# biophytis

LIVE HEALTHIER LONGER

June 2020 I Euronext, 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 Covid-19

Sarconeos (BIO101) for DMD

Macuneos for dry AMD

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

## Our goal

**Prevent disabilities** (mobility and vision) and increase **health span** for patients suffering from **age-related diseases**

**Small molecules** derived from plants which stimulate **biological resilience** developed by **reverse pharmacology**

## Covid-19 & Neuromuscular diseases

Drug Candidate **Sarconeos (BIO101)** in clinical development for :

**Covid-19 phase 2/3**
Respiratory Failure resulting from Sars-Cov2 infection

**Sarcopenia: Clinical phase 2b**
A geriatric chronic muscular dystrophy

**Duchenne's Muscular Dystrophy (DMD): IND granted**
A pediatric genetic muscular dystrophy

## Retinal diseases

Pre-clinical drug candidates

Macuneos

for diseases of the retina,

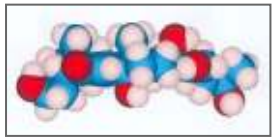
such as Dry Age-related Macular Degeneration (AMD) and Stargard's disease

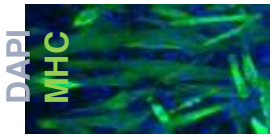
# Modern drug discovery process, inspired by traditional medicine

**Our technology**

**Reverse pharmacology for drug candidates in Age Related diseases**

- Build a proprietary collection of natural molecules & analogs from medicinal plant, produced under biotic or abiotic stress
- Screen in cellular models of age related diseases and identification of targets & pathways
- Selection of best drug candidates based on animal models of aging or genetic diseases






- **Sarconeos (BIO 101)**
- **Macuneos**

- Small molecules: natural and/or NCE
- New target key for aging
- Preclinical proof-of-concept & safety
- IP on use, process and composition of matter

biophytis

# Our clinical pipeline for worldwide development

| Candidates | Indications | Program | Preclinical | Phase 1 | Phase 2 | Phase 3 |
|---|---|---|---|---|---|---|
| Sarconeos (BIO101) | Sarcopenia | SARA | | | Ongoing phase 2b | |
| | Covid-19 | COVA | | (Direct to phase 2/3) | | |
| | DMD | MYODA | | (Direct to phase 1/2) | | |
| Macuneos | Dry AMD | MACA | | | | |
| | Stargardt | | | | | |

- Second generation drug candidates, BIO103 and BIO203, are life-cycle extension candidates in the preclinical Phase

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INSTITUTE OF MYOLOGY

INSTITUT DE LA VISION
PARIS

Biophytis

# Executive team

**Stanislas Veillet - Founder & CEO**

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

**Samuel Agus - CMO**

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

**Pierre Dilda - CSO**

- 20+ years experience in pharmaceutical research, in both academic and industrial settings
- 50+ scientific publications

**Wally Dioh - COO**

- PhD in phytopathology (Paris XI) and MBA
- 21+ years biotech experience in France and the U.S. and R&D at Monsanto

**Evelyne Nguyen- CFO**

- 25+ years of experience in Corporate Finance for International Pharma & Biotech companies ( BMS, LFB)
- Expertise in cross-borders transactions between Europe, US and Asia

Overview

## Sarconeos (BIO101) for sarcopenia

Sarconeos (BIO101) for Covid-19

Sarconeos (BIO101) for DMD

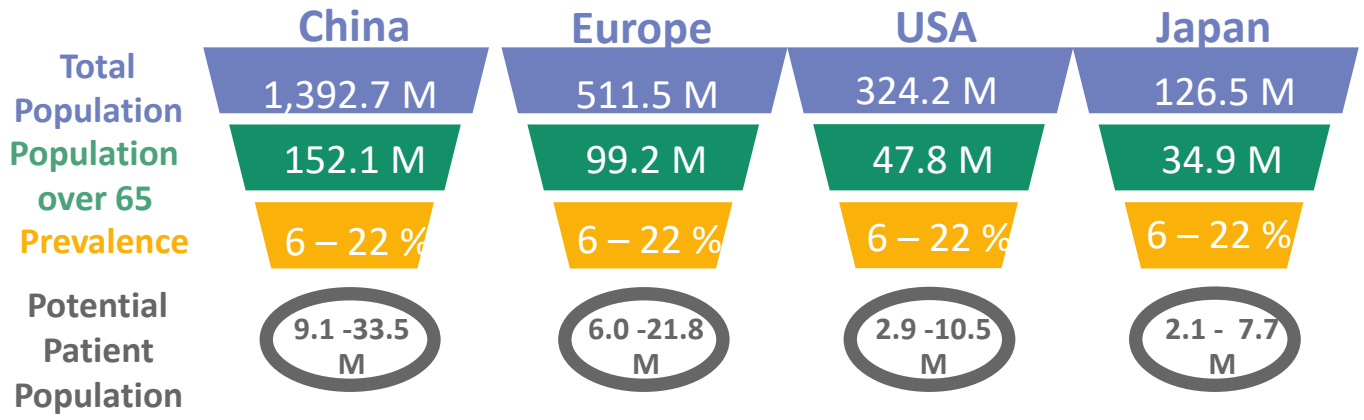
Macuneos for dry AMD

# Sarcopenia: a large unmet medical need with no approved drug

- Age-related degeneration of skeletal muscle characterized by **a loss of muscle mass, strength and functional issues** such as the ability to stand and/or walk
- A major cause of mobility disability, resulting in **a loss of independence and increased risk of adverse events (for example falls)**, which can shorten life expectancy

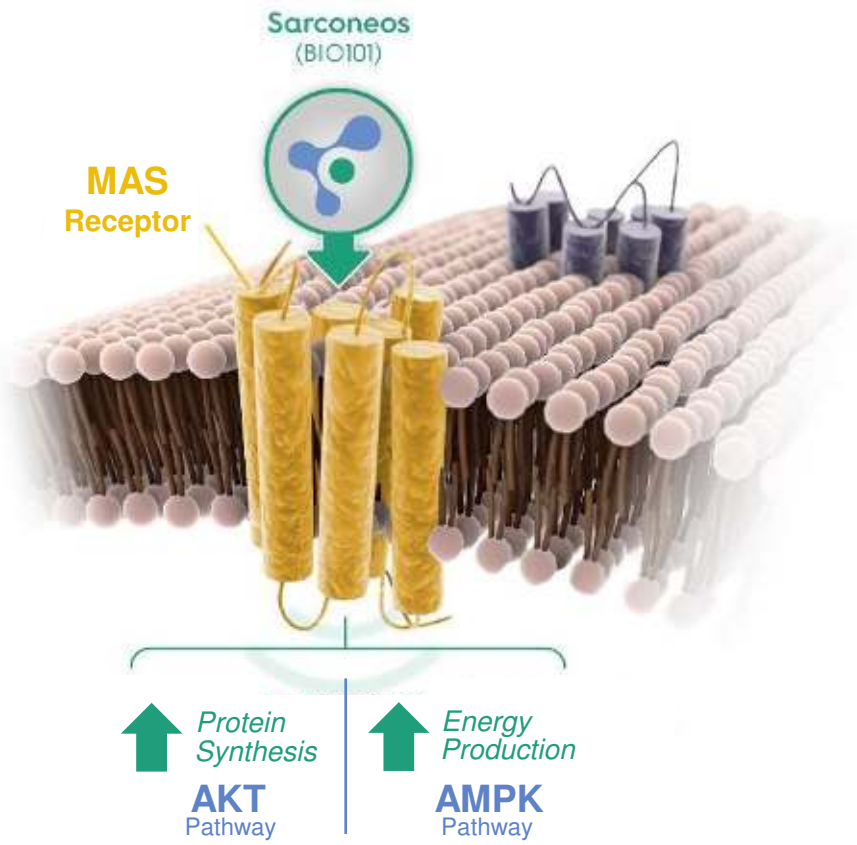
**Sarconeos (BIO101):**

- ✓ **Only drug candidate currently being tested in Phase 2 for sarcopenia**
- ✓ Myostatin inhibitors halted for lack of efficacy in neuromuscular diseases



# Sarconeos (BIO101) activates MAS receptor, a key factor for muscle metabolism

- MAS receptor: a key component of the Renin-Angiotensin System (RAS)
- Trigger two important downstream pathways in myocytes:

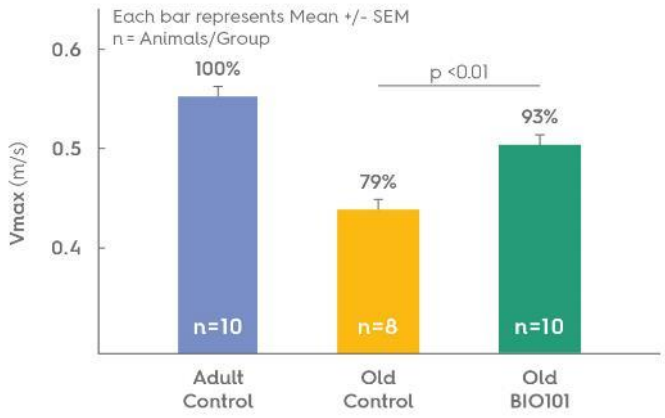



PI3K/AKT/mTOR: Increases **protein synthesis,** preserving muscle mass and increasing **muscle strength**

AMPK/ACC **Stimulates energy production**, increasing muscle strength and **mobility**

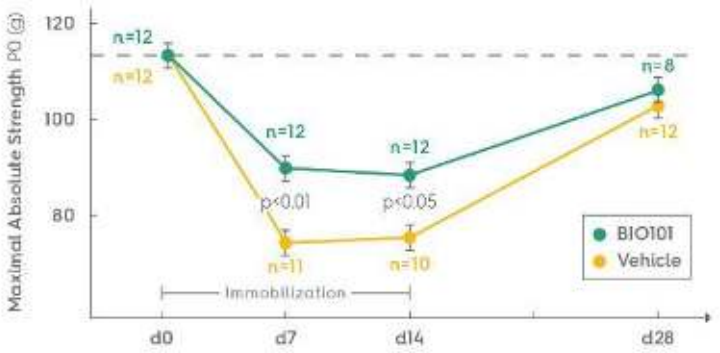
# Sarconeos (BIO101) improves muscle strength and mobility in animal model

## 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. Results were presented in a poster at the SCWD conference in December 2016 in Berlin, Germany.

# SARA-INT: on going Phase 2b clinical trial in sarcopenia

- Global, multicenter, double-blind, randomized, placebo-controlled trial
- Recruitment completed March 2020 for 231 elderly patients with sarcopenia at risk of mobility disability over 22 centers in the US and Belgium

| Objectives | Key Endpoints | Inclusion Criteria |
|---|---|---|
| • 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>• Handgrip strength<br>• 400MWT responder analysis<br>• Patient reported outcomes (PRO) | • 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 |

# SARA-INT: patient enrollment completed March 2020

*"The SARA-INT Phase 2 trial is investigating a new treatment for sarcopenia, a disease of aging which is characterized by loss of muscle mass and function.*

**Dr. Roger Fielding**, PhD, Director of the Nutrition, Exercise Physiology & Sarcopenia Laboratory at **Tufts University** in Boston and Principal Investigator of SARA-INT trial

| Product | 2019 | 2020 | 2021 |
|---|---|---|---|
| 175 & 350 mg (twice daily) of Sarconeos (BIO101) | SARA-INT Phase 2b | | |

- **No safety issue** to date, with multiple DSMB "may proceed" opinions.
- An **Interim analysis is** planned to re-assess the sample size
- Completion of the study, and reporting is expected for **Q1 2021,** depending on Covid-19 pandemic evolution

Source: Clinicaltrials.gov - NCT03452488

Overview

Sarconeos (BIO101) for sarcopenia

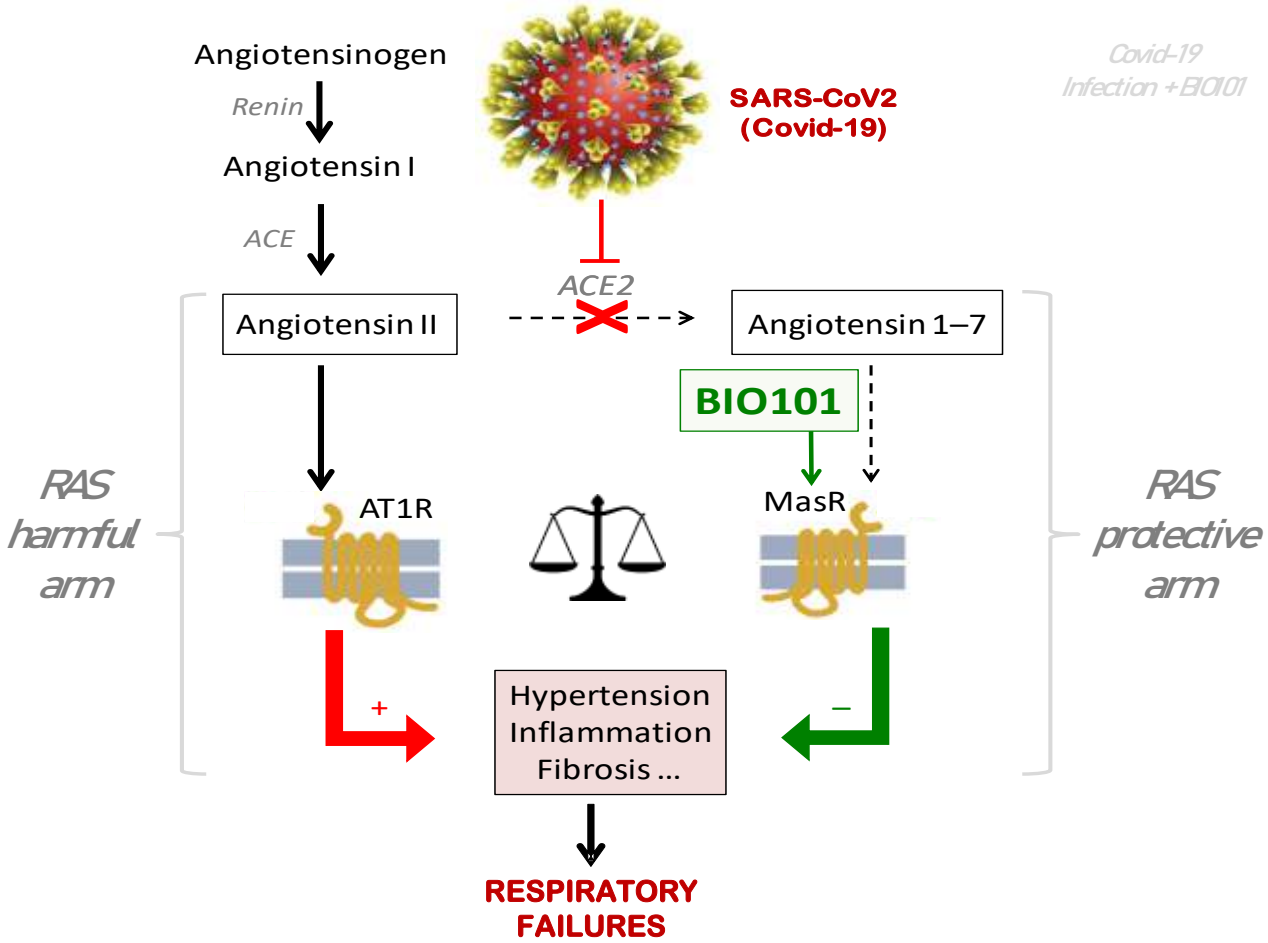
**Sarconeos (BIO101) for Covid-19**

Sarconeos (BIO101) for DMD

Macuneos for dry AMD

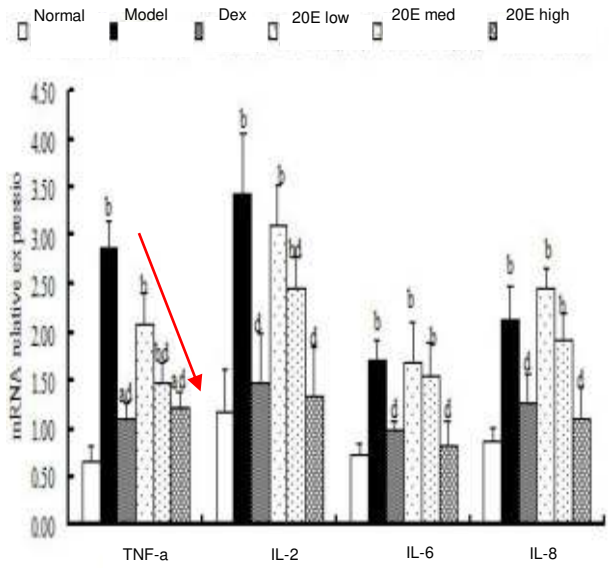
# Sarconeos (BIO101) stimulates respiratory functions by activating RAS

- Sars-Cov-2 uses ACE2 to penetrate into the lungs destabilizing RAS system and causing respiratory failures
- Sarconeos (BIO101) activates MAS receptor, a key component of the protective arm of the RAS system, and re stimulates respiratory function

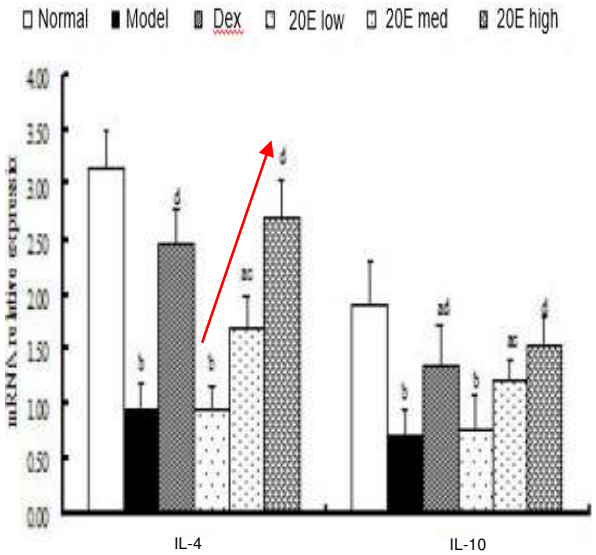


# Sarconeos (BIO101) has anti-inflammatory effects in acute lung injury mice model (ALI)

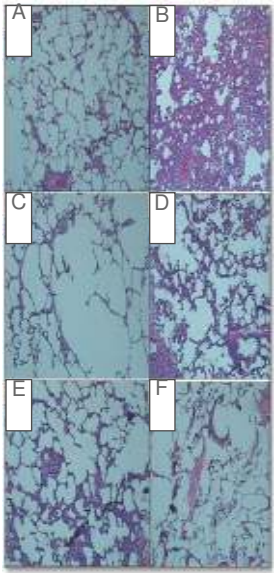
**Dose-dependent decrease of pro-inflammatory cytokines**




**Dose-dependent increase of anti-inflammatory cytokines**




**Dose-dependent improvement of lung lesional profile**



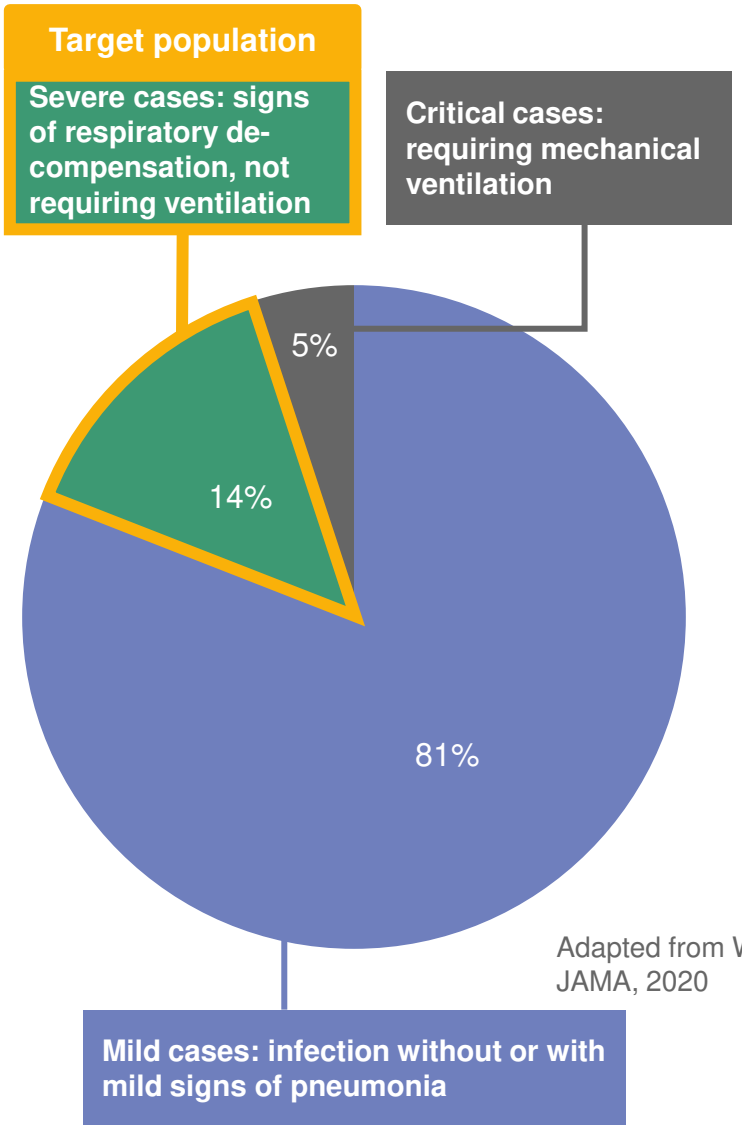

A/ Normal
B/ LPS
C/ Dex
D/ 20E low-dose
E/ 20E med-dose
F/ 20E high-dose

Song et al. 2019

Reduction of pro-inflammatory cytokines (TNF Alpha) and increase in anti-inflammatory cytokines (IL4)

# Target population: severe respiratory manifestations, not intubated

- Patients **aged 65 and above**, with proven Covid-19, respiratory symptoms:
  - With evidence of respiratory decompensation ≤4 days before start of study medication, meeting one of the following:
    - Tachypnea: ≥25 breaths per minute
    - Arterial oxygen saturation ≤92%, on Oxygen at least 3L/min
- Allowed medications: antimalarial, antibacterial and antiviral agents, anti-inflammatory agents and ACE inhibitors / ARB




Adapted from Wu et al. JAMA, 2020

# The COVA study: Sarconeos (BIO101) to prevent respiratory deterioration linked to Covid-19

- A phase 2/3 study
- Multinational, multi-centric
- Double-blind, placebo controlled
- Group sequential (2 parts), adaptive design
- Sarconeos (BIO101) 350mg BID vs. placebo

| Part | Goal | Number of participants |
|---|---|---|
| 1 | 1. Obtain safety and tolerability data on BIO101 in the target population<br>2. Obtain an indication of activity for BIO101 in the target population | 50<br>1:1 randomization |
| 2 | Re-assess the sample size for step 2 | 155 (an addition of 105 subjects)<br>1:1 randomization |
| | Confirmation of the effect of BIO101 in preventing further respiratory deterioration and obtaining a conditional approval | 310 (an addition of 155 subjects)<br>1:1 randomization |

| Product | 2020 | 2021 |
|---|---|---|
| 350 mg of Sarconeos (BIO101) | COVA Phase 2b | |

Overview

Sarconeos (BIO101) for sarcopenia

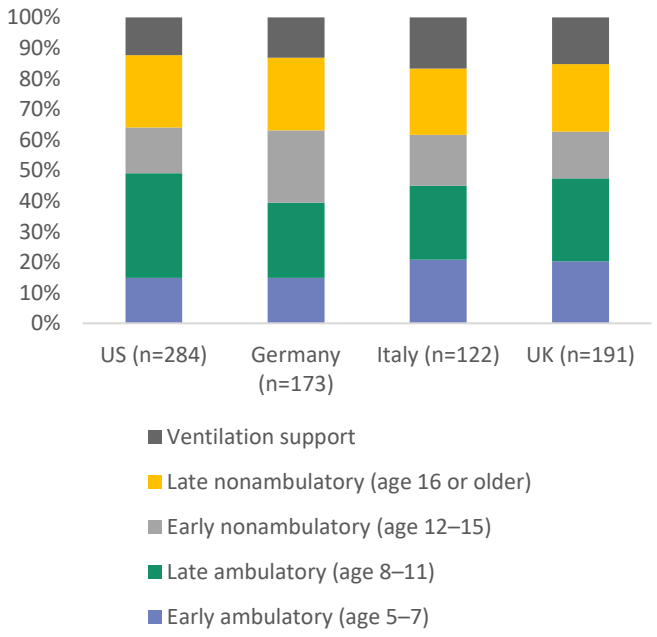
Sarconeos (BIO101) for Covid-19

**Sarconeos (BIO101) for Duchenne's muscular dystrophy (DMD)**

Macuneos for dry AMD

# DMD: No cure and limited treatment options

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

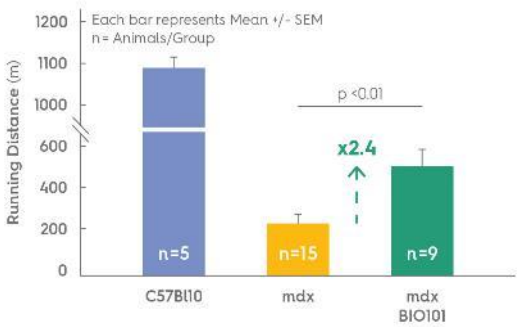



- Rare, genetic neuromuscular disease in male children characterized by accelerated degeneration of muscles, responsible for loss of mobility, respiratory failure and cardiomyopathy, leading to premature death.
- No known cure and limited treatment options, including corticosteroids and targeted therapies (exon-skipping in U.S. & stop codon in EU) that treat approximately 13% of DMD patients with specific genetic mutations.
- Myostatin inhibitors have been developed in DMD by large pharma (Pfizer, Roche) without success
- 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.

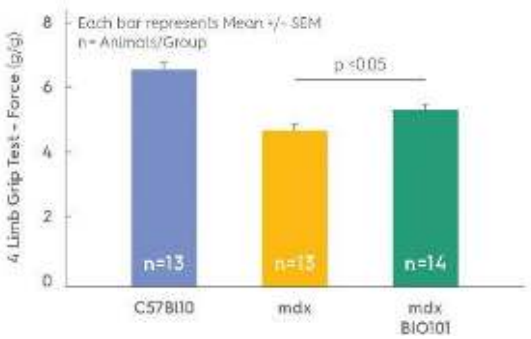
# Proof-of-concept in *mdx* mice models of DMD: Improvements in mobility, strength and respiration

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



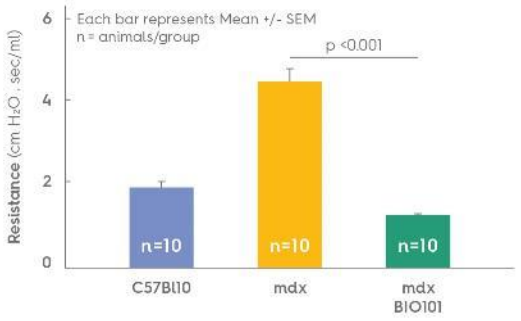

C57BL10-*mdx* mice treated with 50 mg/kg/day of Sarconeos (BIO101) over 8 weeks ran **2.4x farther** than untreated control C57BL10-*mdx* mice

## 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

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

# MYODA-INT: IND granted by FDA to start Phase 1-2 end 2020


## Design

- Global, multicenter, double-blind, placebo-controlled, seamless, Phase 1-2 clinical trial
- Part 1: Safety, tolerability & PK (initial 7 days of dosing of escalating dose of Sarconeos)
- Part 2: Efficacy of Sarconeos (Respiratory and muscle function after dosing for 52 weeks)

## Patients

- Ambulatory and/or non-ambulatory DMD patients:
  - Phase 1-2: 48 patients
- Enrollment in the U.S. and EU
- Patient advocacy group support
  - AFM Téléthon in France

## Regulatory Status

- Pre-IND correspondence with the FDA in October 2018
- Scientific advice meeting with the EMA in December 2018
- IND and European regulatory filings in November 2019
- **FDA – IND granted 12/2019**

Overview

Sarconeos (BIO101) for sarcopenia

Sarconeos (BIO101) for Covid-19

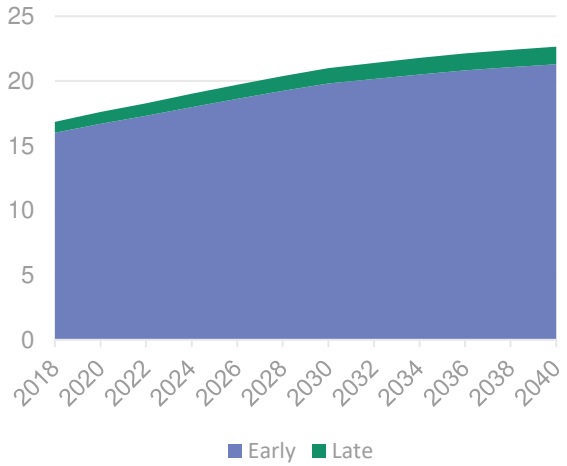
Sarconeos (BIO101) for DMD

## Macuneos for dry AMD

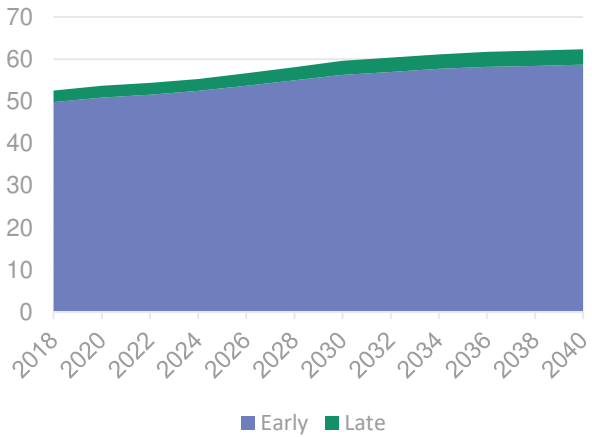
# Dry AMD is an unmet medical need with no approved drugs

- 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]

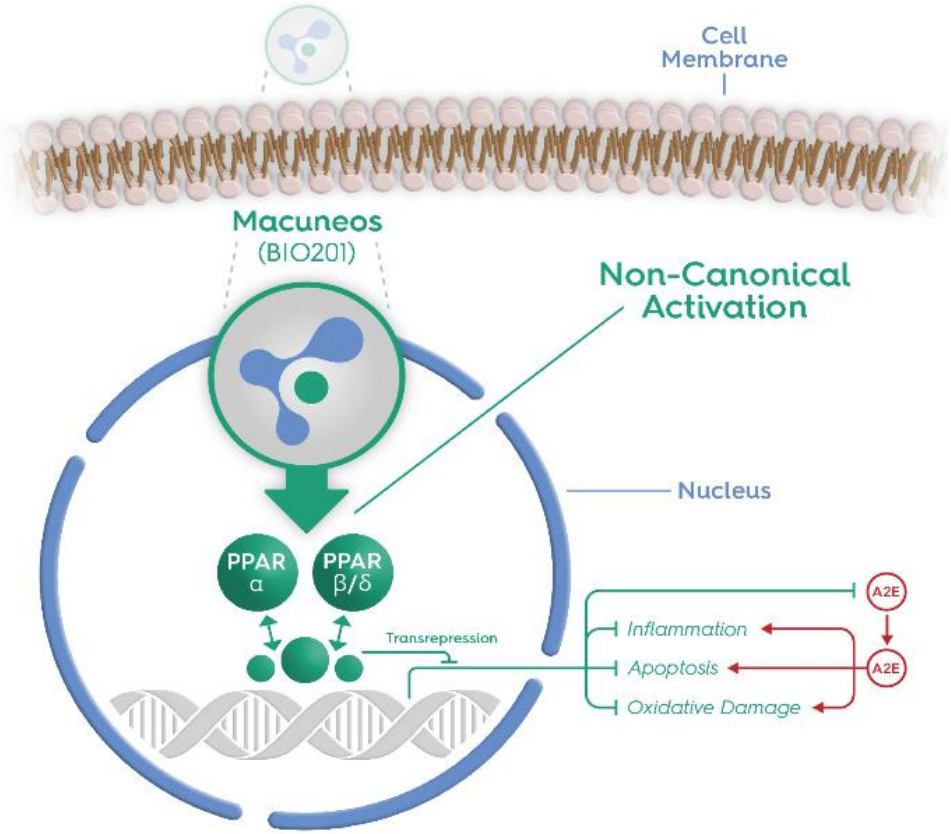



- 85 - 90% of AMD patients have dry AMD in some form; either early, intermediate or late stage, known as geographic atrophy (GA)
- No approved treatments for any stage of dry AMD, including GA
- We are developing Macuneos to treat patients with intermediate dry AMD to prevent the development to advanced 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 mechanism of action: Non-canonical activation of PPARs

- We believe Macuneos 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



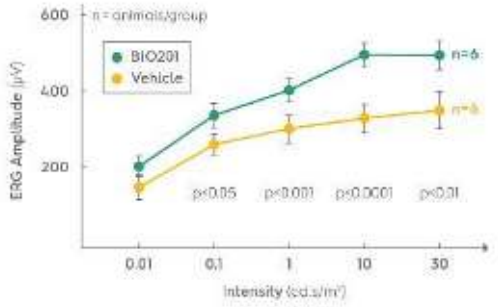

**Anti-inflammatory activity** (promotes the expression of anti-inflammatory genes)

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

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

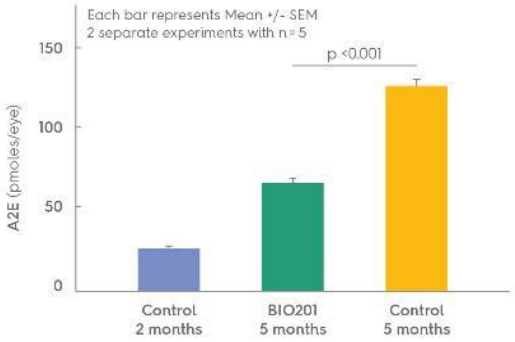
# Macuneos protects the retina in rodent models of dry AMD and Stargardt disease

## Preservation of visual function in mice



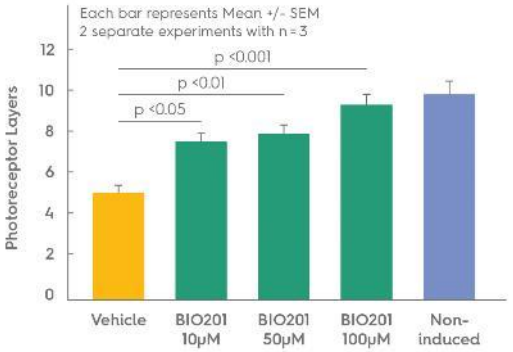

Chronic oral administration of Macuneos for 3 and 6 months **increases ERG amplitude** in ABCA4$^{-/-}$ RDH8$^{-/-}$ mice

## Reduced A2E accumulation in mice




Chronic oral administration of Macuneos 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 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

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 clinical milestones

- ☑ SARA-INT (Phase2b) patient enrollment completed March 2020
- ❑ SARA-INT topline results expected by Q1 2021
- ☑ COVA IND (Phase 2/3) started in Belgium, approved in the UK
- ❑ COVA IND pending approval in the US and France
- ☑ MYODA IND (Phase 1/2) approved in the US and Belgium
- ❑ MYODA First Patient in Q4 2020

# Appendix

# Scientific advisory board

### Pr. Jean Mariani

- Professor of neuroscience and biology of aging and Director of Charles Foix Institute of Longevity at Sorbonne University
- Emeritus Professor (PU-PH) at the Sorbonne University's School of Medicine
- Member of the Board and Executive committee of Gerond'IF

### 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

**Pr. Jean Mariani**

- Professor of neuroscience and biology of aging and Director of Charles Foix Institute of Longevity at Sorbonne University
- Emeritus Professor (PU-PH) at the Sorbonne University's School of Medicine
- Member of the Board and Executive committee of Gerond'IF

**Jean M. Franchi**

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

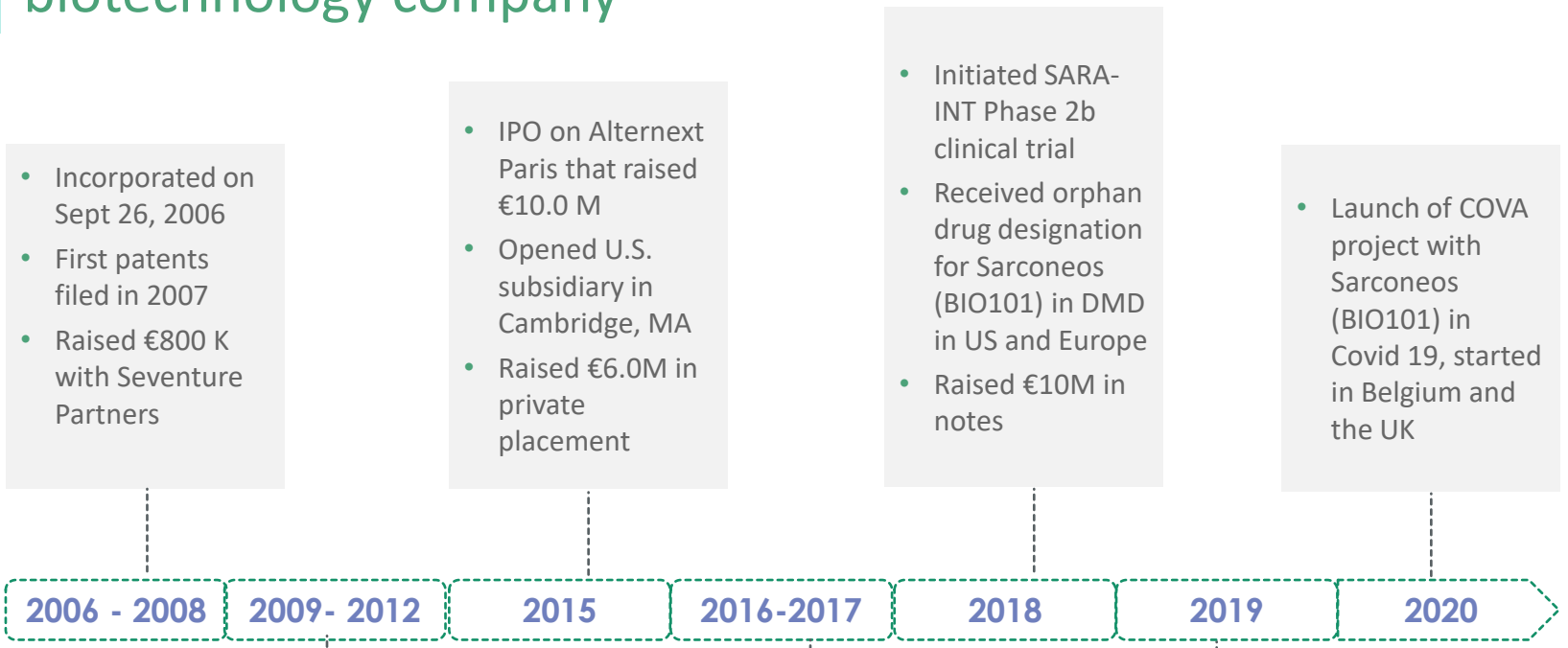
**Dimitri Batsis**

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

**Nadine Coulm**

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

# From a Sorbonne University spin-off to a successful clinical-stage biotechnology company




- Incorporated on Sept 26, 2006
- First patents filed in 2007
- Raised €800 K with Seventure Partners

- 2009 €2.2 M Round A with VC's
- 2009 launched first human clinical trials for Sarconeos (BIO101)
- 2012 €3.0 M Round B with VC's

- IPO on Alternext Paris that raised €10.0 M
- Opened U.S. subsidiary in Cambridge, MA
- Raised €6.0M in private placement

- 2016 initiated and completed SARA-PK Phase 1 clinical trial
- 2017 raised €18.0 M in private placements
- Set up €15M bond financing
- Initiated SARA-OBS clinical trial

- Initiated SARA-INT Phase 2b clinical trial
- Received orphan drug designation for Sarconeos (BIO101) in DMD in US and Europe
- Raised €10M in notes

- Set up €24M bond financing
- Filed and granted IND for Sarconeos (BIO101) in DMD

- Launch of COVA project with Sarconeos (BIO101) in Covid 19, started in Belgium and the UK

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biophytis

# Intellectual Property portfolio – Covid-19 & Neuromuscular diseases

- We hold exclusive commercial rights through licenses of each of our drug candidates.
- IP is jointly owned with Sorbonne University & sometimes with other academic research institutions[1.]
- Patent portfolio covers 10 patent families, including a total of **18** co-owned issued patents and a total of **28** co-owned patent applications.
- Issued patents: 3 European, 2 U.S., and 13 in ROW, including **China, Japan**.
- Pending applications: 2 European, 4 U.S., and 21 in ROW, including **China, Japan, South Korea**

**Neuromuscular diseases**

10 families of patents covering production process, second generation compounds and various applications such as sarcopenia, myopathies (DMD), disuse atrophy, spinal muscular atrophy, respiratory function and Covid 19

# Intellectual Property portfolio – Retinal Diseases

- We hold exclusive commercial rights through licenses of each of our drug candidates.
- IP is jointly owned with Sorbonne University & sometimes with other academic research institutions.
- Patent portfolio covers 5 patent families, including a total of **12** co-owned issued patents and a total of **18** co-owned patent applications.
- Issued patents: 4 European, 2 U.S., and 6 in ROW, including **China, Japan**.
- Pending applications: 1 U.S., and 17 in ROW, including **China, Japan, South Korea.**

**Retinal diseases**

5 families of patents covering 2 classes of compounds and their applications for dry age-related macular degeneration (AMD) and Stargardt disease

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# Thank you

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