biophytis®

NEW THERAPEUTICS FOR AGING DISEASES

Biotech AGORA

Soirée Biotech Agora – 13 décembre 2016

THE BIOTECH SPECIALIST IN AGING DISEASES

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CORPORATE OVERVIEW

BIOPHYTIS is a public company listed on Alternext (Paris, France)

- Share price (December 12th) : €4.24
- Shares outstanding: 6,195 M
- Market capitalization: €26 M
- €16 million raised in 2015 to prepare two Phase IIb trials

BIOPHYTIS is advancing two drug candidates into Phase IIb in 2017

SARCONEOS (ex BIO101)	MACUNEOS (ex BIO201)
MAS activator sarcopenic obesity (SARA Phase IIb start H1 2017)	PPAR activator for dry AMD (MACA Phase IIb start H1 2018)
Preparatory studies: SARA-OBS, SARA-PK	Preparatory studies: MACA-OBS, MACA-PK

BIOPHYTIS spun-out of Université Pierre et Marie Curie in 2006

- BIOPHYTIS' co-founder, René Lafont, assembled a unique small molecule library derived from plants, which is biased for degenerative processes involved in aging
- BIOPHYTIS uses unique cell based assays to identify drug-like small molecules

THE TEAM

Stanislas VEILLET
Founder & CEO
- PhD in genetics
- 15+ years in R&D management (Monsanto, Pharmacia, Danone)
- Created Biophytis in 2006

Jean-Christophe MONTIGNY
Chief Financial Officer
- AgroParisTech engineer, BA from IEP Paris
- 17+ years management experience (Kraft Foods) and entrepreneurship (B.L.O)
- Joined Biophytis in 2009

AN EXPERIENCED MANAGEMENT TEAM

René LAFONT
Co-founder & CSO
- Ecole Normale Superieure
- Professor emeritus at UPMC
- Former Dean of the life sciences department
- 170 publications in biochemistry and physiology

Susanna del SIGNORE
Chief Medical Officer
- MD in geriatrics
- 10+ years in medical regulatory affairs (Sanofi, EMA)
- 20+ years of clinical development in the pharma industry (Sanofi, Servier)

THE BOARD OF DIRECTORS

Stanislas VEILLET
President of the Board
- PhD in genetics, AgroParisTech alumnus
- 15+ years in R&D management (Monsanto, Pharmacia, Danone)
- Created Biophytis in 2006

Marie-Claire JANAILHAC-FRITCH
Indépendant Board Member
- HEC alumnus
- President of the Board, Guerbet
- 10 years as Sales Director in the pharma industry (GSK, Eurorga)
- Fonder and CEO of IRIS and LANATECH (cosmetic industry), sold in 2013

UN CONSEIL D'ADMINISTRATION AUX PROFILS COMPLEMENTAIRES

Nadine COULM
Indépendant Board Member
- HEC Alumnus
- IR Director for FNAC
- 20 years of IR experience with PARISBAS, DANONE & CASINO

Jean-Gérard GALVEZ
Independant Board Member
- INP de Nancy et 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 UPMC
- Co-founder & Scientific Director of Metabrain Research
- 20 years of experiencein drug discovery with MERCK SERONO

KEY MARKET DRIVERS

In 2050

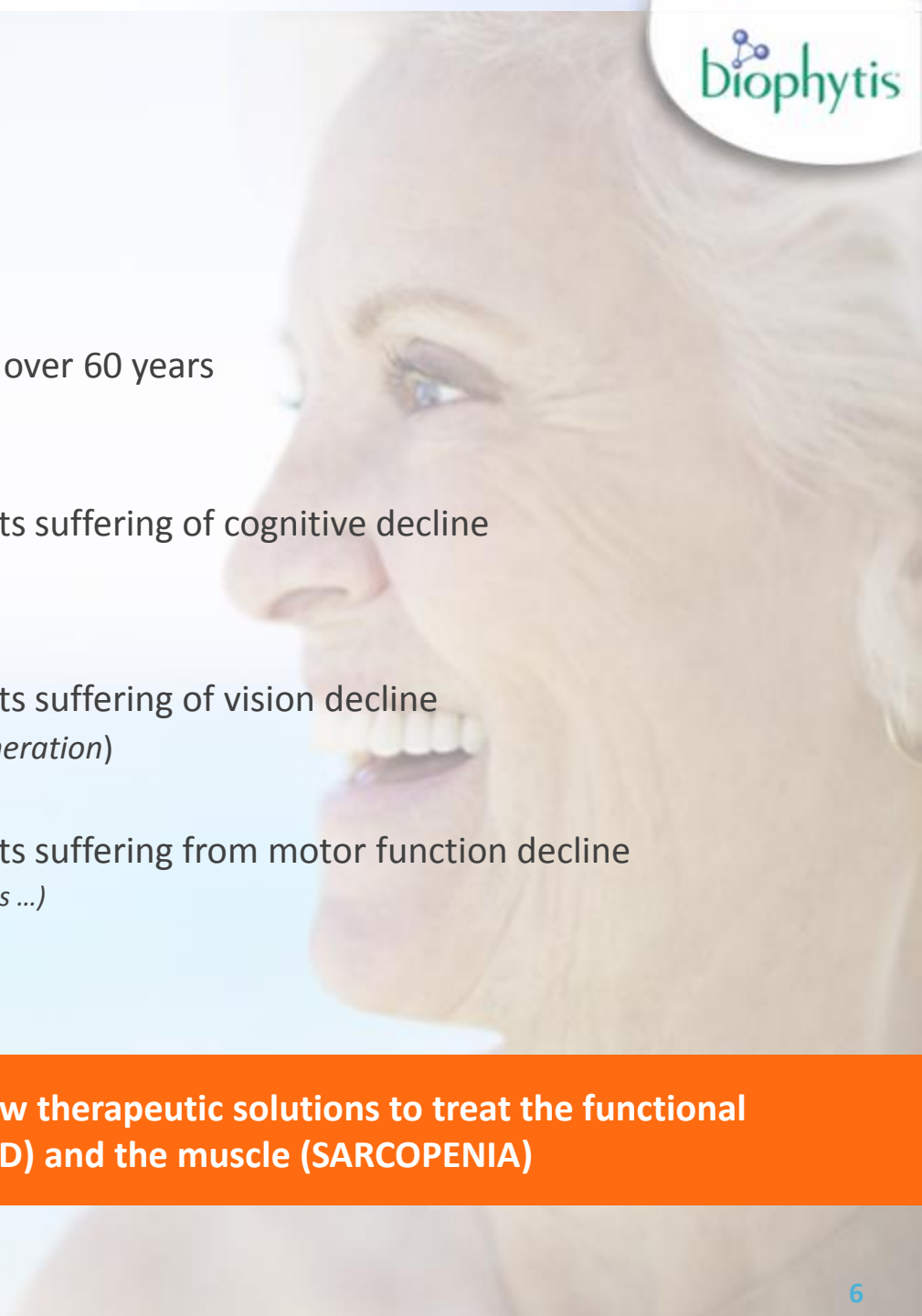
*Sources : OMS – EWGSOP (*European Working Group on Sarcopenia in Older People)

2 billion: Population over 60 years
(versus 680 millions in 2015)

135 million: Patients suffering of cognitive decline
(Alzheimer, senile dementia…)

400 million: Patients suffering of vision decline
(*Age Related Macular Degeneration*)

500 million: Patients suffering from motor function decline
(Sarcopenia, muscular dystrophies …)



BIOPHYTIS develops new therapeutic solutions to treat the functional decline of the eye (AMD) and the muscle (SARCOPENIA)

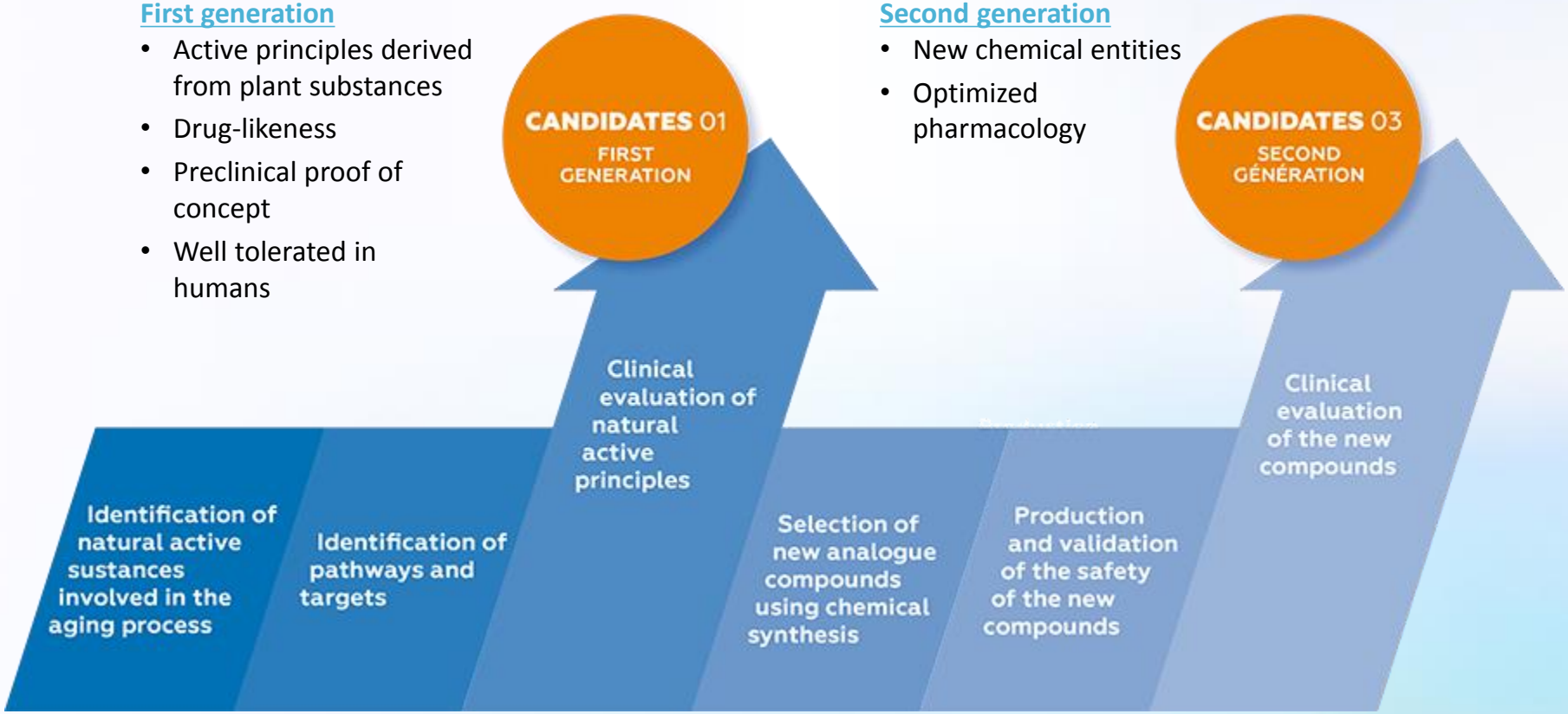
DRUG DISCOVERY & DEVELOPMENT STRATEGY

First generation

- Active principles derived from plant substances
- Drug-likeness
- Preclinical proof of concept
- Well tolerated in humans

Second generation

- New chemical entities
- Optimized pharmacology

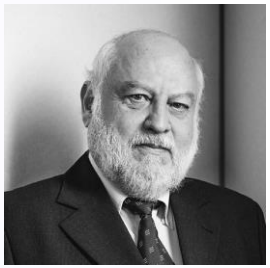


For each drug candidate, BIOPHYTIS develops an aggressive strategy for creation and protection of intellectual property

SCIENTIFIC BOARD

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

UPMC SORBONNE UNIVERSITÉS



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

UPMC SORBONNE UNIVERSITÉS

Pr. José SAHEL
Director of Institut de la Vision

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

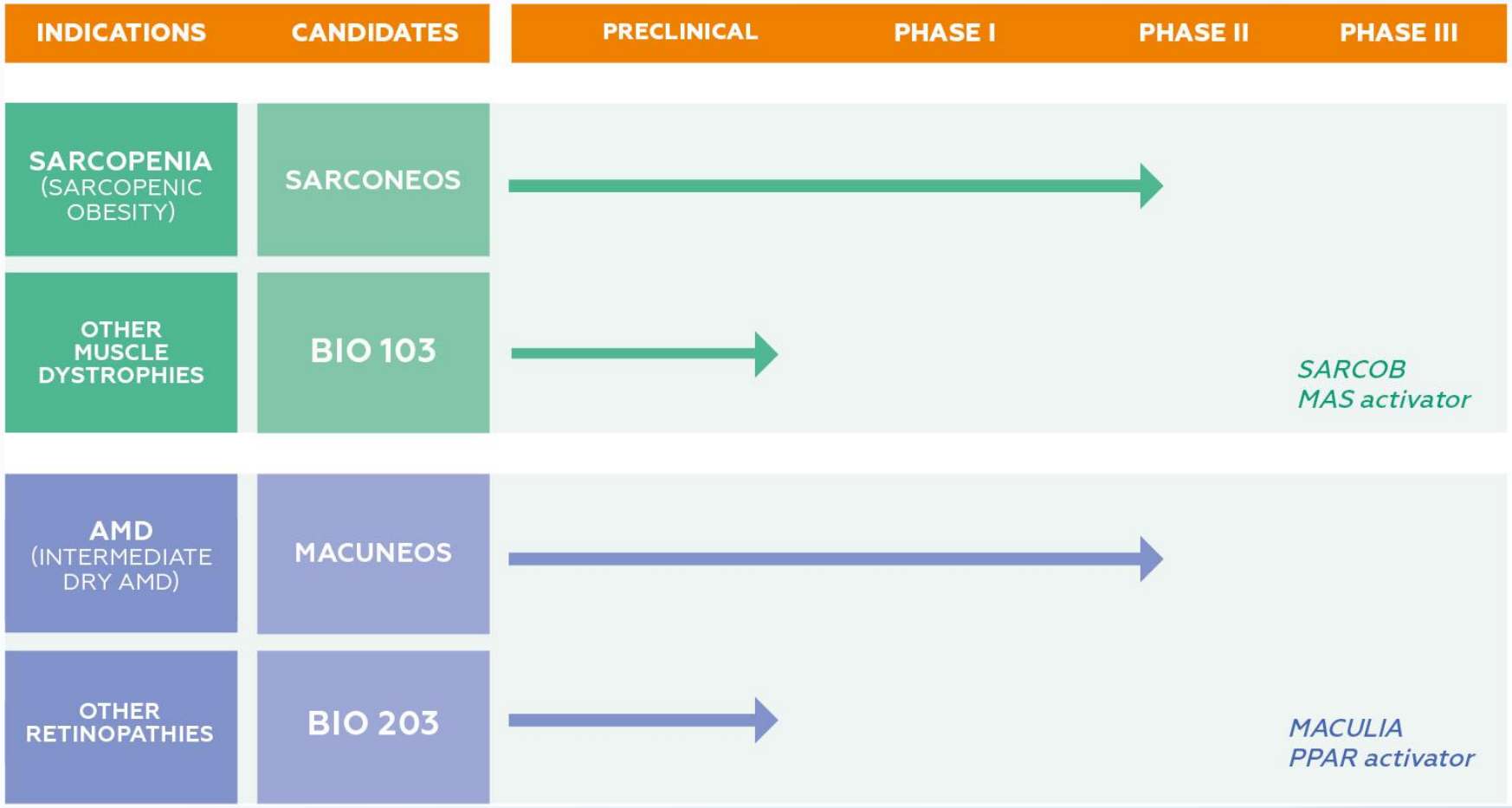
HARVARD MEDICAL SCHOOL

Dr. Philippe GUILLET
MD in geriatrics and neurology
20 + years in clinical development in the pharma industry

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

HARVARD MEDICAL SCHOOL

PIPELINE


INDICATIONS
CANDIDATES
PRECLINICAL
PHASE I
PHASE II
PHASE III
SARCOPENIA (SARCOPENIC OBESITY)
SARCONEOS
OTHER MUSCLE DYSTROPHIES
BIO 103
SARCOB
MAS activator
AMD (INTERMEDIATE DRY AMD)
MACUNEOS
OTHER RETINOPATHIES
BIO 203
MACULIA
PPAR activator

SARCONEOS

Sarcopenia

SARCOPENIA

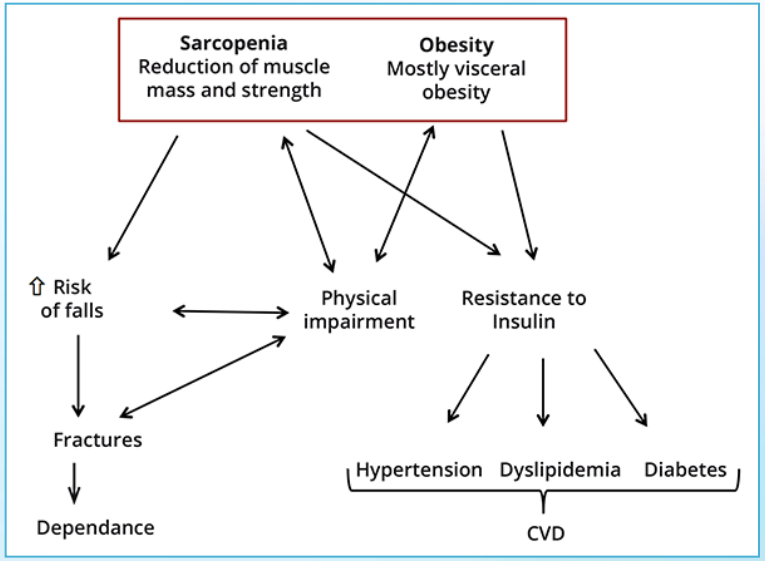
SARCOPENIA IS A DYSTROPHY OF THE SKELETAL MUSCLES
CHARACTERIZED BY LOSS OF MUSCLE MASS AND FUNCTIONALITY ;
SARCOPENIC OBESITY IS WHEN SARCOPENIA OCCURS IN OBESE PATIENTS.

50 million sarcopenic people worldwide

- Muscle loss of 2 % per year as of 50
- 40% of people >80 years of age
- Healthcare cost of sarcopenia is estimated at $18,5 billion

20 million sarcopenic obese patients

- 31% of people > 60 years of age in U.S.
- Serious mobility impairment meaning higher cost of care
- Increased incidence of cardiometabolic disease
- No treatment



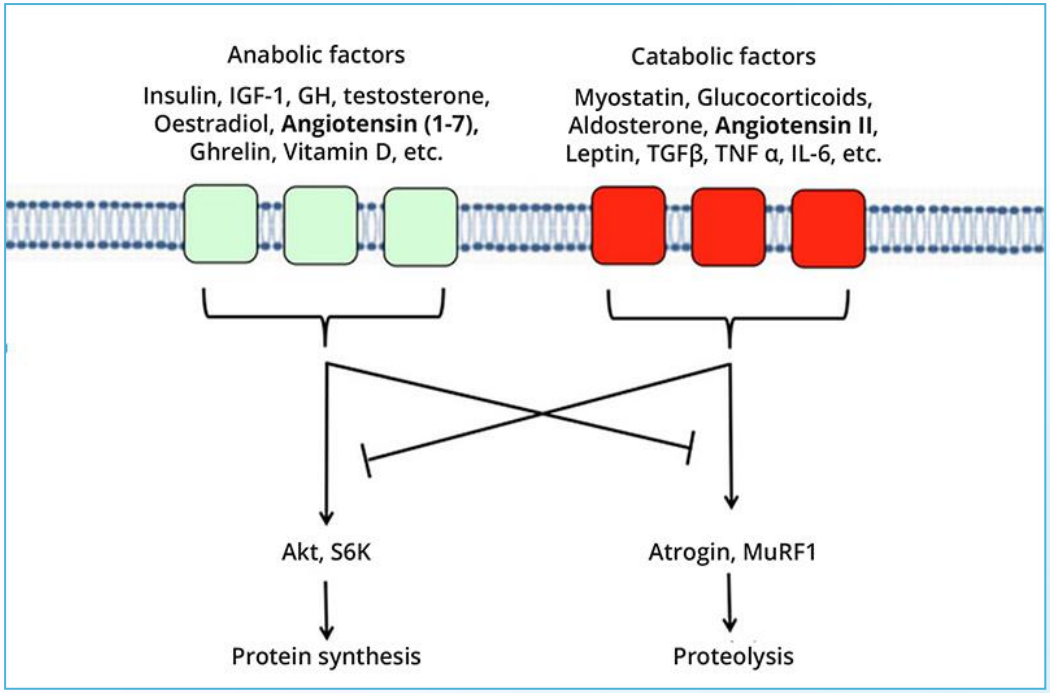
Zamboni 2008

Despite high socio-economic cost, there is no treatment available for sarcopenic obesity
Single recommendation: 30 min physical exercise per day

SARCONEOS TARGETS AN INDICATION WITH NO TREATMENT

	Sarcopenia & Sarcopenic Obesity	Sarcopenia & Cachexia
Standard of care	• **30 min physical exercise / day**	• 30 min physical exercise / day
Products in development	• **SARCONEOS (Phase 2b)**	Anti-myostatin antibodies : • REGN1033 (Regeneron) • BYM338 (Novartis) • LY2495655 (Lilly)
Product attributes	• **Improves mobility** • **Reduces cardiometabolic risk** • **Oral administration**	• Increases muscle mass and strength • No improvement of mobility • Subcutaneous injection

RENIN-ANGIOTENSIN SYSTEM AND SARCOPENIA



Causes of Sarcopenia

- Endocrinal changes associated with aging modulate anabolic/catabolic factors balance, causing the loss of muscle mass and functionality
- Adipose tissue produces anti-anabolic factors accelerating sarcopnia in obese subjects (Sarcopenic obesity)

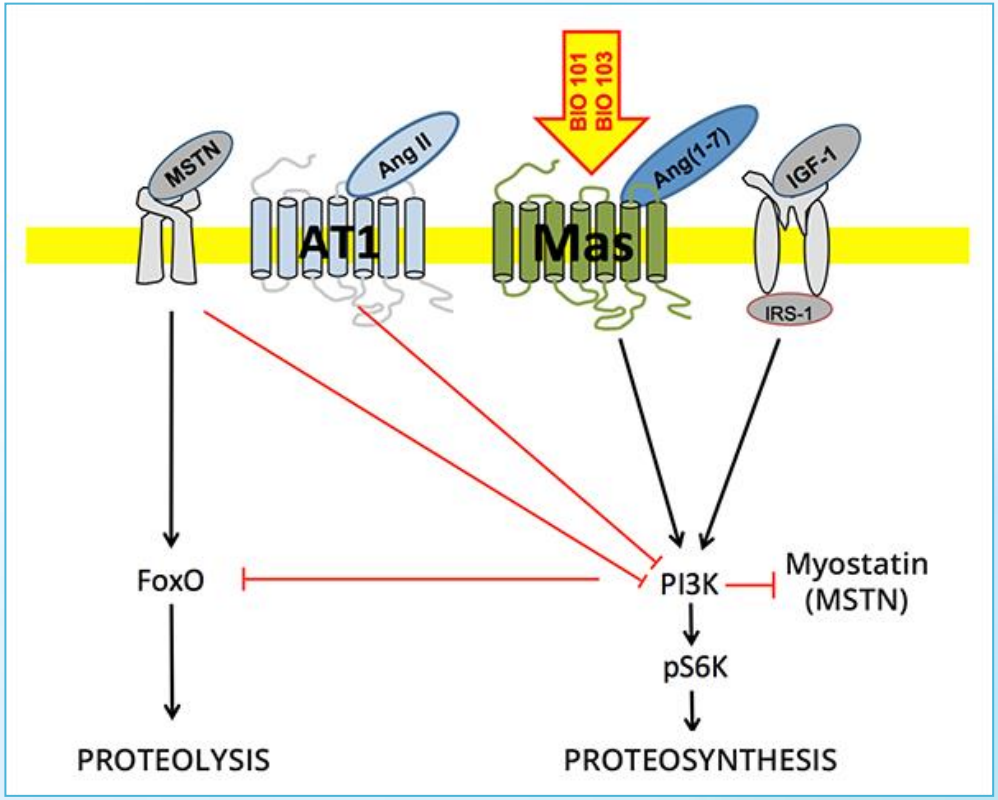
Sarcopenia and Angiotensins

- The Renin-Angiotensin System is a hormonal system involved in the regulation of arterial pressure and the cardiac function, but also the metabolism of muscles.
- Angiotensin II increases with age and obesity causing a loss of muscle mass, and is linked to an increase of cardiovascular risk.
- Angiotensin 1-7 counteracts the effects of Angiotensin II.

MAS RECEPTOR ACTIVATION TO FIGHT SARCOPENIA

The activation of Mas by Angiotensin 1-7 allows stimulation of muscle anabolism, and counteracts the proteolitic effects of Angiotensin II thereby facilitating :

- Increase in myotubes diameter
- Stimulation of protein synthesis
- Stimulation of S6K Phosphorylation
- Inhibition of myostatin production



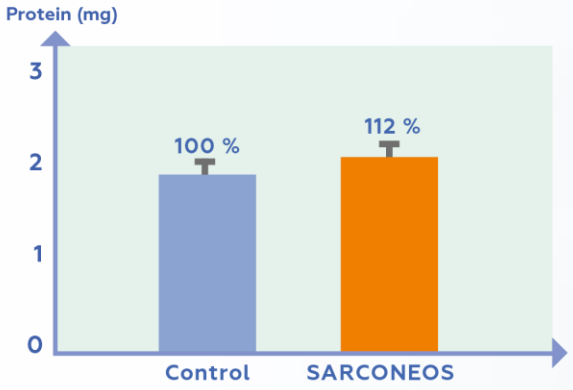
SARCONEOS and BIO 103 are potent Mas activators that stimulate muscle anabolism in preclinical testing

SARCONEOS: PROOF OF CONCEPT

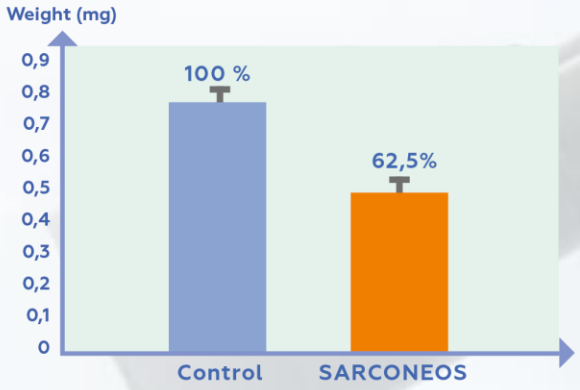
Conclusive preclinical results:

(several rats and mice models of sarcopenia)

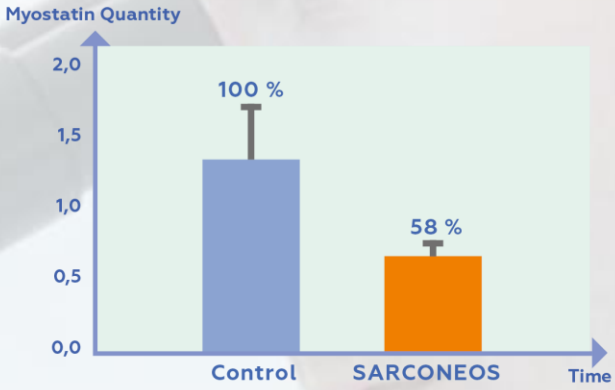
- Increase in running velocity
- Increase in skeletal muscle mass
- Inhibition of myostatin expression
- Reduction of fat mass
- Increase in energy consumption



Increase in protein quantity in soleus muscle



Reduction in adipose tissue storage



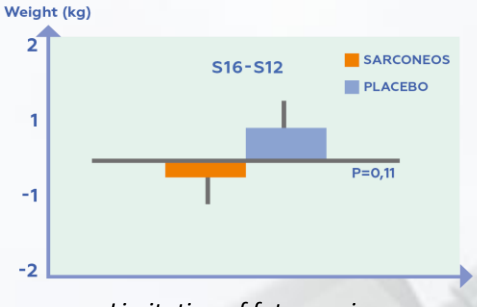
Inhibition of myostatin expression

SARCONEOS: SAFETY AND PHAMACOKINETICS ON HUMANS

Phase I/II Trial:

- Double-blind, placebo-controlled
- 60 healthy obese volunteers
- 12 weeks 40 mg/day oral administration
- No serious adverse events and good tolerability
- Satisfactory bioavailability after oral administration
- Activity on glucose and lipid metabolism

Improvment of sensitivity to insulin



Limitation of fat mass increase

Reduction in adipocytes size

2016: SARA-PK - Pharmacokinetics in elder subjects

- Pharmacokinetics and safety in elder subjects
- Two steps design: SAD step (24 elder and young subjects) + MAD step (30 elder 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 elder subjects
- No influence of age and lunch on pharmacokinetics parameters

SARA-PK will be completed H2 2016 and data used to get approval for SARA Phase 2b

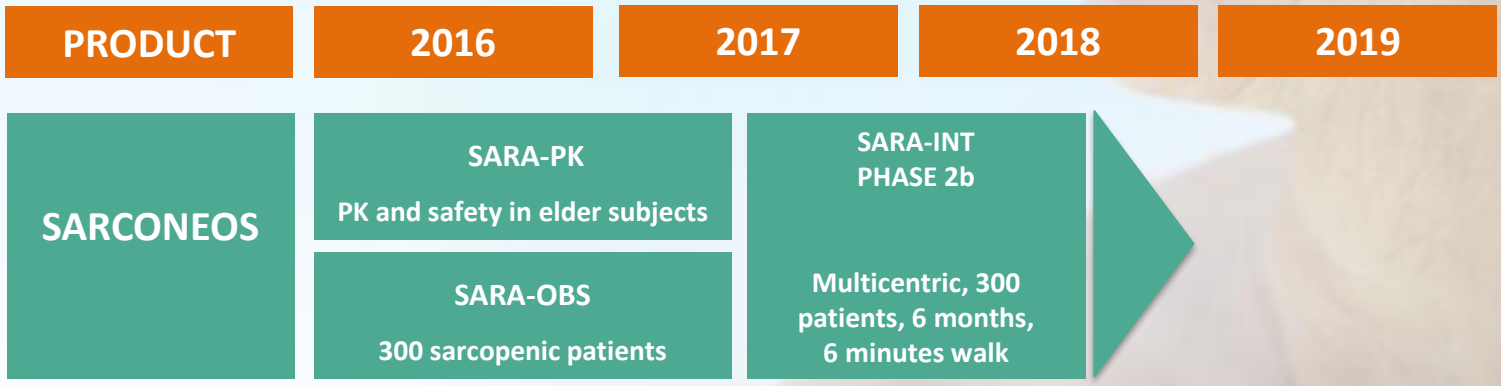
SARA Phase 2b clinical trial

2016: SARA-OBS - Observational study

- Multicentric observational study: eight clinical centers in Europe and the US
- 300 sarcopenic patients: Foundation of NIH inclusion criteria for sarcopenia
- Duration: six months
- Endpoints: 6mn walk test, grip strength, muscle mass and fat mass , plasmatic biomarkers

2017: SARA–INT - Phase 2b clinical trial

- Multicentric, randomized, double-blind, placebo-controlled
- 300 sarcopenic patients
  - Sarconeos 100 mg vs Sarconeos 350 mg vs Placebo
- Duration: six months
- Endpoints:
  - Primary: 6 min walk test
  - Secondary: grip test, SPPB, muscle mass and fat mass



MACUNEOS

Age Related Macular Degeneration

AMD

AGE-RELATED MACULAR DEGENERATION (AMD)
DEGRADES THE CENTER OF THE RETINA
& LEADS TO THE LOSS OF CENTRAL VISION

Leading cause of visual impairment in people over 60

- 20 million people in the world currently suffer from AMD
- A multifactorial pathology (age, heredity, tobacco, life style …)
- Prevalence is double that of Alzheimer's
- 30% risk of AMD in people over 75

No treatment available for dry AMD

- Estimated worldwide market in 2023 for dry AMD treatment is $30 billion per year
- Available treatments target wet AMD (20% AMD population)
- No marketed drugs for dry AMD

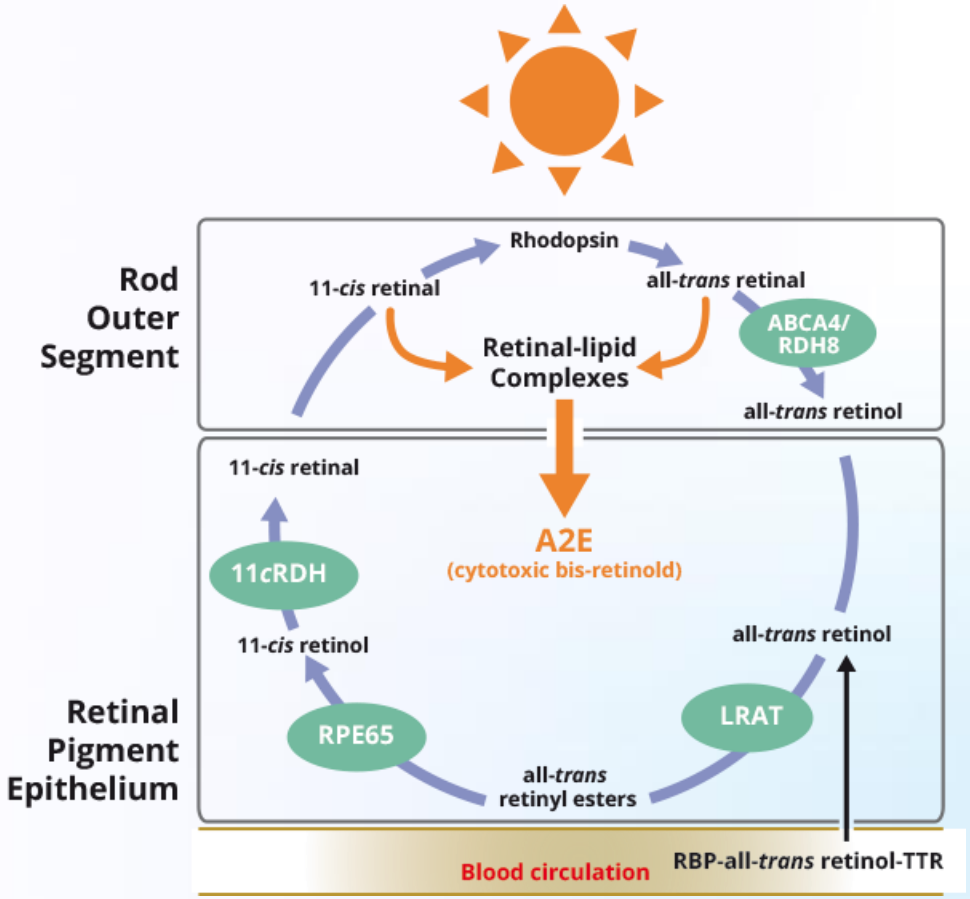
BIOPHYTIS targets dry AMD, an unmet medical need affecting 80% of AMD patients

MACUNEOS FILLS A THERAPEUTIC GAP

	Dry AMD Early & Intermediate	Dry AMD Geographic Atrophy	Wet AMD
Standard of care	• **Zinc + Vitamines C/E (nutraceuticals)**	• None	Anti-VEGF : • Lucentis (Novartis) • Eylea (Bayer)
Products in developement	• **MACUNEOS (Phase 2b)** • **Emixustat (Phase 3, visual cycle modulator)**	Anti-complement factor antibodies : • Lampalizumab (Roche) • LFG316 (Novartis) • Zimura (Ophtotech)	
Product attrbutes	• **Limits A2E accumulation** • **Slows retina degeneration** • **Oral administration**	• Anti-inflammatory • Limits atrophy expansion • Intravitreal injection	• Stops neo-vascularisation • Limits loss of visual acuity • Intravitreal injection

20% of AMD patients

PHOTO-OXIDATIVE STRESS AND AMD



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 AMD

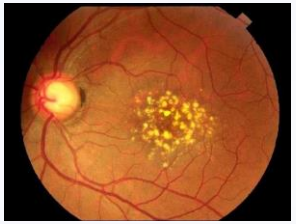
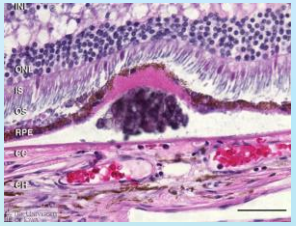


Photo-oxidative stress leads to:

- Lipofuscins accumulation
- Drüsen formation, distorts retina (affecting vision)
- Death of retina cells (progressive blindness)

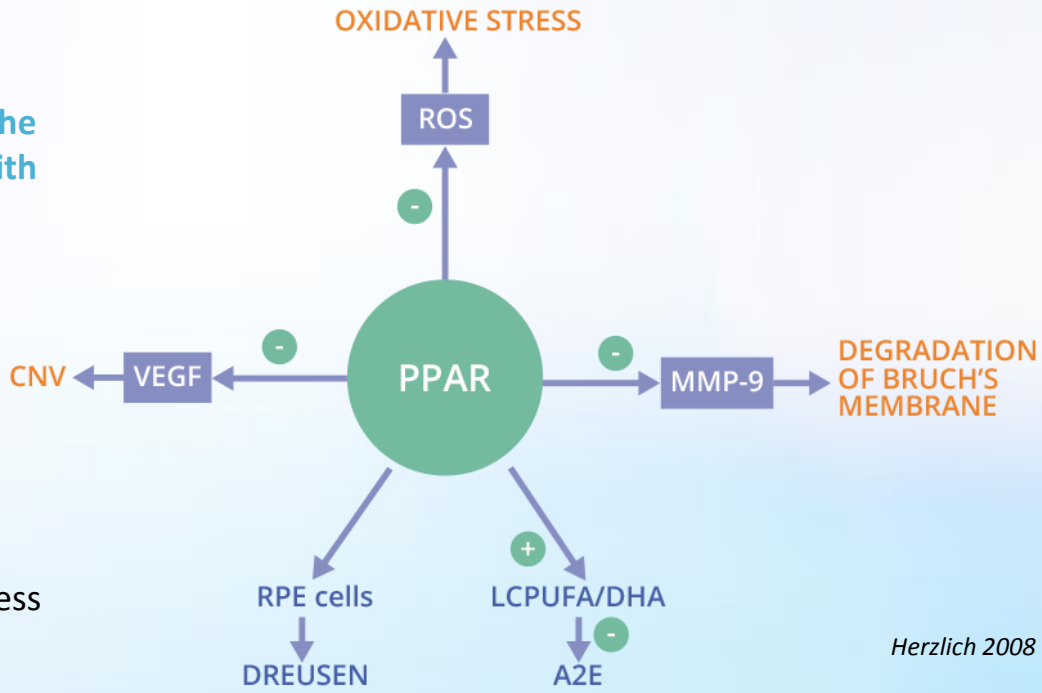


MACUNEOS and BIO 203, identified by BIOPHYTIS, are active in the control of A2E accumulation

PPAR ACTIVATION:
A NOVEL APPROACH FOR AMD TREATMENT

PPAR are nuclear receptors that protect the retina from oxidative stress associated with accumulation of A2E

- Production of free radicals
- Formation of drüsen
- Production of VEGF
- Inflammation
- Cell death associated with oxidative stress

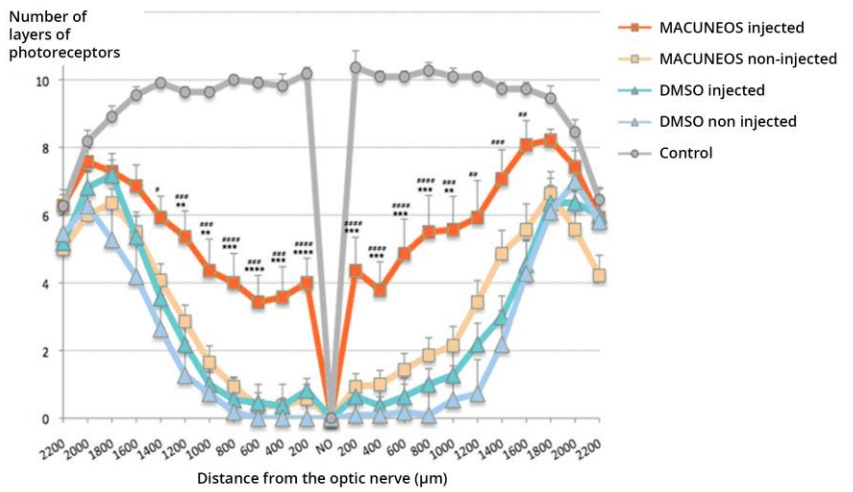


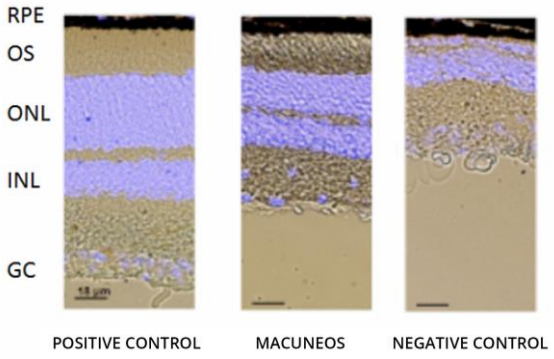
Herzlich 2008

MACUNEOS and BIO 203 are potent, activator of PPAR, and limit retinal degeneration by reducing A2E accumulation in several cellular and animal models

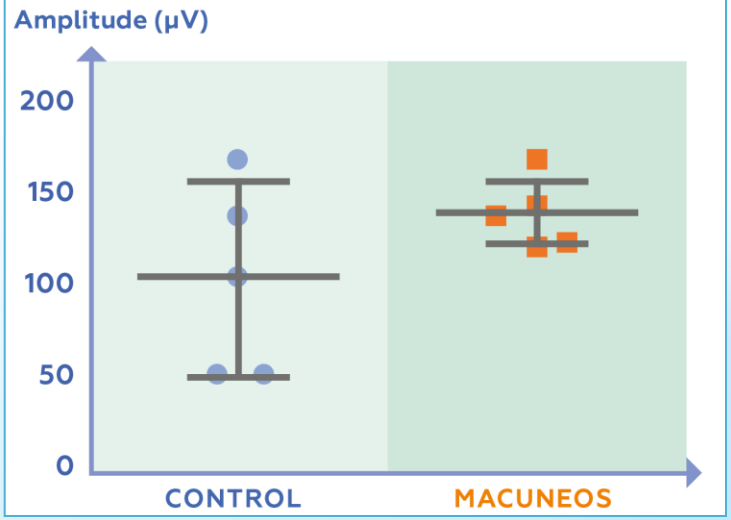
MACUNEOS: PROOF OF CONCEPT

MACUNEOS preserves the number of layers of photoreceptors after a light stress





MACUNEOS preserves the functionality of the retina in chronic oral administration (measured with electroretinography)



MACUNEOS protects the retina and preserves visual function on mice and rat models of AMD

MACUNEOS: SAFETY AND ACTIVITY IN HUMANS

Phase I/II trial

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

MACA-PK – Pharmacokinetics in elder subjects

- Pharmacokinetics and safety in elder subjects
- Two steps design: SAD step + MAD step
- Target: 1H17-2H17

MACA-PK study is mandatory for filling Phase 2b MACA trial approval in 2018

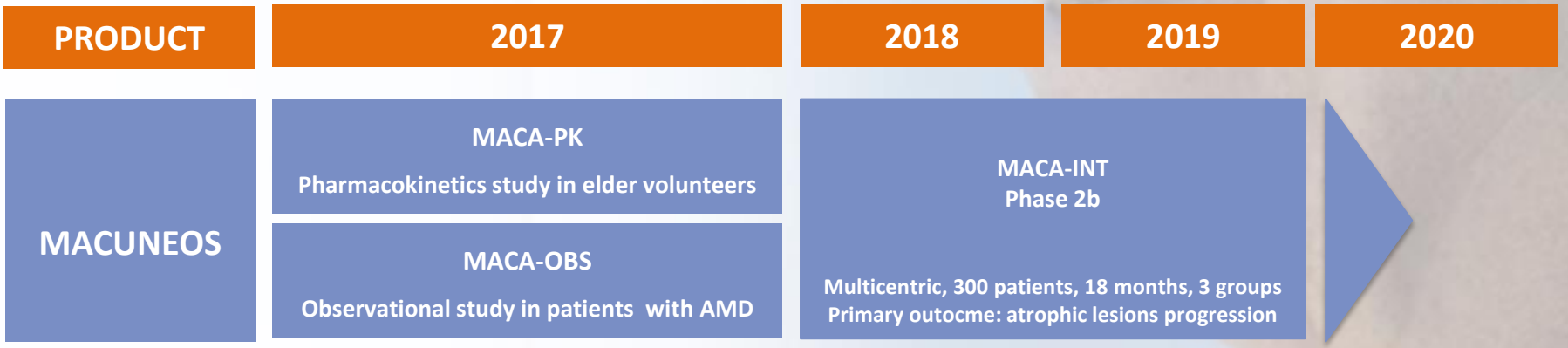
MACA Phase 2b clinical trial

2017: MACA-OBS – Observational study in patients with intermediate dry AMD

- Multicentric observational study: clinical centers in Europe and the US
- 300 patients suffering of intermediate dry AMD
- Duration: 12 months
- Endpoints: atrophic lesion size, ERG, visual acuity

2018 : 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



VALUE CREATION NEWS FLOW

SARCONEOS (BIO 101)

- H2 16: End of pharmacokinetics clinical study SARA-PK (full results Q1 17)
- H2 16: Initiation of obervational study SARA-OBS (ending H1 17)
- H1 17: Initiation of Phase 2b SARA (regulatory approvals)
- H1 18: Interim results of Phase 2b SARA (DSMB)
- H2 18**: Results report of Phase 2b SARA**

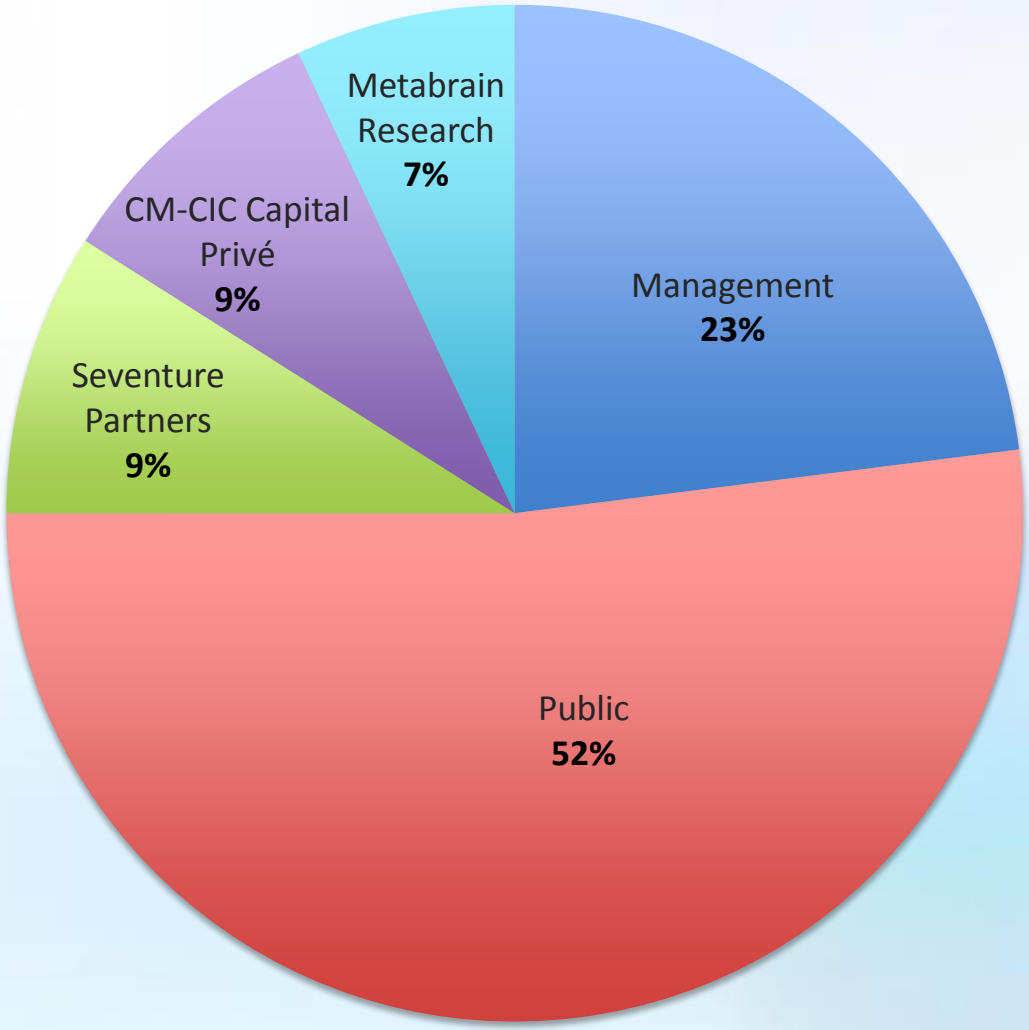
MACUNEOS (BIO 201)

- H1 17: Initiation of pharmacokinetics MACA-PK (ending H2 17)
- H1 17: Initiation of obervational study MACA-OBS (ending H2 17)
- H1 18: Initiation of Phase 2b MACA
- H2 18: Interim results of Phase 2b MACA (DSMB)
- H1 20**: Results report of Phase 2b MACA**

CAPITAL STRUCTURE*

Stock profile

- Market: Alternext of Euronext Paris
- Ticker: ALBPS
- 1st quotation: July 13th, 2015 – €6.0/share
- Number of shares : 6,195 M
- Share value (December 12h): €4.24/share
- Market Capitalization : €26 M



*fully diluted

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INVESTMENT HIGHLIGHTS

1 SARCONEOS to treat sarcopenic obesity

- 20 million patients worldwide
- No treatment on this indication
- SARA Phase 2b trial preparations ongoing (SARA-OBS, SARA-PK studies, H2 2016)

2 MACUNEOS to treat dry AMD

- 15 million patients worldwide, first cause of blindness over 60 years in industrialized countries
- No treatment on this indication
- MACA Phase 2b trial preparations ongoing (MACA-OBS, MACA-PK studies, H1 2017)

3 Value creating newsflow

- SARCONEOS: SARA Phase IIb start 1H 2017 (reporting 2H18**);**
- MACUNEOS: MACA Phase IIb start 1H 2018 (DSMB 1H19; reporting 1H20)

4 Strong intellectual property

- Four patent families for MACULIA covering AMD and retinopathies
- Four patent families for SARCOB covering sarcopenia, related muscular dystrophies and metabolic disorders

5 A technological platform specifically targeting aging pathologies

- Original approach for discovering and protecting novel chemistry involved in degenerative disease
- A unique collection of natural molecules and analogs active on aging processes

Thank you

Investors contact: investors@biophytis.com