



## PRESS INFORMATION

**IXALTIS** is a specialty pharmaceutical company developing proprietary therapeutics to treat genitourinary (GU) disorders with unsatisfied medical need. The company was created from the combined expertise of leading scientists specialised in this field and of experienced managers. IXALTIS has already obtained an exclusive worldwide license for three molecules from SANOFI (IXA-001, IXA-002 and IXA-003). IXALTIS has established a proprietary position covering IXA-001 for use in urogenital and other disorders based on its specific mechanism of action.

The vision of **IXALTIS** is to develop treatments for diseases of the genito-urinary tract where there is still a high-unmet medical need. This will be achieved by developing the molecules in the portfolio and searching for other drugs which have already reached clinical stage, in a different indication, to be potentially repurposed.



*« Our company has the objective of becoming a leading developer of innovative pharmaceutical products for treating disorders of the urogenital tract, bringing to the clinic solutions for diseases that affect many people and for which there are few or no satisfactory treatments ».*

*Roberto Gradnik, CEO*

## IXALTIS FIRST PHASE II CLINICAL STUDY

Protocol Number: IXA-CSP-001

Investigational Medicinal Product: Litoxetine

Indication: Mixed Urinary Incontinence

Phase: II

### Drug used

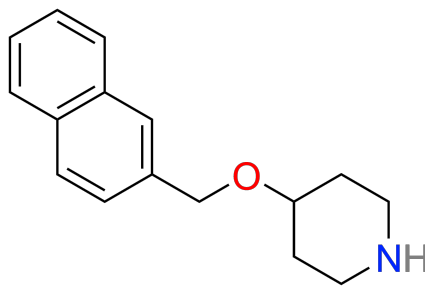
Litoxetine (IXA-001) is a selective serotonin (5-HT) reuptake inhibitor (SSRI) and mixed serotonin agonist-antagonist which will be taken in capsules twice a day. SSRIs affect the chemicals that nerves in the brain use to send messages to one another.

These chemical messengers, called neurotransmitters, are released by one nerve and taken up by other nerves.

Neurotransmitters that are not taken up by other nerves are taken up by the same nerves that released them. This process is termed "reuptake." SSRIs work by inhibiting the reuptake of serotonin, an action that allows more serotonin to be available to be taken up by other nerves.

In addition to these effects, litoxetine has a direct agonist or antagonist effect on specific subtypes of serotonin receptors which makes it particularly appropriate for treating continence dysfunctions.

There are scientific data to suggest that serotonin is involved in the control of micturition and continence, and this study explores if the specific actions of litoxetine on the serotonergic system can improve urinary continence.



### Objectives of the study

The primary objective of this study is to compare the efficacy of 3 doses of litoxetine (10 mg, 20 mg, 40 mg) versus placebo administered orally twice daily (BID) for 12 weeks in female subjects with a diagnosis of mixed urinary incontinence (MUI).

The secondary objectives of this study are to evaluate the safety and tolerability of 3 doses of litoxetine (10 mg, 20 mg, 40 mg) compared to placebo in female subjects with a diagnosis of MUI.

## Target

Approximately 240 subjects are expected to be enrolled, in up to 25 centres in 6 countries : Canada, France, Georgia, Poland, UK and Ukraine.

## Study duration

The study will be double blind randomized placebo controlled and contain a 2 week screening period, a 14 week treatment period followed by a 1 week dose tapering period. Subjects will return to the clinic for a safety Follow-up visit 4 weeks after treatment is completed, for a total study duration of 21 weeks.

## Evaluation criteria

Efficacy of the treatment will be assessed by reduction in numbers of urinary incontinence episodes, the change in Patient Perception of Bladder Condition (PPBC), and the Patient Global Impression of Improvement (PGI-I questionnaires, as well as other).

The tolerance of litoxetine compared to the placebo will be also estimated, and safety assessments will be conducted throughout the trial.



### ***Principal and Coordinating Investigator :***

**Pr. François Haab**, is an urologist surgeon, specialized in functional urology and in particular in the treatment of the urinary incontinence of men and women

## IXALTIS BOARD OF DIRECTORS

### ***Christian CHAVY, MBA. Chairman of the Board***

Christian Chavy is the former CEO of Stallergenes, the worldwide specialist of the Allergy Immuno Therapy. He was previously Chief Operating Officer of Actelion Pharmaceuticals from 2005 to 2008 managing a staff of 1000 and sales of CHF 1.5 billion. At Actelion he has also held the positions of President, Head of Europe, Latin America , Middle East , Africa .

Prior to joining Actelion , he was the Vice-President , Head of Global Therapeutic Area Reproductive Health at Serono International and Managing Director of Serono France .

In 2010, he joined Ares Life Sciences, private equity fund held by the Bertarelli's family, as partner.

He spent five years with Rhone Poulenc Rorer as Managing Director of Rorer France and President of RPR Canada Inc. for both Ethical and OTC activities.

Christian Chavy was educated at ESSEC and holds a Master Degree of Business Management from the Institut de Contrôle de Gestion in Paris ( ICG )

### ***Dr. Roberto GRADNIK, CEO***

Trained as a physician, Roberto Gradnik has more than 25 years' experience in the pharmaceutical and biotechnology sector. After holding various positions with the Knoll Group (a subsidiary of the BASF Group), including that of Vice-President International Marketing Cardiovascular, he joined the Serono Group in 1999 as Italy's General Manager and Head of Southern European Subsidiaries. He was then appointed Executive Vice-President for Europe, in charge of all European markets, and a member of the Executive Committee. He continued in the same position for Merck Serono after the acquisition of Serono by Merck AG. More recently, he was appointed Executive Vice-President, Global Business Unit for Neurodegenerative Diseases for Merck Serono. Since January 1st, 2012 until March 31 st , 2014 he was Chief Executive Officer of Stallergenes, a European biopharmaceutical company specialized in the treatment of severe respiratory allergies with allergen immunotherapy. Roberto Gradnik was President of EBE (European Biopharmaceutical Enterprises) and currently serves on its board.

### ***Dr. Philippe LLUEL***

Dr. Lluel obtained a Ph. D. degree in Pharmacology from the Pierre et Marie Curie University (Paris, France) and a Master degree in Biology and Pharmacology of Ageing. Before founding UROsphere, he spent over 11 years in pharmaceutical companies in drug discovery in the field of experimental urology. Throughout his career he worked closely with various groups charged with development, regulatory affairs and research. His expertise covers the fields of benign prostatic hyperplasia, urinary incontinence, overactive bladder and aging.

Dr. Lluel, in addition to being a board member, also contributes as scientific advisor for IXALTIS.

## **Mario CARIA**

Mario Caria is International Director and Senior Partner at Sofimac Partners France. He joined Sofimac in 2007. After having started and managed Spin Off, Start Up and Business in in clinical diagnostic, medical devices and biotech, he launched Venture Capital funds dedicated to Healthcare, seed and growth. He has been Board Member of numerous companies and currently seats in Boards among which Advanced Perfusion Diagnostic SA, Fine-Heart SA, Centervue SpA.

Previously an Entrepreneur and formerly an Academic and Researcher at CERN, Geneva, he held Chairs in Medical Biophysics and had been teaching Health Technology Assesment in France and Italy. He was Steering Board Member at several initiatives of the European Commission in Bruxelles. He published over 150 papers and 4 books. He holds EMBA from University of Basel, Switzerland and Harvard Business School Certificate. In Ixaltis he brings his sound Corporate knowledge and International network.

## **Jean-Michel PETIT**

Jean-Michel heads the venture capital practice of IRDI Gestion where he manages the seed fund IRDIInov investing in start-ups located in the South-West of France. He serves on the boards of several portfolio companies such as Gamamabs, Fineheart, EnobraQ, Telecom Design, Ademtech and LDL Technology. Before joining IRDI Gestion, he spent 4 years with CDP capital's Life Science venture capital team based first in Montreal and then in Paris. In this position, he made a range of international investments mostly in the US. Before joining CDP capital, he worked for a regional fund based in Montreal. Jean-Michel graduated from Chimie ParisTech and holds and MSc degree from Montreal university and and MBA from McGill.

## **Paolo SIVIERO**

Fund Manager of Principia III, a specialized venture capital fund targeting biotech and medical technology companies. Principia III, the third venture capital fund set up by Principia SGR, become the largest Italian strategic investor in a sector widely expected to be the major driver in knowledge-based economies after the information technology revolution.

Mr Siviero worked for the Italian Medicines Agency (AIFA) from 2007 to 2014 where he led the "Economic Strategy and Pharmaceutical Policy" Unit, responsible for the sustainability of the National Health System with respect to the pharmaceutical sector.

During this time, Mr. Siviero was also appointed as :

- Italian Alternate Member of the European Medicines Agency (EMA) Management Board.
- President of Medicine Evaluation Committee (MEDEV), a group that represent the major European Payers.
- Secretary of the Technical and Scientific Committee of the Italian Medicines Agency
- Secretary of the Pricing and Reimbursement Committee of the Italian Medicines Agency.
- AIFA's Representative at the European Networking of the Competent Authorities for Pricing and Reimbursement of Pharmaceutical.
- Appointed by the Italian Minister of Health as National Expert at the European Network for HTA.

During his career, Mr. Siviero has cooperated several years with the Italian National Research Council,

regarding the development of issues such as the technological transfer, knowledge management and the economical valorization of results obtained through researches.

### ***Hasnaa HAFID (as observer)***

iXO Private Equity is the most important independent private equity General Partner in France dedicated to small, small-mid cap buyout and growth transactions. It manages a 550 €m asset portfolio of capital-investment.

Based in Toulouse, Marseille, iXO Private Equity is meeting the equity needs for the best companies in the Great South of France (Southern West, Southern East) and Rhône-Alpes by investments between 1 et 15 €m.

Our teams long term expertise in this field (Growth Capital, MBO, OBO, Spin-Off, Build-up...) and the focus of the Board of Experts are the major factors contributing to our success. A proprietary deal flow has been developed which help us to target niche markets, local know-how and international exposure companies without any hard competitions. The result is a very long and robust track record in this extended period of time.

More information at : [www.ixope.fr](http://www.ixope.fr)

## **IXALTIS SCIENTIFIC ADVISORY BOARD**

### ***Professor Francois Haab.***

Professor François Haab is an urologist surgeon, specialized in functional urology and in particular in the treatment of the urinary incontinence of men and women.

After a residency in Paris hospitals (APHP) and a training in the USA, François Haab joined in 1994 the service of urology of the Tenon Hospital in Paris.

He becomes professor of university in 2001, within the Faculty of Medicine Pierre and Marie Curie (Paris VI).

In 2007, he becomes chief of the urologic surgery department at the Tenon Hospital (AP-HP).

In 2015, he decided to join the hospital group Diaconesses Croix Saint Simon.

The same year, he also created the Urology center Paris-Opera, dedicated to the care of urinary incontinence.

In 2007, Pr. Haab drafted a report for the Minister of Health on the support of the urinary incontinence in France.

He published, in this domain in particular, more than 200 scientific articles and wrote five books dedicated to the healthcare professionals or to the general public.

***Professor Dudley Robinson, MBBS MD FRCOG***

Dudley Robinson trained at the Royal London Hospital qualifying MBBS in 1991. Throughout his training in obstetrics and gynaecology he has worked in and around London prior to undertaking a research fellowship with Professor Linda Cardozo in the Department of Urogynaecology at Kings College Hospital, London. He has published widely in the field of urogynaecology and research interests include the effect of hormones and drugs on the lower urinary tract. His MD thesis is entitled 'Anti-diuresis in the management of daytime urinary incontinence' and investigated the use of desmopressin nasal spray as a 'designer drug' for women with daytime urinary incontinence. Subsequently he completed a two-year sub-specialty training program in urogynaecology at Kings and was appointed as a Consultant Obstetrician and Gynaecologist with a subspecialty interest in Urogynaecology at Kings College Hospital in 2005. He has published widely in the field of urogynaecology and his specific research interests include 'cure' and the analysis of outcome measures in addition to the influence of drugs and hormones on the lower urinary tract.

He continues to have an active role in research in lower urinary tract dysfunction and is currently Research and Development Lead in Women's Services at Kings

***Professor Stefano Salvatore***

Stefano Salvatore is Professor of Urogynaecology at Vita-Salute San Raffaele University and IRRCS San Raffaele Hospital. From 1995 to 1997 he was a lecturer at the Clinica Ostetrica e Ginecologica of the Insubria University in Varese. In 1999 he became consultant in Urogynaecology at the Bassini Hospital, University of Milan Bicocca and then consultant in Urogynaecology at the Clinica Ostetrica e Ginecologica of the Insubria University in Varese. He is a member of the Scientific and the Nomination Committee of the International Urogynecological Association. He is vice-president of the European Urogynaecological Association. Prof. Salvatore has authored more than 80 articles in peer-reviewed journals.

***Professor Roger Dmochowski, MD, MMHC, FACS***

Prof. Roger R. Dmochowski is Professor at the Department of Urology at Vanderbilt University in Nashville. He is Director of the Section of Female Pelvic Medicine and supervisor of the Fellowship in Pelvic Medicine at Vanderbilt. He is also Clinical Assistant Professor in Surgery at the Uniformed Services University of the Health Sciences in Bethesda, Maryland. Vice Chair, Section of Surgical Sciences Vanderbilt University Medical Center, Associate Director of Quality and Safety, Vanderbilt Health System, Executive Director of Risk Prevention for Vanderbilt Health System, Executive Medical Director for Patient Safety and Quality (Surgery), Associate Chief of Staff, and Medical Director of Risk Management at Vanderbilt University Hospital.

Prof. Dmochowski received his medical degree from the University of Texas Medical Branch at Galveston. He completed an internship and residency in surgery and urology at the University of Texas Medical School at Houston and at the M.D. Anderson Hospital and Tumor Institute in Texas. In addition, Dr. Dmochowski is subspecialty fellowship trained in female urology, neurourology, urodynamics and reconstructive urology. He is board certified in urology.

Prof. Dmochowski has published more than 230 articles and 68 book chapters, and 340 abstracts, and has given over 230 presentations at various national and international meetings. He has been featured in videotapes and CD-ROMS on the management of urinary incontinence. Prof. Dmochowski is on the editorial board for the World Journal of Urology, Neurourology and Urodynamics, and International Journal of Urogynecology and the AUA Office of Education CD-ROM Series, and he is a reviewer for the Journal of Urology, and Urology. He is a Fellow of the American College of Surgeons and a member of the American Urological Association and International Continence Society. Prof. Dmochowski has been granted the Zimskind Award from the Urodynamics Society for his accomplishment in clinical treatment for incontinence. His current research interests are outcomes of incontinence therapies with a particular emphasis on quality of life issues. He also is active in bio materials evaluation.







## IXALTIS MANAGEMENT

### ***Dr. Roberto Gradnik, CEO***

Dr. Gradnik has over 25 years of international pharma and biotech industry experience in top management roles.

Most recently he served as CEO of Stallergenes and before that he was the EVP, Head of the Global Business Unit Neurology for Merck Serono.

Dr. Gradnik is the current president of the European Biopharmaceutical Association (EBE).

### ***Dr. Elisabeth Svanberg, CDO***

Elisabeth Svanberg received her MD and PhD from the University of Gothenburg, and is a board certified general surgeon and associate professor of surgery. She joined Serono International based in Geneva Switzerland in 2000. Initially Elisabeth worked in the field of metabolism, particularly wasting conditions, as a natural continuation of her academic and clinical work. Elisabeth subsequently held roles of increasing responsibilities at Serono/Merck Serono before joining Bristol Myers Squibb (BMS) in the United States in 2007. At BMS, Elisabeth served as development leader (2007 and 2011) for dapagliflozin (Forxiga/Farxiga), a first in class medicine now registered and launched worldwide to treat type 2 diabetes, and subsequently was Vice President and Head of the Intercontinental Medical Department responsible for Canada, LatinAmerica, Middle East&Africa, AsiaPacific and Australia/New Zealand (2011- 2014). In 2014 Elisabeth joined Janssen Pharmaceuticals (a Johnson & Johnson Company) as Vice President, Head of the Established Products group managing a portfolio of 90 products, used by an estimated 150 million patients globally. In 2016, Elisabeth joined Ixaltis as CDO.

### ***Nathalie de Valleuil, Office & Communication Manager***

Nathalie has more than 10 years experience in advertising and communication project management. She worked in various international agencies such as McCann or DDB in Paris and Geneva, assisting companies like L'Oréal, Nestlé, Danone, Pfizer, Sanofi-Aventis or P&G in their local and international communication.

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