



NEW THERAPEUTICS FOR DISEASES OF AGING

**THE BIOTECH  
SPECIALISED IN  
DISEASES OF AGING**

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## CORPORATE OVERVIEW

### BIOPHYTIS is a public company listed on Euronext Growth (Paris, France)

- Share price (January 2nd 2018): €4,72
- Shares outstanding: 13,463,413
- Market capitalization: €63 M
- €16 M raised in 2015; €28 M raised in 2017

### BIOPHYTIS is advancing two drug candidates into Phase II

#### SARCONEOS

MAS activator

Sarcopenia Phase 2b start H1 2018

DMD Phase 2b planned for 2019

#### MACUNEOS

PPAR activator

Dry AMD Phase 1/2a start H1 2018

Stargardt Phase 2b planned for 2020

### BIOPHYTIS spun-out of Sorbonne Université in 2006

- Close collaboration with Sorbonne University labs and world-class institutes (Institut de Biologie Paris-Seine, Institut de Myologie, Institut de la Vision)
- Library of natural compounds active against degenerative processes
- Development of small molecules of therapeutic interest
- Pipeline of back-up compounds and indications

## THE TEAM



**Stanislas VEILLET**

*Founder & CEO*

- PhD in genetics, AgroParisTech alumnus
- 15+ years in R&D management (Monsanto, Pharmacia, Danone)
- Created Biophytis in 2006



**René LAFONT**

*Co-founder & CSO*

- Professor emeritus at Sorbonne Université
- Former Dean of the life sciences department
- 170+ peer-reviewed publications

## A SEASONED MANAGEMENT TEAM



**Jean-Christophe MONTIGNY**

*Chief Financial Officer*

- AgroParisTech engineer, BA from IEP Paris
- 20+ years management experience in fast growing businesses
- Joined Biophytis in 2009



**Susanna del Signore**

*Chief Medical Officer*

- MD in geriatrics
- 10+ years in medical / regulatory affairs (Sanofi, EMEA)
- 20+ years of clinical development in the pharma industry (Sanofi, Servier)



**Manfred HORST**

*Business Development Officer*

- MD, PhD, MBA
- 30+ years pharma industry experience
- 12 years Business Development for MSD

# DRUG DISCOVERY & DEVELOPMENT STRATEGY

## First generation

- Active principles derived from plant substances
- Preclinical proof of concept
- Well tolerated in humans
- IP on use and process

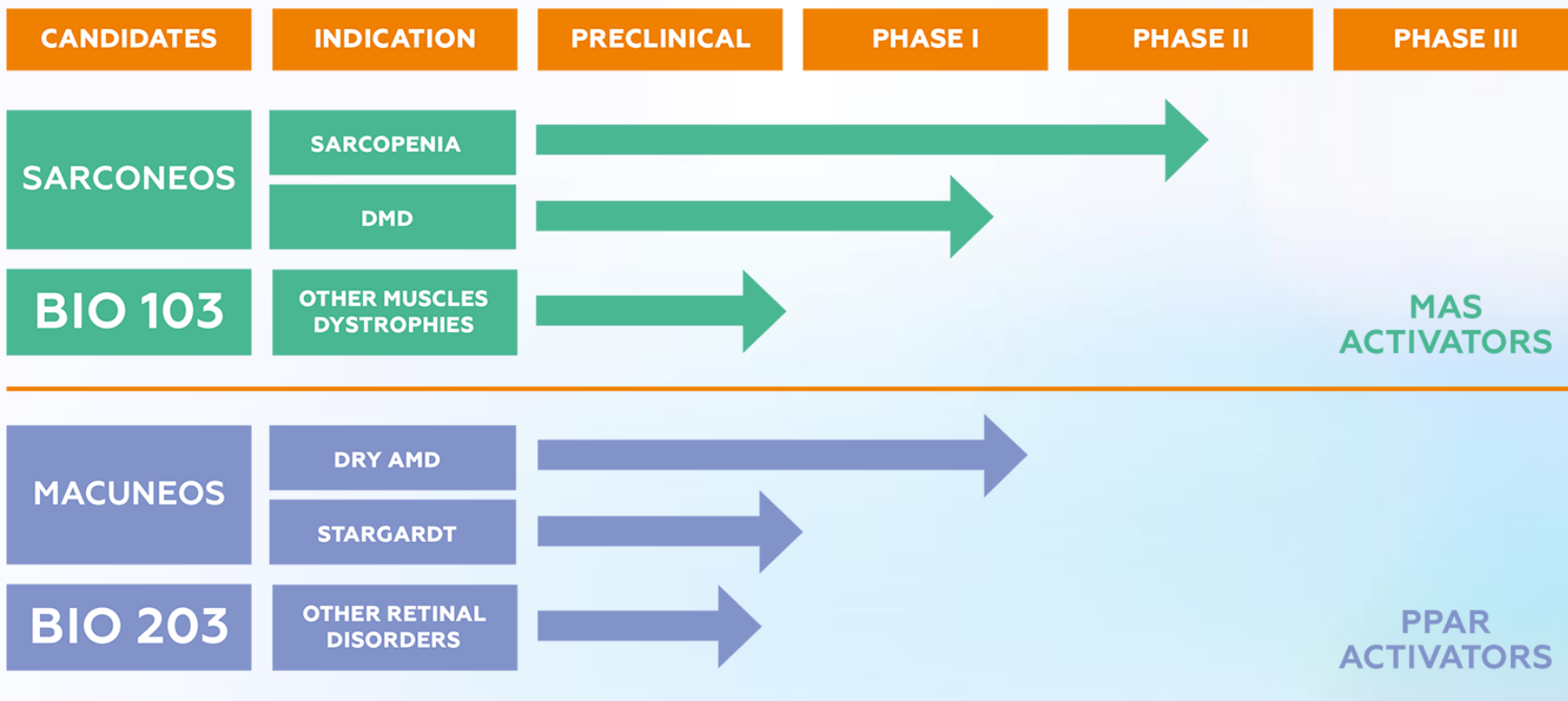
## Second generation

- New chemical entities
- Optimized pharmacology
- IP on composition of matter



Biophytis has identified small molecules derived from plants which counteract the effects of stress on cellular function and slow down degenerative processes associated with aging

# PIPELINE



## SCIENTIFIC BOARD



**Pr. Jean MARIANI**  
Director of Institut de la  
longévité Charles Foix



**Pr. René LAFONT**  
Professor emeritus  
Former Dean of the life  
sciences department



**Pr. José SAHEL**  
Director of  
Institut de la  
Vision



WORLD CLASS SCIENTIFIC LEADERS CONTRIBUTE  
TO THE DEVELOPMENT OF OUR DRUG CANDIDATES



**Dr. Roger FIELDING**  
Professor Nutrition  
Science, Harvard  
Medical School  
Director Clinical  
Nutrition Unit



**Dr. Thomas VOIT**  
Professor, University  
College London,  
Director of the  
Research Centre of the  
GOSH for Children



**Dr. Ivana KIM**  
Professor Harvard  
Medical School,  
Director Retina  
Research, MEEI



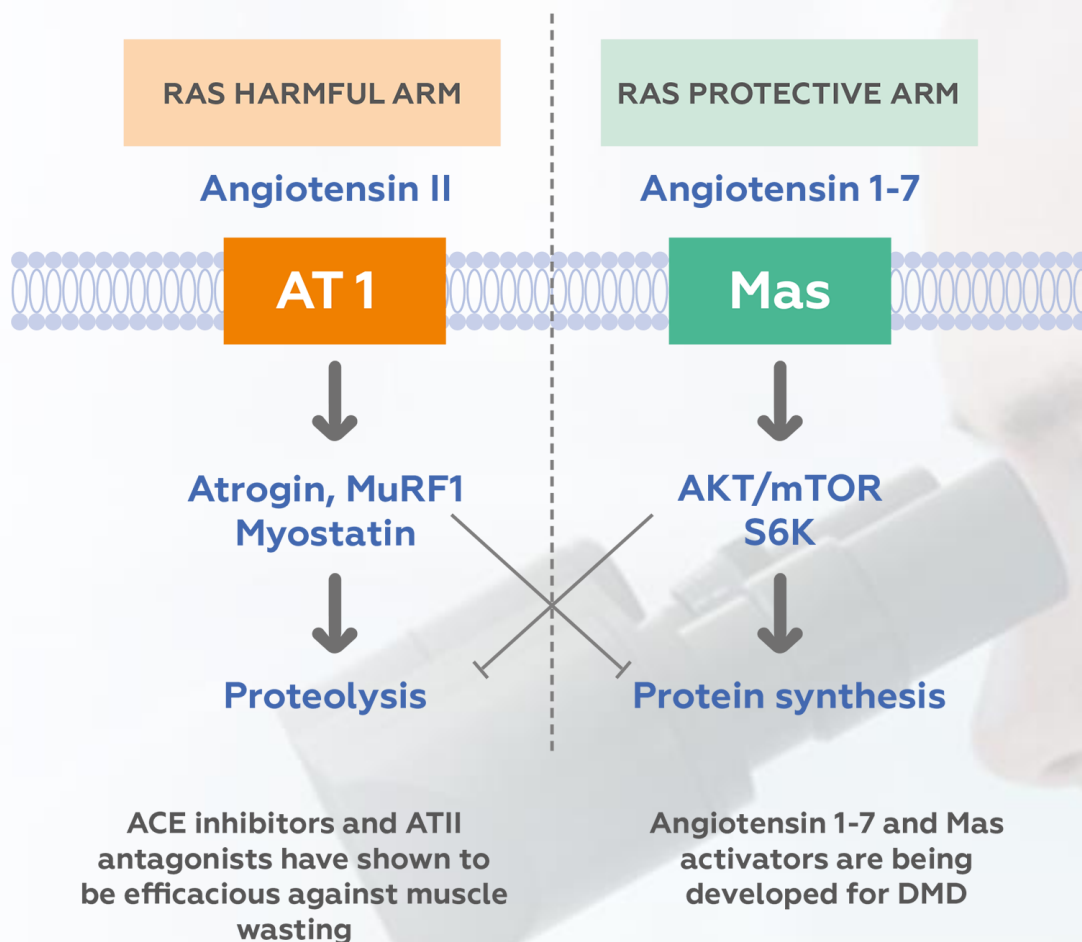
# MAS ACTIVATORS AND MUSCULAR DISEASES

**GERIATRIC CHRONIC DISEASE:  
SARCOPENIA**

**PAEDIATRIC ORPHAN DISEASE  
DUCHENNE'S MUSCULAR DYSTROPHY (DMD)**

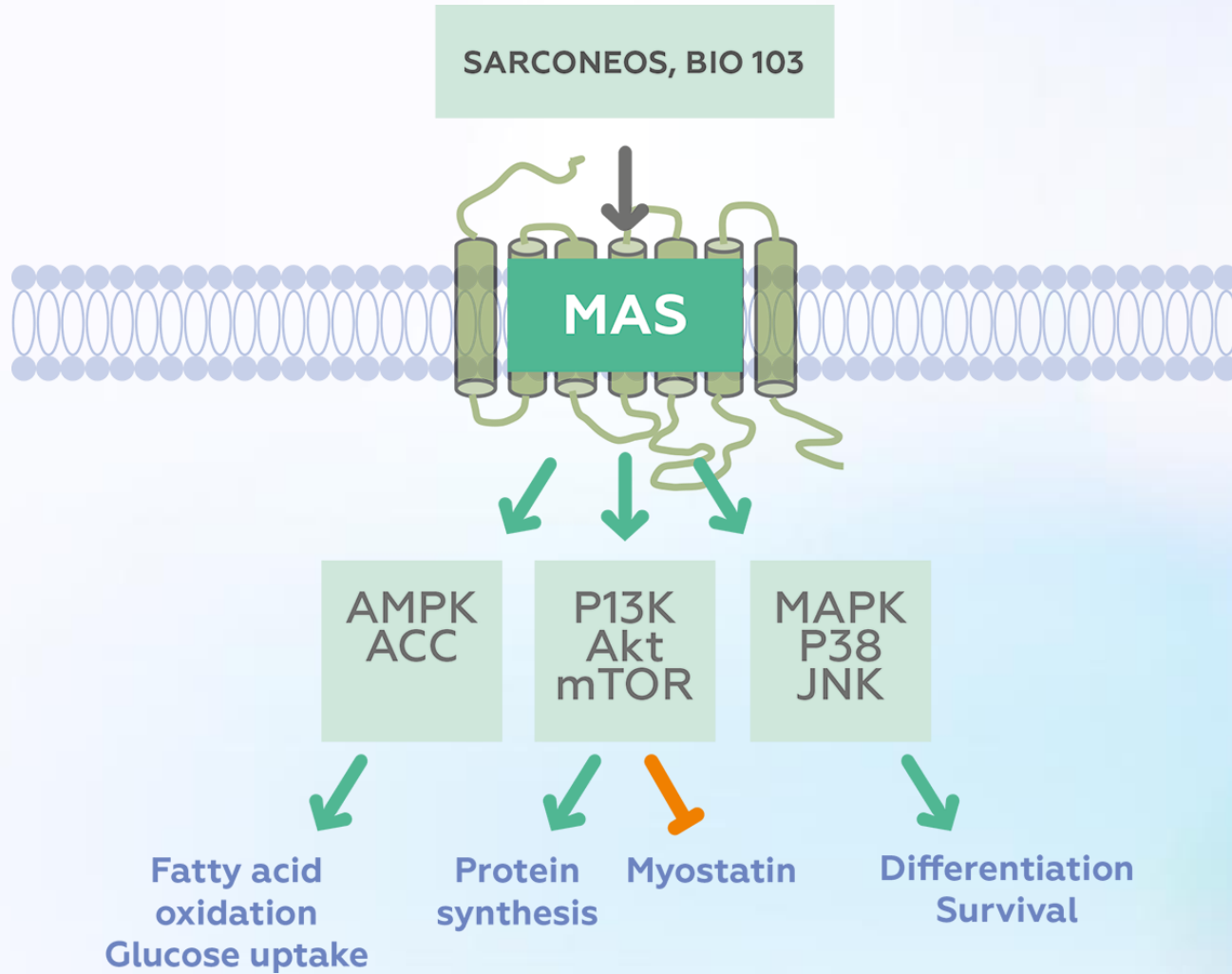


# RENIN ANGIOTENSIN SYSTEM (RAS) AND MUSCLE ANABOLISM



**Targeting RAS stimulates anabolism in muscle and has potential for the treatment of chronic or genetic muscle disorders**

# MAS ACTIVATION



**SARCONEOS is a potent MAS activator that stimulates protein synthesis, energy production and regeneration in muscle**

## SARCOPENIA

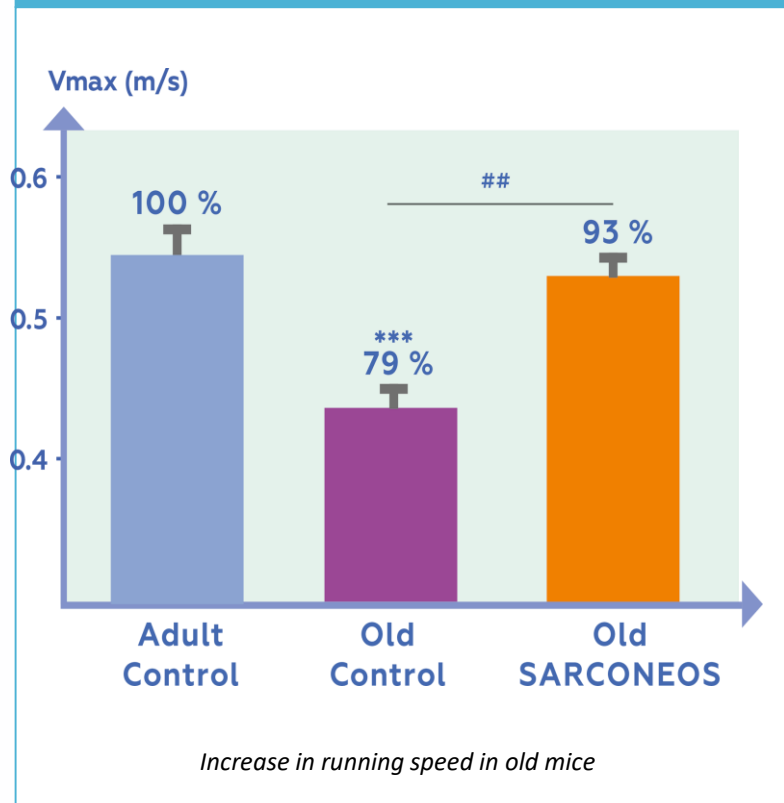


- **Definition:** Low muscle strength and low muscle mass (FNIH criteria)  
ICD-10 Code: M62.84
- **Prevalence:** 50M patients  
Estimated at 5 – 10% in >65 years old
- **Standard of Care:** 30 minutes physical exercise / day  
No currently approved medication

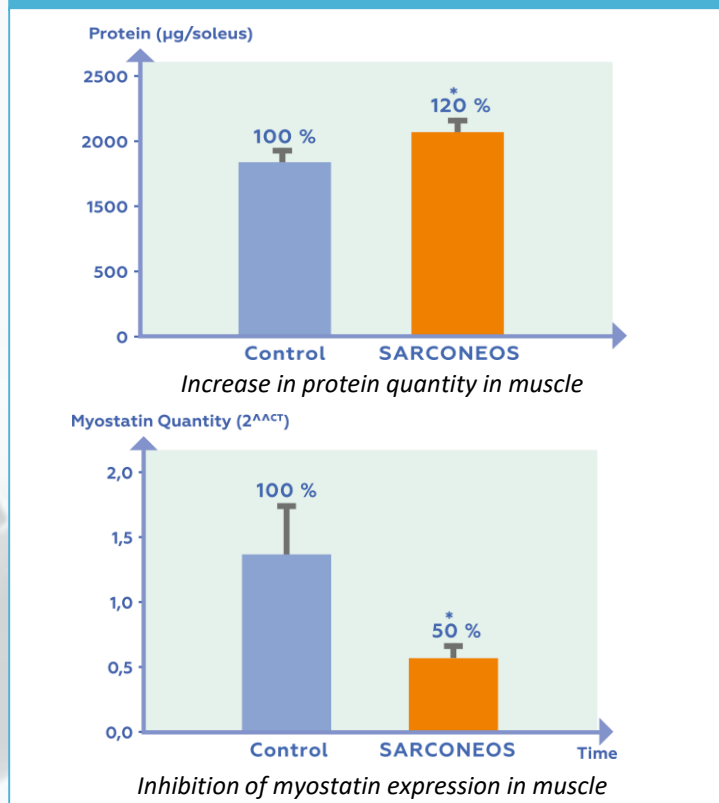
Drug candidates in development	Examples
Myostatin Inhibitors	Antibodies (e.g. Bimagrumab / Novartis) Increase muscle mass and strength, but do not improve mobility
Selective Androgen Receptor Modulators (SARMs)	Enobosarm (GTx / Merck), no longer developed for sarcopenia
Troponin Complex Inhibitor	CK-107 (Cytokinetics / Astellas), developed for COPD and SMA
MAS Activators	SARCONEOS (Biophytis)

# SARCONEOS: PROOF OF CONCEPT IN ANIMALS

## SARCONEOS compensates the effect of ageing on muscle functionality and mobility



## SARCONEOS stimulates anabolism in muscle



**SARCONEOS stimulates anabolism and compensates the effect of ageing on muscle functionality and mobility in mice and rat models of sarcopenia**

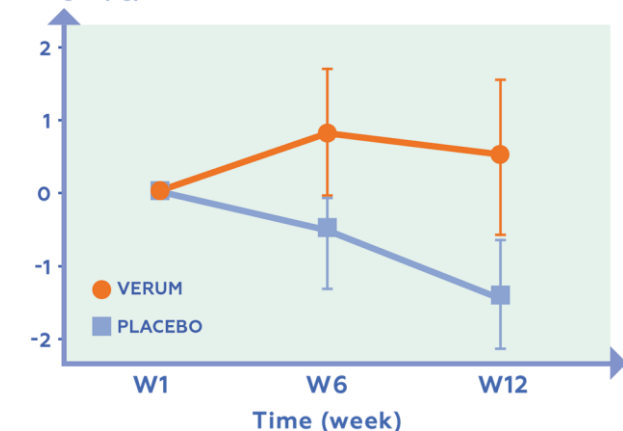
# SARCONEOS: PROOF OF ACTIVITY IN NUTRITIONAL TRIAL

## QUINOLIA – Safety, PK and pharmacodynamic parameters in obese healthy volunteers

- 58 subjects, double-blind, placebo-controlled, nutrition study (dieting)
- Oral administration (40 mg/day) for 12 weeks (6 weeks hypocaloric dieting)
- No serious adverse event and good safety profile in young obese subjects

### Treatment compensates the diet's effect on muscular strength

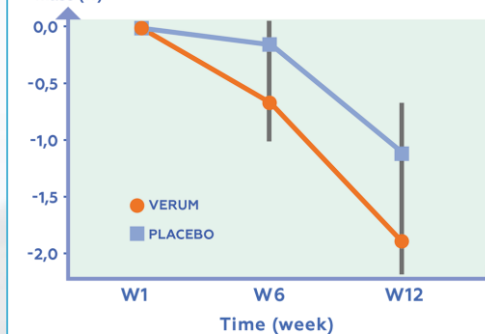
Strength (kg)



Lesser muscle strength loss  
(grip test,  $p=0.09$ )

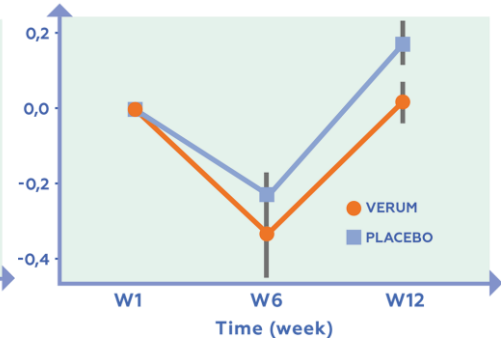
### Treatment accentuates diet's effect both on android fat mass and resistance to insulin

Abdominal fat mass (%)



Stimulation of android fat mass  
loss (%),  $p=0.04$

IR HOMA Index



Reduction of insulin resistance  
(Homa-IR index,  $p=0.06$ )

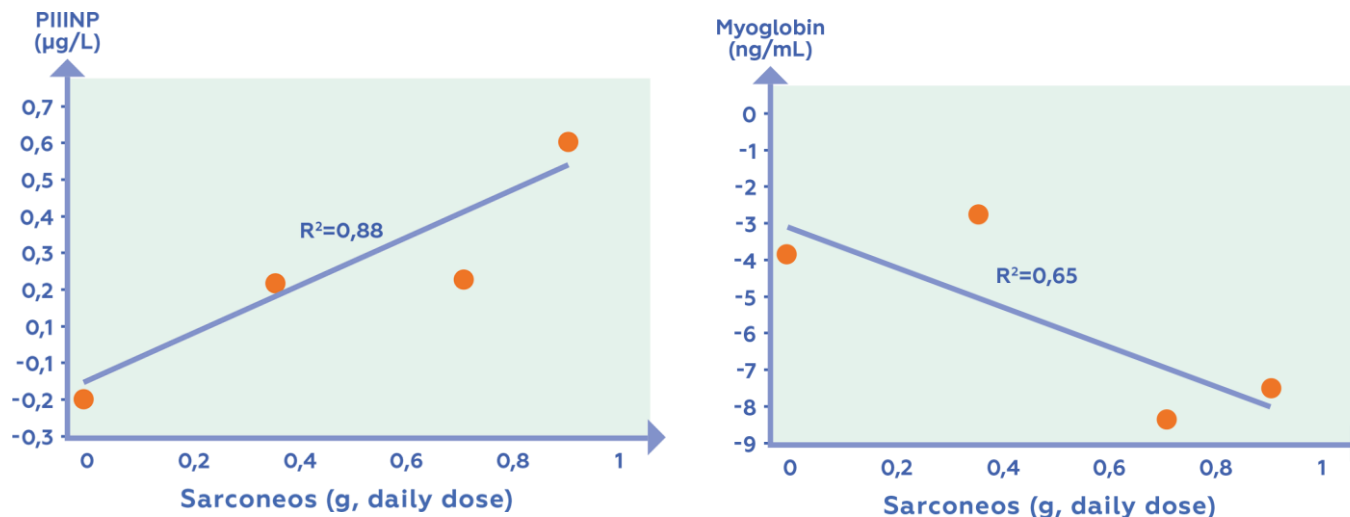
**SARCONEOS active molecule increases the muscle strength, significantly reduces both the android fat mass and the resistance to insulin in obese healthy volunteers**

## SARCONEOS: PROOF OF SAFETY IN PHASE I STUDY

### SARA-PK – Phase 1 – Safety, PK and PD in elderly healthy volunteers

- 54 elderly subjects (>65 years), combined SAD (24 elderly and young subjects) + MAD step (30 elderly subjects)
- MAD after oral administration of 350 mg/day, 700 mg/day or 900 mg/day for 14 days
- No serious adverse event and good safety profile in elderly subjects
- Good pharmacokinetics profile, not influenced by age or meal
- The analysis of pharmacodynamics biomarkers confirms the stimulation of muscular anabolism and the activation of the RAS system in strong doses

#### SARCONEOS stimulates muscular anabolism and reduces catabolism (biomarkers)



Plasmatic level of type III Procollagen Propeptide (PIIINP,  $R^2=0,88$ ) and Myoglobin ( $R^2=0,65$ ) according to SARCONEOS' doses

**SARCONEOS has a good safety and PK profile in young and elder subjects, with *indication* of activity on various biomarkers**

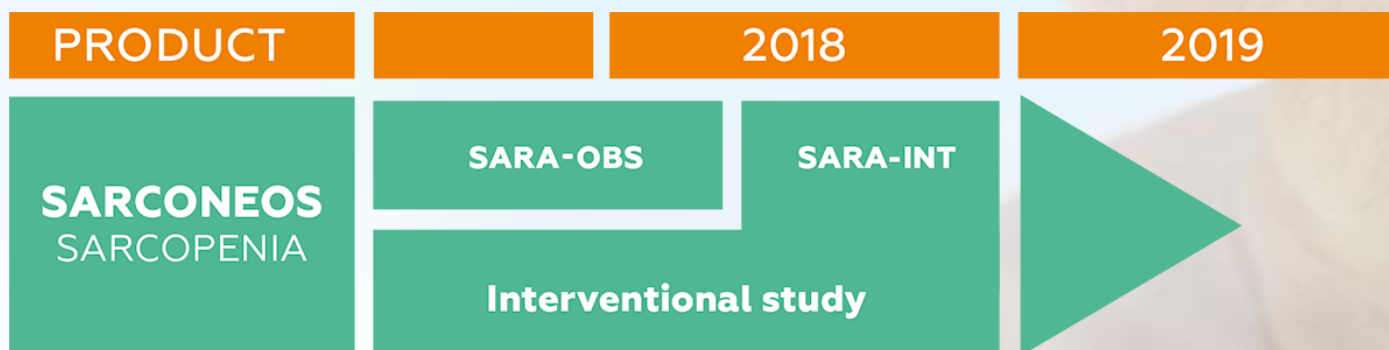
# SARA: PHASE 2b INTERNATIONAL CLINICAL PROGRAM

## SARA-OBS - Observational study

- Multicentric observational study: eight clinical centers in Europe and the US
- Recruitment of sarcopenic patients in Europe and US on going
- 300 sarcopenic patients: Foundation of NIH inclusion criteria for sarcopenia
- Duration: Six months
- Endpoints: 6mn walk test, 400 meters gait speed test, electronically recorded patient-reported outcomes (ePROs): SF-36 QOL questionnaire, measures of muscle strength and muscle mass, plasmatic biomarkers

## SARA-INT – Interventional study

- Multicentric, double-blind, randomized and placebo-controlled
- 334 sarcopenic patients from SARA-OBS and new clinical centers
- Sarconeos 175 mg BID vs 350 mg BID vs Placebo
- Duration: 26 weeks
- Endpoints (EMA Scientific Advice):
  - Primary: **400 meters gait speed test**
  - Secondary: **ePROs (PF-10 subscore of SF-36), Raising from a chair;**  
6mn walk test, stair climbing power test, muscle strength & muscle mass



## DUCHENNE'S MUSCULAR DYSTROPHY (DMD)



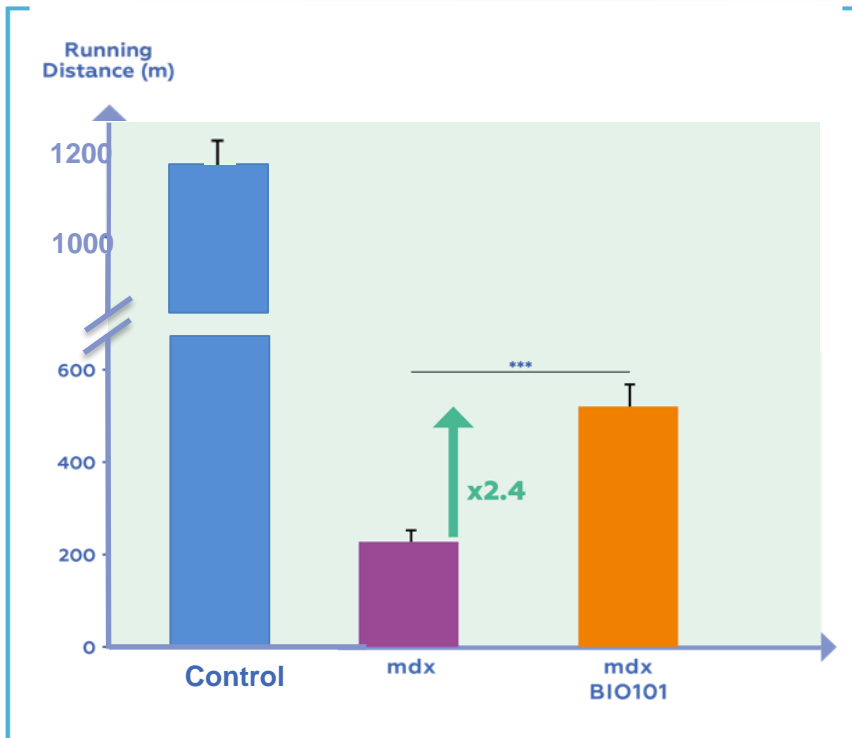
- **Definition:** Genetic disease characterized by progressive muscle degeneration
- **Prevalence:** Around 5 per 100,000 males
- **Incidence:** 1 in 3,500 male births
- **Standard of Care:** Corticosteroids

Drug candidates in development	Examples
Genetic and cell therapy	Exon Skipping (Eteplirsen, FDA-approved) Microdystrophin vectors (preclinical)
Myostatin Inhibitors	Domagrozumab (Pfizer, Phase 2)
Other symptomatic treatment	Ibedenone (Santhera), approved in Israel
MAS Activators	Angiotensin 1-7 (preclinical) SARCONEOS (Biophytis)

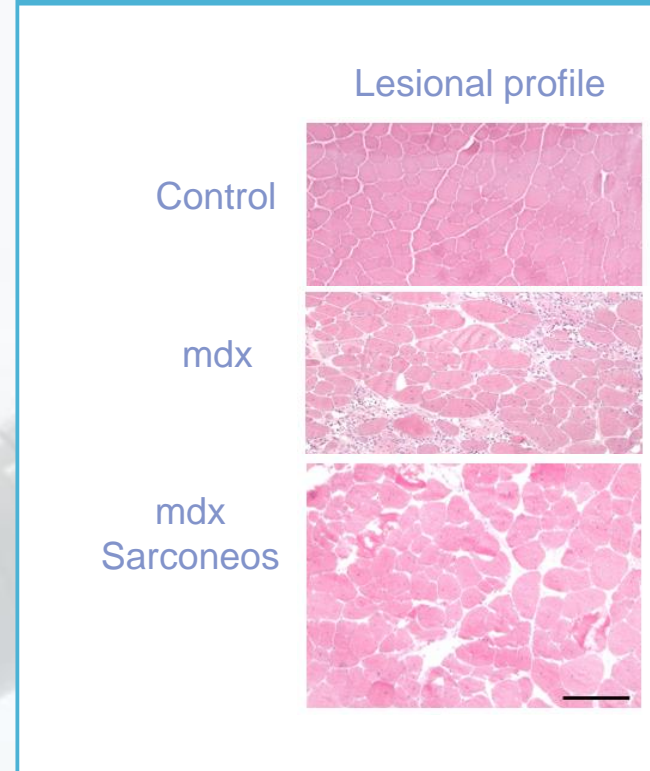


# SARCONEOS: PROOF OF CONCEPT IN ANIMALS

## SARCONEOS improves exercise tolerance in mdx mice



## SARCONEOS reduces fibrosis and lesional profile in mdx mice muscles



**SARCONEOS strongly improves muscle function and decreases muscle fibrosis in the standard animal model for Duchenne’s muscular dystrophy (DMD)**

# SARCONEOS: CLINICAL DEVELOPMENT PLAN IN DUCHENNE'S MUSCULAR DYSTROPHY

## Paediatric PK Study

- Phase 1 trial in ambulant Duchenne boys
- SAD, MAD

## Interventional Phase 2B trial

- Multicentric international clinical trial
- Ambulant Duchenne boys

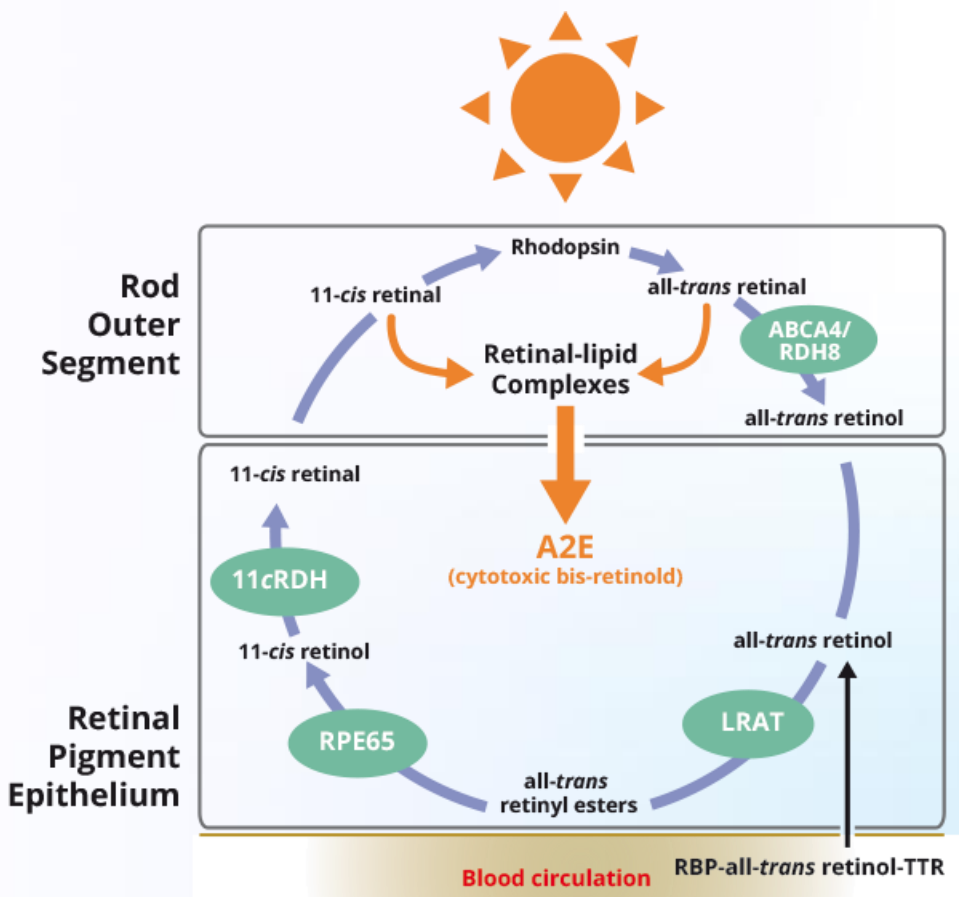


# PPAR ACTIVATORS AND RETINAL DISEASES

**CHRONIC DISEASE:  
DRY AGE-RELATED MACULAR DEGENERATION (AMD)**

**PAEDIATRIC ORPHAN DISEASE:  
STARGARDT'S DISEASE**

# PHOTO-OXIDATIVE STRESS AND MACULAR DEGENERATION



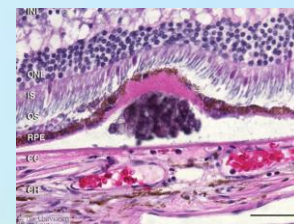
## A2E and oxidative stress

- A2E is a derivative of visual pigment
- A2E accumulates in Retinal Pigment Epithelium (RPE) cells
- A2E is a very reactive molecule that causes oxidative stress with exposure to light, leading to macular degeneration



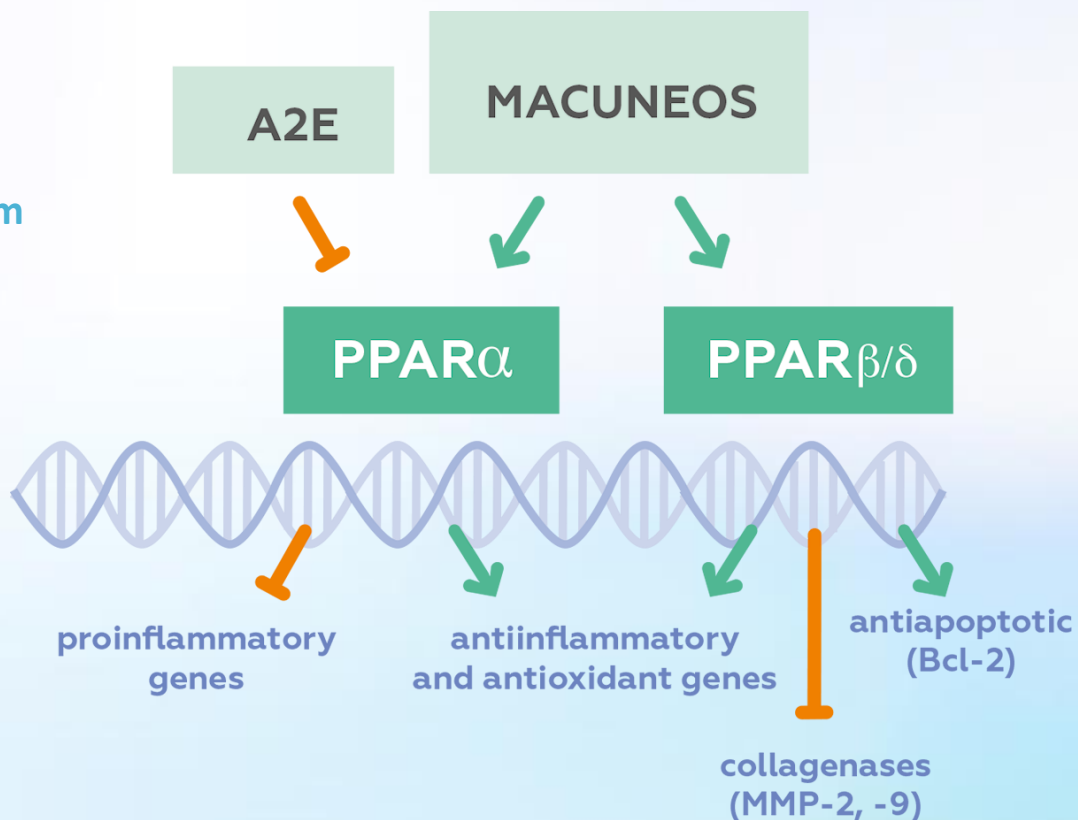
## Photo-oxidative stress leads to:

- Lipofuscin accumulation
- Drusen formation, distorts retina (affecting vision)
- Death of retina cells and progressive blindness



# PPAR ACTIVATION

MACUNEOS activates PPAR nuclear receptors and protects the retina from oxidative stress associated with accumulation of A2E.



- ↓ Cell death
- ↓ Free radicals production
- ↓ VEGF production
- ↓ Inflammation

**MACUNEOS is an activator of PPARs and limits the degeneration of the retina caused by photo-oxidative stress in the presence of A2E**

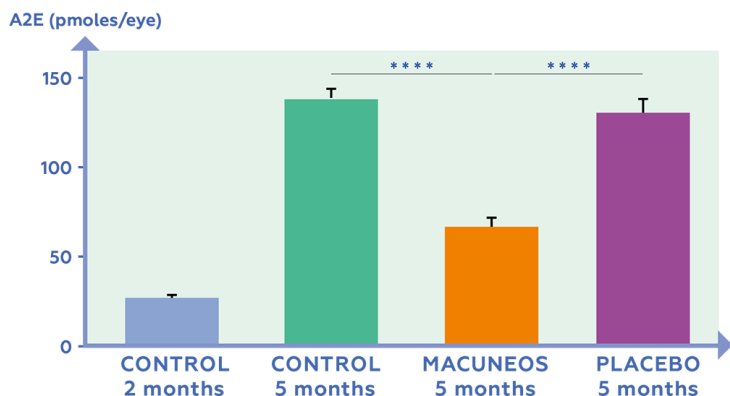
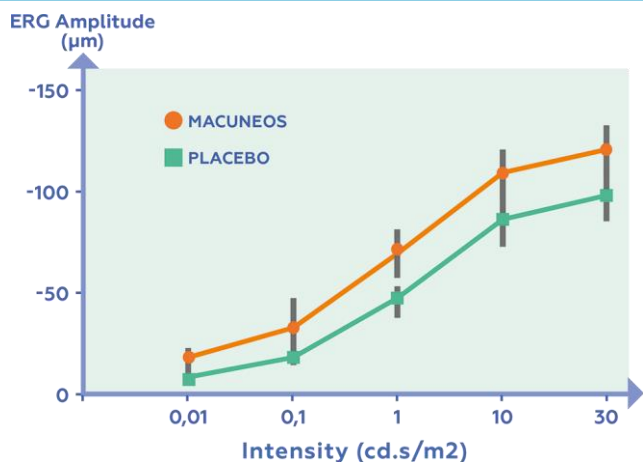


- Definition: All forms of AMD which are not neovascular and exudative
- Prevalence: Estimated at 20M globally
- Standard of Care: Zinc + Vitamines C/E (nutraceuticals)

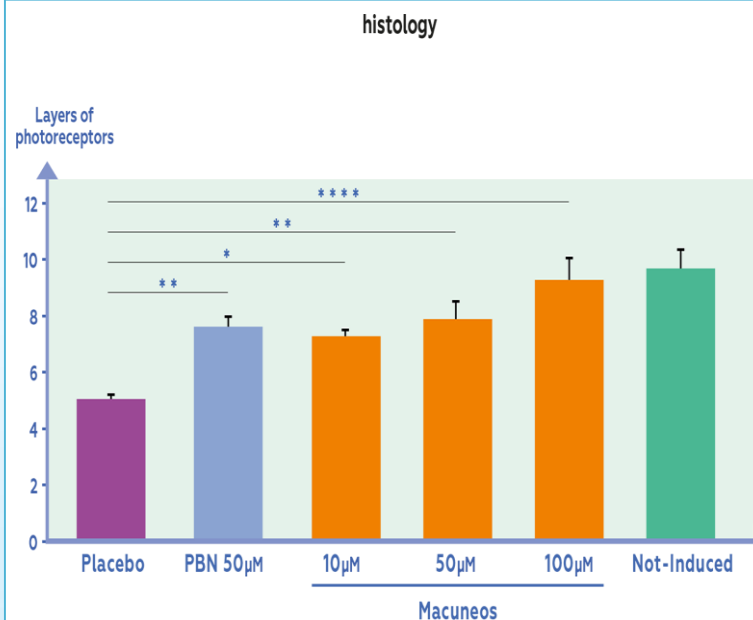
Drug candidates in development	Examples
Anti-complement factor antibodies	Lampalizumab (Roche) – failed in Phase III
Visual Cycle Inhibitors	Emixustat (Acucela) – failed in Phase IIb/III
PPAR Activators	MACUNEOS (Biophytis)

# MACUNEOS: PROOF OF CONCEPT IN ANIMALS

**MACUNEOS preserves the retina's functionality and limits the A2E accumulation after chronic oral administration (ABCA4<sup>-/-</sup> RDH8<sup>-/-</sup> mice model)**



**MACUNEOS preserves the number of layers of photoreceptors after a light stress (Blue light rat model)**



**MACUNEOS protects the retina and preserves visual function in animal models of dry AMD or Stargardt's disease**

## MACUNEOS: SAFETY AND PROOF OF CONCEPT IN HUMANS

### BIXILIA –Safety and PK in healthy volunteers

- 47 healthy volunteers
- Oral administration (35 mg/day) for 12 weeks
- Double-blind, placebo-controlled, nutrition study
- No serious adverse event
- Achieved target for bioavailability

### MACA-PK – Phase 1/2a – Safety, PK and PD in patients with Dry AMD

- Phase 1/2a study, multicentric, international
- Three phases to explore various oral doses of Macuneos
  - SAD step in healthy volunteers (1 center in Belgium)
  - MAD step in 36 patients with dry AMD for 3 months (5 centers in France and Belgium)
- Endpoints
  - Safety and pharmacokinetics
  - Plasmatic biomarkers
  - Visual parameters: ERG, night vision and contrast vision, visual acuity

**MACA-PK study evaluates the safety, the pharmacokinetics and the pharmacodynamics of MACUNEOS in patients with intermediate dry AMD**



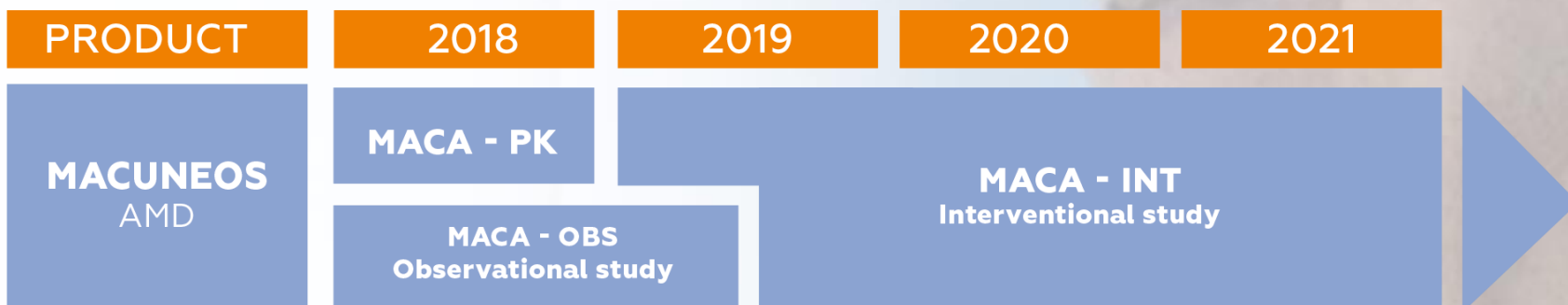
## MACA: PHASE 2B INTERNATIONAL CLINICAL PROGRAM

### MACA-OBS – Observational study in patients with dry AMD

- Multicentric observational study: clinical centers in Europe and the US
- 100 patients suffering of intermediate dry AMD
- Duration: 6 months
- Endpoints: atrophic lesion size, ERG, visual acuity

### MACA-INT – Phase 2b multicentric clinical trial

- Multicenter randomized double-blind, placebo-controlled study
- 300 patients suffering of intermediate dry AMD
  - Macuneos 100mg vs Macuneos 350mg vs placebo
- Duration: 18 months (DSMB : intermediate milestone after 9 months)
- End points:
  - Primary: atrophic lesion size progression
  - Secondary: visual acuity, ERG, accumulation of lipofuscins, evolution towards wet AMD



# STARGARDT'S DISEASE



- Definition: Genetically determined Juvenile Macular Degeneration
- Prevalence: Estimated at 1 in 10,000
- Standard of Care: Eyeglasses / Sunglasses  
Currently no approved therapeutic

## Drug Candidates in Development

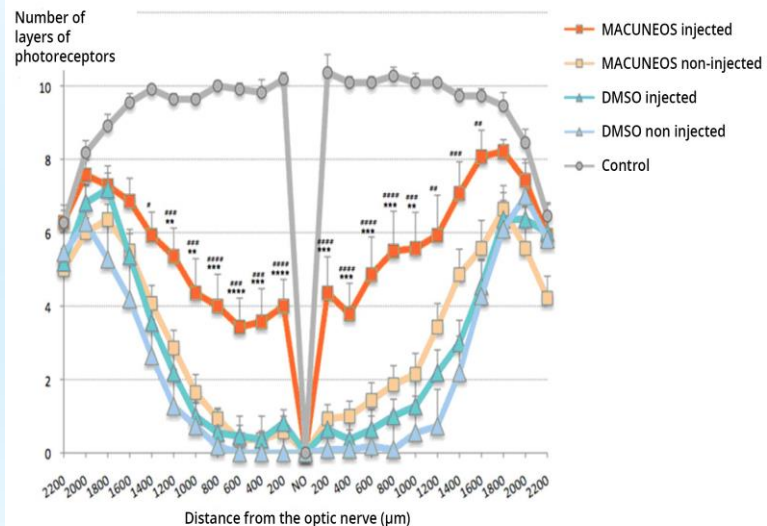
ABCA4 Gene Therapy (Sanofi)

Retinal stem cell grafts (Opis Therapeutics)

Visual Cycle Inhibitor (Emixustat, Acucela)

PPAR Activator (MACUNEOS, Biophytis)

## MACUNEOS preserves the retina structure after intra-vitreal injection (ABCA4<sup>-/-</sup> RDH8<sup>-/-</sup> mice model)



## VALUE CREATION NEWS FLOW

### SARCONEOS in SARCOPENIA

- H1 18: SARA-OBS: Interim results of the observational phase, in Europe and US
- H1 18: SARA-INT: Initiation of the interventional Phase 2b SARA
- H2 18: SARA-INT: Interim results of the interventional Phase 2b SARA (DSMB)
- H2 18: **SARA-INT: Results report of Phase 2b SARA**

### SARCONEOS in DMD

- H1 18: Orphan drug designation
- H2 18: initiation of DMD phase 1/2 clinical program

### MACUNEOS in Dry AMD

- H1 18: MACA-PK: Pharmacokinetics study in patients
- H1 18: MACA-OBS: Initiation of observational phase (ending H2 18)
- H2 18: **MACA-PK: Results report of Phase 1/2a MACA-PK**

## THE BOARD OF DIRECTORS



**Jean M. Franchi**  
*Independent Board Member*

- BA in Finance in Hofstra alumnus
- CFO for Merrimack Pharmaceuticals
- 30+ years as Finance Director for Biotech companies, including 15 years with Genzyme



**Stanislas VEILLET**  
*Chairman of the Board*

- PhD in genetics, AgroParisTech alumnus
- 15+ years in biotech R&D management (Monsanto, Pharmacia, Danone)
- Created Biophytis in 2006



**Marie-Claire JANAILHAC-FRITCH**  
*Independent Board Member*

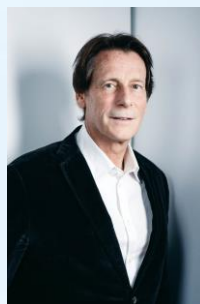
- HEC alumnus
- President of the Board, Guerbet
- 10 years as Sales Director in the pharma industry (GSK, Eurorga)
- Founder and CEO of LANATECH

## A BOARD OF DIRECTORS WITH COMPLEMENTARY PROFILES



**Nadine COULM**  
*Independent Board Member*

- HEC alumnus
- IR Director for Korian
- 20 years of IR experience with FNAC BNP PARIBAS, DANONE & CASINO



**Jean-Gérard GALVEZ**  
*Independent Board Member*

- INP Nancy & MBA Stanford alumnus
- Board member of Implanet & Echosens
- Co-Founder & ex CEO of ActivCard (Nasdaq)



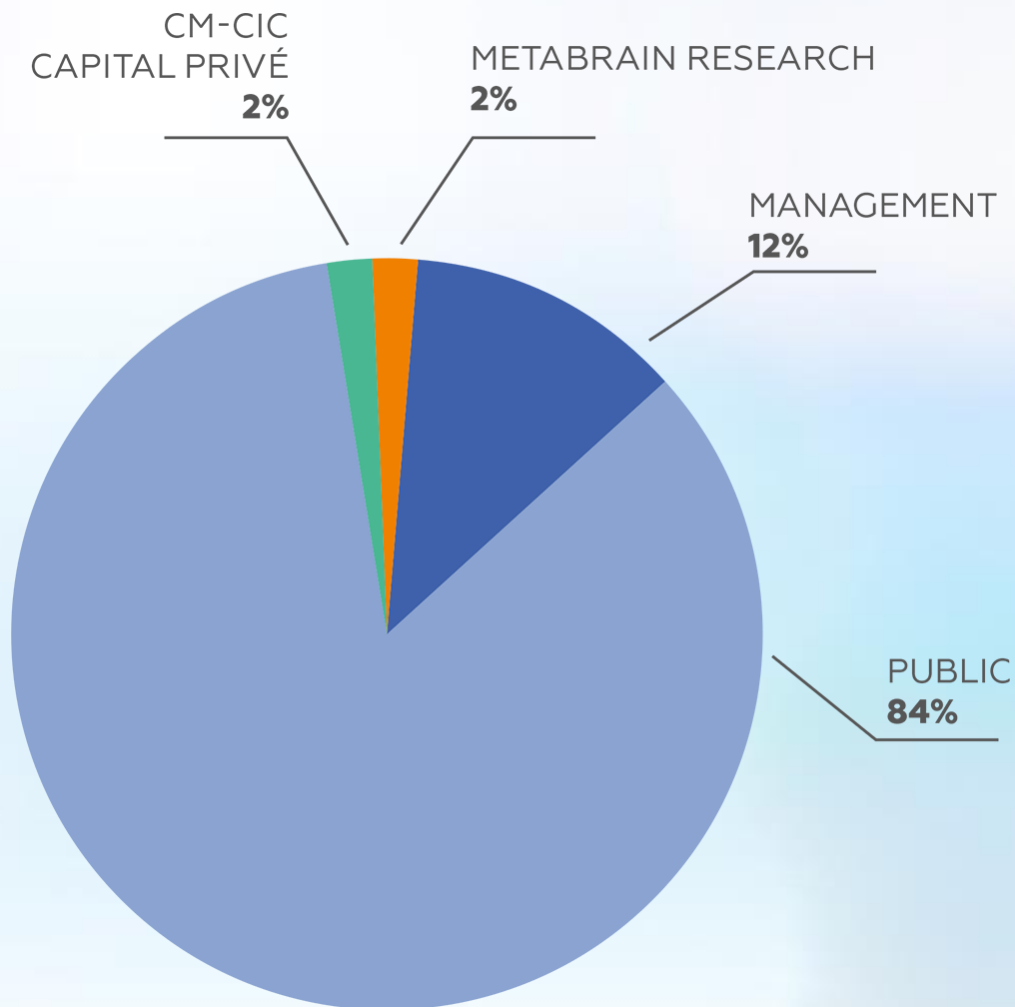
**Micheline KERGOAT**  
*Board Member representing Metabrain*

- PhD in human physiology Sorbonne Université
- Scientific Director of Metabrain Research
- 20 years of experience in drug discovery with MERCK SERONO

# CAPITAL STRUCTURE

## Stock profile

- Market: Euronext Growth of Euronext Paris
- Ticker: ALBPS
- Shares outstanding: 13,463,413
- Share price (January 2<sup>d</sup> 2018): €4,72/share
- Market Capitalization: €63 M



# HIGHLIGHTS

## SARCONEOS to treat sarcopenia and Duchenne's Disease

1

- SARA-INT Phase 2b trial about to start H1 2018, reporting H2 2018
- DMD clinical program planned to start H2 2018

## MACUNEOS to treat dry AMD and Stargardt's Disease

2

- MACA-PK Phase 1 study about to start H1 2018, reporting H2 2018
- Stargardt clinical program planned to start H2 2019

## Strong intellectual property

3

- Six patent families covering sarcopenia and other muscular diseases
- Four patent families covering AMD and other retinopathies

## A technological platform specifically targeting diseases of aging

4

- Original approach for discovering and protecting novel chemistry involved in degenerative diseases
- A unique collection of natural molecules and analogues active on ageing processes

Thank you

Investors contact: [investors@biophytis.com](mailto:investors@biophytis.com)