biophytis® LIVE HEALTHIER LONGER

April 2024 I Euronext: ALBPS – Nasdaq: BPTS

Forward Looking Statements

This presentation contains forward-looking statements. Forward-looking statements include all statements that are not historical facts. In some cases, you can identify these forward-looking statements by the use of words such as **«outlook », «believes», «expects», «potential», «continues», «may», «will», «should», «could», «seeks», «predicts», «intends», «trends», «plans», «estimates», «anticipates» or the negative version of these words or other comparable words. These forward-looking statements include statements regarding Biophytis' anticipated timing for its various BIO101 (20-hydroxyecdysone) clinical trials and expectations regarding commercialization. Such forward-looking statements are based on assumptions that Biophytis considers to be reasonable.**

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therapeutics for muscular, respiratory and metabolic diseases



HQ location: Paris, France Other locations in Sao Paulo, BR and Cambridge, MA US



Founded: 2006



Euronext growth Paris (ALBPS) Nasdaq NYC (BPTS)



Drug discovery : platform for developing drugs for age-related diseases











A clinical-stage biotechnology company specialized in the development of



BIOPHYTIS' People : Expertise & Passion



Stanislas Veillet

CEO, cofounder





Rob van MAANEN Chief Medical Officer





Pierre DILDA Chief Scientific Officer





Waly DIOH Chief Operations Officer





Nicolas FELLMANN Chief Financial Officer





Edouard BIETH

Chief Business Officer





Chiara BACCELLI

Chief Pharmaceutical Operation, Officer & Quality Assurance Director



Our Clinical Pipeline as of today

Candidate	Indication	Program	Preclinical	Phase 1	Phase 2	Phase 3	Regulatory	Market
BIO 101 20-hydroxyecdysone	Sarcopenia	SARA			1			
	Obesity	BA				- 		
	Covid-19	COVA					Ruvembri 20-hydroxyecdysone	
	DMD	MYODA			- 	- - - - - - - - - - - - - - - - - - -		
BIO 201	Dry AMD				 	 		
	Stragardt				- 	- 		

xxx orphan diseases



BIO101 (20-hydroxyecdysone) : Mechanism of Action

- BIO101 (20-hydroxyecdysone) triggers two important MAS receptor downstream signaling-pathways in myocytes:
 PI3K/AKT/mTOR: Increases protein synthesis
 AMPK/ACC: Stimulates energy production
- MAS activation in muscles stimulates muscle metabolism with a potential impact on muscle and/or respiratory functions





BIO101 (20-hydroxyecdysone) is currently in development in 4 indications









BIO101 (20-hydroxyecdysone) in SARCOPENIA



Sarcopenia is an aged related disease

Sarcopenia is a syndrome defined by many consortia including the EWGSOP (The European Working Group on Sarcopenia in Older People) and the SDOC (Sarcopenia definitions and Outcomes Consortium), characterized by **progressive** and generalized loss of skeletal muscle mass, strength and function associated with an increased risk of adverse events such as disability, poor quality of life and death.









Sarcopenia is estimated to influence 10%–16% of the elderly 60+ population worldwide.





SARA

Source : Yuan 2023, Epidemiology of Sarcopenia, Metabolism; Shafiee 2017, Prevalence of Sarcopenia in the world, Journal of diabetes & metabolic disorders; <u>http://dx.doi.org/10.1590/1809-9823.2015.14139</u>



There is no drug treatment registered for sarcopenia

No pharmacological treatment has yet been approved

for either frailty or sarcopenia. Recommendations for the prevention and treatment of frailty and sarcopenia are thus still mainly based on lifestyle interventions, such as nutrition and physical exercise.









Vitamins/dietary supplements

These may improve muscle strength and muscle mass, but no solid clinical evidence

Off label Drugs

The use of off label drugs is based on empiric practice. Data on sub population of large trials exist but not approved.





BIO101 (20-hydroxyecdysone):



First drug candidate to complete Phase 2 (SARA-INT) with clinically meaningful outcome on mobility

On track to prepare the Phase 3 program, through approvals of CTA and granted by EMA and FDA

Other drug candidates including Myostatin inhibitors and SARMs halted for lack of effectiveness in neuromuscular diseases









Source: Tourette et al. 2022. The Journal of Frailty & Aging, vol. 11: S1,22 doi: 10.14283/jfa.2022.22.



SARA-INT: Phase 2 trial overview

Design

- Global, double-blind, randomized, placebocontrolled trial: NCT03452488
- Assess safety and efficacy of two doses of BIO101 (20-hydroxyecdysone) administered orally over 26 weeks, as compared to placebo Treatment effect on improvement of physical
- function (gait speed) and on decrease of risk of mobility disability

Endpoints

Primary

 Gait speed in the 400-meter wal test

Secondary

- Short Physical Performance Ba
- Handgrip muscle strength
- Patient reported outcomes (PRO



	Patient Population
alk	 Age: 65 years old or over Low mobility measured by Short Performance Physical Battery (SPPB) ≤8 out of 12 Able to complete the 400MWT within 15 min without sitting down, help from another person, or use of a walker.
Battery (SPPB)	 Sarcopenia FNIH criteria: ✓lean mass: ALM/BMI < 0.789 in men and 0.512 in women, or ALM <19.75 kg in men and <15.02 kg in women as measured by DXA

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7	(CADA
1	JARA



Promising results obtained in SARA-INT phase 2 trial

BIO101 (20-hydroxyecdysone) significantly improves the 400 MWT gait speed, the primary endpoint, in the PP population after 6 months of treatment

- Global, double-blind, randomized, placebo-controlled trial in patients with aged-related sarcopenia at risk of mobility disability to evaluate safety and efficacy of BIO101 (20-hydroxyecdysone)
- At the highest dose of 350 mg bid: clinically meaningful improvement of 0.10 m/s in the PP population (significant, p=0.008) compared to placebo for the 400MWT gait speed after 6 months of treatment
- This gait speed level of 0.10 m/s is known to be associated with a reduction in mobility disability and mortality in the elderly
- BIO101 (20-hydroxyecdysone) demonstrated the same effects on mobility in the sarcopenic obese subpopulation.





Change from baseline at M6 Gait speed



Treatment effect is nominally significant in PP population at M6 (p =(800.0)





SARA-31 – Phase 3 development plan

Design

- Global, double-blind, randomized, phase 3 placebo-controlled trial
- Assess safety and efficacy of BIO101 (20-hydroxyecdysone) 350 mg BID administered orally over at least 52 weeks, as compared to placebo
- Treatment effect based on estimation of the risk of mobility disability

Endpoints

Primary

 Major Mobility Disability (MMD) assessed by the inability to complete the 400-meter walk test (400MWT) within 15 min

Secondary

- Gait speed 4-meter from Short
- Physical Performance Battery (SPPB)

Handgrip Strength (HGS)

Patient Reported Outcomes (PRO)

Product	2023	2024	202

350 mg b.i.d of	CTA in	SARA-31 Phase 3
BIO101 (20-hydroxyecdysone)	Europe/US	(depending on partnership)
BIOIUI (20-hydroxyecdysone)	Europe/US	(depending on partnership)



Patient Population

- Age: 65 years old or over
- Low mobility measured by Short Performance
 Physical Battery: SPPB 3 ≤ SPPB ≤ 7
- Low Handgrip Strength (HGS < 20 and <35 kg in female and male)
- Slow walkers (gait speed < 0.8 m/s)
- Reporting a loss of motor function over the last year

RO) 125

2026





BIO101 (20-hydroxyecdysone) in Obesity





Muscle weakness associated with obesity and its treatment: an unmet medical need

Obesity is a serious chronic disease



Adults and children are currently living with obesity globally.



The global prevalence of obesity has more than tripled since 1975.

Up to 40%

Total weight loss that comes from muscle when obese patients are treated with GLP-1RA.

nature biotechnology

« [There is a need to] counter the side effects of dramatic weight loss [induced by GLP-1s]. [Biotechs] are searching whether it is possible for people to lose weight on these GLP-1 RAagonists without losing muscle. »

Sources

World Obesity Federation report: https://www.worldobesity.org/news/economic-impact-of-overweight-and-obesity-to-surpass-4-trillion-by-2035 World Health Organization report: https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight McCarthy et al. Weight Loss Strategies and the Risk of Skeletal Muscle Mass Loss. Nutrients 2021, 13, 2473: https://doi.org/10.3390/nu13072473





The global cost of treating obesity-related complications is expected to rise by over \$4 trillion by 2035.

After obesity drugs' success, companies rush to preserve skeletal muscle Nature Biotechnology. 2024 42(3):351-353





According to analysts, 13% of US adult population would be treated with an anti-obesity medication by 2030





Goldman Sachs

"In 2030, we estimate that ~15mn adults in the US will be treated with AOM for chronic weight management (excluding patients treated for type 2 diabetes), which represents ~13% penetration into the U.S. adult population"





Potential attributes of BIO101 (20-hydroxyecdysone) in obese patients treated with GLP-1RA



Effects on muscle wasting:

- Preservation of muscle strength
- Reduction of muscle mass loss
- Improvement of mobility



Effects on fat tissues:

• Increase of fat mass loss

Convenient and safe administration :



- Oral route
- Adequate safety demonstrated in adults from trials in other indications











Supportive preclinical data in obesity



Metabolic effects in obese mice :

Muscle function in mice fed high fat :

hydroxyecdysone) (Serova et al., 2023)



• Protective effect of BIO101 (20-hydroxyecdysone) in mice fed an obesity-inducing high-fat diet, preventing adipose tissue development (Foucault et al., 2012)

• Anti-obesity effect by increase in energy expenditure (Foucault et al., 2014)

• Improved physical performances in adult and old animals orally treated with BIO101 (20-





Android fat mass (p=0.0386)



20-hydroxyecdysone (20E) daily dose of 37.5 mg (given in the form of a dietary supplement) compared to placebo (n=58) 12 weeks study, with weight loss on hypocaloric diet for six weeks (S0-S6) followed by a normocaloric diet for six weeks (S6-S12)



Handgrip strength patients with weight loss >5% (p=0.0974)









- enrolled in the second half of 2024.
- dieting.
- its results are expected in 2025.



 The OBA Phase 2 study is expected to start in mid 2024, upon regulatory approvals, with the first patient to be

• BIO101 (20-hydroxyecdysone) will be evaluated in obese patients treated with GLP-1 RA and following hypocaloric

• The completion of the OBA Phase 2 study and report of





in SARIs

(Severe Acute Respiratory Infections)

Ruvembri[™] is the marketing name for BIO101 (20-hydroxyecdysone) in Covid-19 indication





Global Respiratory Infection treatment market will reach more than 100bUSd by 2031

Medical research, increasing awareness and government initiatives will drive market growth





2031 Total Market

108 bUSD



Source : DataBridge Report on Respiratory Viral Infections 2023



In 2023, Covid treatments represent 29% of the Respiratory **Infections market**

Global treatment market by virus type (2023)









Source : DataBridge Report on Respiratory Viral Infections 2023



17% of patients hospitalized for Covid are still dying

What's happening in reality ?



Patient hospitalized for severe COVID19



Number of comorbidities :	1,2%
Main comoborbidities :	
Hypertension :	33%
Diabetes :	19%
Obesity :	10%



Main symptoms :

Acute Respiratory Failure :

Atrial Fibriliation : 12%





COVA

Source : Comparison of the characteristics, morbidity, and mortality of COVID-19 and seasonal influenza: a nationwide, population-based retrospective cohort study, Lancet Respir Med 2021; 9: 251-59



COVA Study: Targeting Hospitalized Patients with severe respiratory symptoms due COVID-19



Patients aged 45 and above, with proven COVID-19, and severe respiratory symptoms:

 With evidence of respiratory decompensation ≤7 days before start of study medication, meeting one of the following :

- Tachypnea: ≥ 25 breaths per minute
- Arterial oxygen saturation 92% or less

Hospitalized patients with respiratory failure estimated to 15-18% of hospitalized patients: ca 500 new patients per day or 180,000 patients/year in the USA (CDC data, October 27, 2022)



Allowed medications :

- Antiviral agents such as remdesivir, PaxlovidTM
- Anti-inflammatory agents such as dexamethasone[™], tocilizumab[™]





Adapted from Wu et al. JAMA, 2020



Phase 2-3 COVA clinical study to evaluate of Ruvembri[™] in the treatment of severe forms of COVID-19

THE LANCET

EClinicalMedicine Published by THE LANCET

Design

 Administration of 350 mg b.i.d of BIO101 Global, multi-center, double-blind, placebo-controlled group Phase 2-3 sequential (2 parts) adaptive design

• International study including 37 clinical centers in US, Brazil, France & Belgium

Endpoints & Study Follow-Up

Primary endpoint : proportion of patients with respiratory failure or early death within 28 days

• Secondary endpoints : mortality at 28 and 90 days; discharge at 28 days End of study: Q2 2022 (N=237) after early study termination

• Age : 45 years old or over

Inclusion criteria

• Hospitalized for severe respiratory symptoms and with proven **Covid-19 infections**

- All authorized Covid-19 drugs (anti-viral or anti-inflammatory)



Patients with hypoxemia (<92%) or tachypnea (> 25 breaths/min)





Positive results strongly supporting therapeutic potential of **Ruvembri[™] in severe COVID-19 : respiratory failure or early** death

Respiratory Failure or early death : The study met primary endpoint

• Reduction in the risk of early death or respiratory failure at day 28 by 44% (p=0.043, CMH test)

• Time to early death or respiratory failure over 28 days was lower (p=0.022, Kaplan Meier analysis)

• Post hoc analysis confirmed the reduction in the risk of early death or respiratory failure in the ITT population and in the PP population





Proportion without respiratory failure or early death, Kaplan-Meier Analysis, ITT population





Source: Lobo et al., eClinicalMedicine 2023 : 102383. Published Online : https://doi.org/10.1016/j.eclinm.2023.102383

Source: Lobo et al., 2024. www.thelancet.com Vol 68 February, 2024



Positive results strongly supporting therapeutic potential of Ruvembri[™] in severe COVID-19 : mortality and safety

Mortality follow-up over 90 days and safety :

• Kaplan Meier post hoc analysis showed a reduction in the risk of death at day 90 of 43% (p=0.076) in the ITT population and 70% (p=0.016) in the PP population

• Very good safety profile with lower proportion of adverse events, especially respiratory adverse events (57% vs. 64%)

• Lower proportion of patients with severe adverse events compared to placebo (25% vs. 31%)





Proportion without death, Kaplan-Meier Analysis, ITT population

Source: Lobo et al., eClinicalMedicine 2023 : 102383. Published Online : https://doi.org/10.1016/j.eclinm.2023.102383

Source: Lobo et al., 2024. www.thelancet.com Vol 68 February, 2024



Biophytis initiates market access processes for BIO101 treatment of severe forms of COVID-19



Early access :

- program, with initiation expected in 2024





• EAP in France : application for early access will be re-submitted in 2024

• EAP in Brazil: new application to be submitted to ANVISA for an EAP





BIO101 (20-hydroxyecdysone) in Duchenne Muscular Dystrophy



Orphan genetic disease affecting 1/5,000 boys at birth (220,000 patients worldwide)

"Duchenne is every child and parents' worst nightmare come true" (Victoria, Mother of Dougie)



• Degenerative : every muscle is slowly and inexorably damaged (dystrophin deficiency)

• It can affect anyone : 1/3 arise from random spontaneous genetic mutations, which may occur during any pregnancy



MY ODA

Source : AFM Telethon



Despite research progress, no treatment is able to cure or effectively control the progression of the disease



Corticosteroids (Prednisone, deflazacort, vamorolone)

They are the standard of care, but their use is controversial and not uniformly recommended.

- Mobility loss delayed by 2 years



Gene-based Therapies (exon skipping, microdystrophin, etc...)

Gene therapies have been considered to be a revolution for the past 35 years, but what are the concrete results today?

- Limited effectiveness¹
- **Toxicity issues** (several deaths suspected³)
- Outrageously expensive (\$3,2M/patient for Elevidys⁴)



• Serious side effects (weight gain, behaviour disorders, muscle wasting, osteoporosis, cataracts, high blood pressure...) • Long-term use associated with more serious sequelae (69% of complications reported in non-ambulatory patients)

Source : Orphanet J. Rare Dis. doi.org/10.1186/s13023-021-01758-9

• Highly restricted number of addressed patients (e.g. 13% for eteplirsen², and limited to young patients)

MYODA

Source : [1] Expert Opinion on Investigational Drugs, 2021, doi:10.1080/13543784.2021.1868434; [2] Front. Cell Dev. Biol. 2021, doi: 10.3389/fcell.2021.689533 [3] Science, 2023, doi: 10.1126/science.adi8800; [4] Pharmaceutical Technology, 2023.





- No approuved drug for their specific respiratory problems
- Excluded from current clinicals trials
- Average age for tracheostomy is **19 years old**¹
- How do we treat these children who cannot breathe properly as we speak ?
- Ventilatory assistance, mostly invasive, has extended life expectancy by 10 years, BUT with drastic impact on quality of life





Source : [1] Orphanet J. Rare Dis., 2020, doi: 10.1186/s13023-020-01430-8

BIO101 (20-hydroxyecdysone) in DMD : Experts and Stakeholders insights

BIO101 in DMD : the experts speak





"The only barriers to BIO101 adoption by US specialists could be patient access restrictions,

i.e., high price and lack of reimbursement"





(US Payer)

"Your molecule could be life-changing for Duchenne patients"

(French Muscular Dystrophy Association, AFM-Telethon)

"Due to the lack of candidates able to cure or effectively control the disease progression, any drug, such as BIO101, able to improve patient outcomes will be welcomed and prescribed by all specialists

(US Clinical expert)

Source : AEC partners survey for Biophytis, Oct 2023

M~ ODA



Our solution: A first-in-class medication

BIO101 (20-hydroxyecdysone) aims to improve breathing capacity

(PenH) in C57BL10-mdx mice.





Improvement in airway responsiveness

Our solution: A first-in-class medication



BIO101 (20-hydroxyecdysone) aims to improve non ambulatory patients breathing capacity

New therapeutic class New molecular target

- Validated mechanism of action
- Activation of MAS receptor² (renin-angiotensin system)
- Regulation of smooth, cardiac and skeletal muscle metabolism

Good safety profile Low side effects

Clinical trials on motor function

(Sarcopenia, Phase 2)

Clinical trials on respiratory function

(severe Covid-19, Phase 3)

- Preclinical studies in DMD models : motorrespiratory and cardiac function
- Preliminary juvenile tox studies

Remarkable activity in preclinical models

Ease of administration and Affordable cost

- API manufactured at industrial scale
- Advanced CMC
- Oral suspension adapted to DMD patients

Rock-solid IP

• 3 patent families granted in key countries

Orphan designation by EMA & FDA

DMD clinical protocol validated by experts

Highly supported by KOLs & patient associations





M~OD/



Preparing to start phase 1-2 clinical study in DMD

Design

- Randomized, Double-Blind, multi-center A Phase 1-2 Study
- Evaluate the Safety, Efficacy, Pharmacokinetics, and Pharmacodynamics of BIO101 (20-hydroxyecdysone) in Non-Ambulatory DMD Patients with Respiratory Deterioration.
- Pediatric oral formulation (powder) of BIO101 (20-hydroxyecdysone)

Endpoints

- Primary
 - change from baseline in Forced vital capacity (FVC)
- Secondary : The Peak Expiratory Flow (PEF), Performance of Upper Limbs (PUL) scale, Grip strength (MyoGrip)
- Part 1 (N=15): Safety, tolerability & PK 7 days of escalating dose)
- Part 2 (N=45): Safety and efficacy on respiratory function (FVC, PEF) of one dose for 48 weeks

Product	2023	2024	202
BIO 101 (20-hydroxyecdysone)	Amendment to CTA approval	Phases 1-2 study	



Patient Population

- Age: ≥12 years old
- Non-ambulatory DMD patients
- Patients at risk of respiratory failure



Key milestones in the development of BIO101 (20-hydroxyecdysone)

	Achieved in the last 12 months	
SARA	Authorization to start phase 3 SARA-31 study in Belgium and the US	
BA	Preparation of the OBA Phase 2 study New patent application	
CöVA	Phase 2/3 COVA Study : Results published and promising clinical benefits for BIO101 (20- hydroxyecdysone)	
MYODA	Preparation of an amended protocol to regulatory agencies (FDA, EMA)	



Anticipated in the next 12 months

Start of phase 3 SARA-31 study depending on partnership

Start of OBA phase 2 study pending regulatory approval and depending on financial resources

Launch of Early Access programs in France and Brazil

Start of phase 3 study depending on partnership

Start of phases 1/2 study depending on financial resources

Scientific Advisory Board



○ Pr. Jean Mariani, President

Longevity at Sorbonne University

Emeritus Professor (PU-PH) at the Sorbonne University's School of Medicine



René Lafont

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



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- School of Medicine
- Center on Aging



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



Dr. Thomas Voit

- Professor, University College London
- Children





Professor of Medicine, Tufts University

Director and Sr. Scientist Jean Mayer USDA Human Nutrition Research



Pr. Bernard Levy

Professor Emeritus of Physiology and a senior member of PARCC

Headed the physiology department and the Inserm cardiovascular research center at Lariboisière

Director of the Research Center of the Great Ormond Street Hospital for



Dr. Yann Meunier

Professor. Director International Institute of Medicine and Science

Has led clinical trials for new treatments for HIV/AIDS

Financial data



Shareholding structure

Number of shares : 1,404,697,450 (31 March 2024)





Listing Euronext (ALBPS) and Nasdaq (BPTS)

Cash position:

• €5.6m (December 31, 2023)

● €5.4m raised and €4m in convertible bonds

drawn down since June 2023



• H.C. Wainwright – Joe Pantginis, Ph.D.

Kepler Cheuvreux – Nicolas Pauillac

• Invest Securities – Jamila El Bougrini, Ph.D.



THANK YOU

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