biophytis®

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 (October 18th, 2018): €1,65
- Shares outstanding: 13,463,413
- Market capitalization: €22M
- €44M raised since IPO in 2015, €10M loan in 2018

BIOPHYTIS is advancing two drug candidates into Phase II

SARCONEOS	MACUNEOS
MAS activator	PPAR activator
Sarcopenia : Phase 2b started in H1 2018	Dry AMD : Phase 1 ready to start in H2 2019
DMD : Phase1/2 ready to start in 2019	Stargardt disease : Phase 2/3 to start in 2020

BIOPHYTIS spun-out of Sorbonne Université in 2006

- Aging science platform made of long-term collaborations with Sorbonne University
- Development of small molecules that stimulate resilience to stress, selected by reverse pharmacology from a collection of plant secondary metabolites

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

Samuel AGUS
Chief Medical Officer
- MD, PhD
- Board-certified Neurologist
- 15+ years pharma/biotech experience
- Joined Biophytis in 2018

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

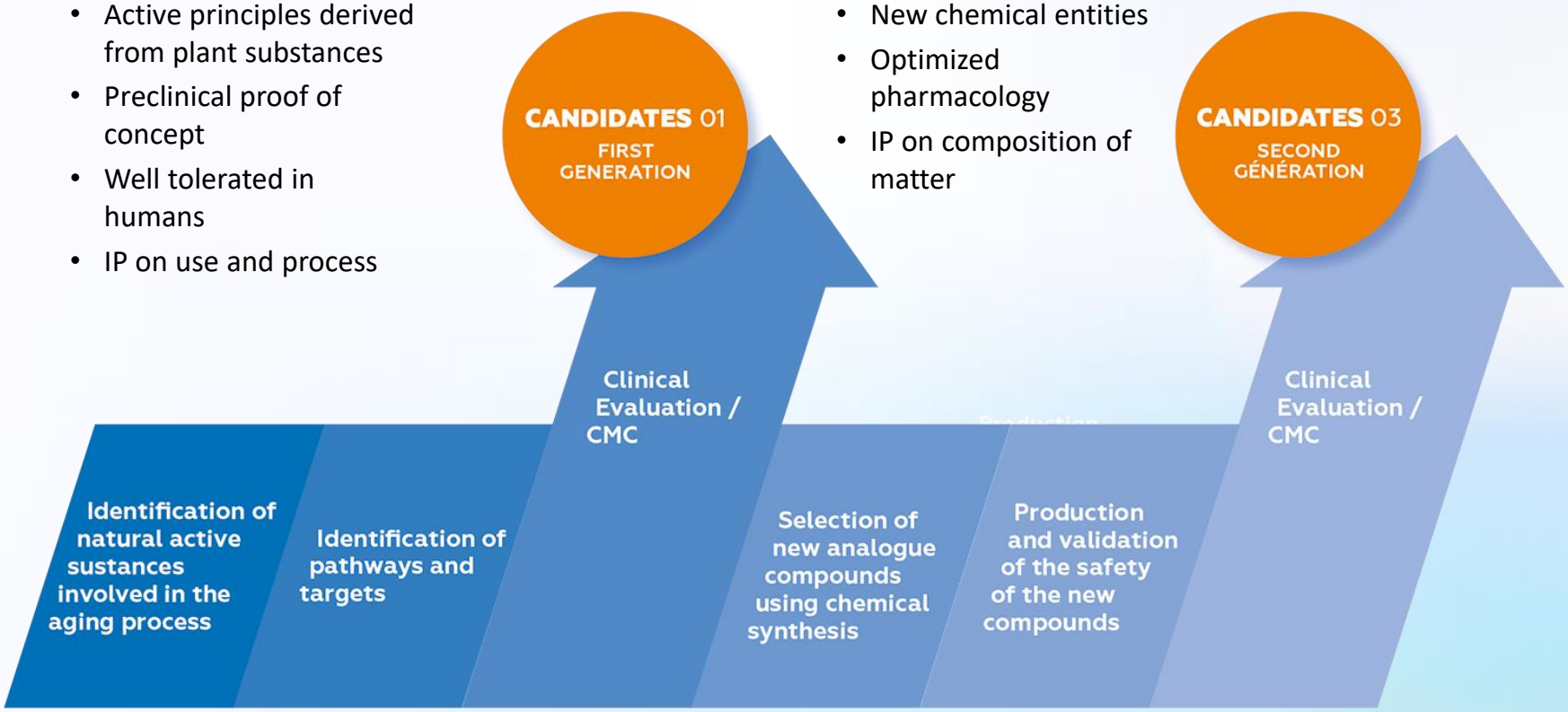
DRUG DISCOVERY & DEVELOPMENT STRATEGY

First generation

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

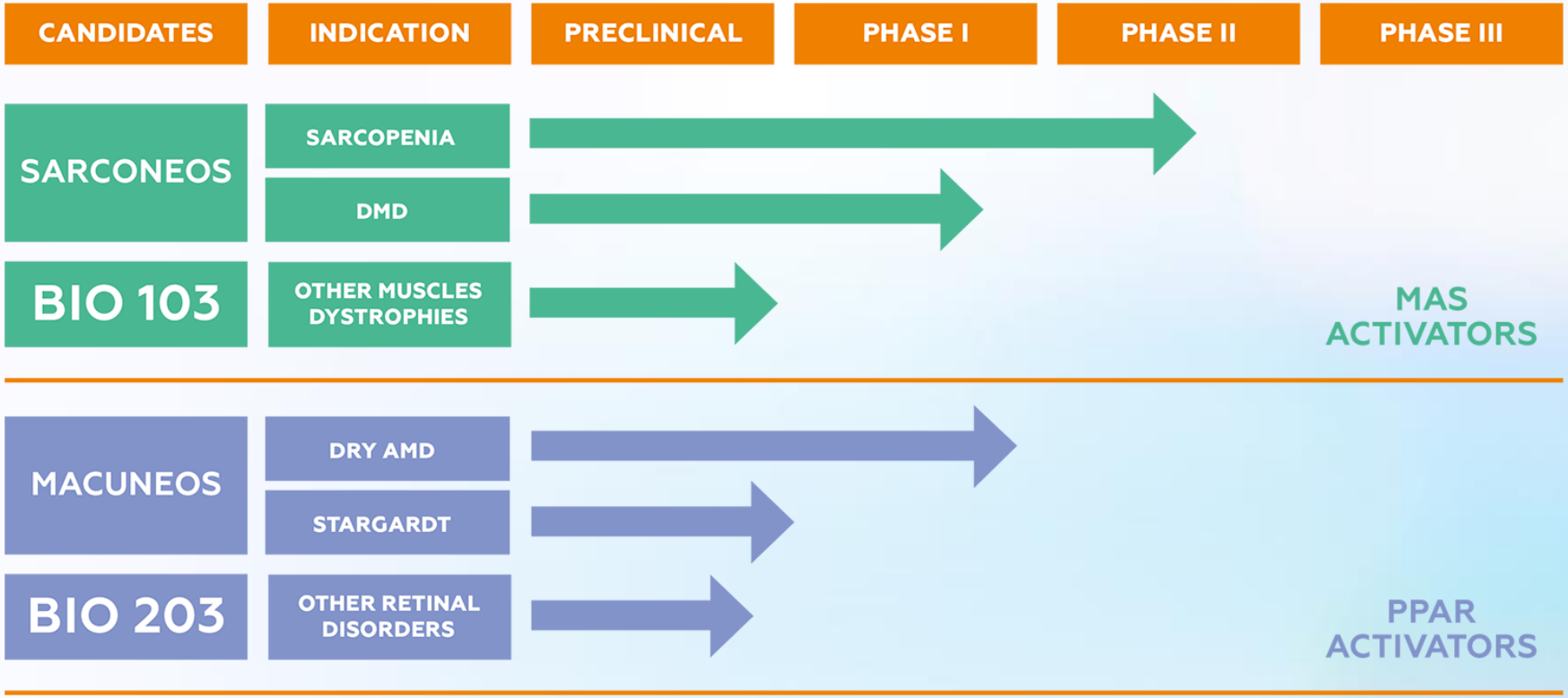
Second generation

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



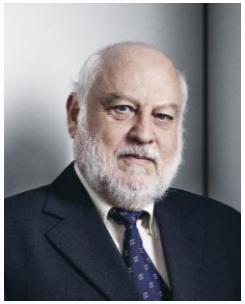
Biophytis has identified small molecules derived from plants which counteract the effects of stress on cellular function and slow down degenerative processes associated with aging

PIPELINE


CANDIDATES
INDICATION
PRECLINICAL
PHASE I
PHASE II
PHASE III
SARCONEOS
SARCOPENIA
DMD
BIO 103
OTHER MUSCLES DYSTROPHIES
MAS ACTIVATORS
MACUNEOS
DRY AMD
STARGARDT
BIO 203
OTHER RETINAL DISORDERS
PPAR ACTIVATORS

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

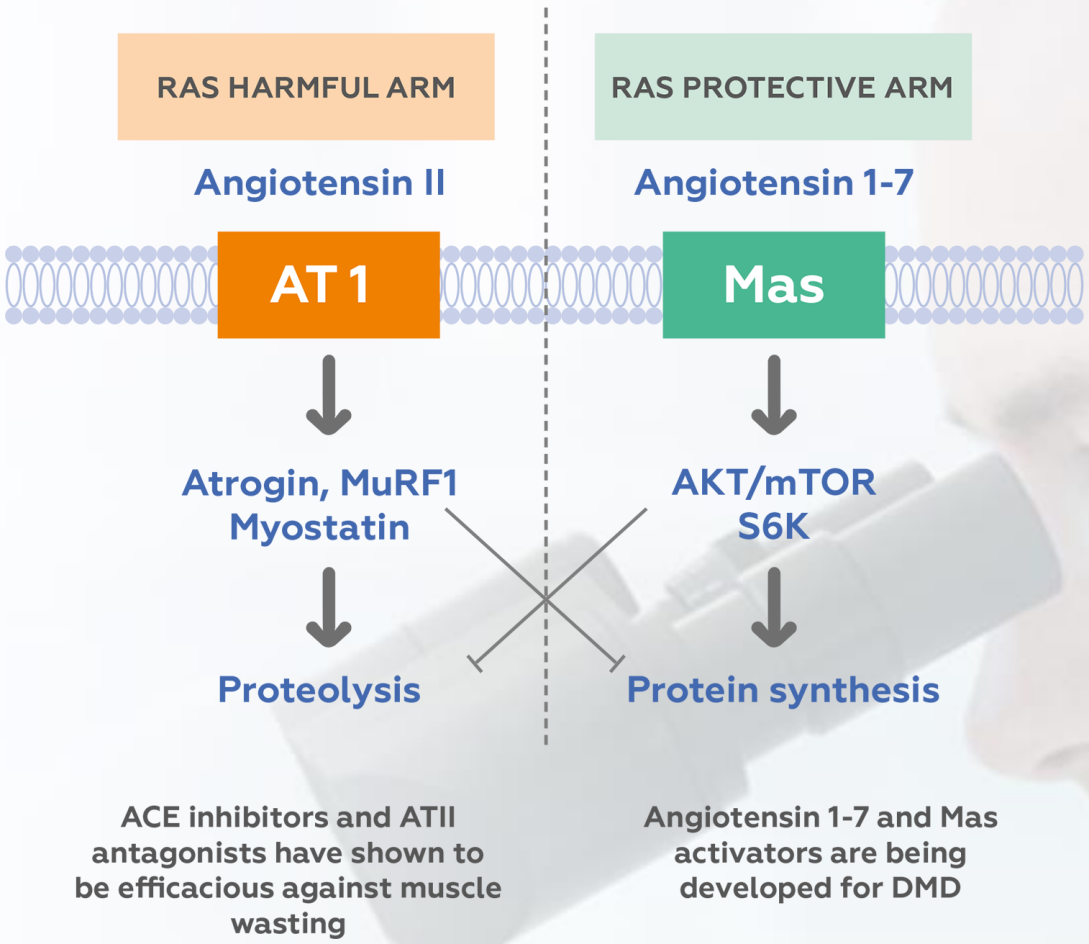
Dr. Ivana KIM
Professor Harvard Medical School,
Director Retina Research, MEEI

MAS ACTIVATORS AND MUSCULAR DISEASES

GERIATRIC CHRONIC DISEASE:
SARCOPENIA

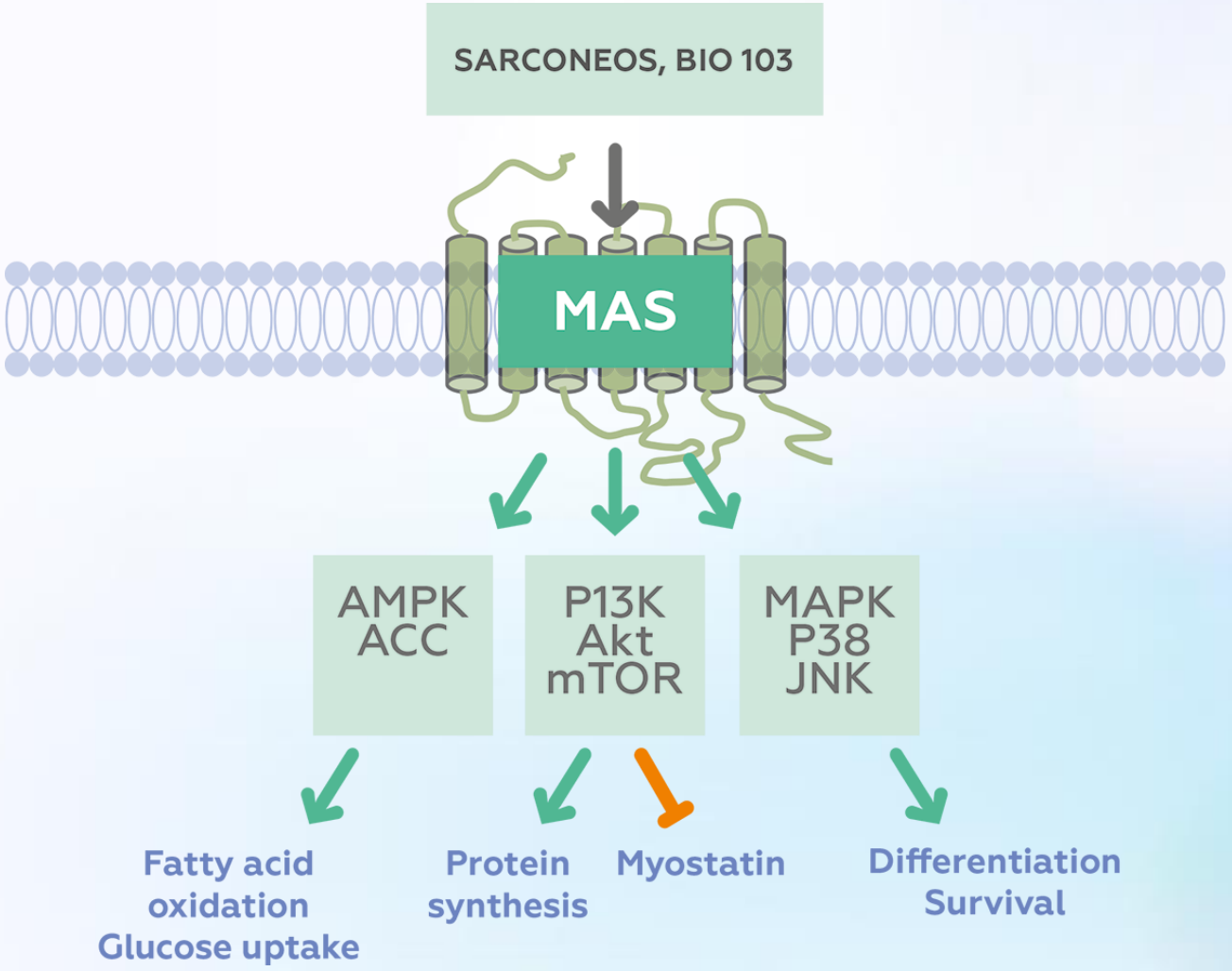
PAEDIATRIC ORPHAN DISEASE
DUCHENNE'S MUSCULAR DYSTROPHY (DMD)

RENIN ANGIOTENSIN SYSTEM (RAS) AND MUSCLE ANABOLISM



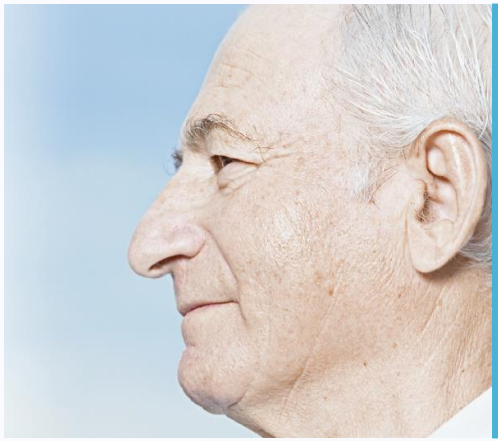
Targeting RAS stimulates anabolism in muscle and has potential for the treatment of chronic or genetic muscle disorders

MAS ACTIVATION



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

SARCOPENIA

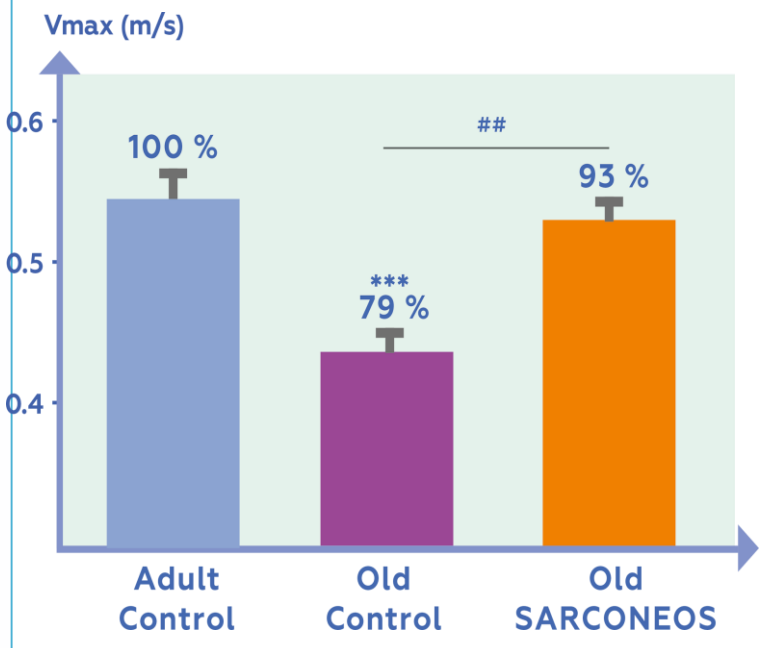


- Definition: Low muscle strength and low muscle mass (FNIH criteria)
  ICD-10 Code: M62.84
- Prevalence: 50M patients
  Estimated at 5 – 10% in >65 years old
- Standard of Care: 30 minutes physical exercise / day
  No currently approved medication

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)

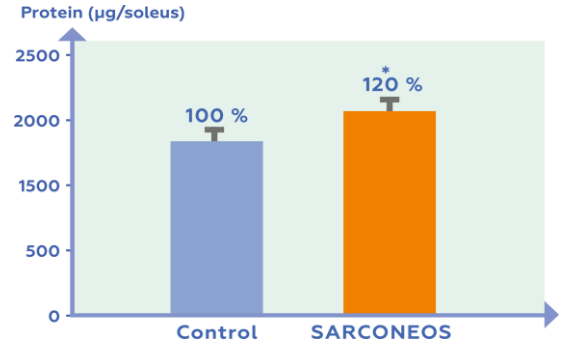
SARCONEOS: PROOF OF CONCEPT IN ANIMALS

SARCONEOS compensates the effect of ageing on muscle functionality and mobility

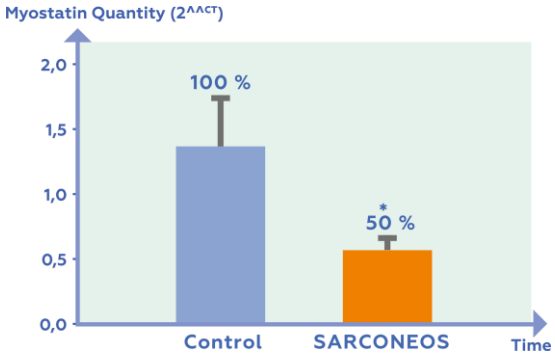


Increase in running speed in old mice

SARCONEOS stimulates anabolism in muscle



Increase in protein quantity in muscle



Inhibition of myostatin expression in muscle

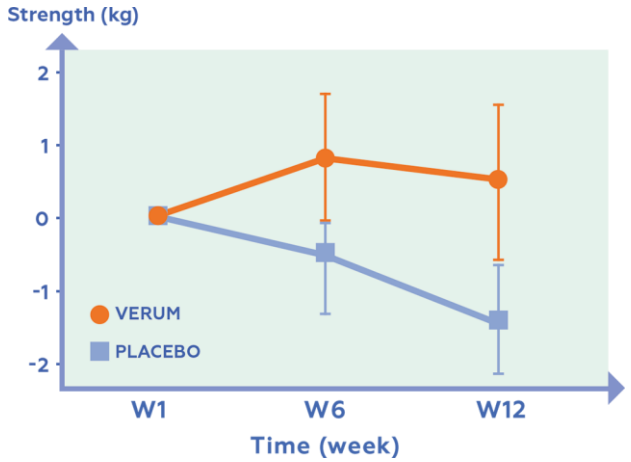
SARCONEOS stimulates anabolism and compensates the effect of ageing on muscle functionality and mobility in mice and rat models of sarcopenia

SARCONEOS: PROOF OF ACTIVITY IN NUTRITIONAL TRIAL

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

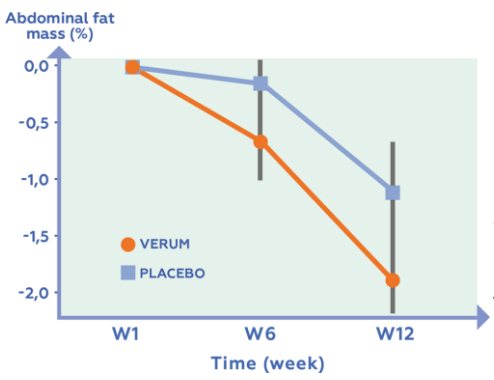
- 58 subjects, double-blind, placebo-controlled, nutrition study (dieting)
- Oral administration (40 mg/day) for 12 weeks (6 weeks hypocaloric dieting)
- No serious adverse event and good safety profile in young obese subjects

Treatment compensates the diet's effect on muscular strength

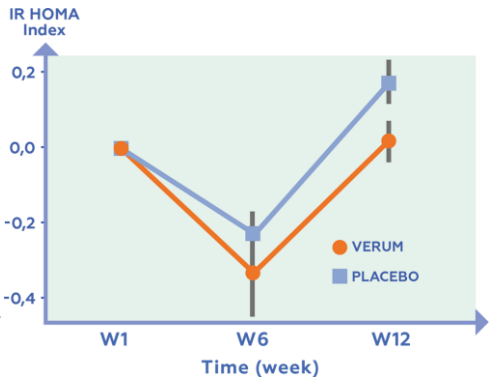


Lesser muscle strength loss (grip test, p=0.09)

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



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



Reduction of insulin resistance (Homa-IR index, p=0,06)

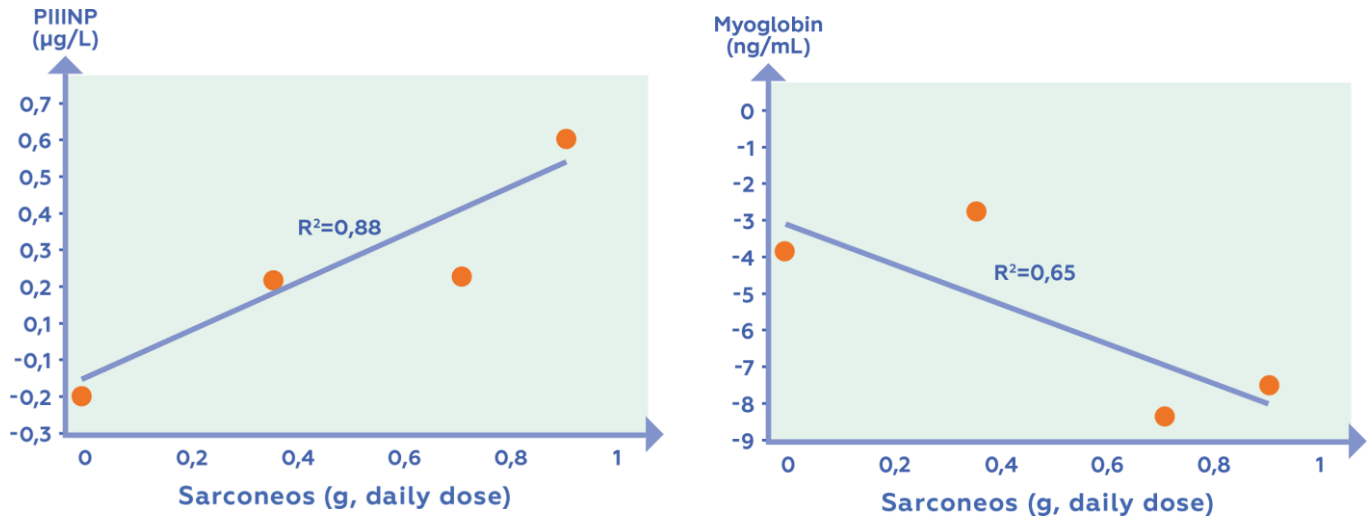
SARCONEOS active molecule increases the muscle strength, significantly reduces both the androïd fat mass and the resistance to insulin in obese healthy volunteers

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

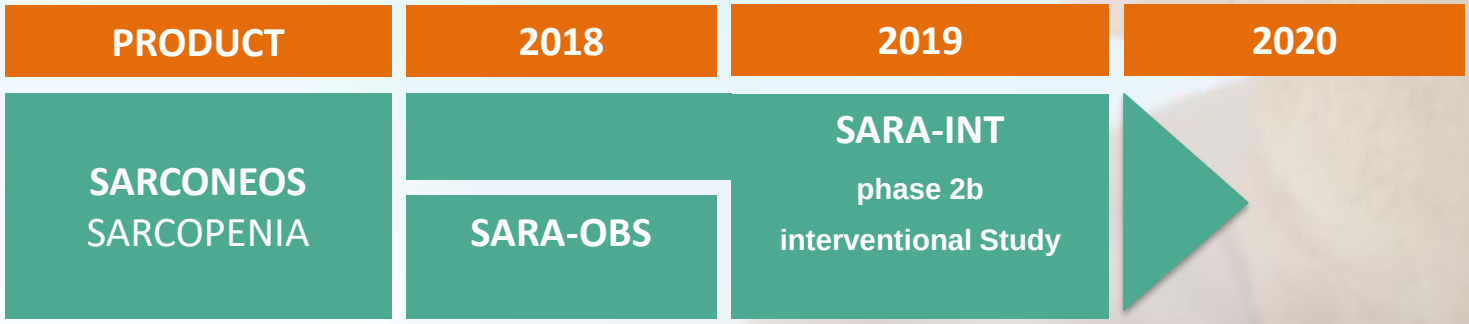
SARA: PHASE 2b INTERNATIONAL CLINICAL PROGRAM

SARA-OBS - Observational study

- Multicentric observational study: nine clinical centers in Europe and the US
- Recruitment of sarcopenic patients in Europe and US on going : 218 patients to-date
- 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 11 additional clinical centers
- Sarconeos 175 mg BID vs 350 mg BID vs Placebo
- Duration: 26 weeks
- Endpoints (EMEA 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



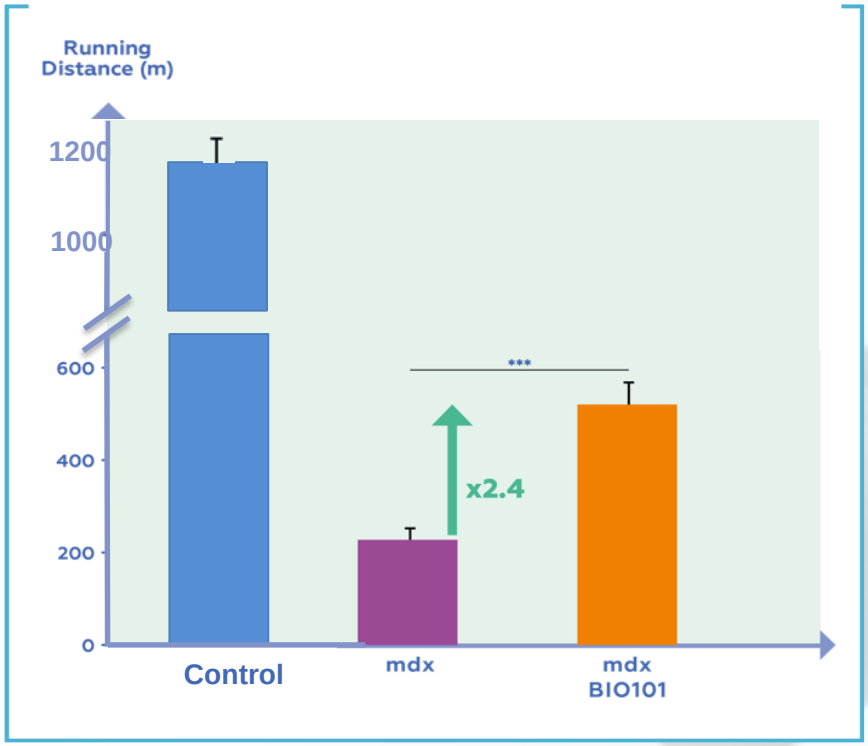
DUCHENNE'S MUSCULAR DYSTROPHY (DMD)

- 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

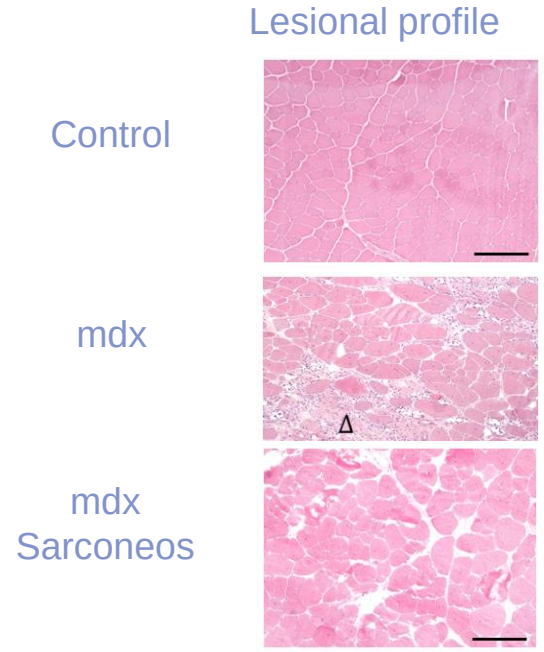
Drug candidates in development	Examples
Genetic and cell therapy	Exon Skipping (Eteplirsen, FDA-approved) Microdystrophin vectors (preclinical)
Myostatin Inhibitors	Domagrozumab (Pfizer, Phase 2)
Other symptomatic treatment	Idebenone (Santhera), approved in Israel
MAS Activators	Angiotensin 1-7 (preclinical)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

SARCONEOS: PROOF OF CONCEPT IN ANIMAL MODEL OF DMD

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

MYODA-PK: Phase 1/2 PK and dose finding study

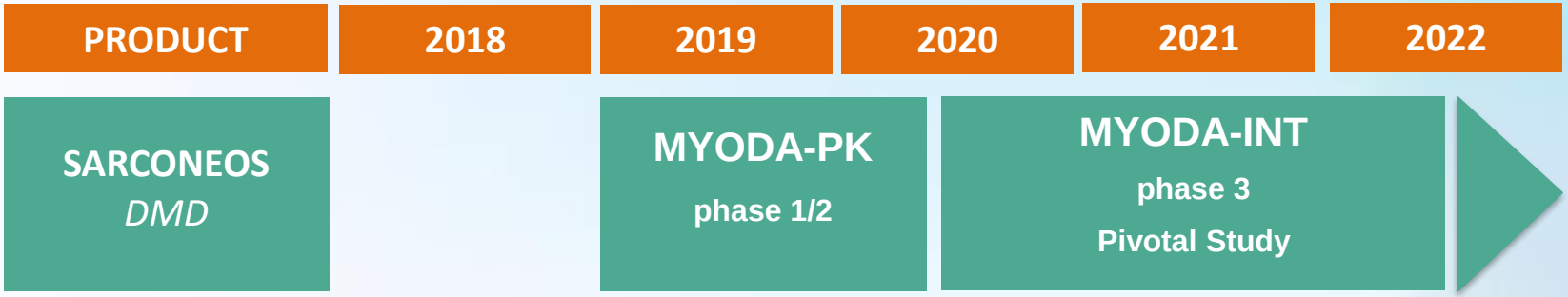
- Phase 1/2 trial, double-blind, placebo-controlled
- 27 ambulatory and non-ambulatory Duchenne patients
- 2 phases: SAD (1 week), dose finding, proof of concept (24 weeks)

MYODA-INT: Pivotal phase 3 study

- Multicentric international clinical trial, randomized, double-blind, placebo-controlled
- 120 ambulatory and non-ambulatory Duchenne patients
- Minimal Duration: 12 months

Primary endpoints :

- Ambulatory patients : change in NSAA score (North Star Ambulatory Assessment)
- Non-ambulatory patients : change in PUL test score (Performance Upper Limb)

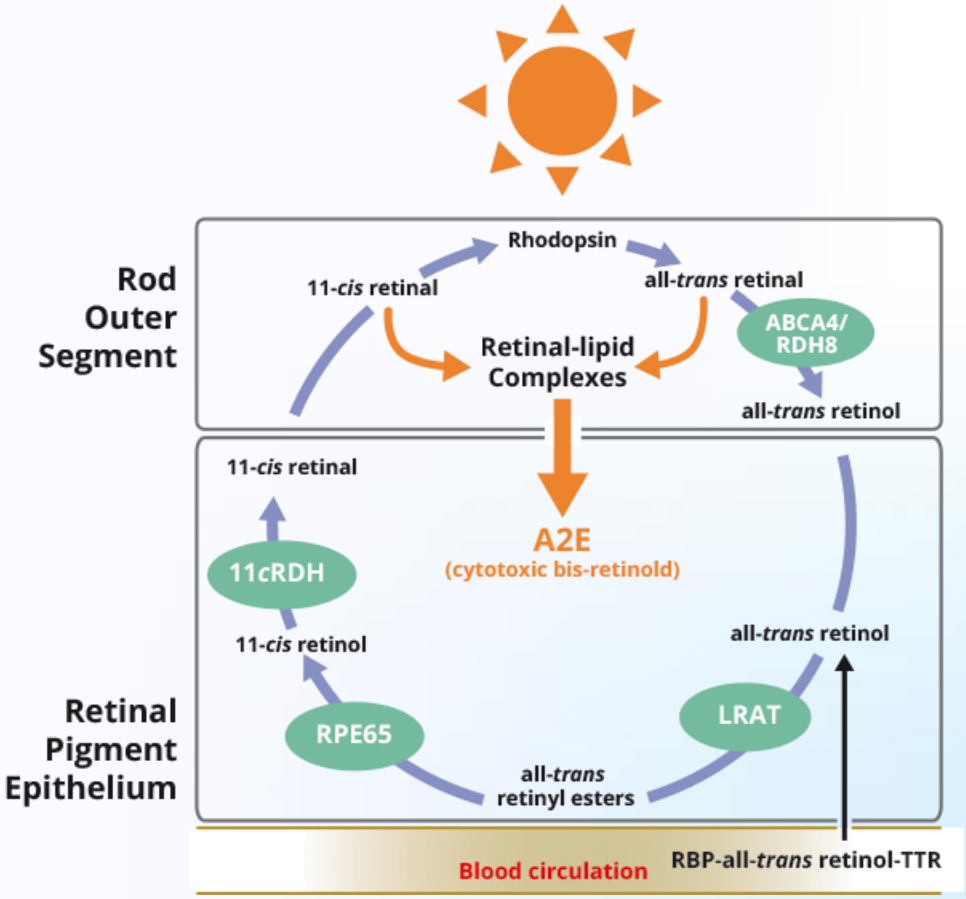


PPAR ACTIVATORS AND RETINAL DISEASES

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

PAEDIATRIC ORPHAN DISEASE:
STARGARDT'S DISEASE

PHOTO-OXIDATIVE STRESS AND MACULAR DEGENERATION



A2E and oxydative 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

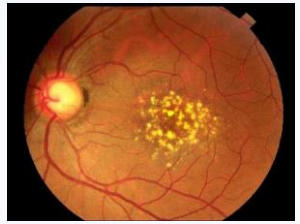
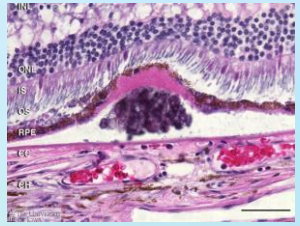


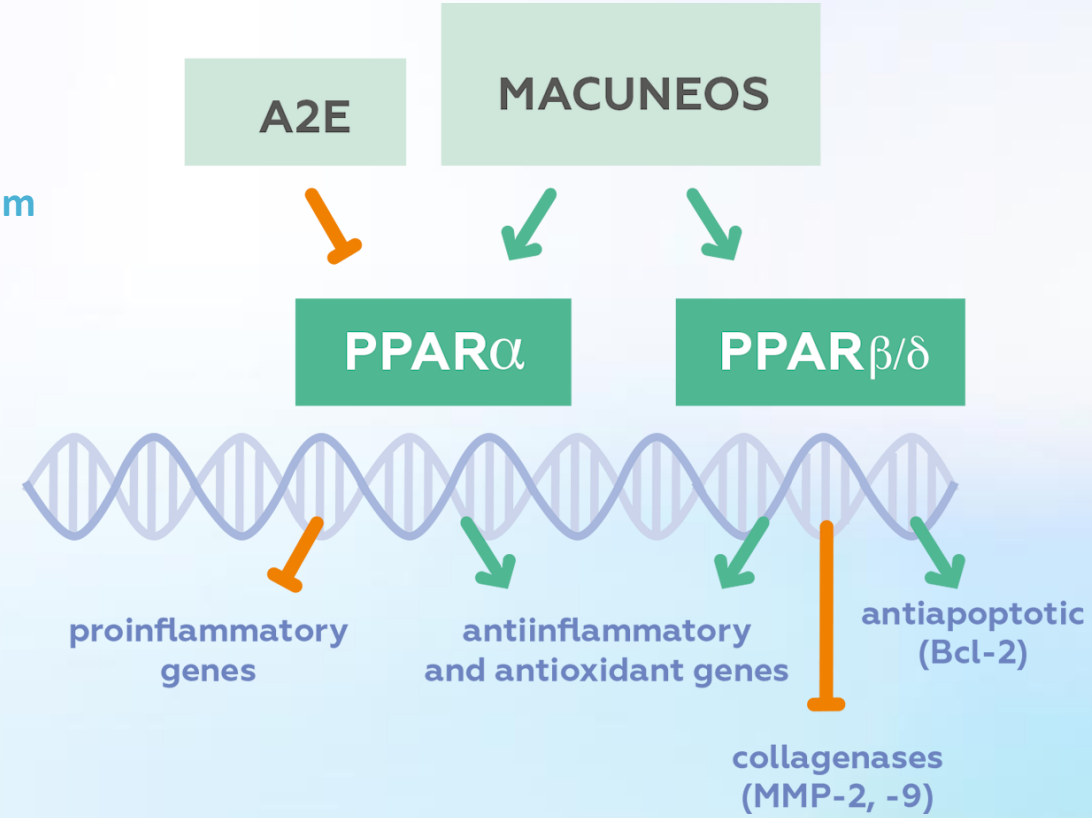
Photo-oxidative stress leads to:

- 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

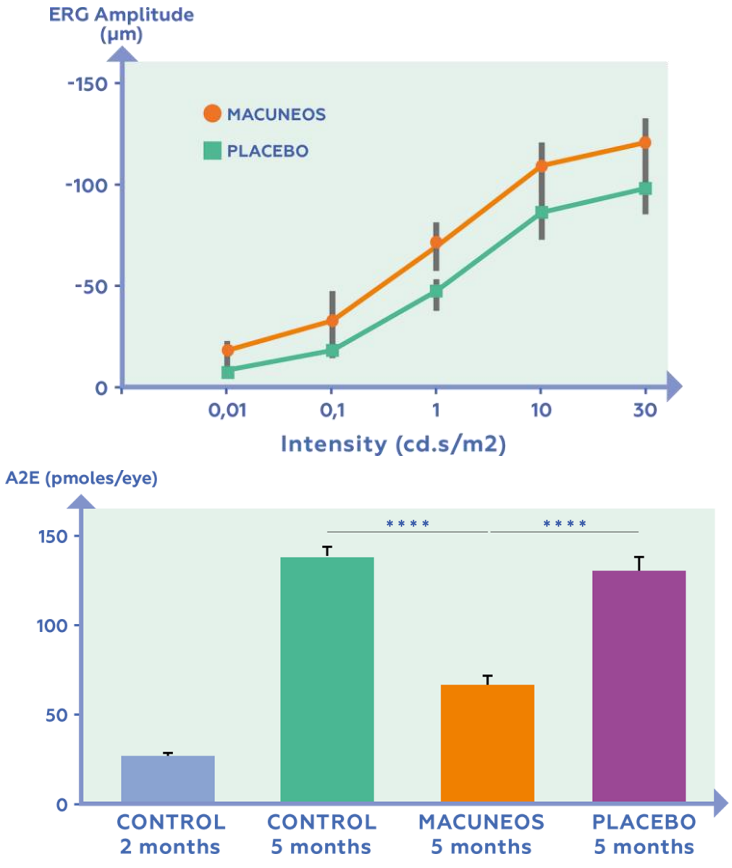
DRY AGE-RELATED MACULAR DEGENERATION (AMD)

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

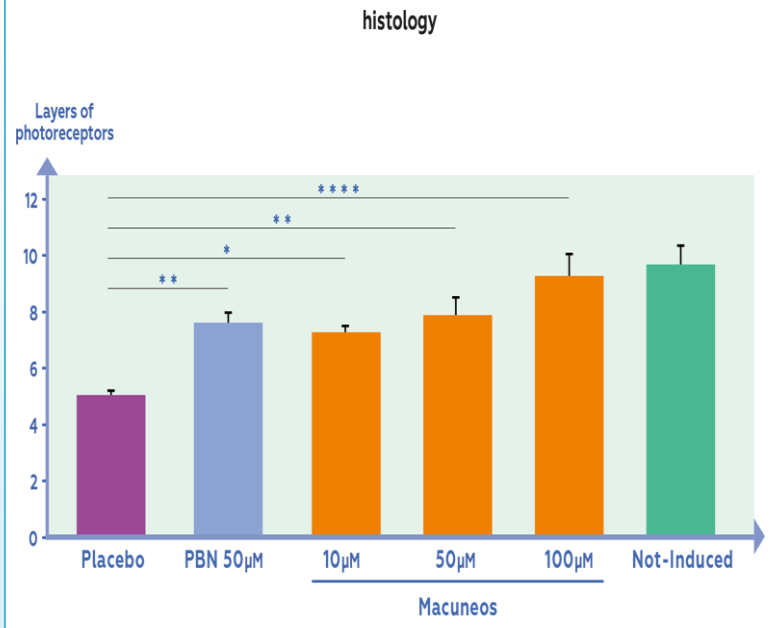
Drug candidates in development	Examples
Anti-complement factor antibodies	Lampaluzimab (Roche) – failed in Phase III
Visual Cycle Inhibitors	Emixustat (Acucela) – failed in Phase IIb/III
PPAR Activators	MACUNEOS (Biophytis)

MACUNEOS: PROOF OF CONCEPT IN ANIMALS

MACUNEOS preserves the retina's functionality and limits the A2E accumulation after chronic oral administration (ABCA4-/- RDH8-/- 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

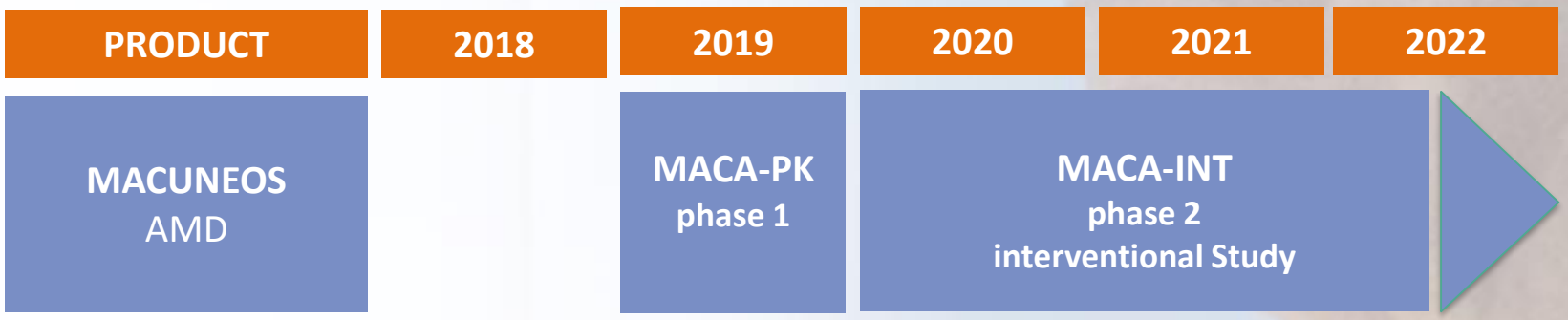
MACA: CLINICAL PROGRAM IN DRY AMD

MACA-PK – Phase 1 – Safety, PK and PD

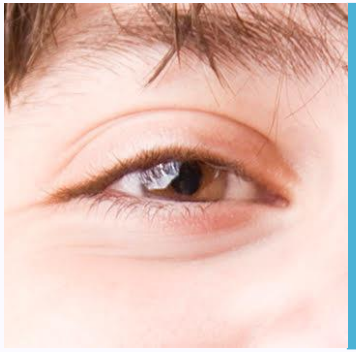
- 2 phases to explore various oral doses versus placebo
  - SAD study in 32 healthy volunteers (2 centers in Belgium)
  - MAD study in 32 healthy volunteers with 14 days follow-up (2 centers in Belgium)
- Endpoints
  - Safety, pharmacokinetics, pharmacodynamics, various plasmatic biomarkers

MACA-INT – Phase 2 multicentric clinical trial

- Multicenter randomized double-blind, placebo-controlled study
- 300 patients suffering of intermediate and late dry AMD (Macuneos 100mg vs 350mg vs placebo)
- Duration: 24 months (interim analysis after 12 months)
- End points:
  - Primary: atrophic lesions size progression
  - Secondary: dark adaptation, accumulation of drusens, evolution towards wet AMD, visual acuity



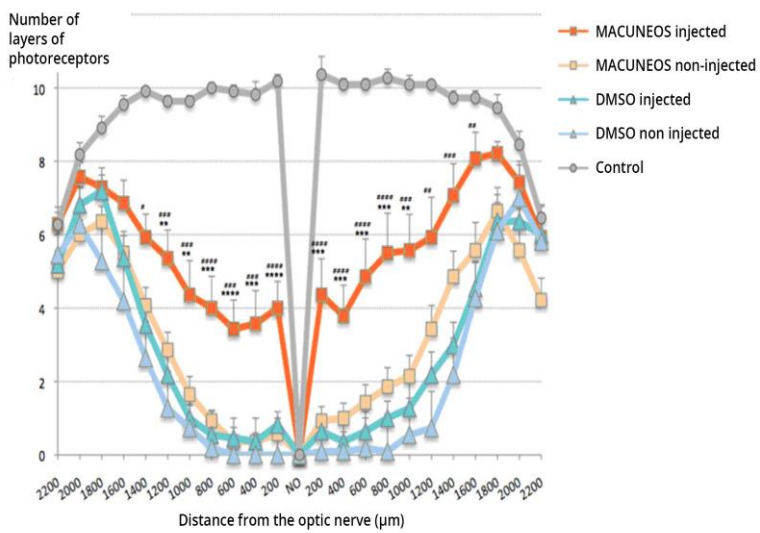
STARGARDT'S DISEASE



- 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 (Opsis Therapeutics)
Visual Cycle Inhibitor (Emixustat, Acucela)
PPAR Activator (MACUNEOS, Biophytis)

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



VALUE CREATION NEWS FLOW

SARCONEOS in SARCOPENIA

- H1 18: SARA-INT: First patient-in in interventional Phase 2b SARA
- H2 18: SARA-OBS: End of observational Study
- H1 19: SARA-INT: Last patient-in in interventional Phase 2b SARA
- H2 19: SARA-INT: Interim results of the interventional Phase 2b SARA (DSMB)
- H2 19**: SARA-INT: Topline results of Phase 2b SARA**

SARCONEOS in DMD

- H1 18: Orphan drug designation
- H2 18: Scientific advices from FDA and EMA on MYODA clinical program
- H1 19: MYODA-PK: Obtention of regulatory approvals of safety and PK Study
- H2 19: MYODA-PK: Safety and pharmacokinetics study on patients
- **H1 20: MYODA-INT: Start of pivotal phase 3 study**

MACUNEOS in Dry AMD

- H1 19: Scientific advice of FDA, AFMPS (Belgium) on MACA clinical program
- H1 19: MACA-PK: Obtention of regulatory approvals of safety and PK Study
- H2 19: MACA-PK: Safety and pharmacokinetics study on healthy volunteers
- H1 20: **MACA-INT: Start of interventional Phase 2 Study MACA-INT**

THE BOARD OF DIRECTORS

Jean M. Franchi
Independant 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

Eric ROWINSKY
Independent Board Member

- President of Rgenix and Oncology Scientific Director at Clearpath Development
- Editor in chief of the *Investigational New Drug* review
- 25 years experience in clinical research and in drug development

A BOARD OF DIRECTORS WITH COMPLEMENTARY PROFILES

Nadine COULM
Independant Board Member

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

Jean-Gérard GALVEZ
Independant Board Member

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

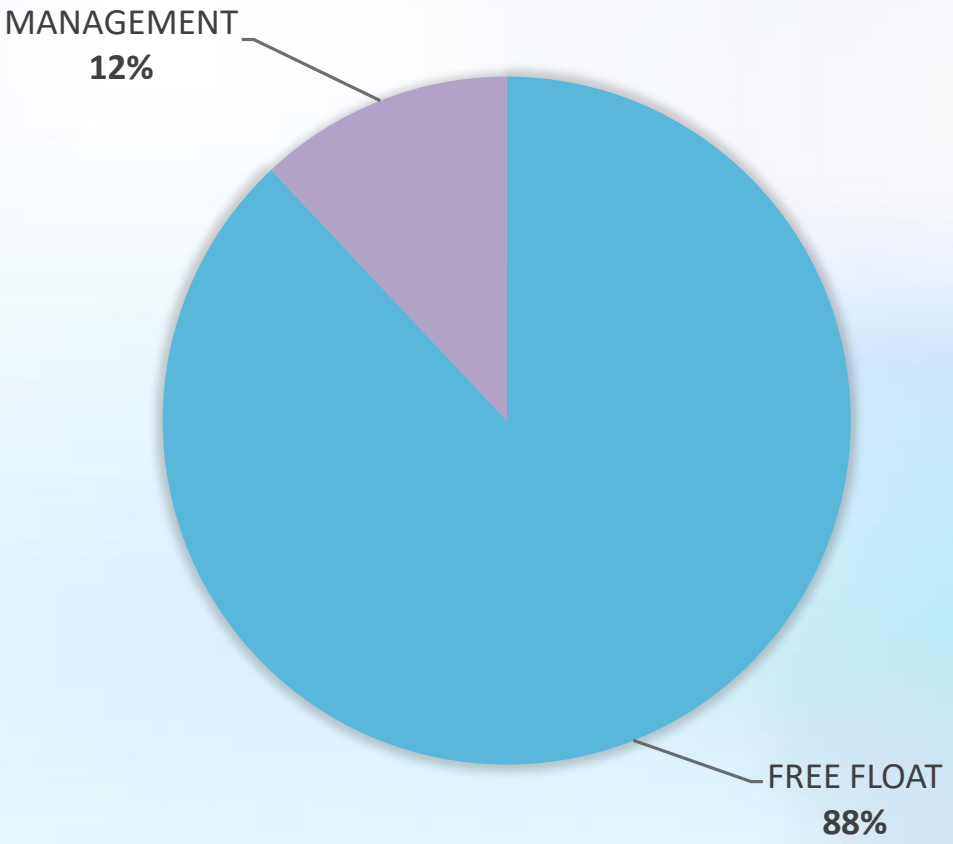
Dimitri BATSIS
Independent Board Member

- Entrepreneur and Business Angel
- Founder of Zeni Corporation and Drone Volt
- 20 years experience in the new technologies' sector

CAPITAL STRUCTURE

Stock profile

- Market: Euronext Growth (Paris)
- Ticker: ALBPS
- Shares outstanding: 13,463,413
- Share price (October 18th 2018): €1,65/share
- Market Capitalization: €22M



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Thank you

Investors contact: investors@biophytis.com