Biophytis SA (BPTS)
Rating: Buy

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Phytochemical Approach for Conditions With Unmet Need; Initiating at Buy and $15 PT

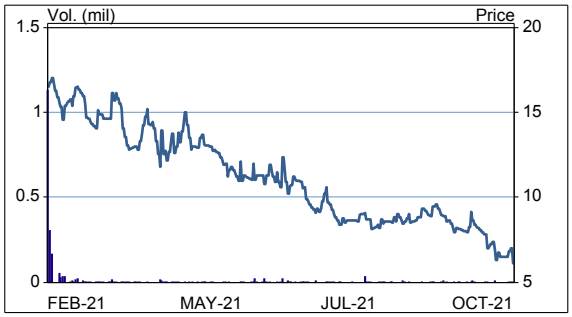
Stock Data	10/22/2021
Price	$6.09
Exchange	NASDAQ
Price Target	$15.00
52-Week High	$18.50
52-Week Low	$6.00
Enterprise Value (M)	$65
Market Cap (M)	$74
Public Market Float (M)	6.2
Shares Outstanding (M)	12.2
3 Month Avg Volume	1,503
Short Interest (M)	0.00
Balance Sheet Metrics	
Cash (M)	€23.0
Total Debt (M)	€13.5
Total Cash/Share	€1.88
Book Value/Share	€0.18

General: U.S. IPO on February 10, 2021

EPS (€) Diluted			
Full Year - Dec	2020A	2021E	2022E
1st Half	$(0.25)	$(0.14)A	$(0.12)
2nd Half	$(0.09)	$(0.11)	$(0.13)
FY	$(0.28)	$(0.25)	$(0.25)

Revenue (€)			
Full Year - Dec	2020A	2021E	2022E
1st Half	$0.0	$0.0A	$0.0
2nd Half	$0.0	$0.0	$2.8
FY	$0.0	$0.0	$2.8

Quarterly EPS may not add to full year due to increases in share count and rounding.



Sarconeos (BIO101) likely a pipeline in a drug. We are initiating coverage on Biophytis with a Buy rating and $15 price target. Based in Paris, France and emerging as a spin-off from Sorbonne University in 2006, Biophytis has built out an intriguing portfolio of therapeutics based on phytochemicals, or compounds derived from plants. Using a proprietary platform, the company focuses on targeting pathways that slow the degenerative processes associated with aging and improving functional outcomes in patients. The company's lead asset, Sarconeos (BIO101) is purified from the plant *Stemmacantha carthamoides*, cultivated in China and used for medicinal purposes in traditional Chinese medicine. Sarconeos (BIO101) targets the MAS receptor of the Renin Angiotensin System (RAS), a complex hormonal signaling pathway implicated in several physiological processes, including blood pressure, inflammation and fibrosis. This mechanism of action allows it to be leveraged across a growing range of indications. The furthest along in clinical development is the company's COVID-19 program, COVA, aimed at treating severe respiratory failure in COVID-19 patients. Sarconeos is also being developed for sarcopenia and Duchenne Muscular Dystrophy (DMD). Sarcopenia is a disorder involving skeletal muscle degeneration, weakness and movement impairment occurring in elderly individuals, has no current approved therapy and afflicts over 17M people in just the U.S. and Europe. DMD is a rare, genetic neuromuscular disease in male children with no cure and limited treatment options. We believe the shares should be attractive to investors based on: (1) potential commercialization of Sarconeos for COVID-19 on the horizon; (2) upcoming clinical milestones across multiple programs; and (3) an expanding portfolio in several indications continues, which could further value of the shares over the long term.

Sarconeos well-positioned to advance in clinical development for sarcopenia. Sarcopenia is an age-associated syndrome characterized by loss of muscle mass and function. With an aging patient population and no currently approved medication or widely accepted standard of care for the disease, there remains are large market potential for Sarconeos. Sarconeos activates key signaling pathways involved in maintaining skeletal muscle strength and mobility (AKT and AMPK) through the activation of the RAS receptor, MAS. In clinical studies to date, Sarconeos has shown a favorable safety and efficacy profile. Topline phase 2 data from the SARA-INT trial have shown that at the highest dose (350 mg bid), Sarconeos treatment led to a clinically meaningful improvement of 0.1 m/s in the 400-meter walk test, the primary endpoint of the study. The company is preparing to start a Phase 3 pivotal program with Sarconeos at the highest dose in 2022. By reaching this milestone, Sarconeos stands to be the only drug candidate in Phase 3 currently being tested for sarcopenia. We believe Biophytis would likely partner Sarconeos for pivotal development.

Taking the path(way) less traveled; Sarconeos as a COVID-19 treatment option. Even with the crucial development of vaccines against COVID-19, there remain breakthrough cases and millions still remain unvaccinated as death tolls progress globally. With incomplete coverage, therapeutics continue to play a key role. With many anti-inflammatory and anti-viral treatments currently in development, Sarconeos has the potential to be a first-in-class treatment option targeting RAS, which is known to be dysregulated upon SARS-CoV-2 infection and induce respiratory failure. Though 80% of COVID-19 are mild, 20% are severe/critical with a high propensity for respiratory infections, the latter of which is the target population of Sarconeos. The competitive landscape of COVID-19 treatments targeting RAS system is still limited, and Biophytis remains a global Phase 2/3 (COVA) studies, and thus far has had two interim analyses with positive feedback from an independent data monitoring committee (DMC). Specifically, DMC feedback results have indicated the trial has no futility, demonstrates a favorable safety profile and a promising zone of efficacy. Taken together, the DMC has recommended the studies proceed unmodified. Biophytis plans to accelerate patient recruitment and anticipates reporting final results in 1H22, along with regulatory submissions for EUA and Conditional Approval expected around the same time. The company is currently scaling up manufacturing activities with a targeted commercialization timeline in 2022.

Sarconeos expands its reach to DMD where poor skeletal muscle performance is a hallmark of disease. DMD develops as a result of the genetic deficiency of dystrophin, rendering muscles unable to repair themselves following mechanical stress which is normal when they contract. As a consequence, patients with DMD progressively lose skeletal, cardiac and in many cases, respiratory functions. Currently, there is no known cure for DMD and treatment options are limited to corticosteroids and precision medicine approaches which target only ~20% of DMD patients that harbor particular genetic mutations. Specific intracellular signaling pathways implicated in both anabolism (Akt/mTOR) and regeneration (MAPK), among others, contribute substantially to the degenerative process in DMD. Of note, both of these pathways feed through the MAS receptor. Emerging studies also implicate systemic mitochondrial defects as a cause of muscle atrophy. Preclinical studies have successfully demonstrated that Sarconeos activates signaling pathways impaired in DMD and increases skeletal muscle performance with improved mitochondrial respiration and anabolism. Biophytis was granted IND approval in December 2019 to initiate a Phase 1/2 clinical proof of concept trial (MYODA-INT) of an oral pediatric formulation of Sarconeos with a primary endpoint of respiratory function. We believe Sarconeos in DMD presents a significant commercial opportunity as there is a clear, well-defined target market of patients with a high unmet need. As the safety profile of Sarconeos has already been established in two other indications, we anticipate a relatively straightforward path for clinical development. Further, and importantly, we believe that Sarconeos has the potential to be complimentary to both approved approaches and the heralded gene therapy approaches currently under development.

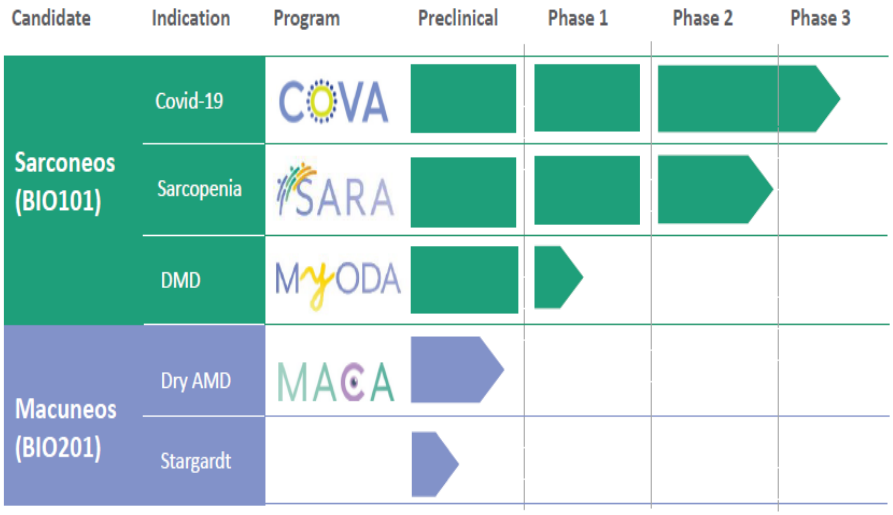
Seeing is believing; Macuneos (BIO201) has blockbuster potential in dry-AMD. The company's second lead molecule Macuneos (BIO201), is designed to treat dry age-related macular degeneration (AMD). Dry AMD accounts for over 85% of AMD cases, and remains largely untreated, affecting nearly 30M people in the US and Europe. As with sarcopenia, dry-AMD is likely to increase in prevalence given the aging demographics of the populations in developed countries. The combination of demographics, growing prevalence and lack of approved therapies to date, creates a market in dry-AMD primed for an innovative, blockbuster drug. Macuneos acts by preventing the photo-oxidative and inflammatory stresses induced by the accumulation of N-retinylidene-N-retinylethanolamine (A2E) in retinal pigment epithelial (RPE) cells, which are responsible for the retinal degeneration observed in AMD. While still several years away from market entry, pre-clinical proof-of-concept data in animal models have shown that Macuneos preserves retinal function and the number of photoreceptors in the eye. Biophytis plans to initiate a Phase 1 clinical trial (MACA-PK) to assess Macuneos safety and PK/PD in healthy volunteers in 2Q21, followed by a Phase 2a/b interventional study (MACA-INT) in patients with geographic atrophy (GA) in one eye and intermediate-stage AMD in the fellow eye. Following MACA-PK in early 2022, Biophytis also plans to explore clinical development of Macuneos for Stargardt disease, the most common form of inherited macular degeneration that typically develops in childhood.

Valuation and risks to price target achievement. Our valuation is based on our clinical net present value (NPV) model, which allows us to flex multiple assumptions affecting a drug's potential commercial profile. We currently value only Sarconeos and its two lead indications, sarcopenia and COVID-19; at this point we are not including Macuneos in our valuation to be conservative, though it has the potential to be a significant contributor to the valuation based on the lack of approved therapies for dry-AMD. Regarding Sarconeos, the two indications referenced contribute approximately 50% each to our valuation. For COVID-19, the revenue opportunity is much closer for the company where we project a 2022 launch and $525 million in peak sales in the U.S. What this does not take into account is: (1) the underlying risk of the need for COVID-19 therapies waning, though we believe the endemic properties of the virus should keep a baseline market for drugs; and (2) the potential recurring revenue opportunity for Sarconeos should any governments look to stockpile the asset and either increase the order over time, or re-up orders based on shelf life of the asset. With respect to sarcopenia, the addressable population is quite large, and therefore we believe that our projections are conservative. The biggest risk, in our belief, is what the regulatory path could look like regarding primary clinical endpoints as this indication continues to be relatively amorphous as to how a first-to-market drug might make it. To this end, we are projecting a 2026 launch off of a 55% chance of success and $1.2 billion in peak sales in the U.S. Moving forward, we believe upside potential to our valuation exists based on: (1) attaining higher market penetration than anticipated; (2) adding additional assets and indications to our valuation, such as Macuneos based on development stage and clinical data; and (3) augmenting projected chances of success based on clinical progress. Factors that could impede reaching our price target include failed or inconclusive clinical trials, the inability of the company to secure adequate funding to progress its products through the development pathway or the occurrence of dilutive capital raises, and lack of commercial success.

Company Background

Biophytis SA is a clinical stage biotechnology company focused on the development of therapeutics aimed at slowing the degenerative processes associated with aging and improving functional outcomes for patients suffering from age-related diseases, including severe respiratory failure in patients suffering from COVID-19. The company was founded in 2006 as a spin-off from Sorbonne University in Paris, where the company's medicinal plant drug discovery platform and collaboration was established. The Sorbonne remains a key partner, and is where the company still holds its offices and where part of the executive committee still remains. Since its founding, the company has focused on developing next-generation therapeutics based on phytochemicals, or compounds derived from plants. As a result, the company currently has two lead molecules, Sarconeos and Macuneos, which target sarcopenia and age-related macular degeneration (AMD), respectively. With regards to Sarconeos, given its mechanism of action, Biophytis has also developed clinical programs expanding its use to such indications as Duchenne Muscular Dystrophy (DMD) and COVID-19. . The company has a strong IP portfolio, with exclusive rights through licenses for each drug candidate and numerous patents issued in Europe, the U.S., China, Japan and South Korea, to date. Across its neuromuscular, respiratory and retinal disease indications, the company's patents cover drug candidate use and process, as well as compound composition and matter. In 2015, the company, based in France, launched an IPO onto Euronext. Earlier this year, the company had a successful IPO on the Nasdaq Capital Market on February 12, 2021, for total gross proceeds of $20.1M.

Biophytis Pipeline



Source: Company Presentation.

Upcoming Company Catalysts

Candidate	Timeline	Milestone	Impact*
Sarconeos			
COVID-19	1Q22	Phase 3 data from COVA study	+++
Sarcopenia	2021-2022	Regulatory feedback for pivotal program design	++
Sarcopenia	2022	Initiate Phase 3 pivotal study	+
DMD	2022	Initiate Phase 1-2-3 clinical program	+
Macuneos			
Dry-AMD	2021-2022	Additional preclinical data and initiate clinical program in dry-AMD	++
Stargardt	TBD	TBD	

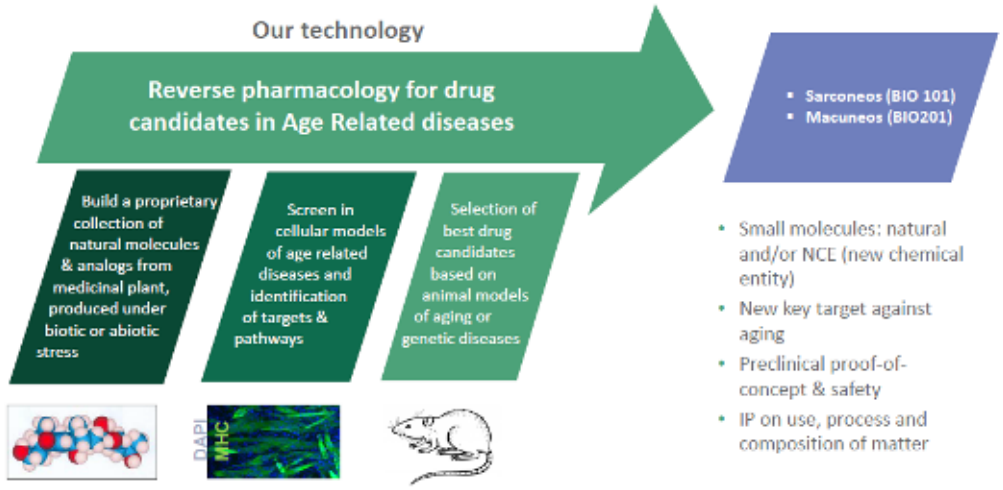
*Source: Company documents. *HCW assessment of milestone's potential to represent a meaningful stock catalyst.*

We Are Bullish on the Shares of Biophytis Based on the Following Six Factors:

1. **Powered by plants; utilizing the power of plants to identify drug discovery candidates for age-related diseases.**

Plants provide a vast reservoir of biologically active compounds, and many synthesize compounds of secondary metabolism including alkaloids and steroids. To this end, Biophytis has built a proprietary collection of natural molecules and analogs of secondary metabolites of plants to focus on degenerative medicine. Specifically, the company seeks to develop small molecules that stimulate biological resilience and can slow down degenerative processes associated with aging, selected by a reverse pharmacology approach, as depicted in the flowchart below.

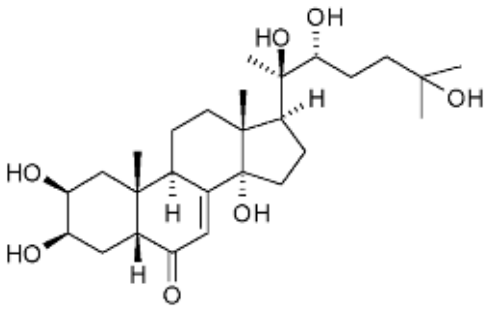
From Plant to Pipeline: Workflow From Screening to Clinical Development



Source: Company Presentation.

The company's lead candidate, Sarconeos is a pharmaceutical-grade (> 97% HPLC) preparation of the ecdysteroid 20E-hydroxyecdysone (20E) (chemical structure illustrated below). 20E is purified from the plant *Stemmacantha carthamoides*, a plant cultivated in China and used for medicinal purposes in traditional Chinese medicine. Though the active pharmaceutical ingredient (API) in Sarconeos belongs to the family of ecdysteroids, it does not interfere with the human hormone system since it is different from mammalian and human steroid hormones.

Chemical Structure of Sarconeos



Source: Company presentation.

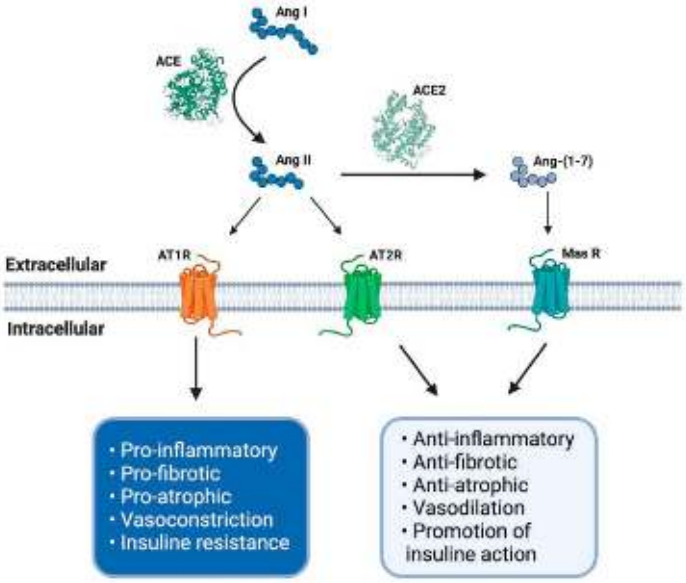
In light of today's global supply chain challenges, we do note that the company's current manufacturing supply chain could be susceptible to risk. In particular, through the use of an American CDMO there are several points along the chain which could pose an issue with successful completion of the full manufacturing process. Namely, the API supply chain goes through three separate countries; plant raw material from China, Austria for API, and finally France for drug formulation. Under normal circumstances this would not pose a significant risk, but we do take it into consideration in our evaluation.

2. A delicate balancing act; RAS is a complex cellular pathway targeted by Sarconeos.

The renin-angiotensin system (RAS) regulates a range of physiological processes including blood pressure, inflammation, carbohydrate metabolism, and fibrosis. It is a complex hormonal axis composed of several peptides that are generated by proteolytic cleavage mediated by RAS-specific enzymes. As illustrated in the schematic below, The RAS signaling pathway is formed by two different axes that counterbalance each other: 1) the "classical" arm through the principal peptide effector Angiotensin II (Ang II) and the G-protein-coupled receptors (GPCRs) angiotensin type I (AT1R) and type 2 (AT2R) receptors, which promotes harmful effects such as inflammation, vasoconstriction, and atherogenesis; and 2) the "non-classical" or ''protective'' arm through the G-protein-coupled MAS receptor and its ligand angiotensin (1-7) (Ang-1-7), which promotes beneficial effects such as vasodilation, and anti-fibrotic and anti-atrophic effects in skeletal muscle cells (Rivera JC *et al*., *Int J Mol Sci.* 2020).

Within the classical arm, the Ang I peptide is converted to Ang II via the proteolytic action of the RAS enzyme, angiotensin-converting enzyme (ACE). Upon conversion, Ang II can bind to the respective AT1R and AT2R receptors. These two receptors play contrasting roles in regulating physiological functions. Upon activation, AT1R-dependent Ang II could result in a signaling cascade that leads to pro-inflammatory consequences, while AT2R-dependent Ang II stimulation promotes downstream anti-inflammatory effects, among other beneficial cellular consequences highlighted below. Within the protective arm, the ACE2 enzyme converts Ang II to Ang-1-7, which mediates beneficial cellular effects through the MAS receptor and promotes similar biological consequences as the AT2R-mediated actions. This axis can increase the activity of such pathways as phosphatidylinositide 3-kinase (PI3K)/protein kinase B (Akt)/mammalian target of rapamycin (mTOR)-p70S6K, favoring protein synthesis, and the AMP-activated protein kinase (AMPK) pathway, promoting increased energy production.

The RAS System and Its Physiological Functions



Source: Gonzalez et. al.,Int. J Mol. Sci. 2020.

Through preclinical studies, the company has linked its lead candidate's activity to the MAS receptor within the protective arm of RAS signaling. RAS dysfunction has been implicated in various pathologies including cardiovascular disease, respiratory failure, inflammation and muscle wasting. As the downstream effectors of this pathway are implicated in wide-ranging cellular processes, the mechanism of action of Sarconeos provides Biophytis an opportunity to go after multiple indications with the same asset, or the proverbial 'pipeline in a drug'.

3. Sarconeos – addressing a very large unmet need in sarcopenia.

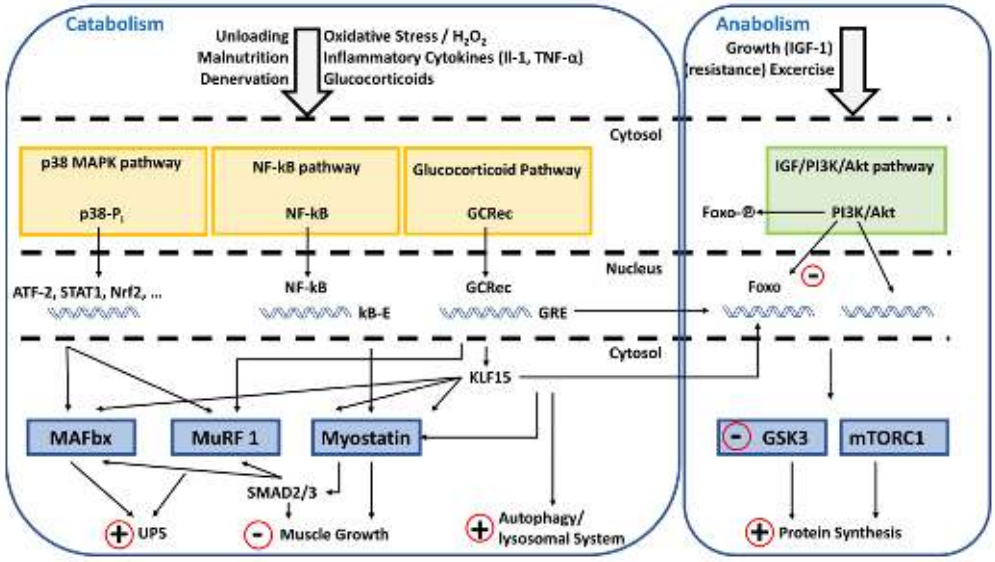
Aging is an inevitable process that involves a progressive multisystem derangement leading to increased risk of developing negative health outcomes. Aging affects almost every organ in the human body including the skeletal muscle, a type of muscle that is under voluntary control and works together with the nerves and the brain as part of the neuromuscular system. Age-related degeneration of the skeletal muscle is defined as sarcopenia and it involves loss of muscle mass, loss of muscle strength and reduced physical performance (Rosenberg IH, *Summary comments. Am J Clin Nutr.* 1989). Muscle mass and strength reach their peaks in early adulthood, followed by a gradual decline after the age of 40 years and a substantial decline after the age of 50 years and onwards. Total muscle mass may decrease by nearly 50% between the ages of 20 and 90 years (Lang T *et al.*, *Osteoporos.* 2010). Sarcopenia is mainly present in the elderly population (greater than 65 years old) with an estimated global prevalence range between 6 to 22% depending on the age-range and is associated with increased risk of adverse health events and hospitalizations, and potential deaths resulting from falls, fractures, and physical disability.

Several lifestyle habits have been identified to play a role in the onset and progression of sarcopenia: low protein diet, poor physical activity, excessive alcohol consumption or cigarette smoking. However, the pathophysiology of the disease and the molecular mechanisms underlying the disease progression are not completely understood. The development of sarcopenia might be the consequence of an imbalance between muscle protein synthesis and degradation, also known as proteostasis, which results in skeletal muscle loss. This can happen due to no other cause expect aging, with subsequent increased apoptosis, increased mitochondrial dysfunction, increased oxidative stress, reduced stem cell proliferation or

uncoupled signaling pathways influencing the synthesis and the breakdown of muscle proteins (Park SS *et al.*, *Osteoporos Sarcopenia*. 2017, Wiedmer P *et al.*, *Ageing Res Rev*. 2021).

The maintenance of skeletal muscle mass depends on the balance between protein synthesis and degradation, which are regulated by anabolic and catabolic pathways, respectively (below). The main anabolic signals in skeletal muscle are exercise and insulin-like growth factor 1 (IGF-1). When IGF-1 binds to its receptor, the Akt pathway is activated leading to increase protein synthesis by inhibiting the glycogen synthase kinase-3 (GSK3) and mTOR, and decrease protein degradation by inactivating the O-type fork head box (FOXO) transcription factor. In contrast, catabolic stimuli such as malnutrition, denervation, oxidative stress, and inflammatory cytokines increase protein degradation via two principal pathways: the p38 mitogen activated protein kinase (MAPK) pathway and the nuclear factor-kappa B (NF-κB) pathway. Additionally, glucocorticoids can directly affect catabolic gene promoter regions. Activation of NF-κB pathway stimulates the secretion of myostatin, a negative regulator of muscle growth by inhibiting Akt pathway. In parallel, myostatin binds the activin type two receptors (ActRIIA/B) and activates SMAD transcription factors which downregulate genes involved in muscle regeneration (Wiedmer P *et al., Ageing Res Rev.* 2021).

Major Signaling Pathways Regulating Muscle Protein Degradation and Synthesis



Source: Wiedmer P et al., Ageing Res Rev. 2021

Sarcopenia poses a major public health issue and is steadily increasing as the global population ages. According to the United Nations World Population Prospects (2017 revision), the global population of people over the age of 60 is expected to be $2 billion by 2050. In accordance, healthcare and long-term care costs for age-related diseases associated with this demographic shift, are expected to rise proportionally. There is currently no consensus for a standard of care to treat sarcopenia. Recommendations primarily focus on lifestyle habit changes for overall health benefits, such as physical activity or strength training, and nutritional intervention. Since effective treatment options for sarcopenia are lacking, medication is not the preferred choice for sarcopenia.

Age-related decrease of circulating levels of anabolic hormones may contribute to changes in muscle mass and function in older individuals. Hormone therapies with testosterone or selective androgen receptor modulators (SARMs) have formed the basis of many of the therapies for sarcopenia investigated to date.

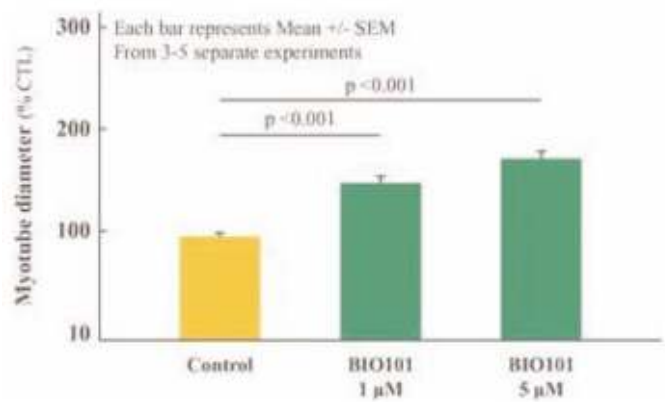
Testosterone increases skeletal muscle mass by promoting hypertrophy of muscle myofibers. However, testosterone treatment is associated with side effects such as elevated prostate-specific antigen (PSA) levels linked to prostate cancer (Srinivas-Shankar U *et al*., J Clin Endocrinol Metab. 2010). Similarly, trials evaluating the SARMs enobosarm (Dalton JT *et al*., *J Cachexia Sarcopenia Muscle*. 2011) or MK-0773 (Papanicolaou DA *et al*., *J Nutr Health Aging*. 2013) reported an increase in total lean body mass and a trend towards improved physical performance over the follow-up period with no statistical significance. Overall, hormonal manipulation did not demonstrate effectiveness on clinically meaningful outcomes such as strength and mobility and have not advanced in the regulatory process (Dennison EM *et al*., *Rev Rheumatol*. 2017).

Latest drug development approaches to treat sarcopenia focus on targeting myostatin, also known as growth differentiation factor-8 (GDF-8). Myostatin is mainly expressed in skeletal muscle cells and inhibits muscle growth through binding with ActRIIA/B (McPherron AC *et al*., *Proc Natl Acad Sci USA*. 1997). Findings from a study investigating LY2495655/landogrozumab, a humanized monoclonal antibody against myostatin in older individuals who have fallen and have muscle weakness, reported that patients under treatment showed increased appendicular lean mass and improved stair climbing time, chair rise with arms, and fast gait speed but failed to improve overall physical performance (Becker C *et al*., *Lancet Diabetes Endocrinol*. 2015, Woodhouse L *et al*., *J Frailty Aging*. 2016). Similarly, a study investigating the potential benefit of BYM338/bimagrumab, which binds ActRIIA/B, in older adults with sarcopenia, found no significant difference between the treatment arm and the placebo group who had six months of adequate nutrition and light exercise. Since physical function was comparably improved in both groups, the study concluded that the effects of sarcopenia can be reduced with proper diet and exercise (Rooks D *et al*., *JAMA Netw Open*. 2020).

As previously mentioned, there are no approved medications for sarcopenia. Clinical trials of SARMs and myostatin inhibitors have been suspended due to lack of evidence of benefit in several studies. Therapeutic development focuses mostly on exercise mimetics, food supplements and dietary measures. Preclinical development of cell therapy and agents that aim to improve muscle function are ongoing, but these have not yet reached human studies. Sarconeos provides a unique approach for the treatment of sarcopenia, activating the anabolic pathway in the muscle.

Sarconeos for Sarcopenia . As previously mentioned**,** pharmacological strategies to prevent and reverse sarcopenia have been largely unsatisfactory and have raised the need to identify novel targets for the development of more effective drugs. Experimental and clinical studies have provided interesting insights on the role of the RAS as a metabolic and regenerative regulator of the skeletal muscle (Sartiani L *et al*., *Clin Cases Miner Bone Metab*. 2015). Preclinical data in C2C12 human myoblasts showed that Sarconeos enlarges myotubes, the main structural units of muscle, a key feature for limiting muscle mass loss and increasing muscle strength (below).

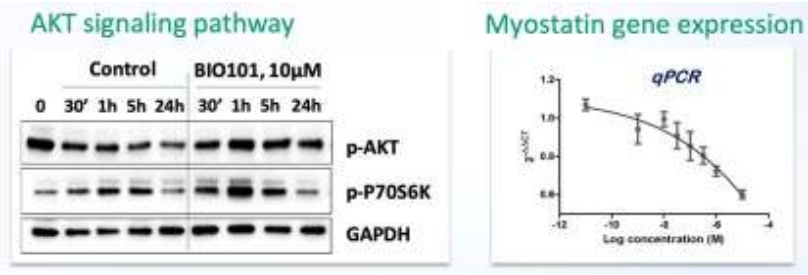
Sarconeos Enlarges Myotubes

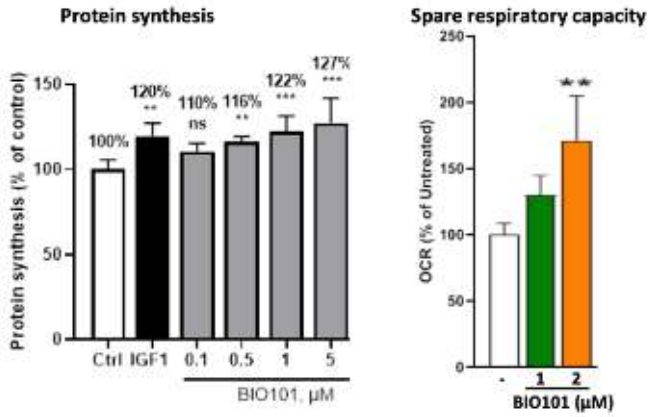


Source: Company presentation.

At the molecular level, Ang-1-7 through MAS receptor, activates the Akt pathway, which prevents the detrimental effects of the classical RAS axis on muscle atrophy (Cisternas F *et al.*, *Clin Sci (Lond).* 2015). In addition, signaling through the AMPK pathway suppresses the expression of AT1R and inhibits the classical RAS pathway, while the expression of MAS receptor and the RAS protective arm is increased (Liu J *et al.*, *Biosci Rep.* 2019). As shown below, Sarconeos stimulates AKT and AMPK signaling pathways (top left figure), and inhibits myostatin gene expression *in vitro* (top right figure), important steps to increase protein synthesis. Accordingly, Sarconeos leads to a significant increase in protein synthesis (bottom left figure), and mitochondrial spare respiratory capacity in differentiated human muscle cells (bottom right figure).

Sarconeos Stimulates Signals for Protein Synthesis *In Vitro*

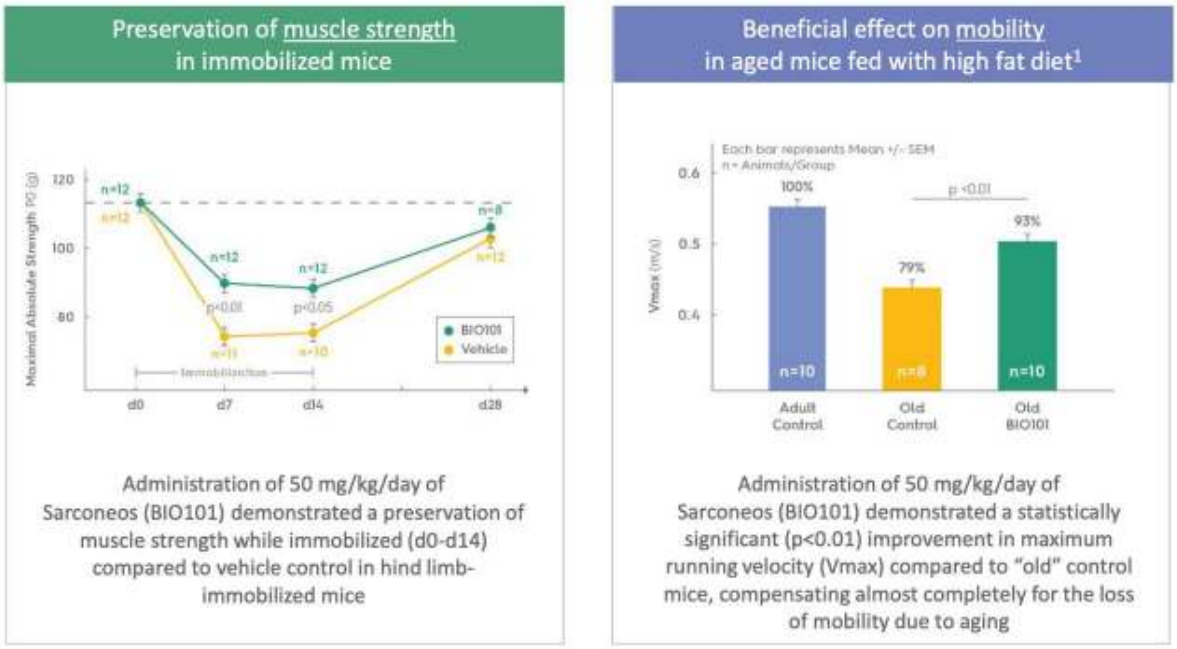




Source: Company presentation.

To model muscle wasting associated with impaired mobility, Biophytis performed *in vivo* experiments where young mice (13 weeks old) were immobilized and administered either Sarconeos at 50 mg/kg/day or a placebo. After 14 days, the immobilization was removed and administration of Sarconeos was continued for additional 14 days. The absolute strength of hind limb muscle was recorded at various times over the 28-day period. Mice treated with Sarconeos demonstrated preservation of muscle strength while immobilized compared to the placebo controls. In order to determine any effects on mobility, Sarconeos was administered (50 mg/kg/day or a placebo) to ''old'' mice (22 months old) that were fed a high-fat diet over 14 weeks. The mice were exercised on a treadmill and maximum running velocity (Vmax) was recorded. Interestingly, results showed that ''old'' mice receiving Sarconeos showed a significant improvement in Vmax, compared to ''old'' control mice ($p < 0.01$), compensating almost completely for the loss of mobility due to aging (below).

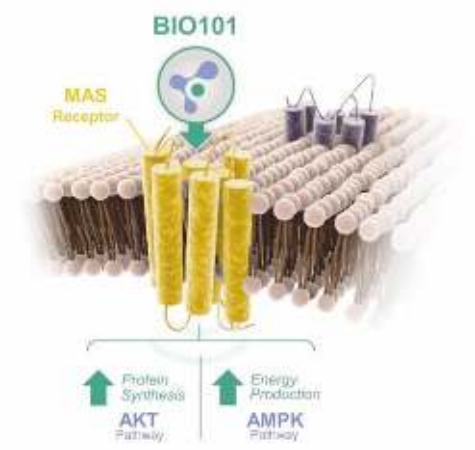
Sarconeos Improves Muscle Strength and Mobility in Mice



Source: Company presentation.

Based on the results from cellular function *in vitro* and from muscle performance *in vivo*, Biophytis believes that Sarconeos improves muscle function and preserves muscle strength and mobility through the activation of the MAS receptor, the protective arm of the RAS. The activation of the MAS Receptor through Sarconeos triggers AKT and AMPK signaling, two key downstream pathways that preserve muscle mass and increase muscle strength under muscle wasting conditions (below).

Sarconeos Mechanism of Action in Skeletal Muscle



Source: Company presentation.

SARA-PK: Phase 1 Study of Sarconeos for Sarcopenia. Biophytis conducted a dose-escalation Phase 1 clinical trial (SARA-PK) to evaluate the safety, pharmacokinetic (PK) and pharmacodynamic (PD) effects of orally administered Sarconeos in 54 healthy adult and elderly volunteers. In the single ascending dose phase, 24 subjects were dosed once with Sarconeos at a range between 100 to 1,400 mg or placebo and no abnormal clinical vital signs or serious adverse events (SAEs) were reported as treatment emergent adverse events (TEAEs). All TEAEs were mild in severity and were resolved by the end of the study. The multiple ascending dose phase included 30 patients who received Sarconeos over 14 days divided into the three groups depicted below, each group consisting of eight active and two placebo per dose. No abnormal clinical vital signs or SAEs were reported. The most common TEAEs were headache and nausea, and were resolved by the end of the study.

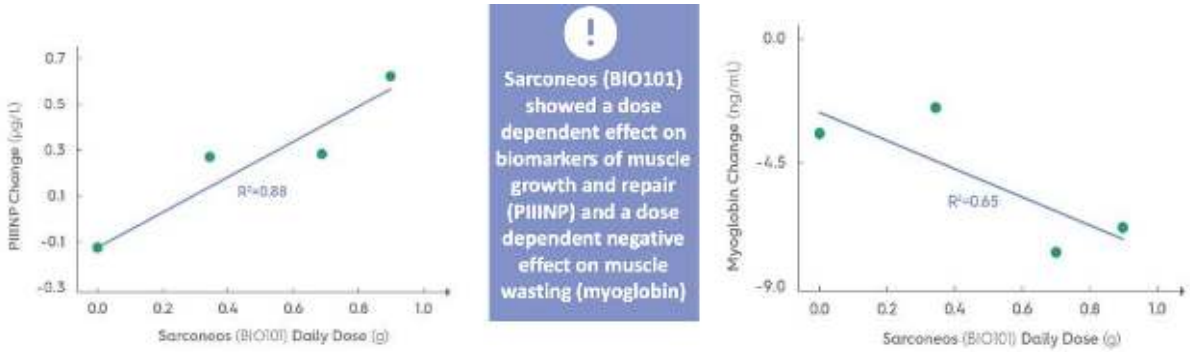
SARA-PK: a Multiple Ascending Dose Study

Source: Company presentation.

The PK analysis determined Sarconeos half-life between three to four hours and a steady state from the second day of administration. No accumulation of the drug was observed in the body at 350 mg qd (accumulation ratio of 1.14). However, a small accumulation was observed at 350 and 450 mg bid (accumulation ratio of 1.31) and therefore, 175 and 350 mg bid were determined as safe and active dosing levels. PD results showed a tendency towards decreased plasma levels of muscle catabolism markers (myoglobin, creatine kinase) and markers of the RAS (aldosterone and renin). Accordingly, Sarconeos treatment over 14 days showed a dose-dependent positive effect on plasma procollagen type III n-terminal peptide (PIIINP) levels, a marker of muscle growth, repair and fibrosis, and a dose-dependent negative

correlation with plasma myoglobin, a marker of muscle catabolism (below). These results align with the proposed mechanism of action of Sarconeos on the RAS activation.

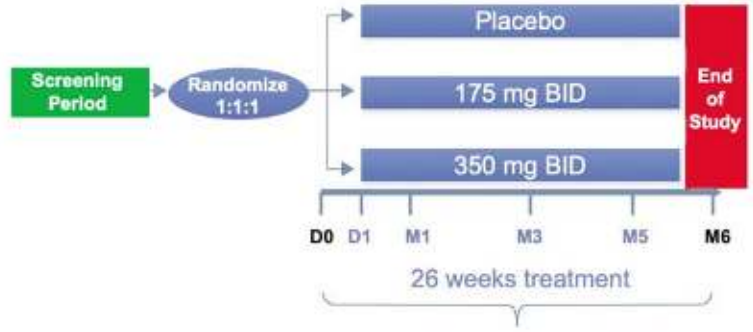
Sarconeos Favors Muscle Growth Versus Muscle Waste



Source: Company presentation.

SARA-INT: Phase 2 Study of Sarconeos for Sarcopenia. Biophytis conducted a Phase 2 clinical trial (SARA-INT) to determine the safety and efficacy of Sarconeos for the treatment of age-related sarcopenia, leading to muscle atrophy and mobility disability (NCT03452488). SARA-INT was a global, double-blind, placebo-controlled study, which included 233 participants enrolled in 22 centers in the USA and in Belgium, who were randomized to 175 mg bid or 350 mg bid or placebo, determined by the Phase 1 SARA-PK study, and followed-up up to six months (adjusted to nine months due to visit restrictions during COVID-19 pandemic) (below). Recruitment for SARA-INT was completed in March 2020 and the last patient completed his final on-treatment visit in December 2020.

SARA-INT Phase 2 Trial Randomization Strategy



Source: Company presentation.

Participants were included on the study based on age (> 65 years old), low Appendicular Lean Mass (ALM) relative to Body-Mass Index (BMI), reduced mobility assessed by the Short Physical Performance Battery index (SPPB ≤ 8), and exercise for least 30 minutes during five days every week. The primary end-point of the efficacy study was gait-speed over the 400-meter walk test (400MWT) in the Full Analysis Dataset (FAS; all randomized 233 participants) and in the Per-Protocol population (PP, subset of 152 participants that complied to the clinical protocol), which represents a measure of the participant's mobility function. A minimum clinically significant benefit is set at 0.10 meter per second (m/sec) in the mean difference between groups. The key secondary end-points were: 1) the chair-stand test, which is one of the mobility criteria that make up the SPPB test; 2) the analysis of the six-minute walking distance test (6MWD); and 3) patient reported outcomes (PROs) as evaluated by the short-form health survey (SF-36 questionnaire), including

the Physical Function domain (PF-10) of the questionnaire (below). Additionally, pre-defined subgroup analyses were performed: 1) a ‘‘very low walking speed subpopulation,’’ defined as having a gait-speed of 0.8 m/sec in the four-meter walk test, a component of the SPPB; 2) ‘‘subpopulation with sarcopenic obesity’’ defined by a body fat percentage of >25% for men and >35% for women; and 3) participants with a chair-stand sub-score of ≤2.

SARA-INT Phase 2 Trial Overview

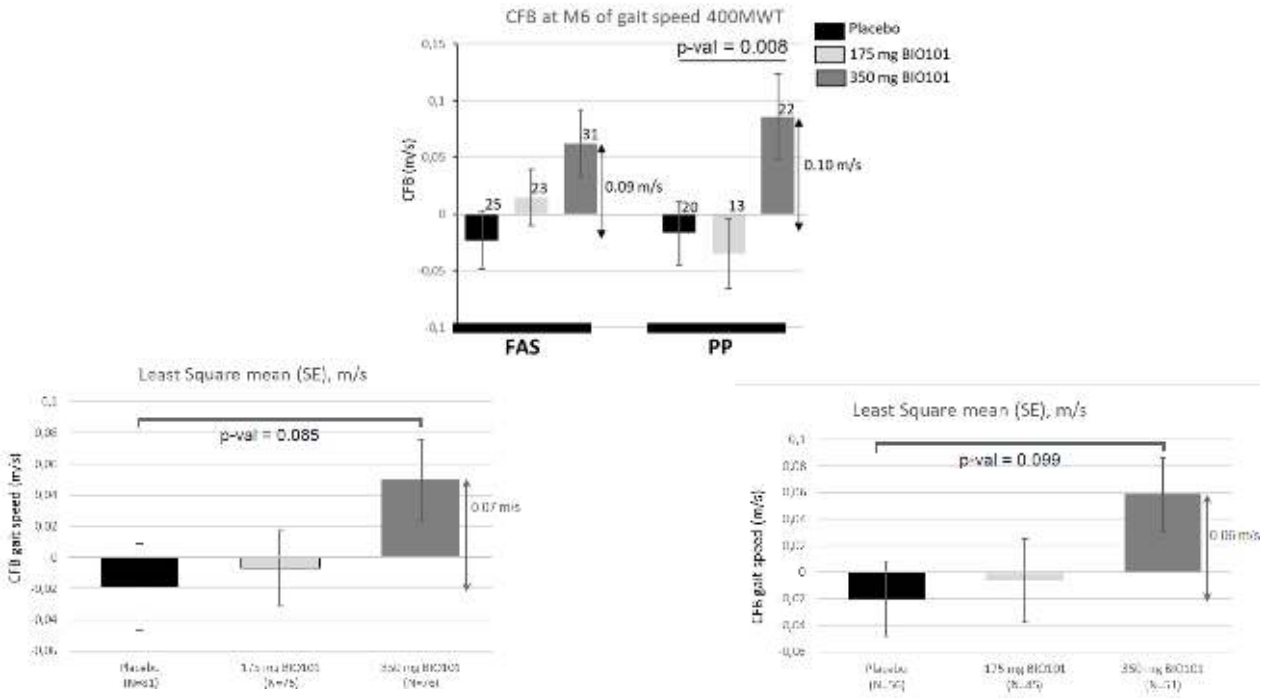
Design	Endpoints	Patient Population
• Global, double-blind, randomized, placebo-controlled trial: NCT03452488 • Assess safety and efficacy of two doses of Sarconeos (BIO101) administered orally with a meal over 26 weeks, as compared to placebo • Treatment effect on improvement of physical function and on decrease of risk of mobility disability	**Primary** • 400-meter walk test (400MWT) - 0.05 m/s is considered the minimal meaningful change **Secondary** • Handgrip muscle strength • Patient reported outcomes (PRO)	• Age: 65 years old or over • Low mobility measured by Short Performance Physical Battery (SPPB) ≤8 out of 12 • DEXA body composition as measured by ALM/BMI (appendicular lean mass / body mass index) • Able to exercise for 30 minutes per day 5 days per week

Source: Company presentation.

Biophytis reported full results from the phase 2 SARA-INT study at the 11th annual International Conference on Frailty and Sarcopenia Research (ICFSR) on October 4, 2021. We should remark that due to the pandemic restrictions, 34% of total participants from the FAS population (final n=79) and 36% from the PP population (final n=55) completed their end of study visit (EoS), despite the extension of their treatment period.

The analysis that included participants with recorded EoS, showed that the highest dose (350mg bid) of Sarconeos led to a clinically meaningful improvement of 0.10 m/s in the PP population (significant, p=0.008) and of 0.09 m/s in the FAS population (not significant) compared to placebo, for the 400MWT in gait speed after six months of treatment (below, top panel). This effect is close to the Minimal Clinically Important Difference (MCID) in sarcopenia (0.1 m/s) known to be associated with a reduction in mobility disability and mortality in elderly. Sarconeos at the lowest dose of 175 mg bid did not show a clinically meaningful difference compared to placebo in gait-speed neither in the FAS nor in the PP population. When the full FAS (n=232; below, bottom left panel) and the full PP (n=152; below, bottom right panel) populations were analyzed, the highest dose of Sarconeos tended to be close to MCID, although it did not reach statistical significance.

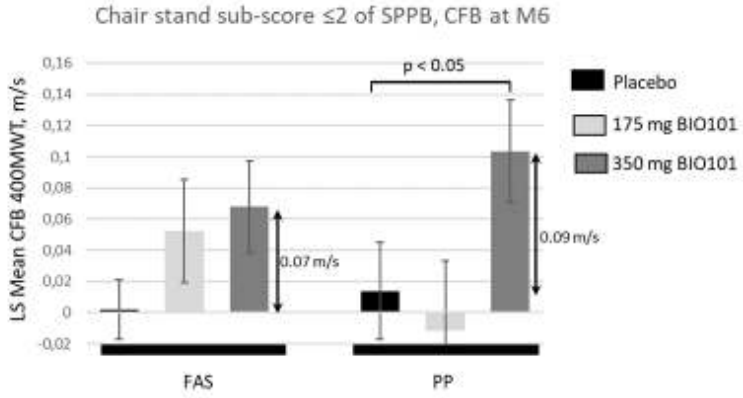
Sarconeos Improves Walking Ability



Source: ICFSR, 2021.

In the PP subpopulation studies with higher risk of mobility disability, Sarconeos at 350mg bid showed positive treatment effect on the 400MWT gait speed in slow walkers (0.07 m/s, p = 0.015), on the obese subgroup (0.09 m/s, p = 0.004), and on the subpopulation with a chair-stand sub-score of ≤2 of (0,09 m/s, p= 0.004), as shown below. These results suggest that the subgroups with higher risk of worsening seem to benefit more from the Sarconeos treatment.

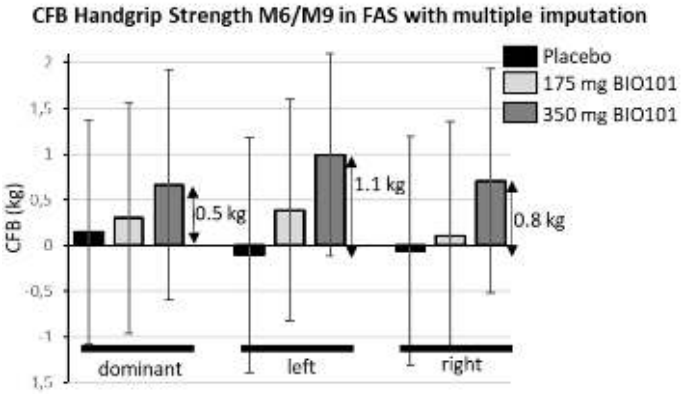
Sarconeos Improves Leg Strength



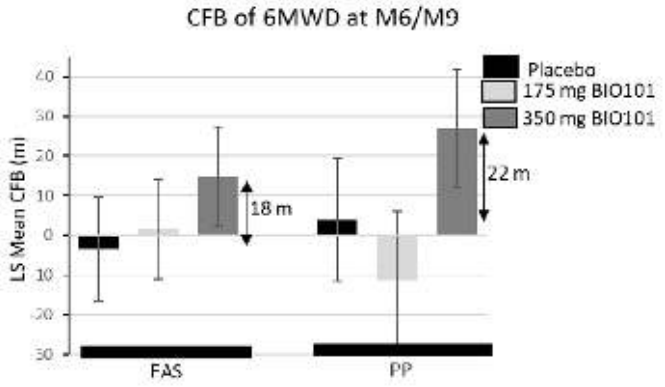
Source: ICFSR, 2021.

As depicted below, no treatment effect was detected on the handgrip strength test (top panel), on the PF10 score of the SF-36 PRO on mobility disability (middle panel), and on the 6MWD test (bottom panel), key secondary end-points of the study. Given the high level of variability observed and the difficulty to reach statistical significance for secondary endpoints, the efficacy of Sarconeos for the secondary end-points could not be concluded.

Secondary End-Point Analyses Reflect Variability But Not Efficacy



	Placebo	175 mg BIO101	350 mg BIO101
Mean PF-10 sub-score at baseline	53.1	50	50.5
LS Mean Square (SE) M6/M9	7.3 (2.5)	7.1 (2.64)	7.1 (2.51)



Source: ICFSR, 2021.

As summarized in the table below, Sarconeos showed a good safety profile after up to nine months of dosing, with no significant differences in adverse events (AEs) between the treatment arms and the placebo group. According to the investigators, none of the serious AEs were related to the product.

Sarconeos Presents a Good Safety Profile

Events	Placebo	175 mg BIO101	350 mg BIO101
# participants	81	75	74
Adverse Events (% of total events)	119 (36%)	123 (37%)	89 (27%)
Number of subjects with any AE	52	51	44
Serious Adverse Events (% of total events)	15 (45%)	14 (42%)	4 (12%)
Number of subjects with any SAE	10	10	4
Treatment Emergent Adverse Events (% of total events)	107 (38%)	101 (36%)	70 (25%)
Number of participants with any TEAEs	48	45	38
Treatment related TEAEs (% of total events)	24 (44%)	15 (27%)	16 (29%)
Number of participants with any treatment related TEAEs	13	10	10
Treatment related Serious TEAEs	2 (100%)	0	0

Source: ICFSR, 2021.

Although COVID-related visit restrictions may have negatively impacted the power of the study and the subsequent analyses, Sarconeos is the first drug candidate to complete a Phase 2 trial with clinically meaningful outcome on mobility. Biophytis plans to start a Phase 3 trial in 2022E with its lead candidate targeting a population of sarcopenic patients at high risk of mobility disability.

4. Stepping up in a world crisis; Sarconeos in clinical development for respiratory infections associated with COVID-19.

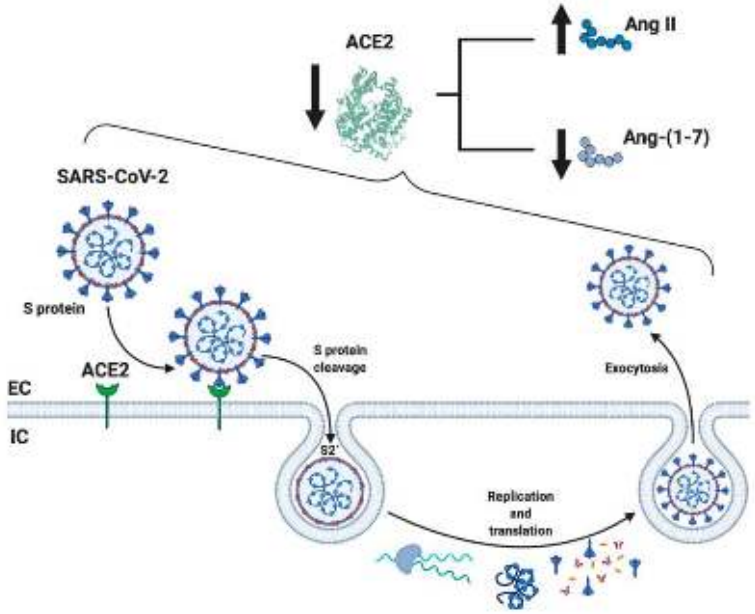
The current severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic, named COVID-19, has resulted in an unprecedented sense of urgency for the development of therapies across numerous companies. In addition to its regulation of myocytes, the Sarconeos-mediated activation of MAS receptor also plays a key role in respiratory functions. Acute Respiratory Distress Syndrome (ARDS) is a hallmark of severe COVID-19 cases. As such, an opportunity to expand into the emerging COVID-19 space was leveraged and Sarconeos is under development as a treatment for respiratory complications, such as pneumonia, following COVID-19 infection.

Sarconeos-mediated activation of MAS receptor as a therapy for respiratory failure in COVID-19. Studies have now shown that SARS-CoV-2 enters the host cell via the ACE2 receptor, which is abundant in microvasculature-rich tissues, including the lungs, being highly expressed endothelial as well as epithelial cells. (Ni et al., *Crit Care,* 2020). In addition, ACE2 is widely expressed in the cardiovascular system, gut, kidneys, CNS and adipose tissue. While respiratory symptoms are predominant, insults to the other aforementioned organ systems have also been documented in COVID-19 patients.

Under physiological conditions, ACE2 is upregulated through a negative feedback mechanism by blocking AT1R, leading to lung protection from virus damage, likely attributable to ACE2 catalyzing Ang II conversion to Ang-1-7 (Wosten-van Asperen et al., *J Pathol.* 2011). When SARS-CoV-2 enters human cells, the interaction of SARS-CoV-2 with ACE2 downregulates the surface expression ACE2 protein, likely due to the enzyme endocytosis complex with virus protein S. This interaction impairs ACE2 activity, rendering the enzyme inactive and ultimately leading to the dysregulation of the RAS, as illustrated in the figure below (Gonzalez et al., *Int. J. Mol. Sci.,* 2020). The ACE2/Ang-1-7/MAS axis (“protective” RAS) counteracts the negative effects of the ACE/Ang II/AT1R axis (“classical” RAS). Through its spike protein, SARS-CoV-2

uses ACE2 to penetrate the lungs and thereby inhibit the protective arm of the RAS signaling axis, increasing the activation of the classical RAS pathway (ACE/Ang II/AT1R), inducing a pro-fibrotic and pro-inflammatory state, vasoconstriction, increased membrane permeability, and apoptosis of lung epithelial cells. Specifically, the ACE2 downregulation, as a result of SARS-CoV-2 binding, enhances the classical RAS arm, leading to lung damage and inflammation with leaky pulmonary blood vessels and fibrosis when the attenuation mediated by the RAS protective arm is reduced (Sarzani et. al., *Am J Physiol Lung Cell Mol Physiol.,* 2020).Taken together, this situation could induce respiratory failure in the form of ARDS.

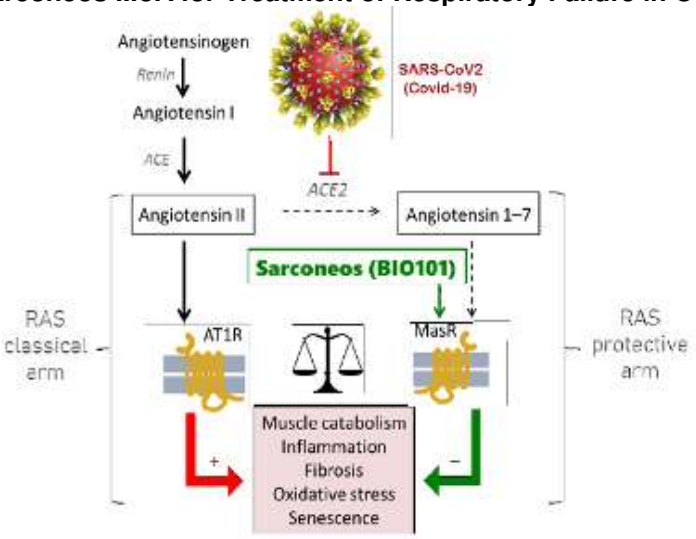
RAS Dysregulation and its Relationship With COVID-19



Source: Gonzalez et. al., Int. J. Mol. Sci. 2020

Enter Sarconeos, which activates the MAS receptor, a key component of the protective arm of the RAS system, and thereby potentially restoring equilibrium between the two RAS arms to mitigate the respiratory distress associated with COVID-19 (as depicted in figure below).With Ang-1-7 being the natural ligand for the MAS receptor, Biophytis has as an opportunity to reactivate respiratory capacity and compensate for the reduction of Ang-1-7 in SARS-CoV-2 with Sarconeos.

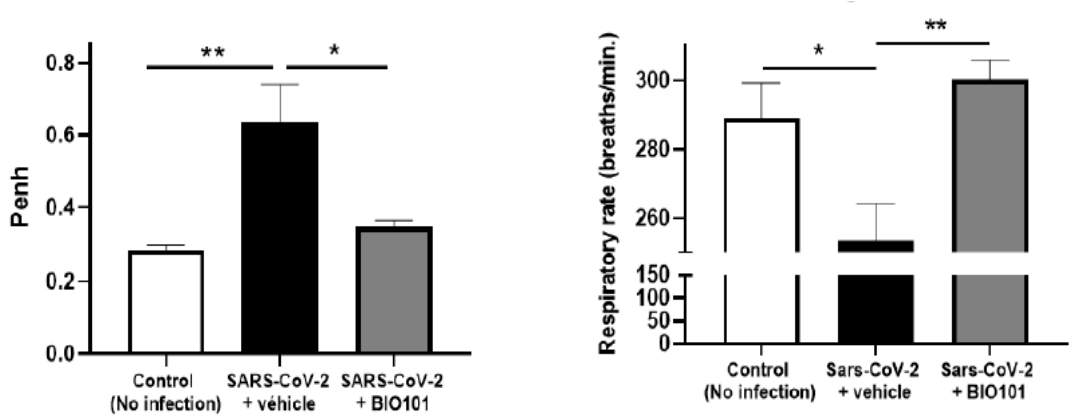
Sarconeos MoA for Treatment of Respiratory Failure in COVID-19



Source: Company Presentation.

Preclinical data suggest that Sarconeos improves respiratory functions in animal models. Using mouse and hamster models, Biophytis has demonstrated significant benefits of treatment with Sarconeos on various respiratory parameters, providing a positive proof-of-concept for further clinical development. Depicted in the figure below are the results of a study evaluating respiratory functions of SARS-CoV-2 infected golden Syrian hamsters after Sarconeos treatment. This animal model harbors a high degree of homology with humans within the region of the ACE2-binding domain of SARS-CoV-2 and is also susceptible to SARS-CoV-2 infection (Chan et al., *Science*, 2020). In this model, six seven-week-old hamsters were inoculated intranasally with SARS-CoV-2 and Sarconeos was administered intraperitoneally daily for seven days. Five days post-infection pulmonary function was assessed using various functional readouts. Two of the key metrics are shown below, including the Enhanced Pause (Penh) (left panel), which is a classically used and derived measure of respiratory distress (Hamelmann et al., *Am. J. Respir. Crit. Care Med.*, 1997). The below results indicate that Sarconeos treatment significantly attenuates respiratory distress, as measured by Penh metrics. Breathing frequency/respiratory rate were also significantly improved in SARS-CoV-2 infected hamsters treated with Saraconeos (right panel below).

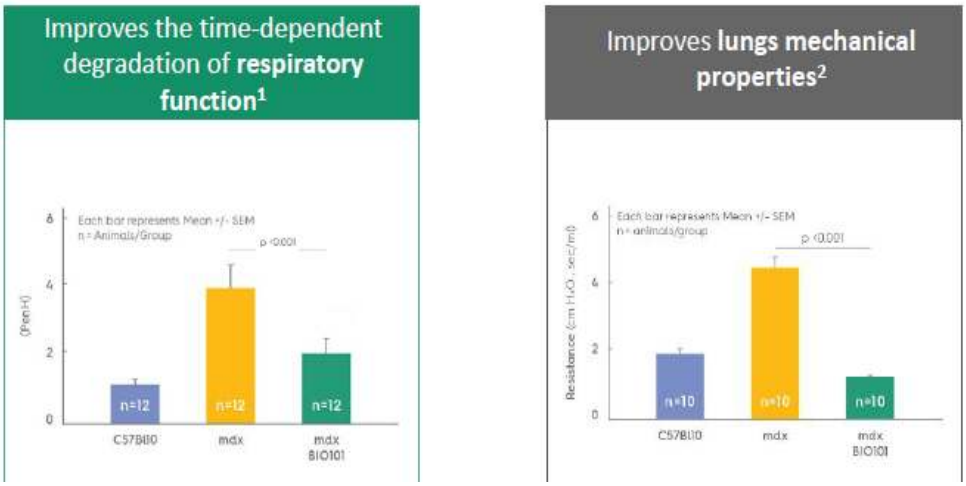
Respiratory Function Evaluation 5 Days After SARS-CoV-2 Infection in Hamsters



Source: Latil et.al; ECCMID 2021

Another *in vivo* model of the clinical benefit of Sarconeos on SARS-CoV-2 mediated respiratory distress is highlighted in the mouse model experiments below. Treating C57BL10-*mdx* mice (an established mouse model used for Duchenne Muscular Dystrophy), with 50 mg/kg/day of Sarconeos over the course of eight weeks showed an improvement in airway responsiveness (Penh) compared to untreated control C57BL10-*mdx* mice (left panel) as well as significantly improving lunch mechanical properties, as measured by airway resistance (right panel). Taken together, these preclinical data suggest that Sarconeos improves respiratory functions and pave the way forward for further clinical development.

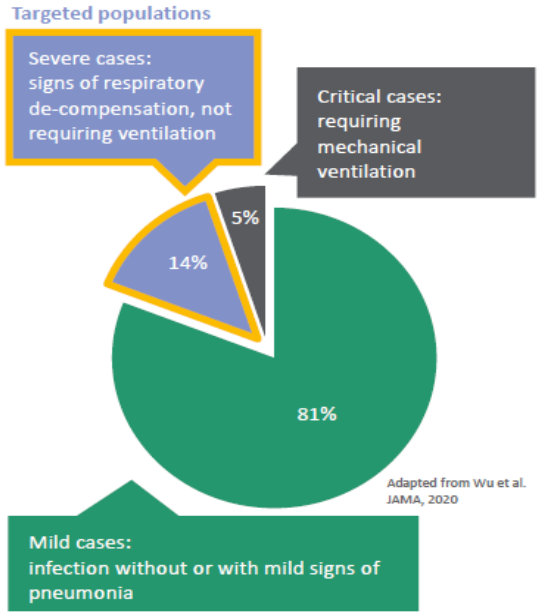
Respiratory Function Evaluation After 8 Weeks of Treatment With Sarconeos



Source: Company Presentation.

Clinical program currently in Phase 2/3 with promising efficacy results. Given the strength of the preclinical data, the company launched the clinical evaluation of Sarconeos in the treatment of ARDS associated with COVID-19 in April 2020. The Phase 2/3 clinical trial first started in France and then extended to other global sites, including Belgium, Brazil and the United States. As a drug candidate, Sarconeos has already demonstrated a positive safety profile during the SARA development program for sarcopenia (described above). The ongoing COVA trial is a global, multicenter, double-blind, placebo controlled, group sequential and adaptive two-part Phase 2/3 study in participants with SARS-CoV-2 pneumonia evaluating prevention of further respiratory deterioration linked to COVID-19. The study targets hospitalized patients, aged 45 years old and above, with proven COVID-19 and severe respiratory symptoms with evidence of respiratory decompensation for seven or less days prior to the start of Sarconeos treatment and meeting one of the following criteria: 1) tachypnea: ≥25 breaths per minute; or 2) arterial oxygen saturation of ≤92%. During the course of study treatment, patients are allowed to also take antiviral agents including Remdesivir and Bamlanivimab, as well anti-inflammatory medications such as Dexamethasone. Study participants are given 350 mg bid of Sarconeos capsules daily for up to 28 days while hospitalized or until a clinical endpoint is reached (Dioh et. al 2021). The COVA study target patient population, as illustrated in the chart below, makes up about 14% of COVID-19 hospitalized patients; they are classified as severe but not yet requiring mechanical ventilation, and thus with the addition of Sarconeos could potentially prevent ICU admission, which remains one of the major burdens on the healthcare system during this pandemic.

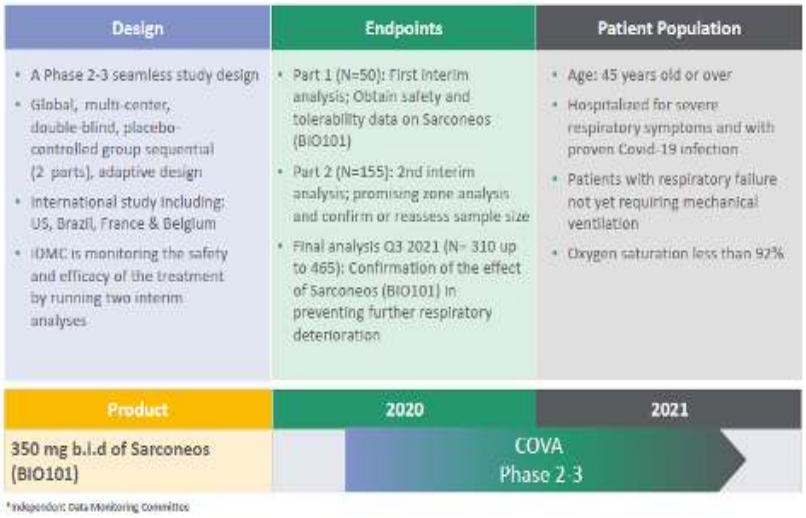
COVA Study: Targeting Hospitalized Patients With Respiratory Failure, and Not Intubated



Source: Company Presentation.

The primary endpoint of the COVA study is the proportion of patients with either all-cause mortality or respiratory failure, and the key secondary endpoint is the proportion of patients who are discharged home. As the table outlining study design and baseline characteristics below indicates, patients in the COVA study are enrolled in two parts, per the recommendation of an independent data monitoring committee (iDMC). As such, there have been two interim analyses evaluating safety and efficacy. The first interim analysis (Part 1 Phase 2 exploratory Proof of Concept) focused on safety and tolerability data from 50 patients and was performed during 1Q20 and based on the results, facilitated patient recruitment for Part 2. Part 2 is a Phase 3 pivotal randomized study to provide further evidence of safety and efficacy of Sarconeos after 28 days of double-blind dosing. More recently (September 15, 2021), the second interim analysis evaluated 155 patients, and the iDMC recommended the COVA study to continue without modifications based upon efficacy results being in the promising zone.

COVA Phase 2/3 Study Design, Endpoints and Target Patient Population



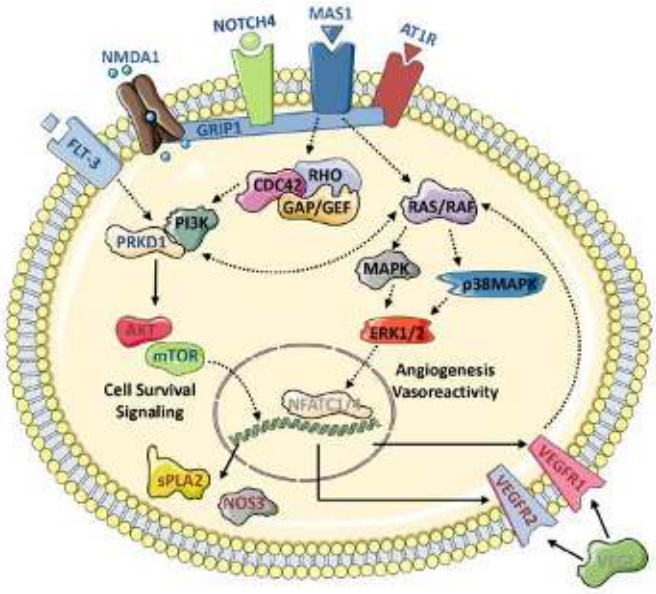
Source: Company Presentation.

COVID-19 second wave has accelerated patient enrollment, with plans for EUA submission quickly approaching. As of September 2021, over 200 patients have been enrolled across 34 sites with a goal of enrolling over 300 (and up to 465) patients by YE21. The company expects to report final topline data from the full COVA study in 1Q22. In anticipation of positive COVA results, the company has scaled up manufacturing operations with a major global CDMO to increase potential supply of Sarconeos. The company could look for EUA in the US and Conditional Approval in Europe as of 2Q22, with potential for early marketing/commercialization for Sarconeos in COVID-19 by 1H22. Though this remains a challenging and dynamic space, the current pandemic has created an environment where finding new therapeutic interventions is imperative. Given the severity of the associated death risk with ARDS, Biophytis could stand to benefit from the same regulatory pathway as Gilead with Remdesivir. Pending topline data and regulatory feedback, Biophytis stands to make rapid progress in the development of its COVA clinical program.

5. Mitochondrial dysfunction is central to DMD progression; enter Sarconeos as a stimulator of mitochondrial activity.

Duchenne muscular dystrophy (DMD) is a 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. DMD affects approximately 2.8 out 100,000 people worldwide (approximately 20,000 new cases annually worldwide). DMD progression is sequential, non-linear and irreversible. DMD develops as a result of a mutation in the X-linked gene *DMD* encoding dystrophin. Deletion mutations in one or more exons of the *DMD* gene shift the translational reading frame and create a premature stop codon, and as a result prohibit dystrophin production. Dystrophin normally protects contracting muscles from injury. Therefore, the absence of dystrophin exposes both skeletal and cardiac muscles to degenerative and regenerative cycles, which ultimately leads to the activation of apoptosis, inflammation, and fibrosis. As a result, muscle degeneration processes become prominent and inhibit regeneration cycles leading to a dramatic muscle fiber loss and the progressive decrease of skeletal, including of the respiratory muscles and ultimately cardiac muscle function until death. Currently, there is no known cure for DMD and treatment option are limited, including corticosteroids and targeted therapies (exon-skipping the U.S. and stop codon in the E.U.). These treatments target about 20% of DMD patients that harbor specific genetic mutations, leaving many patients, primarily those suffering from respiratory function defects, with an unmet medical need. Specific intracellular signaling pathways implicated in both anabolism (Akt/mTOR) and regeneration (MAPK), among others, contribute substantially to the degenerative process in DMD. Of note, both of these pathways feed through the MAS receptor (as illustrated below).

MAS Receptor-Dependent Activation of MAPK Signaling Pathway



Source: Hoffman et. al., Arterioscler Thromb Vasc Biol 2015.

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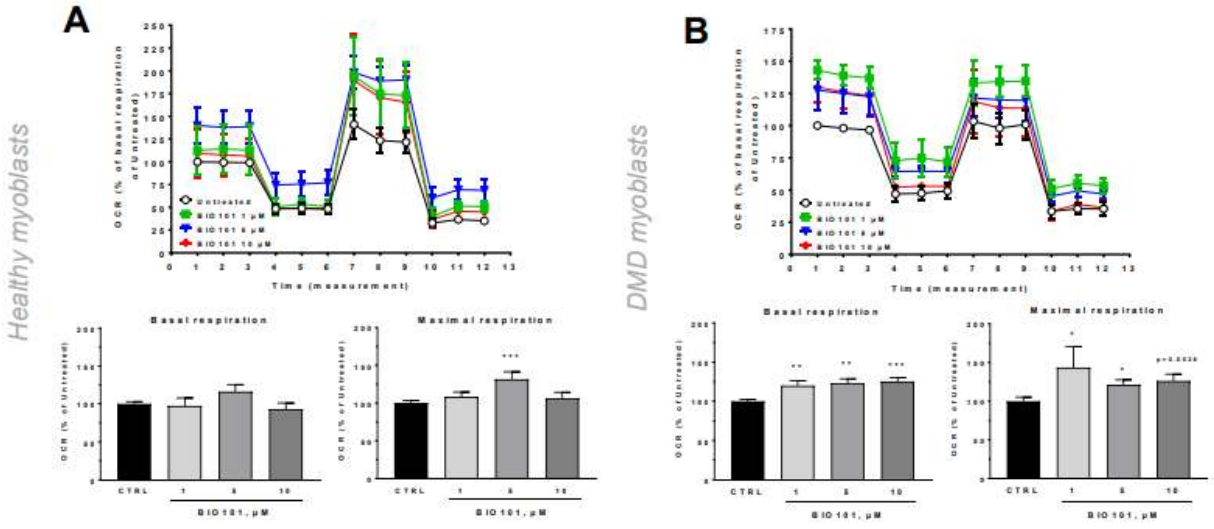
In addition to a lack of dystrophin, studies are also emerging that highlight a link between mitochondrial dysfunction and DMD. In particular demonstrating that DMD is characterized by a systemic mitochondrial defect where increased intra-cellular and inter-mitochondrial calcium has been shown to cause mitochondrial swelling, loss of mitochondrial membrane integrity, cell death and muscle atrophy (Kelly-Worden and Thomas, *Open Journal of Endocrine and Metabolic Diseases*, 2014).

Sarconeos is a small molecule shown to increase muscle performance with improved mitochondrial respiration and anabolism. As described above, RAS is a hormonal complex axis that, under physiological conditions, regulates blood pressure, inflammation, and fibrosis. RAS is also a modulator of muscle mass. By activating the MAS receptor, Sarconeos stimulates anabolism and mitochondrial activity of skeletal muscle cells, resulting in improved muscle strength and mobility. In its initial development designed to combat sarcopenia, Sarconeos demonstrated stimulation of muscle protein synthesis and energy production via the Akt and AMPK signaling pathways. Studies have also shown that ACE2 enzyme levels are elevated in dystrophic skeletal muscle, further validating the potential of Sarconeos in activating the RAS protective arm in DMD (Riquelme et. al., *PLoS One,* 2014). With Sarconeos' profile further solidifying, the asset is now also being evaluated in patients with DMD. The validity and safety of this approach has been extensively investigated by Biophytis in preclinical studies, both *in vitro* and in relevant animal models of DMD.

In the experiment described below, oxygen consumption (mitochondrial respiration) was recorded in healthy (left top and bottom panel) and DMD patient (10 years old, exon 52 mutated) (right top and bottom panel) human myotubes. Using an *in vitro* differentiation system, respective myoblasts (embryonic precursors of skeletal muscle cells) were differentiated for four days and were subsequently treated with increasing doses of Sarconeos for an additional two days. Mitochondrial respiration was measured using a Seahorse analyzer at the end of treatment. The results demonstrate that Sarconeos treatment has beneficial effects in improving mitochondrial respiration in human myocytes, regardless of their dystrophin gene status.

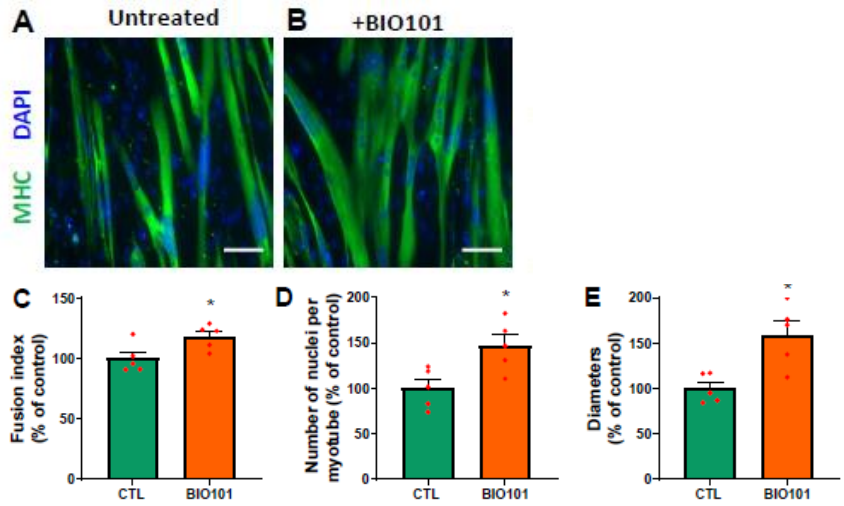
Energy Metabolism is Improved by Treatment With Sarconeos in Human Myotubes



Source: Dilda et al., 23rd International Annual Congress of the World Muscle Society (WMS), 2018

Using the same *in vitro* differentiation system as described above, healthy and DMD myoblasts were differentiated for three days and then incubated with or without Sarconeos at 10µM for a subsequent three days. As shown below, staining of both treated and untreated muscles cells in both the healthy and DMD patient group were stained for Myosin Heavy Chain (MHC), a marker of muscle filaments. Analysis of the stained cells in the treatment and control group showed that there is a significantly increased portion of cells undergoing myoblasts differentiation in the Sarconeos treated group as measured by fusion index, nuclei per myotubes and myotube diameter, in both healthy and DMD mutant muscle cells. Given that DMD muscle tissue can exhibit severely impaired proliferative capacity, and thus defective growth/differentiation potential, this experiment provides further preclinical evident of the utility of Sarconeos in DMD.

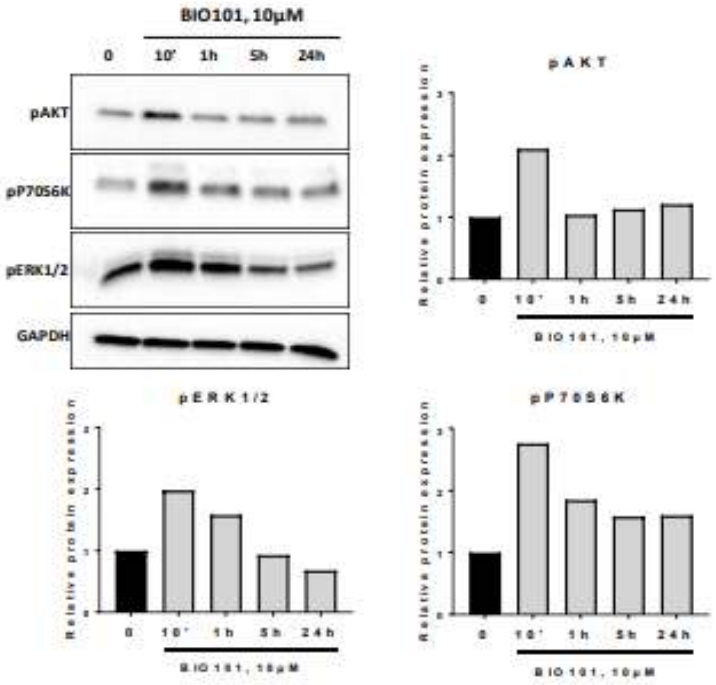
DMD Myoblasts Undergo Increased Differentiation Upon Treatment With Sarconeos



Source: Latil et al., 6th Annual International Congress of Myology, 2019

As noted above, several distinct signally pathways are implicated in DMD, with varying cellular consequences. Signaling pathways involved in anabolism (Akt) and regeneration (mTOR/MAPK) are known to be impaired in DMD muscle. The below series of western blots (graphed on the right) depict a time-course experiment evaluating the effects of Sarconeos on the activation of these three pathways after six days of human skeletal muscle differentiation, followed by a 24-hour treatment with 10µM Sarconeos. Results indicate there is a significant and early activation of each pathway substrate (p-Akt, pP70S6K, pERK1/2), as early as 10 minutes post-treatment.

Sarconeos Activates Signaling Pathways Impaired in DMD

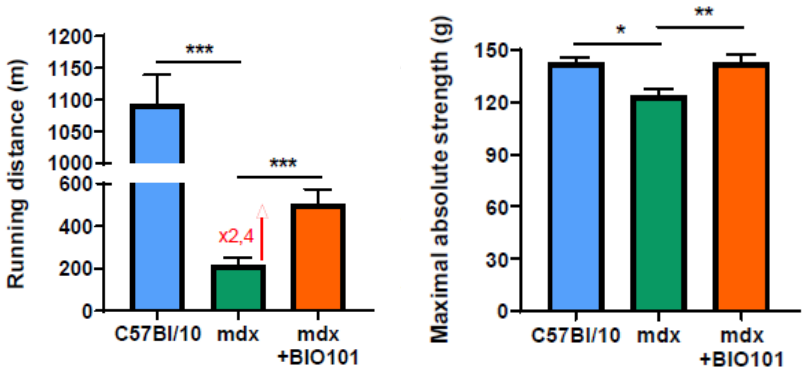


Source: Dilda et al, 23rd International Annual Congress of the World Muscle Society (WMS), 2018

Using the C57BL10-mdx animal model of DMD, the *in vivo* studies below demonstrate the beneficial impact of Sarconeos on skeletal muscle function. Briefly, 12-week-old mice were given Sarconeos (50mg/kg/day) or vehicle control (cyclodextrin) via oral gavage over the course of two months for analysis of exercise tolerance and maximal isometric *Tibalis anterior* (TA) strength. Mice were subjected to chronic exercise (2x/week) until the end of their treatment duration.

Looking at the impact of chronic Sarconeos treatment on running distance, measured in meters, (left graph) shows that mdx mice ran significantly less than the control group (C57Bl/10 mice; -80.4%, $p<0.001$). After eight weeks of treatment, the mdx mice that received Sarconeos ran significantly more than the untreated mdx mice (+136%, $p<0.001$). An *in situ* evaluation of maximal isometric TA muscle strength (right graph), showed that TA muscle strength is decreased in mdx mice compared to control mice ($p<0.05$). A significant increase in the TA muscle strength was observed in the Sarconeos treated mice (+15.3%, $p=0.004$) compared to the untreated mdx mice. Taken together, the overall physical performance of mdx dystrophic mice is significantly improved by two months of Sarconeos treatment (2.4 fold), in conjunction with improved TA muscle strength.

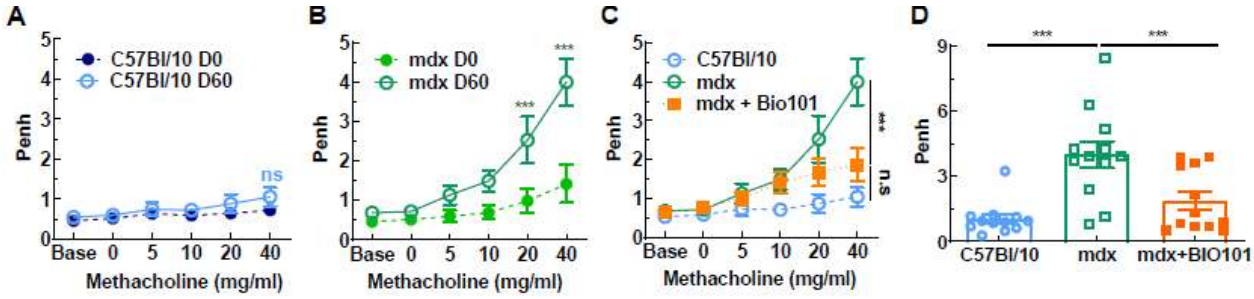
Sarconeos Improves Skeletal Muscle Functionality in DMD Mouse Model



Source: Latil et al., Annual International Congress of Myology 2019

Since the Sarconeos MoA has a role in improving respiratory function, a symptom that can affect many DMD patients, the company also investigated the potential benefit of Sarconeos on this system *in vivo* using the mdx DMD mouse model. In these animal cohorts, 12-week-old C57Bl/10 control mice and mdx mice +/- Sarconeos treatment (as above) were analyzed over the course of two months by plethysmography after methacoline challenge at baseline, one month and two months. Plethysmography tests how much air is in the mouse lungs after taking a deep breath, while the methacoline challenge (also known as bronchoprovacation test) is performed to evaluate lung reactivity/responsiveness. Shown below as plots of each treatment group (panels A-C) and graphical summary together (panel D), are the results of Penh assessment. As described previously in the COVA section, Penh, or enhanced pause, is a metric used to evaluate respiratory distress, via the pressure inside a plethysmograph. As can be seen from the results, mdx untreated, but not control mice, have increased Penh after two months. Sarconeos treatment significantly reduced the observed elevated Penh of mdx mice.

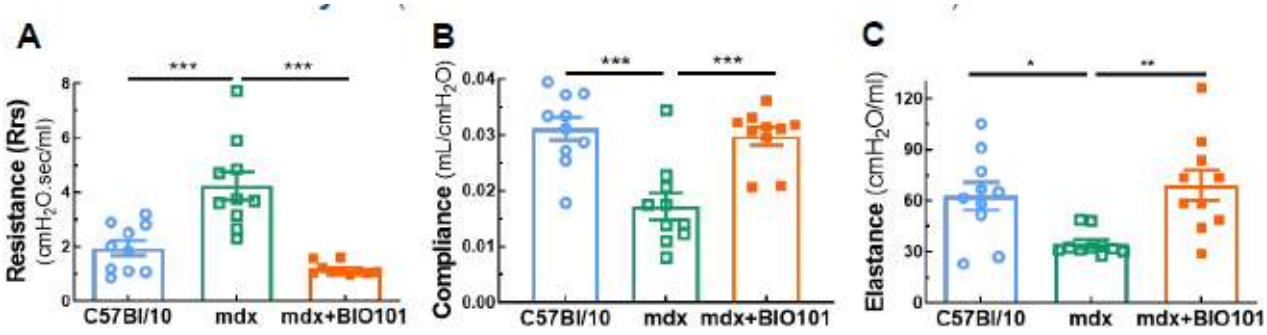
Sarconeos Treatment Improves Respiratory Functions of mdx Treated Mice



Source: Latil et al., Annual International Congress of Myology 2019

The same animals as above underwent flexivent analysis after two months of Sarconeos treatment (results shown below). Three lung mechanical properties were analyzed: resistance, compliance, and elastance. Sarconeos treatment significantly reduced the elevated airway resistance observed in untreated mdx mice (panel A); restored lung compliance, a measure of the lung's ability to stretch and expand (panel B) and improved elastance (panel C). Taken together, Sarconeos treatment improves airway responsiveness as well as deep airway structure, as shown by modifications of mechanical properties (resistance, compliance, and elastance) in mdx mice and protects from lung function degradation in a time-dependent manner.

Sarconeos Treatment Ameliorates Lung Mechanical Properties



Source: Latil et al., Annual International Congress of Myology 2019

Clinical development of Sarconeos in DMD is imminent, pending COVID-19 delays. With the promising pre-clinical package expanding on the use of Sarconeos in DMD, the asset is primed for further clinical development. The company received orphan drug designation in 2018 from the FDA and EMA for Sarconeos in DMD, which could potentially accelerate the approval process. In December 2019, Biophytis was granted an IND approval, from the FDA and the CTA approval from the FAHMP in Belgium to initiate a Phase 1/2 clinical proof of concept trial (MYODA-INT) of a weight-adjusted, oral pediatric formulation of Sarconeos, utilizing a 'seamless' clinical trial design with a primary endpoint of respiratory function.

The company plans to follow the MYODA-INT stage of the trial with a Phase 3 confirmatory stage. The global, double-blind, randomized, placebo-controlled MYODA trial will assess safety and efficacy of two doses of Sarconeos in non-ambulatory young DMD patients with signs of respiratory deterioration, administered orally over the course of 26 weeks, as compared to the placebo arm. An interim analysis is expected to take place after all subjects (48 anticipated) have finished 12 weeks of dosing, and thereafter for every 12-week period until either success or futility is achieved. Upon completion of the MYODA-INT stage of the trial, which will likely take up to one year, participants may be enrolled in an open label extension period. In order to progress from this stage, regulatory approval will be required, and in accordance up to 200 patients will be enrolled and respiratory function will be measured after dosing for 52 weeks (Phase 3).

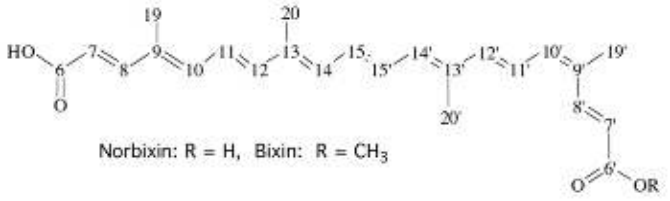
To date however, the trial initiation has been delayed due to COVID-19 pandemic dynamics. Pending the evolution of the pandemic however, Biophytis is set to begin enrollment imminently. With the safety profile of Sarconeos already established in two other indications (Sarcopenia and COVID-19), we anticipate that MYODA-INT will follow a similar path. The implementation of Sarconeos in DMD presents a significant commercial opportunity, as there remains a high unmet need in a well-defined population.

Biophytis believes that because Sarconeos targets various impaired muscle tissues and cells relevant to muscle strength, mobility and respiratory function, it has the potential to be used in all stages of DMD progression, including both ambulatory and non-ambulatory patients (though at this time, the focus remains on non-ambulatory patients only). In addition, management notes that Sarconeos activity is independent of the genetic mutation that causes the disease, it has the potential to be used in conjunction with current approved therapies and other gene therapies under development.

6. Macuneos: avoiding inflammation and eye-cell injury in Dry AMD.

Biophytis´ second candidate is Macuneos and is mainly being developed for the dry form of age-related macular degeneration (dry-AMD). Macuneos is an orally administered small molecule based on Norbixin (9'-cis-norbixin), a 6,6'-di-apo-carotenoid purified from *Bixa orellana* seeds (below).

Chemical Structure of Norbixin, Active Moiety of Macuneos



Source: Fontaine V et al., PLoS One. 2016.

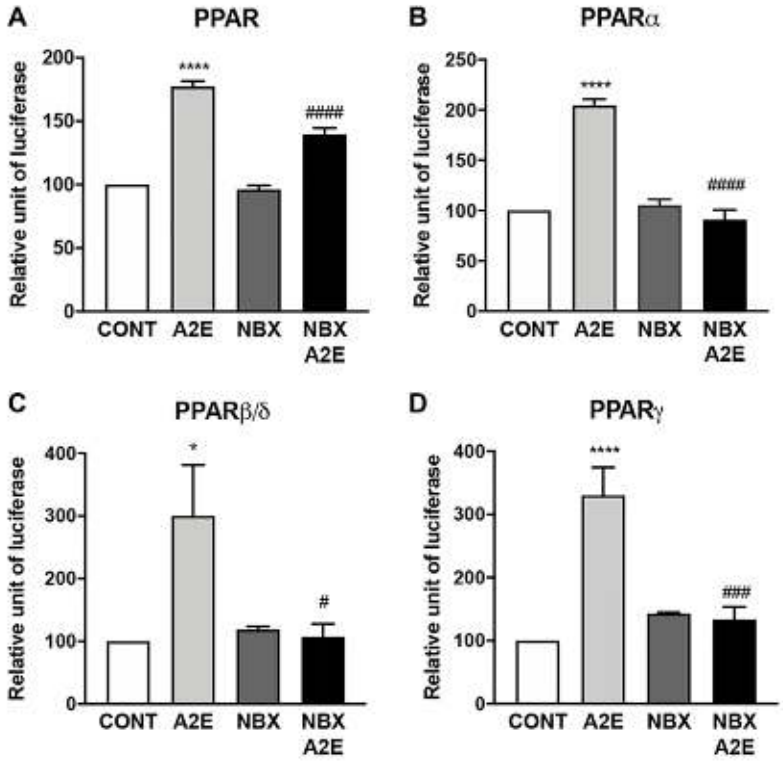
Market is wide open for entry of a blockbuster. The AMD market in the U.S. and E.U. is quite considerable with approximately 11 million and 15 million, respectively. Currently, there are blockbuster drugs on the market for AMD, but only treat the 'wet' form of the disease, which represents only 10% of AMD patients. This leaves 90% of the population with the dry form and no approved therapies, leaving the first potential market entrant (and beyond) with quite a large revenue opportunity, in our belief. To illustrate, the 10% wet AMD population is dominated by Regeneron's (REGN; Buy; King) Eylea, and Roche's (RHHBY; not rated) Lucentis. 2020 revenue for Eylea and Lucentis were $4.95 billion and ~$1.56 billion, respectively. Even if multiple market entrants were to miraculously appear at the same time, even minimal market penetration could be meaningful to a company's valuation, in our belief. Wet-AMD is one of the leading causes of vision loss for patients 50 years of age and older in the U.S. and is characterized by abnormal blood vessel growth at the back of the eye under the macula while also leaking blood and fluid causing damage and scarring to the macula. Dry-AMD, on the other hand, is characterized by the breakdown of light-sensitive cells in the macula due to the death of the supporting retinal pigment epithelium (RPE) cells, which impairs central vision. With obvious blindness ensuing over time, a key phenotypic result of these negative impacts on cells is the formation of what is called drusen, or insoluble extracellular aggregates (scarring). Drusen deposits itself in the retina in the early stages of the disease leading to damage of the retina and to ultimate geographic atrophy (GA), or areas of progressive and irreversible loss of retina function due to the cells wasting away. While the mechanics of the disorder are quite straightforward, it has been difficult to address from a therapeutic standpoint; Macuneos could change this by preventing the photo-oxidative and inflammatory stresses induced by the accumulation of N-retinylidene-N-retinylethanolamine (A2E) in RPE cells, responsible for the degenerative process of the retina in diseases such as AMD.

A2E plays a central role in AMD by inducing angiogenesis and increasing the secretion of inflammatory cytokines (Ablonczy Z *et al.*, *Invest Ophthalmol Vis Sci*. 2013). Certain nuclear receptors, including peroxisome proliferator-activated receptors (PPARs), which accept multiple ligands and are known to regulate a wide spectrum of biological pathways ranging from lipid and carbohydrate metabolisms to cell death, inflammation, and angiogenesis are involved in AMD pathogenesis (Herzlich AA *et al.*, *PPAR Res*. 2008).

Macuneos interferes with the A2E-PPAR duo. When porcine RPE cells were challenged with A2E, Norbixin significantly inhibited endogenous PPAR transactivation by 52% ($p<0.0001$). In addition, when specific constructs coding for PPAR isoforms (PPARα, PPARβ/δ, and PPARγ) were co-transfected with a

luciferase reporter plasmid under the control of the PPAR response element, Norbixin abolished the transactivation of all three PPAR isoforms induced by A2E (below). This observation is the first evidence of Norbixin acting through the PPAR pathway.

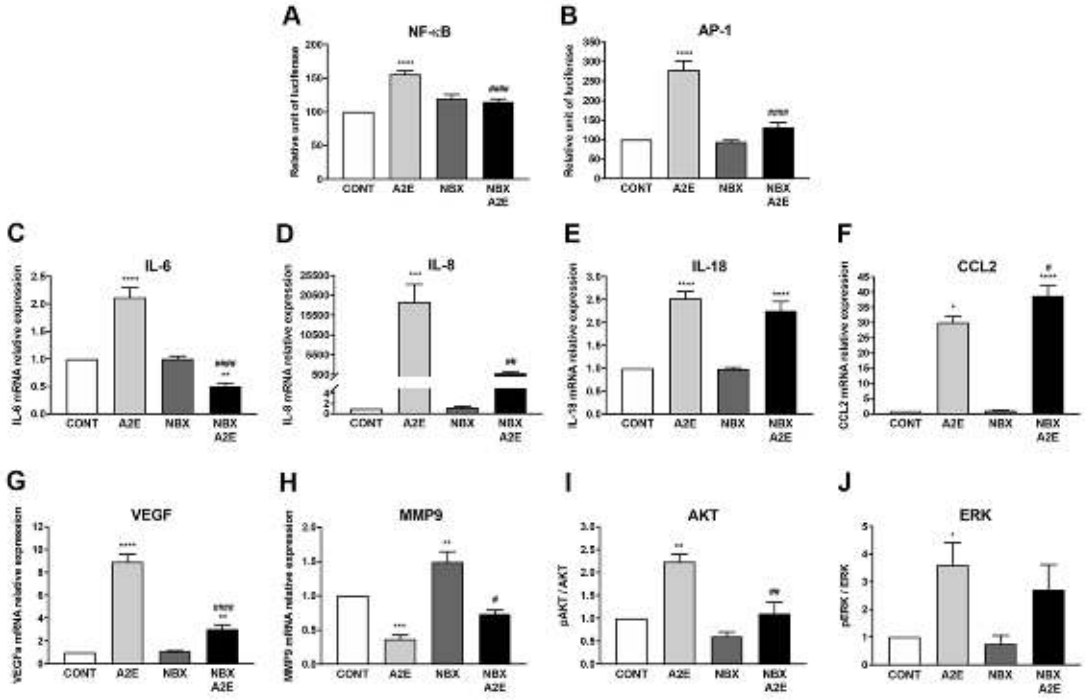
Norbixin Inhibits PPAR Transactivation Induced by A2E *In Vitro*



Source: Fontaine V et al., AGING. 2021.

Interestingly, Norbixin not only inhibits PPAR transactivation induced by A2E but also regulates A2E-induced expression of inflammatory and angiogenic factors. As shown below, treatment with Norbixin strongly downregulated inflammatory mediators and markers such as the transactivation of NF-κB (by 73%, $p<0.0001$) and AP-1 (82%, $p<0.0001$), and the mRNA expression of IL-6 (by 145%, $p<0.0001$) and IL-8 (approximately 23-fold, $p<0.01$) induced by A2E. In contrast, the expression of IL-18 and CCL2 was not inhibited by Norbixin. Although treatment with Norbixin may promote an anti-inflammatory setting, it displays differential modulatory effects on the expression of cytokines. With regards to the drivers of neovascular AMD, VEGF expression was significantly inhibited by addition of Norbixin, but not MMP9 matrix metalloproteinase. It is known that AKT and ERK pathway inhibition suppresses IL-6, IL-8 and VEGF production in RPE cells (Larrayoz IM *et al.*, *Invest Ophthalmol Vis Sci*. 2010). As expected, stimulation of porcine RPE cells with A2E triggered the activation of AKT and of ERK pathways. Treatment with Norbixin prevented AKT phosphorylation but not ERK activation. These observations suggest that the interference of Norbixin with A2E-induced inflammation and neovascularization could be due to direct interactions with PPARs. Although competitive binding experiments using radiolabeled ligands point to a direct communication between Norbixin and PPARs, additional silencing and/or co-immunoprecipitation experiments could further characterize physical interactions between the two molecules.

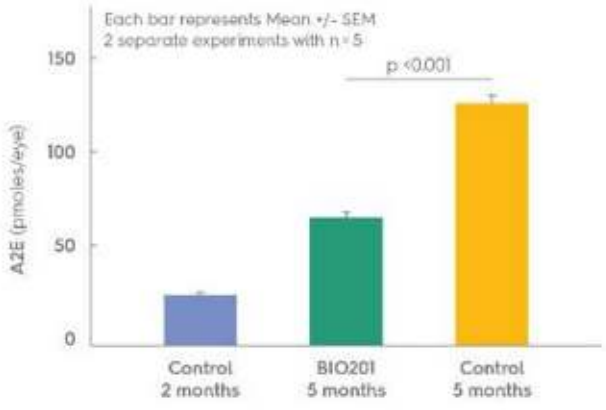
Norbixin Prevents A2E-Induced Inflammation and Neovascularization *In Vitro*



Source: Fontaine V et al., AGING. 2021.

Macuneos says STOP to A2Es in mice. As previously mentioned, accumulation of A2E has been associated with RPE dysfunction and photoreceptor loss. *Abca4*$^{-/-}$*; Rdh8*$^{-/-}$ mice lack critical proteins for retinal clearance and are characterized by an accumulation of A2E in RPE cells owing to an abnormal functioning of the visual cycle. Therefore, *Abca4*$^{-/-}$*; Rdh8*$^{-/-}$ mice develop severe photoreceptor dystrophy at an early age (Maeda A *et al*., *J Biol Chem*. 2008). As depicted below, chronic oral Norbixin supplementation in water during three months decreased A2E accumulation by approximately 45% compared to vehicle control mice. This is an important finding considering that reducing A2E formation and/or accumulation is a target for pharmacological interventions against dry-AMD.

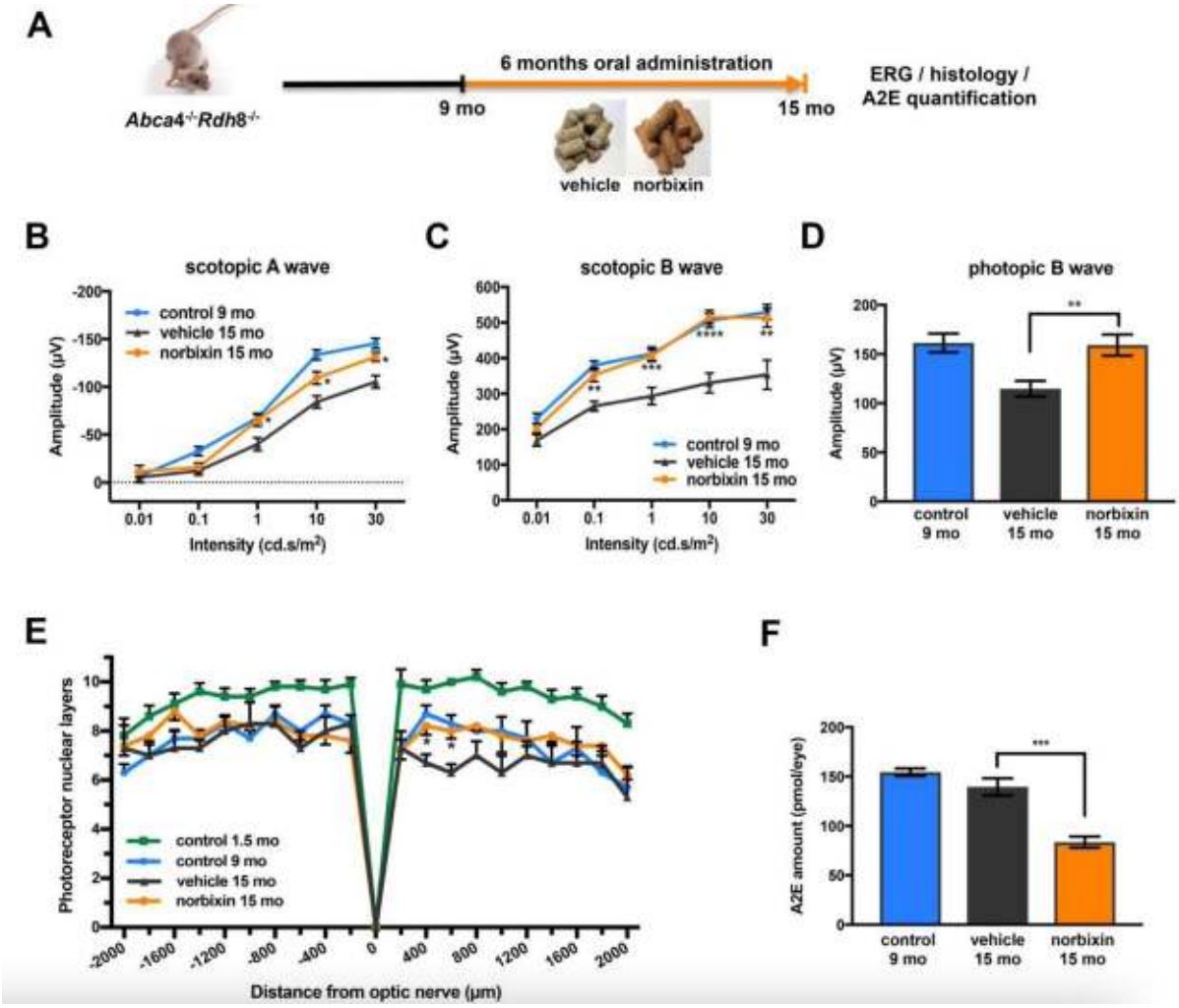
Norbixin Reduces A2E Accumulation of RPE in Mice



Source: Company presentation.

To test the therapeutic efficacy of Norbixin *in vivo*, 9-month-old male *Abca4*$^{-/-}$*; Rdh8*$^{-/-}$ mice were fed with normal pellets or norbixin-containing pellets (below; A). Food-intake measurements determined a daily consumption of 47.5 mg of norbixin (+/- 5 mg) per kg per mouse. After six months of supplementation, a significant preservation of scotopic A- and B-waves (vision under low-light levels), as well as photopic B-wave (vision under well-lit conditions) was observed in mice supplemented with Norbixin (below; B, C, D). In addition, supplementation with Norbixin provided significant protection against photoreceptor layer degeneration (below; E). Consistent with functional protection, A2E accumulation in RPE was 40% lower ($p<0.001$) in mice fed with pellets containing Norbixin compared to mice fed with normal pellets (below; F). These data demonstrate the efficiency of orally given Norbixin through food on the photoreceptor function in the *Abca4*$^{-/-}$*; Rdh8*$^{-/-}$ mouse model.

Norbixin Preserves the Function of Cone Photoreceptors *In Vivo*

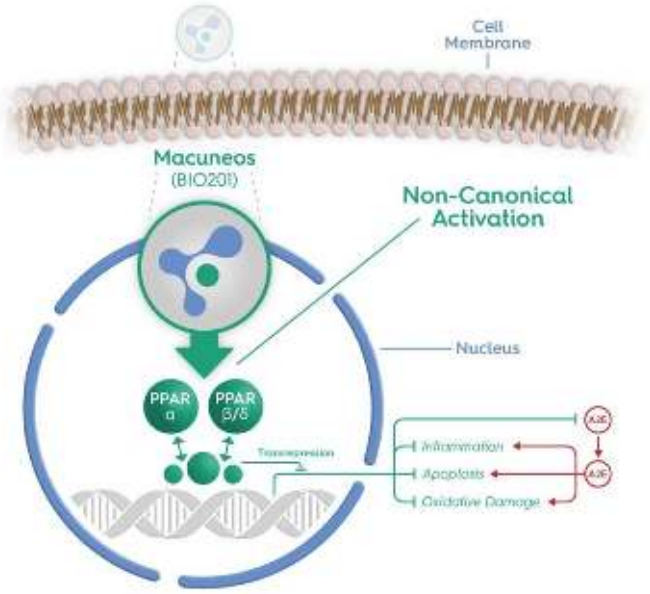


Source: Fontaine V et al., AGING. 2020.

Based on preclinical studies, oral supplementation with Norbixin, the active principal of Macuneos, reduces the concentration of A2E, is neuroprotective, and preserves visual function of *Abca4*$^{-/-}$*; Rdh8*$^{-/-}$ mice, which models retinal degenerative conditions such as dry AMD. The effect of chronic Norbixin supplementation on inflammatory mediators and macrophage activation or differentiation *in vivo* still needs to be assessed. The partial efficacy of Norbixin may be further improved by increasing the doses of Norbixin administered. As depicted below, *in vitro* data suggest that Norbixin might prevent retinal damage caused by A2E

accumulation through the regulation of PPARs and subsequent target genes. The exact mechanisms regulating Norbixin-A2E-PPAR-inflammation/cell damage axis *in vitro* and *in vivo* remain to be determined. However, Norbixin seems to be a promising agent for developing an oral macular degeneration treatment.

Potential Mechanism of Action of Macuneos for the Treatment of Dry AMD



Source: Company presentation.

Clinical development of Macuneos to begin shortly. Biophytis plans to commence a Phase 1 clinical trial (MACA-PK) to assess Macuneos' safety, PK and PD effects in healthy volunteers in 4Q21 or 1Q22, followed by a Phase 2a/b interventional study (MACA-INT) in patients with GA in one eye and intermediate-stage AMD in the fellow eye. Following MACA-PK in early 2022, Biophytis also plans to explore clinical development of Macuneos for Stargardt disease, the most common form of inherited macular degeneration that typically develops in childhood.

Valuation

We value Biophytis at $15 per share. We base our valuation of Biophytis on our probability-weighted clinical net present value (NPV) valuation model. This is an independent, fully taxed snapshot of each drug's perceived value. We believe this method is appropriate in capturing the value of the clinical stage pipeline by allowing us to flex multiple assumptions, including chance of success, peak sales estimates, and year of commercial launch.

Our peak sales estimates (market models below) are found by looking out approximately five years from projected drug launch. Per our market model below, and incorporating the vagaries, and timing of new drug launches, we believe a rough estimate of the market model sales in year five and year six best represent our view of peak. We believe a level of conservatism exists in our valuation model based on our assigned multiple of 17.0x, rather than the sometimes inflated non-profitable biotech multiples in the 30-40x range. It represents a 17x takeout multiple on probability adjusted peak sales for each indication. They are then added up to form a sum-of-the-parts NPV. The table below shows the long-term historical and current P/E values of the top ten Big Pharma companies showing that our assigned 17.0x multiple is at a discount to the long-term medians and averages of the group. Further, the current forward multiples are depressed, in our belief, due to the current market volatility. Our rationale for using Big Pharma multiples, plus a discount, is based on the potential acquisition metrics utilized by Big Pharma in valuing the smaller biotech as part of its overall portfolio. We are currently assigning a 15% discount rate, which is in line for the majority of our covered companies, except for those with higher perceived risks. Our valuation is also based on fully diluted share count.

Average Current and Historical P/E Ratios of Top Ten Pharma Companies

								Through December 2020		
Company	Ticker	Stock Price	Rating	Market Cap ($B)	P/E (2019)	P/E (2020)	P/E (2021)	5-Year Average P/E	10-Year Average P/E	20-Year Average P/E
Amgen Inc.	AMGN	$ 203.61	NR	$ 114.64	18.5	20.7	12.4	27.6	20.8	29.4
AbbVie Inc.	ABBV	$ 108.53	NR	$ 191.86	22.7	29.2	8.6	29.1	NA	NA
Gilead Sciences Inc.	GILD	$ 67.63	NR	$ 84.47	63.9	16.5	9.5	18.1	17.5	33.1
GlaxoSmithKline plc	GSK	$ 38.80	NR	$ 96.16	11.5	16.3	13.9	33.1	25.7	23.2
Jonhson & Johnson	JNJ	$ 159.20	NR	$ 415.12	23.6	23.9	16.4	74.6	45.0	35.1
Merck & Co	MRK	$ 78.95	NR	$ 201.47	18.1	36.0	14.1	37.7	37.1	30.2
Novartis International AG	NVS	$ 82.43	NR	$ 200.60	29.2	20.7	13.0	21.3	17.9	20.1
Pfizer Inc.	PFE	$ 41.42	NR	$ 234.64	26.1	17.7	10.2	21.4	19.3	34.2
Roche Holding AG	RHHBY	$ 48.22	NR	$ 338.96	22.0	21.4	17.8	22.5	19.4	22.3
Sanofi S.A.	SNY	$ 48.22	NR	$ 121.30	10.4	17.4	12.9	23.6	19.0	21.5
				Mean	**24.6**	**22.0**	**12.9**	**30.9**	**24.6**	**27.7**
				Median	**22.3**	**20.7**	**13.0**	**25.6**	**19.4**	**29.4**

Source: FactSet (FDS; not rated) (data as of 10/13/21) and H.C. Wainwright research. Long-term P/E average ratios are calculated through December 2020.

As our clinical NPV valuation model below indicates, we currently value only Sarconeos and its two lead indications, sarcopenia and COVID-19; at this point we are not including Macuneos in our valuation to be conservative, though it has the potential to be a significant contributor to the valuation based on the lack of approved therapies for dry-AMD. Regarding Sarconeos, the two indications referenced contribute approximately 50% each to our valuation. For COVID-19, the revenue opportunity is much closer for the company where we project a 2022 launch and $525 million in peak sales in the U.S. What this does not take into account is: (1) the underlying risk of the need for COVID-19 therapies waning, though we believe the endemic properties of the virus should keep a baseline market for drugs; and (2) the potential recurring revenue opportunity for Sarconeos should any governments look to stockpile the asset and either increase the order over time, or re-up orders based on shelf life of the asset. With respect to sarcopenia, the addressable population is quite large, and therefore we believe that our projections are conservative. The biggest risk, in our belief, is what the regulatory path could look like regarding primary clinical endpoints as

this indication continues to be relatively amorphous as to how a first-to-market drug might make it. To this end, we are projecting a 2026 launch off of a 55% chance of success and $1.2 billion in peak sales in the U.S. As the program matures, we believe both the chance of success and especially the geographical impacts based on future potential business development activities could impact our valuation. A level of distinct conservatism in our valuation exists, in our belief, in that we are only modeling the U.S. opportunity; we believe that ex-U.S. opportunities and their contribution to our valuation could have a significant impact.

Clinical NPV Valuation Model

Drug name	Indication	Status	Projected Launch	Success	Peak Sales (US$)	Economics	Profitability	NPV (US$)
Sarconeos (BIO101)								
	COVID-19	Phase 3	2022	75%	525	100%	30%	7.72
	Sarcopenia	Phase 2	2026	55%	1200	100%	30%	7.40
	DMD	Preclinical	2029	0%	0	100%	30%	0.00
Macuneos (BIO201)								
	Dry-AMD	Preclinical	2031	0%	0	100%	30%	0.00
	Stargardt disease	Preclinical	2033	0%	0	100%	30%	0.00
							Total - US$	**15.11**
							Total - €	**13.03**

Source: H.C. Wainwright research estimates.

Risks

Clinical, regulatory, and market risk. The three primary risks for companies that are developing new therapeutic agents are: (1) regulatory risk including how the clinical data will be assessed by the FDA; (2) potential peers' competition; and (3) the risk of clinical trial failure. Additional regulatory challenges may be faced by the company, which could impede the potential success of a drug candidate. We value the competition and consider that potential comparable therapies may be developed from peers and could already be in later stages of development; however, we believe that Biophytis' approach appears to be generating promising data as well as the potential to generate long term pipeline fill.

Financing risk. As with the majority of development stage biotechnology companies with no regulatory approved drug agents, maintaining funding is a critical necessity for the progression of the candidate pipeline. The company ended 1H21 with €23 million, which management believe provides 12 months of runway. However, cash burn could be significantly impacted based on increasing the number of development programs, which could be potentially offset by partner or collaborative milestone revenue payments. It is also likely that additional equity raises could come in the future based on pipeline expansion and geography expansion.

Commercial risk. Even if approval is obtained for a therapeutic candidate, Biophytis may not generate or sustain revenue from sales of the therapeutic product due to factors such as whether the therapeutic product can be sold at a competitive price and otherwise accepted in the market. Therefore, any revenue from sales of the therapeutic product may not offset the costs of development. The therapeutic candidates Biophytis is developing are based on differentiated plant-based therapeutic approaches. Market participants with significant influence over acceptance of new treatments, such as physicians and third-party payers, may not adopt a treatment based on its therapeutic products, and the company may not be able to convince the medical community and third-party payers to accept and use, or to provide favorable

coverage or reimbursement for, any therapeutic products developed by Tempest and its existing collaborator, or any future collaborators.

Biophytis has benefited from certain reimbursable financial advances and non-reimbursable subsidies from the French government that if terminated or reduced may restrict activities. Biophytis has benefited from certain reimbursable advances and non-reimbursable subsidies from the French government, and it intends to continue to seek advances and/or subsidies from these agencies in the future in order to accelerate the development of its drug candidates. There is no assurance that these benefits will continue to be available to the company in the future. If such benefits and programs were to be terminated or reduced, it could have an adverse effect on Biophytis' business, operating results and financial condition and could deprive it of financial resources necessary for research and development of its drug candidates. Furthermore, the advances and subsidies are generally subject to contractual conditions, including our compliance with agreed upon preliminary budgets and scientific programs, informing the lender of any deviations from such agreed upon budgets and programs, and our compliance with certain financial ratios to ensure Biophytis' solvency. In the event that the company does not comply with the contractual conditions of the subsidies, it may be required to reimburse the French government for any outstanding payments (€832 thousand as of December 31, 2020) on an accelerated basis and could be liable for any damages incurred by such agencies resulting from the breach of contract.

For additional risk considerations, please refer to the company's SEC filings.

($ in millions except per share data)

Profit & Loss - Dec fiscal	2018A	2019A	2020A	2021E	2022E	2023E	2024E	2025E	2026E
Licensing	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
R&D collaborations	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Product and Royalties	0.0	0.0	0.0	0.0	2.8	18.7	48.9	134.7	264.8
Other revenues	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Revenues	**0.0**	**0.0**	**0.0**	**0.0**	**2.8**	**18.7**	**48.9**	**134.7**	**264.8**
CoGS	0.0	0.0	0.0	0.0	0.3	2.2	5.9	16.2	31.8
Gross Profit	**0.0**	**0.0**	**0.0**	**0.0**	**2.5**	**16.5**	**43.0**	**118.5**	**233.0**
Gross margin	*0%*	*0%*	*0%*	*0%*	*88%*	*88%*	*88%*	*88%*	*88%*
SG&A	4.3	6.6	4.0	5.9	7.0	8.2	11.1	13.9	17.4
R&D	9.5	9.1	9.9	15.4	18.8	25.9	37.5	50.7	64.9
Other op ex	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
EBIT	**(13.9)**	**(15.7)**	**(13.9)**	**(21.3)**	**(23.3)**	**(17.7)**	**(5.6)**	**54.0**	**150.8**
EBIT margin	*nm*	*nm*	*nm*	*nm*	*nm*	*nm*	*nm*	*40%*	*57%*
Depreciation	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Amortisation Intangibles	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
EBITDA	**(13.9)**	**(15.7)**	**(13.9)**	**(21.3)**	**(23.3)**	**(17.7)**	**(5.6)**	**54.0**	**150.8**
EBITDA margin	*nm*	*nm*	*nm*	*nm*	*nm*	*nm*	*nm*	*40%*	*57%*
Non operating expenses	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Net Interest Income/Other	(0.2)	(2.1)	(3.1)	(8.3)	(9.2)	(4.0)	(5.0)	(3.0)	(3.0)
Interest expense	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
EBT	**(14.1)**	**(17.8)**	**(17.1)**	**(29.6)**	**(32.5)**	**(21.7)**	**(10.6)**	**51.0**	**147.8**
EBT margin	*nm*	*nm*	*nm*	*nm*	*nm*	*nm*	*nm*	*38%*	*56%*
Provision for taxes	(0.1)	(0.0)	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Net Income	**(14.1)**	**(17.8)**	**(17.1)**	**(29.6)**	**(32.5)**	**(21.7)**	**(10.6)**	**51.0**	**147.8**
Participation of preferred stock	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Net Income to common	**(14.0)**	**(17.8)**	**(17.1)**	**(29.6)**	**(32.5)**	**(21.7)**	**(10.6)**	**51.0**	**147.8**
net margin	*nm*	*nm*	*nm*	*nm*	*nm*	*nm*	*nm*	*38%*	*56%*
NoSH - basic	13.4	16.9	60.0	118.7	129.1	136.8	154.0	158.6	161.2
NoSH - diluted	13.4	16.9	60.0	118.7	129.1	136.8	154.0	158.6	161.2
EPS - basic	**(1.05)**	**(1.05)**	**(0.28)**	**(0.25)**	**(0.25)**	**(0.16)**	**(0.07)**	**0.32**	**0.92**
EPS - diluted	**(1.05)**	**(1.05)**	**(0.28)**	**(0.25)**	**(0.25)**	**(0.16)**	**(0.07)**	**0.32**	**0.92**

Source: Company documents and H.C. Wainwright estimates

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U.S. IPO on February 10, 2021

Half-yearly P&L -Dec fiscal									
$ in millions	FH1'20A	FH2'20A	FY'20A	FH1'21A	FH2'21E	FY'21E	FH1'22E	FH2'22E	FY'22E
Licensing	0.00	0.00	0.0	0.00	0.00	0.0	0.00	0.00	0.0
R&D collaborations	0.00	0.00	0.0	0.00	0.00	0.0	0.00	0.00	0.0
Product and Royalties	0.00	0.00	0.0	0.00	0.00	0.0	0.00	2.80	2.8
Other revenues	0.00	0.00	0.0	0.00	0.00	0.0	0.00	0.00	0.0
Revenues	**0.00**	**0.00**	**0.0**	**0.00**	**0.00**	**0.0**	**0.00**	**2.80**	**2.8**
CoGS	0.00	0.00	0.0	0.00	0.00	0.0	0.00	0.34	0.3
Gross Profit	**0.00**	**0.00**	**0.0**	**0.00**	**0.00**	**0.0**	**0.00**	**2.46**	**2.5**
Gross margin	*nm*	*nm*	*0%*	*nm*	*nm*	*0%*	*nm*	*nm*	*88%*
SG&A	2.27	1.75	4.0	2.92	2.99	5.9	3.22	3.75	7.0
R&D	5.19	4.73	9.9	7.59	7.78	15.4	8.31	10.45	18.8
Other op ex	0.00	0.00	0.0	0.00	0.00	0.0	0.00	0.00	0.0
EBITDA	**(7.5)**	**(6.5)**	**(13.9)**	**(10.5)**	**(10.8)**	**(21.3)**	**(11.5)**	**(11.7)**	**(23.3)**
EBITDA margin			*nm*			*nm*			*nm*
Non operating expenses	0.00	0.00	0.0	0.00	0.00	0.0	0.00	0.00	0.0
Net Interest Income/Other	(2.00)	(1.11)	(3.1)	(5.35)	(2.95)	(8.3)	(4.36)	(4.88)	(9.2)
Interest expense	0.00	0.00	0.0	0.00	0.00	0.0	0.00	0.00	0.0
EBT	**(9.5)**	**(7.6)**	**(17.1)**	**(15.9)**	**(13.7)**	**(29.6)**	**(15.9)**	**(16.6)**	**(32.5)**
EBT margin			*nm*			*nm*			*nm*
Provision for taxes	0.00	0.00	0.0	0.00	0.00	0.0	0.00	0.00	0.0
Participation of preferred stock									
Net Income to common	**(9.5)**	**(7.6)**	**(17.1)**	**(15.9)**	**(13.7)**	**(29.6)**	**(15.9)**	**(16.6)**	**(32.5)**
net margin			*nm*			*nm*			*nm*
NoSH - basic	37.21	82.72	59.97	110.68	126.80	118.74	128.20	130.00	129.10
NoSH - diluted	37.21	82.72	59.97	110.68	126.80	118.74	128.20	130.00	129.10
EPS - basic	**(0.25)**	**(0.09)**	**(0.28)**	**(0.14)**	**(0.11)**	**(0.25)**	**(0.12)**	**(0.13)**	**(0.25)**
EPS - diluted	**(0.25)**	**(0.09)**	**(0.28)**	**(0.14)**	**(0.11)**	**(0.25)**	**(0.12)**	**(0.13)**	**(0.25)**

Source: Company documents and H.C. Wainwright estimates.

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U.S. IPO on February 10, 2021

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RETURN ASSESSMENT

Market Outperform (Buy): The common stock of the company is expected to outperform a passive index comprised of all the common stock of companies within the same sector.

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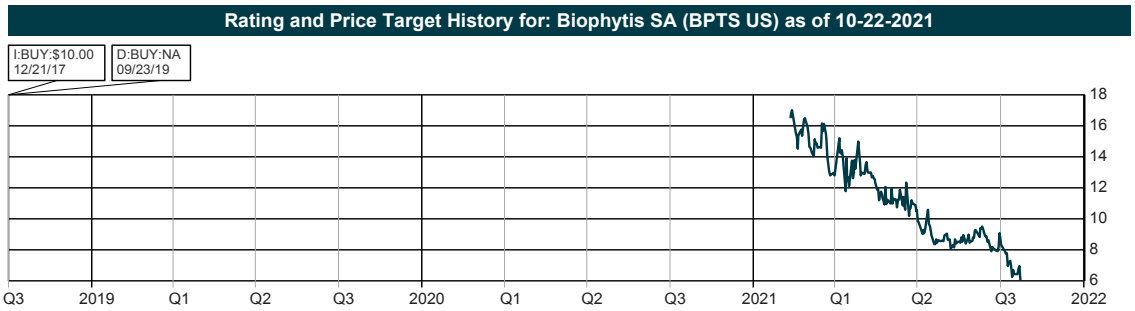

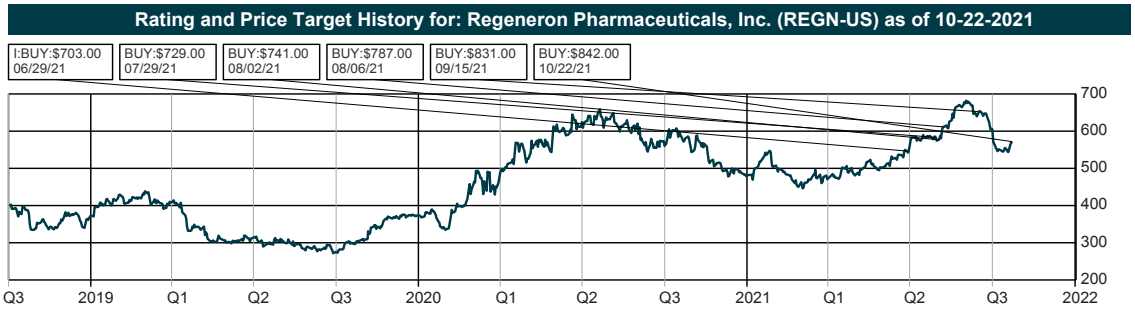

Related Companies Mentioned in this Report as of Oct/22/2021

Company	Ticker	H.C. Wainwright Rating	12 Month Price Target	Price	Market Cap
Regeneron Pharmaceuticals, Inc.	REGN	Buy	$842.00	$572.36	$60159

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Distribution of Ratings Table as of October 22, 2021				
			IB Service/Past 12 Months	
Ratings	Count	Percent	Count	Percent
Buy	537	90.10%	195	36.31%
Neutral	55	9.23%	14	25.45%
Sell	1	0.17%	0	0.00%
Under Review	3	0.50%	1	33.33%

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