The MYODA Seamless clinical trial design: A true innovation for Rare Diseases including DMD

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BACKGROUND

Clinical development of new medications is traditionally broken down into 3 phases. This prevents patients from participating in more than one of the development phases and comes with a burden on site staff (with repeated site initiation and training) leading to prolonged development timelines (up to 10 years) and difficulties in patient recruitment, especially in rare diseases such as Duchenne Muscular Dystrophy (DMD).

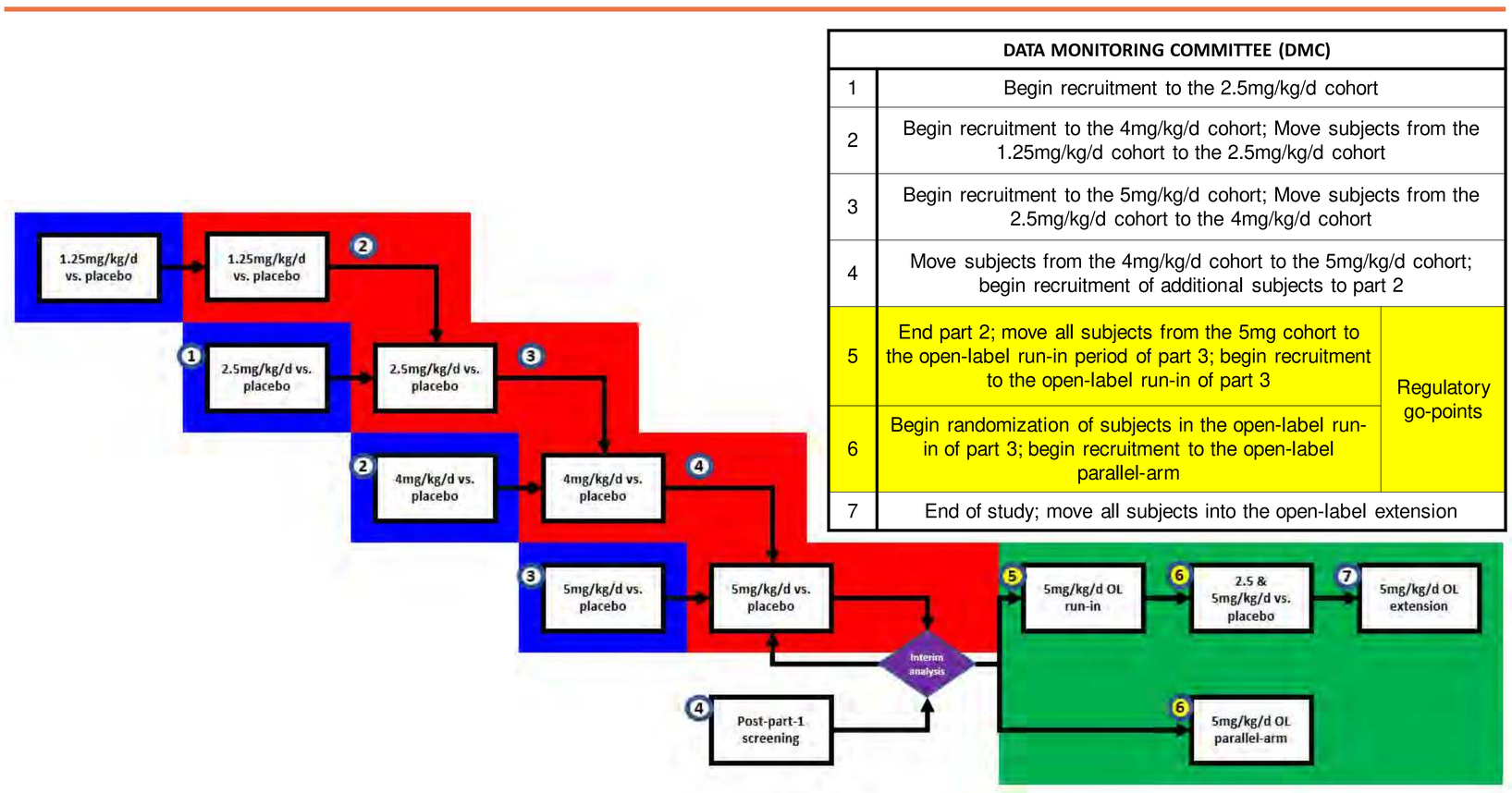
There is a significant need, therefore, for utilization of novel designs, which will make clinical development more approachable for patients and more efficient for study site staff.

Biophytis is developing BIO101 for DMD. The pre-clinical proof-of-concept (PoC) for BIO101 suggests a range of benefit in a broad DMD population (for more details see poster# P11-116-#351). To ensure an optimal and patient-centered clinical development of BIO101 a seamless methodology will be utilized.

DESIGN

Part	Objective	Design	Period / element	Subjects	Length / timing
1	Safety, tolerability Pharmaco-kinetics (PK)	Multiple ascending doses, randomized, blinded, placebo-controlled		4 cohorts, 12 subjects in each (3 placebo, 9 treatment)	7 days
2	Proof-of-Concept (PoC) Biomarkers and pharmaco-dynamics (PD)	Adaptive, randomized, blinded, placebo controlled, with a recurrent interim analysis to assess success and futility	Double-blind period	All subjects, who participated in part 1 continue directly into part 2. Subjects who started in the low doses cohorts will be moved into the higher doses cohort as soon as the data monitoring committee (DMC) will deem this as safe. New subjects are enrolled, as long as the DMC did not deem pat 2 as successful if futile – Subjects will remain on placebo for a maximum of one year, after which they will begin to receive study medication.	3-12 months
			Interim analysis	Assessment for success and futility is done every 3 months by the DMC. In case of futility – the study and all of its procedures will be stopped. In case of success, preparations will begin to gain regulatory approval to move into part 3 and to reach the final design of the part	Every 3 months from the time point, at which all participants in parts 1 and 2 finished at least 3 months of treatment
			Waiting period	Once success was declared by the DMC – all participants will be enrolled into an open label waiting period until regulatory approval to proceed to part 3 was obtained	3-6 months
3	Confirmatory – efficacy and safety	Parallel arms, randomized withdrawal, double-blind, placebo-controlled	Run-in period	For new subjects (who did not participate in part 1 and 2). This period is similar to the waiting period of part 2	3 months
			Double-blind period	All the subjects in the waiting period of part 2 and run-in period of part 3 will be randomized into placebo or treatment. Subjects who were on placebo during part 1 and the double-blind period of part 2 will not be randomized again to placebo.	12 months
			Interim analysis	The DMC will monitor continuously, to identify subjects who have deteriorated due to being randomized to placebo. In addition, a periodic analysis will be made, to identify if study success criteria are met.	TBD
			Open-label parallel arm	Subjects, who will not be eligible to participate in the randomized arms of part 3 will be offered to participate in an open-label arm, which will run in parallel to the randomized arms and will undergo similar assessments as those of the randomized arms.	Until approval
			Open-label extension	After participation in the double-blind periods, subjects will continue to an open-label extension	Until approval

STUDY SCHEME



DATA MONITORING COMMITTEE (DMC)		
1	Begin recruitment to the 2.5mg/kg/d cohort	
2	Begin recruitment to the 4mg/kg/d cohort; Move subjects from the 1.25mg/kg/d cohort to the 2.5mg/kg/d cohort	
3	Begin recruitment to the 5mg/kg/d cohort; Move subjects from the 2.5mg/kg/d cohort to the 4mg/kg/d cohort	
4	Move subjects from the 4mg/kg/d cohort to the 5mg/kg/d cohort; begin recruitment of additional subjects to part 2	
5	End part 2; move all subjects from the 5mg cohort to the open-label run-in period of part 3; begin recruitment to the open-label run-in of part 3	Regulatory go-points
6	Begin randomization of subjects in the open-label run-in of part 3; begin recruitment to the open-label parallel-arm	
7	End of study; move all subjects into the open-label extension	

STUDY POPULATION

Study inclusion is will be non-restrictive as possible.

Patients with DMD, aged 7 and above and FVC <50%, ambulant and non-ambulant, will be included

Patients not eligible for the double-blind period of part 3, will be offered to participate in the open-label parallel arm of part 3

ENDPOINTS AND ANALYSIS

The study population is broad and diverse and patients experience disability in an individual manner, there is a need to assess the efficacy of BIO101 in a manner that will reflect the individual experience.

See more details in the Composite Score poster# P11-128-#459 for more details

DISCUSSION AND IMPLICATIONS

- **The MYODA study is designed to address the challenges that medication development faces, especially in rare disease. It also aims to accommodate the needs of DMD patients while maximizing efficiency and operational excellence**
- **The MYODA study design will also ascertain that it is conducted under the highest standards and scientific rigor. The study will be closely monitored by a data monitoring committee and the regulatory authorities in the countries where it is conducted.**