

Waly Diah<sup>1</sup>, Cendrine Tourette<sup>1</sup>, Carole Margalef<sup>1</sup>, René Lafont<sup>1,2</sup>, Philippe Dupont<sup>1</sup>, Pierre Dilda<sup>1</sup>, Stanislas Veillet<sup>1</sup>, Samuel Agus<sup>1</sup> and Susanna Del Signore<sup>3</sup>

<sup>1</sup> Biophytis, UMPC – BC9, 4 place Jussieu, 75005 Paris, France. <sup>2</sup> Sorbonne Université, UPMC Univ Paris 06, Paris-Seine Biology Institut (BIOSE), CNRS, 75005 Paris, France. <sup>3</sup> Bluecompanion Ltd, London, United Kingdom

## Introduction

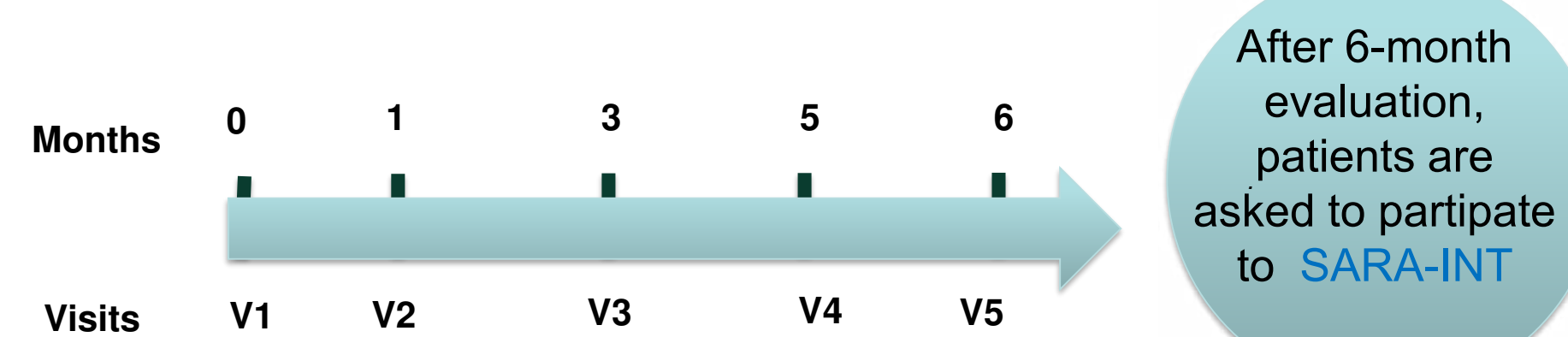
Sarcopenia, is characterized by the loss of muscle mass and muscle strength leading to a global muscle functional impairment and physical disability. Biophytis has developed the drug candidate Sarconeos (BIO101), purified at 97% of 20 hydroxyecdysone (20E), from the edible plant *Stemmacantha carthamoides*. BIO101 has a potential to improve muscle quality and function in *in vitro* and *in vivo* models and accelerates differentiation and enhances mitochondrial function in skeletal muscle cells (see Poster number 4-011). SARA-OBS, is the ongoing observational study dedicated to characterize the population for SARA-INT, the interventional study with the investigational drug BIO101. Both studies are hosted in SARA-Data, an innovative platform for clinical trials. Each of SARA-OBS and SARA-INT study is a 6-month multicenter, clinical trial enrolling community-dwelling persons in Europe and USA and aged 65 years and older at risk of mobility disability. The main objective of SARA-INT is to evaluate 2 selected doses of BIO101 in the targeted sarcopenic population.

## SARA-OBS

Sarcopenia definition used the criteria of the Foundation of NIH (Studenski et al., 2014) with the risk of mobility disability operationalised using the Short Physical Performance Battery (SPPB; Guralnik et al., 1994)

- Absolute ALM (< 19.75 in men and < 15.02 in women) and ALM/BMI (< 0.789 in men, < 0.512 in women) measured by DXA.
- SPPB ≤ 8/12;

## SARA-OBS Clinical study design



### Main objective

• Characterize the target population in Europe and USA and estimate the prevalence of sarcopenia including sarcopenic obesity in the study sample.

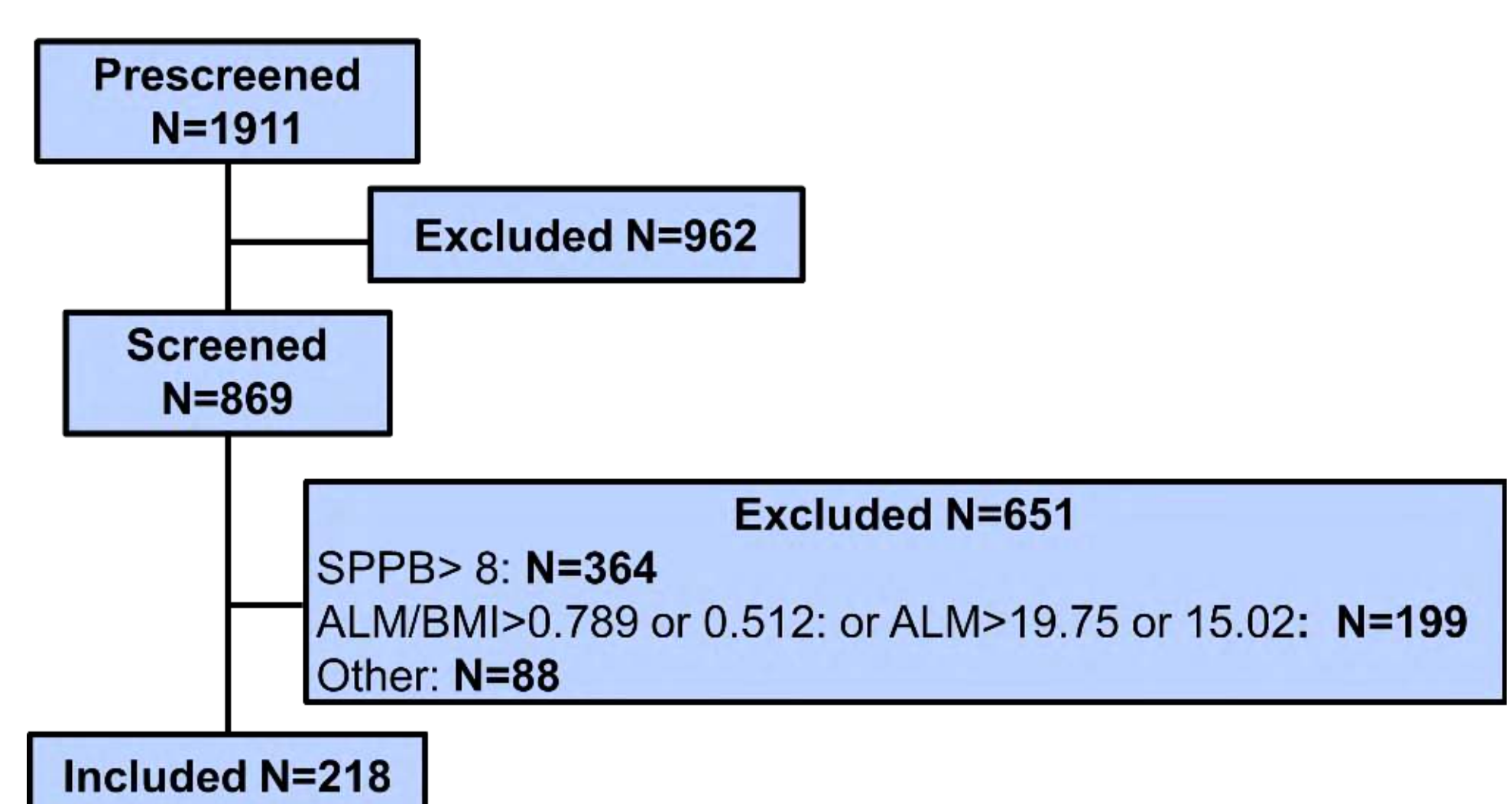
### Primary endpoint:

- 400 m walking test gait speed
- Patient reported outcomes (PROs): Short Form Health Survey (SF-36) and Sarcopenia Quality of Life (SARQOL) and TSD-OC for BMI ≥ 30

### Secondary and exploratory endpoints

- Body composition, Gait speed; Grip strength, 6 minutes walk.
- Actimetry; Biomarkers (Myostatin; PIIINP; IL-6; HsCRP; Aldosterone; Renin; Isolated PBMC, etc...)

## SARA-OBS Workflow



- 50 % of the prescreened patients were not retained. Main reasons were the absence of reported mobility issue and conditions included in SARA-OBS exclusion criteria list.
- Prescreening failure (Prescreened vs included) was rather high: only 11 % of prescreened were selected.
- Screening failure was high, and only 25 % of screened patients were included. Similar or even lower rates were also observed in other sarcopenia clinical trials: 5% (Fielding et al., 2017a), 11% (Fielding et al., 2017b) and 23% (Marzetti et al., 2018)
- Main reasons of screening failure are SPPB > 8 (56%), ALM/BMI > 0.789 or > 0.512 and ALM > 19.75 kg or > 15.02 kg (31%), other screening failures representing 14%.

## SARA-OBS Main characteristics

### Baseline characteristics of SARA-OBS included patients

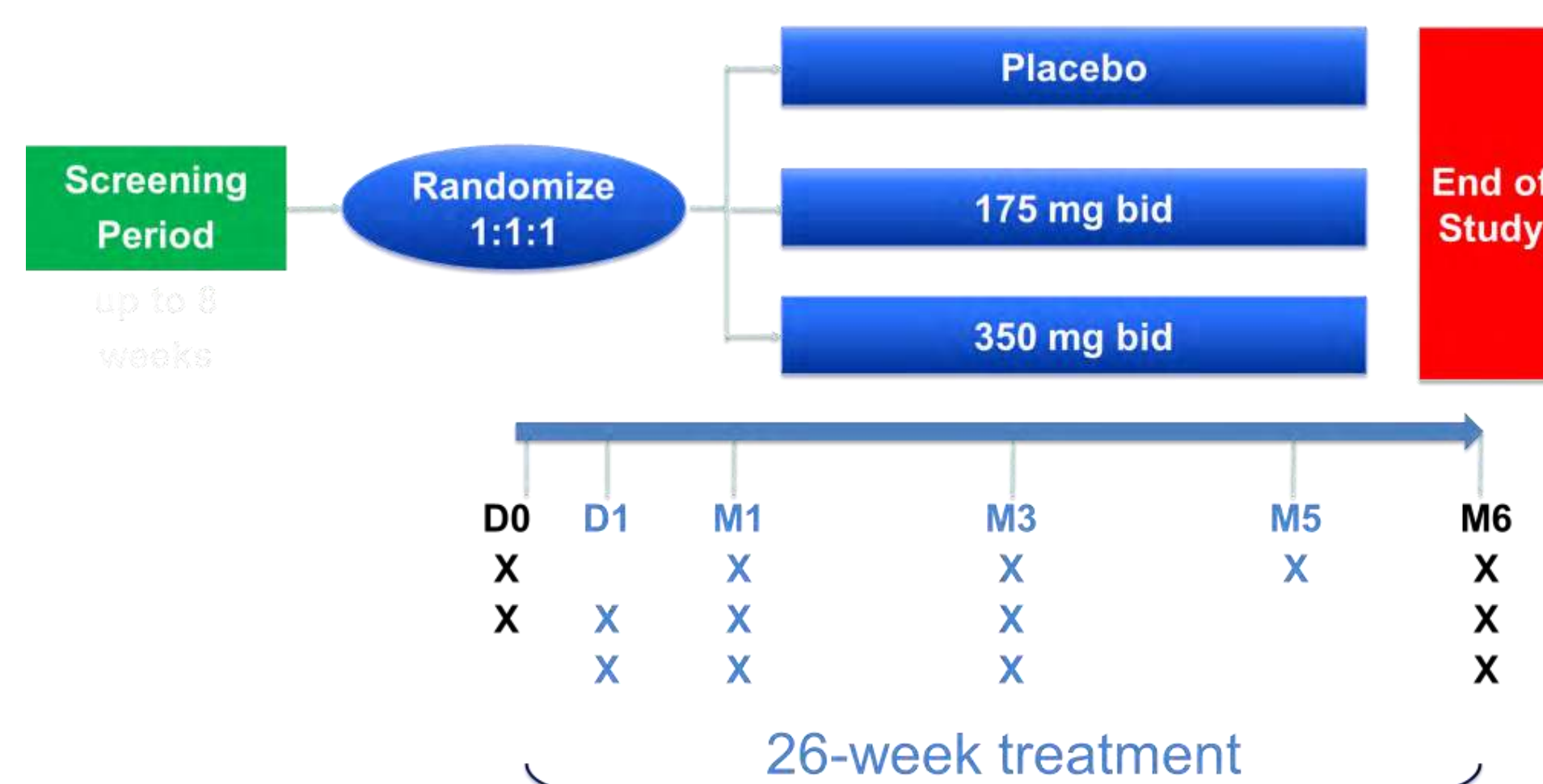
Characteristics	Absolute	Standard deviation	Characteristics	Mean	SD	
Age	79.29	7.39	SF36	Physical function (PF)	52.32	26.08
BMI	29.3	6.8		Role, physical (RP)	42.42	34.47
Male:Female (%)	39:61	NA		Role, emotional (RE)	68.33	29.88
SPPB	6.12	1.83		Bodily pain (BP)	62.29	25.70
Gait Speed in SPPB (sec)	0.70	0.29		Mental health (MH)	68.88	21.82
Chair stand	1.73	0.97		Vitality (VT)	56.47	21.78
				Social function (SF)	73.36	24.96
Appendicular Lean Mass (ALM)	17.17	5.07	General health (GH)	56.87	19.07	
			Maximum Grip strength (kg)	26.7	13.0	
Men	21.30	4.81	Men	31.6	12.8	
Women	14.28	2.69	Women	23.3	12.0	
ALM/BMI	0.59	0.12				
Men	0.69	0.10				
Women	0.52	0.09				
6MWD	295.14	95.99				
400M (min)	8.41	3.20				
Gait speed 400M (m/sec)	0.88	0.27				

- As seen in other large sarcopenia clinical trials, patients showed high BMI allowing to incorporate sarcopenic obese patients.
- 400 m gait speed is similar to the Life study (0.83 m/s at baseline; Pahor et al., 2014).
- Mean SPPB is rather low (6.12/12), corresponding to patients at risk of mobility disability and comparable to other sarcopenia studies (Life study with 7.4±1.6 in the physical activity group, Pahor et al., 2014 and SPRINTT with 6.7±1.4, Marzetti et al., 2018).
- Gait speed SPPB is <0.8 m/s, and fits the EWGSOP definition of sarcopenia and is comparable to value in SPRINTT.
- ALM/BMI in men is lower than the FNIIH threshold (0.69 vs 0.789) but is similar in women (0.52 vs 0.52).
- The 6MWD at 295.14 meters was expected for patients of the mean age (79.29 years) and BMI (29.3). This is low compared to data from sarcopenic patients (575.7±91.8 in men and 523.3±83.4 in women; Pederso-Chamizo et al., 2014) or (461.8 (108.6) in men and 392.8 (118.2) in women; (Gouvea et al., 2013).
- Hand Grip strength was average higher compared to cut points of revised EWGSOP2 (Cruz-Jentoft et al., 2018). Grip strength is <27 kg for 31 % of men, and < 16 kg for 26 % of women.

## SARA-INT

### SARA-INT clinical study design

- SARA-INT is an EU and US double-blind, placebo controlled, randomized interventional clinical trial.
- SARA-INT aims to evaluate safety and efficacy of Sarconeos (BIO101), the investigational drug orally administered for 6 month.
- Most of the sites that participated in SARA-OBS, and additional sites are currently being selected.
- All the patients recruited in the SARA-OBS study are ready to be randomized in the SARA-INT study.
- A pharmacokinetic sub study in Europe is also included in the SARA-INT study



## SARA-INT

### SARA-INT objectives

#### Primary objectives:

- Evaluate the effect of two daily doses of BIO101 versus placebo on gait speed at the 400M test.

#### Key secondary objectives

- Compare the change from baseline of the Patient Reported Outcome (PRO): The Physical Function Domain (PF-10) of the Short Form Health Survey (SF-36).
- Rising from a chair

#### Other Secondary, Tertiary and Exploratory Objectives

- Body composition; Muscle strength; Stair climbing; SPPB;
- PRO (SF-36, SarQoL, TSD-OC);
- Actimetry; Biomarkers (Myostatin; PIIINP; IL-6; HsCRP; Aldosterone; Renin; Isolated PBMC, etc...)

#### Target population

334 sarcopenic patients reporting loss of physical function and considered at risk of mobility disability will be recruited for the SARA-INT study.

The recruitment criteria are similar to the Foundation of NIH (Studenski et al., 2014)

- SPPB ≤ 8/12
- Absolute ALM (< 19.75 in men and < 15.02 in women)
- and ALM/BMI (< 0.789 in men, < 0.512 in women) by DXA

### SARA-INT preliminary results

Characteristics	Absolute	Standard deviation	Characteristics	Absolute	Standard deviation
Age	79.33	6.43	ALM/BMI	0.65	0.13
BMI	28.2	8.6	Men	0.72	0.07
Male:Female (%)	61:39	NA	Women	0.53	0.12
SPPB	7.78	2.02	6MWD	306.32	96.61
Gait Speed in SPPB (sec)	0.85	0.21	400M (min)	8.33	1.96
Chair stand	1.53	0.74	Gait speed 400M (m/sec)	0.85	0.21
Appendicular Lean Mass (ALM)	17.87	5.45			
Men	20.34	5.3			
Women	13.99	3.01			

- As of today, 18 patients are randomized
- 39% of randomized patients are subjects coming from SARA-OBS clinical study
- Overall, SARA-INT population shares the same characteristics as SARA-OBS.
- Mean SPPB score and 400 m gait speed are very similar to the LIFE study (7.78 vs 7.4 and 0.85 vs 0.83 m/s respectively)
- ALM/BMI in men is lower than the FNIIH threshold (0.72 vs 0.789) but is similar in women (0.53 vs 0.52).
- The mean 6MWD at 306.32 meters is low compared to data of sarcopenic patients from other studies (mean from 461.8 to 575.7).

## Conclusions

- Like for other sarcopenia observational studies, SARA-OBS confirmed recruitment opportunities in sarcopenia trials when using the FNIIH criteria (Studenski et al., 2014, ALM/BMI < 0.789 in Men and < 0.512 in Women) and Absolute ALM < 19.75 kg in men and < 15.02 kg in women.
- Similar to SPRINTT study, we selected low performers at SPPB ≤ 8/12 as an index of mobility disability risk.
- Baseline characteristics are comparable to other sarcopenia studies (Life study, Pahor et al., 2014; SPRINTT Marzetti et al., 2018).
- Preliminary analysis confirmed that that target population derived from SARA-OBS is eligible for the SARA-INT phase 2 interventional study.
- SARA-INT clinical trial received all due authorisations from Competent Authorities in USA and Belgium.

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