# biophytis

LIVE HEALTHIER LONGER

September 2019 I **EPA: ALBPS**

# Forward Looking Statements

All statements pertaining to future financial and/or operating results, future growth in research, clinical development, and potential opportunities for Biophytis SA and its subsidiaries (the "Company") and its products, along with other statements about the future expectations, beliefs, goals, plans, or prospects expressed by management constitute forward-looking statements.

Any statements that are not historical fact (including, but not limited to, statements that contain words such as "will," "believes," "plans," "anticipates," "expects," "estimates") should also be considered to be forward-looking statements.

By their nature, forward-looking statements involve risks and uncertainties, including, without limitation, risks inherent in the development or commercialization of potential products, uncertainty in the results of clinical trials or regulatory approvals, need and ability to obtain future capital, and other risks, please refer to the Risk Factors ("Facteurs de Risque") section of the Listing Prospectus upon the admission of Company's shares for trading on the regulated market Euronext Growth of Euronext Paris filed with the AMF, which is available on the AMF website (www.amf-france.org) or on the Company's website (www.biophytis.com).

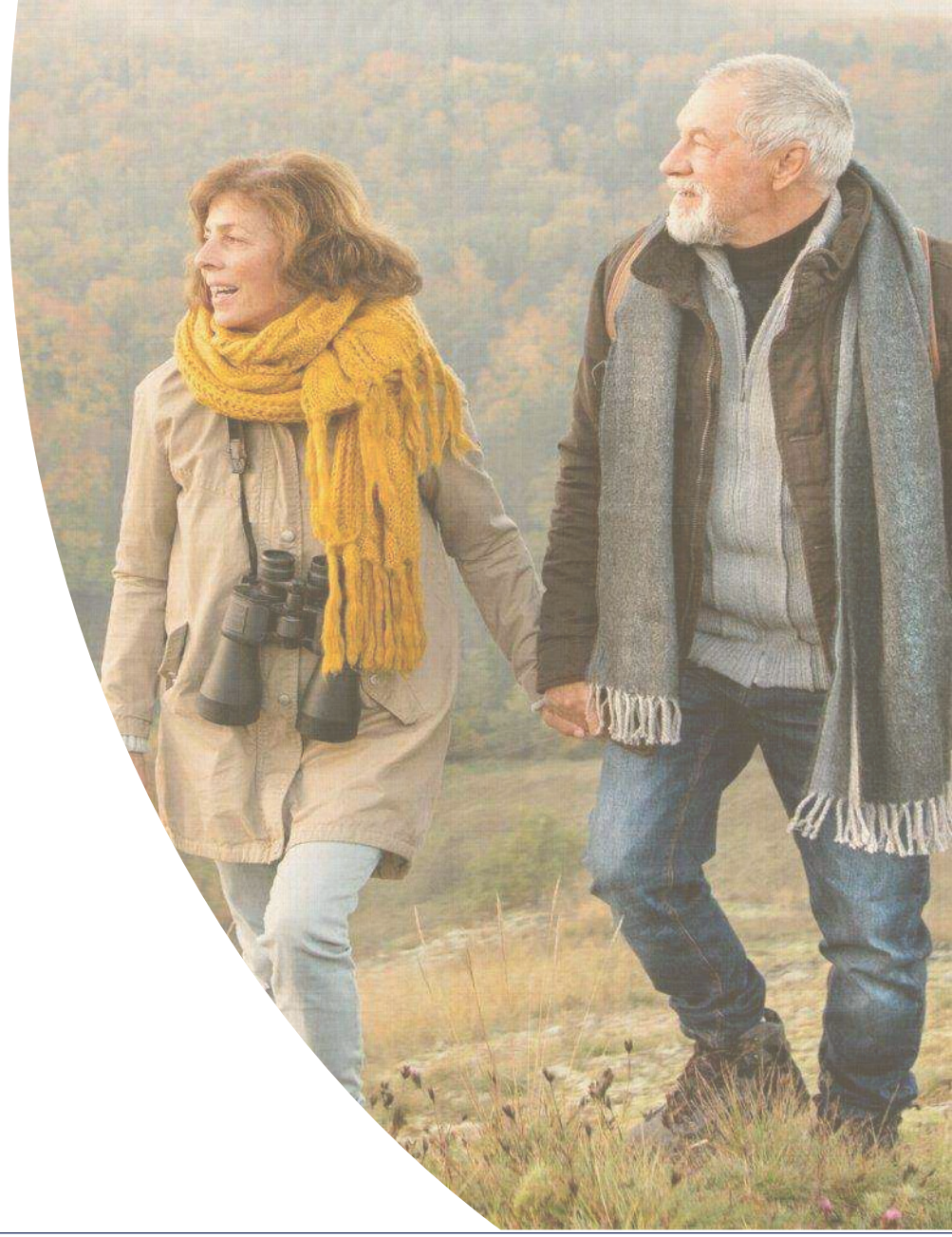
Actual results may differ materially from the results anticipated in these forward-looking statements and as such should be evaluated together with the many uncertainties that affect the Company's business. Any forward-looking statements that we make in this presentation speak only as of the date of such statement, and we undertake no obligation to update such statements to reflect events or circumstances after the date of this presentation, except as required by law.

# Overview

Sarconeos (BIO101) for sarcopenia

Sarconeos (BIO101) for DMD

Macuneos (BIO201) for dry AMD



# A clinical-stage biotechnology company in age-related diseases

## Our goal

Improve functional outcomes (mobility, strength and vision) and healthspan for patients suffering from age-related diseases

## Neuromuscular diseases

Our lead drug candidate Sarconeos (BIO101) is in clinical development for neuromuscular diseases with no (or limited) approved drug treatment options, including sarcopenia and Duchenne muscular dystrophy (DMD)

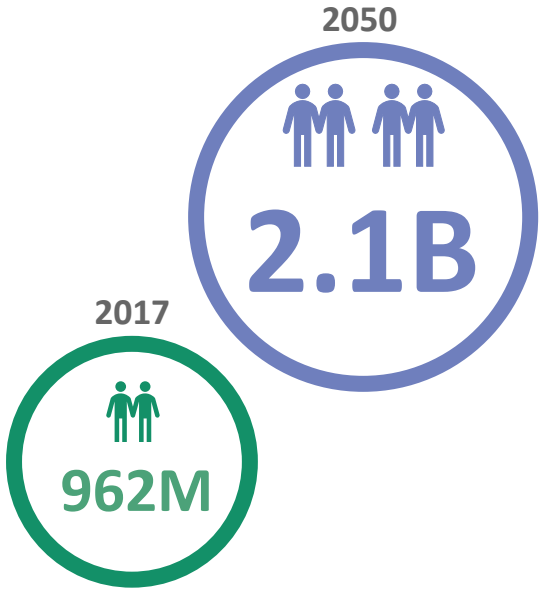
## Retinal diseases

Our second drug candidate Macuneos (BIO201) is in development for diseases of the retina for which there are currently no approved treatment options, including dry age-related macular degeneration (AMD)

# Aging and biological resilience pathways

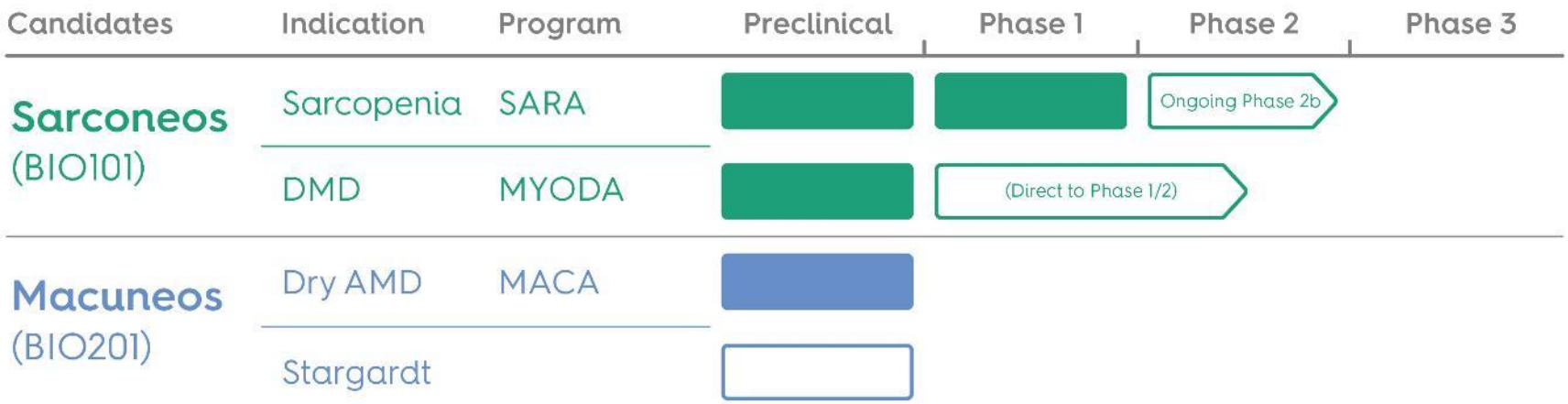
- As we age, our physical (mobility and strength) and visual performances decline due in part to the accumulation of multiple stresses we are exposed to during our lifetime
- We believe this is contributed to by the decline in biological resilience, the natural ability to protect and counteract the effects from these stresses, including inflammatory, oxidative and metabolic stresses
- Our therapeutic approach is aimed at targeting and activating key biological resilience pathways, which we discovered using a reverse pharmacology approach that tested a library of secondary metabolites from medicinal plants[1]

**The global elderly (≥60) population is projected to more than double by 2050[2]**




1. Developed in collaboration with Sorbonne University and its other academic research institutions in Paris, France;
2. Source: United Nations' World Population Prospects: the 2017 Revision.

# Our clinical pipeline



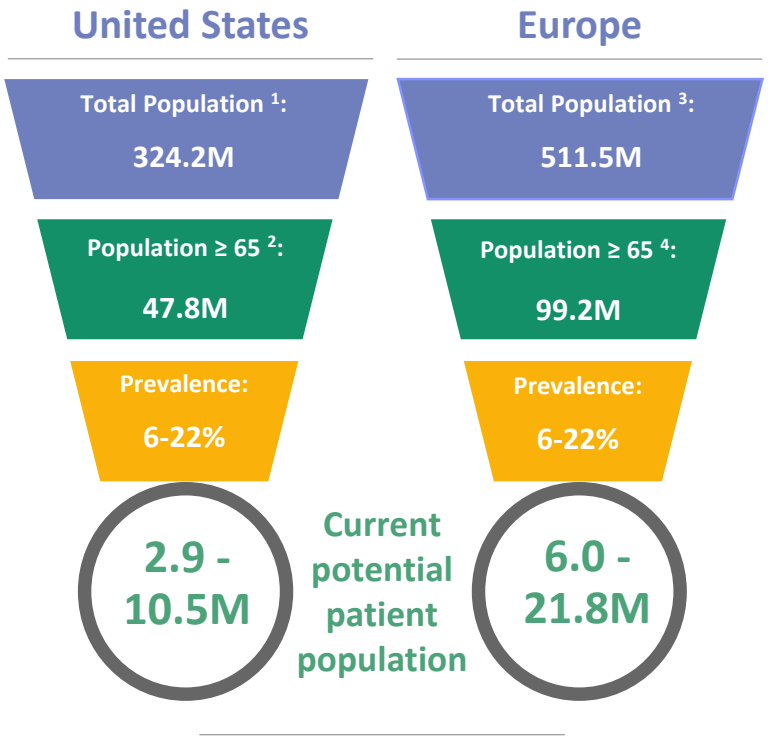
Overview

# Sarconeos (BIO101) for sarcopenia

Sarconeos (BIO101) for DMD

Macuneos (BIO201) for dry AMD

# Sarcopenia is an unmet medical need with no approved drugs

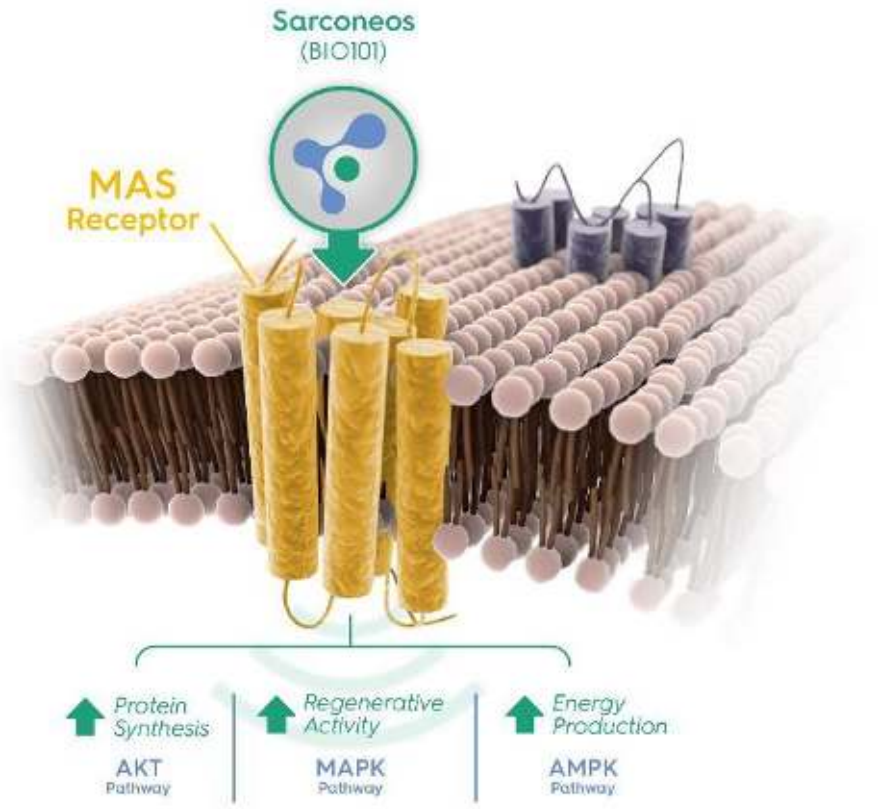



- Age-related degeneration of skeletal muscle characterized by a loss of muscle mass, strength and the ability to stand and/or walk
- A major cause of mobility disability in the elderly (≥65 years) resulting in a loss of independence and increased risk of adverse events
- Currently no approved medication; non-medicinal treatments focus on moderate physical activity and nutritional intervention
- Our approach incorporates multiple interventions, including; 1. protein synthesis, 2. muscle regeneration (stem cell proliferation), and 3. energy production (mitochondrial dysfunction)

1. U.S. census bureau as of January 1, 2017;
2. U.S. census bureau; Facts For Figures: CB17-FF.08 March 27, 2017;
3, 4. Eurostat (www.ec.Europa.eu). Statistics explained, population structure and ageing; data as of January 1, 2017.

# Sarconeos (BIO101) potential mechanism of action: Activates the MAS receptor

- MAS is a key component of the renin-angiotensin system (RAS)
- We believe MAS activation triggers three downstream pathways which may preserve muscle strength, function and mobility in various age-related and muscular wasting conditions



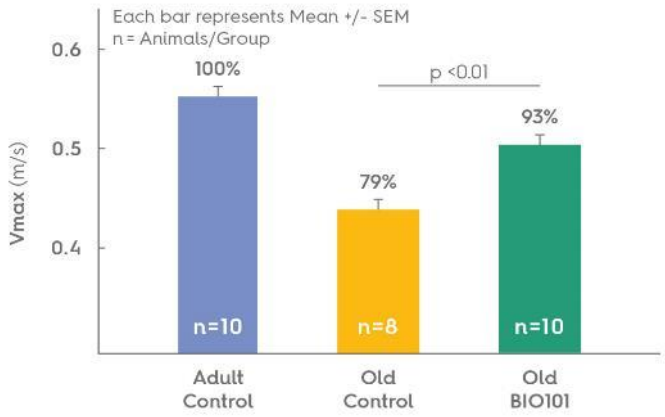

PI3K/AKT/mTOR pathway is involved in increasing protein synthesis, which we believe is a key factor for preserving muscle mass and increasing muscle strength

MAPK/P38/JNK pathway is involved in stem cell proliferation and differentiation, which we believe is a key factor for improving muscle regeneration

AMPK/ACC pathway is involved in stimulating energy production, which we believe is a key factor for increasing muscle strength and improved endurance

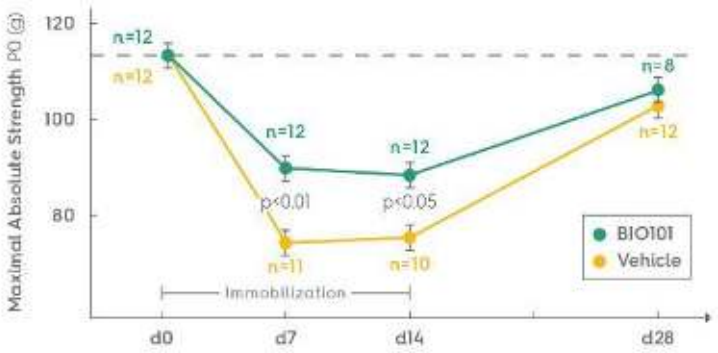
# Sarconeos (BIO101) preclinical data in animal models for sarcopenia suggests improvements in mobility and strength

## Beneficial effect on mobility in aged mice fed with high fat diet[1]




Administration of 50 mg/kg/day of Sarconeos (BIO101) demonstrated a statistically significant (p<0.01) improvement in maximum running velocity (Vmax) compared to "old" control mice, compensating almost completely for the loss of mobility due to aging

## Preservation of muscle strength in immobilized mice




Administration of 50 mg/kg/day of Sarconeos (BIO101) demonstrated a preservation of muscle strength while immobilized (d0-d14) compared to vehicle control in hindlimb-immobilized mice

1. These results were presented in December 2016 at the SCWD conference in Berlin, Germany in a poster presentation.

# SARA-PK: Phase 1 trial completed in 2017

- Single and multiple ascending doses tested in 54 healthy adult and elderly volunteers
- Determined the **two active doses** (175 & 350 mg b.i.d.) for our ongoing SARA-INT Phase 2b clinical trial

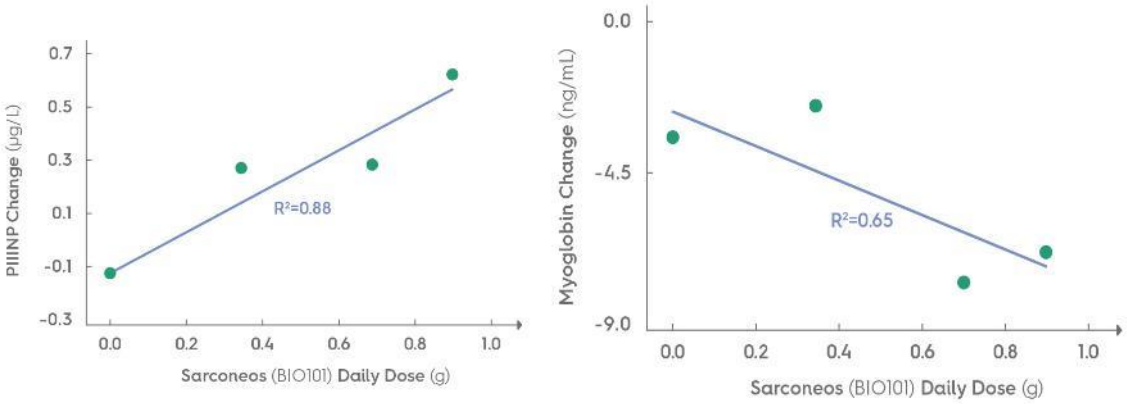
## P1 TRIAL SAFETY RESULTS

**SAD: Dose range between 100 to 1,400 mg**

**MAD: 3 doses from 350 mg q.d., 350 mg b.i.d., and 450 mg b.i.d.**

- No abnormal clinical vital signs were reported as TEAEs in the studies
- All TEAEs were mild or moderate and were resolved by the end of the studies
- No SAEs in the studies

## PD SUMMARY IN MAD PHASE

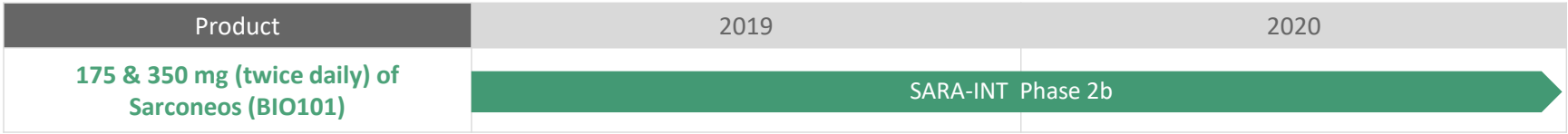



Sarconeos (BIO101) showed a dose dependent effect on muscle growth and repair (PIIINP) and a dose dependent negative effect on muscle wasting (myoglobin)

# SARA-INT: Ongoing Phase 2b clinical trial

**Global, multicenter, double-blind, randomized, placebo-controlled trial in 334 elderly patients with sarcopenia at risk of mobility disability**

| Objectives | Key Endpoints | Subpopulation Analysis |
|---|---|---|
| • Assess safety and efficacy of two doses of Sarconeos (BIO101) administered orally with a meal over 26 weeks compared to placebo<br>• Treatment effect on improvement of physical function and on decrease of risk of mobility disability | **Primary**<br>• 400-meter walk test (400MWT) - 0.05 m/s is considered the minimal meaningful change<br>**Key secondary**<br>• Rise from a chair (part of SPPB)<br>• 400MWT responder analysis<br>• Patient reported outcomes (PRO) | • Very low walking speed<br>• Sarcopenic obesity |



# SARA-INT: Recruiting patients at risk of mobility disability

| Inclusion Criteria | Recruitment |
| --- | --- |
| • Age (≥65 or over)<br>• Low mobility measured by Short Performance Physical Battery (SPPB) ≤8 out of 12<br>• DEXA body composition as measured by ALM/BMI (appendicular lean mass/ body mass index)<br>• Able to exercise for 30 minutes per day 5 days per week | • Recruiting in U.S. and Belgium with 15 sites currently open; expanding to 22+ sites<br>• Awaiting approval to open additional sites in other countries, including France<br>• Enrollment began in May 2018 with **complete enrollment expected in 2020** |

Overview

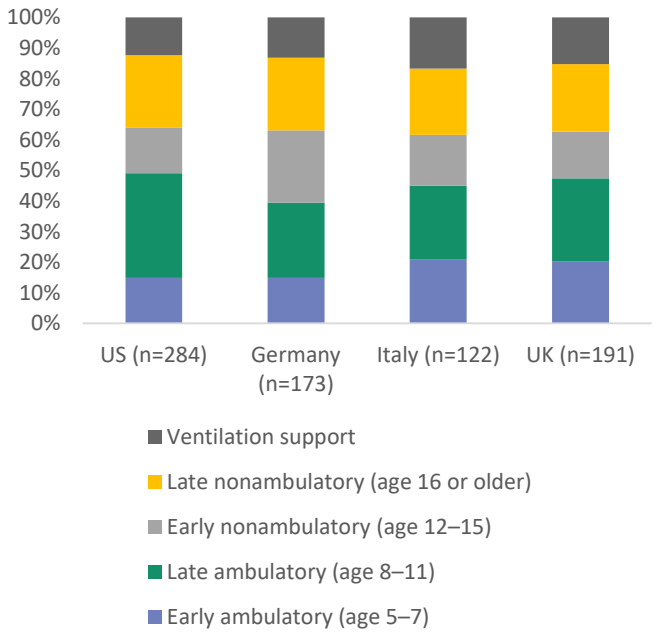
Sarconeos (BIO101) for sarcopenia

## Sarconeos (BIO101) for DMD

Macuneos (BIO201) for dry AMD

# DMD is an unmet medical need with no cure and limited treatment options

**Proportion of ambulatory class in DMD[1]**

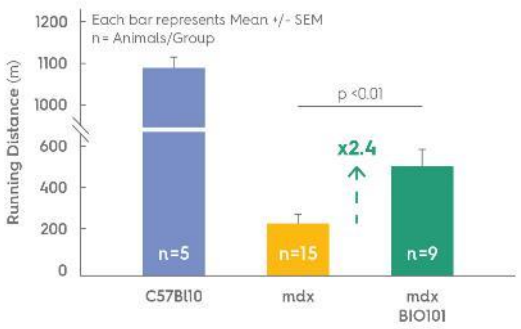



- Rare, genetic neuromuscular disease in male children characterized by accelerated degeneration of muscles, responsible for loss of mobility, respiratory failure and cardiomyopathy, leading to premature death
- No known cure and limited treatment options, including corticosteroids and targeted therapies (exon-skipping in U.S. & stop codon in EU) that treat approximately 13% of DMD patients with specific genetic mutations
- We received orphan drug designation (ODD) in 2018 from the FDA and EMA for Sarconeos (BIO101) in DMD
- We are developing Sarconeos (BIO101) to address all stages of DMD progression, independent of gene mutation and regardless of ambulatory state

1. Source: Landfeldt *et al*., Neurology, 2014.

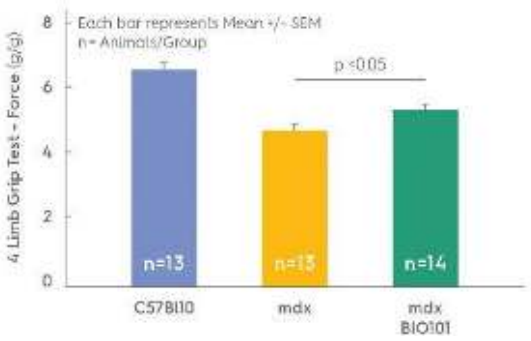
# Proof of concept in *mdx* mice models of DMD: Improvements in mobility, strength and respiration

## Improved **mobility** as measured by running distance[1]



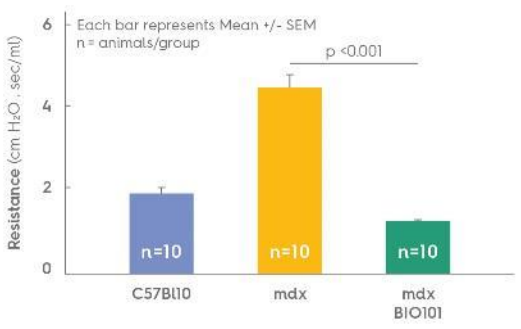

C57BL10-*mdx* mice treated with 50 mg/kg/day of Sarconeos (BIO101) over 8 weeks ran **2.4x farther** than untreated control C57BL10-*mdx* mice

## Improved muscle **strength**, as measured by four-limb grip-test force[1]




C57BL10-mdx mice treated with 50 mg/kg/day of Sarconeos (BIO101) over 8 weeks showed an approximate **14% improvement** in strength as compared to untreated control C57BL10-*mdx* mice

## Ameliorates the time-dependent degradation of **respiratory function**[2]




Chronic (8 week) daily administration of 50 mg/kg/day of Sarconeos (BIO101) **significantly (p<0.001) improved respiratory function** measured by airway resistance

1. These results were presented in October 2018 at the WMS conference in Mendoza, Argentina in a poster presentation;
2. These results were presented in March 2019 at the annual international congress of Myology in Bordeaux, France in a poster presentation.

# MYODA-INT: Seamless clinical trial design (subject to regulatory approval)

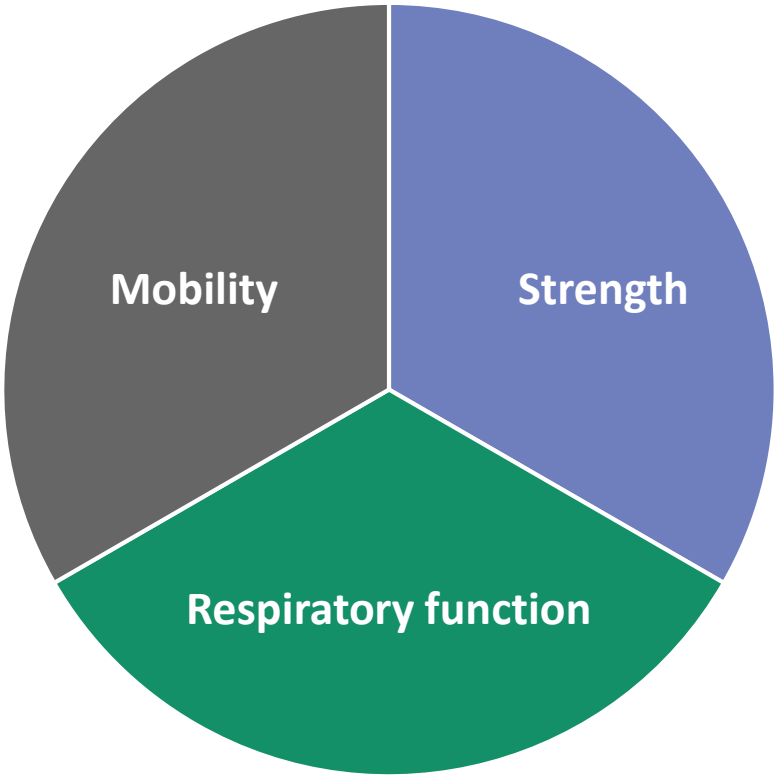
**To test an oral pediatric drug formulation of Sarconeos (BIO101) for DMD patients**

| Design | Patients | Regulatory Status |
|---|---|---|
| • Global, multicenter, double-blind, placebo-controlled, seamless, Phase 1-3 clinical trial<br>  ○ Stop for regulatory interaction after Part 2<br>• Part 1: Safety, tolerability & PK (initial 7 days of dosing)<br>• Part 2: Proof of concept (continued dosing up to week 52)<br>• Part 3: confirmatory / pivotal | • Ambulatory and non-ambulatory DMD patients:<br>  ○ Part 1/2: 48 patients<br>  ○ Part 3: ~100-150 patients<br>• Enrollment in the U.S. and EU<br>• Patient advocacy group support<br>  ○ AFM telethon in France | • Pre-IND correspondence with the FDA in October 2018<br>• Scientific advice meeting with the EMA in December 2018<br>• **IND and European regulatory filings expected H2 2019** |

| Product | 2020 | 2021 | 2022 | 2023 |
|---|---|---|---|---|
| Sarconeos (BIO101) | MYODA-INT (Part 1/2) | | | |

# MYODA-INT: Potential composite score based on function

- Composite endpoints adapted to the stage of severity of the disease in each patient
- Clinical relevance endpoints



Overview

Sarconeos (BIO101) for sarcopenia

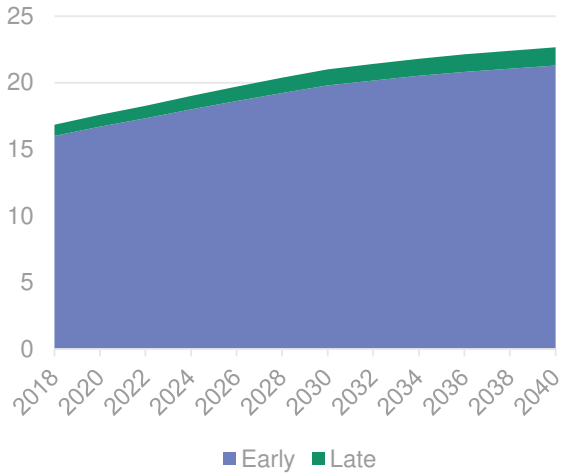
Sarconeos (BIO101) for DMD

## Macuneos (BIO201) for dry AMD

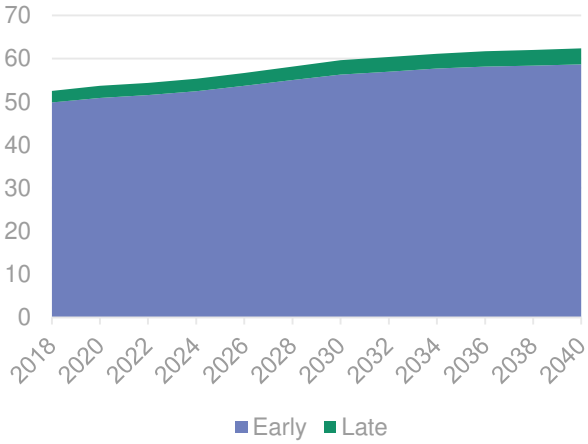
# Dry AMD is an unmet medical need with no approved drugs

- AMD is a common eye disorder among people over 50 that affects the central part of the retina, known as the macula
- Can impair functions such as reading, driving, and facial recognition, and has a major impact on QoL and the ability to live independently
- Multifactorial disease that we believe is mainly caused by accumulation of A2E (a byproduct of the visual pigment cycle) that leads to retinal degeneration

Projection of AMD prevalence in North America (in M, mean projection)[1]




Projection of AMD prevalence in Europe (in M, mean projection)[1]

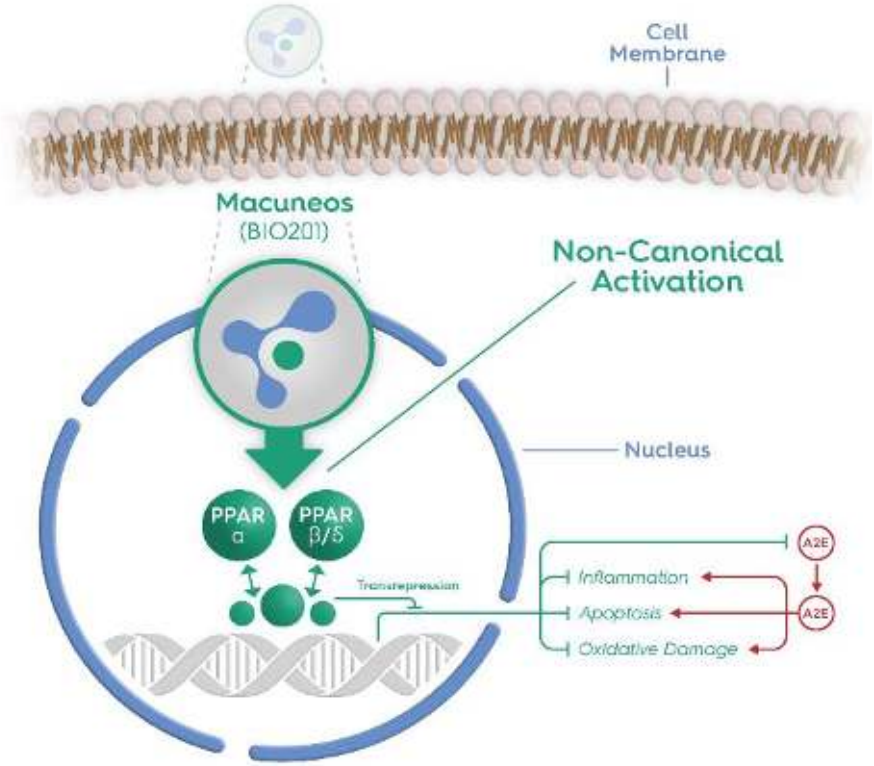



- 85 - 90% of AMD patients have dry AMD in some form; either early, intermediate or late stage, know as geographic atrophy (GA)
- No approved treatments for any stage of dry AMD, including GA
- We are developing Macuneos (BIO201) to treat patients with intermediate dry AMD to prevent the development to advanced stages (wet AMD + GA), which lead to severe vision loss

1. Source: Wang *et al*., Lancet Glob Health 2014; 2: e106–16. Supplemental Table 7: Projection of Number of People with Early, Late and Any AMD by Regions

# Macuneos (BIO201) potential mechanism of action: Non-canonical activation of PPARs

- We believe Macuneos (BIO201) potentially counteracts the phototoxic effects of A2E by selective non-canonical activation of the transrepressive activity of PPARα and PPARβ/δ in the retina
- Most other PPAR ligands mainly exhibit canonical activity and are associated with side effects




**Anti-inflammatory activity** (promotes the expression of anti-inflammatory genes)

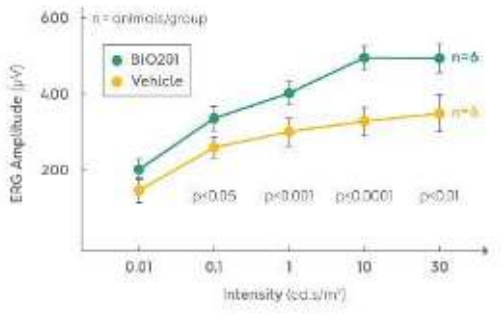
**Anti-oxidant activity** (promotes the expression of anti-oxidant genes)

**Anti-apoptotic activity** (enables pathways that prevent cell death)

# Macuneos (BIO201) proof of concept in rodent models of dry AMD: Protects the retina

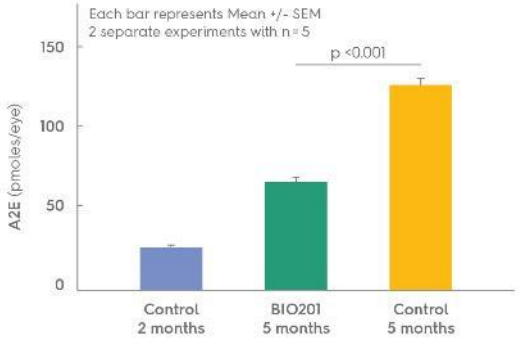
- We are preparing for clinical development through our MACA program and plan to seek regulatory advice in 2H 2019 from European regulatory agencies for a Phase 1 clinical trial

## Preservation of visual function in mice



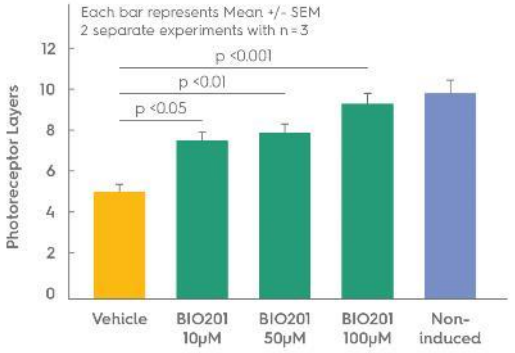

Chronic oral administration of Macuneos (BIO201) for 3 and 6 months **increases ERG amplitude** in ABCA4$^{-/-}$ RDH8$^{-/-}$ mice

## Reduced A2E Accumulation in mice




Chronic oral administration of Macuneos (BIO201) decreased A2E accumulation by **approximately 45%** in Abca4$^{-/-}$ Rdh8$^{-/-}$ mice as compared to vehicle control mice

## Dose-dependent protection of retina integrity in rats




Intraperitoneal injection of Macuneos (BIO201) preserved the number of layers of photoreceptors by **up to approximately 90%** at the maximum dose of 100µM in a standard blue light rat model

These results were presented in May 2016 at the ARVO conference in Seattle, WA in a poster presentation and published in PLoSONE (Fontaine *et al.*; 2016).

# Key milestones in clinical development of BIO101 in neuromuscular diseases

- ☑ SARA-OBS completed enrollment of 218 patients in Oct. 2018
- ☑ SARA-INT (Phase2b) enrolled first patient in May 2018
- ❑ SARA-INT (Phase2b) expected to complete patient enrollment in 2020

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- ☑ MYODA-INT received orphan drug designation in 2018 in U.S. and EU
- ❑ MYODA-INT plan to make IND and EU regulatory filings in 2H 2019

# Executive team

**Stanislas Veillet - Founder & CEO**

- PhD in genetics, AgroParisTech
- 25+ years in biotech; Pharmacia-Monsanto, Danone Group

**René Lafont - Co-founder & CSO**

- Professor emeritus and former Dean of the life sciences department at Sorbonne University
- 185 scientific articles + 59 reviews and book chapters

**Daniel Schneiderman - CFO**

- 17+ years investment banking and corporate finance experience
- Multiple VP roles in healthcare and finance, including MetaStat and HC Wainwright

**Samuel Agus - CMO**

- MD, PhD, Board-certified Neurologist
- 15+ years pharma/biotech experience including Abbott, Shire and Teva Pharmaceuticals

**Manfred Horst - BD Officer**

- MD, PhD, MBA
- 30+ years pharma experience; 12 years BD for Merck & Co.

# Scientific advisory board

**Pr. Jean Mariani**

- Professor of neuroscience and biology of aging and Director of Charles Foix Institute of Longevity at Sorbonne University

**René Lafont**

- Professor emeritus and former Dean of the life sciences department at Sorbonne University
- 185 scientific articles + 59 reviews and book chapters

**Pr. Jose-Alain Sahel**

- Chair of the department of ophthalmology at University of Pittsburgh School of Medicine and director of the UPMC eye center
- Founder and director of the Vision Institute in Paris and professor at the Sorbonne's medical school

**Dr. Roger Fielding**

- Professor of Medicine, Tufts University School of Medicine
- Director and Sr. Scientist Jean Mayer USDA Human Nutrition Research Center on Aging

**Dr. Thomas Voit**

- Professor, University College London
- Director of the Research Centre of the Great Ormond Street Hospital for Children

**Dr. Ivana Kim**

- Associate Professor Harvard Medical School, Massachusetts Eye and Ear
- Co-Director of the Harvard Medical School Department of Ophthalmology AMD Center of Excellence; Associate Scientist, Massachusetts Eye and Ear

# Board of directors

**Stanislas Veillet - Founder & CEO**

- PhD in genetics, AgroParisTech
- 25+ years in biotech; Pharmacia-Monsanto, Danone Group

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

- Merrimack Pharma CFO
- 30+ years as finance director, including 15 years at Genzyme

**Nadine Coulm - Independent Board Member**

- IR Director for Korian
- 20 years of IR experience with FNAC BNP Paribas, Danone & Casino

**Eric Rowinsky - Independent Board Member**

- President of Rgenix and CSO at Clearpath Development Co; board member of Biogen, Fortress Biotech and Verastem
- 25 years in clinical research & drug development

**Dimitri Batsis - Independent Board Member**

- Entrepreneur
- Founder of Zeni Corporation, Drone Volt
- 20 years in the technology sector

# Thank you

Investor relations : investors@biophytis.com