
## DURECT CORPORATION

Fiscal year 2005 was a very strong year for DURECT as the Company completed all of the corporate objectives and key strategic initiatives that we previously communicated.

Today, we continue to make progress in our ongoing development programs, move new programs into clinical development and forge commercial alliances for our products and technologies.

Fiscal Year
05

Project
ANNUAL REPORT

DURECT

## POST-OPERATIVE PAIN DEPOT (SABER™–Bupivacaine)

SABER-Bupivacaine is based on our patented SABER delivery technology and is intended to be administered around the surgical site after surgery to provide 3 days or more of regional pain relief. Our SABER system is a state-of-the-art biodegradable, controlled-release technology that can be formulated for systemic or local administration of active agents.

We successfully completed the first Phase II study for SABER-Bupivacaine in 2005 meting all the primary end-points for the study including safety and pharmacokinetics. In addition, our physician market research indicates that SABER-Bupivacaine would represent a significant advancement over the current commercially available treatments for post-surgical pain.

In January 2006, we announced plans to expand our worldwide development program for SABER-Bupivacaine, by initiating additional Phase II studies for soft tissue and orthopedic surgical procedures. In addition, clinical studies will be conducted in the U.S. under the accepted U.S. Investigational New Drug (IND) application.

Clinical Phase

02

Technology

SABER DELIVERY SYSTEM (INJECTABLE)

Development Partner

DURECT CORPORATION

Indication

POST-OPERATIVE PAIN

Drug

BUPIVACAINE

## POST-OPERATIVE PAIN DEPOT (SABER™–Bupivacaine)

Pain, deemed by the WHO as the "5th Vital Sign," has detrimental physiologic effects that contribute to post-operative complications and may increase the cost of surgical recovery. The current standard of care for post-surgical pain includes oral opiate analgesics and non-opiate analgesics. Opioids commonly cause drowsiness, constipation and cognitive impairment. Because of the fear of opiate addiction and side effects, patients and healthcare providers tend to under treat post-surgical pain. There is a large unmet need for effective, opioid sparing post-surgical pain treatments with improved side effect profiles. Our internal physician market research indicates that SABER-Bupivacaine could assist with a more rapid diagnosis of surgical complications because it has the potential to be opioid sparing, and opioids could mask rare but serious surgical complications that would otherwise be difficult to diagnose. We believe that SABER-Bupivacaine could potentially reduce hospital stays and the amount of traditional post-surgical pain medications needed by patients, as well as the side effects that result from the use of concomitant opioid medications.

Based on our market research to date, there are over 100 million surgical procedures performed each year in the U.S. and the top 5 markets in Europe. According the 275 physicians that participated in our research, SABER-Bupivacaine could be utilized in 32.5 million of the 70 million procedures in the U.S. market covering the following procedures: General surgery; Orthopedics; Obstetrician/ gynecological; Cardiovascular/cardiothoracic; and Plastic surgeries.

Clinical Phase

02

Technology

SABER DELIVERY SYSTEM (INJECTABLE)

Development Partner

DURECT CORPORATION

Indication

POST-OPERATIVE PAIN

Drug

BUPIVACAINE

## REMOXY™ (ORADUR™–Oxycodone)

We are developing Remoxy, an abuse-resistant formulation of oxycodone based on our patented ORADUR technology in collaboration with Pain Therapeutics, Inc., to which we have licensed the worldwide development and commercialization rights. Remoxy and the other ORADUR-based products subject to our license with Pain Therapeutics were sub-licensed to King Pharmaceutiucals, Inc. in 2005. Diversion and misuse are significant issues in the sale and distribution of strong opioids such as oxycodone. We believe the ORADUR technology offers a significant advantage over current sustained release dosage forms as it is more difficult to misuse or abuse (e.g., by crushing or alcohol or water extraction).

According to Pain Therapeutics, Remoxy achieved positive results in a 200 patient Phase III clinical trial in 2005 and successfully completed a Special Protocol Assessment with the FDA which provided guidance for the design of the one remaining pivotal Phase III study to file a New Drug Application.

Clinical Phase

03

Technology

ORADUR (SUSTAINED RELEASE ORAL GEL-CAP)

Development Partner

KING PHARMACEUTICALS, INC.
PAIN THERAPEUTICS, INC.

Indication

CHRONIC PAIN

Drug

OXYCODONE

## TRANSDERMAL SUFENTANIL PATCH (TRANSDUR™–Sufentanil)

Our transdermal sufentanil patch product, which utilizes our proprietary TRANSDUR technology, is intended to provide extended chronic pain relief for up to seven days, as compared to the three days of relief provided with currently available opioid patches. We anticipate that the small size of our sufentanil patch (potentially as small as one-fifth the size of currently marketed transdermal fentanyl patches for a therapeutically equivalent dose) may offer improved convenience for patients.

We licensed the development and commercialization rights of TRANSDUR-Sufentanil for the U.S. and Canadian markets to Endo Pharmaceuticals, Inc. in March 2005. As part of our agreement with Endo, Endo paid us an upfront fee of $10.0 million, with the potential of additional milestone payments of approximately $35.0 million. Endo will be solely responsible for funding the remaining development expenses for this development product for the U.S. and Canadian markets, in which we retain co-promotion rights. We retain all commercial rights in territories outside the U.S. and Canada. In 2005, we reported positive preliminary data from an initial Phase II study of our transdermal sufentanil patch.

Clinical Phase
02

Technology
TRANSDERMAL PATCH

Development Partner
ENDO PHARMACEUTICALS, INC.

Indication
CHRONIC PAIN

Drug
SUFENTANIL

## MEMRYTE™ (DURIN™–Leuprolide)

We are developing Memryte for the treatment of Alzheimer's disease in collaboration with Voyager Pharmaceuticals, Inc., to which we have licensed exclusive, worldwide development and commercialization rights to our DURIN technology under a development and license agreement entered into in July 2002. Memryte uses our proprietary DURIN technology to provide sustained release of the peptide leuprolide acetate, based on Voyager's patented method of treatment of Alzheimer's disease. We will receive from Voyager milestone payments, if specified development milestones are achieved, and, if commercialized, royalties based on sale of the resulting product anywhere in the world. Memryte is currently in Phase III clinical trials.

Alzheimer's disease is an incurable, neurodegenerative disorder that affects over 4 million Americans. This disease is a huge unmet medical problem that typically leads to progressive memory loss, impairments in behavior and language, and physical deterioration. The market potential for Alzheimer's disease treatments is estimated to be in excess of $10 billion.

Our DURIN biodegradable implant technology is a platform for parenteral delivery of drugs for periods of weeks to six months or more. The technology is based on the use of biodegradable polymer excipients, which have a proven record of safety and effectiveness in approved drug delivery and medical device products.

Clinical Phase
03

Technology
DURIN
BIODEGRADABLE IMPLANT

Development Partner
VOYAGER
PHARMACEUTICALS, INC.

Indication
ALZHEIMER'S DISEASE

Drug
LEUPROLIDE ACETATE


## EMERGING SPECIALTY PHARMACEUTICAL COMPANY

Our goal is to become a specialty pharmaceutical company where we commercialize products with significant market potential. To that end, we intend, over the course of a few years, to build up commercial, sales and marketing capability and other required infrastructure in focused specialty areas. We may still choose to enter into strategic alliances from time to time consistent with our strategy to leverage the established sales organizations of third-party collaborators to achieve greater market penetration for some of our products than we could on our own. If we choose to enter into third-party collaborations to commercialize our pharmaceutical systems, we believe we have the flexibility to enter into these alliances under circumstances that allow us to retain greater economic participation because our pharmaceutical systems combine drugs for which medical data on efficacy and safety are available with proven technology platforms.

## Corporate Highlights

2005
### DEC
DURECT Announces Positive Preliminary Results from Transdermal Sufentanil Patch Study in Patients

2005
### NOV
DURECT Highlights Major Commercial Strategic Alliance for ORADUR™ Sustained Release Oral Gel-cap Technology

2005
### NOV
DURECT Corporation Announces Pricing of Public Offering

2005
### OCT
DURECT Announces Positive Preliminary Results from its Phase II Study for its Post-Operative Pain Relief Depot

2005
### OCT
DURECT Corporation Announces Initiation of Dosing for Phase III Clinical Program for Memryte (DURIN™–Leuprolide Implant) Program Under Development with Voyager Pharmaceuticals

2005
### SEP
DURECT Corporation Announces Completion of Dosing in Cohort 3 of its Phase II Study for its Post-Operative Pain Relief Depot

2005
### SEP
DURECT Corporation Announces Positive Phase III Clinical Results for Remoxy, a Novel Oral Pain Medication using the ORADUR™ Gel-Cap

2005
### JUN
DURECT Announces Preliminary Results from Cohort 2 of its On-Going Phase II Study for its Post-Operative Pain Relief Depot

2005
### MAR
DURECT Corporation and Endo Pharmaceuticals Sign Agreement to Develop and Commercialize DURECT's Seven-Day Transdermal Pain Patch

2005
### FEB
DURECT Initiates Phase II Program for Its Sufentanil Patch Product

2005
### FEB
DURECT Completes Dosing of the Phase I Pharmacokinetic Study for Its Sufentanil Patch Product and of the First Cohort of the Phase II Study for Its Post-Operative Pain Relief Depot

2005
### JAN
DURECT Corporation Announces Completion of Clinical Trial Enrollment for DURIN™–Based Leuprolide Product Candidate

## To Our Shareholders

In 2005, we started to capitalize on the investments we started to make since our founding in 1998. Our early investments relating to the drug sufentanil while developing CHRONOGESIC® facilitated our development of a small, elegant seven-day transdermal sufentanil patch (TRANSDUR™–Sufentanil) for which we completed a successful initial Phase II trial and announced preliminary data in 4Q2005. In March 2005, we licensed TRANSDUR-Sufentanil to Endo Pharmaceuticals for the U.S. and Canadian markets. This collaboration put the commercialization of TRANSDUR-Sufentanil in the hands of a specialty pharmaceutical company with a strong track record for successfully launching and building new products in the field of pain management, as well as strengthened our financial position with our receipt of the $10 million upfront payment from Endo.

Through our acquisition of Southern BioSystems, Inc. in 2001, we acquired several proprietary and versatile drug delivery technology platforms, which provide a broad foundation for injectable, implantable and abuse resistant oral products. After several years of research and development, we have now a pipeline of products in Phase II and Phase III clinical development based on these technologies.

We are especially excited about the versatility of the SABER™ technology as a basis for injectable depot and oral products. We have advanced SABER-Bupivacaine, our injectable post-operative pain depot, into Phase II clinical development. If approved, SABER-Bupivacaine would be a first-in-class therapeutic designed to manage local pain after surgery. To date, we have retained full rights to SABER-Bupivacaine. We intend to market this product ourselves in the U.S. as an initial step to achieving our goal of becoming a specialty pharmaceutical company.

The SABER technology is also the basis for our ORADUR™ abuse resistant oral gel cap technology. In collaboration with Pain Therapeutics, Remoxy™, an abuse resistant sustained release formulation of the opioid oxycodone, has progressed to pivotal Phase III clinical trials. We were, furthermore, pleased to have King Pharmaceuticals, Inc. endorse the commercial potential of products based on our ORADUR platform by King's sub-license from Pain Therapeutics of the commercialization rights of Remoxy as well as the remaining ORADUR-based products subject to our license with Pain Therapeutics.

2005 was also the year that the first DURIN™-based product advanced into late stage development. This product, under development with Voyager Pharmaceuticals, Inc., is called Memryte™, a novel therapy for the treatment of Alzheimer's disease, entered Phase III clinical testing.

Our goal to date has been to establish a broad and diverse portfolio of technologies and products in order to minimize the risks inherently associated with drug development. We believe that we have reached that stage with technologies in oral, transdermal, implantable and injectable areas and multiple products in development in large and growing markets in the area of chronic conditions as exemplified by pain and Alzheimer's disease where patients are underserved. Indeed the field of pain management has benefited greatly from controlled delivery technologies and products which have been the basis for innovation and service to patients by delivering medicine to targeted sites, on demand, and for sustained periods of time.

Due to our progress, at the end of 2005, we completed a secondary offering of our common stock that raised net proceeds of approximately $38 million. With our rights in TRANSDUR-Sufentanil, and SABER-Bupivacaine that we can partner overseas and our cash position, we believe we are well positioned to put our efforts towards the goal of becoming a specialty pharmaceutical company.

On behalf of everyone at DURECT, we thank you for your continued support and look forward to the achievement of major milestones in 2006.

Felix Theeuwes, D.Sc
*Chairman and*
*Chief Scientific Officer*

James E. Brown, D.V.M.
*President and*
*Chief Executive Officer*

## Corporate Directory

**Executive Officers**

Felix Theeuwes, D.Sc.
*Chairman,*
*Chief Scientific Officer*
*and Director*

James E. Brown, D.V.M.
*President,*
*Chief Executive Officer*
*and Director*

Jean I. Liu
*Senior Vice President*
*and General Counsel*

Paula Mendenhall,
Pharm D.
*Senior Vice President*
*of Operations*

Su IL Yum, Ph.D.
*Senior Vice President,*
*Pharmaceutical Systems*
*Research and Development*

Harry Guy
*Vice President,*
*Engineering and Safety*

Schond L. Greenway
*Vice President,*
*Investor Relations*
*and Strategic Planning*

Steven C. Halladay, Ph.D.
*Vice President,*
*Clinical and Regulatory*

Jian Li
*Vice President, Finance*
*and Corporate Controller*

Thomas P. McCracken
*Vice President and Chief*
*Patent Counsel*

Andrew R. Miksztal, Ph.D
*Vice President,*
*Pharmaceutical Systems*
*Research and Development*

**Board of Directors**

Felix Theeuwes, D.Sc.
*Chairman,*
*Chief Scientific Officer*
*and Director*

James E. Brown, D.V.M.
*President,*
*Chief Executive Officer*
*and Director*

Simon X. Benito
*Director*

Michael D. Casey
*Director*

David R. Hoffmann
*Director*

Armand P. Neukermans,
Ph.D.
*Director*

Jon S. Saxe
*Director*

**Corporate Secretary**

Jean I. Liu
*Senior Vice President*
*and General Counsel*
Tel: 408.777.1417
Fax: 408.777.3577

**Additional Information**

For more information
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**Annual Meeting**

The company's annual meeting of stockholders will be held at 10:00 A.M. local time June 20, 2006 at Company Headquarters

**Independent Auditors**

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Palo Alto, CA 94304
Phone 650.496.1600
Fax 650.496.4660

**Corporate Counsel**

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& McAuliffe, LLP
2800 Sand Hill Road
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**Transfer Agent**

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**SEC Form 10-K**

A copy of the Company's annual report to the United States Securities and Exchange Commission on Form 10-K is available without charge upon written request to:

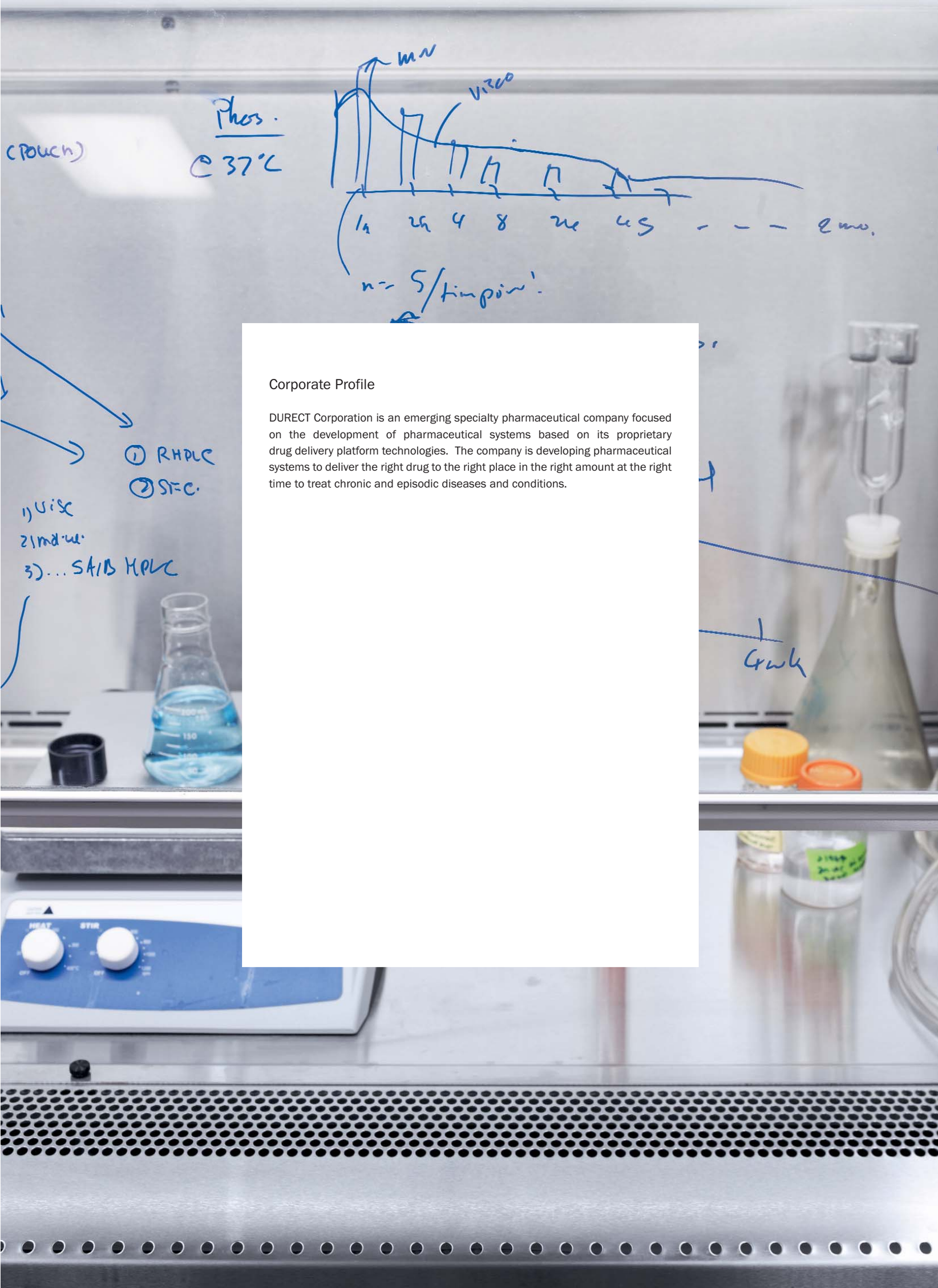
DURECT Corporation
Attn: Investor Relations
2 Results Way
Cupertino, California
95014

**Trademarks**



The statements in this press release regarding DURECT's products in development, product development plans and anticipated markets are forward-looking statements involving risks and uncertainties that can cause actual results to differ materially from those in such forward-looking statements. Potential risks and uncertainties include, but are not limited to, DURECT's (and that of its third party collaborators where applicable) abilities to complete the design, development, and manufacturing process development of the product candidate, obtain product and manufacturing approvals from regulatory agencies and manufacture and commercialize the product candidate, as well as marketplace acceptance of the product candidate. Further information regarding these and other risks is included in DURECT's Annual Report on Form 10-K for the year ended December 31, 2005 filed with the SEC on March 16, 2006 under the heading "Risk Factors."

concept and design: extralarge, a design studio (www.xlstudios.com)




## Corporate Profile

DURECT Corporation is an emerging specialty pharmaceutical company focused on the development of pharmaceutical systems based on its proprietary drug delivery platform technologies. The company is developing pharmaceutical systems to deliver the right drug to the right place in the right amount at the right time to treat chronic and episodic diseases and conditions.


DURECT

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