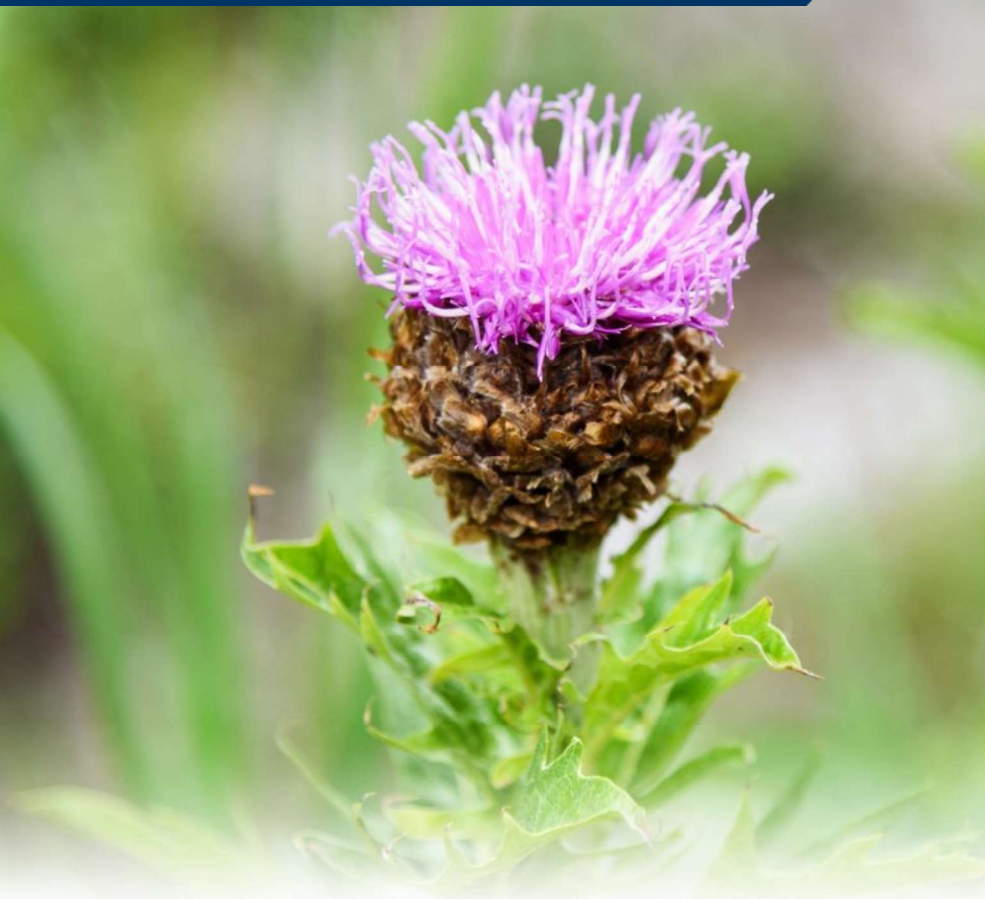


# Biophytis

France | Pharma & biotech | MCAP EUR 42.4m

05 April 2018



## Nature's cure

### What's it all about?

As a developer of plant-derived medicine, Biophytis targets diseases associated with aging, particularly sarcopenia and intermediate age-related macular degeneration (AMD). Its leading asset, BIO101 for sarcopenia, has a clean safety profile. While there is some biomarker and pre-clinical evidence suggesting biological activity, no proof of clinical efficacy has been announced. Moreover, BIO101 reward is likely to be challenging, due to: 1) the risk of failure (e.g. anti-myostatin setbacks); 2) the poor pricing environment (mass market indication); 3) the need for heavy S&M investment; and 4) high COGS, as its active pharmaceutical ingredients (API) are natural. We initiate coverage with a Hold rating and a TP of EUR3.7.

Kepler Cheuvreux and the issuer have agreed that **Kepler Cheuvreux** will produce and disseminate investment research on the said issuer as a service to the issuer.

**Hold** (Not Rated)

|                     |                     |
|---------------------|---------------------|
| <b>Target price</b> | <b>EUR 3.70</b>     |
| Current price       | EUR 3.15            |
| Up/downside         | 17.5%               |
| Change in TP        | none                |
| Change in EPS       | none 18E / none 19E |

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# 360

## in 1 minute

### Investment case summary

Age-related conditions are the leading cause of death and healthcare costs. The dream of fending off old age is as old as human civilisation itself. Given the aging of the global population, developing treatments that preserve health in old age and postpone the onset of age-related diseases is more important than ever. To that end, Biophytis has developed two plant-based screening platforms to identify potential APIs for the treatment of diseases associated with aging. The first platform, Sarcob, identified BIO101, Biophytis's most advanced candidate, which has started its phase IIb in Q1 2018, developed for the sarcopenia indication. Sarcopenia was officially recognised as a disease by the WHO in 2016, and defined as the loss of skeletal muscle mass and strength that occurs with advancing age. Biophytis has already carried out a phase I trial of BIO101, which was deemed to have a clean safety profile. Despite this promising profile, and the potentially lucrative market, BIO101 still needs to demonstrate the clinical efficacy of its lead candidate in the ongoing phase IIb trial SARA-INT. Top-line results of the trial are expected in summer 2019 and will be a key milestone for Biophytis's future prospects.

Biophytis's second screening platform is Maculia, which aims to develop a plant-based API (BIO201) for the AMD (age-macular degeneration) indication. This project is under clinical development and a pharmacokinetics study is expected to start in H2 2018. The next challenge for Biophytis will be to deliver clinical results, following changes to the clinical design of its studies which occurred after its IPO. Moreover, with just EUR20m in cash at end-2017, the company still needs to find additional financing for the clinical proof-of-concept studies of its additional indications and products: BIO101's duchenne muscular dystrophy (DMD) and BIO201's AMD.

### Key findings of the report

In this report we provide:

- A detailed explanation of the mechanisms of BIO101 and BIO201.
- An in-depth overview of the addressed market and the key players involved in the treatment of sarcopenia and intermediate AMD.
- An analysis of the market potential of BIO101 and BIO201.

### Valuation model

Our rNPV models, which are based on the Sarcopenia and AMD indications as we do not yet factor in value for the DMD program, point to a fair value of EUR3.7 per share in our base case scenario. We initiate coverage with a Hold rating and a TP of EUR3.7.

### Company summary

Biophytis is a France-based biotechnology company focused on the development of treatments for diseases associated with aging, particularly those affecting muscular and visual functions. Biophytis's leading assets are BIO101, developed for sarcopenia, and BIO201, developed for the intermediate AMD indication. Both have plant-derived APIs.

#### Management

Stanislas Veillet, CEO  
René Lafont, CSO  
Jean-Christophe Montigny, CFO

#### Key shareholders

Management 13.0%  
CM-CIC 2.0%  
Metabrain research 2.0%

### Market data

|                               |          |
|-------------------------------|----------|
| Bloomberg                     | ALBPS FP |
| Reuters                       | ALBPS.PA |
| Market cap (EUR)              | 42.4m    |
| Free float (%)                | 83.0     |
| No. of shares outstanding (m) | 13       |
| 3m avg. daily vol (EURm)      | 0.5      |
| YTD abs. performance          | -32.8%   |
| 52-week high (EUR)            | 7.02     |
| 52-week low (EUR)             | 2.57     |

### Strengths

- Solid balance sheet with cash run until 2019
- Outsourcing of its R&D drive low cash outflow
- Strong potential to generate deals

### Opportunities

- A number of indications with no addressed medication
- Sarcopenia is an indication of emerging interest for pharma
- Large market potential for the AMD indication

### Weaknesses

- No proprietary technology
- Limited back-up developments
- Limited intellectual property protection for ongoing research

### Threats

- Failure in clinical trials
- Many candidates for the dry AMD indication failed
- Sarcopenia is still not clearly defined by agencies
- Adoption rates of pharmacological treatments for sarcopenia

### Key financials (please see the end of this report for full financials)

| Income Statement (EURm)  | 2013 | 2014 | 2015 | 2016 | 2017  | 2018E |
|--------------------------|------|------|------|------|-------|-------|
| Sales                    | 0.0  | 0.0  | 0.0  | 0.0  | 0.0   | 0.0   |
| % Change                 | na   | na   | na   | na   | na    | na    |
| EBITDA adjusted          | -0.5 | -0.5 | -4.9 | -7.8 | -9.9  | -11.6 |
| EBIT adjusted            | -0.5 | -0.5 | -4.8 | -7.6 | -9.7  | -11.4 |
| Adjusted EBIT margin (%) | na   | na   | na   | na   | na    | na    |
| Net profit reported      | -0.6 | -0.5 | -5.0 | -7.6 | -11.2 | -10.0 |
| Net profit adjusted      | -0.6 | -0.5 | -5.0 | -7.6 | -11.2 | -10.0 |

#### Cash flow statement (EURm)

|                              |      |      |      |      |       |       |
|------------------------------|------|------|------|------|-------|-------|
| CF from operating activities | -0.6 | -0.8 | -4.3 | -8.0 | -11.4 | -10.1 |
| Capex                        | 0.0  | 0.0  | 0.0  | -0.1 | 0.0   | 0.0   |
| Free cash flow               | -0.6 | -0.8 | -4.3 | -8.1 | -11.4 | -10.1 |

#### Balance sheet (EURm)

|                                 |     |     |     |     |     |     |
|---------------------------------|-----|-----|-----|-----|-----|-----|
| Intangible assets               | 0.0 | 0.0 | 2.2 | 2.1 | 2.1 | 2.1 |
| Tangible assets                 | 0.0 | 0.0 | 0.2 | 0.3 | 0.3 | 0.3 |
| Fin. & other non-current assets | 0.0 | 0.0 | 0.3 | 0.1 | 0.1 | 0.1 |

|                            |      |      |      |     |      |     |
|----------------------------|------|------|------|-----|------|-----|
| Total shareholders' equity | -0.4 | -1.1 | 11.6 | 4.5 | 15.9 | 5.8 |
| Pension provisions         | 0.0  | 0.0  | 0.0  | 0.0 | 0.0  | 0.0 |
| Liabilities and provisions | 1.0  | 1.5  | 1.9  | 3.9 | 9.4  | 9.4 |

|                             |     |      |      |      |       |      |
|-----------------------------|-----|------|------|------|-------|------|
| Net financial debt          | 0.4 | 0.7  | -8.6 | -2.0 | -13.3 | -3.2 |
| Working capital requirement | 0.0 | -0.4 | 0.3  | 0.1  | 0.1   | 0.1  |
| Invested capital            | 0.0 | -0.4 | 0.5  | 0.4  | 0.4   | 0.4  |

#### Per share data (EUR)

|                           |    |    |    |      |       |       |
|---------------------------|----|----|----|------|-------|-------|
| EPS adj and fully diluted | na | na | na | high | high  | high  |
| Cash flow per share       | na | na | na | na   | -0.84 | -0.75 |
| Book value per share      | na | na | na | na   | 1.19  | 0.43  |
| DPS                       | na | na | na | 0.00 | 0.00  | 0.00  |

#### Ratios

|         |    |    |        |        |         |        |
|---------|----|----|--------|--------|---------|--------|
| ROE     | na | na | -94.9% | -94.1% | -109.7% | -92.3% |
| ROIC    | na | na | na     | na     | na      | na     |
| Gearing | na | na | -74.2% | -43.7% | -83.5%  | -54.8% |

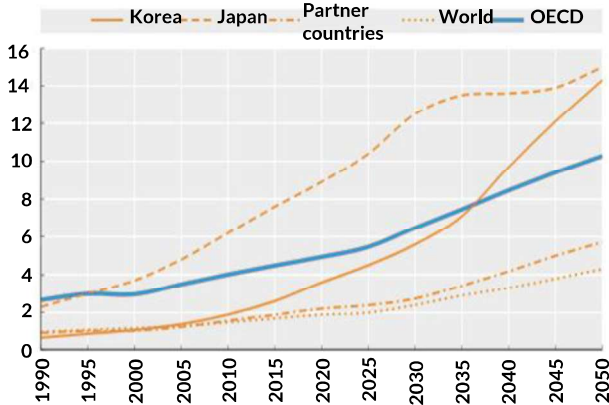
#### Valuation

|                                |    |    |    |      |      |      |
|--------------------------------|----|----|----|------|------|------|
| P/E adjusted and fully diluted | na | na | na | 0.0  | 0.0  | 0.0  |
| P/CF                           | na | na | na | na   | na   | na   |
| P/BV                           | na | na | na | na   | 3.2  | 7.3  |
| Dividend yield (%)             | na | na | na | 0.0% | 0.0% | 0.0% |
| FCF yield (%)                  | na | na | na | na   | na   | na   |
| EV/Sales                       | na | na | na | na   | na   | na   |
| EV/EBITDA                      | na | na | na | na   | na   | na   |
| EV/EBIT                        | na | na | na | na   | na   | na   |
| EV/IC                          | na | na | na | na   | na   | na   |



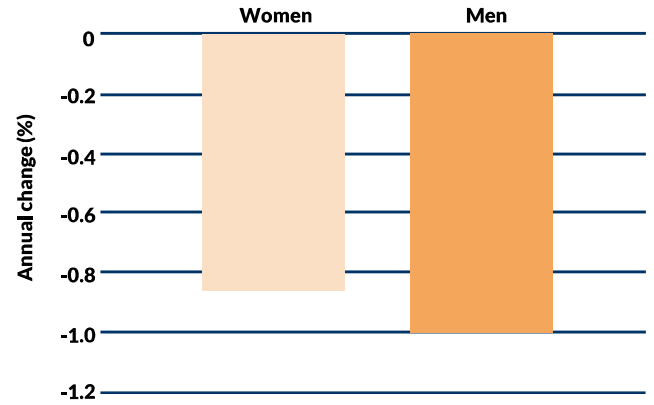
# Investment case in six charts

Chart 1: Share of the population over 80, 1990-2050E



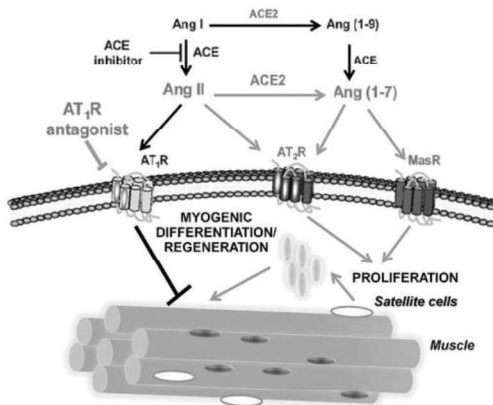
Source: OECD

Chart 2: Skeletal muscle loss over three years in older adults



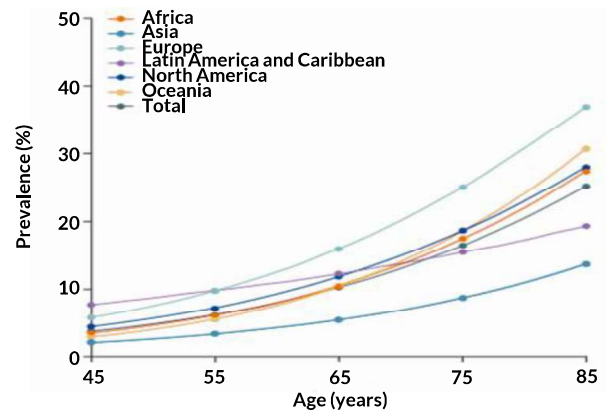
Source: Goodpaster et al., 2006

Chart 3: Renin-angiotensin system (RAS) system



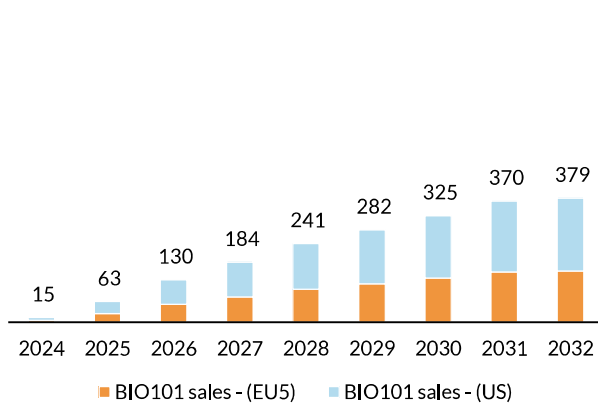
Source: Kepler Cheuvreux

Chart 4: Age trends and prevalence of AMD by region (early-stage AMD)



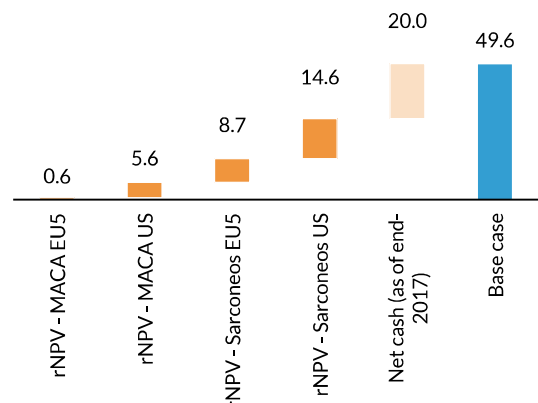
Source: Wong et al., 2014

Chart 5: Sarconeos sales (EURm) 2024-32E



Source: Kepler Cheuvreux

Chart 6: rNPV Biophytis (EURm)



Source: Kepler Cheuvreux

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# Investment case summary

## Sarcopenia the leading opportunity

Biophytis is a pharmaceutical company which specialises in age-related pathologies. More specifically, Biophytis has developed two platforms: 1) Sarcob, which is developing the BIO101 candidate for the sarcopenia indication; and 2) Maculia, which is developing the BIO201's compound for the treatment of intermediate AMD. The company has developed its pipeline based on plant-derived APIs, which traditionally produce fewer side effects than chemically derived APIs. However, a main headwind for these APIs is that they are traditionally more costly to produce and industrialise.

The most advanced programme for Biophytis is its BIO101 candidate which has just started its phase IIb, SARCO-INT, for the sarcopenia indication. Sarcopenia is defined as the loss of skeletal muscle mass and strength that occurs with advancing age. It has been accepted as a disease by the WHO since 2016, and therefore increased interest from large pharmaceutical companies for this mass market pathology is probable. The diagnosis of the disease requires both a muscle mass quality assessment through a hospital-based measurement (DEXA test) and a strength test carried out by GPs. No pharmaceutical treatment option exists for this mass market profile indication, making it an attractive opportunity.

BIO101 is a steroid which directly stimulates the production of muscle proteins. BIO101 has historically been used in Chinese and Russian pharmacopeia. Initially, Biophytis sought to develop BIO101 for the metabolic syndrome indication. However, a change in the regulatory environment made the company shift its strategy and decide to develop BIO101 for sarcopenia. In pre-clinical testing, the candidate displayed both *in vitro* and *in vivo* anabolic properties, which resulted in improved functional performance in old animals. Due to these positive results, Biophytis carried out a phase I trial called SARA-PK and accorded a clean safety profile to BIO101. Despite this promising profile and the potential lucrative market, BIO101 still needs to demonstrate the clinical efficacy of its lead candidate in the ongoing phase IIb trial SARA-INT. Topline results of the trial are expected in summer 2019, and are a key milestone for Biophytis's future prospects.

## Maculia: the second pillar

Biophytis's second platform, Maculia, aims to develop plant-based APIs for the AMD indication. Intermediate AMD precedes the two late-stage forms which are commonly known as dry AMD (or geographic atrophy (GA)), and wet AMD. While some approved anti-VEGF treatments can help patients with wet AMD, no option exists either for dry AMD or intermediate AMD. AMD epidemiology is booming due to the aging of the global population.

Intense R&D activity is ongoing in the dry-AMD field. However, due to the heterogeneity of dry AMD's etiology, no success has been recorded in clinical trials. The only partial improvement seen in the past decade was the use of an anti-oxidative nutritional regimen. As such, AMD is a notoriously difficult disease to address for the pharmaceutical industry.

Biophytis currently has one asset in clinical stage, BIO201, developed for intermediate-AMD. The drug-candidate targets the formation of A2E, a phototoxic by-product of the visual cycle, which is part of the root cause of vision loss in AMD patients. In AMD, it has been observed that the deregulation of this cycle leads to oxidative stress on eye cells due to the accumulation of A2E, which kills the important retinal pigment epithelium (RPE) cells. Biophytis aims to prove BIO201's ability to reduce this stress with a proof-of-concept clinical trial, called MACA-INT, which should start in 2019. Before then, a phase I/IIa trial to prove the clean safety profile of the asset is planned for 2018 (MACA-PK). Full results of MACA-INT are expected for the H2 2021, and as such the Maculia platform is far from producing any tangible results.

### Deconstructing the forecasts

Biophytis has two assets in clinical trial: BIO101 was developed for the sarcopenia indication, and BIO201, which is set to start its clinical life for the AMD indication. As such, we developed two distinct sales models taking into account the most recent data on prevalence, diagnosis and current treatment rates. We also took into consideration the competitive environments, as well as the current pricing context in the mass pharmaceutical market field. As such, due to the APIs not being new molecular entities (NME), and their well-known profile, we estimate that both Macuneos (BIO201) and Sarconeos (BIO101) should be priced at around EUR1500 and EUR800 respectively (US pricing).

### Valuation, target price and risks

In our valuation of Biophytis, we focus on BIO101's potential to treat severe sarcopenia, and BIO201's efficacy against intermediate AMD. For both candidates, we take the hypothesis of a licensing deal at the end of their respective phase IIb trials (SARA-INT and MACA-INT). As such, we think that Biophytis will not look to commercialise its own candidates. Biophytis has sufficient means to finance its own operations until end-2019. We value each project with a risk-adjusted net present value (rNPV). Our base case valuation of Biophytis stands at EUR3.7 per share.