioma cell line, did not express wild-type merlin and carried a frame-shift mutation in exon 7 of the NF2 gene (Burns et al., 2011). We have also established luciferase-expressing Ben-Men-1 meningioma cells. Bioluminescence imaging of intracranial Ben-Men-1 and KT21MG1 xenografts in SCID mice detected tumor growth over time. Ben-Men-1 xenograft-bearing mice fed chow containing AR-12, decreased tumor size by about 42% after one month and 65% after three months, compared to mice fed normal diet. Treatment with AR-42 reduced tumor size by about 86% after one month and 94%





# NF2 Compass

## A QUARTERLY ADVOCURE ONLINE NEWSLETTER



Formerly known as "Flutterby"

after three months. Volumetric MRI confirmed these results. Our results indicate that both AR-42 and AR-12 are potential treatments for NF2-deficient meningiomas.

#### **(4) Nf2Nestin conditional knockout (CKO) mice:**

We have generated a tamoxifen-inducible Nf2 knockout mouse model (Nestin-CreER;Nf2flox2/flox2) in which the Nf2 gene can be inactivated in neuroprogenitor cells at different times during development (Akhmamyeva et al., 2011). We found that Nf2 inactivation in these Nestin-CreER;Nf2flox2/flox2 mice during mid-to-late gestation resulted in schwannomas and lymphomas at a high frequency (~52%). The Nf2Nestin CKO mice that we have generated may serve as an alternative model for NF2-associated schwannomas.

#### **(5) Transgenic NF2-T mice:**

Several lines of transgenic mice carrying different lengths of the NF2 promoter-driven SV40 T antigen were produced. Interestingly, transgenic NF2P2.4-T and NF2P0.9-T carrying a 2.4- or 0.9-kb NF2 promoter, respectively, efficiently developed malignant peripheral nerve sheath tumors (MPNSTs) or schwannomas as early as 3 months old and with 100% penetrance (Chang et al., 2011). We have used the schwannomas developed in these NF2-T mice to those in Nf2-deficient mice for their sensitivity to pathway-specific small-molecule inhibitors.

#### **(6) Wap1-Cre;Nf2flox2/flox2 and Blg-Cre;Nf2flox2/flox2 mice:**

To examine whether Nf2 has any role in mammary gland development and tumorigenesis, we have inactivated Nf2 in mammary epithelial cells using three mammary-specific Cre drivers, MMTV-Cre, Wap1-Cre, and Blg-Cre (Huang et al., 2011). We found that while MMTV-Cre;Nf2flox2/flox2 embryos died during mid-gestation, both Wap1-Cre;Nf2flox2/flox2 and Blg-Cre;Nf2flox2/flox2 mice show defects in postnatal mammary gland development and 100% mammary tumor formation. Our results suggest a link between NF2 and breast cancer.

#### **Abstracts/Presentations:**

- (1) Welling DB. Clinical Trial Update in NF2. Invited lecturer, Children's Tumor Foundation NF Forum 2010, Las Vegas, NV, April 10, 2010.
- (2) Welling DB. Radiation Treatment and Hearing Preservation in NF2. Invited lecturer, Children's Tumor Foundation NF Forum 2010, Las Vegas, NV, April 10, 2010.

(3) Welling DB. NF2 Trials: Have We Defined the Right Patient Population? At What Stage of NF2 Should the Patient Be? Invited lecturer, NF2 Meeting: The State of the Clinical Trial, Las Vegas, NV, May 5, 2010.

(4) Welling DB. Vestibular Schwannoma: Pathogenesis and Clinical Applications. Invited lecturer, Fifth Annual Ann B. and Julius N. Hicks Lectureship in Otolaryngology, University of Alabama School of Medicine, Birmingham, AL, May, 14, 2010.

(5) Welling DB. Reaching Consensus in NF2 Clinical Trials and an Update on Key Ongoing NF2 Trials. Invited lecturer, CTFn Annual NF Conference, Baltimore, MD, June 5, 2010.

(6) Merlin is Essential for Neurulation and Neuroepithelial Progenitor Proliferation in Mammalian Brain Development. Oral presentation (Elena Akhmayeva, MD), Children's Tumor Foundation Annual NF Conference, Baltimore, MD, June 7, 2010.

(7) HDAC42 and OSU-03012, Novel Small-Molecule Inhibitors for the Treatment of Vestibular Schwannomas. Oral presentation (Janet Oblinger, PhD), Children's Tumor Foundation Annual NF Conference, Baltimore, MD, June 8, 2010.

(8) Welling DB, Lee T, Akhmayeva EM, Huang J, Burns S, Bush ML, Packer MD, Kulp SJ, Chen CS, Giovannini M, Jacob A, Chang LS. Growth Inhibitory and Anti-Tumor Activities of OSU-03012, a Novel PDK1 Inhibitor, on Vestibular Schwannoma and Malignant Schwannoma Cells. Collegium Oto-Rhino-Laryngologicum Amicitiae Sacrum, Budapest, Hungary, August 24, 2010.

(9) Welling DB. Obtaining Funding for Clinical and Translational Research. Invited presenter, Miniseminar, American Academy of Otolaryngology - Head and Neck Surgery Foundation Annual Meeting, Boston, MA, Sept 29, 2010.

(10) Welling DB. Meniere's Disease Update: 2010. The New York Otolaryngology Update. New York, New York, Oct 27, 2010.

(11) Vestibular Schwannoma: Pathogenesis and Treatment. The New York Otolaryngology Update. New York, NY, Oct 27, 2010.

(12) Bush M, Oblinger J, Davletova S, Burns S, Chang LS, Welling DB, Jacob A. Treatment of Vestibular Schwannoma Cells with ErbB Inhibitors. Combined Otolaryngology Society Meeting (American Neurotology Society). Chicago, IL. April 30, 2011.

\*Awarded American Neurotology Society Fellow Research Award

(13) Burns, S.S., E.M. Akhmayeva, J.L. Oblinger, M.L. Bush, J. Huang, V. Senner, M. Giovannini, C.-S. Chen, A. Jacob, D.B. Welling, and L.-S. Chang. 2011. AR-42 and AR-12 Potently Inhibit the Growth of NF2-deficient Human Meningiomas. The 2011 NF Conference, Jackson Hole, Wyoming.

(14) Bush, M.L., J.L. Oblinger, V. Brendel, G. Santarelli, J. Huang, E.M. Akhmayeva, S.S. Burns, J. Wheeler, J. Davis, C.W. Yates, A. Ray-Chaudhury, S. Kulp, C.-S. Chen, L.-S. Chang, D.B. Welling, A. Jacob. 2011. The Growth Inhibitory Effect of AR42, A Novel Histone Deacetylase Inhibitor, on Vestibular Schwannomas. The 2011 NF Conference, Jackson Hole, WY.

(15) Bush, M.L., A. Bratasz, V. Brendel, A. Manning, J.L. Oblinger, L.-S. Chang, D.B.





# NF2 Compass

A QUARTERLY ADVOCURE ONLINE NEWSLETTER



Formerly known as "Flutterby"

Welling, A. Jacob, K. Powell. 2011. The Use of Magnetic Resonance Spectroscopy (MRS) in Monitoring Vestibular Schwannoma Growth and Treatment Effect. The 2011 NF Conference, Jackson Hole, Wyoming.

(16) Akhmametyeva, E.M. J. Huang, S.S. Burns, C.Y. Kuan, D.B. Welling, and L.-S. Chang. 2011. Opposing Roles of Merlin during Neural Tube Development and Tumorigenesis. The 2011 NF Conference, Jackson Hole, Wyoming.

(17) Huang, J., E.M. Akhmametyeva, S.S. Burns, M. Giovannini, D.B. Welling, and L.-S. Chang. 2011. Merlin plays important roles during mouse mammary gland development and tumorigenesis. The 2011 NF Conference, Jackson Hole, Wyoming.

(18) Chang, L.-S., E.M. Akhmametyeva, S. Burns, J. Huang, A. Ray-Chaudhury, and D.B. Welling. 2011. The Neurofibromatosis 2 (NF2) gene promoter directs transgene expression to Schwann cells. The 2011 NF Conference, Jackson Hole, Wyoming.

### **Publications and Submitted Manuscripts:**

(1) Bush, M.L., J. Oblinger, V. Brendel, G. Santarelli, C. Hrelec, J. Davis, J. Huang, E.M. Akhmametyeva, S.S. Burns, S. Kulp, C.-S. Chen, M. Giovannini, L.-S. Chang, D.B. Welling, A. Jacob. 2011. HDAC42, A Novel Histone Deacetylase Inhibitor, as a Potential Therapy for Vestibular Schwannomas and Meningiomas. *Neuro-Oncology*, 2011 Jul 21. [Epub ahead of print] PMID: 21778190.

(2) Yates, C., D.B. Welling, L.-S. Chang. 2011. Research Advances in Therapeutics for Neurofibromatosis Type 2-Associated Vestibular Schwannomas. In *Advances in Neurofibromatosis Research*, K.S. Cunha and M. Geller (Eds.). Nova Science Publishers, Inc., Hauppauge, N.Y.

(3) Bush, M.L., S.S. Burns, J. Oblinger, S. Davletova, L.-S. Chang, D.B. Welling, A. Jacob. 2011. Treatment of Vestibular Schwannoma Cells with ErbB inhibitors. *Otol. Neurotol.*, In Revision.

(4) Akhmametyeva, E.M., S.S. Burns, J. Huang, A. Ray-Chaudhury, D.B. Welling, L.-S. Chang. 2011. Efficient Induction of Malignant Peripheral Nerve Sheath Tumors and Schwannomas in Transgenic NF2 Promoter-Driven T Antigen Mice. *Genes Cancer*, In Revision.

(5) Blakely J, Evans DG, Adler J, Brackmann D, Chen R, Ferner R, Hanemann CO, Harris G, Huson SM, Jacob A, Kalamirides M, Karajannis M, Korf B, McClatchey A, Miao H, Plotkin SR, Slattery W, Stemmer Rachamimov A, Welling DB, Wen P, Widemann, Hunter-Schaedle K, Giovannini M. Consensus Recommendations to Accelerate Clinical Trials for Neurofibromatosis Type 2: An Update. Submitted Clin Cancer Res.

## Extraordinary NF2er - Parker

*"That's life, that's what all the people say. You're riding high in April, shot down in May... But I know I'm gonna change that tune.... when I'm back on top, back on top in June..."*



Those lyrics by Frank Sinatra kind of became my motto last year. I have a Frank shirt and sing that song lots! My name is Parker and I'm fourteen years old. My family and friends think of me as a silly pankster or call me "Mr. Giggle Pants." I can't get enough of football and the MN Vikings are my favorite team. I've learned to deal with frequent losses! I played football for five years and was also on the All-Star team where there were back to back practices. I really miss being part of those teams. I had two surgeries on my arm because my hand quit working, but I was still able to play football with a splint on. My right arm became

so strong that I could do a one-handed pull up! I had to stop playing football ten months ago after a surgery (craniotomy) to remove a couple of tumors at my brainstem. I feel good now though. I try not to think about NF2. I really just want to be a normal fourteen year old, so I don't ever talk about it. I do worry a lot though, so I understand what you are going through if you have a lot of worries about NF2. I had a great summer boating, tubing, hitting the water park, and hanging out with my friends. I have an older sister and brother, and one younger brother. We live in Iowa and my care is directed by Dr. Tonsgard at the University of Chicago. It's 5 1/2 hours away, but they take great care of me (I don't want my parents to know I agree with them)! No thank you to any more surgery! I hope you are all able to see good doctors and are doing well.

**\*\*\*Written by fourteen year old Parker - August, 2011.\*\*\***

Note from Parker's mom, Julie: "As a family, we have raised over \$25,000 for the Iowa chapter of CTF in the last 5 years. We keep at it!" **If you have any questions for Julie or would like to connect with another parent of a child with NF2, please feel free to email her: [jelmquist@aol.com](mailto:jelmquist@aol.com)**





# NF2 Compass

A QUARTERLY ADVOCURE ONLINE NEWSLETTER



Formerly known as "Flutterby"

## Fundraising:



### ZazzleTM - 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 [click here](#).



Another easy way to contribute to NF2 is to visit us and donate on [Facebook](#).

**2011 NF2 Fundraising Plan – A Halloween Bash!!!! A benefit through Advocure NF2 to fund children’s tumor research: Saturday, October 22nd, 2011**

**Vice Niteclub  
1251 Arroyo Way,  
Walnut Creek, CA**



"...This year will be the 7th annual Halloween Bash and our goal is to raise \$100,000. All donations will be matched by the Thoms family so we could conceivably raise a total of \$200,000. Of this money, \$0 will go to administrative causes. All of it will go to research being performed by doctors and scientists working on a cure/therapy to control tumor growth. While we are not close to eliminating **NF2**, we are extremely close to containing it and preserving the quality of life for Camille and thousands of others affected..." **Contact Roland Thoms for more info at: 925-575-1593 (California) or [roland@advocurenf2.org](mailto:roland@advocurenf2.org)**

## NF Symposiums or Conferences With an NF2 component

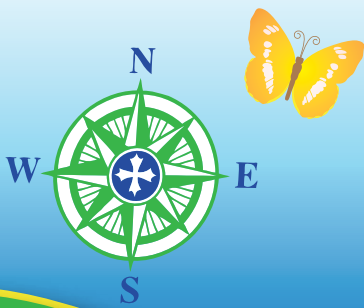


- **Oct 1-6, 2011 • Washington, DC, USA**  
[2011 CNS Annual Meeting](#)  
Hosted by the [Congress of Neurological Surgeons](#).
- **Oct 7-9, 2011 • Columbus, OH, USA**  
[Ohio Gathering](#)  
Coordinated by the [NF2 Crew](#)
- **Oct 15, 2011 • St. Louis, MO, USA**  
[NF Symposium](#)  
Hosted by [Neurofibromatosis Midwest](#)
- **Dec 5, 2011 • Borden Auditorium, Monmouth Medical Center, 300 Second Avenue, Long Branch, NJ, USA**  
[Brainstorm: Psychosocial Support for Brain Tumor Families](#)  
Brought to you by the [National Brain Tumor Society](#).

## Forward to a friend?

Know someone who would like to read this online newsletter? Why not [forward it to them?](#) Thanks!





# NF2 Compass

## A QUARTERLY ADVOCURE ONLINE NEWSLETTER

Formerly known as "Flutterby"



### NF2 Clinical Trials & Studies:

- **Phase II Study of Everolimus (RAD001) in Children and Adults With Neurofibromatosis Type 2**

ClinicalTrials.gov Identifier: NCT01419639

**This study is not yet open for participant recruitment.**

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.

- **A Single Arm, Monocenter Phase II Trial of RAD001 as Monotherapy in the Treatment of Neurofibromatosis Type 2 - Related Vestibular Schwannoma**

ClinicalTrials.gov Identifier: NCT01345136

**This study is ongoing, but not 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. Secondary objectives include determining if RAD001 treatment will improve hearing ability in **NF2** patients.

- **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 currently 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.

- **Investigation of the intra-tumoural concentration and activity of Nilotinib in cutaneous schwannomas**

Study No: CAMN107GB05T

This study aims to provide important information about the way a drug (Nilotinib) is taken up into the skin (or cutaneous) tumours of patients who have the condition called **Neurofibromatosis 2 (short NF2)**, a condition which is caused by changes to the genetic material inside body cells. **NF2** is difficult to manage clinically, and a new drug that targets specific molecules in the cells, and could offer a better treatment for patients with this condition.

Principle Investigator: **Prof. Dr. C. Oliver Hanemann MD, FRCP**, Peninsula College of Medicine and Dentistry, UK

- **A Phase II Trial of the Combination of Bevacizumab (Avastin™) and Everolimus in Patients with Refractory, Progressive Intracranial Meningioma**

ClinicalTrials.gov Identifier: NCT00598351

**This study is currently 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.





# NF2 Compass

## A QUARTERLY ADVOCURE ONLINE NEWSLETTER

Formerly known as "Flutterby"



- **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).

- **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.

- **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)**.

- **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.

- **Phase II Trial of Bevacizumab (Avastin™) in 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..

- **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.

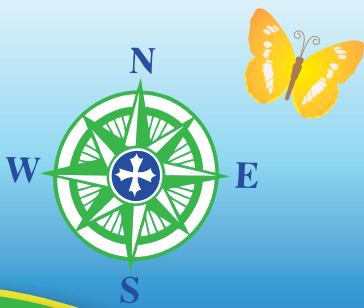
- **Phase II Trial of Sunitinib (SU011248) in Patients with Recurrent or Inoperable Meningioma**

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





# NF2 Compass

## A QUARTERLY ADVOCURE ONLINE NEWSLETTER

Formerly known as "Flutterby"



### **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.

### **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)**.

### **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**

• **Neurofibromatosis Type 2 Clinical Trial Overview**

• **Neurofibromatosis Type 2 Trial FAQ**

### **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 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.

### **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.





# 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**
- **Lapatinib** (Tykerb™)
- Caffeic Acid (**BIO30™**)
- **RAD001**
- **BEZ-235**

- **Valproic Acid**
- **Rapamycin**
- **Cetuximab**
- **Trastuzumab** (Herceptin™)
- Vandetanib (**Zactima™**)
- **Nilotinib** (Tasigna™)
- **Curcumin**
- **Dasatinib**

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](mailto:contact@advocurenf2.org). For more trials and/or studies, please see: [this link](#). When there, please try inputting "Neurofibromatosis type 2", or a NF tissue type, such as; "Vestibular Schwannoma", "Schwannoma", "Meningioma", "Glioma", "Ependymoma", or "Astrocytoma", within the relevant search field.



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

Email: [contact@advocurenf2.org](mailto:contact@advocurenf2.org)  
Web: [www.advocurenf2.org](http://www.advocurenf2.org)



## How To Help

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

