

DURECT Results

With more than 30 years
experience in developing innovative
drug-delivery technologies,

Dr. Felix Theeuwes as
chairman and chief scientific

officer of Durect, is directing
the start-up company

with the goal of
commercializing

pharmaceutical systems that

deliver the right drug to
the right place in the right
amount at the right time.



BY KIM RIBBINK

Photos: Scott Lewis
Courtesy: Studioslp.com

THERE ARE CERTAIN CHARACTER TRAITS THAT ALL GOOD SCIENTISTS HAVE — vision, patience, and a methodical dedication to the principles and theories that surround discovery. For a scientist in the pharmaceutical field, those core values and abilities become even more critical if the goal of taking a discovery to the market is to be realized.

“Scientists need to have the ability to forecast certain outcomes,” says Felix Theeuwes, D.Sc., chairman and chief scientific officer of Durect. “Practicing science means being able to predict the future. As a scientist in the drug-discovery business, it is important that I combine knowledge with foresight to ensure that the company is working toward an outcome that is realistic, that is timely, and that is affordable.”

Time and time again, Dr. Theeuwes has proven that he has the vision, the knowledge, and the determination to turn theoretical formulas into tried-and-true products. His successes at Alza Corp., where he began his pharmaceutical career, and now at Durect speak for themselves — from the development of the Alzet mini osmotic pump to laying the groundwork for many of Alza’s most enduring drug-delivery programs. He is continuing along that focused path at Durect, leading the company in its goal of developing pharmaceutical systems and products to treat chronic debilitating diseases and enabling biotechnology drugs.

For Durect, pharmaceutical systems products are defining a new industry at the convergence of the biotechnology, pharmaceutical, and medical-device industries. While the pharmaceutical, biotechnology, drug-delivery, and medical-device industries have increased overall life expectancy and improved patient quality of life, many chronic debilitating diseases continue to be inadequately treated with current drugs or medical devices.

Because of its strong technological foundation and the unique pharmaceutical systems approach to delivering a drug in the right amount to the right place at the right time, Durect is positioned to capitalize on the advancements currently being made and address challenging problems in the health-care industry.



“This flexibility allows us to work with a variety of drug candidates including small molecules, proteins, peptides, or genes,” Dr. Theeuwes says. “I have tried to build an organization that is based on good science, on transparency, and on limiting bureaucracy to ensure efficiency.”

A NEW BEGINNING

In July of 1998 Durect was spun out from Alza Corp., which was founded in 1968 by Dr. Alejandro Zaffaroni, who had the vision that medicine could be improved through delivery technology that would culminate in enabling a precise amount of drug to be delivered to the right site at the right time.

Dr. Theeuwes, Tom Schreck, and James Brown, D.V.M., with guidance from Dr. Zaffaroni, founded Durect following the successful completion of a technology licensing agreement with Alza. Under the license agreement, Alza granted Durect exclusive, worldwide rights, including patents, trade secrets, and know-how, to develop and commercialize products based on Alza’s Duros technology in the fields of: the delivery of drugs by catheter to the central nervous system to treat selected central nervous disorders, the delivery of drugs by catheter to the middle and inner ear, the delivery of drugs by catheter into the pericardial sac of the heart, the delivery of selected drugs by catheter into vascular grafts, and the delivery of selected cancer antigens for cancer immunotherapy.

Alza successfully developed technologies that facilitated precise and time-controlled

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believe in teaching by example. I like to make sure that the issues that are at hand are objectively discussed and can be debated. I try to instill in people a belief in the work so that they take ownership of their work and feel able to make a contribution.

drug delivery, which are now widely used in many pharmaceutical products, including Procardia XL, Transderm-Nitro, and NicoDerm CQ. In June 2001, a wholly owned Johnson & Johnson subsidiary was merged with and into Alza, which retained its name and survives as a direct, wholly owned subsidiary of J&J.

Dr. Theeuwes joined Dr. Zaffaroni at Alza in 1970 where he remained until June 1999 directing research, technology development,



and product development for a variety of controlled drug-delivery systems. His work led to the product introduction of the Alzet mini osmotic pump series for animal research, and the Oros systems series of products. He directed research in transdermal research and development, initiated the electrotransport/iontophoresis program, as well as the Duros osmotic implant program. Dr. Theeuwes holds more than 210 U.S. patents covering these systems and has published more than 80 articles and book chapters.

There were some difficult years for Alza, including a period where the company faced bankruptcy before being rescued by Ciba-Geigy and injected with funding of \$43 million. Nevertheless, Dr. Theeuwes foresaw the long-term significance of Alza's drug-delivery programs.

"Even though the company did not do well for a long time and I had many opportunities to go to academia or other places, I stayed because the dream of drug delivery had not been realized," he says. "Alza's technologies were the best in the world. I continued to work to develop those into products because I knew someday that these were going to be very important both from a technical and business point of view."

AMERICAN CONNECTION

Dr. Theeuwes' successes at Alza might never have been realized were it not for a letter from a professor at the University of Kansas and a chance meeting with another highly regarded scientist.

As a scientist in the drug-discovery business, it is important that **I combine knowledge with foresight** to ensure that the company is working toward an outcome that is realistic, that is timely, and that is affordable.

While working as a research fellow at CERN in Geneva and completing his doctorate in physics through the University of Leuven in Belgium an opportunity to work in the U.S. presented itself. Richard Bearman, a professor of statistical mechanics at the University of Kansas, wrote to a professor at Leuven, inquiring if he knew of anybody with the experimental capability to prove out the theories that he was developing on models to describe ideal fluids.

The professor recommended Dr. Theeuwes. The move to the U.S. was, Dr. Theeuwes says, a real eye-opener in the best possible sense.

"While in graduate school in Belgium, we had to think ahead because it took a long time for equipment to arrive, and to get anything done," he says. "So we spent a lot of time

working through theoretical problems. When I arrived at the University of Kansas, I made a list of equipment that I wanted to have and presented the list to the director of laboratories, Jack Rose. He replied, 'would you like to have them tomorrow or this afternoon?' I was totally flabbergasted by that quick turnaround capability."

Dr. Theeuwes spent four years at the University of Kansas, first as a post-doctoral fellow, then as a visiting assistant professor under Professor Bearman, developing equipment, and measuring the thermodynamic properties of two noble gasses — liquid krypton and xenon — as well as thermal conductivities of saline solutions.

Dr. Theeuwes was the first person to measure the thermodynamic properties of liquid krypton and xenon.

While Dr. Theeuwes describes the work as mental gymnastics having only theoretical, or academic interest, with no link to product outcome, his achievements caught the eye of a prominent scientist.

"I had the good fortune to meet Takeru Higuchi, who was as Dr. Bearman said, the best applied thermodynamicist of his generation," Dr. Theeuwes says. "He was a physical organic chemist who had gone to the field of pharmacy to make the art of pharmacy a science, and he's called by many the father of physical pharmacy. I met him at a social function in 1970 and during our conversation he said I should join this nascent company called Alza. I told him that I knew nothing about drugs, but he replied that the research was not about drugs, rather it was about thermodynamics."

And so Dr. Theeuwes was persuaded to join Alza's Institute of Pharmaceutical Chemistry in Lawrence, Kan., under the direction of Mr. Higuchi, who was the founding chair of the Department of Pharmaceutical Chemistry at Kansas University.

"At the time I made the switch to the pharmaceutical industry people believed that in academia one did very elegant work on irrelevant problems and that in the pharma industry one did very relevant work but fairly superficially," he explains. "But I found out that in fact it is possible to do very relevant work in a very fundamental way, so that was why I switched."

What attracted him to, and kept him at Alza was the company's approach to enhancing the value of therapeutic compounds by optimizing their delivery into and within the body.

"Alza was founded with the goal to revolutionize the business of drug development by using new techniques of drug delivery," Dr. Theeuwes says. "Alza founder Dr. Zaffaroni and Tak Higuchi both envisioned that what was needed was to find a fresh approach to drug development. Alex gave us the mission of where to go, and Tak really set out the method to achieve it."

Alza's goals were firmly rooted in science, and what Dr. Theeuwes brought to the table was a deep understanding of theory, combined with a dedication to the discipline of science, which had been drummed into him during his schooling and university years in Europe.

"I had the good fortune of having terrific high school teachers in math and science," he says. "They taught us the beauty of mathematical solutions and the elegance of science — and how the world hangs together."

"In Europe at that time, a lot of emphasis was placed on theoretical aspects and on the finer and deeper understanding of how the world works, and how different subjects correlated and inter-related," Dr. Theeuwes says. "Computers were not readily available, so in science and mathematics the focus was on forming elegant analytical solutions to problems that could then be used to try to predict future events."

In addition, Dr. Theeuwes spent several years early in his career teaching physics, mathematics, chemistry, and biology to high school students in Belgium. That experience, he says, helped ground his understanding of the subjects and how to put that knowledge into practice.

"They say in order to know a subject one must see one, do one, teach one," he says. "Teaching helped me understand how to convey the message and offer explanations by building a correlation rather than just offering anecdotal information. Building a correlation to previous materials helps not only in the teaching process, but also in research and development."

Dr. Theeuwes credits his parents with instilling in him a thirst for knowledge, the determination to succeed, and an understanding that he would need to work to overcome obstacles.

"My parents lived through two world wars, and people who have lived through those experiences are tempted to give their children a dose of reality and conservatism," he says. "My mother was very supportive, and believed that her children could achieve anything we put our minds to. And my father was the sort of person who believed it was important to do something relevant, something that would

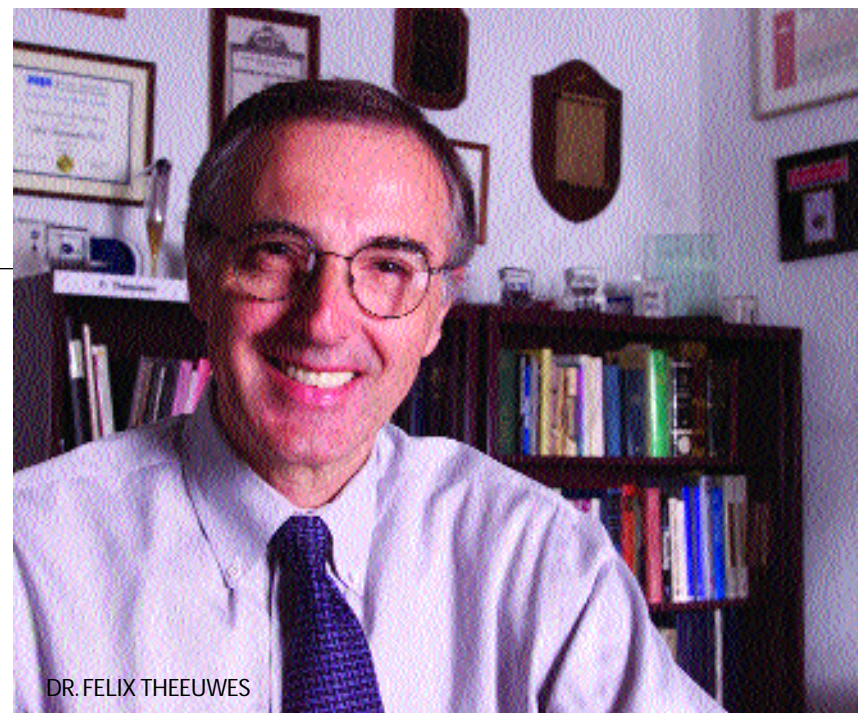
make a difference. They also believed very strongly in education as a way to further our prospects."

A LEGACY OF ACHIEVEMENT

Dr. Theeuwes' findings have attracted attention, earning him several awards and distinctions for his scientific achievements. He is particularly proud of two of these honors.

"I was the Inventor of the Year in Silicon Valley in 1980, and that's obviously a prestigious award in an area where so much relevant and so much important work is being done," he says. "That award was for the establishment of osmotic therapeutic systems technology at Alza. The second award that I am proud of is the Founders Award I received from Alza, which was put in place to emphasize the successes of the company's technology and products. I received the first of those awards in recognition for the contribution I made to the company's scientific foundations."

Dr. Theeuwes' achievements at Alza have



DR. FELIX THEEUWES

Making a Durect Connection

IN AN EXCLUSIVE INTERVIEW WITH PHARMAVOICE, FELIX THEEUWES, D.SC., CHAIRMAN AND CHIEF SCIENTIFIC OFFICER AT DURECT, DISCUSSES THE ALZA SPIN OFF'S BEGINNINGS, ITS GOALS, AND ITS PIPELINE.

WHAT LED TO THE FORMATION OF DURECT?

In the late 1980s, the Alza management team collectively decided that we were going to be commercially more important and successful if we were to develop our own products. We had set up partnerships, or balance-sheet financing mechanisms, including TDC (Therapeutic Discovery Corp.) and Crescendo, to fund the work for about \$750 million. This meant that we could not afford to spend extra money for research. In the meantime, I had hired Jim Brown from Syntex to lead the development of the Duros system, which led to the commercialization of the first product called Viadur (leuprolide acetate implant) to treat the symptoms of advanced prostate cancer. (Viadur is marketed by Bayer Corp.)

We met up with Tom Schreck, who eventually became Durect's third co-founder, and we talked about applications of site-specific drug delivery using the Duros technology. We tried to get these things done in Alza and to become an entrepreneurial activity, but we couldn't do it from within since the stock value and the value of the com-

pany would have been too depressed. So we had to find new monies and new investors and create new ownership, and we then reached an agreement with Alza to spin out these discoveries, and we founded Durect.

WHAT IS IN THE PIPELINE AT DURECT?

We started out with a license from Alza for the Duros technology, which is a miniature drug-dispensing pump that releases minute quan-

been numerous and have contributed greatly to the company's success.

"I started at Alza in 1970 when the company was a bag of money and a good idea, but there was no technology, and I set out to develop osmotic systems," he explains. "I invented and developed the Alzet mini osmotic pump, the elementary osmotic pump, and the push-pull system technologies, which are the basis for the oral drug -delivery business of Alza. That was my most important contribution to the company."

Among the scientist's other achievements were initiating the program to develop the Duros system — a miniature drug-dispensing pump that releases minute quantities of concentrated drug formulations in a consistent flow over months or years using an osmotic engine, which was the starting point for Durect.

LASTING IMPRESSIONS

Having spent more than 30 years at Alza, and now at the spin-off company Durect, Dr. Theeuwes understandably has had quite an impact on the way the companies conduct and organize business.

"As a manager, I see an organization as a pipeline through which work flows, and I like to build a pipeline that works, that has a minimal number of obstacles, that is simple, that is transparent," he says.

Dr. Theeuwes was the **Inventor of the Year** in Silicon Valley in 1980, which he calls a prestigious award in an area where so much relevant and important work is being done.

Part of ensuring that those goals are achieved is to create a work environment in which everyone is able to make a contribution and has an opportunity to succeed. To encourage others to reach their potential, Dr. Theeuwes tries to set an example with his own work ethics.

"People are inspired by example, so I believe in teaching by example," he says. "I like to make sure that the issues that are at hand are objectively discussed and can be debated. I try to instill in people a belief in the work so that they take ownership of their work and feel able to make a contribution."

Many of the lessons Dr. Theeuwes is now passing onto young scientists and others at the company are those he learned from his mentors — his parents, Mr. Higuchi, Professor

Bearman, and others. "I have tried to learn from all my mentors, and to pass on the concepts and habits I learned from them," he says. "I try to steer people in the right direction, to correct habits, because in the long run habits that people have and the discipline that they bring to their job are extremely important."

CYCLE OF DISCOVERY

"Our goal is to develop pharmaceutical systems that have the potential to be a more convenient, patient-friendly product that may provide an alternative to current therapies for long-term treatment of various chronic conditions," Dr. Theeuwes says. "The distinct advantage to the patient and the physician is convenience and control, respectively. The patient receives a continuous dose and does not have to worry about taking pills, receiving injections, or changing patches. The physician has the added assurance that the patient is getting the right dose of medicine and does not have to worry about the possibility of a lost prescription or non-compliance."

For a person to inspire others they need to be inspired themselves, and Dr. Theeuwes finds plenty to be excited about with regard to the possibilities of drug-development technology.

He believes there is nothing more fulfilling than taking a drug from an intention to the marketplace, and to witness the contributions to patient well-being. He offers a couple of examples of how research at Alza has had an

tities of concentrated drug formulations in a continuous, consistent flow over months or years using an osmotic engine. We have built that up also to include Duros delivery to site-specific areas with a catheter attachment. Our most advanced product in that series is the Chronogestic Pain Therapy System, which combines the Duros technology with a proprietary formulation of sufentanil, a potent opioid currently used in hospitals as an anesthetic. The system, which delivers sufentanil over a three-month period, is entering Phase III in the middle of this year. We also added technologies from a company called Southern Biosystems Inc., which we acquired in 2001. With that acquisition, Durect gained broad capabilities with three platform technologies: Saber erodable depot injectables, Durin erodable implant technology, and Microdur injectable microcapsule technology. (See related box on pages 60 and 61 for more details.)

WHAT ARE DURECT'S LONG-TERM GOALS?

We founded Durect with the focus on the high-end added value of drug delivery, which is to help treat chronic debilitating diseases. If all medicine in the U.S. was given away free of charge, the savings in healthcare costs would be less than 10%, since the majority of healthcare costs reside with long-term hospital care and in geriatric institu-

tions. Furthermore, people suffering from debilitating conditions have a poor quality of life.

Our aim at Durect is to combine devices with drugs to create pharmaceutical systems that are ambulatory. In other words, patients can walk away with the product and lead a normal, independent life. Not only does that give the patient a high quality of life, it also saves a lot of the cost to society.

In addition, we are focusing on enabling biotechnology molecules to reach the marketplace, because many of those will only be laboratory curiosities unless they can be developed to target the part of the body where they are required and at dosage levels where they can have an impact.

WHAT ROLE DO YOU EXPECT TO PLAY IN ADVANCING THESE TECHNOLOGIES?

Firstly, my goal is to define the mission as well as the technical approach of the company. Through experience, I have seen many dead ends, so I am working to keep people away from areas where there are potential failures. That's where experience pays off. As the chairman of the company, I am focused on the strategy, the objectives, and am working with the board's input to make this a successful company.

impact both on people's lives and on bottom-line results.

"While doing research with Pfizer, we started working with nifedipine (Procardia XL), which at the time was used only for the treatment of angina," he says. "We developed that product as a treatment for both angina and hypertension and by doing so we expanded the market for that substance from \$200 million to \$1.4 billion. We also expanded the

benefits of the product, by allowing people to take the medicine once a day."

While at Alza, Dr. Theeuwes was instrumental in developing several other proprietary drug-delivery technologies that expanded the use of established compounds, such as fentanyl, which is marketed as Duragesic by Janssen Pharmaceutica, a J&J company. Duragesic is a transdermal patch system approved for treating chronic pain.

"When we began our research, there was a product called fentanyl, which was a hospital-room anesthetic only used in a very controlled setting by an anesthesiologist, and which generated about \$35 million a year," Dr. Theeuwes explains. "By developing fentanyl as a transdermal patch that allowed a patient to be mobile and pain-free for three days at a time, it became an \$800 million product."

Dr. Theeuwes and his team at Durect are expanding on this technology with the Chronogesic Pain Therapy System, which incorporates sufentanil, an opioid that is currently used in hospitals as an analgesic.

"We are taking sufentanil, which is a hospital-room anesthetic that is 7.5 times more potent than fentanyl, and transforming it into a very safe medication that people can use as a treatment for chronic pain," he says.

FUTURE OPPORTUNITIES

It is not only work being conducted at Alza and Durect that captures Dr. Theeuwes' imagination, but the expansion of the therapy possibilities stemming from biotechnology and gene therapy.

"In pharma, there have been great contributions in the anti-viral area, the treatment of AIDS," he enthuses. "We also see new developments of vaccines, which are essentially curative and have an enormous impact on the cost of care since they prevent disease from happening. In the biotechnology area it is the development of monoclonal antibodies, which are disease modifying, as opposed to the palliative treatments that pharma has in the past spent most of its time developing. We also are seeing gene therapy come of age."

Furthermore, the device industry is starting to play an enormous role, he says. "The contribution that stents have made to the cardiovascular field rivals, or even surpasses, that of drug treatment in many ways," he says. "The combination of drug substances coming from biotech and pharma with the device capability — which is the pharmaceutical systems business that Durect is pioneering — allows the industry to build new dimensions in treatment that will have an enormous impact on people's lives and on healthcare."

Furthering its mission, in April 2001, Durect acquired Southern BioSystems Inc., a privately held company located in Birmingham, Ala.

SBS develops, manufactures, and sells biodegradable polymer and non-polymer drug-delivery systems. SBS also provides bulk supply of biodegradable polymer for seven FDA approved products sold by five customers.

As part of this acquisition, Durect acquired intellectual property, including three issued

Theory and Practice: A Journey in Science

FELIX THEEUWES — RESUME

JULY 1998 TO PRESENT. Chairman, chief scientific officer, and co-founder, Durect Corp. Durect was established in 1998 as a spin off from Alza Corp. to focus on the development of pharmaceutical systems and products to treat chronic debilitating diseases and enabling biotechnology drugs.

AUGUST 1998 TO JULY 1999. Chief scientist, Alza Corp., Palo Alto, Calif.

AUGUST 1997 TO AUGUST 1998. President, new ventures and chief scientist, Alza.

1995 TO AUG 1997. President, Alza R&D and chief scientist, Alza.

1994 TO 1995. President, Alza Technology Institute and chief scientist, Alza.

1991 TO 1994. Executive VP, R&D, and chief scientist, Alza.

1987 TO 1991. Senior VP, research, and chief scientist, Alza.

1982 TO 1987. VP, research, and chief scientist, Alza.

1980 TO 1982. VP, product research and development, Alza.

1974 TO 1980. Principal scientist, Alza.

1971 TO 1974. Research scientist, Alza.

1970 TO 1971. Research scientist, Alza Institute of Pharmaceutical Chemistry, Lawrence, Kan.

1968 TO 1970. Visiting assistant professor of chemistry, The University of Kansas.

1966 TO 1968. Postdoctoral, Department of Chemistry, The University of Kansas.

1964 TO 1966. Research Fellow at CERN, Geneva, Switzerland.

1961 TO 1964. Research Fellow, National Fonds, Belgium high school teacher of physics, mathematics, chemistry, biology, at St. Vincent, Westerlo, Belgium.

EDUCATION:

1961. Licentiaat, Physics, The University of Leuven (Louvain), Belgium.

1962. Agregaat Hoger Secundair Onderwijs.

1966. D. Sc., Physics, The University of Leuven (Louvain), Belgium.

1993. Stanford Executive Program.

MILITARY SERVICE:

1964-1965. Lieutenant, Meteorological Service, Belgian Air Force.

HONORS:

1966. D. Sc. with Great Distinction.

1980. Inventor of the Year, Peninsula Patent Law Association, for invention and continued development of Osmotic Therapeutic Systems.

1981. Louis W. Busse Lecturer, University of Wisconsin, Madison, Wisc.

1983. Award for the Advancement of Industrial Pharmacy presented by the Academy of Pharmaceutical Sciences.

1985. Third Annual Sidney Riegelman Lecturer, University of California, San Francisco.

1988. Fellow of the American Association of Pharmaceutical Scientists.

1993. First recipient of Alza Corp.'s Founder's Award.

U.S. patents, covering SBS's proprietary drug delivery technologies. SBS has three drug delivery platforms: the Saber delivery system, Microdur (microspheres injectable), and Durin (drug-loaded implants).

The Saber technology is a patented and versatile depot technology with a simple manufacturing process. Saber is intended to be injected subcutaneously as a liquid, via a needle and syringe, and remains in a highly viscous liquid form following injection to conform to body shape.

Microdur uses microencapsulation, the process of trapping the active agent in a solid polymer shell, which results in a free-flowing powder controlling the rate of drug release through a number of variables.

The microspheres can be formulated for

oral, parenteral, dermal, or other routes of administration.

Durin technology is drug-loaded implants that can be used for delivering an active compound through parenteral and other routes of administration.

Drug-delivery implants consist of an active and a polymeric excipient that are formed into a fiber, rod, film, or other shapes to control drug release through a number of variables.

All these developments will change the way that medicine is practiced and will improve quality of life for patients, Dr. Theeuwes contends.

"New treatments will go from palliative to restorative and curative," he says. "Patients will gain more freedom, and doctors will

become healers, as they're supposed to be. Much of the medicine we have today can be equated to a wooden leg — it's a crutch on which you walk every day but it doesn't restore the body to normalcy. Antibiotics are a class of drug that basically eradicate a pathogen and the patient is essentially cured. But very few other medications can do this. In the future, we will see more curative treatments."

Nevertheless, Dr. Theeuwes remains realistic about the obstacles the industry faces.

"Regulations and politics often place hurdles in the way of development," he notes. "In my lifetime in the pharmaceutical industry, I have seen the cost of developing a new medicine increase from \$200 million to \$800 million. There has been a great increase in the

Durect Product Pipeline

Durect Corp. is pioneering the development and commercialization of pharmaceutical systems for the treatment of chronic debilitating diseases and enabling biotechnology-based pharmaceutical products. Durect's goal is to deliver the right drug to the right site in the right amount at the right time.

Durect's pharmaceutical systems combine technology innovations from the medical-device and drug-delivery industries with proprietary pharmaceutical and biotechnology drug formulations. These capabilities can enable new drug therapies or optimize existing therapies based on a broad range of compounds, including small-molecule pharmaceuticals as well as biotechnology molecules such as proteins, peptides, and genes.

The company's focus is on the treatment of chronic diseases including asthma, cancer, cardiovascular disease, central nervous system disorders, and pain. Durect holds an exclusive license from Alza Corp., a Johnson & Johnson company, to develop and commercialize products in selected fields based on the Duros implant technology.

ASTHMA

Durect, in April 2002, filed an Investigational New Drug application to investigate the delivery of cromolyn sodium for the treatment of asthma. The IND was filed as part of an ongoing program to develop a product for the treatment of asthma and allergic rhinitis (seasonal allergies) using one of the company's proprietary biodegradable drug-delivery platforms. Cromolyn sodium, a non-steroidal anti-allergy medication, is a FDA-approved drug for the management of mild-to-moderate persistent asthma and is recommended for early intervention and daily anti-inflammatory therapy.

BIOTECHNOLOGY

Drugs developed out of the biotechnology industry are mainly administered by repeated, frequent injection. The desirability of dosage forms that can reliably administer proteins for long periods of time is

readily acknowledged. Durect is researching products using its biodegradable platform technologies in combination with protein molecules having known efficacy against major diseases with a goal to develop products that require less frequent administration than products available on the market.

CARDIOVASCULAR

In collaboration with the University of Maastricht in The Netherlands, Durect is working to develop methods for treating ischemic heart disease and other chronic cardiovascular diseases through continuous pericardial delivery. Research in animal models suggests that ischemic heart disease may be treated by continuously delivering an angiogenic factor to spur new blood vessel growth, thereby increasing blood flow, and restoring function to the diseased heart.

CENTRAL NERVOUS SYSTEM

Durect has a collaboration with the Johns Hopkins University, Department of Neurology/Neurosurgery, exploring the feasibility of treating tumors of the brain stem by site-specific delivery of a chemotherapeutic agent directly to the tumor via a Duros system attached to a catheter. The program is in preclinical development studies in primates. The company is developing its Duros platform technology in combination with various catheter systems for targeted delivery of drugs to treat select CNS disorders. Durect also is developing bioerodible platform technologies for systemic and targeted delivery of select CNS disorders.

PAIN

With its lead product, the Chronogesic (sufentanil) Pain Therapy System, Durect intends to target patients with opioid responsive chronic pain that results from a variety of causes. The Chronogesic product delivers sufentanil continuously within the therapeutic window, at physician prescribed doses for three months of pain therapy. Sufentanil is an opioid that is currently used in hospitals as an analgesic. The Chronogesic product addresses the potential problems of peaks (too much medication) and

length of time to develop such medications. The challenge to society will be to strike an optimal balance between regulation and policy; between the scientific aspects, and the freedom to develop medicine.”

In the meantime, Dr. Theeuwes strives to make his contribution to fulfilling the goals of medicine by helping Durect achieve its milestones.

“Everyday we have to make a difference, so I start by looking at which obstacles are keep-

ing people back and which new concepts or ideas we should pursue to add to the capabilities that we have,” he says. “As I stand farther and farther back from the work, my main focus is on the horizon.”

Because of its strong technological foundation and its unique pharmaceutical systems approach to delivering a drug in the right amount to the right place at the right time, Durect is well-positioned to capitalize on the advancements currently being made and

address the challenging problems in the healthcare industry. The completion of the sequencing of the human genome will revolutionize drug discovery, but Durect believes that delivery technology is required to transform these molecules emerging from biotechnology into real medicine. ♦

PharmaVoice welcomes comments about this article. E-mail us at feedback@pharmalinx.com.

Research

Focus: **SABER™ Oral**

Indication: Various

Drug: Various Compounds

Focus: **Biotechnology**

Indication: Various

Drug: Various Agents

Focus: **Antipsychotic**

Indication: Psychotic Disorders

Drug: Anti-Psychotic Agent

Preclinical

Focus: **SABER™ Injection**

Indication: Post-Operative Pain

Drug: Local Anesthetic

Focus: **Brain Tumor Local Delivery**

Indication: Brain Cancer

Drug: Anti-Tumor Agent

Focus: **Spinal Delivery**

Indication: Chronic Pain

Drug: Opiate

Focus: **Pericardial**

Indication: Coronary Disease

Drug: Angiogenic Factors

Phase I Program

Focus: **Asthma**

Indication: Asthma

Drug: Cromolyn

Phase III Program

Product: **CHRONOGESIC™**

Indication: Chronic Pain

Drug: Sufentanil

Commercial Products

IntrEAR®

ALZET®

LACTEL®

troughs (too little medication) associated with pills and patches. This product will provide an alternative to current therapies for the treatment of chronic pain and may provide for less risk of potential misuse, abuse, and diversion than traditional pills or patches. The ability of the Chronogestic product to provide controlled dosing will allow physicians to prescribe and safely administer to patients, a clinically necessary opioid for moderate-to-severe chronic pain for three months.

In 2001, Durect made significant progress in the development of the Chronogestic product. The company completed a Phase II trial in which patients preferred the Chronogestic product by a two-to-one margin versus their previous pain medication. Patients not only reported a reduction in side effects when compared with their previous medications, but also reported improved quality of life, such as improved sleep patterns. In 2001, the company also completed a pilot Phase III study that confirmed its conversion strategy for transitioning patients from other opioid medications to the Chronogestic product. Chronogestic's potential is to improve the quality of life of patients suffering from chronic pain and will be evaluated in pivotal Phase III clinical trials starting in 2002. The primary objectives are to demonstrate that patients can be safely transitioned from a variety of existing opioids, such as pills and patches, to the Chronogestic product, as well as to demonstrate that Chronogestic provides safe and effective pain relief at least equivalent to the patient's existing pain therapy. The Chronogestic product uses the Duros drug-delivery technology.

LOCAL POST-OPERATIVE PAIN

Durect is developing a sustained-release formulation of a local anesthetic using its Saber Delivery System for the treatment of post-surgical pain. This analgesic will be injected by the physician at the time of surgery and placed adjacent to the surgical site. By delivering effective amounts of a potent analgesic to the location from which the pain originates, local pain control can be achieved with minimal exposure to the remainder of the body, and hence minimal side effects. The company is currently conducting preclinical studies on this product.

SPINAL DELIVERY PAIN

Infusion of opiates into the spinal fluid has become accepted medical therapy in patients who find high-dose oral or transdermal opioids ineffective or who experience side effects that make systemic therapy unacceptable. Although there are many implantable infusion pumps on the market today, these pumps tend to be relatively large and require a costly surgical procedure to implant. A need exists for a minimally invasive, spinal infusion device that has an improved cost benefit for patients with chronic pain. Durect's strategy is to develop an infusion system that can deliver an opioid into the spinal fluid via a catheter. This product will be considerably smaller and less invasive than currently available spinal infusion pumps, allowing for implantation on an outpatient basis. The company is currently conducting preclinical studies on this product.