



# Excellence in Drug Development for Metabolic Disorders

We work to find a better way.

We work to raise standards and deliver more.

We break new ground to make progress possible.



# Excellence in Metabolic Disorders

## **The experience you need from the people you trust.**

ICON's therapeutic focus capitalizes on expertise in drug development, biomarkers and management of global trials in diabetes, obesity, dyslipidemia and metabolic syndrome.

ICON has made the strategic decision of developing a leadership position in this area to apply speed, science, flexibility, and superior quality to your development needs.

## **“The ICON added value.**

The in-depth expertise in Metabolic Disorders of ICON Clinical Research, ICON Development Solutions, and ICON Central Laboratories, enables us to share a unique experience and insight into the management of clinical programmes, and development plans in this therapeutic area.

Your product will be in the capable hands of teams familiar with the challenges of programmes in Metabolic Disorders. ”

## **Didier Saur, MD**

**Global Therapeutic Head of Metabolic Disorders**

# The Global Epidemic

## “The Global Epidemic” (WHO, 1997)

According to the World Health Organization at least 180 million people worldwide have diabetes today and the experts are predicting that by 2030 the figure will have doubled to reach 360 million. It is estimated that approximately 2.9 million deaths per year are attributable to diabetes.

The disease is most prevalent in working age adults in developing countries and disadvantaged minorities and is driven by an aging demographic profile and an increase in obesity.

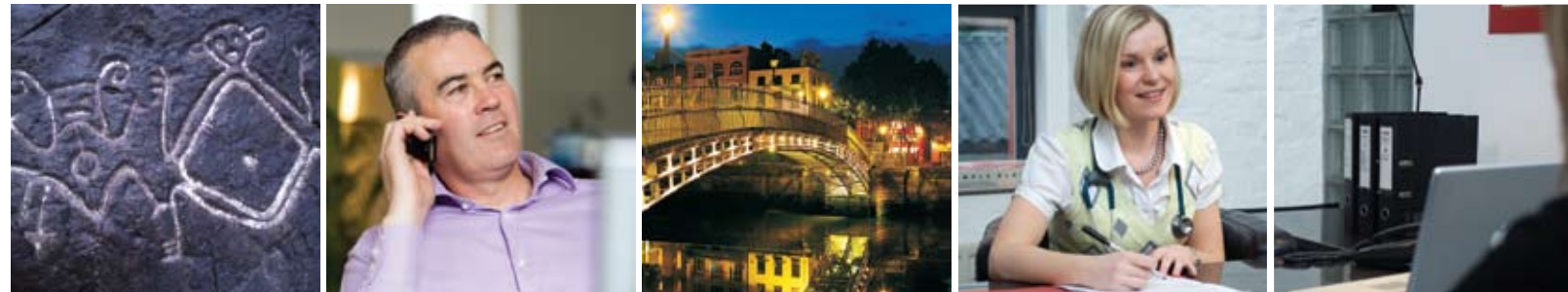
It is estimated that globally 1.6 billion adults are overweight and at least 400 million are obese.

While considered initially a problem in high-income countries, obesity is now dramatically on the rise in low- and middle-income countries, particularly in urban settings.

According to IMS Health, sales for diabetes treatments were US\$6 billion in the USA in 2007. Global anti-diabetic drugs sales are expected to grow dramatically over the next years to over US\$22 billion in 2012 as the patient population rises and demand increases.



While for sponsors the development of new and improved diabetes compounds present significant market opportunities there are some major challenges to overcome if new drugs can be released on schedule and within budget.



# The ICON Solution

To overcome the challenges of clinical development in Metabolic Disorders, we have created the Therapeutic Area Groups. A group of experts in Metabolic Disorders for the level of support your program needs.

## Therapeutic Area Group (TAG)

Clinical development of a product in diabetes is driven by FDA and CHMP Regulatory guidelines, however several options are available and to avoid the potential pitfalls, expertise in drug development and clinical data generation is critical.

At ICON we do believe that therapeutic expertise is a key component of the successful delivery of our programmes.

- The TAG members are from different ICON departments and divisions, but share a common expertise in Metabolic Disorders in their area of competence: medical, operations, statistics, laboratory, consulting.
- ICON's TAG members provide therapeutic indication training to the project team that will enable the team to get up and running sooner and meet aggressive timelines.
- TAG members accompany and provide support to the Project Manager during the course of the project. They are a permanent resource for the project team.



# Challenges and Solutions

## Accelerated Patient Recruitment

One of the biggest challenges in Diabetes trials is recruiting patients that are treatment naïve. In Western Europe, US or Australia, diabetic patients are treated in an early stage of the disease and in accordance with international accepted guidelines e.g. ADA, IDF or national guidelines.

- New regions for clinical research such as Eastern Europe, India and South America have been found to have a larger pool of patients with higher rates of patient retention.
- ICON has a network of offices across these regions and has developed strong relationships with highly motivated sites.
- Our PER (Patient Enrolment and Retention) group has developed tools and collaborations to accelerate patient recruitment in studies in Metabolic Disorders.
- Our experience in diabetes trials contributes to accelerated rates of patient enrolment.

## Efficient, Effective and in Compliance

Clinical trials in new regions require understanding of local regulation, health care systems and cultures.

- Our Feasibility group has an extensive experience in the conduct of comprehensive feasibility studies. Their expertise in feasibility coupled with the ICON experience in Metabolic Disorders allow us to develop the best strategy for country and site selection.
- ICON's Regulatory specialists provide the expertise required for the submission of Ethic Committee and Regulatory dossiers enabling rapid start-up for the sponsor.
- We provide insight into obstacles that may arise, for example placebo controlled studies in selected countries, technical requirements of sites and competing studies in Metabolic Disorders.
- We have developed an extensive network of qualified investigators in every region and every country to support clinical studies in Metabolic Disorders. As testified in industry surveys, at ICON we believe in investigators relationships.

# Expertise and Support

## Influential Key Opinion Leader Support

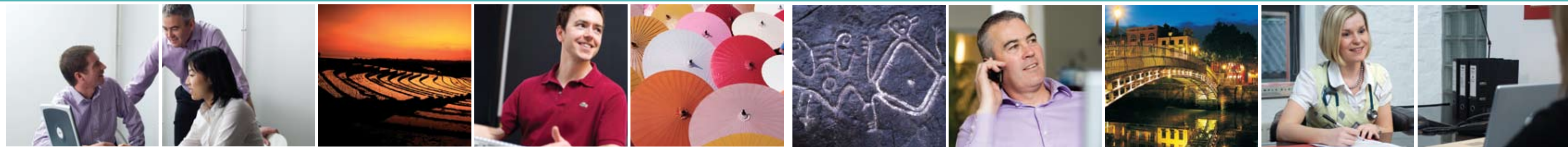
Key opinion leaders can be crucial to the success in developing and marketing drugs. Conducting trials in new regions brings the challenge of ensuring that the drug discovery gains the appropriate profile in the Western European and US medical community to be able to contribute to the overall success of the project.

- Development of a communication and relationship management plan ensures that critical information is communicated to the right people at the right time and through the most effective channels.
- ICON understands the issues and can provide the solution to ensure your clinical trial is planned to take advantage of new territories with the balance of KOL support in Western Europe and the US.

## Project Management Expertise

Multinational clinical trials can present challenges in coordination and communication.

- ICON's project management and monitoring experience extends to local, regional and multinational studies in Metabolic Disorders, providing the sponsor access to a wide range of study design options suited to individual product development needs.
- Our extensive domain knowledge of trials in Metabolic Disorders together with our global full service capabilities can expedite the successful delivery of compounds to market.



ICON has extensive experience in running global studies in Metabolic Disorders. We use this experience to design trials that meet our sponsor's objectives and consistently deliver quality data and results.

We apply our knowledge and expertise to successfully solve the challenges that arise during every clinical study.

# Excellent Experience

## Our Experience In Diabetes Includes:

- Insulins, insulin secretagogues, thiazolidinediones, metformin, DPP-IV inhibitors and other new classes.
- Recruitment of diverse patient populations: treatment naïve, monotherapy, combination therapy, including insulin add-on, diabetic complications.
- Placebo or active controlled studies, pivotal or proof of concept studies (including clamp studies), HbA1c or cardiovascular outcome studies

Our experience in **dyslipidemia** covers statins, fibrates or other drugs, and the latest drugs have been tested in the **obesity** studies performed by ICON.

Through our work in this area we have a deep understanding of the safety and development issues associated with these classes of drugs.

## Case Studies

### Prevention of diabetic retinopathy progression in Diabetic type I & type II patients

**Number of patients:** 5,231  
**Number of sites:** 310  
**Global:** 30 countries

**Key Challenges:**  
 Patient recruitment and retention  
 Competing diabetes studies

**ICON solution:**  
 ICON used its previous experience and database to develop targeted patient recruitment strategy

**Outcome:**  
 Completed on schedule  
 Patient retention of 94% over 7 years

### Cardiovascular outcome study in diabetic type II patients

**Number of patients:** 5,238  
**Number of sites:** 321  
**Global:** 19 countries

**Key Challenges:**  
 Patient recruitment and retention  
 Competing diabetes studies

**ICON solution:**  
 ICON appointed a dedicated resource to lead and used its geographical reach and experience to choose sites that met key criteria

**Outcome:**  
 Completed ahead of schedule  
 Only 2 patients lost to follow-up (average follow-up: 34.5 months)



# Our People Make the Difference

At ICON we have highly skilled individuals from various disciplines who can provide you with advice on your metabolic disorder programme.

They provide guidance in the following areas:

- Drug development planning
- Project management
- Regulatory Affairs
- Medical affairs and pharmacovigilance
- Biometry
- Laboratory and biomarkers
- Imaging and central reading

We continue to invest heavily in highly qualified professionals with specific experience in Metabolic Disorders drug development.

Region	CRAs	CPMs
US	232	67
EU	247	56
ROW	97	22
<b>Total</b>	<b>576</b>	<b>145</b>

In each region we have a large number of CRAs and Project Managers with experience in Metabolic Disorders. More than 40% of our PMs have experience managing projects in diabetes or related disorders.

# Our Global Metabolic Disorders Experience

ICON has an extensive experience in running projects in Metabolic Disorders. Our teams have conducted 229 projects over the last 5 years, representing more than 100,000 patients, and 14,000 sites.

ICON's global experience over the past 5 years in Metabolic Disorders

Indication	No. of Studies	Regions	Patients	Sites	Phase
Diabetes mellitus	152	Asia, Central Europe, Latin America, North America, South Africa, Western Europe	40,391	9,170	Phase I, IIa, IIb, III, IIIb, IV
Diabetes mellitus, dyslipidemia	1	North America	1,100	160	Phase III
Diabetes mellitus, hormone deficiency	1	United States	130	11	Phase IV
Diabetes mellitus, obesity	3	Latin America, North America, Western Europe	2,430	218	Phase I, IIb, III
Diabetic nephropathy	5	Asia, Central Europe, North America, Western Europe	4,568	906	Phase III, IIIb
Diabetic neuropathy	10	North America	3,276	206	Phase I, II, III
Diabetic retinopathy	1	Australasia, Central Europe, Western Europe	5,231	309	Phase III
Hypercholesterolemia	31	Australasia, Asia, Central Europe, Latin America, North America, South Africa Western Europe	33,218	2,729	Phase I, IIb, III, IIIb, IV
Hypercholesterolemia, obesity	1	Australasia, Latin America, North America, Western Europe	1,980	66	Phase III
Metabolic syndrome	2	NA	NA	NA	C
Obesity	22	Australasia, Latin America, North America, Western Europe	7,884	492	Phase IIb, III, IV
<b>TOTAL</b>	<b>229</b>		<b>100,208</b>	<b>14,267</b>	

Table correct as of June 2008

Metabolic Disorders represents a strong area of business for ICON, and we continue to invest heavily in highly qualified staff with specific experience in diabetes drug development and related diseases.



A Symbol of Excellence

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