First Orphan Drug Designation for Fragile X

By Carlo Paribello, M.S.M., M.D., President, FXRFC

In a recent announcement, the Food and Drug Administration (FDA) in the United States granted Neuropharm Group Plc an Orphan Drug Designation for the use of Fenobam in the treatment of Fragile X. Neuropharm Group Plc is a UK based speciality pharmaceutical group dedicated to the development of products for the treatment of disorders of the central nervous system.

Orphan Drugs are those drugs used to treat rare diseases, and Fragile X is considered to be a rare disease because it affects less than 1 in 1,000 people. Several countries, such as the U.S.A., Britain, and Japan have implemented an “Orphan Drug Act/Policy” to provide tax incentives and market protection for pharmaceutical companies. The purpose is to make it financially worthwhile for these companies to develop drugs for the very small market share represented by the rare disorders.

What does this mean to Canadian families affected by Fragile X? While Canada does not have an orphan drug policy, it does have a mechanism in place whereby Canadians can access drugs that have received an Orphan Drug designation and marketing approval in the U.S. It is done through the normal drug approval process in Canada, via the EDRP (Emergency Drug Release Program) or SAP (Special Access Program). This means that Canadians should be able to access the medication once it has been released in the U.S. as an “orphan drug”.

Fenobam is an drug that acts as an mGluR5 antagonist (or blocker). It can now be developed by Neuropharm Group Plc for use in clinical trials and treatment of Fragile X within the next few years. Researchers have found a specific excess of metabotropic glutamate receptor (mGluR) signaling in Fragile X brains, and studies...
indicate this may be a common mechanism underlying many autism spectrum disorders. Research on animal models has shown that it is possible to regulate this hyperactive brain mechanism with compounds such as Fenobam, which block mGluRs and may reverse the major deficits of Fragile X such as cognitive impairment, anxiety, and autistic behaviours.

Scientists at the labs of a Johnson & Johnson subsidiary developed Fenobam in the 1970s. It was studied in clinical trials in patients with anxiety disorders and demonstrated some effectiveness and a good safety profile, but exactly how it worked was unknown. It was not until twenty years later that researchers at Hoffmann LaRoche discovered that it is an mGluR5 antagonist, making it a promising potential treatment for Fragile X. I am very hopeful that this drug, and others like it, will help compensate for the abnormal brain functions seen in patients with Fragile X as well as autism.

FXRFC & Surrey Place Centre participate in Fragile X Clinic Consortium

On February 12, 2007, Dr. Carlo Paribello and Nurse Practitioner Leeping Tao of the Surrey Place Centre Fragile X Clinic in Toronto, were invited to attend the first ever Fragile X Clinics Consortium meeting in St. Louis Missouri. They represented one of the thirteen Fragile X clinics currently operating in North America. The Consortium will have many purposes including the development of a knowledge base for treatment of difficult cases and the establishment of a structure for collaborative research efforts, including drug trials.

The meeting was sponsored by the National Fragile X Foundation in the U.S. The clinic listings can now be found at www.fragilex.org under “CLINICS” in green. The page entitled “FRAGILE X CLINICS, UNITED STATES AND CANADA” is a result of more than four years of collaboration between the NFXF and the growing number of Fragile X clinics. The information that you see in the document will be updated regularly. Many other facts about the clinics will be displayed so that families and physicians will be better equipped to choose a particular clinic according on their individual needs. To arrange for a consultation at the Surrey Place Centre Fragile X Clinic in Toronto, you can call 905-453-9366, or e-mail Dr. Carlo Paribello at fxrfc@on.aibn.com.
Fragile X Protein May Play Role in Alzheimer’s Disease

Researchers Jim Malter and Cara Westmark at the University of Wisconsin-Madison have made an unexpected finding in the Fragile X knockout mouse. It appears that the Fragile X mental retardation protein (FMRP), which is missing in Fragile X, may regulate the material responsible for the plaques and cell death seen in the brains of Alzheimer’s patients. If these findings can be confirmed in humans, there is hope for developing a treatment for Alzheimer’s disease as well.

The characteristic plaques in the neurons of patients with Alzheimer’s disease contain remnants of dying cells and clumps of a small, sticky piece of a protein called beta-amyloid. When the beta-amyloid builds up in the brain, it can clump together, causing damage to the neurons and ultimately killing them. It is not known what triggers toxic beta-amyloid accumulation in the brain, but the sticky bits are made when a larger amyloid precursor protein (APP) is broken up into pieces by enzymes.

The amyloid precursor protein is already known to be important at the sites of connections between neural cells and unusually high levels have been reported in patients with other developmental disorders, including autism and Down’s syndrome. However, this does not mean that patients with Fragile X also have Alzheimer’s disease, despite having excessive levels of APP. Conversely, patients with Alzheimer’s disease don’t have excessive levels of APP. It is possible that damage to the brain cells of Alzheimer’s patients can occur because of abnormal metabolism of APP, which leads to toxic accumulation of certain by-products.

This raises the exciting possibility that the same mGluR antagonists or blockers that we believe will eliminate the core symptoms of Fragile X, may also decrease the production of APP and therefore prevent disease progression in Alzheimer’s.

Wear A Fragile X Awareness Wristband This Summer!

Our bright green silicone wristbands say “Support Fragile X Research” and show the FXRFC logo. It’s a great way to raise public awareness about Fragile X, raise money for research and look “summer-stylish” at the same time!

Order 1-4 wristbands at $3 each or save, and order 5 or more wristbands at $2 each.

Try selling them at work as a fundraiser, or use them as a great gift idea for your child’s teachers or daycare at the end of the school year!

Call the FXRFC headquarters at (905) 453-9366 and order yours today!
Michael Spero - Is there life on Gabriola after 23 years in Toronto?

By Lawrence Spero, Gabriola, British Columbia, Pharmacologist, FXRFC Board Member

In September of 2005 our family moved from Toronto to the Island of Gabriola in the Straits of Georgia about a 20 minute ferry ride from Nanaimo on Vancouver Island. Nearly 19 months later Michael, 25 yrs. old, is probably known by a quarter of our population of 4,050 and has become a part of the community, something that never happened in Toronto. In the first few months we met a support worker whose job was actually in Victoria but who spent 2-3 days a week on Gabriola. She took Michael under her wing and before long they were collecting leaves and seaweed for compost one day a week and working in our community centre. This led to a volunteer position in our food bank one morning a week. Michael helps collect the donations, packs the food and is very proactive in telling people they really should try this. The 30-40 people who use the food bank all have issues of one sort or another and they have adopted Michael into the group.

Our first contacts with “the system” were remarkably pleasant and this has continued. It’s so nice to be able to park outside their office, not have to wait in line and have people who actually answer their phone and respond to questions. They are very caring and supportive and by November Michael was receiving a support cheque from the Provincial Government, a free bus pass for Nanaimo and a half-price ferry pass. Yes, after a few training trips Michael takes the ferry by himself to Nanaimo and can now use the bus system to at least three different locations. He signed up with two agencies whose fees are paid directly by the Province. One provides an afternoon of recreation in Nanaimo, one supports a morning of volunteer work at the Nanaimo Hospital. Michael also now fills and mails envelopes on a fourth morning and actually is paid for this work. So Michael is working 4 half days a week.

We live about a 20 minute walk from our mail box. Michael goes to fetch the mail every day. The box is next to a farm with 23 alpacas so Michael generally “talks” to them and can take up to an hour for the round trip. He also walks to the village store, about 15 minutes further down the road and has been known to walk home from the ferry (when we are late picking him up) and that’s an hour walk. Michael has lost a lot of weight, his clothes fit and best of all his cholesterol levels and BP are now normal. We gave Michael a credit card with a low limit and he uses this to go shopping in the Village, to buy snacks in Nanaimo and just for emergencies.

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It's the 4th Annual FX Foundation Family Fun Day!!

Sunday June 24th, 11am-2pm
Once again our Fun Day will be held at Variety Village!
Mark your calendar NOW!

That’s right, you’ll enjoy an all expenses paid, action packed day of amazing games & fantastic gourmet food (free hotdogs, burgers, veggie burgers, drinks) along with other incredible FX families, just like yours! Feel free to bring along aunts, uncles, grandparents or whoever supports you & your family. This is your chance to meet other families, connect, relax & let the kids play together at a great facility. There is a fenced-in outdoor green space & patio as well as reserved indoor space in the fieldhouse in case the weather does not co-operate.

Please make sure you let us know if you plan on attending no later than June 16th, so we can bring along enough food for everyone.
Call Lori Beesley at (416) 261-2666 and tell her how many people you’re bringing.

So bring along your smiles - but not your pets (sorry Rover, you are not allowed) and get ready to have a great time, with lots of fun and laughter! There will be some play equipment provided, but feel free to bring your ball & glove, frisbees etc.

See you there - rain or shine!
For directions and more details, please see next page.
Variety Village is located at 3701 Danforth Avenue
Toronto, Ontario M1N 2G2

for more info. on Variety Village, visit  http://www.varietyontario.com/village/

Please note you can only exit south off the 401 at Warden Ave. or Brimley Rd. Also be aware that Danforth Rd. & Danforth Ave. are both in this area. Variety Village is on Danforth Ave. It’s on the south side, and sits next to a high school. You can park in the school lot if the Village lot is full, then follow the walkway to Variety Village. There is a set of traffic lights at Variety Village, so just turn in where you see the sign out front!

Remember to let Lori know by June 16th!

Call Lori Beesley (416) 261-2666 - please specify how many adults & children when you call (the more the merrier) and please leave a number where you can be reached, just in case.

Thank you and hope to see you June 24th!
He sits with his mom, Tessa, when the card statement comes in and matches the slips. His grasp of numbers has improved as well as his notions about the value of money.

Michael feeds and waters and collects eggs from our six hens every day. In fact he is always looking for (and finding) things to do such as taking out the garbage or the compost, emptying the dishwasher or even sweeping the kitchen floor. His sense of well being has improved. He actually responds when people say hello – and on Gabriola everyone who passes says hello, except perhaps for tourists. Perhaps best of all he has found a friend, A.J., who is very quiet and quite different from Michael but they enjoy each other’s company, watch movies together and occasionally make pizzas.

Michael is now so much better able to care for himself that we have left him for a few days at a time, including last September for 10 days. We arranged for someone to drop in but mostly Michael said he was okay and their visit was rather short. We are very proud of how well he coped and he often asks when we are going to leave him again – he enjoyed it!

Moving to Gabriola is the best thing that could have happened to Michael. Tessa and I came because it was what we thought would be best for us and hoped that it would work for Michael. Boy did it ever!

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**Birthday Fundraiser**

*On the occasion of FXRFC Treasurer David Doritty’s 50th Birthday, his close friends got together and raised $2,000 for David’s favourite charity, FXRFC.*

*The organizers, Susan and Peter Sainsbury wrote the following note about the occasion!*

Michael Doritty is 14 years old and already a legend in his own time. His presence brightens the day of his many friends, whether they be from his neighbourhood in North Toronto, or from his cottage in Georgian Bay or from skiing at Georgian Peaks... or for that matter, any place else! Michael brings joy and laughter to all he meets.

Michael also happens to have Fragile X. Michael’s life is a success story that highlights the efforts of The Fragile X Research Foundation of Canada, and its Treasurer, David Doritty. David, his wife Ann and a group of other parents founded the Foundation 1996. Their mandate is to promote scientific research that will lead to effective treatment for Fragile X.

David is a wonderful father to Michael and always displays a positive and encouraging love for his youngest son. Their family concentrates on Michaels ABILITIES - not his disabilities. David’s favourite thing is to take Michael to his hockey games - Michael plays in a League called Special Hockey for Heart and his team is the Don Mills Diamonds. He also participates in Special Olympics and loves his basketball team, his skiing group at Earl Bales Park, and is excited about the start of the softball team in May.
On April 13th, 2007, in honour of David’s 50th birthday, a donation of $2,000 was made to the Fragile X Research Foundation by some of Michael’s family and friends, in the hope that Michael’s success story can be repeated... again and again.

Happy Birthday, David!

The following is the thank you note sent by Ann Doritty to David and her their wonderful friends!

When Michael was 2 years old, he was diagnosed with Fragile X Syndrome. We had no idea what it was - or even what a “genetic disorder” was. We were told he would be mentally challenged, physically awkward, would not be able to live on his own but in a group home, and would be dependant on us for the rest of our lives - then it would be up to his siblings to care for him. YIKES!

Imagine - we walked in with our beautiful golden haired boy with the gorgeous smile and blonde curls - and had all our dreams of him having a “normal life” taken away. We were devastated. Personally, it was a real heartbreak for me to learn that I was the carrier. I wanted to “fix it”, to control things, to find a cure - or a drug - or another doctor who would give us hope... anything.

The Child Development Clinic at Sick Kids Hospital tried to answer our questions and help with our fears, but there were no services at all for families with Fragile X Syndrome in Canada. So in 1996, a group of us, all parents, started The Fragile X Research Foundation of Canada. The mandate - to promote scientific research that will lead to effective treatment for Fragile X.

David has worked tirelessly on this charity for 10 years and is so proud of how much it has grown and what it has done to help families affected by Fragile X. In fact, we now have our very own FX Clinic Clinic at Surrey Place - how I wish we had been able to have access to a Clinic like that when Michael was first diagnosed

FXRFC is a national, non-profit, tax-exempt organization administered totally by volunteers. Your donation MAKES A DIFFERENCE... a big one! We are determined to improve the quality of lives of the thousands of children across Canada who live with Fragile X. So thank you so much for all you have given.

On a personal note, I want to thank each and every one of you for the role you have played in Michael’s life. As Johanne says “Michael is ALL of ours” and I believe it is true. All of you and your families have embraced him. Whether it is at the cottage, the Peaks, in the neighbourhood, he feels at home and he feels safe. You can’t imagine how important that is - not just to him, but to us. I know what an impact he has had on all of you - and your kids. He has taught us all a lot and brought us much joy.
Michael truly is the gem in our family. Having a child like “Mikes” has made us travel down roads that we may not have travelled - and that has been a positive thing in most cases. He has taught us about the importance of acceptance and of unconditional love.

The last person I want to talk about is David. He has never, ever complained - not once. Instead he is the one bragging about Michael’s latest escapades! I have the normal reactions of thinking “I wish Michael had more friends, was at a regular school, were on a Select Hockey team, or ski racing…” but David always has a positive response for me. It takes a special person to believe the way he does. And he truly believes in Michael.

I can’t imagine our life without Michael. I am thankful for all that he has given our family. We know that his siblings Robyn and Jonathan have such empathy and understanding because of their brother. I hope he will continue to grow and thrive the way he has - and that he will continue to be a part of ALL of our lives in the future.

So... here’s to Michael and here’s to his amazing Dad!!!

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**Bringing Awareness & Lunch to the Mayor**

_by Chris Beesley_

May is “Community Living Month” in Ontario. It’s intended as a month to raise awareness and celebrate the contributions of people with an intellectual disability within the community.

To kick off the month, Community Living Toronto organized the “Appetite for Awareness” program which delivers lunches and information kits to various media, educational and political people of influence in the community.

This year, Mitchell and I volunteered to take part in the program and we delivered lunch to Toronto’s Mayor, David Miller! As you can see by the photo, Mitchell was a little shy around the mayor, but he did a great job shaking the mayor’s hand and giving him the lunch. In doing so, the mayor was able to meet a person with an intellectual disability who is active in the community. He also received information about Community Living Toronto and a great lunch!

As an added bonus, Mitchell and I spent a fun day together. We’ll definitely do it again next year and who knows, maybe the Queen will be in town!
If you have an announcement or request to make that is related to Fragile X, and would like other families to know about it, please e-mail the Foundation at fxrfc@on.aibn.com, or fax us at (905) 453-0095. You can also check out our website at www.fragile-x.ca. The Website is an integral part of the Foundation. Not only does it provide scientists with information about our research grant program, but it also allows us to educate the public about Fragile X and keep you updated on the research that your donations are funding. We also have back issues of the FXRFC newsletters posted so you can read interesting articles you might have missed. With a click of the mouse button, you can access a multitude of useful links related to Fragile X, learn about the research projects that we fund, and find out about events in your area.

**FXRFC Support Groups**

We are very interested in starting support groups in the other provinces and territories and will provide assistance to anyone able to help out. If you would like to network with other parents of children with Fragile X, or if you would like to volunteer for fundraising events in your area, please contact any of the people below.

**National Headquarters**
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E-mail: fxrfc@attglobal.net

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**Ontario**
Kitchener-Waterloo
Teresa Burch, Co-ordinator
62 Corfield Drive, Kitchener, Ontario
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**British Columbia**
Pam Winthrope
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V4C 4Y6 Phone: (604) 590-6822
E-mail: pwinthrope@hotmail.com
Web: http://fragilexbc.tripod.com/fragilexbc

**Fundraising and Public Awareness Contacts**
Kirsten J. Madsen
4022 West 28th Ave.
Vancouver BC V6S 1S8
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(collect calls accepted)

**FXRFC Newsletter**

This newsletter is published regularly and is sent to friends of the Fragile X Research Foundation of Canada (FXRFC). Permission is granted to reproduce and distribute this newsletter for noncommercial purposes.

The Fragile X Research Foundation of Canada (FXRFC) is a national, nonprofit, tax-exempt organization; charitable # 88643 3762 RR0001. You can become a friend of the FXRFC for a tax-deductible donation of $35 or more per year. The FXRFC is a 100% volunteer organization run by parents and professionals - which means more of your donation goes directly towards research. We now accept VISA and Mastercard payments; simply phone (905) 453-9366 and pass on the details. You may send your cheque or money order to:

The Fragile X Research Foundation of Canada • 167 Queen St. W., Brampton, ON, Canada L6Y 1M5

Come visit our site on the web at: http://www.fragile-x.ca