

# New cancer drugs excite investors

CHICAGO

BY ANDREW POLLACK

The early success of a new class of cancer drugs, revealed in test results released here over the last several days, has raised hope among the world's top cancer specialists that they may be on the verge of a milestone in the fight against the disease.

The excitement has spread to Wall Street. Shares of Merck and Bristol-Myers Squibb, which are developing such drugs, both rose more than 3 percent on Monday after data from their studies were presented over the weekend at the meeting of the American Society of Clinical Oncology.

The drugs, still generally in early testing, work in an entirely new way, by unleashing the immune system to attack cancer cells much as it attacks bacteria. That could be an alternative to often-debilitating chemotherapy.

Finding ways to use the body's own defenses has been a goal since the late 1800s, when a New York surgeon named William B. Coley noticed that cancer disappeared in a patient who had a severe bacterial infection.

He then began injecting bacteria into cancer patients to rev up their immune systems. His claims of success were disputed, and most attempts since then to harness the immune system have not worked.

The new drugs work by disabling a brake on the immune system called the programmed death 1 receptor, or PD-1. And although the data presented at the meeting were from the earliest stage of testing only, the drugs were the center of attention here, with some doctors predicting that cancer treatment was about to shift.

"If you look five years out, most of this meeting will be about immunotherapy," said Dr. Mario Sznol, a professor of medical oncology at Yale.

Analysts, who predict billions of dollars in sales, are trying to determine which of the three front-runners — Merck, Bristol-Myers and Roche — has the best drug and how soon the drugs could reach the market. Some think it could be as early as a year and a half from now.

"I think all of you recognize this is a very special moment in oncology," Dr. Roger M. Perlmutter, head of research and development at Merck, told analysts Sunday at a standing-room-only meeting.

Harnessing the immune system is appealing for several reasons. It might be applicable to many different types of cancer. It might produce longer remissions than can be achieved by chemotherapy or the newer targeted drugs. And it seems somehow more natural and holistic.

"It seems the right thing to do to stim-

ulate our body's defense, rather than take some kind of poison," said Dr. Therese Bocklage, a cancer patient and pathologist from Albuquerque, New Mexico.

Dr. Bocklage thought she had bruised her leg moving a Christmas tree in late 2011. It turned out to be the return of the melanoma she thought had been successfully eradicated by surgery 20 years earlier.

She has been taking Merck's experimental PD-1 inhibitor, lambrolizumab, as part of a clinical trial since January 2012, and her tumors have disappeared. "If I had had this turn up not last year but six years ago, most likely I'd be dead," she said.

But there are reasons to be cautious. This is cancer, after all. Many other hoped-for miracles have failed to materialize. This is a conference that has hailed drugs that extend lives by only a few weeks as breakthroughs.

"We're so used to failure, we get excited very easily," said Dr. Kim Mar-

**"It seems the right thing to do to stimulate our body's defense, rather than take some kind of poison."**

golin, an expert on melanoma and immune therapies at the Seattle Cancer Care Alliance.

Most of what is known about the PD-1 drugs is that they shrink tumors significantly in 15 percent to 50 percent of patients. It is still not clearly established, though there are some hints, that the drugs will let people live longer.

And results seen in trials, under idealized conditions, do not translate perfectly to the real world. One poster presented here looked at use in Britain of Yervoy, a melanoma drug approved in 2011 that disables a different immune system brake. Median survival has been only about half of what had been seen in clinical trials.

Moreover, just because the immune system is involved does not make something safe. Ask anyone with lupus, multiple sclerosis or other diseases caused by an aberrant immune system.

Yervoy, made by Bristol-Myers, has some serious side effects caused by overstimulation of the immune system. The newer PD-1 drugs seem remarkably well tolerated so far, though lung inflammation has been seen in some patients.

For the last decade or so, the emphasis in oncology has been so-called targeted therapy, in which drugs counteract particular genetic mutations that drive tumor growth. These were supposed to displace conventional chemotherapy, which tends to poison fast-growing cells, both cancerous and healthy ones, causing serious side effects.