



Annual Report 2004



**Dyax Corp.** brings together science, technology and drug development – independently or with partners – to deliver novel biotherapeutic products that will expand treatment options for physicians, and improve the quality of patients' lives.



## To Our Valued Shareholders:

I am very pleased to report that 2004 was a year of considerable progress for Dyax, highlighted by positive results from three clinical development programs involving our small protein product candidates, DX-88 and DX-890. Additionally, the first antibodies and peptides from Dyax libraries were advanced into Phase I clinical trials by Dyax collaborators. With respect to new revenue generating collaborations, we enjoyed a year of unprecedented growth, particularly in the use of our antibody libraries. And for our own pipeline of clinical candidates, we completed preclinical animal studies against numerous new targets and plan to advance at least one antibody into formal development at Dyax during 2005.

The core components of Dyax's business model – therapeutic development, new drug discovery, revenue generating collaborations, and ultimately, product commercialization – combine to secure the promise of an increasingly bright future for Dyax, our partners and our shareholders.

### **Clinical Progress**

#### ***DX-88 for HAE***

During 2004, we reported positive results from Phase II clinical trials of DX-88 for the treatment of a rare, life-threatening acute inflammatory condition called hereditary angioedema (HAE).

**The DX-88 for HAE program, which is in a joint venture with Genzyme Corporation, is at the forefront of bringing a desperately needed therapy to market** in the US, where no FDA approved treatment for acute attacks of HAE is available to patients.

In November of 2004, Dyax and Genzyme reported final results from our placebo-controlled Phase II trial of DX-88 in HAE, known as EDEMA1. The data demonstrated that the drug was well tolerated and provided a statistically significant clinical benefit ( $p=0.0169$ ) to HAE patients who were dosed intravenously with DX-88 (n=40) versus those





who were administered a placebo (n=8). The median time to significant relief of HAE symptoms in this trial was 70 minutes for patients who received DX-88, compared to greater than 240 minutes for patients in the placebo group.

More recently, in January of 2005, we reported positive interim results on the first 61 HAE attacks treated intravenously with DX-88 in our ongoing, open-label, Phase II, repeat dosing trial known as EDEMA2. These interim results again support the good tolerability of DX-88 at all three dose levels tested, and reinforce DX-88's ability to elicit rapid relief of HAE symptoms, with a median time to onset of relief of HAE symptoms of only 35 minutes.

In EDEMA2, designed to dose patients with DX-88 multiple times for separate HAE attacks, patients have been treated up to twelve times. To date, there has been no decrease in efficacy or safety observed, nor have antibodies to DX-88 been detected.

Analysis of initial response and durability of response to DX-88 at various dose levels tested has allowed us to identify a single optimal dose level. This is important as we accelerate the development of a subcutaneous formulation of DX-88 for at-home administration, and as we prepare to initiate a pivotal Phase III trial, referred to as EDEMA3. We expect successful completion of EDEMA3 to be a final step toward filing a Biologics License Application (BLA) for FDA approval of DX-88 for HAE.

#### **DX-88 for CABG**

A Phase I/II clinical trial to evaluate the use of DX-88 during open heart surgery – specifically, on-pump coronary artery bypass grafting (CABG) procedures – has demonstrated positive safety and clinical benefit. The trial results, announced in late December 2003, raised the visibility of the DX-88 for CABG program during 2004. The data highlighted that patients treated with DX-88 had a significant reduction of approximately 50% in their need for blood transfusion products versus patients receiving placebo, as measured 24 hours from the start of cardiopulmonary bypass (CPB).

Preclinical animal studies conducted during 2004 demonstrated that DX-88 may also reduce reperfusion injury that can occur during open-heart surgery, suggesting a potentially broader market for this product.

Given its greater than anticipated market potential and costs of clinical development, we believe it is in the best interest of the Company to partner DX-88 prior to initiating

major Phase II trials. **Our objective is to partner this product with a company experienced in the marketing and development of cardiovascular products.** To this end, discussions are underway, and we look forward to initiating new trials with a partner's input and support.

#### **DX-890**

With respect to development of our second product in the clinic, DX-890, in February of 2004 we announced positive results on safety and pharmacokinetics from a second Phase IIa study of DX-890. This trial involved children with cystic fibrosis and was conducted by our partner Debiopharm SA, who has more recently initiated a placebo-controlled Phase II trial at various sites in Europe. This 63-patient trial includes a clinical endpoint for lung function.

Although I am very pleased that this efficacy trial has begun, the cystic fibrosis program has advanced at a much slower pace than planned, and it has been difficult for Dyax to effect more rapid progress. **We have come to a mutual decision with Debiopharm to restructure our agreement in a way that will benefit both companies.**

We expect the amended agreement to allow Debiopharm to proceed independently with DX-890, while Dyax advances a pegylated (PEG) version of the molecule for disease areas outside of cystic fibrosis. Our interest in this variant of DX-890 is based on animal study results received in 2004, demonstrating that pegylation substantially extends DX-890's half life, and our ensuing belief in its potential to treat chronic indications such as chronic obstructive pulmonary disease (COPD).

#### **Productive Collaborations Exceed Goals, Advance to the Clinic**

With an original focus on small proteins and peptides, Dyax has now emerged as a strong presence in the field of antibody discovery. While we were not the first in this area, I believe our innovative libraries are the best available today. The growth in our antibody collaborations reflects the industry's recognition of the speed and precision at which high quality clinical candidates can be isolated from Dyax's libraries.

**Our team at Dyax is vigilant about uncovering opportunities to leverage our powerful technology in order to generate licensing and product development revenues,** while at the same time utilizing our internal capabilities to fuel Dyax's own pipeline. We look forward to advancing our next clinical candidate into Development, and to monitoring our collaborators' progress.

# Advancing Novel Biotherapeutics

Through a library licensing agreement with ImClone Systems Incorporated, **two fully human monoclonal antibodies derived from Dyax's libraries have entered into Phase I clinical development for their potential as cancer therapeutics.**

In addition, two peptides from Dyax libraries moved into Phase I clinical development during 2004; one at Amgen Inc. and one at EPIX Pharmaceuticals.

Dyax also entered into a number of other important new collaborations in 2004, most notably an agreement with Biogen Idec for identification and characterization of therapeutic and/or diagnostic antibodies against up to thirty Biogen Idec targets per year. Other new collaborations include those with Amgen, Inc., Baxter Healthcare Corporation, Genzyme Corporation, Inhibitex, Inc. and Tanox, Inc.

The majority of our more than 75 collaborations and licenses include upfront fees, renewal fees, success based milestone payments, and royalties on products that advance to market.

## Summary of Financial Results

For the year ended December 31, 2004, revenues from continuing operations were \$16.6 million, approximately equivalent to revenues for the year ended December 31, 2003. Increases in revenues from library licensing activities during 2004 largely offset any decreases in revenues from funded research and development. And, while the costs associated with compliance with new Section 404 rules (Management's Reports on Internal Control Over Financial Reporting) of the Sarbanes-Oxley Act are substantial, I'm pleased to say that Dyax is fully compliant.

For the year ended December 31, 2004, the Company reported a net loss from continuing operations of \$33.1 million or \$1.06 per share, as compared to a net loss from continuing operations of \$24.5 million or \$1.04 per share for the previous year.

Regarding Dyax's financial outlook for the year 2005, we expect net cash consumption for the year 2005 to be approximately \$30 million.

## Employees Who Drive Our Success

Dyax's progress during 2004 was made possible by the extraordinary effort of an employee base that combines independent thinking and teamwork to achieve set goals. **Each and every Dyax employee has a unique influence on our success.** And, a highly accomplished senior management team draws on individual experience and leadership skills to guide all activities toward Dyax's shared



Henry E. Blair – Chairman, President and Chief Executive Officer

goals. Beyond our corporate objectives, I'm proud to say that over 80% of our employees worldwide contribute to staff-initiated community outreach efforts. Beneficiaries include The Salvation Army, a local homeless shelter, a community food bank and other charities. This speaks volumes about the character and integrity of the Dyax family, and is one of the many reasons I am certain of our continued success, both as a leading biopharmaceutical company and as a good corporate citizen.

## Building Value

In closing, and in view of our past several years of progress, it is evident that **Dyax is on a clear and steady path toward our most important goal of delivering novel biotherapeutic products to patients in need.** As we continue to build this company, we remain focused on this goal which, I believe, is the key to building long-term shareholder value.

Sincerely,

A handwritten signature in black ink that reads "Henry E. Blair".

Henry E. Blair

Chairman, President and Chief Executive Officer





OUR PIPELINE

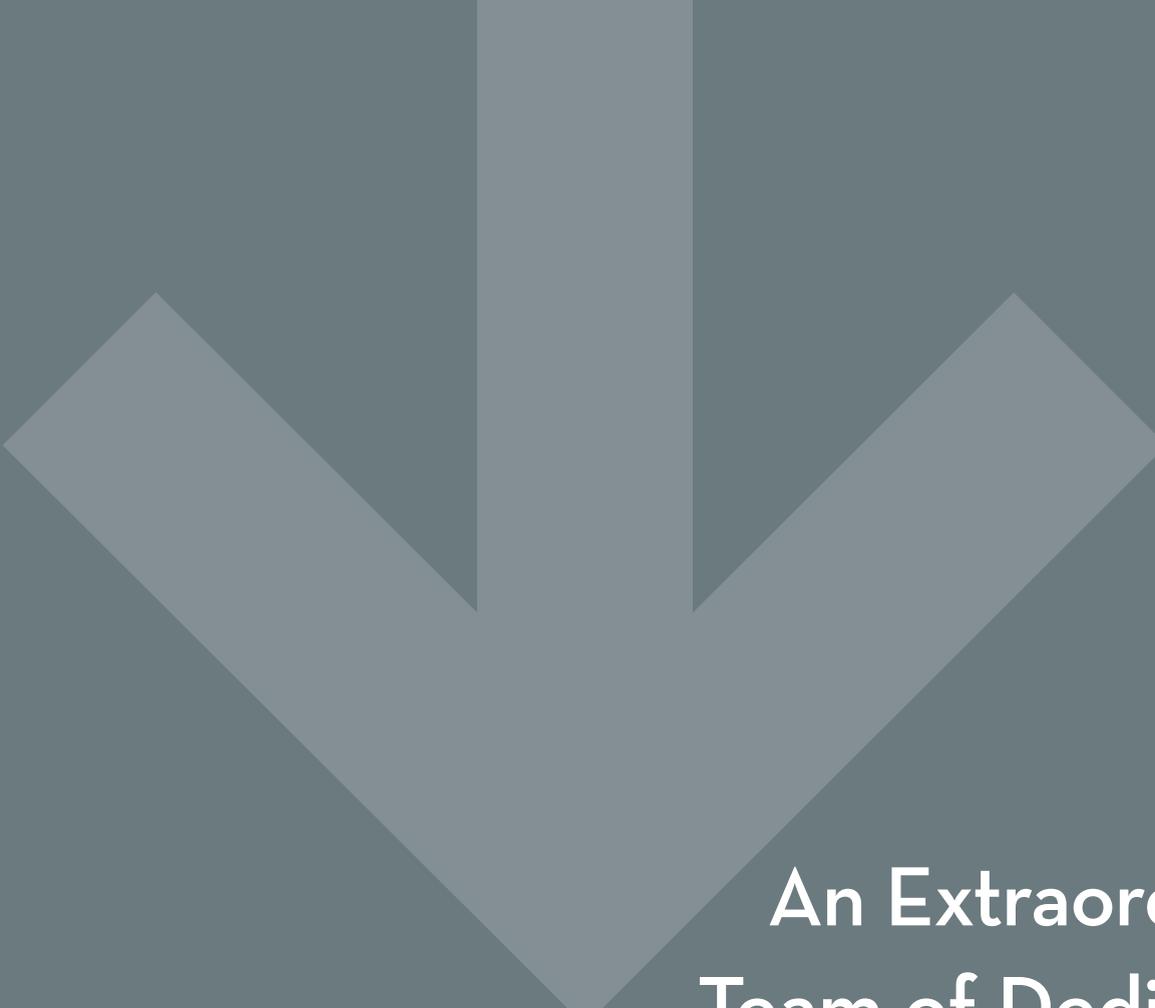


## → A Pipeline that Fuels Our Future

A strong pipeline of new clinical candidates helps to secure Dyax's future growth. Our focus is on areas of expansive opportunity: treatments for cancer and inflammation. We have the unique advantage of utilizing our proprietary phage display libraries of antibodies, small proteins and peptides for new drug lead discovery.

The unparalleled diversity of our "in demand" fully human monoclonal antibody libraries allows us to isolate the highest quality drug candidates for clinical development. Our integrated automation platform is used for high throughput selections and screening, which dramatically shortens the discovery process and enables our research groups to move leads into Development with remarkable precision and speed. On average, we can move Fabs on phage to soluble Fabs in nine weeks, and to whole IgGs in just twelve weeks.

During 2004, we tested six new compounds in animal studies ("in vivo") against a variety of disease targets. We expect to advance at least one antibody from this group into Development during 2005.



# An Extraordinary Team of Dedicated Professionals

Dyax's progress is directly related to the remarkable commitment and camaraderie of our employees. In our fast-paced and competitive industry, teamwork is an essential element of our success, and a fundamental part of the Dyax culture.

Our business development and discovery research groups, for example, work closely together to understand, meet, and often exceed the expectations of our collaborators. And internally, all departments are represented in making strategic decisions for the Company, such as which compounds to advance into clinical trials, and which programs to partner versus pursue independently.

Dyax currently has over 100 employees worldwide, of which approximately 25% have M.D. or Ph.D. degrees, and approximately 75% work in research and development.

Dyax employees earn respect every day by their initiative, accountability, and a willingness to give 100% to reach Company goals.



OUR TEAM





dedication



leadership



teamwork

commitment



integrity



# Strategic Partnerships that Generate Revenue

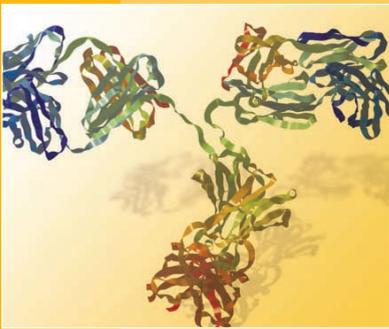
Through co-development agreements, funded research, patent licenses and library licenses, Dyax leverages its proprietary phage display technology to establish strategic partnerships and collaborations. These agreements give us many more “shots on goal,” by allowing for a multitude of potential biotherapeutic products isolated from Dyax libraries to be simultaneously developed for potential commercialization.

The power and precision of our technology continues to offer ample opportunity for the development of therapeutics by Dyax as well as by our many partners. Dyax entered into an unprecedented seven new antibody and two new peptide collaborations during 2004, and has over 75 revenue generating collaborations and licenses in place, several of which we expect to increase in value to the Company as products in development advance toward marketing approval.

One of our major collaborations is our joint venture partnership with Genzyme Corporation for the development of our lead product, DX-88, for the potential treatment of hereditary angioedema. Under this collaboration, Dyax is responsible for development and Genzyme is responsible for sales and marketing, contingent on DX-88 receiving FDA approval for commercialization.



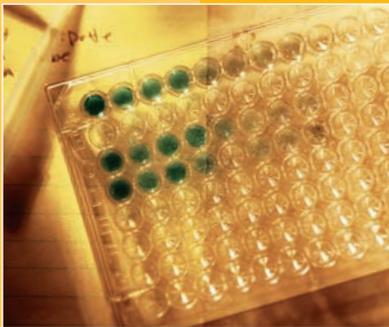
OUR PARTNERS



biogen idec



AstraZeneca 



genzyme

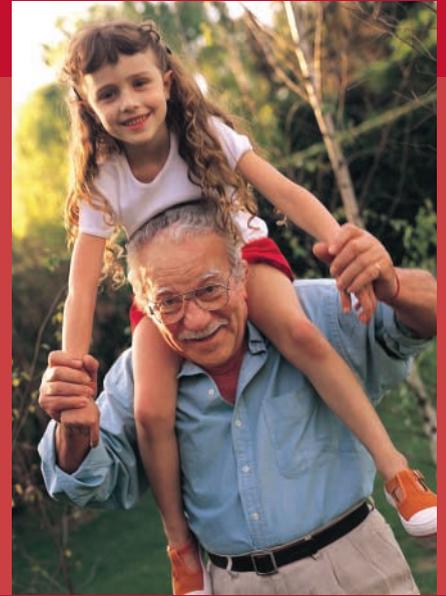
  
ImClone Systems  
Incorporated

**EPIX** Pharmaceuticals





PHYSICIANS  
AND PATIENTS



## → A Shared Trust with Physicians and Patients

Physicians and patients are indispensable partners, working with us toward our common goal – to bring to market new therapies that will profoundly improve the lives and health of patients in ways previously unachievable. Our active clinical development programs aim to serve:

**Families with hereditary angioedema (HAE).** HAE is a debilitating condition, characterized by unpredictable episodes of severe inflammation and pain, including life-threatening swelling of the larynx. With DX-88, we aim to provide a safe and effective treatment for these patients, many of whom are seeking an alternative to managing their attacks with anabolic steroids, which have significant side effects.

**Patients undergoing on-pump open-heart surgery (CABG).** This bypass procedure is performed over 500,000 times annually in the US alone. Blood loss, systemic inflammatory responses and neurological deficit are possible risks for these patients. DX-88 holds the potential to greatly reduce these risks.

**Patients with cystic fibrosis (CF).** CF is a serious genetic disease that compromises lung function, primarily in children, and significantly shortens their life span. CF requires constant care and medication to fight respiratory infections. DX-890 may help block the cycle of inflammation, infection and destruction of the lung tissue in patients with CF.

# Looking forward...

At Dyax, we have entered the year 2005 with great confidence in our current and upcoming clinical development programs, in the value that our collaborations provide, and in the unique ability of our internal proprietary discovery technology to continue to generate drug candidates today and long into the future.

Dyax is not a one-product company, but instead is actively engaged in the development of numerous compounds. Our discovery capabilities allow us to strategically choose which of the antibodies, small proteins or peptides from Dyax libraries to develop independently, and which to partner with experienced biotechnology and/or pharmaceutical companies. As financial resources and strategic fit allows, it is our ultimate goal to independently develop and market biotherapeutic products for patients in need of better, safer medicines.

We have successfully completed several clinical trials and are fully committed to moving those programs forward. We anticipate initiating new trials to further evaluate DX-88 in hereditary angioedema, including a pivotal Phase III trial and importantly, a Phase I volunteer study to evaluate the safety and pharmacokinetics of a subcutaneous formulation of DX-88. We are accelerating the development of a subcutaneous product because we believe that a formulation that can be easily administered will give patients the most control over the debilitating effects of HAE and will also maximize the market potential for DX-88 in this indication.

Also on the clinical trial front, once we have partnered the CABG indication, we anticipate starting Phase II trials for DX-88 in on-pump, open-heart surgery.

With respect to active clinical studies, we have additional results pending from our Phase II EDEMA2 trial of DX-88, as well as results from Debiopharm SA from their placebo-controlled Phase II trial of DX-890 in cystic fibrosis.

**Dyax remains focused on advancing its proprietary products – from discovery research, to clinical development, and ultimately into the marketplace – to make patients' lives better and to build value for our shareholders.**

We are very excited about our pipeline of clinical candidates against oncology and inflammation targets, and we expect to advance at least one of these into formal development this year. We also expect that trial results from our collaborators will further validate the quality of leads isolated from Dyax libraries.

We hope you share our enthusiasm for what Dyax has accomplished in 2004, and the potential that we see for growth and success in 2005 and beyond.

# Corporate Information

## DIRECTORS

### Henry E. Blair

Chairman, President and Chief Executive Officer, Dyax Corp.

### Constantine E. Anagnostopoulos, Ph.D.

Managing General Partner, Gateway Associates, LP

### Susan B. Bayh, J.D.

### James W. Fordyce

Managing Partner, Fordyce & Gabrielson, LLC

### Mary Ann Gray, Ph.D.

President, Gray Strategic Advisors, LLC

### Thomas L. Kempner

Chairman and Chief Executive Officer, Loeb Partners Corporation

### Henry R. Lewis, Ph.D.

Former Director, Genzyme Corporation

### David J. McLachlan

Senior Advisor and Former EVP and Chief Financial Officer, Genzyme Corporation

## EXECUTIVE OFFICERS AND KEY EMPLOYEES

### Henry E. Blair\*

Chairman, President and Chief Executive Officer

### Stephen S. Galliker, CPA\*

EVP Finance and Administration and Chief Financial Officer

### Lynn G. Baird, Ph.D.\*

SVP Development

### Robert C. Ladner, Ph.D.

SVP and Chief Technology Officer

### Ivana Magovčević, Ph.D., J.D.\*

SVP Legal Affairs and Chief Patent Counsel

### Clive R. Wood, Ph.D.\*

SVP Discovery Research and Chief Scientific Officer

### E. Fayelle Whelihan, Ph.D.

SVP Discovery Research and General Manager, Dyax SA

## TRANSFER AGENT

American Stock Transfer & Trust Company  
59 Maiden Lane  
New York, NY 10038

## LEGAL COUNSEL

Palmer & Dodge LLP  
111 Huntington Avenue  
Boston, MA 02199

## INDEPENDENT ACCOUNTANTS

PricewaterhouseCoopers LLP  
One Post Office Square  
Boston, MA 02109

## ANNUAL MEETING OF SHAREHOLDERS

Dyax's 2005 Annual Meeting of Shareholders will be held at 2:00 p.m. EST on Thursday, May 19, 2005 at Dyax Corp., 300 Technology Square, 8th Floor, Cambridge, MA. You are cordially invited to attend.

## STOCK LISTING

Common stock has been traded on the Nasdaq Stock Market under the symbol DYAX since our initial public offering in August 14, 2000.

The following table gives the quarterly high and low sales prices of our common stock for the last three years.

	2002		2003		2004	
	High	Low	High	Low	High	Low
First Quarter	\$11.38	\$3.10	\$2.25	\$1.52	\$14.54	\$7.56
Second Quarter	\$4.68	\$3.20	\$4.90	\$1.67	\$15.65	\$9.20
Third Quarter	\$4.20	\$1.65	\$7.50	\$2.58	\$11.97	\$6.30
Fourth Quarter	\$2.68	\$1.05	\$9.05	\$4.45	\$9.80	\$5.46

## FORM 10-K

Additional copies of Dyax's Annual Report on Form 10-K for the Fiscal Year 2004, as filed with the Securities and Exchange Commission, are available without charge upon request from:

Dyax Corp.  
300 Technology Square  
Cambridge, MA 02139  
ATTN: Investor Relations

## SAFE HARBOR

This annual report contains forward-looking statements regarding Dyax Corp., including statements regarding its revenues, results of operations, financial position, research and development expenditures and programs, clinical trials and collaborations. Statements that are not historical facts are based on Dyax's current expectations, beliefs, assumptions, estimates, forecasts and projections for Dyax and the industry and markets in which Dyax competes. Such statements are not guarantees of future performance and involve certain risks, uncertainties and assumptions, which are difficult to predict. Therefore, actual outcomes and results may differ materially from what is expressed in such forward-looking statements. Important factors which may affect future revenues, operating results, financial position, research and development programs, clinical trials and collaborations include Dyax's dependence on the expertise, effort, priorities and contractual obligations of its collaborators in the development, clinical trials, manufacture, marketing, sales and distribution of biopharmaceuticals developed by Dyax or its collaborators; the risk that biopharmaceuticals developed by Dyax or its collaborators may not show therapeutic effect or an acceptable safety profile in clinical trials or could take a significantly longer time to gain regulatory approval than Dyax expects or may never gain approval; Dyax's ability to obtain and maintain intellectual property protection for its products and technologies; the development of technologies or products superior to Dyax's technologies or products; and other risk factors described or referred to in Dyax's most recent Form 10-K and other periodic reports filed with the Securities and Exchange Commission. Dyax cautions investors not to place undue reliance on the forward-looking statements contained in this annual report. These statements speak only as of the date of this annual report, and Dyax undertakes no obligation to update or revise these statements, except as may be required by law.

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\*Executive Officer

# Advancing Novel Biotherapeutics



**Dyax**

**Dyax Corp.**

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**Other Offices**

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