ESTERN Medical CRO
Diagnostic Radiological Imaging Research & Innovation in Radiopharmaceuticals for MRI/MRA/CT/PET Clinical Research Trials
ESTERN Medical is the CRO of choice for Diagnostic Radiological Imaging Clinical Trial studies across Latin America.
The last 10 years have seen the emergence of a major conceptual change spanning several medical disciplines. This movement has led to the creation of translational medicine. The concept of translational medicine is based on an effort to bridge preclinical and clinical trial phases for strictly similar biological targets (and consequently clinically pertinent) and on monitoring therapeutic treatments, both for developing new molecular entities and monitoring responses to treatment through biomolecules already on the market. Translational research constitutes a very positive trend for medical imaging, and in particular, molecular imaging.

Molecular imaging makes it possible to visualize processes that are the very basis of life. The revolution within molecular biology has contributed in recent years to the development of imaging, making it possible to understand the inner mechanisms of cell function within its environment. The ability to be able to perform this identification within a living organism is the objective of molecular imaging.

**MAJOR TRENDS IN MOLECULAR IMAGING**

“Functional” imaging is currently in a phase of significant expansion in response to a need to describe with precision certain biological processes, within the framework of anti-tumour products; eg. antiangiogenic or antivascular molecules. The benefits of this approach are substantial, contributing significantly to a better understanding and diagnosing pathological processes. Furthermore, it leads to the development of new treatments as well as monitoring their effect on patients.

It is easy to anticipate that these two concepts (that are of course linked) will in the medium term considerably contribute to advances in medical imaging:

- Medicine referred to as “personalized” requiring the availability of validated biomarkers;
- “Theranostics” is the association of a targeted therapeutic agent and an agent with a targeted diagnostic application, or an agent contributing to monitoring the efficacy of treatment.
- Anatomical Imaging
- Functional Imaging
- Molecular Imaging
I. CARDIOVASCULAR DISEASES
KEY FACTS

Cardiovascular illness is the leading cause of mortality in the world (29% of mortality worldwide) or 17.1 million deaths.\(^{(1)}\)

- 42% of these deaths are the result of coronary heart disease
- 33% of these deaths are the result of a cerebral vascular accident (CVAs)\(^{(2)}\)

**Needs**
Preventing the risk of CVAs.

**The Trial Challenges**
Develop a clinical trial product capable of discriminating at risk from stable plaques. The rupture of vulnerable plaque is one of the primary causes of CVAs.

*Sources:*
(1) World Health Organization (WHO), September 2009
(2) World Health Organization (WHO), most recent statistics, 2004

II. CANCER
KEY FACTS

2nd cause of death in the European Union.\(^{(1)}\)
3.4 million new cases of cancer diagnosed and 1.8 million deaths caused by cancer in Europe in 2008.\(^{(2)}\)

**Needs**
Adapting treatments to the patient (personalized medicine). Identifying the incidence of recurrence reliably.

**The Trial Challenges**
Developing a specific product for the detection of ovarian cancer recurrence and the monitoring treatments.

Developing an agent to evaluate prognosis before treatment and monitor the antitumor therapies, more specifically targeted therapies.

*Sources:*
(1) International Agency for Research on Cancer (IARC), Lyon, 2007

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**Examples of key molecular imaging applications**

- **Prevention**
  - Prevention of CVAs
    - Detection of at risk atheromatous plaque

- **Diagnostics**
  - Diagnosis of Alzheimer disease
    - Protection of the build up of Aβ plaques

- **Aid for treatment**
  - Evaluation of tumoral exeresis by imaging

- **Monitoring**
  - Cellular therapy
    - Monitoring stem cell implants
  - Monitoring antiangiogenic treatment
    - Evaluation of the efficacy of glioma treatment
  - Monitoring treatment by an anti-atheroma agent
    - Evaluation of the inflammatory response of carotid plaque
III. INFLAMMATORY AND NEURO-DEGENERATIVE DISEASES

KEY FACTS

In the USA & Europe, Alzheimer’s disease affects more than 14 million people.

The total cost of healthcare for patients affected by this disease is estimated at $100 billion US/Dlls per year.

Needs
Contribute to early and reliable diagnosis of Alzheimer’s disease to improve treatment responses.

Facilitate evaluation of the efficacy of new treatments.

The Trial challenge
Develop a contrast agent to detect neural inflammatory processes associated with Alzheimer’s disease lesions.

Developing a specific product allowing direct visualization of lesions and contributing to improve monitoring of treatment.

A major research initiative

- Our goal is to push the boundaries of MRI applications
- Contribute to the evolution of MRI to meet new diagnostic requirements
- Move from anatomical to molecular imaging
- Increase sensitivity in contrast and spatial resolution
- Meet the challenges posed by increased magnetic fields
- Adopt an integrated vision of the technology product machine concept

CONCLUSION

Since the early 2000’s, ESTERN Medical CRO has contributed to major advances in clinical trials medical Diagnostic Radiological Imaging to achieve improved patients care throughout the world.

Through its recognized expertise in CT, PET and MRI and its extensive product range (MRI and Nuclear Medicine), ESTERN Medical assists in the Pharmaceutical, Biotech & Medical Device R&D of healthcare companies and professionals (radiologists, cardiologist, oncologists...) in achieving better diagnosis of patients and better targeting of their treatment.

ESTERN Medical intends to deploy its scientific and clinical expertise and innovation in the service of the major Pharmaceutical and Medical Device health care challenges of the 21st century. Our mission is to guide, support and contribute as a CRO to advances in diagnosing major pathologies by proposing innovative and effective imaging trial solutions to achieve improved patient care throughout the world.

We know that future products will target anomalies at the molecular level and will make it possible to apply personalized treatment solutions for highly disabling pathologies. To achieve this objective and invent a new generation of contrast agents, ESTERN Medical Research and Clinical Development teams, to maximize their own efforts at innovation, are supported by many years of productive scientific and technological partnerships, notably through highly reputed international Research Networks of Excellence.

This commitment to innovation focused on improving the care and treatment provided to patients also requires close collaboration with sponsors and clinical practitioners.

Our Knowledge is in:

*Evaluating cardiovascular risk
*Achieving more precise diagnosis of tumors and evaluating the therapeutic response
*Early detection of Alzheimer’s disease
OUR BROAD RADIOLOGICAL TRIAL EXPERIENCE

ESTERN Medical personnel and senior executive management provide Pharmaceutical & Medical Device companies with considerable experience using radiological imaging as part of clinical trials.

In Latin America we have successfully managed a wide range of radiological imaging studies across multiple imaging modalities looking at a diverse a number of indications; products that are now on the global market.

OUR NET RADIOLOGICAL IMAGING COVERAGE ACROSS LATIN AMERICA

ESTERN Medical is able to offer scientific and senior team members that not only have considerable hands-on clinical trial experience, but who also have excellent relationships with imaging investigators and key opinion leaders.

With rapid access to eligible patients across a wide geographical area – ESTERN Medical has the unique ability to tap into underutilized patient populations in diverse locations in Latin America - which has allowed us to build a reputation as the primary CRO to be relied upon to meet or exceed patient recruitment targets.

This includes considerable experience in securing patients for studies where timely recruitment has been a problem, through opening up sites in new geographies and working with clinical sites that have a track record for rapid recruitment.

We utilize our proprietary database of key clinical sites to drive recruitment targeting specific or general patient populations for any indication.
OUR LEADERSHIP EXPERTISE & TRACK RECORD

Dr. Jorge L. Estrella M.D.
President & Chief Medical Officer.

Dr. Estrella is the founding President & Chief Medical Officer of ESTERN Medical, Clinical Research Organization (CRO) Group Globally.

Dr. Estrella brings more than 15 years of experience in the clinical research development programs in diverse global corporate pharmaceutical and medical device companies, with an extensive experience in the areas of Cardiovascular, CNS, Infectious Diseases and Diagnostic Imaging clinical research development.

Prior to founding the ESTERN Medical CRO Group, Dr. Estrella has held diverse positions in the clinical development research field, at EPIX Pharmaceuticals Inc., as the Director Clinical Development, in Cambridge-Boston, Massachusetts, during the business and R&D collaboration-partnership with Schering Pharmaceuticals AG & Berlex Laboratories LLC. (Now known as BSP - Bayer Schering Pharma AG).

During his work life at EPIX he was in charged of two of the most important company novel drug development clinical compounds INDs & NDAs agents at EPIX Pharmaceuticals brand name Vasovist® (gadofosveset Trisodium) or also know as ABLAVAR®. The First Imaging Agent Approved For Magnetic Resonance Angiography (MRA / MRI) in the U.S. an injectable intravascular contrast agent designed to provide improved imaging of the cardiovascular and peripheral artery system through magnetic resonance angiography imaging (MRA / MRI) approved for global marketing in the United States, Europe and in 40 countries and EP-2104R a diagnostic radiological imaging novel pharmaceutical agent under present development, designed for enabling detection of blood clots using Magnetic Resonance Imaging.

Prior to joining EPIX Pharmaceuticals, he worked in the Medical Device industry as as the Senior Physician Director-Clinical Trials Coordinator at Guidant Corporation Inc., (ACS) Advanced Cardiovascular Systems in Santa Clara California Peripheral & Stent Division, (now known as Boston Scientific Inc). Having culminating with Guidant, with the HERCULINK® Stent platforms.

A CNS extensive knowledge working in collaboration in the global clinical CNS development of RISPERDAL® (Risperidone) and Antipsychotic drugs used to treat symptoms of psychiatric disorders such as schizophrenia and bipolar disorder, where he held a positions in the medical clinical research department at Janssen Pharmaceuticals Inc.
Robert Morgan, J.D., M.S. & B.S.
Head Scientific Regulatory Legal Affairs & Quality

Mr. Robert Morgan, is the Head Scientific Regulatory Legal Affairs & Quality at ESTERN Medical CRO Global Group. He is one of the key members of ESTERN’S Corporate Scientific Advisory Board since April 2009. Mr. Morgan also serves as the Senior Vice President, Regulatory Affairs, Quality, and Clinical Development and has served in that capacity since June 2006 at ZIOPHARM Oncology, Inc.

Mr. Morgan is a Multi-faceted, hands-on, senior level Clinical and Regulatory Executive, with over 25 years experience in all areas of drug development, in the United States, Canada, Europe, India, Pacific Rim and Latin America. Author of numerous successful IND, NDA and Orphan Drug submissions, specializing in innovative treatments across multiple therapeutic areas, particularly Oncology and Diagnostic Radiological Imaging.

His Diagnostic Radiological imaging Track Record:
*EPIX Pharmaceuticals Inc., Previous Senior Executive Director of Regulatory. Key project Vasovist® First Imaging Agent Approved For Magnetic Resonance Angiography (MRA / MRI) in the U.S. an injectable intravascular contrast agent designed to provide improved imaging of the cardiovascular and peripheral artery system through magnetic resonance angiography imaging approved in (40) countries & EP 2104R, an MRI imaging contrast agent designed for the detection of blood clots.

• Dupont Pharmaceutical® / Bristol Myers Squibb / now known as Lantheus Medical Imaging as Previous Director Regulatory.
• Cardiolite®/Miraluma® (Technetium Tc99m Sestamibi for Injection), the world’s leading cardiac perfusion imaging agent and also approved as breast cancer imaging agent; DEFINITY® Vial for (Perflutren Lipid Microsphere) Injectable Suspension, the leading cardiac ultrasound contrast agent in the US.

Mr. Morgan received his Law Degree from the Massachusetts School of Law, and completed his Masters, in Radiation Biophysics at the University of Kansas City. He studied his BS in Zoology from the University of Massachusetts.

Claudia M. Hernandez Castro. B.S., RPT. & MRI-Tech.
Director Clinical Operations Latin America

Mrs. Hernandez most recently prior to join in the ESTERN Medical CRO Group was the senior manager of clinical, technical and education training support for Medrad Inc. a subsidiary of Bayer-Schering Pharma AG, where she initiated a strategy that helped transform Medrad Inc. in Latin America from a distribution platform company to a fully independent clinical and training network structure in South America. Ms. Hernandez spent 10 years with Medrad Inc. culminating in her role with two of the most important company platforms, the Avanta cardiovascular interventional injector and most important the Stellant Dual Injector System for Multi-slice CT clinical support training for the Latin American region.
She develop the key strategies for Schering Pharmaceuticals in diverse diagnostic imaging compounds (e.g Magnevist, lopamidol and Levovist), contrast media agent sfor MRI & CT Intra- Individual Dose Comparison continuing clinical trials studies in Latin America Phases III -IV.

Prior to joining Medrad Inc., she was the senior manager of clinician MRI specialist for Siemens Medical Latin America with diverse responsibility from clinical training through commercialization. Previous to her experience in the pharmaceutical & medical device industry she endure her clinical experience as a chief of MRI technologist in South America and as clinical physical therapist where she did practice as clinician for more than 10 years. Mrs. Hernandez is internationally well recognized for her broad expertise in clinical and diagnostic field, in some of the most prestigious medical institutions in the field of cardiovascular, peripheral vascular diseases, interventional cardiology and diagnostic CT, MRI imaging.

Mrs. Hernandez holds BS in Clinical & Physical Therapy from the University of the Rosario in Bogotá, Colombia and Masters in Technical Diagnostic Imaging from the University of Santander in Bogotá, Colombia.

Mike Webb  
Head of Corporate Advisory Board Member at ESTERN Medical.

Mr.Webb was previously the CEO of EPIX Pharmaceuticals, Inc. from 1994 through 2005.

With key success approval of Vasovist® Contrast Media Agent for MRI & MRA, approved in (40) countries & EP 2104R, an MRI imaging contrast agent designed for the detection of blood clots.

Dr. Juan E. Gutierrez M.D.  
Senior Corp. Diagnostic Radiological Imaging Scientific Advisory Board

Dr. Gutierrez has nearly 15 years experience in clinical drug development in the fields of radiology and oncology. Previously at Bayer Health Care Pharmaceuticals (Former Berlex Laboratories) as the Director Medical Development Diagnostic Imaging, Dr. Gutierrez held increasing responsibilities for the operations, strategic planning and corporate development of a growing portfolio of radiopharmaceutical business. His key early phase experience includes multiple variations of early-phase Cardiology, CNS and Oncology trial designs including traditional dose-escalating maximum tolerated dose design as well as various optimal dose designs for targeted agents.

Dr. Gutierrez later phase oncology, cardiology & CNS experience includes extensive pivotal trial experience in the United States, Western and Eastern Europe, Latin America, and Asia-Pacific. With such clinical trials projects under his belt of clinical design and global implementation with Bayer Health Care (e.g. Vasovist, Magnevist, Gadovist, Ultravist and Iopamiron and Also with Guerbet Pharma Group with Dotarem).
As a clinician, scientist and investigator, Dr Gutierrez focus his knowledge with the clinical community with a bast track record of scientific clinical journals and book publications.

Dr. Gutierrez holds a fellowship Interventional Radiology at the Jacksonville Memorial Hospital at Miami, Florida a Neuroradiology Research Fellowship from Thomas Jefferson University in Philadelphia. He received his medical degree from the CES University in Medellin, Colombia and he completed residency training in Clinical Radiology at the Javeriana Pontifical University in Bogota, Colombia.

Dr. Gutierrez is currently an Assistant Professor of Radiology Division of Neuroradiology at The University of Texas Health Science Center in San Antonio, Texas, USA.

Dr. John Amedio Ph.D.,
Scientific Advisory Board Member at ESTERN Medical.

Dr. Amedio is currently Vice President, Manufacturing & Process Development at Seaside Therapeutics, LLC & he previously was the Executive Director, Analytical and Chemical R&D, at EPIX Pharmaceuticals Inc., and key developer for Vasovist® (MS-325) Contrast MRI/MRA Media Agent & EP 2104R, a MRI imaging contrast detection of blood clots.

Dr. Alfonso Lozada M.D.,
Clinical Scientific Advisory Board Member at ESTERN Medical.

Dr. Lozada, has more than twenty years of experience as a clinician & radiologist in the MRI & MRA radiopharmaceuticals clinical industry. He formerly served as the Executive Medical Director & Clinical Development for Bayer-Schering Pharma AG., where he develop and guided broad clinical launches of diverse pharmaceutical products such as Magnevist, Iopamiron, Gadovist, Levovist some of the world’s top radiopharmaceuticals for more than 20 years.
OUR CRO ADVANTAGE

With a heritage specializing in imaging, we have successfully managed more imaging compounds than any other CRO across Latin America for Global Sponsors.

Our management team are respected professionals in clinical imaging, regulatory affairs, radiology technology, clinical operations, business development, and clinical trial management.

Our local Monitors and Regulatory Affairs Associates in each of the regional countries will expedite study start-up and facilitate excellent relationships with the sites.

Our years of experience working in the emerging market countries across Latin America and our excellent long-term relationships with the local regulators allows us to offer rapid study start-up and provide access to qualified sites with which we have successfully worked with on numerous occasions. This enables us to provide our sponsors with rapid patient recruitment and quality data to assure a high standard of study conduct.

Our Strong Project Management ensures that studies are run efficiently, maintaining consistency across sites and providing quality deliverables. We offer highly experienced professionals with many years of experience to manage these studies, and to develop contingency plans to assure timely completion of these studies within budget and to the highest quality standards.
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