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## Chronic Believer

Susan Desmond-Hellmann helped make Genentech a leader in oncology. Now she wants to make cancer livable.

1981-2006

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HBA WOMAN OF THE YEAR

There are people who hope cancer,  
one day, will become  
a manageable disease.  
Then there are those who *know* it.  
Meet Susan Desmond-Hellmann.

# *Chronic Believer*

BY JOANNA BREITSTEIN, EXECUTIVE EDITOR

**T**here's something barbaric about cancer treatment. Doctors cut patients open, slice pieces away, burn people with radiation, and pump them full of harsh chemicals. This modern healing ritual is the best we've come up with. And even for the patients who endure the treatment and survive the disease, they are still left to wonder, "Will it come back? Will I have to go through this again?"

It doesn't have to be that way, or so it seems to a growing number of visionaries. Prominent among them is Andrew von Eschenbach, MD, FDA's acting commissioner, who has been talking about a new era of cancer treatment for years. Back in 2001, when he was tapped to head the National Cancer Institute, he articulated a sweeping vision of how medical progress would transform cancer into a chronic disease—a manageable condition—and how new drugs would make the disease an affliction to be lived with, not to die from.

Von Eschenbach's goal is to reach that point by 2015. That leaves a lot to accomplish in just nine years. Currently, more than six million patients die each year from cancer—some succumb slowly and painfully, while others are swept away with shocking speed. And although von Eschenbach is talking about treating cancer, not curing it, the oncology community on the whole isn't hopeful that his vision will become reality in the next decade.

But Susan Desmond-Hellmann, MD, head of product development at Genentech, is more optimistic than her peers about how cancer care can improve for patients—she even articulated this same vision years before von Eschenbach. "If you'd asked me ten

*Photography by Kenneth Probst*



Genentech's Susan Desmond-Hellmann says she is driven to innovate cancer care in order to create a more livable disease for patients.



years ago to predict how far we'd come by 2005, I may have underestimated," says Desmond-Hellmann. "While some people are uncomfortable calling cancer a chronic disease, I do appreciate the notion. Perhaps one day, a patient who's been diagnosed with cancer could feel like they do when they talk to their doctor about high blood pressure or diabetes, or other illnesses that are difficult, but treatable. Cancer won't feel or sound like a death sentence."

Certainly, Desmond-Hellman has played a pivotal role in hastening that day by bringing some of the most promising and innovative oncology drugs to market: Rituxan (rituximab), the first drug to use monoclonal antibodies, which works by attacking specific types of cancer cells; Herceptin (trastuzumab), which opened the doorway to personalized medicine by targeting the

**"One day, patients who've been diagnosed with cancer could feel like they do when they talk to their doctors about high blood pressure or diabetes, illnesses that are difficult, but treatable."**

HER2 gene, which defined a specific subtype of breast cancer; and Avastin (bevacizumab), the first angiogenesis inhibitor to stop tumors by preventing the formation of new blood vessels.

In 2005, Genentech had total product sales of \$5.5 billion. A substantial portion of that, thanks to Desmond-Hellman's contributions, came from oncology. But if you ask her, a woman who describes herself as a simple Catholic girl who spends weekends skiing and cycling with her husband, she'll say she's just trying to help cancer patients lead livable lives. This focus on patient benefit sets the tone for drug development at Genentech, which, in turn, is setting an industry-wide agenda for oncology therapeutics. (See "Following Science," *Pharm Exec*, October 2005.)

"As a physician who has been engaged in the care of human beings, not just rats or yeast or cells, her greatest contribution may be bringing the eyes of a true clinician to a major biotech company," says David Johnson, MD, who heads the cancer unit at Vanderbilt University and is a former president of the American Society of Clinical Oncology (ASCO). "She understands at a core level what disease is."

Susan Desmond-Hellmann is not a secret. The *Wall Street Journal* ranked her sixth of its "50 Women to Watch" in 2005, and *Fortune* magazine included her among the "50 Most Powerful Women" for the fourth time. Most recently, the Healthcare Businesswomen's Association (HBA) bestowed another recognition on Desmond-Hellmann, naming her its 2006 "Woman of the Year."

"Sue has made an amazing impact in her corporate role at Genentech and, at the same time, remains dedicated to patient care, a critical combination in today's healthcare environment," says Debra Newton, president of HBA and the Newton Grey agency. "Her colleagues credit her with making the world a better place to live."

Even as Desmond-Hellmann's work advances a new model of cancer treatment, it also charts the rapid evolution of pharma companies and shows that what's good for patients can be good for business. Under her leadership, a new vision—and practice—of cancer as a chronic disease has begun to emerge.

### Always Wanted to Be a Doctor

Desmond-Hellmann didn't set out to be an oncologist. But, growing up in Reno, Nevada, she did know she wanted to be a doctor. Her father co-owned the local Keystone Owl Rexall drugstore, and her mother was an English teacher. Desmond-Hellmann and her six siblings were brought up to value education. "There was a lot of emphasis on being a good student, on studying, and discussion about science and about medicine," she says. "When I was growing up, I was very much the nerdy student. I admired people who were smart."

Working as a bookkeeper at the pharmacy, she listened to her father talk with patients about their illnesses. She and her brothers and sisters were also inspired by their physician and family friend, Dr. Smirnoff. (Today, he's 101.) The early influences took root. Four of the seven children now work in health or science.

All the Desmond kids went to the University of Nevada, Reno, because it was inexpensive and let them save money by living at home. After graduating as valedictorian of her high school class and blasting through college in three years, Susan Desmond enrolled in the university's medical school in 1978.

She planned to work in sports medicine, but something clicked the first time she went to the cancer wards of the Veterans Administration Hospital. "My first rotation was with an oncologist, Dr. Stephen Hall," she recalls. "He was such a good doctor—and the patients had such difficult medical problems. It was just a one-month rotation, but it was the first time I was in the hospital as a medical student, and I was inspired to try to do something. After that, I switched to focusing more on internal medicine, and then oncology."

By 1982, she had begun an oncology residency at the University of California, San Francisco, where she met her husband, Nicholas Hellmann, a fellow resident who was treating patients in the new and terrifying AIDS epidemic. She took a master's in public health at Berkeley, doing a research project on the epidemiology of patients with Kaposi's sar-

#### HBA WOMAN OF THE YEAR

The Healthcare Businesswomen's Association is dedicated to advancing women in the healthcare industry. Each year, the group honors a woman who they believe exemplifies strong leadership capabilities, has proven mentoring skills, and has made substantial contributions to the community at large.

#### PAST HBA WOMAN OF THE YEAR RECIPIENTS

SOURCE: HBA Website

**2005**  
**Lynn O'Connor Vos**  
President & CEO  
Grey Healthcare Group

**2004**  
**Christine Poon**  
Worldwide Chairman,  
Medicines &  
Nutritionals  
Johnson & Johnson

**2003**  
**Catherine Angell  
Sohn, PharmD**  
VP Worldwide Business  
Development  
GSK Consumer  
Healthcare

**2002**  
**Sarah S. Harrison**  
Vice President,  
Customer Strategy  
Integration  
AstraZeneca

coma, a disease that sits at the intersection of AIDS and cancer. In 1991, the Rockefeller Foundation invited the couple to conduct AIDS research and teach at Makerere University in Kampala, Uganda.

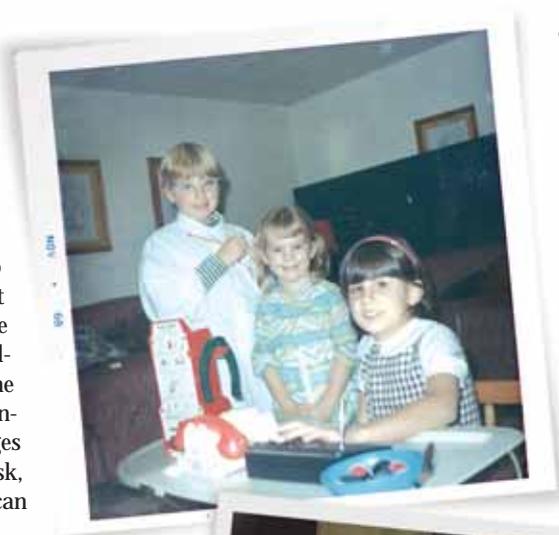
“Taking care of patients in the beginning of the epidemic, I felt so overwhelmed with the sense that young people were dying and there was so little to do,” says Desmond-Hellmann, who watched medicine transform AIDS into a chronic manageable condition. “That challenges us working in other fields to ask, ‘How could it work for us? How can we have the kind of molecular breakthroughs that were seen in HIV?’”

The couple returned to the United States in 1993 as changed people, and settled into private practice in Lexington, Kentucky, where Nicholas grew up. Desmond-Hellmann was working in a two-person oncology practice, and her husband was one of the few doctors that treated AIDS patients in the region.

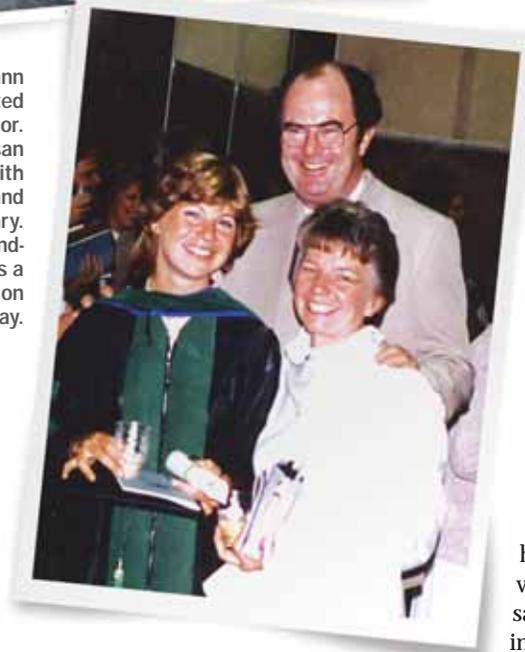
“It was a difficult time,” says Desmond-Hellmann. “There weren’t as many therapies to treat patients with HIV and AIDS. My husband and I would commiserate about the conversations that no physician wants to have with a patient—about their impending demise or their suffering or their pain.” She pauses. “Fifteen years later, oncologists still have those conversations.”

Within a few years, Desmond-Hellmann was ready to try something new. It was hard to keep working when so many conversations with patients ended, she remembers, with “I’m sorry, we don’t have anything else to try.”

So when Bristol-Myers Squibb called her husband in 1993 to work in its HIV division, she went along and became the project team leader of Taxol (paclitaxel). Her mother, Jennie, would later take the drug in her successful battle against breast



Desmond-Hellmann knew she wanted to be a doctor. (Top) Young Susan plays the part, with sister Theresa and cousin Mary. (Right) Desmond-Hellmann, always a top student, on graduation day.



cancer. Taxol became one of the biggest chemotherapy drugs ever developed for cancer. But even a blockbuster success could not quiet her misgivings about traditional chemotherapy.

### Vision Finds a Home

“What’s exciting to me about the future of cancer therapy is that some of the most feared side effects—hair loss, nausea and vomiting, bone marrow suppression—aren’t part of the new targeted therapies,” says Desmond-Hellmann. “That’s good for patients.”

It was a project related to side effects that brought Desmond-Hellmann to Genentech. It was 1995, and researchers at the company had just identified thrombopoietin as a key mediator in making platelets. The drug had an obvious potential use in cancer—treating chemotherapy-induced anemia. But Genentech had a series of disappointments over oncology drugs in the clinic, and was still very much focused on cardiovascular and growth hormone drugs.

“At the time, Genentech had no presence in oncology whatsoever and wasn’t necessarily guaranteed to make inroads,” says John Park, MD, who spent time as a visiting scientist at Genentech, but

is currently an associate professor of medicine at the University of California at San Francisco, where Desmond-Hellmann still teaches epidemiology and statistics.

Just a few months after Desmond-Hellmann arrived, Arthur Levinson replaced Kirk Raab as CEO. Levinson, who had worked on the early research that would lead to understanding HER2 and launching Herceptin, reinvigorated the oncology program. He invested 50 percent of revenues into R&D, promoted

#### PAST HBA WOMAN OF THE YEAR RECIPIENTS

##### 2001

**Carrie S. Cox**  
EVP, President of  
Global Prescription  
Business  
Pharmacia

##### 2000

**Myrtle Potter**  
President, US  
Cardiovascular/  
Metabolic  
Bristol-Myers Squibb

##### 1999

**Tamar Howson**  
SVP and Director,  
Worldwide Business  
and Corporate  
Development  
SmithKline Beecham

##### 1998

**Kathy Giusti**  
Former Executive  
Director, Searle;  
Founder and President,  
Multiple Myeloma  
Research Foundation

##### 1997

**Maureen Regan**  
CEO  
Regan Campbell Ward

##### 1996

**Lynn Gaudioso**  
VP, Business  
Development,  
Consumer Health Care  
Pfizer

Desmond-Hellmann to vice president of medical affairs, and less than two years later, to chief medical officer.

“When she became head of clinical affairs, the company kicked it up a notch further and made a full-court press toward oncology,” says Park. “She really oriented the company toward thinking about the best ways to develop new drugs for oncology, and in some cases, somewhat creative ways.”

## Upholding Standards

For a practitioner of some of the world’s most complex science, Genentech’s Susan Desmond-Hellmann has a remarkably straightforward philosophy toward drug development: “R&D is just a matter of asking and answering questions,” she says. “When you do, great things can happen.”

Certainly, you need those questions and answers to find new cures for cancer. But Desmond-Hellmann’s contribution has been to link the newest science with the most rigorous drug development.

“There are very few people who are translational,” says David Johnson, who heads the cancer clinic at Vanderbilt University. “The bench scientists wouldn’t know a patient if they sat on them. On the other hand, very often clinicians don’t understand the basic science. What you want is a world made up of people who do basic research that has clinic applicability and can compress the timeline from discovery to development.”

Desmond-Hellmann has been able to straddle the R&D world and is now looking to biomarkers and diagnostics to help speed drugs through the pipeline. However, at times, the head of Genentech’s product development has had to choose between better, slower science that wouldn’t move the needle on revenue and faster clinical trials that beat out the competition. She let patient benefit be her guide—which in turn, was the right guide for Genentech.

“AstraZeneca raced to the finish with Iressa [gefitinib], but Genetech sauntered to the finish line with Tarceva,” Johnson says. “I personally believe the drugs are virtually identical. But Sue’s team did it in the best possible way—she sought out the right people to work with and then stuck to her guns while her detractors went on.” The careful clinical trials paid off: Since June 2005, FDA has limited access to AstraZeneca’s Iressa, citing too few non-small cell lung cancer patients that have responded to the therapy. Instead, FDA suggests, physicians should think about prescribing Tarceva.

Desmond-Hellmann arrived at Genentech at a time when the company was just realizing the power of its own pipeline drugs. It had recently licensed Rituxan from IDEC, and the clinicians expected the drug to be modestly effective, but extremely safe. But the tumors in the first patient treated with Rituxan broke down so fast—it was that effective—that the body could not handle the toxic effects. “The patient’s kidneys were threatened,” she says. “The patient had medical difficulty as a result of this tumor lysis syndrome.”

Herceptin challenged researchers for another reason. Preclinical testing indicated that the drug only worked in one

quarter of the patients, but it appeared to be extremely effective for that small group. What the scientists needed to understand was the genetic difference between the 25 percent of tissues that responded and the remainder that did not. Genentech found that the drug was effective in the presence of the HER2 gene. When the scientists developed a diagnostic test to identify patients with this gene, they were ready for the clinic. Without the diagnostic, the drug would have been effective in just one in four patients and would have failed by traditional standards.

In this way, instead of becoming another abandoned compound, Herceptin opened the door to a new era of personalized medicine. “She created what some people perceived to be almost impossible studies by targeting the drug against a very defined breast cancer population,” says Johnson. “There was a lot of skepticism: If the study, one, could be done and, two, was necessary. Not only did they demonstrate it, but they did so with remarkable outcomes.”

Desmond-Hellmann herself was inspired by what she learned from Herceptin. “It teaches you that the marker, HER2—which is kind of like a competitive advantage for the tumor—can be identified and then turned into a treatment target. That the very asset of the cancer turns into its Achilles’ heel,” she explains.

Herceptin was a major development when it launched, but it started to look even bigger this past year, when Genentech presented new clinical results at the ASCO meeting. Herceptin was

given to women with early-stage HER2-positive breast cancer in addition to standard adjuvant therapy following surgery—chemotherapy, hormone therapy, or both—the risk of cancer recurrence was cut in half.

“It showed that we have the opportunity to treat patients and have their cancer never come back,” she says. “That’s what we ought to be doing.” Desmond-Hellmann also notes that breakthroughs like this—which keep cancer in remission longer—edge medical professionals toward managing cancer as a chronic disease.

“Now that Herceptin has shown its usefulness in that setting,

### PAST HBA WOMAN OF THE YEAR RECIPIENTS

**1995**

**Carol A. Webb**  
President  
Ortho Biotech

**1994**

**Carolyn Koestenblatt**  
Former Vice President  
Novartis

**1993**

**Carolyn Glynn**  
Vice President,  
Public Policy and  
Communications  
Hoffmann-La Roche

**1992**

**Joan Keith**  
Former Vice President,  
CV Strategic Business  
Planning Worldwide  
Bristol-Myers Squibb

**1991**

**Jane Townsend**  
Co-founder  
Gross Townsend Frank  
Hoffman

**1990**

**Karen Katen**  
President,  
US Pharmaceuticals  
Pfizer



stock fell 10 percent in one day.

Desmond-Hellmann remembers the year as a time when she questioned what she was doing. Shareholders complained. Her clinical trials budget was threatened. And the company as a whole understood the risk of losing Avastin.

“Some of your most important lessons come from adversity,” she says. “When the Avastin breast cancer study was negative, there was a lot of criticism about the amount of money we had invested, about what we were thinking. It provided me with a opportunity to reflect on what we intended to do.”

To get through those stressful times, says Desmond-Hellmann, “You have to have a lot of confidence in the integrity of the company. That’s your anchor and your compass.” To contend with pressures—like high prices and clinical setbacks—she says she has “to be at a company that has good values, and wants to do good things for patients.”

Desmond-Hellmann remained a realist. She didn’t expect Avastin to work in all tumor types, but she was confident about anti-angiogenesis because of the positive data generated in the pre-clinical work. The investigators on the study told her they still believed in the drug as well—but they thought they were treating the patients too late.

we are talking about eradicating breast cancers, not just controlling them,” says Park.

### Staying the Course

Of course, product development is never a sure thing. Over and over, promising molecules prove ineffective, or unexpected dangers crop up in late-stage trials. For most pharma people, the hopeless mantra of “fail earlier” is about the best they can hope for. What’s admirable about Desmond-Hellmann is her seemingly instinctive ability to know when to ignore that advice, and take risks.

“I would bet that instincts are just a form of data,” says Hal Barron, chief medical officer of Genentech. “She always follows the data.”

When Desmond-Hellman was chief medical officer, back in 1997, Genentech began clinical trials of Avastin. Researcher Napoleone Ferrara had demonstrated that an antibody directed at the vascular-endothelial growth factor (VEGF), the key regulator in angiogenesis, could slow tumor growth in pre-clinical models. Angiogenesis—the process of creating new blood vessels—is an important part of how tumors grow. So scientists hoped the drug would have wide application.

Genentech bet heavily on Avastin. But in September 2002, when the company had already invested more than \$100 million in the drug, bad news hit hard: The Phase III results of Avastin in late-stage breast cancer came back negative. The

Desmond-Hellman arrived at Genentech at a time when the company was just realizing the power of its own pipeline drugs. Ten years later, in 2005, Genentech posted \$5.5 billion in revenue.

“It reinforced for me the importance of working in a place where you really respect your colleagues, and you’re very data driven,” says Desmond-Hellmann. “It also showed the power of listening, and getting input when something goes differently than you wanted.”

Desmond-Hellmann continued to roll out the studies. Finally, six years after clinical trials on Avastin commenced, in May 2003, the long-awaited colon-cancer data was announced. Avastin not only slowed tumor growth, but it also helped colon-cancer patients live longer—an endpoint Desmond-Hellmann introduced to showcase the drug’s effectiveness.

Desmond-Hellmann remembers the group assembled to enjoy that success. “There were ten of us or more in the room—Art [Levinson] even called Napo Ferrara in Italy in the middle of the night to tell him that the trial had been successful,” she recalls. “For me, there was this sense that something important was going to happen for patients, and that I was part of this team that was so talented, with different people doing very different things to contribute.”

The clinical studies validated the strategy of angiogenesis, and in doing so, helped cement the future of Avastin and Genentech. The stock did more than just jump at the news—it climbed 45 percent that day. Some analysts say Avastin is now set to be the best-selling cancer drug of all time.

The cancer community has made it clear how highly it values the drug and Desmond-Hellmann's role in bringing it to market. In 2005, she was elected as the first industry representative in more than 20 years to sit on the board of directors of the American Association of Cancer Research. Margaret Foti, president of the association, compares Avastin to another ground-breaking drug: "When we look at Gleevec [imatinib], one has to recognize that it would not be on the street without the sheer determination of Alex Matter [the scientist who led the Gleevec effort at Novartis], who kept that drug in the forefront of the minds of the people in the company. Susan did the same thing for Avastin."

### Tomorrow's Vision, Today

Desmond-Hellmann is proud of the progress targeted therapies have made. People who might have suffered horribly during radiation or chemotherapy endure fewer side effects with therapies she has pioneered. But even as she and her colleagues lead the industry toward new indications for antiangiogenics and other drugs, Desmond-Hellmann is still not satisfied.

"There was an important moment in drug development for HIV/AIDS when people started to use viral load as a surrogate measure for good outcome in patients with HIV infection," she says. "A dream that I have had for a long time is that we would have in oncology an excellent surrogate marker—simple blood tests that could help us understand very quickly, not just if this is the right patient for this therapy, but is it working? That would be a huge thing for oncology, and really change the pace with which we could discover and develop new drugs."

Desmond-Hellmann still looks back to her husband's early experiences in the AIDS clinic. "What I thought was most inspiring was the pace with which new therapies were coming forward with HIV," she remembers. "What was once a death sentence was changed to a chronic disease. I found it both challenging to see him and his colleagues deal with the HIV/AIDS epidemic, but then inspiring the kinds of scientific breakthroughs that happened."

For Desmond-Hellmann, this provides a natural link to her vision for cancer. "From the time the HER2 gene was identified, to the adjuvant therapy was 20 years," she says. "We should challenge ourselves to say, 'What would the world look like if we could do that in 10 or 15 years?'"

To pick up the pace of development, Desmond-Hellmann wants her employees to keep taking risks. Richard Scheller, executive vice president of research, shares her view: "We've

been so successful, and Sue has been so successful, over the last years, that one could imagine that you would pull back a little and become conservative for fear of failing," he says. "Sue says you go forward with the knowledge that not everything is going to work, but that you're never going to make huge strides forward without taking risk. For me, that meant not to be afraid to put forward molecules in the development portfolio

**Clinical studies initiated by Desmond-Hellman helped cement the future of Avastin—and Genentech. Some analysts say Avastin is set to be the best-selling cancer drug of all time.**

lio that have totally new mechanisms of action that we don't know if they'll end up working in the clinic yet."

Second only to her focus on patients, Desmond-Hellmann is devoted to pure research. "I always tell drug developers who ask me for advice, if you love drug development, look at the research. All good that happens in drug development comes from great molecules. These are the researchers' babies, and they look to us to guide them through the trials. It all starts with research, and that's been the great gift at Genentech—having these scientifically-driven molecules and making them into drugs."

Desmond-Hellmann still keeps the focus on patients, even as she turns her attention increasingly to hiring, mentoring, and thinking about how to create the best work environment at Genentech. The company is growing quickly, not least because it has won a reputation as a wonderful workplace. For eight consecutive years Genentech has appeared on *Fortune* magazine's list of the best companies to work for—and in 2006, it took the number one slot. But Desmond-Hellmann will continue to push the next generation of leaders to remain true to the ideals that she helped establish.

"No one person at Genentech really does as much as Sue has done to ensure the culture is focused on doing what's best for patients," says Barron. "When someone has a singular focus like that, it's a call to action for the entire company. Once everybody in the culture adopts that focus, it becomes part of Genentech."

Hal Barron thinks Desmond-Hellmann's influence is broader than she knows.

"Go down ten levels below her and ask somebody why they are at Genentech, there's a good chance they will say, 'I'm here because I think I can make the biggest difference to patients.' They might not ascribe that to her; they might not necessarily even have ever met her; but I think that the entire workforce comes here and stays here because of that belief." ❁

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