

ICON plc annual report

2005



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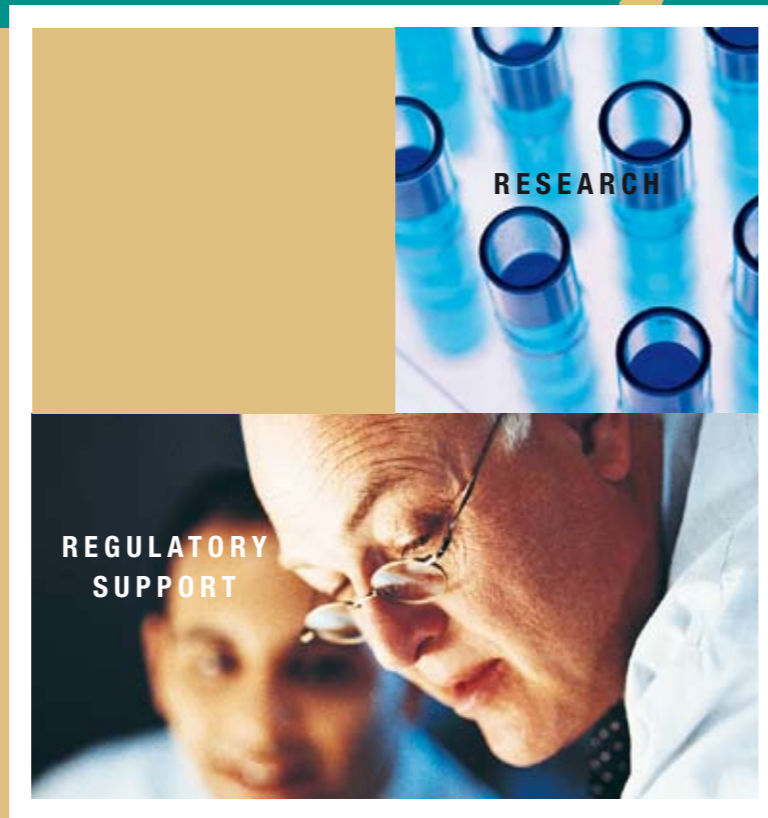
ICON offers a full range of clinical research and related support services to the biopharmaceutical and medical device industries.



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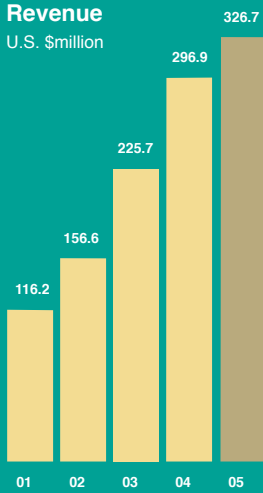
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# Global Full Services Drug Development 41 Offices in 27 Countries

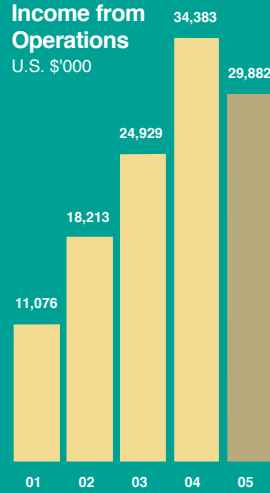


# Financial Highlights

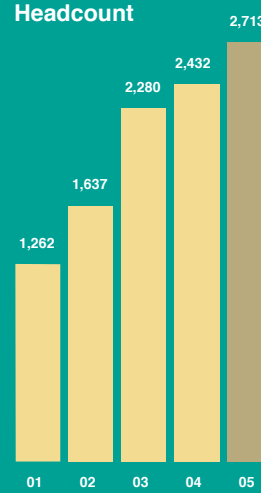
**Revenue**  
U.S. \$million



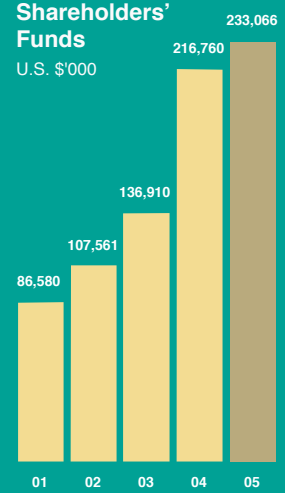
**Income from Operations**  
U.S. \$'000



**Headcount**



**Shareholders' Funds**  
U.S. \$'000



These services include strategic development and regulatory support, project management and execution of phase I-IV clinical trials, medical and safety support, data management, statistical analysis, central laboratory services for samples and images, interactive voice response systems and bioanalysis.



# Letter to Stockholders

The year to May 31, 2005 was a difficult one, representing the first year in 4 in which our earnings per share declined. Nonetheless we made significant progress in our strategic development and expect to resume growth in 2006, capitalising on continued strength in our underlying market.

The challenges in the year were largely driven by an exceptional level of cancellations in our clinical business during our first quarter ended August 2004, when projects valued at approximately \$47 million were stopped or were not commenced. While normally our cancellation rate is between 1-2% of our backlog, this level of cancellations represented 10%, and left us with significant excess capacity which took time to re-book. The reasons for these cancellations were outside of ICON's influence: 75% of them were related to decisions taken by clients in consultation with the FDA about the efficacy of the drugs in question or the appropriateness of the studies concerned and the remainder were related to internal budget allocation decisions by clients. These cancellations impacted primarily on our US Clinical business.

These challenges were compounded by a greater than anticipated impact of the European Clinical Trials Directive on our Phase I business in the UK. While, following the introduction of this legislation, the approvals process continued to operate quickly and efficiently, clients, anticipating delays and bureaucracy, placed their Phase I projects in countries other than the UK, leading to a drop in bookings and revenue for our unit, which in turn led to losses.

At the same time, our Central Laboratory business, having moved to a new facility in February 2004, continued to struggle with disappointing revenues, while costs increased as a result of the move and through the introduction of new testing capabilities.

Against this challenging backdrop, nonetheless, significant progress was made: the Lab achieved steadily increasing new business bookings through the year culminating in bookings of over \$20 million in the fourth quarter and total bookings for the year of \$49 million against revenues of \$26 million – a strong indicator of improved revenue performance in the year ahead; Strong overall bookings of \$327 million were achieved in the last three quarters compared to revenues of \$248 million in the same period – again a strong indicator of a resumption of growth; and our European and Rest of World Clinical business produced its best ever performance both in revenue and margin terms.

## **Strategic Development**

The market environment in which we are operating continues to be positive. We broadened our customer base, diversified our revenues and received record levels of "Request for Proposals" (RFPs) from customers and potential customers. We continue to believe that the use of outsourcing is growing and that global, full service providers are well positioned to meet the needs of the bio-pharmaceutical industry, particularly as it seeks to access broader patient groups in less developed regions of the world, and therefore expect continued strong business flows as a result.

Events in the industry in recent times have increased focus on safety monitoring of marketed drugs and of the need for more formal post approval studies.

While market growth continues, the approach being taken by our customer base varies. Small and mid-sized companies are seeking full service providers with strong scientific support. Some larger companies are seeking “strategic partnerships” with limited numbers of CROs in which pipeline visibility and resource availability is shared by the partners. Other large companies are continuing to use CROs on a purely tactical basis, while a couple of large companies are pursuing a “functional service provider” (FSP) approach whereby the many activities involved in clinical trials are outsourced on a function-by-function basis to different providers. ICON is working with all of these models. We recognise that we are a service oriented business and therefore must deliver to each of our customers the service that they specifically want.

Japan, the second largest pharmaceutical market in the world, has traditionally had a unique approach to clinical research. ICON has for a number of years aspired to establish an operational presence there, but remained cautious pending progress in the wider adoption of ICH/GCP practices. With significant progress having been made in this regard, we increased our commitment to the Japanese market during the year and were rewarded with our first major project win in that country towards the end of the financial year. We expect to build on this in the year ahead and aspire to become a leading CRO in the Japanese market over the next five years.

Events in the industry in recent times have increased focus on safety monitoring of marketed drugs and of the need for more formal post approval studies. ICON has, over the last several years, been developing its stand-alone pharmacovigilance capabilities, and achieved significant progress in marketing this service during the year. In addition, we established a specialised group to design and manage Phase IV (safety) programmes, and they have already won business and have a growing pipeline of opportunities.

Our interactive voice response systems division (IVRS) continued to grow strongly during the year, driven by increasing demand for, not only automated patient randomisation and drug supply management, but also electronic patient diary systems. As we discussed in this letter last year, many trials can best be served using simple phone technology for data collection rather than more complex web-based systems. Nonetheless, there are also many trials that require more detailed data, where web-based systems are more suited. Recognising this, we entered into a partnership with Medidata Systems Inc. during the year. As a result, when clients request electronic data capture for more complex trials ICON is recommending and collaborating with Medidata in responding. While the transition from paper collection of clinical data continues to be slow, momentum is building, and we believe our partnership with Medidata positions us well in this regard.

# Letter to Stockholders

As ICON approaches 3000 employees we reflect on the exciting journey we have made over the last 15 years from a minor regional CRO to a leading global player.

## The Future

With strong innovation continuing among biotech and specialty companies, we believe we will increasingly need to provide strong scientific and medical input to such companies. Recognising this we have acquired a number of key businesses in recent years including our Phase I unit, and regulatory and drug development consultancies. We have recently unified these specialist units and intend to expand them both through acquisition and organic growth.

The increasing globalisation of clinical research has created strong growth opportunities for our operations in Eastern Europe, Latin America and Asia including China and India. We anticipate further strong growth in these areas in the years ahead as we respond to client needs.

Meanwhile our core activities in the US and Europe continue to grow organically, and we expect to make further acquisitions to build on our strengths and supplement our services in these regions.

As ICON approaches 3000 employees we reflect on the exciting journey we have made over the last 15 years from a minor regional CRO to a leading global player. This could not have been achieved without the efforts and dedication of all of our staff and we would like to extend our appreciation to them on behalf of you, our shareholders.

**Dr. John Climax**  
*Chairman*

**Peter Gray**  
*Chief Executive*



# PHASE I-IV

ICON manages Phase I-IV clinical trials in all major therapeutic areas and focuses on delivering quality data on or ahead of schedule. ICON has the global resources, systems and infrastructure in place to take on global mega trials, but remains flexible enough to provide an individual, highly personalised service for locally managed projects.





# PHASE I

Phase I clinical trials have traditionally focused on assessing safety and tolerability in man. In modern drug development, successful companies must decide very quickly whether to proceed with their development strategies or to abandon further development based on the safety, tolerability, pharmacodynamic and pharmacokinetic properties on biologicals and new chemical entities (NCEs). Moreover, additional regulatory requirements include studies evaluating drug-drug interactions, effects of food on absorption and metabolism, special populations such as the elderly, renally-impaired, or hepatically-impaired subjects, and other studies targeted to better understand the characteristics of the drug before broad exposure to patients.

ICON has extensive experience in the design, implementation and interpretation of clinical pharmacology studies in all major therapeutic areas. We have one of the world's most innovative and internationally recognised Phase I units. The clinical pharmacology team can assist with traditional pharmacokinetic studies such as First in Man (FIM) studies as well as cutting-edge pharmacodynamic assessment as a means of assessing the potential efficacy of biologicals and NCEs prior to Phase II studies in patients.

Our consultancy services provide expert solutions based on extensive experience with biologicals and novel NCEs and a focus on the dose-scaling from animals to man, enabling us to identify and develop potential surrogate markers and models for use in later clinical development phases.

Once the biologicals and NCEs have been extensively studied in normal volunteers (100-200 volunteers) to determine the maximally tolerated dose, absorption, distribution, metabolism, excretion, and potential pharmacodynamic properties, it can then be introduced into the target patient population.

Phase II studies are designed to evaluate the short-term effectiveness of biologicals and NCEs and to enhance the understanding of its dose-response and safety profile in patients. This second phase of testing may last from several months to two years, and involve up to several hundred patients. Most Phase II studies are randomised trials. One group of patients will receive the experimental drug, while a second “control” group will receive a standard treatment or placebo. Often these studies are “blinded” – neither the patients nor the researchers know who is getting the experimental drug. Only about one-third of experimental drugs successfully complete both Phase I and Phase II studies.

Identifying the right patient population is essential when entering into Phase IIb/III. ICON’s global feasibility group has conducted hundreds of feasibility assessments for our clients in all therapeutic areas. This focused area of expertise reduces the risk in patient identification and recruitment by systematic evaluation of the clinical investigator site, standard of care, and the regional distribution of centres to meet the objectives of the study protocol.

Regulatory agencies often require an end of Phase II meeting and review of the data before companies expand into larger global Phase III studies. These meetings help companies to define protocol efficacy and safety measures as well as total patient exposure to the NCE. From these meetings, a final Phase III development plan is agreed upon, and Phase III trials can begin.

# PHASE II





# PHASE III

In a Phase III study, a drug is tested in several hundred to several thousand patients. These large-scale studies provide the pharmaceutical company and regulatory agencies with a more thorough understanding of the drug's effectiveness, benefits, and the range of possible adverse reactions. Most Phase III studies are randomised and blinded trials.

Phase III studies typically last several years. Seventy to 90 percent of drugs that enter Phase III successfully complete this phase of testing. Once a Phase III study is successfully completed, a pharmaceutical company can request approval for marketing the drug.

Phase IIIb studies are often done while awaiting, or after, regulatory approval to find additional uses for the drug or to prove that prolonged use enhances mortality and/or quality of life.

As our clients reach Phases III and IV they find more often than not that as the patient numbers increase the patient costs also increase. At ICON, we have developed many innovative ways to reduce these costs while maintaining exceptional and reliable data.

Phase IV studies occur after the product receives regulatory approval. These studies are used to characterise the effectiveness and safety of a product in the general patient population under conditions of typical use. In some cases, regulatory agencies may mandate post-marketing surveillance studies as part of the approval process. Typically, very large numbers of patients are involved in these studies which may also be global in reach.

ICON's Phase IV and peri-approval services help sponsors respond to regulatory needs and marketplace opportunities. ICON's strategy is to create cost-effective study solutions for late phase requirements by marrying the expertise acquired from early development to innovative, streamlined processes developed specifically to enhance large scale studies. Utilising the breadth of ICON's resources and knowledge, this area offers a wide variety of research methodologies aimed at defining and communicating the value of products to the marketplace so that good products can achieve their maximum potential.

# PHASE IV

# Overview

The financial year to May 31, 2005 was a difficult one, due to the exceptional level of cancellations we experienced in the first quarter of the fiscal year. Despite these challenges we achieved revenue growth of 10% with Group revenues of over \$326 million for the year. Growth was strong across most of the regions, ICON's European region grew over 20% and ICON's Rest of World region grew 73%, while ICON's US region only grew 1% in the year, as the cancellations we suffered significantly impacted on this region.

ICON has continued to see the volume and value of requests for proposals (RFPs) increase significantly, indicating that the market for our services continues to strengthen. During the financial year we were awarded over \$436 million of new business, of which over \$52 million related to our Central Laboratory. As a result our total backlog at May 31, 2005 was over \$528 million, up 14% from the previous year.

Operating margins declined in the period to 9.1% from 11.6% in fiscal 2004. Given the challenges it faced, ICON's Clinical business performed satisfactorily, with operating margins of 12.1%. ICON's Central Laboratory business had another poor year recording losses of \$6.5 million.

## Growth

At May 31, 2005 ICON employed 2,713 people of whom 1,470 were located in the USA, 1,043 were located in Europe and 200 were located in ICON's Rest of World region. The acquisition of 70% of Beacon Biosciences Inc. added approximately 45 employees in the USA.

To accommodate this growth and to enable future growth ICON has continued to expand its existing infrastructure and also expanded its geographic presence with the creation of operations in Chennai, India, São Paulo, Brazil and Mexico City, Mexico.

Beacon, ICON's specialist medical imaging group, focused on the centralised management, processing and reading of digitised medical images generated in clinical trials has provided ICON with an excellent foothold in the developing centralised imaging market. The integration of Beacon progressed well during the year.

ICON's revenue growth in fiscal 2005 was lower than has been traditionally achieved, which may appear contradictory when you consider the strength of the Phase I-IV outsourcing market. Indeed ICON's European and Rest of World Phase II-IV businesses benefited greatly from the strong market fundamentals. Unfortunately, ICON's US Phase II-IV business did not grow as we would have expected, as it had to overcome the challenge of cancellations in the early part of the year. ICON's Phase I business in the UK also had to overcome the challenge of the European Clinical Trials Directive which was introduced during the year and the Central Laboratory business, while having great success in winning new business, will not see the benefit from these awards in terms of revenue growth until next year.

At May 31, 2005 ICON employed 2,713 people of whom 1,470 were located in the USA, 1,043 were located in Europe and 200 were located in ICON's Rest of World region.

We continue to focus on ways to enhance margins and shareholder value. We expect good growth in the coming year and believe we are well positioned to achieve it.

### **The Future**

Despite the challenges of the year we have continued to invest in infrastructure, systems, technology and people. During the year we invested heavily in a number of collaboration, training and communication tools, which will facilitate the ongoing growth of the organisation and assist ICON in maintaining its client-focused culture.

We have also introduced ICON's new project management system which has been in development for a number of years. This system is the new backbone infrastructure for clinical project management and will play a pivotal role in ensuring the quality execution of clinical trials managed by ICON. ICON has also launched a systematic internal process review project. The purpose of this review is to find and implement improvements in ICON's processes, to ensure the organisation is operating at the highest standards and also to ensure that all processes and procedures are as efficient as possible. This project is aptly named IMPROVE and is affecting all levels and groups within ICON.

We have come through a difficult year, our Phase I business has recovered from the effects of the European Clinical Trials Directive, our US Phase II-IV business is hiring strongly and our Central Laboratory makes good progress towards the achievement of a breakeven performance.

We continue to focus on ways to enhance margins and shareholder value. We expect good growth in the coming year and believe we are well positioned to achieve it.

# Directors and Other Information

## Directors

John Climax *Chairman*  
Peter Gray *Chief Executive Officer*  
Ronan Lambe *Director*  
Edward R. Roberts *Director* †§x  
Thomas G. Lynch *Director* †§x  
Shuji Higuchi *Director*  
Bruce Given *Director* †§x

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Ciaran Murray

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Ireland

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10005 USA

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Chartered Accountants  
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Ireland

Ronan Lambe  
*Director*



Shuji Higuchi  
*Director*



Thomas G. Lynch  
*Director*



Bruce Given  
*Director*



Peter Gray  
*Chief Executive Officer*



John Climax  
*Chairman*



Edward R. Roberts  
*Director*

† Member of Audit Committee  
§ Member of Compensation Committee  
x Member of Nomination Committee

Statements made in the Annual Report that are not descriptions of historical fact may be forward-looking statements that are subject to risks and uncertainties. ICON's actual results could differ materially from those currently anticipated due to a number of factors including, but not limited to, those identified in Form F-1 and Form 20-F as filed with the SEC. All references to historical financial information are based on US accounting principles.

**ICON plc**

American Depository Shares are traded on  
the NASDAQ National Market (Symbol ICLR)

**Depository for ADS**

Bank of New York  
101 Barclay Street  
New York 10286

**Register for Ordinary Shares**

Computershare Services (Irl) Limited  
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