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Dear Friends,

The University of Colorado Cancer Center's sole purpose is to discover, develop and deliver the most effective treatment for those diagnosed with cancer. This booklet highlights just a handful of ways we're doing this work in adult cancer, including leading the country in testing tumors for gene anomalies, developing one of the only translational research and care programs for young women with breast cancer and providing survivors of all ages with programs to help the transition from oncology care to primary care.

Our adult clinical care program is the busiest in Colorado, with nearly 100,000 outpatient cancer visits to University of Colorado Hospital in the 2009-2010 fiscal year. Our infusion center completed almost 18,000 procedures—a near tripling since it was opened in 2002. Our busy radiation oncology center saw more than 26,000 visits last year. These numbers explain why University of Colorado Hospital is expanding the Anschutz Cancer Pavilion, adding two radiation vaults and nearly doubling the number of infusion bays.



Our clinical trials program—hands down the most robust in the Rocky Mountain region—continues to grow, with 1,110 people enrolled in therapeutic trials and nearly 9,000 people enrolled in prevention trials last year. The Anschutz Cancer Pavilion expansion will also increase our clinical research space by nearly 12,000 square feet. And we're expanding our clinical outreach program, bringing clinical trials to people with cancer in rural and mountain Colorado towns.

But all of this activity doesn't mean much if it's not positively impacting our patients. You can turn to page 16 to see our center's 5-year survival rates for major cancer types. We can confidently say that people treated by our physicians have better 5-year survival rates, especially those with late-stage cancers.

Everything we do in cancer at University of Colorado Hospital is backed by hundreds of basic and translational scientists working at the University of Colorado Anschutz Medical Campus, University of Colorado at Boulder and Colorado State University. And as one of our nation's elite cancer centers—just one of 40 designated as a comprehensive cancer center by the National Cancer Institute—University of Colorado Cancer Center will continue to lead our region and the nation in our battle against cancer.

Sincerely,

Dan Theodorescu, MD, PhD Director, University of Colorado Cancer Center

Genetic variations in cancers drive breakthroughs in treatment

A unique laboratory at the University of Colorado Cancer Center is propelling the latest breakthroughs in oncology research into treatments to extend survival rates for patients across the country.

The Colorado Molecular Correlates Laboratory (CMO-CO) tests tumor tissue from nearly a dozen types of cancer for minute genetic mutations that can be treated with targeted therapies. It is one of just a handful of laboratories across the nation that can perform these tests—tests that are quickly becoming standard of care for effective treatment.

"Because of the research we were doing, we saw the need very early on for molecular testing and began developing the idea for this lab," says Wilbur Franklin,

MD, CMOCO director and professor of pathology at the University of Colorado School of Medicine. "This is the culmination of 15 years of attempts to bring laboratory medicine to the bedside."

CMOCO is playing a pivotal role in newly discovered targeted therapies in head-and-neck cancer, bladder cancer and melanoma, such as the widely publicized BRAF inhibitor. Some of the greatest advancements have come in advanced-stage lung cancer. Researchers have identified 10 different gene mutations within lung cancer that can be directly targeted with drugs that either inactivate the cancer or make it more vulnerable to conventional therapies, such as chemotherapy.

"We have now revealed that what was once believed to be one disease—lung cancer—is, in fact, several different diseases at the molecular level," says D. Ross Camidge, MD, PhD, director of the lung cancer clinical program at the University of Colorado Hospital, UCCC's adult clinical partner. "Each one of the diseases may need a different treatment."

In October, Camidge and colleagues reported in the *New England Journal of Medicine* that more than half of patients with a particular gene mutation, known as ALK, present in 5 percent of lung cancers responded positively to a particular drug that didn't work in the vast majority of patients. By identifying and treating these specific mutations, UCCC has achieved patient survival rates that are double the national average.

"It's crucial to know which patients have which genetic mutation," Franklin says. "You must know the result before treatment because if a patient without the mutation is treated, the outcome is considerably worse than no treatment. This information is absolutely essential today."

Patients do not have to travel to Colorado to reap the benefits since testing is performed on tumor tissue that can be sent to the lab. CMOCO provides genetic testing for known genetic markers in cancers of the bladder, breast, cervix, colon, gastrointestinal stroma (GIST), head-and-neck, skin, prostate and stomach. Certified by the Centers for Medicare and Medicaid Services and the College of American Pathologists, testing at the lab is covered by most insurance plans as well as Medicare.

CMOCO is one of just 14 labs across the country that is part of an effort to test 1,000 lung cancer patients over the next two years for the 10 known genetic mutations. The project, known as the Lung Cancer Mutation Consortium, is being funded by a \$5.2 million grant through federal stimulus money.



"The majority of people diagnosed with Stage 4 lung cancer die within a year," Camidge says. "But we

now have a way to help some of those people live much longer. The key, however, is properly identifying and treating the unique genetic components of each patient's disease."



Opposite: Wilbur Franklin, MD, Fred Hirsch, MD, PhD, Marileila Varella-Garcia, PhD, Paul Bunn, MD; Above: D. Ross Camidge, MD, PhD

Melanoma trials eke out months of hope for advanced-stage patients

Nearly 70,000 people in the United States will be diagnosed with melanoma this year. While the vast majority will have early stage melanoma that is cured by removing it from the skin, a small but significant percentage will have cancer that has spread into the lymph nodes or organs.

Hope for these patients comes in clinical trials and the ability of treating physicians to understand how to craft treatment plans in a sequence that will not preclude the patient from being eligible for a different treatment down the road. The goal is to eke out weeks and months of quality life before the cancer recurs, while always leaving another option in reserve.



"The question always is: What do we do next?" says Karl Lewis, MD, assistant professor of medical oncology at the University of Colorado School of Medicine and a melanoma specialist at the University of Colorado Cancer Center (UCCC). "It's never easy. We try to leave as many doors open as possible. Unfortunately, some patients come to us after

they've been treated with something we know to be ineffective that then excludes them from a trial."

This year, the UCCC melanoma program treated nearly 500 new patients and enrolled more than 100 patients in dozens of clinical trials, ranking it as one of the top 10 melanoma programs in the country. Over the past 15 years, the program has enrolled more than 1,200

melanoma patients in clinical trials. UCCC is one of just 14 centers in the world—and the third largest test site—with access to the new BRAF inhibitor, PLX4032, that is showing remarkable results in advanced-stage melanoma.

The Center also recently participated in the Phase III trial of an immunologic drug that shows the first-ever survival benefit in melanoma patients. The drug, called ipilimumab, blocks a cell receptor that prevents the body's immune system from attacking cancer cells.

"This is the only drug that has ever shown improved survival results in melanoma," says Rene Gonzalez, MD, director of the melanoma program. "And we have it right now, even before it's been approved by the FDA."

Shannon Clark is one of the many patients benefitting not just from UCCC's clinical trials program but also from its seamless integration with its clinical program. By accessing physicians who are intimately involved in the moment-by-moment advancements being made in melanoma treatment, Clark's Stage IV melanoma is stable two-and-a-half years after her diagnosis.

Clark was first treated with biochemotherapy, which stopped her tumors from growing until January 2010. By that time, UCCC was conducting the PLX4032 trial, and Clark qualified for one of the few remaining slots. Within days, her tumors started shrinking and they continue to be stable nearly one year later.

"While our ultimate goal is always to find a cure, it may be more realistic to think of cancer as a chronic disease," Lewis says.

Photo: Andrea Buchmeier, Karl Lewis, MD, Rene Gonzalez, MD



Colorado Cancer Center focuses on breast cancer in new mothers

Virginia F. Borges, M.D. niceraty of Colorado Cancer Cente

Pepper Schedin, PhD, and Virginia Borges, MD, MMSc

A woman's chance of developing invasive breast cancer significantly increases for up to six years after giving birth, with more than 15,000 young mothers expected to be diagnosed in 2010 in the United States. And incidence is on the rise due to trends of delayed childbirth, since risks for the disease increase for women who give birth after age 35.

The co-directors of the University of Colorado Cancer Center's Young Women's Breast Cancer Translational Program are leading the nation in understanding the disease's mechanisms and finding ways to combat it.

Pepper Schedin, PhD, and Ginger Borges, MD, MMSc, propose that two naturally occurring processes—pregnancy-induced immune suppression and post-pregnancy breast tissue inflammation—cause this increased risk. Earlier this year, they showed for the first time in humans that mammary gland tissue creates a tumor-promoting and metastatic environment as it reverts to its normal state following birth and/or breast feeding.

"We now know that the involution process that occurs when the breast is returning to its normal state uses wound healing and inflammatory programs including proliferation of pro-tumor macrophages," says Schedin, professor of medical oncology at the CU medical school. "This environment is not only more likely to grow tumors but also to cause metastases."

The study, published in the American Journal of *Pathology*, helps explain why recently pregnant women experience higher rates of metastases and poorer outcomes. Schedin and Borges, associate professor of medical oncology at the CU medical school, co-authored the study. Both women are considered to be among the world's foremost experts in breast cancer in young women and pregnancy-associated breast cancer. Schedin was recently elected by peers throughout the world to chair the prestigious 2011 Mammary Gland Biology Gordon Research Conference.

About one in 200 women in the United States will develop invasive breast cancer before hitting her 40s—considered "young women's breast cancer"— and about 45 percent of those cases are attributed to pregnancy-associated breast cancer, Borges says.

Some studies show that perhaps just 40 percent of women diagnosed within two years of giving birth are alive five years later, compared with a 70 percent survival rate in women who are at least 15 years postpartum when diagnosed.

UCCC's Young Women's Breast Cancer Translational Program is unique in the United States, specializing in diagnosis and treatment breast cancer patients under age 50 and women diagnosed with pregnancy-associated breast cancer. The program's research arm ensures that these women have access to the latest understanding and clinical trials in this specialized area.

Schedin and Borges are currently conducting preclinical trials into the effectiveness of several potential treatments for reducing the inflammation that creates the tumor-promoting environment during involution. They are testing celecoxib (Celebrex) and fish oil, both of which are safe for pregnant and nursing women to use. In particular, they studying whether taking either treatment can reduce inflammation during the weeks between breast cancer diagnosis and surgery for new cases of young women's breast cancer. The trials are seeking patients from throughout the United States.

"If we can blockade the increased risk of metastasis by having women take fish oil or regular anti-inflammatory medications, how beautiful would that be?" Borges says.



Targeting cancer stem cells may improve survival

In the war against cancer, researchers at the University of Colorado Cancer Center (UCCC) believe they may have found the enemy's commanding officers—cancer stem cells.

Cancer stem cells make up less than 0.1 percent of tumors, but they are the toughest type of cancer cells to kill. Seemingly impervious to chemotherapy and radiation, they hide deep behind the lines waiting to send out new troops at any time. Some researchers



believe it's these cells that are responsible for initiating and maintaining cancer, just as normal stem cells cultivate normal tissue.

Researchers at the University of Colorado this year launched the nation's first program focused on identifying and testing drugs that tar-

get and destroy cancer stem cells. The Cancer Stem Cell-Directed Clinical Trials Program (CCTP) is a collaboration between UCCC and the Charles C. Gates Center for Regenerative Medicine and Stem Cell Biology, both located at the University of Colorado School of Medicine in Aurora, Colo.

"We want to know whether stem cells are generating cancer, driving it or sustaining it," says Antonio Jimeno, MD, PhD, an associate professor of medical oncology at the CU medical school specializing in head-and-neck cancer and CCTP director. "We believe we can change the way most cancers are treated by targeting tumorinitiating cells."

The CCTP is testing several drugs that target cancer stem cells, including IPI-926, a hedgehog pathway inhibitor, in combination with standard chemotherapy in head-and-neck cancer patients. UCCC has been one of the leading centers in developing this drug in humans. UCCC also is the lead center in the newly launched clinical trial of PX-866, a targeted inhibitor of the PI3K pathway (key in cancer stem cells) that is being tested in combination with docetaxel for treatment of multiple types of advanced cancers, including head-and-neck and lung cancers. A third study that will be supported by the CCTP will evaluate a gamma-secretase inhibitor in pancreatic cancer, a collaboration with Johns Hopkins University led by Wells Messersmith, MD, associate professor and deputy chief of medical oncology at the CU medical school.

In these cases, the chemotherapeutic agents act like bombs that wipe out entire fields of cancer cells but at the cost of collateral damage to normal cells. The biological agents are expected to act like "drones" that specifically locate and kill the cancer stem cells. Eventually researchers hope to be able to achieve better results with lower doses of chemotherapy or radiation therapy.

"It is really exciting to translate the work we have conducted in the lab over the last years to our patients," Jimeno says. "This is what bench to bedside is all about."

In some cases, the drugs needed to destroy cancer stem cells are already in existence. Yosef Refaeli, PhD, assistant professor of dermatology at CU medical school, screened more than 80 leukemia drugs and found three that killed leukemia stem cells. UCCC researchers believe they can use this technology to isolate stem cells in other types of cancers and elicit antibodies that successfully attack them.

"We hope that by targeting the cancer stem cells, we can ultimately bring solid tumor cure rates in line with those for some blood cancers—upwards of 75 percent, with our ultimate goal being 100 percent," Jimeno says.

Above: Yosef Refaeli, PhD; Opposite: Antonio Jimeno, MD, PhD and patient Katrina







Antonio Jimeno M.D., P Assistant Professo Medical Oncology



Cancer survivors get support through education and research in Colorado

Thanks to increasingly effective cancer treatments, nearly one in every 25 Americans has fought and beat cancer.

But the battle is long from over for these survivors. People who have been through cancer treatment at any point in their lives are at higher risk for a host of health problems, including infertility, heart problems, cataracts, hypothyroidism, memory problems and more. Cancer survivors also have unique emotional challenges, including anxiety about recurrence or survivor guilt.

"Late effects are becoming more and more important for us to understand because there are now more than 12 million cancer survivors in America," says Alison Jones, ND, director of the LIVESTRONG[™] Cancer Survivorship Center of Excellence at the University of Colorado Cancer Center (UCCC).

UCCC is a National Cancer Institute designated comprehensive cancer center in Aurora, Colo., that serves patients throughout the Rocky Mountain region. Its survivorship program, which includes both patient support as well as research into late effects, is one of only eight LIVESTRONG centers in the country.

UCCC offers three programs to help survivors—and their primary care physicians—understand their risk for late effects and the best ways to reduce that risk. Two of the programs, called TACTIC and HOPE, are for adult survivors of childhood cancers. The third program, THRIVE, is for adult cancer survivors.

"Even if you have a cure, we're beginning to treat cancer like a chronic disease, such as diabetes, that needs regular monitoring," says Kristin Kilbourn, PhD, a psychologist with the UCCC's survivorship program and an assistant professor at the University of Colorado School of Medicine. "In our clinics, we can educate survivors and hopefully help them educate their primary care physicians about preventing recurrences and other illnesses."

UCCC researchers are engaged in numerous studies to help better understand late effects of cancer treatment. UCCC has received one of eight LIVESTRONG Survivorship Centers of Excellence grants, as well as support from the NCI to conduct this research. Current projects include:

Betsy Risdendal, PhD, associate research professor at Colorado School of Public Health, is working to identify factors that might predict why some people do better after cancer than others and to develop ways to better intervene and improve cancer survivorship and quality of life. She is also studying the effectiveness of the TACTIC and THRIVE clinics.

- Anna Baron, PhD, professor at the Colorado School of Public Health, Tim Byers, MD, associate dean of the Colorado School of Public Health, and Risdendal are working on a long-term study of Latina breast cancer survivors, called the SUNSHINE Study.
- Tom Beresford, MD, professor at CU medical school, is investigating how psychological adaptive styles might predict who does well in cancer survivorship.



- Ellyn Matthews, PhD, assistant professor at University of Colorado College of Nursing, is studying interventions for insomnia, pain, psychosocial distress and symptom management in cancer populations. She has an NIH grant to test therapy for chronic insomnia after completion of breast cancer treatment.
- Michael Galbraith, PhD, associate professor at University of Colorado College of Nursing, is researching quality of life, relationship satisfaction, intimacy, communication and symptoms in couples who are long-term survivors of prostate cancer.
- Linda Burhansstipanov, DrPH, associate professor at UCD SOM, leads the Native American Cancer Education for Survivors project, which aims to improve quality of life for Native American breast cancer patients from diagnosis through survivorship.

Above: TACTIC physicians Brian Greffe, MD, Linda Overholzer, MD, and Tim Garrington, MD

Hub-and-spoke research models moves research quickly to bedside

If you're trying to track cancer research at the University of Colorado Cancer Center, you might want to bring a few homing devices with you. And a very large spreadsheet.

Thanks to a unique approach introduced 11 years ago by nationally renowned translational scientist Gail Eckhardt, MD, research at the comprehensive cancer center moves up, down and sideways so rapidly that it can be tough to keep up with the more than 500 clinical trials and thousands of laboratory studies. Driving this seemingly ceaseless need for speed is the intense desire to move treatments from the lab to the bedside.

"The main thing that sets us apart from community cancer centers is our ability to offer patients access to huge numbers of Phase I studies, which are highly regulated and require experienced investigators," says Eckhardt, division chief of medical oncology at the University of Colorado School of Medicine and program



leader for UCCC's developmental therapeutics program.

"But our Phase I program doesn't stand alone. It is integrated with disease-specific programs so that when a drug shows promise, it can be moved into that disease area seamlessly without having to be handed off to a different team."

The model is called the hub-andspoke, and it attracts renowned

researchers from around the world to this campus just on the outskirts of Denver and minutes from the international airport. Laboratories doing bench research are located in the same buildings as clinical research, both of which are just across manicured commons from patient clinics.

More important than the physical proximity, however, is the staffing proximity. A clinical researcher from

each of 10 different cancer areas plus UCCC's stem cell program sits on the Phase I clinical trials team, ready to pounce if a drug shows promise in a specific patient population.

"A lot of centers build huge stand-alone Phase I programs, but when re-

search needs to transition to expanded cohorts of Phase 2, it has to transfer to a new group," Eckhardt says.

A breakthrough treatment for lung cancer is a prime example of how this model moves research quickly from safety testing to a particular group of patients. Shortly after beginning Phase 1 trials for a new drug called crizotinib, Ross Camidge, MD, PhD, director of the lung cancer clinical program at the University of Colorado Hospital and a member of UCCC's Phase I research oversight team, saw marked improvement among a subset of lung cancer patients. He quickly moved the drug into his division and was soon able to identify that the drug worked effectively for patients with a particular gene mutation, known as ALK, present in only about 5 percent of lung cancers.

"That is, without a doubt, the most successful example of how our model works," Eckhardt says. "We have multiple examples of taking drugs from Phase I to Phase 2 studies very rapidly because of this mechanism."



Several other innovative programs at the CU medical school complement the cancer clinical trials program in its effort to help move research rapidly forward, such as the newly developed Cancer Stem Cell-Directed Clinical Trials Program (CCTP). Researchers also benefit by a unique model that allows them to implant human tumor tissue directly from patients into mice. This allows laboratory researchers to test drugs in Phase I trials against tumors, allowing concurrent research on safety and dosing ranges while also testing for effectiveness in specific cancers, resulting in a fasttrack to Phase 2 trials.

Using this model, UCCC researchers recently discovered three biomarkers to help identify patients who

will best benefit from drugs in development. These biomarkers are so unique that other cancer centers, including the University of Chicago and Mayo Clinic, are now using them in their trials. These biomarkers also are being used for patient selection in trials of three different drugs by the National Cancer Institute's prestigious Cancer Therapy Evaluation Program.

"The thing we're most excited about right now is the ability to use biomarkers to find genetic pathways that when targeted in combination with standard treatments will lead to better outcomes," Eckhardt says.

Opposite: S. Gail Eckhardt, MD; Gastrointerology Cancer Tumor Board; Above: University of Colorado Cancer Center researcher



UCH: Cancer Tumor Registry | COLORADO- Colorado Central Cancer Registry | NATIONAL- National Cancer Data Base

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UCH: Cancer Tumor Registry | COLORADO- Colorado Central Cancer Registry | NATIONAL- National Cancer Data Base

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Colorado's only federally designated cancer center tackles cancer problem from all angles

The University of Colorado Cancer Center is the hub of cancer research in Colorado. We are a consortium of more than 400 researchers and physicians at three state universities and six institutions, all working toward one goal: translating science into cancer survivorship.

Through collaboration and innovation, UCCC members discover, develop and deliver breakthroughs that improve cancer care for people and companion animals. We focus on:

- Personalized care that embraces the best clinical practices of prevention, diagnosis, treatment and survivorship.
- > Innovative interdisciplinary research.
- > Premier clinical and scientific training.
- > Creative partnerships.



Founded in 1988, UCCC is the only comprehensive cancer center designated by the National Cancer Institute in Colorado and the Rocky Mountain region. Our founding director, Paul A. Bunn, Jr., MD, led the organization until 2009. In 2010, Dan Theodorescu, MD, PhD, ushered UCCC into a new era.

UCCC is headquartered on the Anschutz Medical Campus in Aurora, Colo., in the University of Colorado School of Medicine. Member institutions include University of Colorado Denver, University of Colorado at Boulder, Colorado State University, University of Colorado Hospital, The Children's Hospital, Denver VA, Denver Health, National Jewish Health and the Kaiser Permanente's Institute of Health Research. Our clinical outreach program extends through Colorado and neighboring states.

Highlights and Accomplishments

UCCC is known clinically for its robust and diverse Phase I clinical trials program and personalized cancer treatment. Our scientific expertise ranges from understanding how chromosome structure controls cancer cell behavior, to understanding how the immune system impacts cancer. Other strengths include:

Lung cancer care and research: UCCC is one of the world's best lung cancer research and treatment programs. We are the coordinating center for the Lung Cancer Mutations Consortium, funded by a \$5.3 million American Reinvestment and Recovery Act Grand Opportunities grant.



- Cancer survivorship: one of 8 Lance Armstrong Foundation LIVESTRONG Survivorship Centers of Excellence, home to the region's three full-scale cancer survivorship clinics: The HOPE clinic for young adult survivors of cancer at The Children's Hospital, the TACTIC clinic for adult survivors of childhood cancer at University of Colorado Hospital, and the THRIVE clinic for transitioning adult cancer patients back to primary care.
- Cancer Screening: The Colorado Colorectal Screening Program is a national model for ensuring uninsured Coloradoans who meet certain financial and risk criteria receive colon cancer screening and follow-up care at no cost to them.

- Molecular tumor testing. UCCC has developed tests that find specific gene defects that can be targeted with new drugs and, positioned UCCC as a national leader for clinical trials of "targeted" drugs.
- Tumor Explants. UCCC is on the cutting edge of personalized cancer treatment, developing laboratory methods to test cancer therapy by explanting living cancers from patients into a special breed of mice. The mice receive different treatments to identify the drug combination that the patient's tumor will best respond to.
- Cancer Clinical Trials. With the largest human and companion animal cancer clinical trials programs in

the region, UCCC provides patients across the state and region with access to cutting-edge cancer care UCCC's Phase I Trials program is the only program of its kind in the region.

- Structural Biology. UCCC's NMR spectroscopy and X-Ray facilities are among the best in the world and have helped recruit world-class scientists to use them. The machines, housed in UCCC's Structural Biology core, help scientists solve structures of cancer molecules to develop drugs with precise molecular targeting.
- Animal Cancer Treatment and Clinical Trials. The Colorado State University Animal Cancer Center is the world leader in research and treatment of spon-

taneously occurring cancers in companion animals, especially dogs. UCCC's members at CSU collaborate with researchers in human cancers, and clinical trials in dogs have led to new treatments for people.

- Stereotactic Body Radiation Therapy (SBRT). UCCC members Dr. Brian Kavanagh and Dr. Tracey Schefter led the development of SBRT, a highly precise, high dose radiation treatment that noninvasively targets tumors inside the liver and other organs.
- Pregnancy-Associated Breast Cancer. Drs. Pepper Schedin and Ginger Borges are world experts on breast cancer that arises as a complication of pregnancy, which affects about 30,000 young women each year.

Learn more:

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ANSCHUTZ MEDICAL CAMPUS



