Results of two clinical trials in vulnerable populations support the evaluation of BIO101 (20-hydroxyecdysone), a MAS Receptor activator as a candidate oral treatment for rare pediatric neuromuscular diseases

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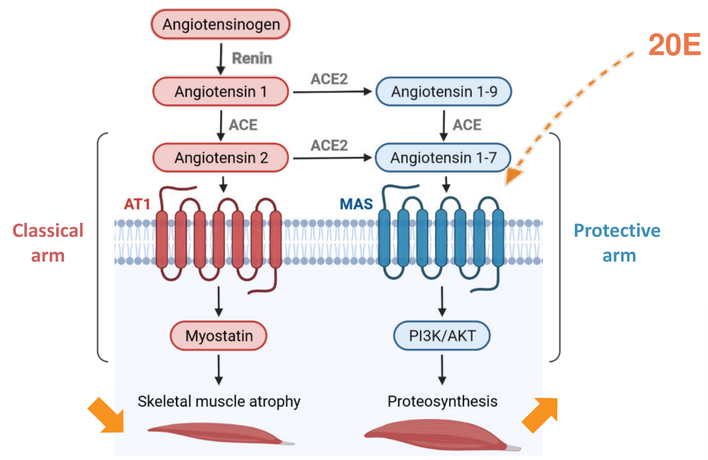
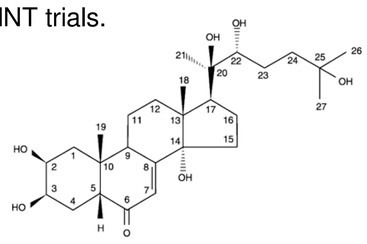
BIO101 (20-Hydroxyecdysone - 20E)

BIO101 (20-hydroxyecdysone – 20E) is a new oral drug candidate activating the MAS receptor (a major receptor in the renin-angiotensin system) leading to muscle anabolism, which already demonstrated meaningful activity in animal models of muscular dystrophies (Lafont *et al.*, 2022) and respiratory function. Furthermore, BIO101 (20E) has also demonstrated beneficial effects in two vulnerable populations in clinical settings, in the COVA and SARA-INT trials.





BIO101 (20E) is a pharmaceutical grade preparation of 20-hydroxyecdysone. BIO101 is a MASR activator

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20-Hydroxyecdysone activates the protective arm of the RAAS via the MAS receptor

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Affiliations + expand

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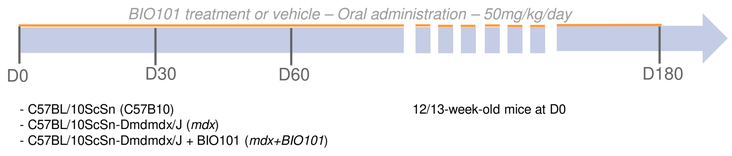
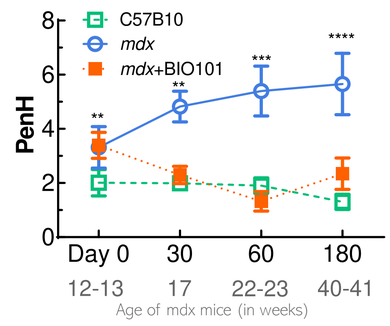
Duchenne Muscular Dystrophy Preclinical Data on respiratory function in mdx mice

- ***Whole body Plethysmography***





Sustainable 20E (BIO101) effects on lung reactivity in C57B10 mdx mice. The enhanced pause (Penh) of mdx, BIO101 treated mdx mice, and WT C57B10 was measured in response to 40 mg/ml of methacholine by plethysmography *p<0.05, **p<0.01, ***p<0.001, ****p<0.0001. Bonferroni test compared to control at each time point.

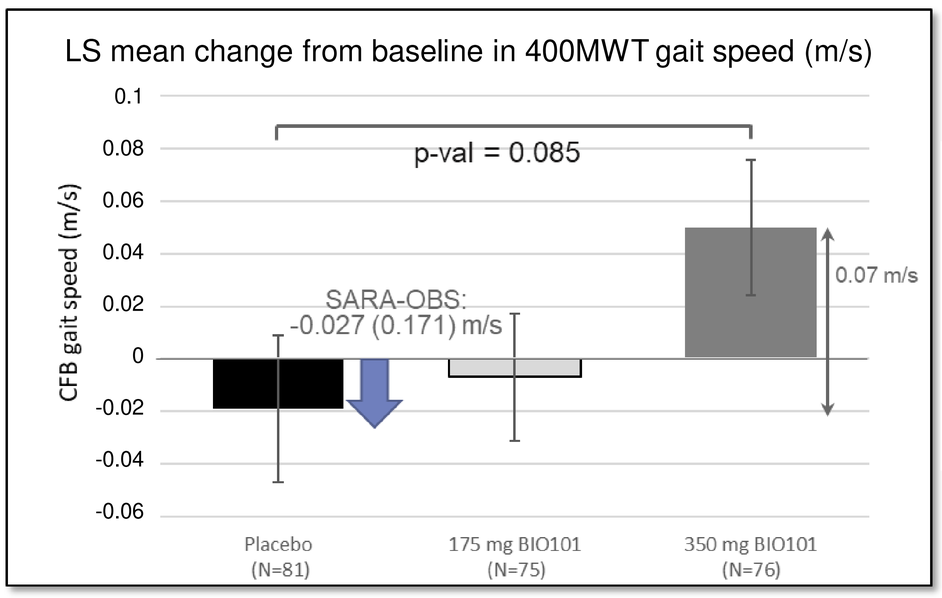
- ***BIO101 treatment significantly improves airway responsiveness as measured by PenH (normalization of Penh values in mdx mice vs control mice).***
- ***BIO101 effects are sustained for 6 months.***

➢ ***For full preclinical proof of concept, see Poster #P083***

SARA-INT trial

233 Sarcopenic seniors aged 65+ (FNIH criteria + SPPB ≤8) treated with BIO101 at 2 doses (175 mg / 350 mg bid BIO101 versus placebo) up to 9 months

Secondary statistical analysis of Change From Baseline (CFB) in 400MWT gait speed based on Multiple Imputation for subjects without on-site visit data at M6 and adjusted Bayesian Imputation for non completers at M6 in the FAS population

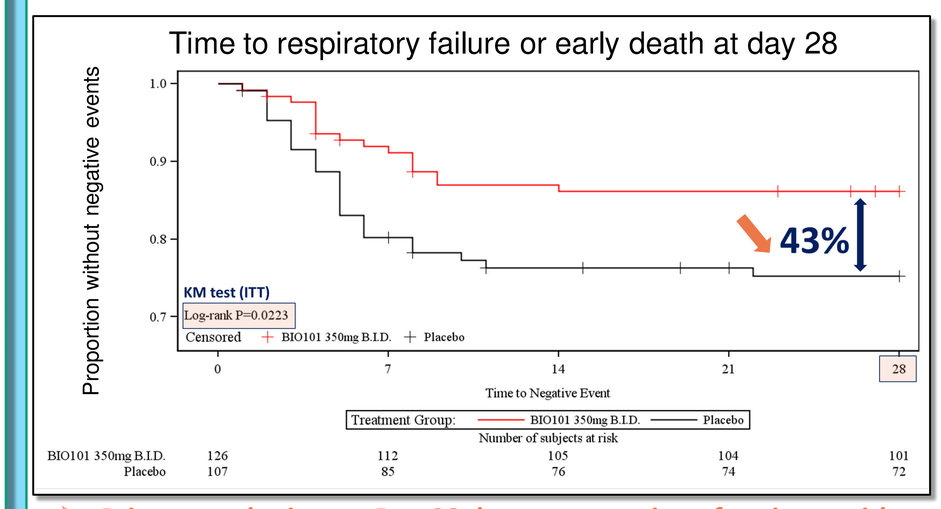


- ***Natural deterioration in gait speed in placebo group, comparable to OBServational study***
- ***Trend for a dose effect***
- ***Close to statistical significance and close to clinical significance at the highest dose, consistent with other physical assessments***

COVA trial

233 hospitalized patients with severe COVID-19 having signs of pneumonia who may or may not require oxygen supplementation, and who are not on invasive mechanical ventilation or ECMO (extracorporeal membrane oxygenation), treated with BIO101 350 mg bid (n=126) versus placebo (n=107) up to 28 days.

KM analysis in the ITT population showed a difference in proportion of patients with respiratory failure or early death between BIO101 and placebo, p=0.0223, with a reduction of 43% in the treatment arm.



- ***Primary endpoint : at Day 28, lower proportion of patients with respiratory failure or early death in BIO101 group versus placebo, CMH test, p=0.0426, with a relative risk reduction of respiratory failure or early death of 43.8%***
- ***Reduction in the relative risk of early death by 43.8% at day 90***
- ***Trend in the adjusted difference in the proportion of patients with hospital discharge of 11% in BIO101 group versus placebo in ITT population, p= 0.0586 – CMH test***

BIO101 (20E) safety profile

BIO101 (20E) was administered to 253 vulnerable adults and showed a very good safety profile:

- In the SARA-INT trial, BIO101 (20E) showed a good safety profile after up to 9 months of dosing, with no significant difference between treatment arms and placebo for TEAEs, related TEAEs and SAEs as well as biliary imaging studies, ECG, safety laboratory parameters and vital signs.
- The COVA study showed a lower proportion of patients with TEAEs in the BIO101 350 mg bid group than in the placebo group (57% vs 64.4%) and in particular, a lower frequency for serious respiratory TEAEs (25% vs 30.8%).

MYODA proposed trial design

Proposed Trial design	Study Endpoints	Patient Population
• A Randomized, Double-Blind, multi-center Phase 1-2 Study • Approximately 12 clinical centers US/EU • Evaluation of the Safety, PK, PD and Efficacy of BIO101 in Non-Ambulatory DMD Patients with Respiratory Deterioration • Pediatric oral formulation (powder suspension) of BIO101	• Part 1 (N=15): Safety, tolerability & PK- initial 7 days of dosing of escalating dose of BIO101 (1.25 up to 4 mg/kg) • Part 2 (N=30 + 15 from Part1): Efficacy of BIO101 - Respiratory function after treatment for 48 weeks • Endpoints: respiratory function (FVC, PEF), muscle strength (PUL, Myogrip), QoL questionnaires	• Age: ≥12 years old • Non-ambulatory DMD patients, regardless of the genetic mutation • Patients with respiratory failure not yet requiring mechanical ventilation

- **BIO101 (20E) is a promising oral treatment for DMD patients with respiratory deterioration.**
- Beneficial effects on motor function in sarcopenic patients (SARA-INT phase 2b) and beneficial effects on COVID-19 patients with respiratory failure (COVA phase 2/3)
- Favorable safety profile (SARA-PK phase 1, good safety data on 149 SARA-INT participants with at least 6 Months of treatment and 126 adults in the COVA study)
- ODD granted in Europe and US, Biophytis plans to start the Phase 1/2 MYODA clinical trial after last regulatory interactions.