

# Colorado Companies Tackle CANCER

A cure for cancer is the Holy Grail of modern medicine. But so far, despite more than a half-century of research and a handful of incremental successes, researchers have yet to make a giant breakthrough.



Photo courtesy of Allos Therapeutics, Inc.

The scope of the problem is clear: cancer is the No. 2 killer of Americans, second only to cardiac disease, taking 500,000 lives a year. And the incidence of cancer is rising in developing nations as people live longer, making cancer a truly global disease.

Cancer is a syndrome of many diseases, all characterized by uncontrolled cell growth, and those cells ability to invade other tissues. Treatments include chemotherapy, radiation and surgery. Cancer treatment itself can be so debilitating that counteracting its effects has proven a multibillion dollar market. And in most cases, cancerous cells re-emerge after treatment, eventually leading to death.

“It’s a few yards and a cloud of dust,” says Leonard Shaykin regarding modern cancer research. Shaykin, chief executive officer of Tapestry Pharmaceuticals, continues, “There have not been any major leaps in cancer treatment; it’s all been very incremental because our knowledge is really so sparse.”

Founded in 1992 as NaPro BioTherapeutics, Boulder-based **Tapestry** is one of Colorado’s oldest biotechnology firms. The publicly traded company is among more than a half dozen Colorado firms at work on cancer treatments.

Tapestry initially grew, harvested and sold paclitaxel, the generic form of an early broad-spectrum chemotherapy drug. Oncologists still use taxanes such as paclitaxel in cancer chemotherapy, often in combination with other medications.

In 2003 Tapestry sold its paclitaxel business and turned its attention to developing a third-generation taxane designed to overcome the body’s resistance to the earlier medication. The company expects to put the compound, TPI 287, into Phase II clinical trials this year.

Taxanes attack cells’ microtubules, small fibrous cell components that are fundamental to cell division. Taxanes cause those microtubules to stick together; preventing cell division, and eventually spurring cell suicide.

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The problem, explains Tapestry's Chief Financial Officer Gordon Link, is that tumors become resistant to taxanes, much like bacteria grow resistant to antibiotics. After a while, tumor cells overproduce a protein that grabs foreign substances and pumps them out of the cell.

"Our compound is designed to overcome that resistance," Link says. "We have very good in vitro data, and nice in vivo data suggesting that's the case. We are now in the clinic in patients. Time will tell – keep watching."

Chemotherapy drugs are poisons. They are designed to kill cancer cells, while allowing surrounding healthy tissue to live. Inevitably, the process is imprecise, and healthy cells die, too.

Now cancer researchers are capitalizing on decades of research into what makes cancer cells different from the rest of the body. That has resulted in so-called "targeted therapies" that attack specific chemical markers or chemical pathways in tumor cells.

The resulting drugs can attach to tumor cell surfaces or enter the cells themselves, interfering with ongoing functions. Unlike older chemotherapy, targeted therapies have the potential to slow down cancer cell growth while doing minimal damage to the rest of the body.

Eight-year-old publicly traded **Array BioPharma** is at the forefront of the targeted chemotherapy revolution. Its lead candidate, currently in Phase I trials, is a MEK inhibitor. MEK is an enzyme that plays a role in the cascade of interactions that leads to cancer cell growth.

"If you think of cancer cells like a copy machine that went crazy, and just kept producing copy after copy, the drug interferes with the copy machine at the point of the MEK protein," explains Array Spokeswoman Tricia Haugeto.

Array, which has facilities in Boulder and Longmont, was founded by scientists who left bioscience giant Amgen in 1998. The company has four other targeted medications in the pipeline. The 270-person firm has invested \$164 million in research to date, and struck deals with AstraZeneca and Genentech.

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Chemotherapy sends drugs to kill cancer cells. Cancer immunotherapy, on the other hand, stimulates the body's natural defense system to attack tumors. A fast-growing Colorado firm, **GlobeImmune**, has a cancer vaccine ready to enter Phase II clinical trials this year

The 53-person Louisville firm, based on technology licensed from the University of Colorado, develops therapeutic vaccines called Tarmogens using brewer's yeast. Unlike traditional

vaccines that shore up the body's defenses against a future infection, these vaccines drive the immune system to fight cells it has come to live with, however uncomfortably. GlobeImmune's cancer vaccine stimulates a T cell response against cells with genetic mutations that lead to wild proliferation. The firm genetically engineers yeast to contain proteins "specific to the disease we are trying to combat," explains Kirk Christoffersen, the company's senior director of corporate development.

After the Tarmogens are injected, "antigen-presenting cells pick up this yeast, they chop it apart with molecular scissors, and they take the pieces and present them to the immune cells," Christoffersen says. "Those T cells get activated, and they go and hunt for any cell that has the same marker – in this case, every cancer cell that displays certain proteins."

GlobeImmune is also working on a Hepatitis C vaccine, and considering applications of its yeast-based technology in AIDS and influenza. The company, which raised \$38.4 million in a Series B financing in 2005, is committed to Colorado.

"We've had great venture capital support locally," Christoffersen says. "Colorado has a great quality of life, and there's a really interesting, growing biotech community that has enabled us to stay and recruit top talent here."

Radiation therapy is used to treat almost every kind of solid tumor, and a handful of Colorado companies – including Boulder-based RxKinetix and Westminster-based Allos Therapeutics– are working to make it more effective.

Radiation works best in tumor cells that have a high concentration of oxygen. Oxygen-deficient tumor cells, such as some brain tumor cells, call for two to three times as much radiation before they are killed.

Publicly traded **Allos Therapeutics'** drug Efavoxyn was created to solve this problem by increasing the release of

hemoglobin circulating in and around tumors. The company hopes by mid-2006 to complete enrollment in Phase III clinical trials for Efavoxyn, looking at its application in brain metastases that have spread from breast cancer.



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Photos courtesy of RxKinetix and Array BioPharma

Privately held **RxKinetix** is also working to improve radiation by making it more tolerable. The 23-person firm has high hopes for a compound to ameliorate a miserable side effect of head and neck radiation – oral mucositis: painful ulcers that form in the patient's mouths. These sores make it difficult to talk, eat or swallow, and patients often need opiates to manage their pain.

RxKinetix, founded on technology licensed from the University of Colorado, has developed an innovative gel infused with an anti-oxidant medication. The gel, RK-0202, is liquid at room temperature and viscous when it warms up. The patient swishes the medicated gel around his mouth, effectively coating the mucous membrane and protecting it from harmful irradiation.

While RK-0202 doesn't entirely prevent oral mucositis, it slows its progression, allowing patients to finish their therapies and keeping them out of the hospital, says Joanna Money, RxKinetix vice president of corporate development.

No drugs today treat this condition, she adds. "This is a huge quality of life issue for patients, and for the health-care system there is a huge pharmacoeconomic benefit."

Phase II trials were completed in 2005, and a Phase III trial is planned for completion in 2008. To that end, the firm has raised \$26 million to date, primarily from Colorado-based Aweida Venture Partners.

RxKinetix sees initial potential for RK-0202 in the approximately 40,000 people who are diagnosed with head and neck cancer each year.

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“But we believe the market opportunity for this drug is even bigger,” Money says. “It could easily be expanded to other (radiation) patients. And a lot of chemotherapy patients get this disease as well.”

While many Colorado pharmaceutical companies are developing cancer treatments, one medical devices company is on the attack as well.

2006 will be **Valleylab’s** year of microwave ablation, a technology that destroys cancer lesions by “cooking” them from the inside out.

The 39-year-old Boulder-based company, a wholly owned subsidiary of Tyco International as part of its Tyco Healthcare division, is well-known in the medical community for radio frequency ablation technology. Its Cool-tip RF ablation system is used by surgeons to treat inoperable liver cancer.

Using radio frequency current, the Cool-tip system quickly heats and coagulates large volumes of tissue. RF ablation procedures can be performed during open surgery percutaneously or laparoscopically, depending on the physician’s discretion. It is an excellent alternative or adjunct therapy for patients with non-resectable liver lesions who may otherwise be unable to be successfully treated with surgery or chemotherapy.

Valleylab has been working on microwave ablation since July 2005 when Tyco Healthcare purchased Vivant Medical Inc., which developed the technology. Microwave ablation works similarly to RF ablation as a treatment for inoperable tumors. The technology is being tested in clinical trials, and the company expects to be able to commercialize it this year, said Donna Ford-Serbu, director of marketing for ablative therapies.

“There’s a lot of excitement for this new technology,” Ford-Serbu says, which is being targeted toward lung, liver, kidney and bone metastases.

The new technology drove much of the 1,200-employee company’s hiring in the past year, Ford-Serbu says. Direct sales and R&D staff has grown by 150 percent and 200 percent, respectively.

**OTHER COLORADO COMPANIES** developing or marketing oncology care products include Pharmion, Amgen, OSI Pharmaceuticals, Cytologic, SomaLogic, Thinc Pharmaceuticals, Newellink USA, Radiological Imaging Technology, Cell-Point and CeMines.

