Clinical trial triumph

A drug developed at the Masonic Cancer Center and brought to patients with philanthropy’s help is finding early success

In June of 2012, University of Minnesota physics professor Cynthia Cattell, Ph.D., discovered that her nagging fatigue was something more serious than just end-of-semester burnout. She had aggressive B-cell lymphoma, a blood cancer that required immediate, intensive treatment.

That treatment—chemotherapy, radiation, and two bone marrow transplants—was brutal, leading Cattell into and out of the hospital for months. Worse, it wasn’t working; her cancer kept growing back. Then last spring, her doctor told her about a Phase I clinical trial underway at the U and asked if she was interested.

“I thought about it for about five minutes,” Cattell says, “then said, ‘Absolutely!’ Once you’re in a place where everything has failed, what do you have to lose?”

Developing DT2219

Cattell was now on a trajectory to meet Daniel Vallera, Ph.D., a University colleague she had never heard of who heads a research lab at the Masonic Cancer Center, University of Minnesota. Vallera, Lion Scholar and a professor in the Department of Therapeutic Radiology, had retooled his lab in 2000 so he could focus solely on producing cancer drugs.

With guts and grace, grateful patient finds a source of energy

An infusion of genomics experts will bolster U team

Report confirms link between taconite and mesothelioma

continued on page 2
“It was a difficult decision,” says Vallera, who’s been studying cancer for more than 30 years, “because research geared toward producing specific drugs is expensive, is very hard to fund, and has high liability. But my career goal had become [to] produce a drug that will cause complete remission in a patient with cancer, and that’s what I’ve focused on: developing new anticancer agents and getting them into the clinic as quickly as possible.”

His weapon of choice in the war against B-cell lymphomas is something called a “targeted toxin.” Simply put, that means he treats the molecular strands like series of Lego blocks, snipping out segments here, snapping in new segments there, to create entirely new DNA strands that don’t exist in nature. By manipulating the genes, he can make biologic agents that home in on specific types of cancer cells and deliver a death blow. It’s a much more precise approach than traditional chemotherapy, which kills not just cancer cells but healthy cells as well.

Using the bacteria diphtheria as his toxin, Vallera created the innocuously named DT2219, the drug Cattell would soon encounter in the clinic.

Into the clinic

Vallera is a research scientist who doesn’t see patients, so to get DT2219 into the clinic, he first had to find a physician interested in launching a Phase I clinical trial with him. He found that person in Masonic Cancer Center colleague Veronika Bachanova, M.D., Ph.D.

“I was aware of the drug that Dan had developed,” says Bachanova, who sees lymphoma and leukemia patients in University-affiliated clinics, “and was immediately interested in bringing the drug to clinic for patients whose standard treatment options had failed.”

The first step was to complete a Phase I clinical trial, through which the research team identifies the drug dose that is both well tolerated and effective. Bachanova designed the study protocol and quickly enrolled 10 patients, including Cattell, who responded beautifully. While she suffered minor side effects—primarily weight gain from water retention, and a low white blood cell count—Cattell felt healthy throughout the treatment, which was delivered in four separate infusions over the course of eight days. One month later, Bachanova found a whopping 75 percent reduction in the size of Cattell’s tumor.

Although the parameters of the trial called for just one course of treatment, Bachanova felt Cattell might benefit even more from a second course.

“They asked me if I would be willing to do it again,” says Cattell, “and I said yes immediately. On the scale of what I’d had to deal with in the other treatments, the side effects were very manageable. And it was working!”

One month after her second round of DT2219, Cattell’s tumors had vanished and, nine months later, she remains in complete remission.
Two extraordinary supporters

What Vallera does—working at the molecular level to develop drugs—is painstaking, rigorously regulated, and seriously expensive. While the National Cancer Institute has supported his work for more than 30 years, Vallera says he never could have brought DT2219 to this clinical trial without the help of two extraordinary philanthropists.

Both donors have been touched personally by the devastating blood and bone marrow cancer acute lymphoblastic leukemia (ALL)—one with a son who survived the disease and one whose son died. Both became committed to finding a cure. Early on, when they studied the field to find out who was doing promising research, Vallera’s name kept popping up.

“I got into supporting this research the hard way,” says Jeff Lion, a California resident whose son, Josh, was diagnosed with ALL at 18 months old and then relapsed a few months before his fifth birthday. “He’s 20 now, and fine, but along the way I saw so many children die.”

Lion now has a veteran’s knowledge of not just ALL, but of how the research system works and what it takes to bring new drugs to market. He generously supports Vallera’s research and encourages others to open their checkbooks.

“At the end of the day, scientists like Dan are going to cure cancers one at a time; it won’t be the same cure for all,” Lion says. “A disease like ALL?

Ultimately, there might be 10 or 12 cures for it, and they’ll all be expensive to develop.”

The second donor, who has provided significant support to Vallera over many years, as well, prefers to remain anonymous.

Face to face

On a cold day in late November, Vallera got a rare opportunity to come face to face with Cattell, who had gone into complete remission because of a drug he had developed.

“It was amazing to meet her,” says Vallera, “and all the better because she turned out to be a University colleague.”

Says Cattell: “To meet the person who developed the drug that saved your life? Incredible. I’m so grateful for the work he’s done, and I hope that by participating in the trial, I’ve helped them learn more about the drug and that it will help save other people.”

Vallera and Bachanova are now taking DT2219 to the next level with a Phase I-II clinical trial, which includes both patients with lymphoma and ALL. That begins in February.

“We’re so excited by the responses we saw in the first phase and have high hopes for this next trial,” says Bachanova.

“As a research scientist,” adds Vallera, “you’re not always thinking about how patients struggle through treatment, about how parents make tough decisions for sick kids. Working with Jeff [Lion], meeting Cindy, that’s really caused me to think about my work in a new way. It reminds me that there are very real people out there, waiting, and their need is urgent.”

Josh and Jeff Lion (Photo courtesy of Jeff Lion)
For a person going through Stage IV colon cancer treatment that’s exhausting at best and grueling at worst, Danna Mezin is surprisingly energetic. Mezin, 53, a former executive at UnitedHealthcare, now lives laser-focused on advancing research on treatments for the disease that has overwhelmed her life since she was diagnosed in September 2013. “Every step forward helps somebody,” Mezin says. “That keeps fueling me. When you don’t have any control over your own destiny, you think, ‘What can I be doing instead of just saying there are no options? What can I be doing to make a difference?’ And while I probably won’t be able to make a difference for me, I am hoping that what we’ve started is something that will keep going and will be able to make a difference for a lot of other people.”

What she’s started, with her husband, Dick Koats, is the Mezin-Koats Colon Cancer Research Fund at the Masonic Cancer Center, University of Minnesota. Since April 2014, they’ve inspired more than 300 gifts totaling $125,000 and have disbursed $25,000 to each of two promising Masonic Cancer Center research efforts.

All roads

The day her cancer was diagnosed, Mezin’s physician referred her to University colon and rectal surgeon and Masonic Cancer Center member Robert Madoff, M.D. The chief medical officer at UnitedHealth Group also recommended him. “All roads led to Dr. Madoff,” Mezin says.

Madoff then set her up with oncologist Anne Blaes, M.D. Mezin says she has been continually impressed by the “over-the-top” compassionate care she has received as well as the depth of talent and knowledge at the U.

“I’ve been in health care for 25 years, and I can’t say I’ve experienced care the way I’ve seen it at the U.” she says.

Moving forward

The first project receiving Mezin-Koats Colon Cancer Research funding is led by scientist Tim Starr, Ph.D., and aims to understand how genes work together to cause colon cancer. His goal: designing targeted treatments. The second, led by physician-scientist Emil Lou, M.D., Ph.D., seeks to discover better information about how colon cancer cells communicate and become resistant to treatment.

Mezin knows the reality of research: it takes a lot of money and a long time to make significant progress. But she wanted to provide meaningful support to projects that stand to make a difference in her lifetime—however long that might be.

Starr hopes that the Mezin-Koats funding he’s receiving provides the seed needed to prove that his ideas work. “Because we are developing new methods, most granting agencies are not willing to give money for our research because they deem it too risky,” he says.

For Mezin and Koats, that’s the point—taking risks to make progress faster. “We are driven by people who have colon cancer today,” Mezin says. “We appreciate what colon cancer patients go through and how important research really is.”
Support through a lifetime—and beyond

Your annual gifts to support cancer research, education, and care at the University of Minnesota make a real difference to patients and their families. Did you know that you can continue to make a difference after your lifetime by including the University of Minnesota Foundation in your estate plan?

Here are three ways to continue your support for the Masonic Cancer Center:

• Leave a specified dollar amount or a percentage of your estate to the University of Minnesota Foundation through your will or living trust.
• Name the University of Minnesota Foundation as a beneficiary of your retirement plan account or a life insurance policy.
• Arrange a gift that will provide payments to you or others.

If you’ve already included a gift for the Masonic Cancer Center in your estate plan, we hope you will let us know so we can work with you to ensure that your future gift is directed to the program you wish to support. You can share your gift intentions with us and still remain anonymous.

For more information, contact Jay Kautt of the University of Minnesota Foundation at 612-626-0510 or jkautt@umn.edu.

Exploiting new information

An infusion of genomics experts at the U aims to make a wealth of new scientific knowledge relevant to patients faster

They hear it all the time: work smarter, work faster. Even as they make groundbreaking discoveries in human genomics, Masonic Cancer Center scientists are constantly challenged to do more.

A tactical hiring initiative currently underway at the University of Minnesota aims to help researchers do just that by creating a jump-started team of investigators that will arrive later this year.

Early in 2014, the Medical School’s new dean, Brooks Jackson, M.D., M.B.A., charged his scientists with proposing a so-called “cluster hire” to quickly expand work already in progress at the U. In response, a group of Masonic Cancer Center researchers put together a comprehensive proposal to hire five experts in functional genomics, which is a rapidly growing field dedicated to understanding the function of every gene in the genome—the proteins they produce, how those proteins affect the body, and what happens when things go wrong.

The new team being brought to the U under the “cluster hire” will focus on gastrointestinal tract cancers, complementing existing expertise at the Masonic Cancer Center.

“With this hiring approach, you’re able to develop a lot of scientific synergy very quickly,” says Anja Bielinsky, Ph.D., Genetic Mechanisms of Cancer program coleader, who cochairs the search with colleague Scott Dehm, Ph.D.

Bringing in a group of scientists all at once requires painstaking preparation, but the payoff can be enormous. And, with the groundwork carefully laid, the U is now positioned to attract the best and brightest physicians and scientists in the field.

“Our technology has evolved to enable us to look at all the cancer genes in a cell at the same time,” says Bielinsky. “Now we need to exploit that knowledge and make it clinically relevant as quickly as possible. These hires will help us do just that.”
Building support

Following a $25 million gift from Minnesota Masonic Charities and to recognize the Masons’ legacy of support, the University of Minnesota in October renamed its children’s hospital University of Minnesota Masonic Children’s Hospital.

The gift will be used to enhance the hospital experience for children and families and advance research in areas such as neurobehavioral development, rare and infectious diseases, and stem cell therapies.

Minnesota Masonic Charities is the single largest donor to the U of M. When combined with other gifts the Masonic Fraternity has made over the last six decades—including $75 million to support cancer research and care since 2008—it brings the Masons’ total support to more than $125 million.

UMN Health opens Phase I clinical trials unit

University of Minnesota Health now has a state-of-the-art facility for Phase I clinical trials. The Early Phase Clinical Research Unit opened on August 31 and currently accepts patients who are participating in research studies at the U.

The unit is located on University of Minnesota Medical Center’s 5th floor in the Blood and Marrow Transplant (BMT) Unit. Renovated last year, the BMT Unit has single-patient rooms that are used exclusively for clinical trials.

The Early Phase Clinical Research Unit is staffed by a skilled care team that specializes in working with research patients. The unit’s nursing staff will work closely with the research nurse and pharmacist to prepare participants for the study treatment. Patients could be on the unit for six to 18 hours, depending on the study protocol.

Opening the Early Phase Clinical Research Unit will help U of M experts translate breakthrough lab research into new therapies for patients.

Nine active oncology clinical trials are currently open for enrollment. To learn more, visit www.cancer.umn.edu/clinical-trials.
The final report on a University of Minnesota study investigating the health of Minnesota’s taconite industry workers shows an association between mining dust exposure and cases of a rare cancer and, in response, urges increased monitoring and disease prevention initiatives for employees.

Findings from the project, called the Minnesota Taconite Workers Health Study, were released December 1.

“Mining is of great importance to the people of Minnesota and to our state’s economy,” says School of Public Health Dean John Finnegan, Ph.D., who led the project with principal investigator Jeffrey Mandel, M.D., M.P.H. “The state invested significant funds and time into the Taconite Workers Health Study, and we felt it was important to indicate follow-up activities in order to continue to improve the health and safety of all miners moving forward.”

The study was launched in 2008 at the request of the State Legislature after the Minnesota Department of Health detected an unusually high number of cases of mesothelioma, a rare cancer of the lung lining, in Minnesota taconite workers.

The study sought answers to three major questions:

**Is working in the taconite industry associated with mesothelioma and/or other diseases?**

The study found that taconite workers had higher than expected death rates from three diseases when compared with the general Minnesota population: mesothelioma (2.77 times higher than the expected mortality rate), lung cancer (1.16 times higher than expected), and heart disease (1.10 times higher than expected). In instances of lung cancer and heart disease, working in the mining industry was not believed to be the prominent cause of the illnesses.

**What factors, particularly dust from taconite operations, are associated with mesothelioma and other respiratory diseases?**

Researchers found that the length of time people worked in the mining industry was specifically linked to higher rates of mesothelioma. For each year in the industry, researchers noted a 3 percent increase in the worker’s risk of developing mesothelioma.

Specifically, exposure to a fiber-like mineral—referred to as elongate mineral particle (EMP)—was linked to mesothelioma. The investigators determined EMP exposure could be from either dust generated in mining and processing or from its most widely known source, commercial asbestos exposure.

**Are workers at risk for common dust-related lung diseases, and are their spouses at risk for the same diseases?**

A health screening of current and former taconite workers and their spouses in 2010–11 showed X-ray evidence of dust-related scarring of the lung and lung lining (pleura) in workers but not in their spouses.

Read the full report at z.umn.edu/taconitestudy.
A study out of the Masonic Cancer Center and Johns Hopkins University suggests that cruciferous vegetables such as broccoli sprouts could be more than just part of a healthy diet. They may even have cancer-preventing properties.

Nearly 300 participants in the study, published in the June edition of Cancer Prevention Research, drank either a “tea” made from dried broccoli sprouts, pineapple juice, and lime juice or a placebo. The participants—all of whom were recruited from a rural area in China where exposure to airborne pollutants are substantial—consumed the beverages every day for eight weeks.

Participants’ urine samples were evaluated in Minnesota by the Masonic Cancer Center’s Stephen Hecht, Ph.D., and colleagues.

“We analyzed the samples using mass spectrometry, which is something we specialize in,” says Hecht, who holds the Wallin Land Grant Professorship in Cancer Prevention. “The results were very striking. It showed that the people who consumed the broccoli sprout tea had a much greater amount of detoxification.”

Being that air pollution has been linked to lung cancer and cardiopulmonary diseases in research time and again, this study shows that intervening with broccoli sprouts could be an inexpensive way to lessen the long-term health effects of exposure to air pollution.

“There is no magic bullet to preventing cancer,” Hecht says, “but there are factors we can control, including some dietary changes.”