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Gaining on Prostate Cancer

Drug Firms Advance Rapidly After Long Drought, but Treatments Are Pricey

By [RON WINSLOW](#)

Drug companies have scored a string of recent successes against advanced prostate cancer, ending a long drought during which there seemed to be few weapons to combat the disease.



WSJ's Ron Winslow has details of the success by some drug companies in developing treatments against advanced prostate cancer. Photo: Ramsay de Give for The Wall Street Journal

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Medivation Prostate Cancer Drug Well-tolerated in Trial

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In the latest evidence of progress, researchers reported Tuesday that an experimental drug from San Francisco-based [Medivation Inc.](#) extended survival by nearly five months in a 1,199-patient study.

A second drug, a radiation-emitter being developed by [Bayer AG](#) and [Algeta ASA](#) of Norway, targeting prostate cancer that has spread to the bone, improved survival by nearly three months in a 922-patient study.

Results of both trials were released ahead of their presentation at the American Society of Clinical Oncology's Genitourinary Cancers Symposium being held this week in San Francisco.

If the drugs win approval soon from the Food and Drug Administration, it would mean that after decades of frustration, the pharmaceutical industry will have turned out five new treatments for advanced prostate cancer within just three years.

Those already approved within the past two years include [Dendreon Inc.](#)'s Provenge, Jevtana from [Sanofi SA](#), and Zytiga from [Johnson & Johnson](#).

The pharmaceutical industry is increasingly looking for ways to speed development of new drugs—including the realization that closer ties to academic researchers can aid in discovery.

Medivation's compound, called MDV3100, is notable for how it was developed—largely in the research laboratory of Charles Sawyers, a scientist at Memorial Sloan-Kettering Cancer Center with a track record in drug discovery.

Medivation expects to file its application with the FDA this year. Assuming all goes well, the drug could be on a track to win approval about five years after it was first tested in people. "By any standard, that would be considered very, very quick," said David

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Hung, Medivation's chief executive officer.

Also helping progress is a growing understanding of the biology of prostate cancer, a disease fueled largely by the male hormone testosterone.

The new treatments aren't cures and individually their impact on survival is modest—in clinical trials each added a median of roughly three to five months to patients' lives. Their high cost is likely to complicate adoption for many patients. Provenge, for

instance, costs \$93,000 for a course of three treatments while Zytiga's price is about \$5,000 for a monthly supply of pills.

But some researchers believe that the options will lead to new strategies where the drugs are used either sequentially or in combination to significantly extend survival. The new treatments are expected to cause the world-wide market for prostate cancer therapies to surge to \$4 billion by 2015, according to Morningstar Inc., up from about \$1 billion currently.

"The whole equation for prostate cancer is completely different," said Christopher J. Logothetis, chief of genitourinary medical oncology at M.D. Anderson Cancer Center, Houston. "It is [now] among the solid tumors that should be considered highly treatable."

New Options
Recent progress in treatment for men with advanced prostate cancer:

PROVENGE
Company: Dendreon
COST OF TREATMENT:
\$93,000 one-time course of three treatments
Status: Approved

JEVTANA
Company: Sanofi
COST OF TYPICAL TREATMENT:
\$48,000 six 3-week treatment cycles
Status: Approved

ZYTIGA
Company: Johnson & Johnson
COST OF TYPICAL TREATMENT:
\$40,000 eight-month course
Status: Approved

ALPHARADIN
Company: Bayer and Algeta
Status: Late-stage trial completed

MDV3100 (no brand name yet)
Company: Medivation and Astellas
Status: Late-stage trial completed

Source: WSJ research

All of this stands in contrast to just a decade or so ago when the disease was considered resistant to almost any treatment. Drug companies would say "nothing has worked in 35 years. Why are we going to throw our [new] drug at that?" said Bruce Roth, professor of medicine and an oncologist at Washington University, St. Louis. "Now we're starting to see a payoff in the investment in research about the biology of prostate cancer."

MDV3100 is a case in point. Dr. Sawyers, a Howard Hughes Medical Institute investigator, played important roles in the development of [Novartis](#) AG's breakthrough leukemia drug Gleevec and a second-generation version called Sprycel from [Bristol-Myers Squibb](#) Co.

In the mid-1990s, while at University of California at Los Angeles, Dr. Sawyers became interested in why men with prostate cancer relapsed on hormone therapy—the standard treatments, which starve prostate tumors of testosterone, the primary fuel that makes them grow.

Conventional wisdom was that once a patient relapsed, the so-called androgen receptors—structures that protrude from tumor cells like a lock to attract the testosterone "key" that activates them and promotes tumor growth—were no longer driving the disease. Dr. Sawyers was skeptical. In a series of experiments with mice, he and his colleagues found that drug-resistant patients actually had elevated (not lower) levels of androgen receptors. Drugs were now activating them instead of blocking out the testosterone.

"It wasn't destroying dogma, but it wasn't what people expected," Dr. Sawyers said. "It put a spotlight on the androgen receptor as a drug target."

But he said he wasn't able to persuade any drug companies to pursue the lead. So he teamed up with a chemist, Michael Jung, at UCLA to design a drug themselves.

Scouring patent databases, Dr. Jung discovered a compound made by the former French drug maker Roussel Uclaf that locked onto the androgen receptor about 100 times more strongly than the commonly used prostate-cancer drug, Casodex.

Using that drug as a template, and taking on a task normally performed by drug-industry scientists, Dr. Jung fashioned some 200 slightly different molecules, which the researchers tested against tumor samples in their own version of the drug industry's high-volume screening technology. They came up with a promising candidate, tweaked it so it would be absorbed in the blood as a pill and then performed the key experiment—testing it in mice to see if it would shrink tumors.

"It did, very dramatically," Dr. Sawyers said. But academic scientists aren't positioned to take the drug across the "valley of death"—the chasm between a promising compound discovered in the lab and the work required to test it in humans, said Dr. Sawyers, who as an inventor of MDV3100 is entitled to royalties on any sales.

In 2005, Medivation agreed to license the drug. The company confirmed the researchers' findings, tested the molecule and altered its formulation to make it suitable for humans, and filed an application with the FDA to start human studies.

Howard Scher, a veteran of prostate-cancer studies and chief of the genitourinary oncology service at Memorial Sloan-Kettering Cancer, agreed to run the research, which began in 2007. Aided by a 13-center research consortium group funded by the Defense Department and the Prostate Cancer Foundation and intended to speed development of medicines for the disease, researchers ultimately and rapidly enrolled 140 patients, with promising results.

In 2009, Medivation, in collaboration with [Astellas Pharmaceuticals](#) Inc. of Japan, launched a late-stage trial, the results of which Dr. Scher reported Tuesday.

Dr. Scher reported that the 800 patients treated with the drug had a median survival of 18.4 months compared with 13.6 months for those given a placebo. In addition, 54% of MDV3100 patients—compared to 1.5% of those on placebo—had a greater than 50% reduction in a marker called prostate specific antigen—an indicator of a positive response to the drug. Side effects included fatigue.

During a news conference to announce the findings, Nicholas J. Vogelzang, chairman and medical director of the developmental therapeutics committee of US Oncology, a cancer treatment company, called the results "unprecedented." He added: "This is definitely going to change the way we take care of patients every day in the office."

Dr. Scher said the first patient he treated four and a half years ago is still alive and on the drug. "That's the beauty of a targeted agent," he said.

For Medivation, the successful study contrasts with news two weeks ago that, along with partner [Pfizer](#) Inc., it was pulling the plug on development of an Alzheimer's drug called dimebon after it failed to show benefit in a late stage, 1003-patient study.

Write to Ron Winslow at ron.winslow@wsj.com

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