For almost thirty years, William Kuhens worked on Staten Island as a basketball referee for the Catholic Youth Organization and other amateur leagues. At seventy, he was physically fit, taking part in twenty games a month. But in July of 2013 he began to lose weight and feel exhausted; his wife told him he looked pale. He saw his doctor, and tests revealed that his blood contained below-normal numbers of platelets and red and white blood cells; these are critical for, respectively, preventing bleeding, supplying oxygen, and combatting infection. Kuhens was sent to the Memorial Sloan Kettering Cancer Center, in Manhattan, to meet with Eytan Stein, an expert in blood disorders. Stein found that as much as fifteen per cent of Kuhens’s bone marrow was made up of primitive, cancerous blood cells. “Mr. Kuhens was on the cusp of leukemia,” Stein told me recently. “It seemed that his disease was rapidly advancing.”
Leukemia is a disorder of the blood cells, which form in the bone marrow. For reasons not always clear to scientists, immature cells fail to develop properly into mature ones and instead continue to multiply, crowding out normal blood cells. Patients are at risk of massive bleeding and sepsis, a severe complication of infection. There are many kinds of leukemia, depending on the type of blood cell involved and the pace at which the cancer advances. Kuhens was developing acute myelogenous leukemia, or A.M.L., which is estimated to occur annually in at least fifty thousand people worldwide, most of them adults, and is usually lethal; fewer than a quarter of patients survive for more than five years. Kuhens knew that his prognosis was grim, likely measured in months. Stein treated him with four courses of chemotherapy, to no significant effect.

The only options were experimental. Stein had sent a sample of Kuhens’s bone marrow to be analyzed for the presence of thirty or so gene mutations that are known to be associated with blood cancers. The tests revealed one notable mutation, in a gene that produces an enzyme called IDH-2. Normally, the enzyme helps to break down nutrients and generate energy for cells. When mutated, it creates a molecule that alters the cells’ genetic programming. Instead of maturing, the cells remain primitive, proliferate wildly, and wreak havoc.

About fifteen per cent of all A.M.L. patients carry the mutated enzyme. In recent months, Stein had been participating in a Phase 1 clinical trial of a drug, AG-221, designed to target it; the drug was developed by the pharmaceutical company Agios. Phase 1 studies represent the very first tests of a new drug in humans; they are mainly meant to assess a new drug’s safety, with little expectation that the treatment will help. Of the first ten patients who had been treated, three had died from their disease before the drug’s effects could be evaluated. But the data on six of the seven remaining patients were striking: five had gone into complete remission and one entered a partial remission. (The other patient did not improve, and his leukemia continued to grow.)

Stein described one patient to me, a woman in her late sixties with A.M.L. She had already undergone a bone-marrow transplant, had relapsed, and then had more chemotherapy; nothing helped. To Stein’s surprise, after three months on AG-221, her leukemia had gone into complete remission and her blood count had returned to normal. “It was transformative,” Stein said. “She gained weight and told me that the pep in her step was back.” Another patient, a sixty-year-old man with A.M.L., also had failed to benefit from several regimens of chemotherapy, and he, too, went into remission after taking AG-221. Moreover, the side effects of the medication, which is given orally, have been manageable—mostly mild nausea and a loss of appetite.
This past spring, Kuhens entered the drug trial and received his first dose. Within weeks, the leukemic-cell count in his bone marrow had fallen from fifteen per cent to four per cent, and his counts of healthy blood cells improved markedly; he has been in complete remission for four months. The most noticeable side effect has been a metallic taste in his mouth. “For some reason, I can’t stand mayonnaise,” Kuhens told me recently. He just celebrated his fiftieth wedding anniversary. “I want to be around for a while,” he said, “and I don’t know how long this drug will last.”

In April, Stein presented his findings to a packed auditorium at the annual meeting of the American Association for Cancer Research, in San Diego. It was the first public airing of the results of AG-221; patients with progressive A.M.L. had never improved so quickly and definitively.

I received the news with tempered excitement. In the nineteen-seventies, when I trained in internal medicine, and later in hematology and oncology, acute myelogenous leukemia was the cancer to beat. The disease typically overwhelms its victims, relegating them to the intensive-care unit, where they require intravenous antibiotics, blood transfusions, and, as their lungs and heart fail, support on ventilators. The most effective initial treatment was, and still is, a pair of highly toxic chemotherapy drugs, daunorubicin (or sometimes a related one, adriamycin) and cytarabine. The side effects are profound: the first family of drugs causes arrhythmias and heart-muscle damage, often leading to cardiac failure; the second drug is toxic to the central nervous system, particularly the cerebellum, resulting in severe lack of balance and coördination. Combined, the two agents might kill the leukemic cells in the marrow, but they also kill healthy blood cells, causing patients to enter a limbo with an “empty marrow,” during which we doctors used to pray that their normal cells would regrow. Daunorubicin and adriamycin have a distinctive red color, and in my day medical interns referred to them as “the red death,” because most of the patients who took them ultimately died of their disease. In response, my mentors argued that “desperate diseases require desperate measures.”

By comparison, Stein’s results were breathtaking. Still, his trial hadn’t involved many patients, and they hadn’t been followed for long. Cancer is wily, and some drugs that target mutations can show benefits that soon evaporate as the tumor adapts. In June, however, at the European Hematology Association conference, in Milan, Stéphane de Botton, a hematologist at the Institut Gustave Roussy, near Paris, presented updated results that were equally promising. The findings covered thirty-five patients, most of them with A.M.L. Ten had died within a month of entering the trial,
from complications related to the disease. But fourteen patients had improved on AG-221,
including nine whose leukemia went into complete remission. Five were stable but showed no
change; in six, the leukemia continued to grow. The patients also experienced few side effects, de
Botton told me recently, and some patients have been in remission for more than six months.

“These data signal the first real advance for A.M.L. in thirty years,” Stephen Nimer, the director of
the Sylvester Comprehensive Cancer Center, at the University of Miami, and an eminent leukemia
researcher and clinician, told me. “It’s a huge step forward.”

The breakthrough is notable in part for the unconventional manner in which the drug attacks its
target. There are many kinds of cancer, but treatments have typically combatted them in one way
only: by attempting to destroy the cancerous cells. Surgery aims to remove the entire growth from
the body; chemotherapy drugs are toxic to the cancer cells; radiation generates toxic molecules that
break up the cancer cells’ DNA and proteins, causing their demise. A more recent approach,
immunotherapy, coöpts the body’s immune system into attacking and eradicating the tumor.

The Agios drug, instead of killing the leukemic cells—immature blood cells gone haywire—coaxes
them into maturing into functioning blood cells. Cancerous cells traditionally have been viewed as a
lost cause, fit only for destruction. The emerging research on A.M.L. suggests that at least some
cancer cells might be redeemable: they still carry their original programming and can be pressed
back onto a pathway to health.

Most cancers, once they spread, are incurable. Cancer researchers are desperate to raise the
number of patients who go into remission, to prolong those remissions, and to ultimately prevent
relapse. So when a new way of attacking cancer comes along, it is often greeted with incautious
euphoria and an assumption that the new paradigm can be quickly converted into a cure for all
cancers.

In 1971, President Nixon announced the War on Cancer, based on the mounting belief, born of
research in the nineteen-sixties, that cancer is caused by viruses. As it turns out, although viruses
often cause cancer in lower animals, they do so less frequently in humans. In 1989, Harold Varmus
and Michael Bishop won the Nobel Prize for their discovery, thirteen years earlier, that normal
genes could mutate into cancer-causing oncogenes, which appear to drive the unchecked growth
and behavior of malignant cells. Cancer was now seen as a genetic disease, and in some cases, such
as familial breast cancer, genetic tests were developed that could indicate whether an individual was at high risk for the malignancy.

Advances in DNA technology and in computing led to the mapping of the healthy human genome, and of other genomes, including those of various cancers. Scientists assumed that they would soon decipher how tumors arise and find a way to stop them. In the case of some cancers, that promise has been fulfilled, but for most, especially once they have spread, it has not. In 1998, after the development of new drugs that could shut down certain cancers by choking off their blood supply—an advance, known as anti-angiogenesis, that has given rise to the drug Avastin—the Nobel laureate James Watson predicted that this work would “cure cancer in two years.” Immunotherapy has recently been shown to be highly effective against melanoma and kidney cancer, but many other cancers manage to evade this type of therapy.

The more scientists learn about cancer, the more diverse and vexing their opponent appears. Most cancers have several potential ways of developing. Even within a single tumor, individual cancer cells may follow separate road maps. A drug designed to target one pathway may succeed in destroying only a fraction of the tumor, leaving the rest to grow, spread, and kill. The IDH-2 mutation is just one of many enzyme mutations that are found in acute myelogenous leukemia. Recently, Timothy Ley, a researcher at Washington University, in St. Louis, and an expert on the genetics of blood cancers, published a study involving two hundred patients with A.M.L.; he found that each patient harbored a unique set of mutations. “It’s complex, but I’m not daunted,” Ley told me. “At least now we know what we’re dealing with.”

Agios hopes that AG-221 will become a key in treating those cancers which are driven by IDH-2. In March, the company launched clinical trials of another drug, AG-120, which targets a different mutated enzyme, IDH-1. The mutation occurs in as many as ten per cent of A.M.L. patients, but it’s also found in seventy per cent of patients with a type of brain tumor called a glioma and in fifty per cent of cases of cancer of the cartilage. The treatment of cancer, which traditionally adopted a destroy-the-village strategy, is becoming ever more like precision warfare. “We treat people with the specific mutation who may benefit,” David Schenkein, the C.E.O. of Agios, told me. “We don’t treat people who would not respond to the drug.”

One day in July, I visited the Agios laboratory, not far from the M.I.T. campus, in Cambridge, Massachusetts. Precision medicine has been made possible in part by advances in computer
technology, enabling scientists to depict enzymes, receptors, and other key cellular molecules in exquisite, three-dimensional detail. Pharmaceutical companies like Agios have large databases that keep track of known drugs and their physical contours. Finding or creating a drug for a cancer-causing molecule can be a matter of deciphering the molecule’s shape and determining what sort of drug would best match it, like fitting a key to a lock.

AG-221 came to exist in much this manner. For several years, scientists had been aware that some patients with acute myelogenous leukemia carry the mutated IDH-2 enzyme. The healthy enzyme helps the cell generate energy by breaking down a molecule called isocitrate, leaving another, called alpha-ketoglutarate, as a by-product. In 2009, Agios researchers discovered that the mutated enzyme leaves a different by-product, a molecule called 2-hydroxyglutarate, or 2-HG, which appears to switch off certain genes in the cell nucleus. As a result, the cell fails to mature into a fully functioning blood cell and instead multiplies dangerously. An Agios team soon devised AG-221, which binds to the abnormal enzyme and prevents it from creating 2-HG.

The researchers were nonetheless surprised when the malignant cells matured into healthy ones. As it turns out, a cell containing the mutated IDH-2 enzyme also still contains the healthy enzyme; the healthy one functions correctly, but its benefits to the cell are swamped by the effects of the aberrant enzyme. Once the mutant enzyme is neutralized, the healthy one puts the cell back on track. In effect, the leukemic cell harbors the genetic program to behave normally; the drug allows the program to be accessed and enables the cancer to grow up.

At Agios, a bioanalytical chemist named Kelly Marsh showed me how the drug works. In a large laboratory space, Marsh and her colleagues were preparing to test the efficacy of a second-generation version of AG-221. She sat at a lab bench with a plastic tray the size of an index card; it had ninety-six wells, each containing a few drops of clear liquid—suspensions of leukemic cells with the IDH-2 mutation. Some of the wells had been treated with increasing doses of the drug; others were untreated, to serve as controls. Marsh’s analysis would show how effective the drug was at neutralizing the errant enzyme.

The most prominent object on the lab bench was a mass spectrometer—a machine about the size of a steamer trunk, with fine plastic tubing emanating from it. Marsh lined up the plastic tray so that an automated pipette drew up about a tenth of a drop from each of the wells and sent it through the tubing and into the machine. Within the spectrometer, the liquid would be heated into a gas and
passed through a powerful electric field, where its mass could be calculated to several decimal points and its molecular makeup could be determined. A computer readout indicated how much 2-HG, the by-product of the aberrant enzyme, remained in each well.

Marsh would have to run the test scores of times before she had sufficient data to draw statistically valid conclusions. Still, the results from this run were easy to grasp. As the dose of the drug was increased, the amount of 2-HG fell, in some cases as much as ninety per cent. The leukemic cells had been neutralized, as they had been in the clinical study of patients like William Kuhens.

That afternoon, I examined microscope images of the bone marrow of a patient who had not been treated with the drug. As a hematologist, I often dread taking in this view. Up close, healthy marrow looks like an Impressionist painting—a variegated landscape of cell types and colors. Leukemic marrow is a monotonous canvas of cancer cells; the images I was looking at showed hardly any normal blood cells being made. Then I examined images from a patient who had received the Agios drug. Typically, when a patient with A.M.L. is treated with high doses of chemotherapy, the marrow is emptied of all living cells; what’s left is a moonscape of fat globules and fibrous tissue. The images at Agios showed robust marrow: the leukemic cells had been forced to mature and had reverted to functioning white blood cells, red blood cells, and platelets. They were transformed.

I had seen something similar only once before. The first scientific paper I ever wrote, some thirty-five years ago, was about an unusual blood cancer called acute promyelocytic leukemia, or A.P.L.
My paper noted that patients typically died from massive hemorrhage and that even after intensive chemotherapy their remissions lasted only a year or so. In the nineteen-eighties, the disease became a curiosity for scientists, because of a new drug that was being employed against it, one whose effects mirror those of AG-221.

The drug, called all-trans-retinoic acid, or ATRA, causes leukemic cells to abandon their relentless growth and to mature into white blood cells. ATRA and AG-221 attack different molecules in their respective cancers: AG-221 targets an enzyme that, when not mutated, is essential to the cell’s metabolism; ATRA attacks a hybrid protein—the result of chromosomes breaking and faultily recombining—that should not otherwise exist. Nonetheless, when ATRA came into use, it was the first time that a cancer had been neutralized by forcing its cells to mature. The slides I saw of marrow from patients treated with AG-221 looked a great deal like the slides I’d seen from patients with acute promyelocytic leukemia who had been treated with ATRA. The principle was the same: cancer cells could be made healthier again.

The idea for ATRA grew out of research by Zhen-yi Wang and Zhu Chen, of the Ruijin Hospital, in Shanghai. They were studying acute promyelocytic leukemia and wondered whether there was another way to treat the cancerous cells besides killing them. Wang was inspired by a passage from the Analects of Confucius: “If you use laws to direct the people, and punishments to control them, they will merely try to evade the punishments, and will have no sense of shame. But if by virtue you guide them, and by the rites you control them, there will be a sense of shame and of right.” Wang later wrote, “If cancer cells are considered elements with ‘bad’ social behavior in our body, ‘educating’ rather than killing these elements might represent a much better solution.”

Wang and Chen were aware of work by Leo Sachs, a researcher at the Weizmann Institute of Science, in Israel, who had found that some leukemic cells seemed to have retained their ability to mature into healthy cells, at least in laboratory experiments. For a treatment agent, the Chinese scientists turned to all-trans-retinoic acid, a derivative of Vitamin A, which in Shanghai had just been approved to treat skin diseases such as psoriasis and acne. When the researchers exposed leukemic cells to ATRA, they appeared to mature, released from their primitive state.

In 1985, Wang treated his first patient with ATRA: a five-year-old girl with acute promyelocytic leukemia who had not improved with chemotherapy and was dying. Within a week of treatment, she had begun to improve, and by three weeks she “miraculously went into complete remission,”
Wang and Chen wrote in 2008, in the journal *Blood*. The authors noted that she was now twenty-six years old and healthy. In 1988, the Shanghai Institute of Hematology had published the results of a study in which twenty-four patients were given ATRA: twenty-three entered a complete remission, their leukemic cells having matured. This success was soon confirmed by other hematologists across the globe.

But researchers discovered that the benefits of the drug often were not lasting. The leukemic cells, reprogrammed to mature and behave, exhibited a strong tendency to become cancerous again within three to six months. Chen, drawing on the work of researchers at Harbin Medical University, in northeastern China, experimented with arsenic trioxide as a follow-up agent. (Arsenic compounds were an active ingredient in an anticancer remedy popular among local healers.) It seemed that arsenic trioxide caused mature blood cells to commit suicide, a process called apoptosis. The resulting treatment was a one-two punch: ATRA triggered the leukemic cells to mature, whereupon they became vulnerable to the second drug, which destroyed them. Three decades ago, the remission rate for acute promyelocytic leukemia was forty per cent. Today, with the combination therapy, it is ninety-five per cent, and most of those patients are cured.

The effectiveness of ATRA was long viewed as an anomaly, but today researchers working on AG-221 and acute myelogenous leukemia often cite it as an inspiration. “A.M.L. is a disease that we all fear,” Harold Varmus, who has followed the ATRA research for years, told me. “There were findings in the laboratory suggesting that leukemia cells could differentiate, and it is gratifying to see this approach moving into the patient setting.”

The critical question is how long the benefits of AG-221 will last. “The issue is durability,” Martin Tallman, the chief of the Leukemia Service at the Memorial Sloan Kettering Cancer Center and a professor at Weill Cornell Medical College, told me. “Some patients have been in remission for six to eight months. But, based on prior studies in acute leukemia, the concern is that these people may ultimately relapse.” Tallman believes that the next step in treatment should involve combining AG-221 with a chemotherapy drug, as well as with other targeted inhibitors of gene mutations, or with bone-marrow transplantation.

One potential virtue of highly targeted drugs is that their side effects are far less severe than those of traditional chemotherapy drugs. “No major toxicity with AG-221 has been observed so far,” Tallman said. “And it seems that, as you increase the dose, patients go into remission more
quickly.”

In medical school, we were taught that although cancer comes in many forms, it has one immutable characteristic: it is composed of immature cells. The research on these blood cancers, however, suggests that this trait may be reversible after all, and that the cancer cells, when prompted to mature, become susceptible to therapies to which they would otherwise remain resistant.

Blood cancers are a fairly small subset of cancers as a whole. Recently, scientists working with solid tumors of the lung, ovaries, and pancreas have had success in forcing those cancer cells to mature into something like normalcy. These achievements have sprung from research not on metabolism but on stem cells. In the early nineteen-sixties, the Canadian biologists James Till and Ernest McCulloch showed that, in mice, all blood cells originate from primitive, undifferentiated cells in the bone marrow. These blood-forming stem cells are rare—perhaps one in a hundred thousand cells—and are unremarkable when seen under the microscope: small, bland, and round, offering no indication of their marvellous capacity to reconstitute the entirety of our blood system. Scientists have since shown that many of our body tissues also arise from specialized stem cells; there are neural stem cells in the brain, intestinal stem cells in the gut, and cardiac stem cells in the heart. Researchers are now investigating what triggers these cells to differentiate and develop into our various tissues, and to what extent those instructions can be manipulated.

In 1994, John Dick, now a professor at the Princess Margaret Cancer Center and at the University of Toronto, posited that cancer, too, might originate from its own particular stem cell. Dick’s work was highly controversial, but subsequent researchers have reported evidence of stem cells in breast cancer, colon cancer, and melanoma, as well as in cancers of the prostate, the lung, and the pancreas. The definitions can be unclear. To some scientists, the leukemic cells in A.M.L. include cancer stem cells; to others, they are simply immature blood cells. And not everyone sees the same value in the research.

“I understand full well the attractiveness and the seduction of the cancer-stem-cell model,” William Kaelin, a cancer biologist at Harvard’s Dana-Farber Cancer Institute, told me. “But so far it hasn’t made any predictions that I wouldn’t have otherwise made. I think we already knew that cancers tended to coöpt stem-cell pathways that are important for normal stem cells. And I think we already knew that many genes that are involved with stem-cell biology were occasionally mutated in cancers.”
Nonetheless, investors and drug companies have leaped at the notion of cancer stem cells. Robert Weinberg, a prominent cancer researcher at M.I.T., recently co-founded a company called Verastem, while Regeneron, an established biotech company, added cancer stem cells to its research portfolio. In 2004, scientists at the University of Michigan and the University of Texas joined the molecular biologist Larry Lasky and a lawyer, Robert Gavin, to start OncoMed, which is investing heavily in cancer-stem-cell research. The company has five drugs in early-phase clinical trials, under the direction of the oncologist Jakob Dupont; some six hundred million dollars in hand; and potential funding of more than five billion dollars, should its milestones be met, from pharmaceutical giants like Bayer, GlaxoSmithKline, and Celgene.

Whether or not cancer stem cells actually exist, the search for them has highlighted at least one useful insight, involving a mutation in a gene that plays a key role in prompting stem cells to mature. The mutation was discovered in 1917, by Thomas Hunt Morgan, an American biologist who revealed the importance of chromosomes in heredity. Much of Morgan’s work was performed at Columbia University, where he studied mutations in *Drosophila melanogaster*, the common fruit fly. Morgan found that a certain gene, when mutated, produced a cleft in the fly’s wing. The gene, called Notch, has turned out to be critical in the development of mammalian embryos, including humans, helping to make sure, for instance, that our blood vessels are patterned correctly. But when the gene is mutated it can become overly active and prevent the cell that contains it from reaching maturation.

In 2008, OncoMed began a clinical trial of an experimental drug. Like AG-221, it was designed for a distinct subset of patients, in this case those whose cancers carry a mutated form of the Notch gene. The drug effectively dampens the overactive gene, enabling cells to mature. One of the first patients was a woman with ovarian cancer; her tumors had metastasized and could not be cured by surgery, and she had undergone a dozen treatment regimens, including chemotherapy. All failed. But the anti-Notch drug stopped the cancer, after a fashion: her tumors did not shrink, which in oncology is the classical criterion for response, but neither did they grow. Her cancer seemed to have entered a kind of equilibrium, as if frozen or paralyzed. This arrest in its growth lasted for more than five hundred days. But the effects eventually waned, the cancer regrew, and she died of the malignancy.

So far, the trial has included fifty-five patients; more than a third of them have shown a similar response. Cancers of the pancreas, lung, and ovary have been paralyzed for a hundred days or more. Further research has found that targeting the Notch mutation in these three cancers can prompt the
cells to mature and more closely resemble normal tissue cells. I studied microscope images of some of those cancers. Before the anti-Notch therapy, the malignant cells of a pancreatic tumor were primitive and aggressive in appearance, with large nuclei, and multiplying profusely. After treatment, the changes were striking: the cancer cells resembled mature pancreatic tissue.

The Notch blocker “pushed the cells down the differentiation cascade,” John Lewicki, the chief scientist at OncoMed, told me. “What we’ve largely observed in all our pre-clinical work to date is that when you block these pathways you largely get stable disease. To me, that’s not surprising, because we’re not necessarily killing cells.” In recent clinical trials, the Notch blocker has been given to patients in conjunction with chemotherapy. “When you combine these agents, you change the stem cells’ fate,” Lewicki said. “You not only differentiate them but you make them much more susceptible to the impact of chemotherapy.”

This spring, I spoke with Gerald Wildes, a sixty-seven-year-old former truck designer in Tennessee. In November of 2011, he developed pancreatic cancer and underwent surgery; he was also treated with radiation and chemotherapy. About a month later, the cancer showed up in his lungs. Wildes entered the Notch study in combination with chemotherapy.

“The way I understand it, this treatment is supposed to get to the intelligence of the tumor,” Wildes said. “At the time, I was probably the first primate in Tennessee—something above a hog, anyway—to jump into the program.” During his first fifteen months of treatment, he experienced no new growths of cancer, and the tumors in his lungs shrank slightly. Since then, the benefits have faded, but Wildes told me that he was grateful for the quality time he gained.

In October of last year, Usha Malik, a forty-six-year-old homemaker in New York City, learned that she had pancreatic cancer that had spread to her liver. Surgery was not an option. She saw Eileen O’Reilly, a pancreatic-cancer researcher at the Memorial Sloan-Kettering Cancer Center, and O’Reilly got her into the experimental trial.

“It was a tough decision,” Malik told me. “I have a daughter who is twenty-two years old. My husband needs me and my daughter needs me.” Malik received the anti-Notch drug along with standard chemotherapy. The treatment regimen gave her nausea and diarrhea and left her exhausted. But the tumors in her liver nearly disappeared, and the mass in her pancreas became markedly smaller. “I was back driving, trying to do everyday work,” Malik said. The benefit was
sustained for six months, until a CT scan revealed that one of her tumors had grown slightly.

O’Reilly noted that the survival rate for pancreatic-cancer patients like Malik, whose disease has spread to the liver, is typically no more than several months. “Pancreatic cancer is a disease where new approaches are keenly needed,” O’Reilly said. “This experimental drug appears to get at, at least theoretically, one of the fundamental issues of cancer resistance to treatment.” OncoMed is planning to test the Notch-blocking approach by comparing the results of treatment using a combination of standard chemotherapy and the Notch drug with the outcome of treatments based on standard chemotherapy alone.

Cancer does not have one fatal flaw. It advances along many paths, sometimes incrementally, often unpredictably, like the science arrayed against it. Nonetheless, these latest findings offer an unanticipated opportunity for scientists to reëxamine what many of us took for granted: that cancer cells must be destroyed if the patient is to improve. These discoveries could enable researchers to target cancers that were previously beyond treatment. For patients, they offer evidence that it is possible to live longer, and better, with cancer—and they provide hope that scientists are advancing on a cure. ♦

•

•

•

•