

ROS1 derings

A newsletter by and for the ROS1 cancer community

Issue 2

YOU Can Accelerate ROS1 Research

If you have a medically necessary biopsy, surgery, or pleural fluid drain in your future, please consider donating tissue or fluid to the ROS1 Cancer Model Project!

Why do we need cancer models?

Cancer models allow researchers to study cancer outside the human body. One type consists of immortalized human cancer cells in a lab dish called cell lines. Another consists of human cancer cells growing under the skin of a mouse--called a patient-derived xenograft (PDX) mouse.

Cancer researchers use these models to examine ROS1 biology and drug resistance, develop new biomarker tests, and find new treatment options. In early 2017, only a few ROS1 cell lines and one ROS1 PDX model existed, and none of the

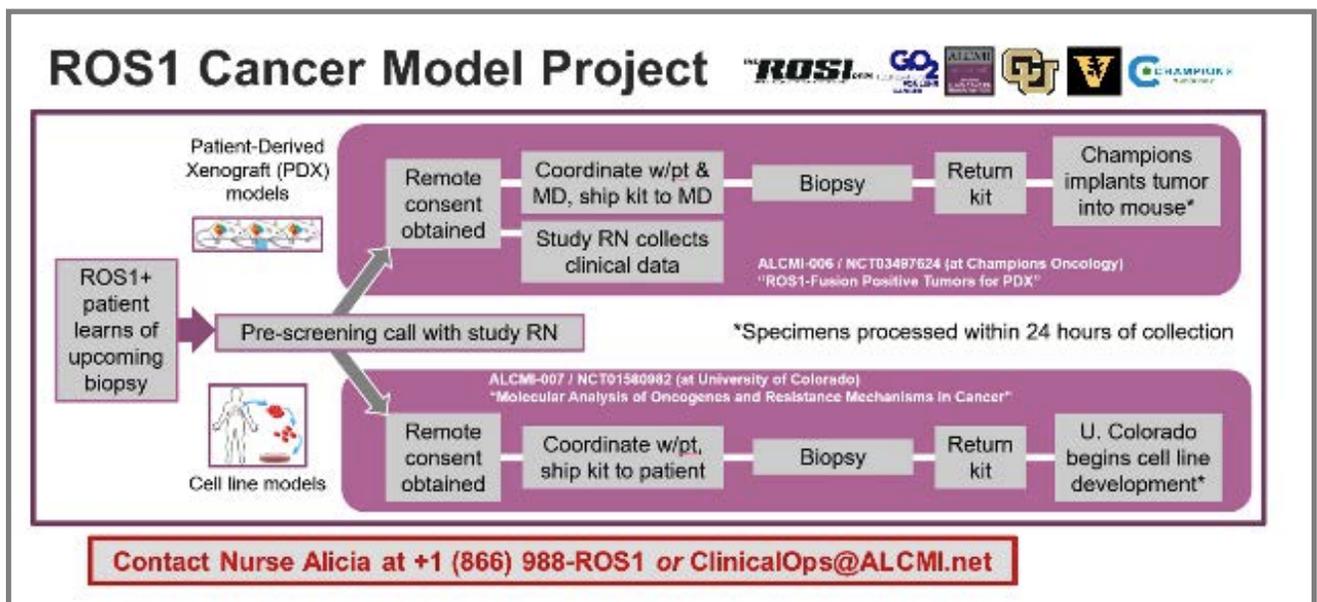
cell lines were from tumors that had developed resistance to ROS1 drugs.

What is the ROS1 Cancer Model Project?

To make more cancer models, we need ROS1 patients to donate live cancer cells. The ROS1 Cancer Model Project is making that happen.

Here's how it works. Before a biopsy, ROS1 patients arrange to donate excess tissue or fluid to the Doebele Lab in Colorado (to create cell lines), or Champions Oncology (to create PDX mice).

Here's the great news. **Tissue and fluid donations have already created four new ROS1 cell lines, doubling the number of ROS1 cell lines available for research. They have also started development of three mouse models.**



What happens to cancer models created from ROS1der donations?

Cancer models created from ROS1der donations are shared freely with academic researchers to accelerate research. They are also available, for a fee, to the pharmaceutical industry. We are working to set up a system to annotate our cell lines with information from medical records. This will make them even more useful to researchers.

So far, cell lines created from our donations have been shared with five other institutions researching ROS1 cancers:

- [University of California San Francisco](#)
- [Huntsman Cancer Institute](#)
- [National Institutes of Health](#)
- [Moffitt Cancer Center](#)
- [Ignyta \(now part of Roche\)](#)

ROS1der cell lines have also been used in published studies about ROS1 biology, resistance, and biomarker testing:

- [Differential Subcellular Localization Regulates Oncogenic Signaling by ROS1 Kinase Fusion Proteins](#)
- [Resistance Mechanisms to Targeted Therapies in ROS1+ and ALK+ Non-small Cell Lung Cancer](#)
- [Comparison of Molecular Testing Modalities for Detection of ROS1 Rearrangements in a Cohort of Positive Patient Samples](#)

One attempted PDX model was abandoned because it did not grow. This highlights the difficulty in creating these models and the importance of receiving more fresh tissue and pleural fluid from ROS1 patients.

You can help make this ROS1 research happen. See page 5 for a full update on how.

YOU can stay in touch with our progress! We'll keep you updated on our progress. Look for the chart on the right in each

ROS1derings newsletter issue and on [The ROS1ders website](#).

	Cell Lines	PDX
Unique donations received	6	5
Models in process	0	3
Models created	4	0
Models sequenced	3	0
ROS1 fusion partners	CD74 (2), TPM3 (1), Pending(1)	N/A
Sites that received our models	5	0
Published studies using our models	3	0



This research is grabbing important attention for the ROS1 cause. Ros1ders founders (L to R) Lisa Goldman, Janet Freeman-Daily and Tori Tomalia were nominated for the inaugural 2019 C2 Catalyst for Precision Medicine Award.

The Few...The Proud...

The ROS1ders! By Luna Okada

I usually start my cancer story on the day I entered an emergency room for abdominal pain and learned I have metastatic disease. Since my story took a turn 8 weeks later, this time I will start by letting everyone know that 6 ½ years later, I'm alive and well. Although most years have been good, there have also been dark and scary times. I was 54 years old and I had a single 3 cm lung tumor that had seeded my liver and many of my bones, (cervical vertebrae, spine, shoulders, sternum, ribs, pelvis, and femoral heads.) My liver was ginormous, (hence the abdominal pain), and all liver tests were abnormal.

I tested negative for EGFR and ALK mutations, and started on traditional IV chemotherapies. After two rounds, I had disease progression. My oncologist wanted to test for mutations in a newly described gene called ROS1, but the biopsy had to be delayed due to bleeding risks associated with one of my chemo meds, Avastin. While waiting to have a second biopsy, I had a round of docetaxel which kicked my @\$\$. I was so sick that I had serious conversations with my husband about discontinuing therapy. I needed his support in choosing death. Thankfully, before the second round of docetaxel, my biopsy found I was ROS1 positive. I started crizotinib in March, 2013 and continue on it today. I had side effects early on, but most have dissipated over time. I still manage nausea, but most days do well.

In 2017, I had a small brain met that was successfully treated with CyberKnife. CT scans and brain MRI every four months show that my disease is stable. I have no breathing problems, but continue to struggle with bone achiness. My liver is back to normal, with liver enzymes, mostly, within normal limits.

Since December of 2012, I've spent loads of time and energy managing my health. I've also exerted time and energy doing what I can to be a balanced human being. Here are a few things I do and think about a lot:

1. I work. I'm a genetic counselor 3 days a week in a busy practice. I love my job, which is good since I need to work for good health insurance. (crizotinib is a covered benefit. Whew.)
2. I work out every day. No exception. Sweating and feeling my heart pump helps me feel I'm making myself strong. Some of this is for physical health, but mostly it is for emotional and mental strength.
3. A few years ago, I decided my goal is to be the healthiest looking sick person I know.



4. I travel whenever possible. I used to bank PTO for that big trip I would take someday. Now, although I bank vacation days in case I need time off for illness, I'm focused on time to travel with my family, visit family and friends, and experience new places. I always thought I'd travel in retirement, but since I may not get there, I'm doing it now.
5. The weight of being sick is more than just a personal burden. My illness has profoundly affected my husband, children, and mother. Since day one, I've done my best to maintain an active role as wife, mother and daughter...because I love them so much. It's often exhausting, but I choose this.

Given that I'm not in control of this diagnosis, I've opted to incorporate my illness into my life. I plan to not only salvage the years I have ahead, but to live the best and fullest life I can. I can't control my diagnosis, but I'm controlling my response to it.

I am humbled by and grateful for many things, including my fellow ROS1ders. I've learned so much about my disease from this group, and greatly appreciate the collective effort to share information and advance research. It's all for us and I am proud.

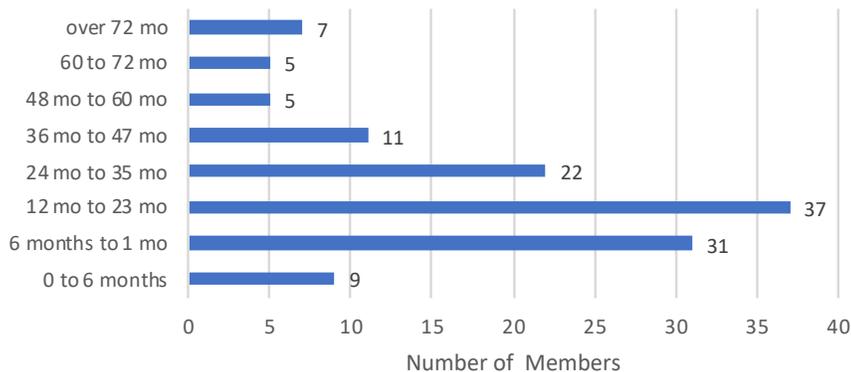
Note: A couple weeks after discovering my cancer, I started blogging. Occasionally, I go back and read where I've been. It's my cancer diary, but it also reminds me to savor life's joys (trips, weddings, babies, graduations) and brace myself for life's other crap (mother's stroke, home burglary, brain met, hip replacement and femur fracture). My blog: "Cancer....An Unexpected Journey" is at lunaoblog.blogspot.com.

ROS1 by the Numbers

By Jeff Wynne

This graph shows how long some of ROS1ders have been on Xalkori. The data represents the people that are still on Xalkori, as far as we know from what has been shared on the Facebook page. My data shows that 50 members have been on the drug over 2 years and 28 members have been on the drug over 3 years. Seventeen have been on for over 4 years.

Members currently on Xalkori
Number of months on this treatment



Fundraising Update

By Lisa Goldman



We are so excited to share that - with your hard work and amazing support - we have raised an incredible \$340,000 (and counting!) to support two ROS1-specific research studies aimed at better understanding and treating ROS1+ cancer through the Addario Lung Cancer Medical Institute and the GO2 Foundation for Lung Cancer. Congratulations and thank you for supporting these studies so enthusiastically!

We are still actively fundraising towards our goal of \$500,000, so we still need your help. If you haven't already, you can create your own personal fundraising page [at this link](#) and begin fundraising today! If you've already created your page and begun fundraising, a great next step is to share this exciting fundraising update with your network and ask for support from your family, friends, and coworkers to help us to reach our \$500,000 goal. Fundraising in support of these two studies is a powerful and unique opportunity to effect change in our own, specific disease by supporting research aimed at changing the future of ROS1+ cancer. Please help us reach our goal!



Here's how you can help us accelerate ROS1 Research!

Donate Tumor Tissue or Fluid

As soon as you know that, unfortunately, you need a biopsy, surgery, or draining of pleural fluid, contact Nurse Alicia at +1 (866) 988-ROS1 or

ClinicalOps@ALCMI.net. She'll need at least three days notice to ship collection kits to you (for the cell lines) or your doctor (for the PDX models). A week would be better. Please ask for your procedure to be scheduled on Monday through Thursday, if possible.

Tissue and fluid donations must be received at the lab for processing within 24 hours to give researchers the best chance of creating a successful model. This, and differences in research regulations in other countries, limits our opportunity to accept donations from other countries. This is truly unfortunate. Currently, tissue and fluid donations can be accepted from patients in the USA (including Puerto Rico) and Canada. We are working on

making this research opportunity accessible in other countries through Champions or other academic centers.

Donate to our Research Fund

The labs creating our cancer models are funding some of the work via grants and internal funding. The ROS1ders have raised over \$340,000 to fund the Cancer Model Project. You can donate to The ROS1ders patient-driven research projects by giving to any of [the ROS1 fundraising pages here](#). All funds go into a dedicated ROS1 fund at GO₂ Foundation for Lung Cancer, a 501(c)(3) nonprofit.

Spread the word!

Share the information on this page with your doctor. Or, print out the letter to physicians that we have shared on the ros1cancer.com website and share it with your doctor. You can find it here: <https://ros1cancer.files.wordpress.com/2019/04/cancer-model-project-alcmi-006-letter-to-share-with-doctor-23apr2019.pdf>

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**OUR TISSUE AND FLUID DONATIONS ARE MAKING A DIFFERENCE!
WILL YOU HELP?**

**YOU CAN HELP ACCELERATE
ROS1 CANCER RESEARCH!**

If you have an upcoming biopsy or pleural fluid draining
(in the USA, Puerto Rico, or Canada),

PLEASE CONTACT NURSE ALICIA
866-988-ROS1 (866-988-7671)
at least 3 days before the procedure

Thanks from all of us at 

Travel Tips *By Jeff Wynne*

When I was diagnosed in December of 2015, I stopped waiting for “someday” to do the traveling I wanted to do. My wife and I have traveled over 100,000 miles since then.

Here are tips that ROS1ders have posted about seeing the world with stage 4 cancer:

- Invest in 1-2 pairs of thigh-high compression **socks** to combat edema and reduce risk of blood clots — especially during flights.
- Drink at **LEAST** eight glasses of water daily to avoid dehydration.
- Medications:
 - Pack meds in prescription bottles. **ALWAYS** keep them with you in a purse or carry-on. **NEVER** pack them in a checked bag.
 - Bring a list of your prescription meds. For any drug not available in the country you’re visiting, get a letter from your doctor explaining why you need them. Some countries confiscate unapproved drugs. I haven’t needed my letter yet, but better safe than sorry.
- Ask your doctor about getting a prescription for a broad-spectrum antibiotic to take with you, just in case.
- To reduce risk of picking up a virus:
 - Avoid touching any part of your face unless you’ve just washed your hands.
 - Take a packet of Clorox wipes. Wipe down airplane arm rests and tray table.
 - Take plenty of hand sanitizer for when you can’t wash your hands.
 - Avoid touching escalator or stair rails, doorknobs, etc with bare hands
 - Take an N95-rated ventilator to wear in case of bad air quality, heavy smoke, or airplanes with passengers coughing nearby.
- You may want a mask to sleep on the flight.
- Sea bands (wrist bands) can help for nausea.
- If you have balance issues, bring a folding cane.
- Get all appropriate vaccinations.
- Learn something about the healthcare available in your destination, such as the names of preferred hospitals and the local emergency numbers. Note: 911 doesn’t work all over the world!
- Obtain the names of qualified, English-speaking doctors and medical providers in your destination.



- Learn whether ambulances can be trusted to transport you in the event of emergencies. In some places it's safer and faster to take a cab.
- Learn about pharmacies in your destination Are they reliable? Open at night? If you take medication regularly pack two supplies and place one in your carry-on luggage.
- Travel with a first-aid kit.
- Buy a good travel insurance policy. Travel insurance is a plan you purchase to protect you from financial risks and losses that can occur while traveling. These losses can be minor, like a delayed suitcase—or significant, like a last-minute trip cancellation or a medical emergency overseas. For **pre-existing conditions**, the plan has to be purchased within 5 to 21 days of the initial trip deposit. Members have recommended **Travelex**, **Allianz** or **AIG Travel Guard** for travel insurance.
- Also, **GeoBlue** is medical insurance for international travel that covers emergency medical transportation. The plan covers pre-existing conditions if you buy the choice plan. You can purchase the plan anytime before your trip. It does not reimburse you for any trip cancellation costs.
- **Medjet** will arrange medical transfer to the hospital of their choice within their home country with no pre-existing condition exclusions (under age 75), health questions, deductibles or claim forms. Regardless of medical necessity, the plan covers you if you are hospitalized 150 miles or more from home.

Current ROS1 Research

Below are the abstracts from the 2019 annual meeting of the American Association for Cancer Research (AACR) that are germane to ROS1-positive cancer.

[Exceptional responses to Crizotinib in breast cancer patients with somatic MET and ROS1 alterations](#)

Two patients with metastatic breast cancer with MET and ROS1 somatic alterations treated with off-label single-agent Crizotinib.

[Repotrectinib, a new generation ROS1 inhibitor, is highly potent against fusion ROS1s and emerging resistance mutations](#)

The activity of Repotrectinib against multiple fusion ROS1s and corresponding resistance mutations is outlined.

[Entrectinib in locally advanced or metastatic ROS1 fusion-positive non-small cell lung cancer \(NSCLC\): Integrated analysis of ALKA-372-001, STARTRK-1 and STARTRK-2](#)

Entrectinib is highly active in patients with ROS1 fusion-positive NSCLC, including those with CNS disease.

[Multicenter study evaluating the ROS1 status in lung adenocarcinoma using the novel SP384 immunohistochemistry clone. Towards a new algorithm for ROS1 status assessment in routine?](#)

The ROS1 SP384 clone demonstrates superior sensitivity for the detection of ROS1 rearrangements.

[Repotrectinib demonstrates promising activities in ROS1 wild-type and solvent-front mutant lung cancer patients-derived preclinical models](#)

Superior antitumor activity of Repotrectinib in both wild-type and mutant ROS1 fusion, providing a rationale that Repotrectinib may be an effective subsequent or upfront treatment option for patients with ROS1-positive NSCLC who have relapsed on the available TKIs as well as TKI naïve, including patients with progressive CNS metastases.

[Novel NOTCH1-ROS1 gene fusion drives distinct molecular mechanisms in a rare pediatric angiosarcoma](#)

While both NOTCH1 and ROS1 are established proto-oncogenes and have been separately involved in gene fusions across diverse cancer types, this is a previously unreported fusion in this rare pediatric cancer.

About this newsletter..

ROS1derings is a quarterly newsletter of The ROS1ders patient advocacy group. The ROS1ders is a group of patients and caregivers dealing with ROS1+ cancer. We strive for better outcomes for all ROS1 cancers by supporting patients and caregivers, increasing awareness and education, accelerating research, and improving access to effective diagnosis and treatment.

We will use this space to share updates about our progress, to feature questions frequently asked by the ROS1 community, and to invite all ROS1 patients to join us in our mission. [Learn about the ROS1ders.](#)