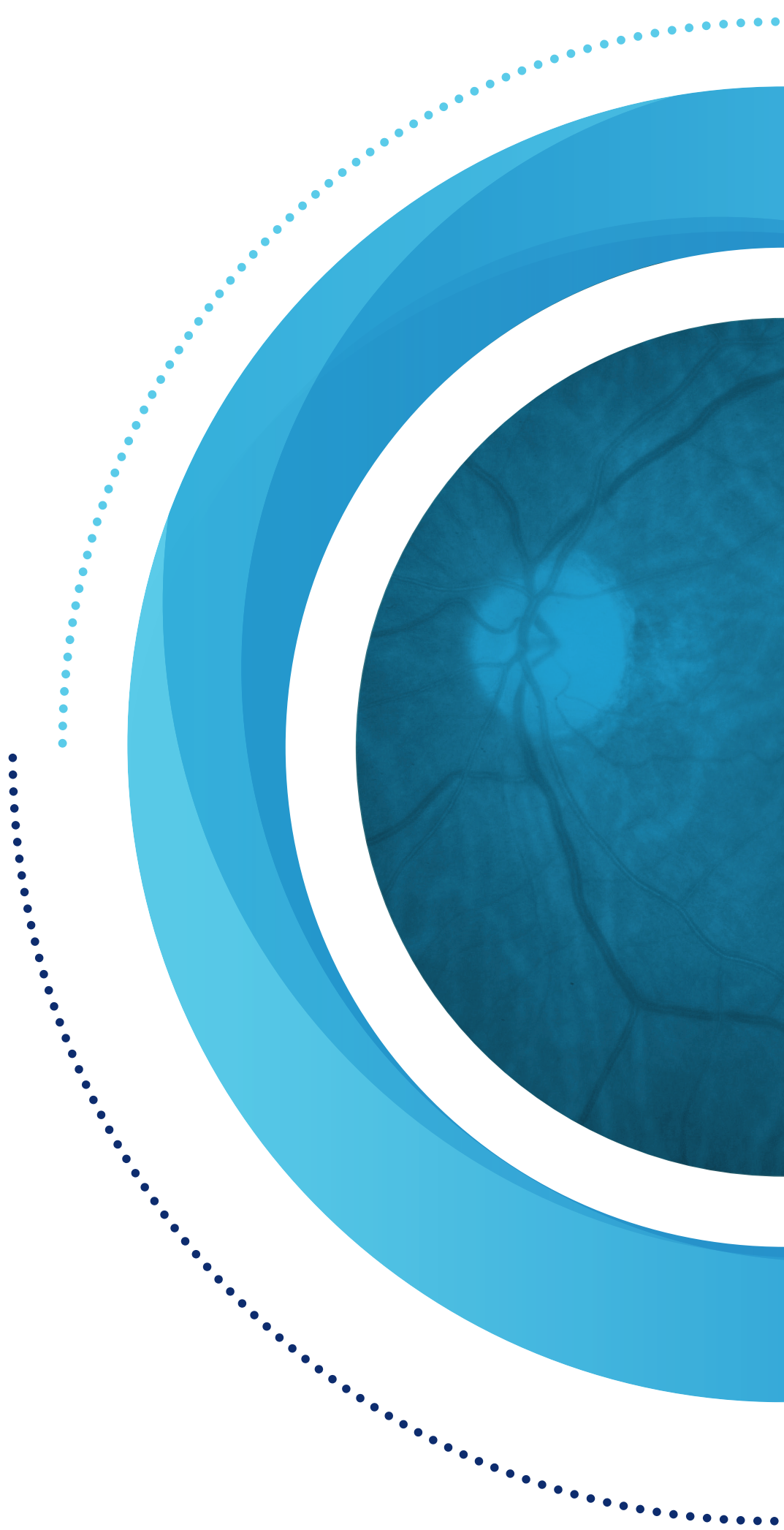


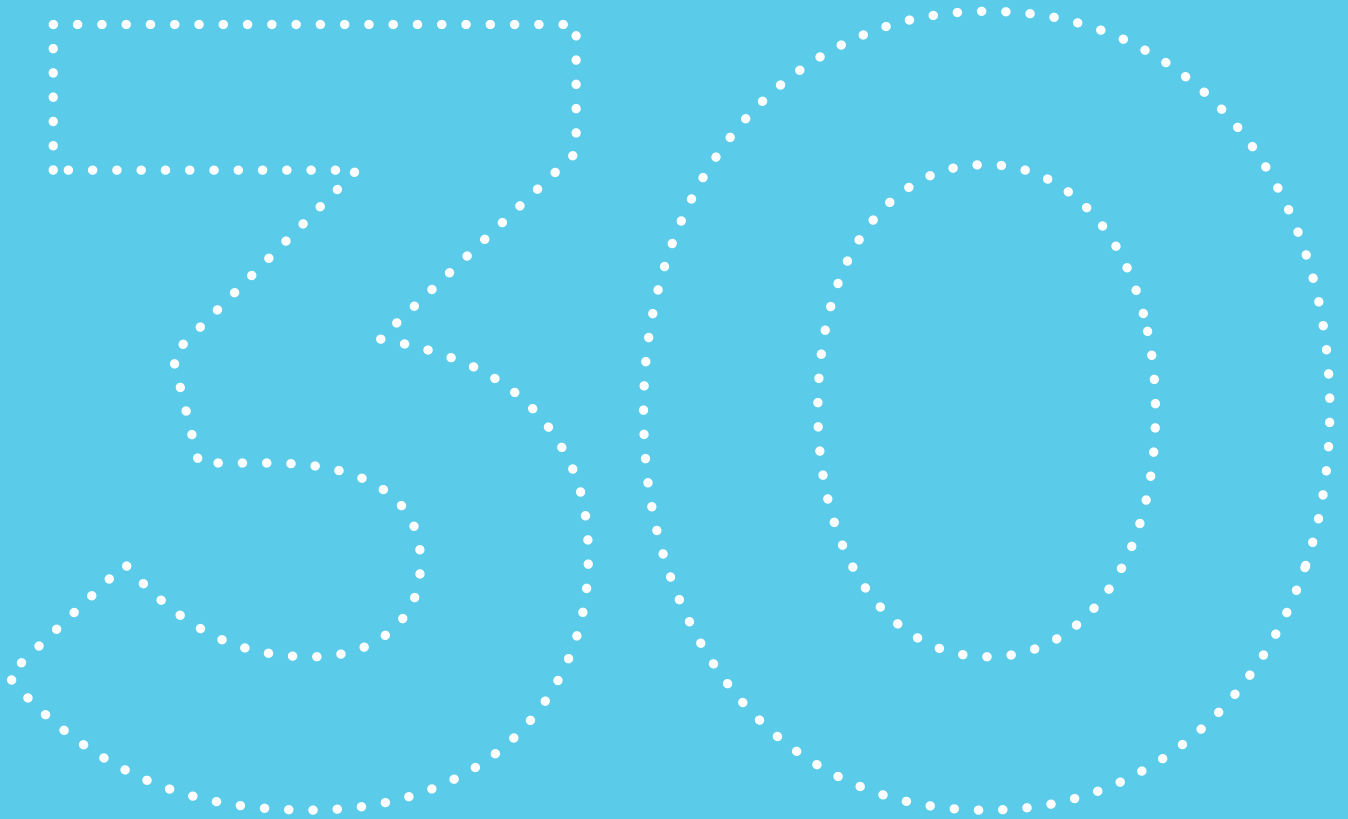


2019  
REPORT



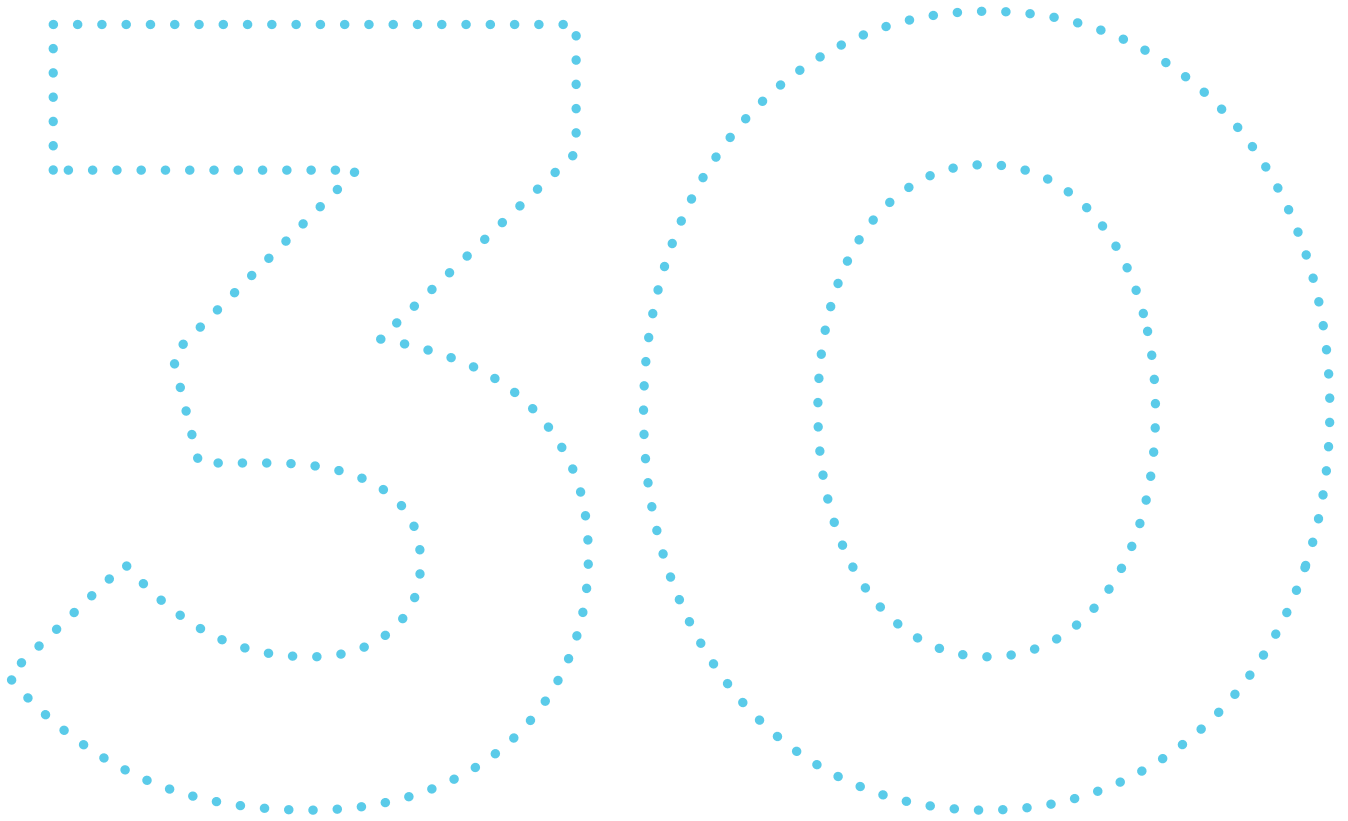


# 2019 REPORT



YEARS OF EXCELLENCE





YEARS OF EXCELLENCE



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## MESSAGE FROM THE PRESIDENT

AIBILI - Association for Innovation and Biomedical Research on Light and Image, was founded thirty years ago.

Its main goals were to contribute with innovative solutions to our knowledge in the areas of ophthalmology, neurosciences, imaging and pharmacology and to develop tools to improve health care delivery. The scientific work performed at AIBILI has been published regularly in the best international scientific journals and has led to the development of new products.

AIBILI is recognised internationally and has now a leading role in European eye research by coordinating a network of more than 100 clinical research centres (EVICR.net). AIBILI is a sought after research partner that has contributed extensively to translational research, developing new biomarkers of disease progression and treatment response. It is now in the process of coordinating a European network of translational research centres.

AIBILI has achieved during these thirty years a reputation of scientific excellence, adherence to highest and most exigent quality standards and is now an active partner in joint projects with reference centres, such as Harvard Medical School (USA), University of Paris and Institut de La Vision (France), Moorfields Eye Hospital (London, UK), University of Bonn (Germany), University of Milano (Italy), University of Antwerp (Belgium) and Vall d'Hebron Institute of Research (Spain).

AIBILI has been recognized as an Interface Centre by the Portuguese Ministry of Economy, and is the only one in the health sector.

I can say that the main objectives set thirty years ago have been generally fulfilled and I am convinced that in the next thirty years AIBILI will continue to pursue its path on research and innovation in the Health Sector, contributing to the development of scientific knowledge, international collaboration and the economy of Portugal.

José Cunha-Vaz  
President



# 1

## INTRODUCTION

AIBILI - Association for Innovation and Biomedical Research on Light and Image is a Research Technology Organisation in the health area dedicated to the development and clinical research of new products for medical therapy and diagnostic imaging. It is an Interface Centre of the Portuguese Network of the Economy Ministry.

It is a private not-for-profit organisation, founded in 1989, established to support technology transfer and translational research in the health area.

AIBILI main areas of activity are:

- Coordination of clinical trials at both national and multinational levels
- Performance of clinical studies
- Centralized grading of eye examinations
- Research and development of new technologies for medicine in the area of imaging
- Health technology assessment
- Data Centre

AIBILI is ISO 9001:2015 certified for all its activities. Clinical research is performed in accordance with ICH - Good Clinical Practice (GCP) Guidelines and national and European regulatory requirements.

AIBILI is located in the area of the Health Campus of Coimbra University since 1994 and has its own building with 1.454 m<sup>2</sup> and state-of-the-art equipment funded by European Union funds.

Regarding human resources it has a permanent staff of 57 including medical doctors, researchers, engineers, pharmacologists, technicians, project managers, statisticians data managers, study coordinators and administrative personnel. Another 54 professionals collaborate regularly in research activities.

The main goals of AIBILI are translational research and innovation contributing to the conversion of basic research knowledge into practical applications in order to improve human health and well-being.



## INTERFACE CENTRE IN THE HEALTH SECTOR



AIBILI is an Interface Centre in the Health Sector of the National Technology Network of the Economy Ministry. This recognition identifies AIBILI as the technology transfer centre acting as the facilitating partner between scientific institutions, enterprises and industry in order to bring novel products to the market.

AIBILI strategy for the period 2019-2021 focuses on its role as Centre for Technological Interface of Portugal in the Health Sector. The innovation and technological objectives focus on:

- Maintaining its position as a Reference Centre for coordination and logistical support of clinical research activities in Europe
- Development of imaging biomarkers of disease progression and response to treatment
- Research on diseases related to ageing of the eye and brain
- Assessment of economic viability in the process of development of new products

In the area of clinical research coordination and logistical support activities it is crucial to maintain its present status of international recognition. The internationalization already achieved with EVICR.net and C-TRACERs Networks create unique opportunities for Portuguese SMEs and research centres to participate in new studies. AIBILI will

continue to expand its partnerships with Portuguese companies and universities in order to foster the development of new products.

Innovation is focused in the development of imaging biomarkers of progression and response to treatment of retinal and brain diseases. Ageing of the eye and brain is a research focus of AIBILI. AIBILI will continue contributing to the development of screening programmes using tele-ophthalmology particularly in primary health care centres, promoting clinical research and reaching out to different population of patients. Another focus of AIBILI research is the area of artificial intelligence applications to image analysis of eye images. A main goal of AIBILI is the development and validation of new imaging biomarkers thus creating opportunities for companies of the health sector to develop and market new products.

In the course of the development of new products it is intended by AIBILI to evaluate the economic viability of medicines, design of the value strategy, regulation and translation of technology that will allow greater knowledge of the chain value and transfer of knowledge to SMEs, market access, as well as follow-up and effectiveness after commercialization.



## BIOTECHNOLOGY AND LIFE SCIENCES FOCUS: HUMAN HEALTH

FINANCIADO POR



## AIBILI Associates

### Founding Associates

- FLAD - Fundação Luso-Americana para o Desenvolvimento (Honorary Associate)
- IAPMEI - Instituto de Apoio às Pequenas e Médias Empresas e à Inovação
- José Cotta - EMS, S.A.
- José Cunha-Vaz
- Laboratório EDOL - Produtos Farmacêuticos, S.A.
- Biofísica da Faculdade de Medicina da Universidade de Coimbra
- Farmacologia da Faculdade de Medicina da Universidade de Coimbra
- Serviço de Dermatologia do Centro Hospitalar Universitário de Coimbra
- SUCH - Serviço de Utilização Comum dos Hospitais

### Other Associates

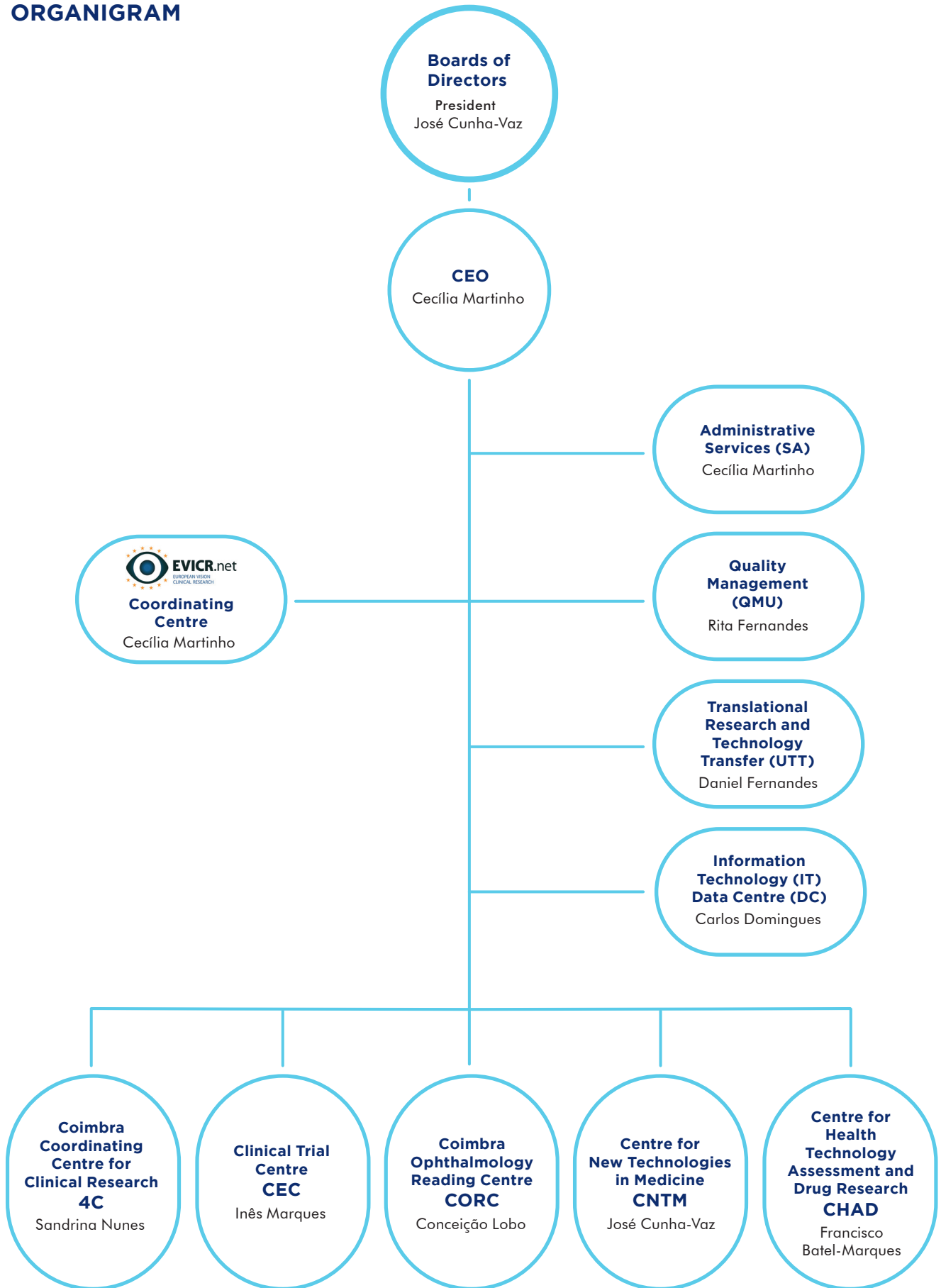
- Alcon Portugal - Prod. e Equip. Oftalmológicos, Lda.
- BIAL - Portela & C<sup>ª</sup>, SA
- Centro de Oftalmologia da Universidade de Coimbra
- Conceição Lobo
- Francisco Batel Marques
- Fundação Champalimaud (Honorary Associate)
- Hospital CUF Coimbra / José de Mello Saúde
- Laboratórios Pfizer, Lda.
- Novartis Farma, SA
- Universidade de Coimbra (Honorary Associate)

## AIBILI Board of Directors (2017-2020)

- José Cunha-Vaz, President
- José Cotta - EMS, SA, Vice-President (Conceição Lobo)
- BIAL - Portela & C<sup>ª</sup>, SA (Tice Macedo)
- Fundação Champalimaud (António Parreira)
- Laboratórios Edol, Produtos Farmacêuticos, SA (Gonçalo Pimpão)
- Serviço de Dermatologia do Centro Hospitalar Universitário de Coimbra (Américo Figueiredo)
- Francisco Batel Marques

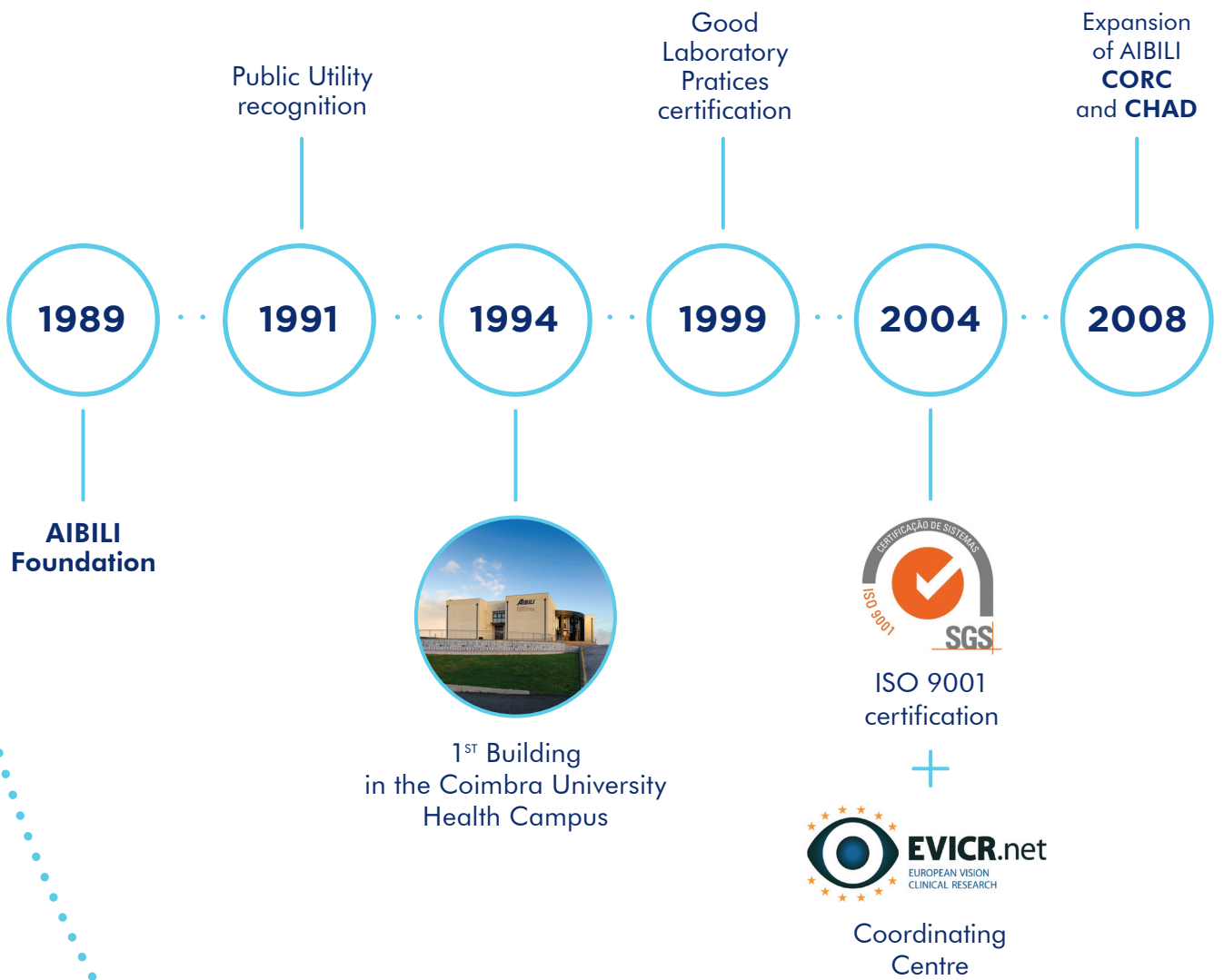


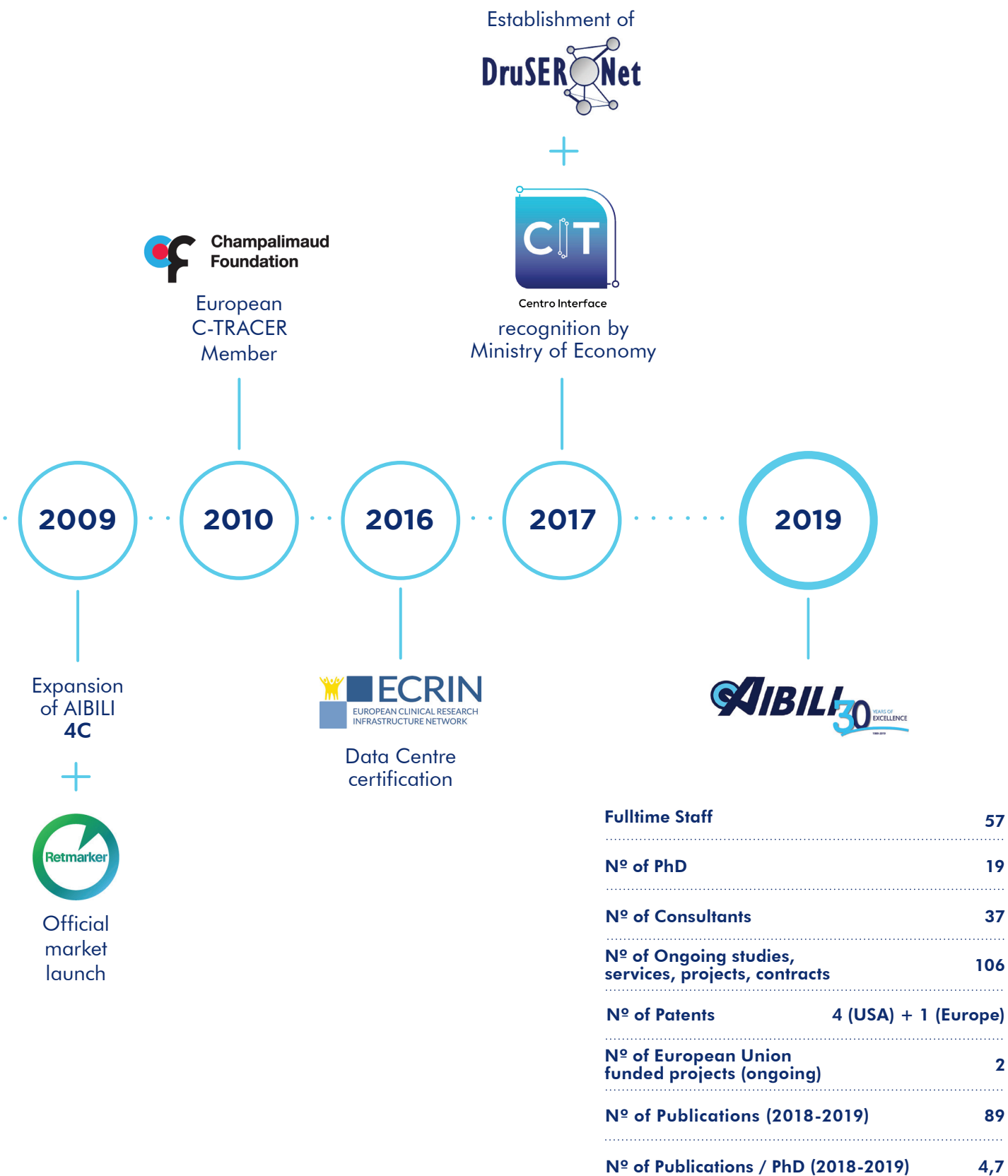
# ORGANIGRAM



# 2

## 30 YEARS AT A GLANCE





|  |                      |
|--|----------------------|
| Fulltime Staff                                       | 57                   |
| Nº of PhD  | 19                   |
| Nº of Consultants                                    | 37                   |
| Nº of Ongoing studies, services, projects, contracts | 106                  |
| Nº of Patents  | 4 (USA) + 1 (Europe) |
| Nº of European Union funded projects (ongoing)       | 2                    |
| Nº of Publications (2018-2019)                       | 89                   |
| Nº of Publications / PhD (2018-2019)                 | 4,7                  |

# 3

## AIBILI RESEARCH CENTRES AND UNITS

AIBILI is organized in Research Centres and Organizational Units.

The Research Centres are:

- Coimbra Coordinating Centre for Clinical Research (4C)
- Clinical Trial Centre (CEC)
- Coimbra Ophthalmology Reading Centre (CORC)
- Centre for New Technologies in Medicine (CNTM)
- Centre for Health Technology Assessment and Drug Research (CHAD)
- Data Centre (DC)

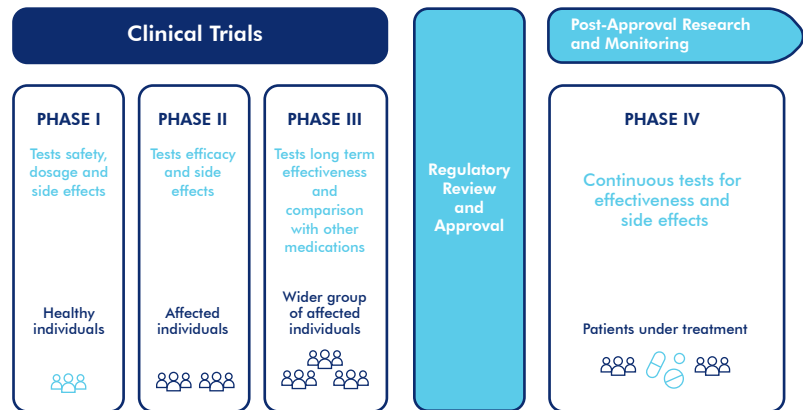
Organizational Units are:

- Administration (SA)
- Quality Management Unit (UGQ)
- Translational Research and Technology Transfer Unit (UTT)
- Information Technology Unit (IT)

### In Vitro and In Vivo Study



### Clinical Development



From Pre-Clinical To Clinical  
CHAD and 4C

Design, Conducting and Monitoring Clinical Studies  
CEC, 4C and CHAD

HTA and Market Access  
CHAD

Effectiveness and Pharmacovigilance  
CEC, 4C and CHAD

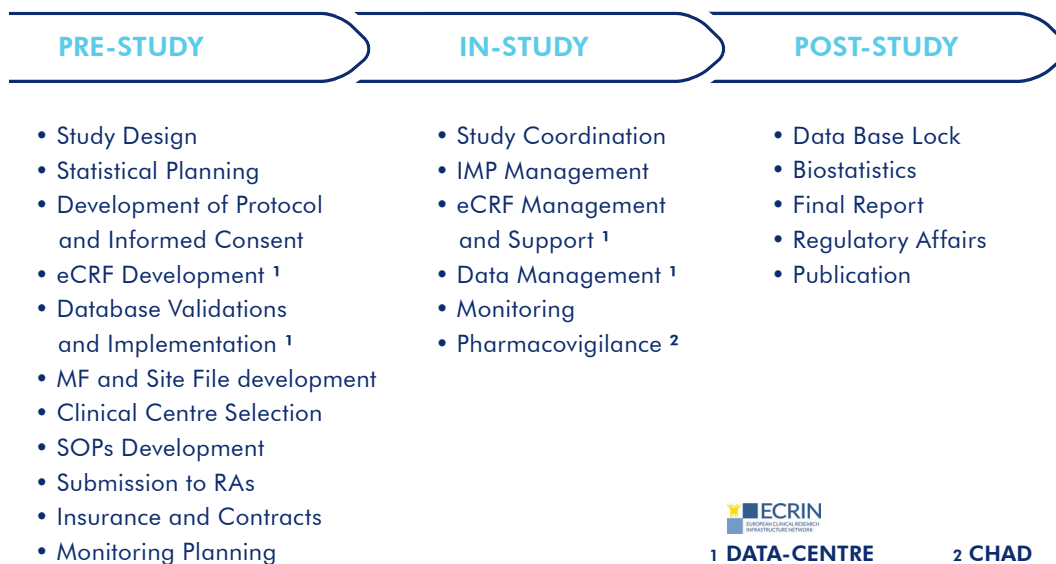
# 4C - COIMBRA COORDINATING CENTRE FOR CLINICAL RESEARCH



Director: [Sandrina Nunes](#), PhD

Staff: Beatriz Melício, Cecília Martinho, Conceição Lobo, Daniel Fernandes, Daniel Silva, Joana Tavares, Laura Seco, Liliana Carvalho, José Cunha-Vaz, Maria Viegas Nascimento, Mónica Fernandes, Pier Basile, Rita Coimbra, Rita Fernandes, Sónia Simões, Vanessa Santos

The Coimbra Coordinating Centre for Clinical Research (4C) is a structure to support the development and coordination of Investigator Initiated and Industry Sponsored Clinical Research by providing the following services:



Contacts  
 Sandrina Nunes, PhD  
 Phone: +351 239 480 137  
 E-mail: [sandrina@aibili.pt](mailto:sandrina@aibili.pt)

ECRIN  
 EUROPEAN CLINICAL RESEARCH INFRASTRUCTURE COORDINATION  
**1 DATA-CENTRE**      **2 CHAD**

## Nº of Projects Coordinated by 4C (2017-2019)

| Year        | Coordination of Clinical Studies (nº) |                    |          | Total     |
|-------------|---------------------------------------|--------------------|----------|-----------|
|             | Investigator Initiated                | Industry Sponsored | Other    |           |
| 2017        | 22                                    | 2                  | 4        | 28        |
| 2018        | 16                                    | 2                  | 3        | 21        |
| <b>2019</b> | <b>14</b>                             | <b>2</b>           | <b>4</b> | <b>20</b> |



## Representative Publications

Figueira J, Fletcher E, Massin P, Silva R, Bandello F, Midena E, Varano M, Sivaprasad S, Eleftheriadis H, Menon G, Amaro M, Ayello Scheer S, Creuzot-Garcher C, Nascimento J, Alves D, Nunes S, Lobo C, Cunha-Vaz J; For the EVICR.net Study Group: **Ranibizumab Plus Panretinal Photocoagulation versus Panretinal Photocoagulation Alone for High-Risk Proliferative Diabetic Retinopathy (PROTEUS Study).** *Ophthalmology*. 2018 May; 125(5):691-700. doi: 10.1016/j.ophtha.2017.12.008.

Finger RP, Schmitz-Valckenberg S, Schmid M, Rubin GS, Dunbar H, Tufail A, Crabb DP, Binns A, Sánchez CI, Margaron P, Normand G, Durbin MK, Luhmann UFO, Zamiri P, Cunha-Vaz J, Asmus F, Holz FG; on behalf of the MACUSTAR consortium: **MACUSTAR: Development and clinical validation of functional, structural and patient-reported endpoints in intermediate age-related macular degeneration.** *Ophthalmologica* 2018. Aug 28:1-12.

Nunes S, Alves D, Barreto P, Raimundo M, da Luz Cachulo M, Farinha C, Lains I, Rodrigues J, Almeida C, Ribeiro L, Figueira J, Santos L, Silva R: **Adherence to a Mediterranean diet and its association with age-related macular degeneration. The Coimbra Eye Study-Report 4.** *Nutrition*. 2018 Jul - Aug;51-52:6-12.

Simó R, Hernández C, Porta M, Bandello F, Grauslund J, Harding SP, Aldington SJ, Egan C, Frydkjaer-Olsen U, García-Arumí J, Gibson J, Lang GE, Lattanzio R, Massin P, Midena E, Ponsati B, Ribeiro L, Scanlon P, Lobo C, Costa MÂ, Cunha-Vaz J, for the European Consortium for the Early Treatment of Diabetic Retinopathy (EUROCONDOR): **Effects of Topically Administered Neuroprotective Drugs in Early Stages of Diabetic Retinopathy. Results of the EUROCONDOR Clinical Trial.** *Diabetes*. 2018 Nov 2. pii: db180682. doi: 10.2337/db18-0682.

Rosenblatt A, Udaondo P, Cunha-Vaz J, Sivaprasad S, Bandello F, Lanzetta P, Kodjikian L, Goldstein M, Wilner ZH, Loewenstein A, for the ARTES study group: **A Collaborative Retrospective study on the Efficacy and Safety of intravitreal dexamethasone implant (Ozurdex) inpatients with Diabetic Macular Edema (DME). THE EUROPEAN DME REGISTRAR STUDY (ARTES).** *Ophthalmology* (2019), doi:10.1016/j.ophtha.2019.10.005.





# CEC - Clinical Trial Centre

Director: [Inês Marques](#), MD

Staff: Aida Vitorino, Ana Maria Nunes, Ana Rita Santos, Catarina Eloy, Céu Simões, Conceição Lobo, Eugénia Cardoso, Filipe Martins, Isabel Pires, Luisa Ribeiro, João Figueira, José Costa, José Cunha-Vaz, Maria da Luz Cachulo, Maria Viegas Nascimento, Marcela Pascoal, Marta Lopes, Miguel Amaro, Patrícia Barreto, Patrícia Martins Oliveira, Paulo Marques, Pedro Faria, Rufino Silva, Sandra Pardal, Sílvia Simão



Contacts  
 Inês Marques, MD  
 Phone: +351 239 480 148/124  
 E-mail: [ipmarques@aibili.pt](mailto:ipmarques@aibili.pt)

The Clinical Trial Centre (CEC) performs randomized clinical trials with special emphasis on ophthalmology. CEC has dedicated facilities and updated ophthalmological equipment. Clinical patient-oriented research involves characterizing disease progression and testing new discoveries by carrying out controlled research studies in patients, i. e., clinical trials. This includes testing not only new drugs, but also new methods, devices, imaging and surgical procedures as well as well-designed prospective, non-interventional, longitudinal studies.

Our research is focused in age-related eye diseases with special emphasis on diabetic retinopathy and age-related macular degeneration. The CEC has proven expertise and scientific publications in these areas and is a certified Clinical Site of Excellence by the EVICR.net - European Vision Institute Clinical Research Network since 2006. The CEC has experienced and qualified staff and the necessary equipment to perform clinical research according to ICH GCP Guidelines and uses an Electronic Medical Record in its daily routine.



## Nº of Investigator Initiated and Industry Sponsored Studies performed at CEC (2017-2019)

| Year        | Nº of Clinical Studies |                    | Total     |
|-------------|------------------------|--------------------|-----------|
|             | Investigator Initiated | Industry Sponsored |           |
| 2017        | 6                      | 23                 | 29        |
| 2018        | 6                      | 15                 | 21        |
| <b>2019</b> | <b>5</b>               | <b>13</b>          | <b>18</b> |



## Investigator Initiated Studies

### Diabetic Retinopathy

**1. PROGRESS – Progression of Diabetic Retinopathy. Identification of Signs and Surrogate outcomes**  
ClinicalTrials.gov n° NCT 03010397

**2. CORDIS - Characterization of retinal vascular disease in eyes with mild to moderate Nonproliferative diabetic retinopathy in Diabetes type 2, using novel non-invasive imaging methods, in a longitudinal and prospective clinical study with 2 years of duration**  
ClinicalTrials.gov n° NCT03696810  
Financial support: Portugal 2020 - 02/SAICT/2017 - Project n° 030375

### Age-Related Macular Degeneration

**3. MACUSTAR - Intermediate AMD: Development of novel clinical endpoints for clinical trials in patients with a regulatory and patient access intention**  
ClinicalTrials.gov n° NCT03349801  
Financial Support: European Union and EFPIA - Innovative Medicines Initiative 2 Joint Undertaking - Grant Agreement n° 116076

### Retinal Degenerative Diseases

**4. STAR - Development of a Model for Advanced Screening for Timely Treatment of Age-Related Eye Diseases**

**5. EYEMARKER - Characterization of potential biomarkers of Eye Disease and Vision Loss**  
ClinicalTrials.gov n° NCT02500862

## Industry Sponsored Clinical Trials

### Diabetic Macular Edema

**1. An Open Label, Registry Study of the Safety of ILUVIEN® 190 Micrograms Intravitreal Implant in Applicator (IRISS)**  
ClinicalTrials.gov n° NCT01998412

**2. An open-label, randomized, active-controlled, parallel-group, Phase-3b study of the efficacy, safety, and tolerability of three different treatment regimens of 2 mg aflibercept administered by intravitreal injections to subjects with diabetic macular edema (DME) (VIOLET - BAY 86-5321/17613)**  
EudraCT n° 2014-004938-25

**3. A phase III, multicentre, randomized, double-masked, active comparator-controlled study to evaluate the efficacy and safety of RO6867461 in patients with diabetic macular edema (Rhine)**  
EudraCT n° 2017-005105-12

**4. A two-year, three-arm, randomized, double-masked, multicentre, phase III study assessing the efficacy and safety of brolicizumab versus aflibercept in adult patients with visual impairment due to diabetic macular edema (KESTREL)**  
EudraCT n° 2017-004742-23

**5. A randomized, double-masked, placebo-controlled exploratory study to evaluate safety, tolerability, pharmacodynamics and pharmacokinetics of orally administered BI 1467335 for 12 weeks with a 12 week follow up period in patients with non-proliferative diabetic retinopathy without center-involved diabetic macular edema (ROBIN Study)**  
EudraCT n° 2016-002971-91

### Age-Related Macular Degeneration

**6. An open-label, randomized, active-controlled, parallel-group, Phase-3b study of the efficacy, safety, and tolerability of 2 mg aflibercept administered by intravitreal injections using two different treatment regimens to subjects with neovascular age-related macular degeneration (nAMD) (AZURE)**  
EudraCT n° 2012-003763-22

**7. A Multicenter, Double Masked, Randomized, Dose-Ranging Trial to Evaluate the Efficacy and Safety of Conbercept Intravitreal Injection in Subjects with Neovascular Age-Related Macular Degeneration (PANDA)**  
EudraCT n° 2017-004825-34

### Glaucoma

**8. Long-Term Surveillance Study of Latanoprost to Monitor Hyperpigmentation changes in the eye in Pediatric Populations (A6111144)**

### Neurological Disorders

**9. A multicenter, randomized, double-blind, parallel-group, placebo-controlled variable treatment duration study evaluating the efficacy and safety of Siponimod (BAF312) in patients with secondary progressive multiple sclerosis (EXPAND)**  
EudraCT n° 2012-003056-36

**10. A multi-site, open-label extension Trial of Oral RPC1063 in relapsing Multiple Sclerosis (RPC01-3001)**  
EudraCT n° 2015-002500-91

**11. Multicenter, randomised, double-blind, parallel-group, active-controlled, superiority study to compare the efficacy and safety of ponesimod to teriflunomide in subjects with relapsing multiple sclerosis (AC-058301 - OPTIMUM)**  
EudraCT n° 2012-000540-10

**12. Multicenter, non-comparative extension to study AC-058B301, to investigate the long-term safety, tolerability, and control of disease of ponesimod 20 mg in subjects with relapsing multiple sclerosis**  
EudraCT n° 2016-004719-10

### Cancer

**13. A randomized, open label, multicenter Phase 2/3 study to evaluate the efficacy and safety of rogaratinib (BAY 1163877) compared to chemotherapy in patients with FGFR-positive locally advanced or metastatic urothelial carcinoma who have received prior platinum-containing chemotherapy**  
EudraCT n° 2016-004340-11



## Representative Publications

Ribeiro L, Pappuru R, Lobo C, Alves D, Cunha-Vaz J: **Different Phenotypes of mild nonproliferative diabetic retinopathy with different risks for development of macular edema (C-TRACER study)**. *Ophthalmic Res* 2018;59:59-67.

Marques IP, Alves D, Santos T, Mendes L, Santos AR, Lobo C, Durbin M, Cunha-Vaz J: **Multimodal Imaging of the Initial Stages of Diabetic Retinopathy. Different Disease Pathways in Different Patients**. *Diabetes*. 2018 Dec 6. pii: db181077. doi: 10.2337/db18-1077.

Santos AR, Santos T, Alves D, Marques IP, Lobo C, Cunha-Vaz J.: **Characterization of Initial Stages of Diabetic Macular Edema**. *Ophthalmic Res*. 2019;62(4):203-210. doi: 10.1159/000499117.

Farinha C, Cachulo ML, Alves D, Pires I, Marques JP, Barreto P, Nunes S, Costa J, Martins A, Sobral I, Láins I, Figueira J, Ribeiro L, Cunha-Vaz J, Silva R.: **Incidence of Age-Related Macular Degeneration in the Central Region of Portugal: The Coimbra Eye Study - Report 5**. *Ophthalmic Res*. 2019;61(4):226-235. doi: 10.1159/000496393.

Farinha C, Martins A, Neves A, Soares R, Ruão M, Ornelas M, Neves P, Gomes Rodrigues F, Coelho C, Silva R. **Ranibizumab for the Treatment of Diabetic Macular Oedema in the Real-World Clinical Setting in Portugal: A Multicentre Study**. *Ophthalmologica*. 2019;241(1):1-8. doi: 10.1159/000489046.



Director: [Conceição Lobo](#), MD, PhD

Staff: Adozinda Simão, Alda Baltar, Amélia Martins, Ana Paula Pascoal, Ana Raquel Branco, Ana Rita Santos, Carla Sofia Gomes, Catarina Neves, Christian Schwartz, Cláudia Farinha, Inês Marques, Isa Sobral, Isabel Pires, João Gil, João Pedro Marques, José Cunha-Vaz, José Filipe Costa, Marco Marques, Mariana Costa, Maria Luísa Ribeiro, Maria da Luz Cachulo, Marta Lopes, Patrícia Ferro, Renata Castanheira, Rui Alberto Pita, Sílvia Simão, Telmo Miranda



Contacts  
Conceição Lobo, MD, PhD  
Phone: +351 239 480 135/149  
E-mail: [clobo@aibili.pt](mailto:clobo@aibili.pt)

The Coimbra Ophthalmology Reading Centre (CORC) focus its activities in grading retinal diseases on fundus images and OCT images of the retina, as well as functional evaluations of the retina using mfERG and visual fields.

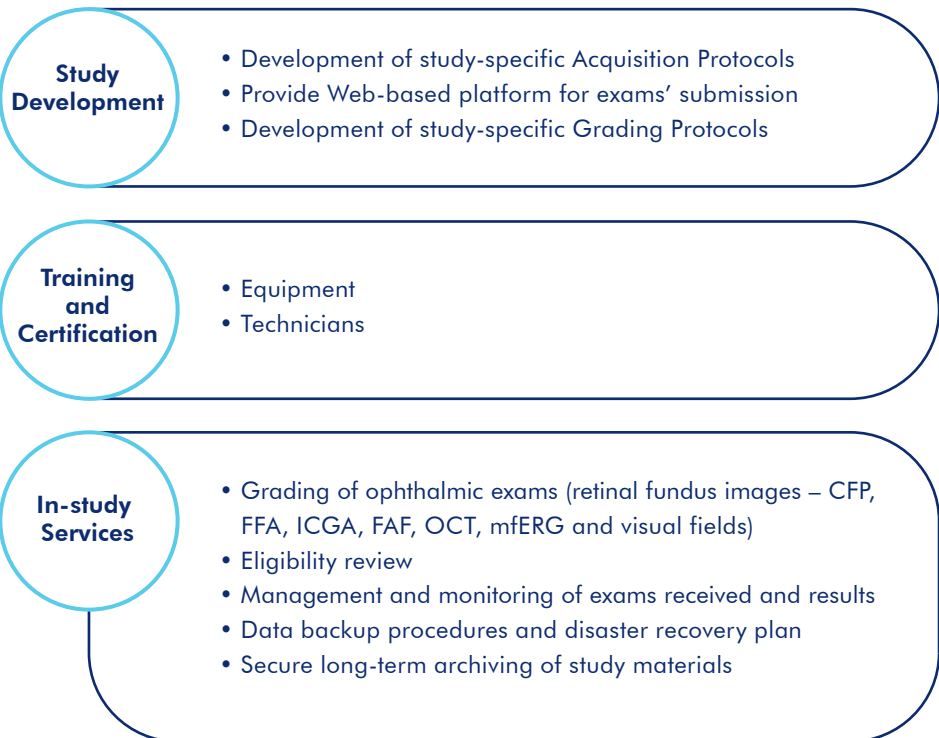
It serves as central Reading Centre for a series of multinational/multicentric clinical studies, mainly in Diabetic Retinopathy (DR) and Age-related Macular Degeneration (AMD). CORC is also the central Reading Centre for the Diabetic Retinopathy Screening Programme of the Central Region of Portugal since 2011.

CORC has a secure custom-designed web based tool to transmit images between Clinical Sites and

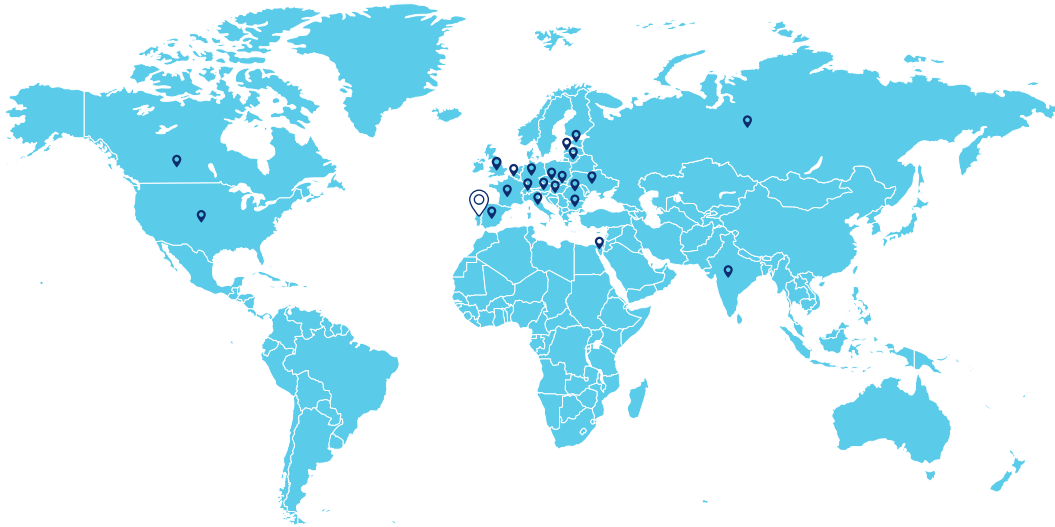
CORC (<https://studies.corc.pt/>). This system is hosted in the AIBILI's Data Centre.

For grading purposes CORC uses licensed software from the equipment suppliers, such as Cirrus HD-OCT (Carl Zeiss Meditec), Heidelberg Eye Explorer (Heidelberg Engineering), RETIsystem (Roland Consult), Topcon OCT (Topcon Corporation), etc.

For research, CORC has novel in-house developed software to assess microaneurysm turnover in DR (RetmarkerDR®), classify and quantify AMD lesions (RetmarkerAMD) and perform segmentation of the retinal layers on OCT.



## Receive and Grade Exams from



- 📍 AUSTRIA
- 📍 BELGIUM
- 📍 BULGARIA
- 📍 CANADA
- 📍 CZECH REPUBLIC
- 📍 ESTONIA
- 📍 FRANCE
- 📍 GERMANY
- 📍 HUNGARY
- 📍 INDIA
- 📍 ISRAEL
- 📍 ITALY
- 📍 LATVIA
- 📍 LITHUANIA
- 📍 POLAND
- 📍 PORTUGAL
- 📍 ROMANIA
- 📍 RUSSIA
- 📍 SLOVAKIA
- 📍 SPAIN
- 📍 SWITZERLAND
- 📍 UK
- 📍 UKRAINE
- 📍 USA

## N° of Projects at CORC (2017-2019)

N° of Projects

| Year        | Diabetic Retinopathy | AMD      | Other    | Total     |
|-------------|----------------------|----------|----------|-----------|
| 2017        | 11                   | 3        | 1        | 15        |
| 2018        | 10                   | 7        | 1        | 18        |
| <b>2019</b> | <b>8</b>             | <b>8</b> | <b>2</b> | <b>18</b> |



## Representative Publications

Soares M, Neves C, Marques IP, Pires I, Schwartz C, Costa MÂ, Santos T, Durbin M, Cunha-Vaz J. **Comparison of diabetic retinopathy classification using fluorescein angiography and optical coherence tomography angiography.** Br J Ophthalmol. 2017 Jan;101(1):62-68. doi: 10.1136/bjophthalmol-2016-309424.

Figueira J, Fletcher E, Massin P, Silva R, Bandello F, Midena E, Varano M, Sivaprasad S, Eleftheriadis H, Menon G, Amaro M, Ayello Scheer S, Creuzot-Garcher C, Nascimento J, Alves D, Nunes S, Lobo C, Cunha-Vaz J; EVICR.net Study Group. **Ranibizumab Plus Panretinal Photocoagulation versus Panretinal Photocoagulation Alone for High-Risk Proliferative Diabetic Retinopathy (PROTEUS Study).** Ophthalmology. 2018 May;125(5):691-700. doi: 10.1016/j.ophtha.2017.12.008.

Farinha C, Cachulo ML, Alves D, Pires I, Marques JP, Barreto P, Nunes S, Costa J, Martins A, Sobral I, Láins I, Figueira J, Ribeiro L, Cunha-Vaz J, Silva R. **Incidence of Age-Related Macular Degeneration in the Central Region of Portugal: The Coimbra Eye Study – Report 5.** Ophthalmic Res. 2019;61(4):226-235. doi: 10.1159/000496393. Epub 2019 Mar 1. PubMed PMID: 30820012.

Marques IP, Alves D, Santos T, Mendes L, Santos AR, Lobo C, Durbin M, Cunha-Vaz J. **Multimodal Imaging of the Initial Stages of Diabetic Retinopathy: Different Disease Pathways in Different Patients.** Diabetes. 2019 Mar;68(3):648-653. doi: 10.2337/db18-1077. Epub 2018 Dec 6. PubMed PMID: 30523027.

Marques JP, Pires J, Simão J, Marques M, Gil JQ, Láins I, Alves D, Nunes S, Cachulo ML, Miller JB, Vavvas DG, Miller JW, Husain D, Silva R. **Validation of RetmarkerAMD as a semiautomatic grading software for AMD.** Eye (Lond). 2019 Oct 23. doi: 10.1038/s41433-019-0624-7. PubMed PMID: 31645672.



# CNTM - CENTRE FOR NEW TECHNOLOGIES IN MEDICINE

Director: José Cunha-Vaz, MD, PhD

Staff: Celina Canguero, Luis Mendes, Rufino Silva, Telmo Miranda, Torcato Santos



The Centre for New Technologies in Medicine (CNTM) develops new medical diagnostic techniques with special emphasis on the area of eye fundus imaging.

The eye offers unique opportunities to obtain in a non-invasive manner information on the body, in general and of the retina and brain in particular. It is, in fact, a window to the body. We are particularly interested in methodologies that allow repeated observations and measurements in order to identify early alterations that

may allow timely therapeutic interventions, e.g., precision medicine.

Our group has been able to identify novel biomarkers of disease progression, such as microaneurysm turnover in diabetic retinopathy identified automatically by software developed in-house, the Retmarker®, and fluid quantification in the retinal diseases by identifying noninvasively changes in the Blood-Retinal Barrier in the retina, using a novel patented algorithm, the OCT-Leakage.



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**Research Focus**

- Multimodal imaging of retinal disease
- Characterization of capillary closure as the main alteration that identifies diabetic retinopathy progression
- OCT-Leakage. Layer by layer fluid analysis of the retina
- Characterization of prognostic biomarkers of retinal disease progression using artificial intelligence
- Characterization of response to anti-VEGF treatment in Diabetic Macular Edema

## Nº of Projects at CNTM (2017-2019)

| Year        | Nº of Projects                      |                         | Total     |
|-------------|-------------------------------------|-------------------------|-----------|
|             | Imaging/<br>Artificial Intelligence | Diabetic<br>Retinopathy |           |
| 2017        | 10                                  | 1                       | 11        |
| 2018        | 7                                   | 3                       | 10        |
| <b>2019</b> | <b>6</b>                            | <b>5</b>                | <b>11</b> |



## Representative Publications

Cunha-Vaz J, Santos T, Alves D, Marques I, Neves C, Soares M, Lobo C: **Agreement between OCT-Leakage and Fluorescein Angiography to identify sites of alteration of the Blood-Retinal Barrier in Diabetes.** Ophthalmology Retina 2017;1:395-403.

Durbin MK, An L, Shemonski DS, Soares M, Santos T, Lopes M, Neves C, Cunha-Vaz J: **Quantification of Retinal Microvascular Density in Optical Coherence Tomography Angiography Images in Diabetic Retinopathy.** JAMA Ophthalmol. 2017;135(4):370-376.

Santos AR, Alves D, Santos T, Figueira J, Silva R, Cunha-Vaz JG. **Measurements of retinal fluid by Optical Coherence Tomography Leakage in Diabetic Macular Edema: A Biomarker of Visual Acuity Response to Treatment.** Retina. 2019 Jan;39(1):52-60. doi: 10.1097/IAE.0000000000001905.

Farinha C, Santos T, Santos AR, Lopes M, Alves D, Silva R, Cunha-Vaz J.: **Optical Coherence Tomography Leakage in Neovascular Age-Related Macular Degeneration: identification of choroidal neovascularization activity by location and quantification of abnormal fluid under anti-vascular endothelial growth factor therapy.** Retina. 2019 Jan 24. doi: 10.1097/IAE.0000000000002470.

Marques IP, Alves D, Santos T, Mendes L, Santos AR, Lobo C, Durbin M, Cunha-Vaz J: **Multimodal Imaging of the Initial Stages of Diabetic Retinopathy. Different Disease Pathways in Different Patients.** Diabetes. 2018 Dec 6. pii: db181077. doi: 10.2337/db18-1077.





# CHAD - CENTRE FOR HEALTH TECHNOLOGY ASSESSMENT AND DRUG RESEARCH



Director: [Francisco Batel-Marques](#), PhD

Staff: Alexandra Escada, Ana Penedones, Carlos Alves, Carlos Fontes Ribeiro, Daniel Fernandes, Diogo Mendes, Inês Ribeiro, Maria Viegas Nascimento, Óscar Lourenço

The Centre for Health Technology Assessment and Drug Research (CHAD) focus is on evaluation of medicines and other medicinal products for market access purposes, aiming at financing and reimbursement and pharmacovigilance.

CHAD provides scientific information to support the decision making in healthcare policy and practice. Health Technology Assessment studies are necessary to ensure equity in the access to medicines and the most favourable benefit/risk and cost/effectiveness ratios in the drug use process. It is, therefore, of capital importance in both drug reimbursement decisions at both ambulatory and hospital settings.

CHAD is also a qualified resource to work closely with Pharmaceutical Industry in all the different phases of drug development.

CHAD provides pharmacovigilance services necessary in clinical studies. It has a pharmacovigi-

lance software fully compliant with the regulations, directives, and the general guidance related to electronic reporting of adverse events (US FDA 21 CFR part 11 and EMA's Good Pharmacovigilance Practice (GVP) Guidelines) for this purpose, as well as SOPs ICH-GCP compliant to perform pharmacovigilance clinical research. It has a license to use MedDRA, a standardised international medical terminology designed for use in safety monitoring of medicinal products through all phases of the development cycle (i.e., from clinical trials to post-marketing surveillance) that supports ICH electronic communication within the E2B Individual Case Safety Report.

Since 2008 CHAD has been responsible for a Pharmacovigilance Unit of the National Pharmacovigilance System which is contracted with the National Authority of Medicines and Health Products (INFARMED, IP).



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#### Main Activities

- Health Technology Assessment, pricing and reimbursement (medicines and medical devices)
- Primary research (Patient-based outcomes and real-world effectiveness studies)
- Secondary research (Literature searching and evaluation, Systematic reviews and meta-analysis, Indirect/mixed treatment comparisons according to methodological guidelines, Comparative effectiveness studies, and Expert reports)
- Pharmacovigilance and Risk Management services



## Nº of Projects at CHAD (2017-2019)

| Year        | Nº of Projects |             | Total     |
|-------------|----------------|-------------|-----------|
|             | Market Access  | Drug Safety |           |
| 2017        | 22             | 7           | 29        |
| 2018        | 21             | 7           | 28        |
| <b>2019</b> | <b>16</b>      | <b>8</b>    | <b>24</b> |

### Representative Publications

Penedones A, Alves C, Batel Marques F. **Recommendations to conduct and report systematic reviews in medical literature: a scoping review.** BMC Med Res Methodol. 2019;19(1):234.

Alves C, Mendes D, Batel Marques F. **Fluoroquinolones and the risk of tendon injury: a systematic review and meta-analysis.** Eur J Clin Pharmacol. 2019 Oct;75(10):1431-1443. doi: 10.1007/s00228-019-02713-1.

Batel-Marques F, Pereira D, Mendes D, Alves C, Penedones A. **Effectiveness in clinical practice versus efficacy of dipeptidyl peptidase-4 inhibitors in clinical trials for type 2 diabetes: protocol for systematic review.** BMJ Open. 2019 Sep 17;9(9): e032522. doi: 10.1136/bmjopen-2019-032522.

Penedones A, Alves C, Batel Marques F. **Risk of non-arteritic ischemic optic neuropathy with phosphodiesterase type 5 inhibitors: a systematic review and meta-analysis.** Acta Ophthalmol. 2019 Sep 27. doi: 10.1111/aos.14253.

Mendes D, Alves C, Silverio N, Batel Marques F. **Prevalence of undiagnosed hypothyroidism in Europe: a systematic review and meta-analysis.** Eur Thyroid J. 2019 Jun;8(3):130-143. doi: 10.1159/000499751.



## DC – DATA CENTRE

Director: [Carlos Domingues](#), BSc

Staff: Celina Canguero, Hugo Morgado, José Monteiro, Patrícia Silva, Telmo Miranda, Torcato Santos



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AIBILI Data Centre was built specifically to support AIBILI's information systems but the existing space and environment conditions allow to grow up to store clients/partners data and information. Inside the Data Centre, the server racks are connected to two separate power circuits, protected by two redundant Uninterruptable Power Supplies (UPS). These redundant power supply units ensure that a failure of one power supply unit does not cause any problems and that power is always supplied to servers. The UPS also ensures that the quality remains constant. It compensates for voltage and frequency fluctuations and thereby effectively protects sensitive computer electronic components and systems. Block batteries ensure that all operating applications can run for almost three hours. For Data Centre cooling AIBILI has implemented a cold air container solution with redundant air conditioning units. The air is directed to the container through the floor and flows through the racks, dissipating the heat produced by servers and providing adequate temperature and humidity for electronic equipment's. Water detection sensors on the floor and automatic fire extinguisher (based on gas-based suppression system FM200) complements the Data Centre asset-protection.

Presently Information Technology Unit maintains more than 30 servers, either virtual or physical supported on different operating systems and technologies. There are specific Standard Operating Procedures (SOPs) in place, developed according IT best practices such as Informa-

tion Technology Infrastructure Library (ITIL), and project management standards such as recommended by the Project Management Institute (PMI). All changes in the production environment are preceded by testing and validation processes, according to GAMP5 V-model and methodology. This Unit is responsible to guarantee the safety and integrity of the data and images collected all in compliance with GCP Guidelines and applicable national legislation. AIBILI specific SOPs for Information Technology and Data Centre also comply with US FDA 21 CFR part 11 (Guidance for Electronic Records) and ISO 27001 (Information Security Management). Regular internal audits and penetration tests are performed to ensure the safety and integrity of data.

All this information is categorized and specific backup policies are defined according information value. Long term storage procedures are in place to assure all the information lifecycle. Information Technology Unit manages over than 30 TB of useful storage (clinical images and databases, administrative information, project information and long term storage).

AIBILI Data Centre is certified by ECRIN - European Clinical Research Infrastructure Network ([www.ecrin.org](http://www.ecrin.org)) since April 2016. Compliance with ECRIN v3 standards confirms AIBILI capacity to provide appropriate and effective data management services for multinational, randomised controlled studies.



**Main  
Activities**

- CDMS (Clinical Data Management System) validation, implementation and support
- eCRF (Electronic Case Report Form) development and support
- Key users helpdesk
- CORC-IT platform support
- Data export and biostatistics support
- Long Term Storage
- EVICR.net webinar platform
- Software development

**N° of Projects at DC (2017-2019)**

| Year        | N° of Projects    |           |
|-------------|-------------------|-----------|
|             | Projects/Services | Total     |
| 2017        | 15                | 15        |
| 2018        | 16                | 16        |
| <b>2019</b> | <b>15</b>         | <b>15</b> |



# ORGANIZATIONAL UNITS

## ADMINISTRATION

CEO: [Cecília Martinho](#)

Staff: Laura Seco, Mara Miraldo, Marco Santos, Paulo Barros, Tânia Melro

The Administrative Services are responsible for the management of AIBILI and to perform all the necessary administrative tasks, including finances and accountability, human resources management, as well as maintenance of infrastruc-

ture according to the institution's needs. The Administrative Services establishes a direct liaison between the Board of Directors of AIBILI and its Centres and supporting Units.



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## QUALITY MANAGEMENT UNIT (QMU)

Staff: Cecília Martinho, Rita Fernandes, Marta Ventura

The Quality Management Unit (QMU) guarantees that AIBILI has the necessary resources to provide the services and meet the needs of its Clients and interested parties.

The QMU assures that the Quality Management System (QMS) is maintained effective and efficient permitting improvement.

AIBILI is ISO 9001 certified for the activities of: Research and Development in New Technologies for Medicine with particular emphasis in the Areas of Imaging, Optics and Photobiology; Performance of Clinical Studies; Planning, Coordination, Monitoring of Clinical Research Activities; Health Technology Assessment; Grading of Eye Exams; and Data Centre Activities.

It has a Standard Operating Procedure (SOP) Manual which contains general organizational SOPs and specific SOPs for each process, in compliance with ISO 9001:2015, ICH-GCP Gui-

delines, requirements for Certification of ECRIN Data Centres, General Data Protection Regulation (EU) 2016/679 and applicable national law, as well as other regulatory requirements, statutory and legal, applicable to AIBILI activities.

Currently the paper Document Management System (SOP Manual) is being transposed into a digital format to streamline the access to management information, approvals, records and archiving.

Internal auditing is a guarantee that procedures are followed at AIBILI and the QMS is in improvement to enhance customer satisfaction by meeting customers' requirements.

AIBILI's Quality Management Unit also provides consultancy services to other healthcare institutions to implement quality systems ISO 9001 and ICH-GCP compliant due to its long and vast experience in this field.



### Contacts

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## TRANSLATIONAL RESEARCH AND TECHNOLOGY TRANSFER UNIT (UTT)

Staff: Cecília Martinho, Daniel Fernandes, Maria Madeira



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The Translational Research and Technology Transfer Unit is responsible to provide all the support to facilitate and promote the transfer of R&D activities and pre-clinical studies to the development of clinical studies and to enhance the adoptions of best practices in the community. It is responsible for identifying perspectives and perform analysis of technology transfer, creating the conditions for contracting with industry and other stakeholders, namely intellectual property implications.

This Unit is responsible to identify opportunities and apply for external funding, namely R&D programs in the health market. Currently it is responsible for AIBILI participation in European Union projects and supporting the other partners on administrative and legal issues.

The Translational Research and Technology Transfer Unit is responsible for promoting AIBILI and its Centres and is the main contact point for establishing partnership and collaborations with other institutions.

## INFORMATION TECHNOLOGY UNIT (IT)

Staff: Celina Canguero, Carlos Domingues, Hugo Morgado, Patrícia Silva, Telmo Miranda, Torcato Santos, José Monteiro



### Contacts

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The Information Technology Unit is responsible for the management and maintenance of AIBILI Data Centre, IT networks and information systems. The Data Centre, built in 2014 for storing AIBILI's critical information, houses all AIBILI servers/systems: the Electronic Medical Record that is daily used to collect patient clinical information at CEC; the custom-designed web based platform used to exchange grading data and images by CORC (<https://studies.corc.pt/>); the Clinical Data Management System that is used in the development of eCRFs for each clinical study; the PhVC Manager – Extedo that is used for pharmacovigilance in clinical studies by CHAD as well as the Clinical Trial Management

System (CTMS) used for the management of multiple multinational clinical studies by 4C. There are also other administrative information systems supported in AIBILI's Data Centre. AIBILI's Data Centre houses EVICR.net website ([www.evicr.net](http://www.evicr.net)), EVICR.net Educational Programme webinar platform ([https://cloud.aibili.pt/evicrnet\\_webinars](https://cloud.aibili.pt/evicrnet_webinars)) and also supports other administrative/office information systems.

AIBILI Data Centre is certified by ECRIN - European Clinical Research Infrastructure Network ([www.eclin.org](http://www.eclin.org)) and is part of the ECRIN Data Centre Network. AIBILI Data Centre can provide safe, secure, compliant and efficient management of clinical research data.



# ETHICS COMMITTEE

AIBILI has an Independent Ethics Committee (IEC/IRB) that is responsible for protecting the rights, safety and wellbeing of human subjects involved in clinical studies (not involving Investigational Medicinal Products (IMP's) or medical devices) performed at AIBILI according to the Portuguese Law n° 97/95 of 10 May.

AIBILI Ethics Committee is available to be called upon CEIC's request, in case it is needed for the review of ophthalmology clinical trials or studies since it has expertise in this scientific area.

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## MEMBERS

### President

André Dias Pereira, PhD  
(Director of the Centre for Biomedical Law of the University of Coimbra and Professor at the Faculty of Law, University of Coimbra)

### Vice-President and Secretary

Margarida Duarte Ramos Caramona, PhD  
(Emeritus Professor at the Faculty of Pharmacy, University of Coimbra)

José António Moura Pereira, MD  
(Ophthalmologist at the University Hospital of Coimbra)

Maria Elizabete Batista Geraldês, MD  
(Endocrinologist at the University Hospital of Coimbra)

Paulo Simões, BSc  
(Father, Director of University Institute of Justice and Peace, Coimbra)

Filomena Maria Ferreira Ramos Mena, BSc  
(Nurse at the National Institute of Forensic Medicine, Coimbra)

Maria Cecília Martinho, BSc  
(AIBILI CEO)



# 4

## RESEARCH AND INNOVATION

Throughout its thirty years of existence, AIBILI has created an excellence track record in ophthalmology clinical research, being internationally recognized for its innovation in the area of imaging biomarkers and diagnostics.

With the huge acceleration in innovation in the past years, and the increased complexity in medical needs, it has become crucial to science to escort this acceleration. Researchers must provide

more insight on disease understanding and deliver more healthcare solutions to promote and protect human health. Likewise, AIBILI also needs to keep up its pace in innovation.

In order to promote science and technology advancement and bring potential new treatments and diagnostic tools to the market, in 2019 AIBILI has assumed an integrated Strategic Research Plan with five main research pathways.



# DIABETIC RETINOPATHY RESEARCH PROGRAM

Coordinator: [João Figueira](#)

Research Team: Ana Rita Santos, Inês Marques, José Cunha-Vaz, Luis Mendes, Luisa Ribeiro, Maria Madeira, Mário Soares, Torcato Santos

Diabetic Retinopathy (DR) remains a major cause of blindness as the prevalence of diabetes is expected to approximately double globally between 2000 and 2030. DR progresses over time at different rates in different individuals with only a limited number developing significant vision loss due to the two major vision-threatening complications, clinically significant macular edema and proliferative retinopathy.

Good metabolic control is important to prevent and delay progression, but whereas some patients escape vision loss even with poor control, others develop vision loss despite good metabolic control. Our research group has been able to identify three different DR phenotypes character-

ized by different dominant retinal alterations and different risks of progression to vision-threatening complications. Microaneurysm turnover (MAT) has been validated as a prognostic biomarker of development of clinically significant macular edema, whereas subclinical macular edema identified by Optical Coherence Tomography (OCT) appear to be also a good candidate as organ-specific bio markers of DR. Haemoglobin A1c (HbA1c) remains the only confirmed systemic prognostic biomarker of DR progression.

The identification of different phenotypes of DR with different risks for development of vision-threatening complications opens new avenues for the comprehension of DR onset.



#### Contacts

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## Research Program Main Goals

Identify new biomarkers of DR progression and their correlation with different risks for development of vision-threatening complications, offering new perspectives for understanding DR and for its personalized management.

## Projects

### **PROGRESS – Progression of Diabetic Retinopathy. Identification of Signs and Surrogate outcomes**

ClinicalTrials.gov n° NCT 03010397

PROGRESS is a project dedicated to characterize the 5-year progression of mild non-proliferative DR (NPDR), in patients with diabetes type 2, to vision-threatening complications.

Through this work, the predictive risk of ocular and systemic markers will be accessed to identify prediction methods for disease development and progression. Moreover, in the retinal neurodegenerative steps in different stages of DR will be explored.

### **CORDIS - Characterization of retinal vascular disease in diabetes type 2, using novel non-invasive imaging methods**

ClinicalTrials.gov n° NCT03696810

Financial support: Portugal 2020 - 02/SAICT/2017 -

Project n° 030375

The main objective of this project is to better characterize, using new methods, OCTA and OCT-Leakage, the evolution and progression of phenotypes B and C of DR identifying eyes that show worsening and disease progression to sight-threatening DR (progression phenotypes), allowing for a better characterization of the two main features of the leaky or ischemic progressor phenotypes, using non-invasive methodologies.

### **RECOGNISED - Retinal and cognitive dysfunction in type 2 diabetes: unravelling the common pathways and identification of patients at risk of dementia**

Sponsor: VHIR, Barcelona, Spain

Financial support: Horizon2020 – SC1-BHC-2019 –

Project n° 847749

RECOGNISED is a multicentre, multinational study that aims to investigate the common mechanisms involved in the pathogenesis of DR and cognitive impairment in the type 2 diabetes (T2D). At the end, a main goal is to use the retina as a tool to identifying individuals with T2D at a higher risk of developing cognitive decline or dementia.

## Representative Publications

Marques IP, et al. **Multimodal Imaging of the Initial Stages of Diabetic Retinopathy: Different Disease Pathways in Different Patients.** *Diabetes.* 2019 Mar,68(3):648-653. doi: 10.2337/db18-1077. Epub 2018 Dec 6. PubMed PMID:30523027.

Lobo C, et al. **Subclinical Macular Edema as a Predictor of Progression to Central-Involved Macular Edema in Type 2 Diabetes.** *Ophthalmic Res.* 2018,60(1):18-22. doi: 10.1159/000486792. Epub 2018 Mar 6. PubMed PMID: 29510401.

Ribeiro L, et al. **Different Phenotypes of Mild Nonproliferative Diabetic Retinopathy with Different Risks for Development of Macular Edema (C-TRACER Study).** *Ophthalmic Res.* 2018,59(2):59-67. doi:10.1159/000484666. Epub 2017 Dec 22. PubMed PMID: 29268280.

Santos AR, et al, **Functional and Structural Findings of Neurodegeneration in Early Stages of Diabetic Retinopathy: Cross-sectional Analyses of Baseline Data of the EUROCONDOR Project.** *Diabetes.* 2017 Sep,66(9):2503-2510. doi: 10.2337/db16-1453. Epub 2017 Jun 29. PubMed PMID: 28663190.

Cunha-Vaz J, et al. **Diabetic Retinopathy Phenotypes of Progression to Macular Edema: Pooled Analysis From Independent Longitudinal Studies of up to 2 Years' Duration.** *Invest Ophthalmol Vis Sci.* 2017 May 1,58(6):BIO206-BIO210. doi: 10.1167/iovs.17-21780. PubMed PMID: 28785768.



# AGE-RELATED MACULAR DEGENERATION RESEARCH PROGRAM

Coordinator: [Rufino Silva](#)

Research Team: Cláudia Farinha, José Cunha-Vaz, Luis Mendes, Maria Luz Cachulo, Maria Madeira, Patrícia Barreto, Torcato Santos

Age-related macular degeneration (AMD) is the leading cause of adult blindness in developed countries, which affects almost 30% of the older population. In fact, with the aging of population, AMD will become globally an increasingly important and prevalent disease worldwide. The hallmark of the early phases of AMD are macular drusen and pigmentary changes, and it progresses slowly from early AMD to intermediate AMD (iAMD) and ultimately late-stage AMD with severe and frequently irreversible lesions. Of note, it is probable that the early and intermediate forms of AMD do not represent a single disease, but rather a collection of sub-

types, which ultimately progress to the advanced forms. Therefore, elucidating these subtypes and their underlying pathogenesis will be critical in developing effective therapies for these earlier stages of AMD.

The aetiology of AMD is complex, and although genome-wide and gene-candidate studies have been enabled to identify genetic variants associated with AMD pathogenesis, studies on gene-environment interactions have gained increased relevance on the disease onset. Hence, an healthy diet and the use of nutritional supplements created the environment for prevention in this area.



#### Contacts

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## Research Program Main Goals

Contribute to the understanding of the pathophysiology of AMD, and to identify novel targets for future treatments of this condition and innovative diagnosis methods, focusing on:

- Structure and function relation in AMD
- Genomics and metabolomics of AMD
- Lifestyle and genetics interplay in AMD onset and progression
- Drug safety and effectiveness in AMD
- Development of innovative approaches, based on Artificial Intelligence, to facilitate AMD diagnosis

## Projects

**Metabolomics, Genetics and Environment - A novel integrative approach to Age-Related Macular Degeneration** (IN0654) Network with MEEI and the Harvard Medical School, Boston, USA.

This project purposes to characterize the metabolome of AMD progression over five years and evaluate the relationship between metabolomics and genetics in AMD and identify new candidate AMD-metabolite associations.

It will provide unique insights into the AMD pathogenesis and progression and has the potential to identify novel potential future biomarkers, which can ultimately lead to precision medicine in AMD.

**COIMBRA EYE STUDY - Epidemiological study of the prevalence and incidence of Age-Related Macular Degeneration in Portugal**

ClinicalTrials.gov n° NCT01298674 and NCT02748824

**Age-related Macular Degeneration in Portugal - Prevalence, incidence and risk factors in the era of multimodal imaging**

The main objective of this project is to take advantage of multimodal evaluation of possible risk factors and biomarkers, demographic factors, genetics and structural markers, to evaluate a possible progression biomarker and infer on an association with fast progressor AMD phenotype or another particular phenotype.

**Age-Related Macular Degeneration: Genetic susceptibility, Nutrition and Lifestyle**

The purpose of this project is to determine the effect modification on the risk of AMD onset and progression of high-risk-patients due to nutrition and lifestyle. It will assess on what grounds food, nutrients and lifestyle protect or not patients at genetic risk for AMD.

**ATLANTIC - A Randomized, Double-masked, Sham-controlled Phase 4 Study of the Efficacy, Safety, and Tolerability of Intravitreal Aflibercept Monotherapy Compared to Aflibercept With Adjunctive Photodynamic Therapy in patients with Polypoidal Choroidal Vasculopathy**

EudraCT n° 2015-001368-20  
ClinicalTrials.gov n° NCT02495181

Atlantic is a multicentre study dedicated to compare the efficacy and safety of intravitreal aflibercept (IVA) with sham photodynamic therapy (sPDT) versus IVA with verteporfin photodynamic therapy (sPDT) in a Caucasian population with treatment-naive PCV, enrolling in a treat and extend regimen.

**Phenotypic and genotypic characterization of Polypoidal Choroidal Vasculopathy (PCV) in Caucasian populations. A multicenter retrospective study**

This study aims to characterize the genetic, anatomical and imaging features of PCV in a large Caucasian population in order to provide a better understanding of this condition in this specific ethnicity.

**MACUSTAR - Intermediate AMD: Development of Novel Clinical Endpoints for Clinical Trials in Patients with a Regulatory and Patient Access Intention**

Sponsor: UKB, Bonn, Germany  
ClinicalTrials.gov n° NCT03349801  
Financial Support: European Union and EFPIA - Innovative Medicines Initiative 2 Joint Undertaking - Grant Agreement n° 116076

The major objective of MACUSTAR is to develop novel clinical endpoints for clinical trials with a regulatory and patient access intention in the area of functional, structural, and patient-reported outcome measures in patients with intermediate age-related macular degeneration (iAMD). MACUSTAR will also characterize visual impairment in iAMD and its progression, as well as identify risk factors for progression to late-stage AMD.

## Representative Publications

Laíns I, et al. **Human Plasma Metabolomics in Age-Related Macular Degeneration: Meta-Analysis of Two Cohorts.** *Metabolites.* 2019 Jul 2,9(7). pii: E127. doi: 10.3390/metabo9070127. PubMed PMID: 31269701, PubMed Central PMCID: PMC6680405.

Laíns I, et al **Urine Nuclear Magnetic Resonance (NMR) Metabolomics in Age-Related Macular Degeneration.** *J Proteome Res.* 2019 Mar 1,18(3):1278-1288. doi: 10.1021/acs.jproteome.8b00877. Epub 2019 Feb 6. PubMed PMID: 30672297.

Farinha C, et al. **Optical Coherence Tomography Leakage in Neovascular Age-Related Macular Degeneration: Identification of Choroidal Neovascularization Activity by Location and Quantification of Abnormal Fluid Under Anti-Vascular Endothelial Growth Factor Therapy.** *Retina.* 2019 Jan 24. doi: 10.1097/IAE.0000000000002470. PubMed PMID: 30689620.

Farinha CVL et al. **Incidence of Age-Related Macular Degeneration in the Central Region of Portugal: The Coimbra Eye Study - Report 5.** *Ophthalmic Res.* 2019,61(4):226-235. doi: 10.1159/000496393. Epub 2019 Mar 1. PubMed PMID: 30820012.

Farinha C, et al. **Ranibizumab for the Treatment of Diabetic Macular Oedema in the Real-World Clinical Setting in Portugal: A Multicentre Study.** *Ophthalmologica.* 2019,241(1):1-8. doi: 10.1159/000489046. Epub 2018 Jun 8. PubMed PMID: 29886497.



# IMAGING BIOMARKERS RESEARCH PROGRAM

Coordinator: [Conceição Lobo](#)

Research Team: Ana Rita Santos, José Cunha-Vaz, João Figueira, Luis Mendes, Maria Madeira, Telmo Miranda, Torcato Santos

The eye offers unique opportunities to obtain in a non-invasive manner information on the body, in general and of the retina and brain. It is, in fact, a window to the body. The retinal circulation and the retina can be examined using a variety of methods. Fundus Digital Photography, Optical Coherence Tomography (OCT) and Optical Coherence Tomography Angiography (OCTA) are non-invasive examinations that offer extremely promising perspectives as the information collected can be analysed automatically. The analysis of the data can also be tailored to specific purposes, allowing val-

uating imaging biomarkers of disease. These imaging biomarkers may give information on retinal and eye disease but also may serve as indicators of systemic disease, such as brain degenerative diseases and circulatory disorders.

Our group has been able to identify biomarkers of disease progression, such as MA turnover in diabetic retinopathy identified automatically by software developed in-house, the Retmarker®, and identify non-invasively changes in the Blood-Retinal Barrier in the retina, using also a novel AIBILI patented algorithm, the OCT-Leakage.



## Contacts

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## Research Program Main Goals

Development of new imaging techniques of the eye fundus without disturbing in any way the ocular and body environment. Particular interest is given to methodologies that allow repeated observations and measurements in order to identify early alterations and the degree of activity of these alterations when present over time.

## Projects

### Identification of Capillary Closure in using Optical Coherence Tomography Angiography

The major goal is to identify reliable methods to quantify retinal vascular alterations, which allow disease characterization and identification of the different disease progression groups. As ultimate goal, we aim on facilitate disease stage identification in clinical practice, as well as to facilitate the identification of patients with higher risk for progression.

### OCT-Leakage. Layer by layer fluid analysis of the retina

Our group is developing applications that resort to advanced imaging algorithms to enable analysis of OCT data, focusing on the segmentation of the different layers of the retina and the permeability of the Blood-Retinal Barrier. A novel analysis "Method and device for the non-invasive indirect identification of sites of alterations of the Blood-Retinal Barrier" was published under the Patent Cooperation Treaty number WO2016/174637A1.

### Artificial intelligence for characterization of retinal biomarkers

The purpose is the development, testing, and validation of cognitive computing methods applied to state-of-art imaging data to be used in the screening and management of eye disease.

### FILTER - Framework to Develop and Validate Automated Image Analysis Systems for Early Diagnosis and Treatment of Eyes at Risk in Blinding Age-Related Diseases

Financial support: Portugal 2020 - 02/SAICT/2017 - Project n° 032412

FILTER aims to development and validation of a prototype to be used in the screening and management of blinding age-related diseases.

The prototype will allow the detection, characterization, and follow-up of lesions associated with AMD and DR. Novel methods will be developed for the analysis of OCT imaging data and CFP images.

### ADRIAN - Development and Validation of a Machine Learning Algorithms for Automated Prediction of Diabetic Retinopathy Progression

Partnership with Roche.

With this collaboration, ROCHE and AIBILI expects to develop and validate a machine learning (ML) algorithms that automatically predict Diabetes Mellitus patients that are at high risk for progression in Diabetic Retinopathy severity and vision-threatening conditions.

## Research Contracts and Partnerships

Quantification of Retinal Microvasculature in Retinal Disease  
Sponsor: Carl Zeiss Meditec, USA

ADRIAN - Development and Validation of a Machine Learning Algorithms for Automated Prediction of Diabetic Retinopathy Progression  
Sponsor: Roche, Switzerland

## Representative Publications

Marques IP, et al. **Multimodal Imaging of the Initial Stages of Diabetic Retinopathy: Different Disease Pathways in Different Patients**. *Diabetes*. 2019 Mar;68(3):648-653. doi: 10.2337/db18-1077. Epub 2018 Dec 6. PubMed PMID:30523027.

Santos AR, et al. **Characterization of Initial Stages of Diabetic Macular Edema**. *Ophthalmic Res*. 2019;62(4):203-210. doi: 10.1159/000499117. Epub 2019 Apr 23. PubMed PMID: 31013506.

Santos AR, et al. **Measurements of Retinal Fluid By Optical Coherence Tomography Leakage In Diabetic Macular Edema: A Biomarker of Visual Acuity Response to Treatment**. *Retina*. 2019 Jan;39(1):52-60. doi: 10.1097/IAE.0000000000001905. PubMed PMID: 29077605.

Durbin MK, et al **Quantification of Retinal Microvascular Density in Optical Coherence Tomography Angiography Images in Diabetic Retinopathy**, *JAMA Ophthalmol*. 2017, vol. 135, N 4, pp 370-376.

Cunha-Vaz J, et al. **Agreement between OCT Leakage and Fluorescein Angiography to Identify Sites of Alteration of the Blood-Retinal Barrier in Diabetes**. *Ophthalmol Retina*. 2017 Sep - Oct;1(5):395-403. doi: 10.1016/j.oret.2017.02.002. Epub 2017 Mar 29. PubMed PMID: 31047568.



# DRUG EVALUATION RESEARCH PROGRAM

Coordinator: [Francisco Batel-Marques](#)

Research Team: Alexandra Escada, Ana Penedones, Carlos Alves, Diogo Mendes, Inês Ribeiro, Maria Viegas Nascimento

The demands on health services and the challenges of drug development, in the light of increased aging of population, changing patterns of disease and increased costs of medicines, creates the need for research on the effectiveness, the safety and the economics of drugs R&D and reimbursement.

In the Centre for Health Technology Assessment and Drug Research (CHAD) research is performed through several interconnected ongoing projects, aimed at study real world outcomes, safety, economics and market access of drugs.



#### Contacts

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### Research Program Main Goals

To strengthen the evaluation of medicines for the benefit of public health, through research and development of methodologies to assess their safety, effectiveness and efficiency.

## Projects

### DruSER.Net – Drug Safety and Effectiveness Research Network

The DruSER.Net is a research network of Hospitals and Primary Healthcare Centres, which is coordinated by the Pharmacovigilance Unit of Coimbra. The main objective of the DruSER.Net is to investigate and monitor safety and effectiveness of medicines used in routine clinical practice and therefore contributing for patient safety through the conduction of research projects using real-world data

### The Portuguese survey on anticoagulated patients register (START-Portugal-Register)

ClinicalTrials.gov n° NCT03977363

The purpose of the PT-START-Register study is to record the clinical history of patients who initiate anticoagulation prospectively and without interfering with current clinical practice to generate evidence to assess the safety and effectiveness of the various therapeutic options.

### ESSENCE - The Effectiveness, Safety and Patient Experience on Oncology Treatments: Achieving Real-World Evidence

The main objective of ESSENCE Study is to assess whether the outcomes of patients with breast, lung and ovarian cancer treated under real-world conditions reflect the results obtained from clinical trials.

This study also aims to identify the healthcare resources consumption and associated costs implicated in the treatment of cancer patients in routine clinical practice.

### Systematic review: role in drug safety and clinical effectiveness assessment

The aim of this research is to understand the actual role of systematic reviews in drugs' safety assessment and to compare the methodologies of the two major orientations to plan and conduct systematic reviews. It will be analysed the combination of several types of studies (from experimental data to case reports) when performing a systematic review of drug safety.

### Economic evaluation of ophthalmic medicines: does the results estimated based on pre-marketing evidence correlates with clinical practice?

The main objective of this project is to clarify the role of pharmaco-economic studies as a tool to inform policy decision making of ophthalmic drugs. The research will also identify, characterize and assess the methodological quality of pharmaco-economic studies of ophthalmic drugs, and it will evaluate if the results of economic studies reflect the findings from real-world clinical practice evidence.

### Network Meta-analysis

The aim of this research is to assess whether it is possible to produce reliable risk estimates from a network meta-analysis including simultaneously clinical trials and observational studies in order to establish comparisons between treatments which would not be possible to compare based exclusively on data from experimental studies.

### Coimbra Pharmacovigilance Regional Centre

The main aim is to validate the post-marketing adverse drug reactions reported to the Coimbra Regional Unit of the Portuguese Pharmacovigilance System, by assessing causality, seriousness and previous knowledge. Different techniques for safety signals generation are being tested and applied.

## Representative Publications

Ribeiro I, Batel-Marques F, Alves D, Alves C. **An analysis of the effectiveness outcomes of economic studies evaluating ophthalmic drugs: a systematic review.** Acta Ophthalmol. 2020 Jan 30. doi: 10.1111/aos.14362.

Alves C, Mendes D, Batel Marques F. **Fluoroquinolones and the risk of tendon injury: a systematic review and meta-analysis.** Eur J Clin Pharmacol. 2019 Oct;75(10):1431-1443.

Batel Marques F, Pereira D, Mendes D, Alves C, Penedones A. **Effectiveness in clinical practice versus efficacy of dipeptidyl peptidase-4 inhibitors in clinical trials for type 2 diabetes: protocol for systematic review.** BMJ Open 2019;9:e032522.

Penedones A, Alves C, Batel Marques F. **Risk of non-arteritic ischemic optic neuropathy with phosphodiesterase type 5 inhibitors: a systematic review and meta-analysis.** Acta Ophthalmol, 2019, doi: 10.1111/aos.14253.

Mendes D, Alves C, Loureiro M, Fonte A, Batel-Marques F. **Drug-induced hypersensitivity: A 5-year retrospective study in a hospital electronic health records database.** J Clin Pharm Ther. 2019;44(1):54–61.





# TRANSLATIONAL VISION RESEARCH PROGRAM

Coordinator: [António Francisco Ambrósio](#)

Research Team: Ana Raquel Santiago, Elisa Campos, Henrique Alves, José Cunha-Vaz, Maria Madeira, Rosa Fernandes

AIBILI and the Faculty of Medicine of the University of Coimbra have an historical relationship, particularly with the Coimbra Institute for Clinical and Biomedical Research (iCBR, former IBILI) that represents a critical opportunity in the facilitation of translational research and of innovation from the laboratory in vision research.

To (re)start a new research area at AIBILI, named 'Basic and Translational Vision Research' in collaboration with the Retinal Dysfunction and Neuroinflammation Lab from iCBR is one of our priorities and strategies to reinforce the field of translational research in this specific area.



## Contacts

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## Research Program Main Goals

To promote innovative translational vision research, not only by translating laboratory science into new therapeutic strategies, but also by using human samples to find new biomarkers of disease, disease progression and response to therapy.

## Projects

### Identification of new biomarkers of disease, disease progression and response to therapy

With a clear translational perspective, and with the aim of bridging the gap between fundamental and clinical research and find new biomarkers, we intend to analyse ocular fluids (tears, aqueous humour, vitreous humour) and blood, namely at a molecular level, to access proteins, microRNAs, mitochondrial DNA and antimicrobial peptides (AMPs).

### Using the retina as a window to assess pathologies that affect the brain

Taking advantage of the communication between retina and brain, we will assess structural, functional, cellular and molecular changes in the retina and will try to establish correlations with changes occurring in the brain in the context of Alzheimer's disease, and Attention Deficit Hyperactivity Disorder (ADHD).

### Development of new potential therapeutic strategies for retinal diseases

Target the unmet need of novel potential therapeutic strategies to retinal degenerative diseases, focusing on test the efficacy of molecular entities that have been selected based on our studies focused on the mechanism of disease, and new delivery routes, such as biodegradable implants or microparticles loaded with drugs of interest.

## Representative Publications

Boia R, et al. **Treatment with A2A receptor antagonist KW6002 and caffeine intake regulate microglia reactivity and protect retina against transient ischemic damage.** *Cell Death Dis.* 2017, 8(10):e3065. doi: 10.1038/cddis.2017.451.

Aires ID, et al. **Blockade of microglial adenosine A2A receptor suppresses elevated pressure-induced inflammation, oxidative stress, and cell death in retinal cells.** *Glia.* 2019, 67(5):896-914. doi: 10.1002/glia.23579.

Boia R, et al. **Porous poly( $\epsilon$ -caprolactone) implants: a novel strategy for efficient intraocular drug delivery.** *J. Control. Release.* 2019. 316:331-348. doi:10.1016/j.jconrel.2019.09.023.

Chiquita S, et al. **Retinal thinning of inner sub-layers is associated with cortical atrophy in a mouse model of Alzheimer's disease: a longitudinal multimodal in vivo study.** *Alzheimers Res. Ther.* 2019, 11(1):90. doi: 10.1186/s13195-019-0542-8.

Aires ID, et al. **Intravitreal injection of adenosine A2A receptor antagonist reduces neuroinflammation, vascular leakage and cell death in the retina of diabetic mice.** *Sci Rep.* 2019, 9(1):17207. doi: 10.1038/s41598-019-53627-y.

# 5

## INTERNATIONAL NETWORKING

### EVICR.net - EUROPEAN VISION INSTITUTE CLINICAL RESEARCH NETWORK



AIBILI is the Coordinating Centre of EVICR.net, that is responsible for the management of the Network, coordination of multinational clinical research studies as well as developing training activities.

The EVICR.net is a network of European Ophthalmological Clinical Research Centres, dedicated to perform multinational clinical research in ophthalmology with the highest standards of quality, following the European and International Directives for Clinical Research according to harmonized SOPs.

EVICR.net strengthens the capacity of the European Union to explore the determinants of ophthalmic diseases and to develop and optimise the use of diagnostic, prevention and treatment strategies in ophthalmology, by performing multinational clinical research.

It is a platform for ophthalmology multinational clinical research in Europe and a structure to support multinational Investigator-Initiated Research (IIR). EVICR.net is also a resource for Industry in

the development of new drugs and medical devices in ophthalmology.

In order to become a member of EVICR.net, each Clinical Research Centre must apply to the Network and fulfil basic requirements such as dedicated space to perform clinical studies, qualified and experienced personnel, experience of multinational clinical research and to agree to implement organizational Standard Operating Procedures (SOPs) according to ICH GCP Guidelines.

Once a member, the Clinical Site adopts/harmonises EVICR.net SOPs with the help of the Coordinating Centre in order to become a certified Clinical Site of Excellence of EVICR.net.

Scientifically it is organized by ophthalmology subspecialty Expert Committees namely: Age-Related Macular Degeneration; Retinal Dystrophies; Diabetic Retinopathy and Vascular Diseases; Glaucoma; Anterior Segment; and Ocular Surface, Inflammation, Dry-Eye & Allergies. It also has Transversal Sections in Rare Diseases, Medical Devices and Reading Centres.

At present, EVICR.net has 100 Clinical Ophthalmological Research Centres members from 15 European countries.

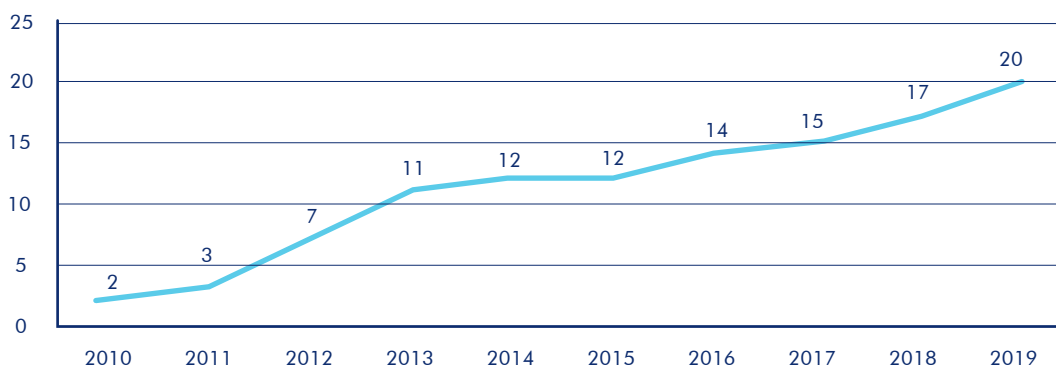
#### Clinical Studies and Registries

AIBILI as EVICR.net Coordinating Centre, assumes the leadership of coordination and management of Investigator Initiated Research (IIR) in ophthalmology across Europe through the Network. EVICR.net Members have the opportunity to participate in IIR within the Network as

well as to submit abstracts for IIR to the Coordinating Centre in order to be evaluated by a specific Expert Committee. When approved, they will have access to support in coordinating and implementing the IIR within EVICR.net.

## Multinational Clinical Research Studies (2010-2019)

Number of Multinational Clinical Research Studies



EVICR.net investigator initiated research (IIR) has been growing in the last years, giving the opportunity for investigators to perform multinational clinical research of high quality in compliance with ICH-GCP Guidelines assuming that the rights, safety and wellbeing of the trial subjects are protected and that the clinical data are credible.

EVICR.net has contributed to the improvement of diagnostic, prevention and treatment strategies in ophthalmology. In 2019 there were eight ongoing multinational clinical research studies of which 3 are European Union funded projects.

### Ongoing Projects and Activities

#### Age-Related Macular Degeneration

- ATLANTIC (IIR, Industry grant)
- MACUSTAR (IIR, EU funded – IMI2)
- MADEOS (External-sponsored)

#### Retinal Dystrophies

- IRD Survey (Industry Collaboration)

#### Diabetic Retinopathy

- RECOGNISED (IIR, EU funded – H2020)
- IRIS (Industry-sponsored)

#### Anterior Segment

- REDCAKE (IIR, Flemish grant)
- ANIRIDIA-NET (EU funded - COST)



## Educational Programme

The EVICR.net has developed a continual training and educational programme with webinars on ophthalmology clinical research. The Educational Programme is organized in modules each with three webinars of one hour. Currently the following modules are available at <https://www.evicr.net/webinars/webinars/>:

| Module   | Multinational Clinical Research Organization | Diabetic Macular Edema Understanding and Management | Diabetic Macular Edema, Imaging, Biomarkers and Anti-VEGF Management | Glaucoma Risk Factors and Management | Dry Eye Diagnosis and Treatment      |
|----------|--|---|--|--------------------------------------|--------------------------------------|
| WEBINARS | <b>WEBINAR #1</b>                            | <b>WEBINAR #4</b>                                   |  | <b>WEBINAR #8</b>                    | <b>WEBINAR #11</b>                   |
|          | How to setup a clinical research study       | DME definition, classification and imaging          |  | Landmark clinical trials in glaucoma | Dry eye syndrome: signs and symptoms |
|          | S. Nunes                                     | J. Cunha-Vaz  |  | E. Normando                          | J. Gil                               |
|          | <b>WEBINAR #2</b>                            | <b>WEBINAR #5</b>                                   |  | <b>WEBINAR #9</b>                    | <b>WEBINAR #12</b>                   |
|          | Clinical research organization               | Predicting progression and treatment response       |  | Risk factors in glaucoma             | Diagnosis in dry eye syndrome        |
|          | L. Ribeiro                                   | J. Cunha-Vaz  |  | F. Cordeiro                          | J. Gil                               |
|          | <b>WEBINAR #3</b>                            | <b>WEBINAR #6</b>                                   | <b>WEBINAR #7</b>  | <b>WEBINAR #10</b>                   | <b>WEBINAR #13</b>                   |
|          | SOPs – quality and certification             | Treatment of DME                                    | Anti-VEGF treatment of DME   | Glaucoma - Who to treat and when     | Treatment of dry eye syndrome        |
|          | C. Martinho<br>R. Fernandes                  | J. Cunha-Vaz  | J. Cunha-Vaz   | S. Gandolfi                          | E. Costa                             |

More information: [www.evicr.net](http://www.evicr.net)

## Representative Publications

Finger RP, Schmitz-Valckenberg S, Schmid M, Rubin GS, Dunbar H, Tufail A, Crabb DP, Binns A, Sánchez CI, Margaron P, Normand G, Durbin MK, Luhmann UFO, Zamiri P, Cunha-Vaz J, Asmus F, Holz FG; on behalf of the MACUSTAR consortium. **MACUSTAR: Development and Clinical Validation of Functional, Structural, and Patient-Reported Endpoints in Intermediate Age-Related Macular Degeneration.** *Ophthalmologica.* 2019;241(2):61-72. doi: 10.1159/000491402. Epub 2018 Aug 28. Review.

Martinho C, Fernandes D: **European Network of Clinical Research in Ophthalmology Information Update.** *Ophthalmic Research.* 2018. DOI: 10.1159/000496497.

Rosenblatt A, Udaondo P, Cunha-Vaz J, Sivaprasad S, Bandello F, Lanzetta P, Kodjikian L, Goldstein M, Wilner ZH, Loewenstein A, for the ARTES study group: **A Collaborative Retrospective study on the Efficacy and Safety of intravitreal dexamethasone implant (Ozurdex) inpatients with Diabetic Macular Edema (DME). The European DME Registrar Study (ARTES).** *Ophthalmology* (2019), doi:10.1016/j.ophtha.2019.10.005.

Cursiefen C, Cordeiro F, Cunha-Vaz J, Wheeler-Schilling T, Scholl HPN; EVI Steering Board: **Unmet Needs in Ophthalmology: A European Vision Institute-Consensus Roadmap 2019-2025.** *Ophthalmic Res.* 2019;62(3):123-133. doi: 10.1159/000501374. Epub 2019 Aug 5.



## C-TRACER - CHAMPALIMAUD TRANSLATIONAL CENTRE FOR EYE RESEARCH



AIBILI is recognized as a C-TRACER - Champalimaud Translational Centre for Eye Research by the Champalimaud Foundation for its activities in translational eye research.

This Network is of great relevance because it brings together under the Champalimaud Foundation three major eye research institutions in the world and creates links between three major continents: Asia, Europe and South America.

The C-TRACERs Network brings together the LV Prasad Eye Institute in Hyderabad, India; AIBILI and the Institute for Vision at the Federal University of S. Paulo at S. Paulo, Brazil.

More information:

<http://first.fchampalimaud.org/en/champalimaud-research/c-tracer/>

## ECRIN - EUROPEAN CLINICAL RESEARCH INFRASTRUCTURES NETWORK



ECRIN-ERIC is a network dedicated to improving the health of patients and citizens across the world through clinical research. ECRIN-ERIC supports multinational collaboration in clinical research, acting through correspondents hosted in national clinical research hubs and networks. ECRIN is based on the connection of coordinating centres for national networks of clinical research centres and clinical trials units, able to provide support and services to multinational clinical research.

AIBILI as Coordinating Centre of EVICR.net, a disease oriented network in ophthalmology for clinical research, is an Affiliate Partner of ECRIN-ERIC. Thus, EVICR.net serves as a resource to ECRIN-ERIC in the area of vision and ophthalmology multinational clinical research, particularly by providing scientific and medical expertise, access to patients and research capacity.

More information:

<https://www.ecrin.org/>



## EATRIS - EUROPEAN INFRASTRUCTURE FOR TRANSLATIONAL MEDICINE

**eatris**

European infrastructure  
for translational medicine

EATRIS is a client driven, non-profit organization comprising European academic centers of excellence in translational research. EATRIS partner institutes support in bringing innovative ideas for novel preventive, diagnostic or therapeutic products towards first in human application and on to clinical proof of concept. EATRIS partner institutes provide services and expertise in the following areas: Advanced therapy medicinal products and biologics, Biomarkers, Imaging and tracing, Small molecules, and Vaccines. AIBILI, is member of EATRIS and has capacities in the Biomarkers and Imaging and tracing platforms.

More information:  
<https://eatris.eu/>

## ERN-EYE - EUROPEAN REFERENCE NETWORK ON RARE EYE DISEASES



The European Reference Network (ERN) on Rare Eye Diseases (ERN-EYE) is led by Prof. Hélène Dollfus (Strasbourg, France) and is composed of 29 healthcare providers from 13 European countries. ERN-EYE is organized in thematic groups: Retinal, Neuro-ophthalmology, Paediatric Ophthalmology and Anterior Segment.

EVICR.net is a member of the Scientific, Medical and Ethical Advisory Board (SMEAB). EVICR.net collaborates with ERN-EYE through the Rare Diseases Transversal Section and with its long experience in Quality Systems and certification of Clinical Sites as well as by providing overall management and logistical support needed in multinational investigator initiated studies in rare eye diseases.

More information:  
<https://www.ern-eye.eu/>



## PARTNERS



### ARSC – Health Administration of the Centre Region of Portugal

ARSC regulates the organization and functioning of healthcare institutions and services in the Centre Region of Portugal.

The Protocol between AIBILI and ARSC is of great relevance as the area of primary healthcare is a major research interest of AIBILI as screening and prevention are priorities for AIBILI research particularly in imaging diagnostics.

Since 2011, AIBILI-CORC is the Reading Centre for fundus images of Screening Programme for Diabetic Retinopathy in the Centre Region of Portugal.



### FMUC – Faculty of Medicine of the Coimbra University

The Faculty of Medicine of the University of Coimbra (FMUC) is one of the most important schools of medicine in Portugal due to its vast research areas. The partnership between AIBILI and FMUC allows AIBILI to coordinate clinical research from FMUC investigators.



### HCP – Health Cluster Portugal

AIBILI is member of the Health Cluster Portugal (HCP) whose main objective is the promotion and implementation of initiatives and activities leading to the consolidation of a national cluster for competitiveness, innovation and technology in the health area.

AIBILI is part of the Ophthalmology sub-cluster within HCP with the aim to increase Portuguese participation in international partnerships, attract national and foreign investment and make Portugal an active partner in ophthalmology healthcare and research.

More information:  
[www.healthportugal.com](http://www.healthportugal.com)



### iCBR – Coimbra Institute for Clinical and Biomedical Research

Coimbra Institute for Clinical and Biomedical Research (iCBR), formerly IBILI, is a Multidisciplinary Research Unit from the Faculty of Medicine, University of Coimbra (FMUC). Research at iCBR aims to investigate molecular and cellular mechanisms underlying the pathophysiology of chronic diseases, to identify innovative therapeutic strategies and disease biomarkers, as well as to unveil and implement new approaches to promote the quality of life and wellness.

The partnership between AIBILI and iCBR aim on filling the gaps between Pre-Clinical and Clinical Research, setting the ground for the development of innovative projects, translating basic science into new therapeutic strategies, but also by using human samples to find new biomarkers of disease, disease progression and response to therapy.



### **i3S – Institute for Research and Innovation in Health of the University of Porto**

The i3S consortium, headed by the Porto University, brings together institutions and researchers from several schools of the Porto University. This wide participation of schools, research institutions and hospitals in a research institute is unique in Portugal and is a valuable asset for science and technology development, while creating an environment that feeds real breakthrough research and translation of discoveries into the clinic.

The partnership between AIBILI and i3S will increase the participation in innovation and translational projects as well as to have a more complete and robust value chain for their clients, particularly, for companies.



### **INFOCUS Clinical Research**

INFOCUS is an ophthalmology focused full-service contract research organization (CRO) based in the USA.

AIBILI and INFOCUS are currently providers of ophthalmology clinical research development support services, respectively, in Europe and North America and are organizing themselves to be able to provide a global ophthalmology clinical research support.



### **INFARMED - National Authority of Medicines and Health Products, I.P.**

INFARMED, IP is a Government agency accountable to the Health Ministry, that evaluates, authorises, regulates and controls human medicines as well as health products, namely, medical devices and cosmetics for the protection of Public Health. AIBILI has a protocol with INFARMED to collaborate in the framework of the national strategy for the development of clinical research in the pharmaceutical sector.

Since 2008 that AIBILI-CHAD has been responsible for a Pharmacovigilance Unit of the National Pharmacovigilance System contracted with INFARMED, IP.



### **José de Mello Saúde – Hospital CUF Coimbra**

The CUF Coimbra Hospital provides access to excellent health services, both inpatient and outpatient with a comprehensive and innovative offer in diverse medical-surgical areas in terms of the technology used and its processes.

The partnership between AIBILI and CUF Coimbra Hospital has as main goal the coordination and promotion of clinical research facilitating the exchange of scientific and technical knowledge.







### **P-BIO – Portugal's Biotechnology Industry Organization**

P-BIO is the only association that brings together the vast majority of companies linked to the biotechnology and life sciences sector. P-BIO seeks to develop an environment that is favourable to the creation and growth of start-ups, promoting their corporate development domestically and internationally.

The partnership with AIBILI allows P-BIO companies to have access to differentiated support to evaluate the economic viability of medicines, value strategy design, regulation and translation of technology, market access and effectiveness after commercialization as well as to the coordination and overall management of clinical research studies.



### **PtCRIN – Portuguese Academic Clinical Research Infrastructures Network**

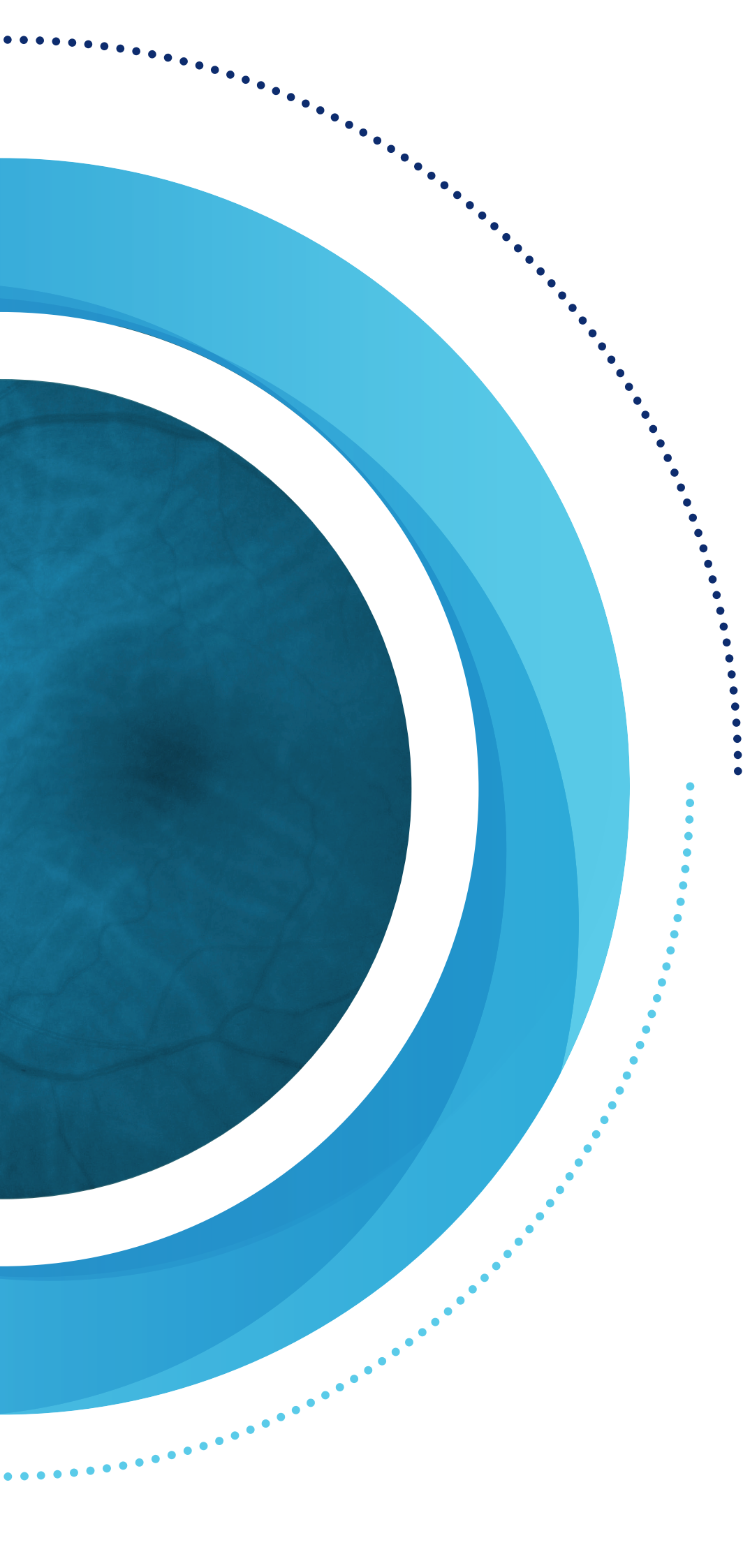
PtCRIN ([www.ptcrin.pt](http://www.ptcrin.pt)) is the national clinical research network aiming to facilitate and improve quality in clinical research and to increase national and international research collaboration for the benefit of patients, citizens and the health-care system. PtCRIN is the Portuguese member of ECRIN-ERIC.

AIBILI is a founding member of the PtCRIN and it is a Clinical Trial Unit and a Clinical Research Centre. AIBILI has the only ECRIN Certified Data Centre since 2016 in Portugal.



FINANCIADO POR





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association for  
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research on light and image