

INVESTOR UPDATE WEBINAR PRESENTATION

Melbourne, Australia – 6 February 2025: Percheron Therapeutics Limited (ASX: PER) ('the Company'), an international biotechnology company focused on the development of novel therapies for rare diseases, is pleased to provide investors with further information on the Company's phase IIb clinical trial results. The attached presentation will be delivered at the Company's webinar to be held at 9am (AEDT) Thursday 6 February 2025.

Percheron Chief Medical Advisor, Dr Cathryn Clary, will share findings from the company's analysis of the trial data. Thereafter, she and Percheron CEO, Dr James Garner, will be pleased to respond to questions from shareholders.

To register in advance please use the link below:

https://us02web.zoom.us/webinar/register/WN_Ex9lCP6AQ_63SGulZlCogA

The company will endeavour to make a recording of the webinar available afterwards for those shareholders unable to attend.

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About Percheron Therapeutics Limited

Percheron Therapeutics Limited [ASX: PER | US OTCQB: PERCF] is a publicly listed biotechnology company focused on the development and commercialisation of novel therapies for rare diseases. The company's lead program is avicursen (ATL1102), an antisense oligonucleotide targeting the CD49d receptor, which has been investigated in a range of inflammatory conditions, including multiple sclerosis and Duchenne muscular dystrophy.

For more information, please contact info@PercheronTx.com.

This announcement has been authorized for release to the Australian Securities Exchange by the Board of Directors.



Phase IIb Study of Avicursen (ATL1102) in Duchenne Muscular Dystrophy

Review of Six-Month Data

Dr Cathryn Clary
Chief Medical Advisor

6 February 2025



Forward-Looking Statements

This presentation contains **forward-looking statements** within the meaning of the safe-harbor provisions of the Private Securities Litigation Reform Act of 1995. These statements do not relate strictly to historical or current facts and may be accompanied by words such as ‘could,’ ‘would,’ ‘may,’ ‘potentially,’ ‘suggest,’ ‘believes,’ ‘expects,’ ‘should,’ ‘intends,’ ‘plans,’ ‘forecasts,’ and similar words or expressions.

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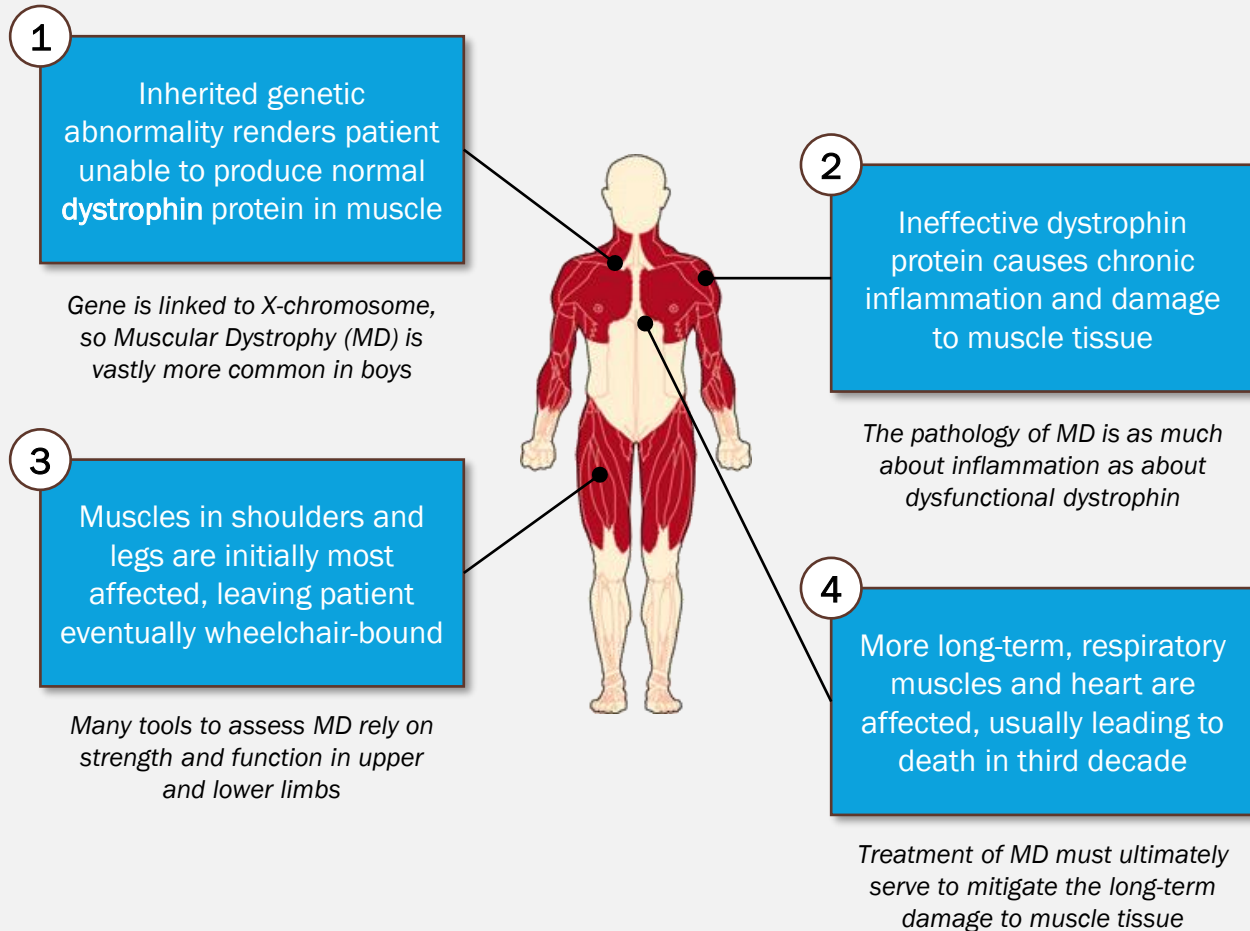
Any forward-looking statements contained in this presentation speak only as of the date this presentation is made, and we expressly disclaim any obligation to update any forward-looking statements, whether because of new information, future events or otherwise, except as may be required by law.

Introduction

- Antisense Therapeutics previously completed an open-label phase IIa pilot study of ATL1102 in nine non-ambulant boys with Duchenne muscular dystrophy (DMD).
 - The study was conducted at the Royal Childrens' Hospital in Melbourne, one of the leading DMD treatment centres in the Southern Hemisphere, from 2018 – 2020.
 - The study was formally a single-arm safety study, and the primary endpoints were safety and tolerability.
 - PUL2.0 was measured, and showed a favourable result at 6 months, with an average change in total PUL2.0 score of +0.9 points.
- On the basis of these results, the company originally sought to move directly into a phase III study.
 - However, FDA would not permit dosing for more than six months or at doses higher than 25mg until a 9-month toxicology study had been completed.
 - Moreover, the large phase III study that was originally contemplated would have been very challenging to finance.
- In late 2021, the strategy was changed, and the company launched an international phase IIb study that reduced time and expense while still keeping open the possibility of an early registration.
 - The phase IIb study was a randomised controlled trial, which is the level of evidence typically required by regulatory agencies and large pharma partners.
 - The study was placebo-controlled, which reduced the impact of confounding factors on relatively subjective endpoints such as PUL2.0.
 - PUL2.0 was selected as the primary endpoint because it is the presumptive approval endpoint for FDA and European agencies in non-ambulant DMD.
 - The study was conducted in thirteen hospitals in five countries, which provides a broader and more diverse sample of day-to-day clinical care.
 - The study otherwise aimed to recruit a similar population to the earlier phase IIa study.

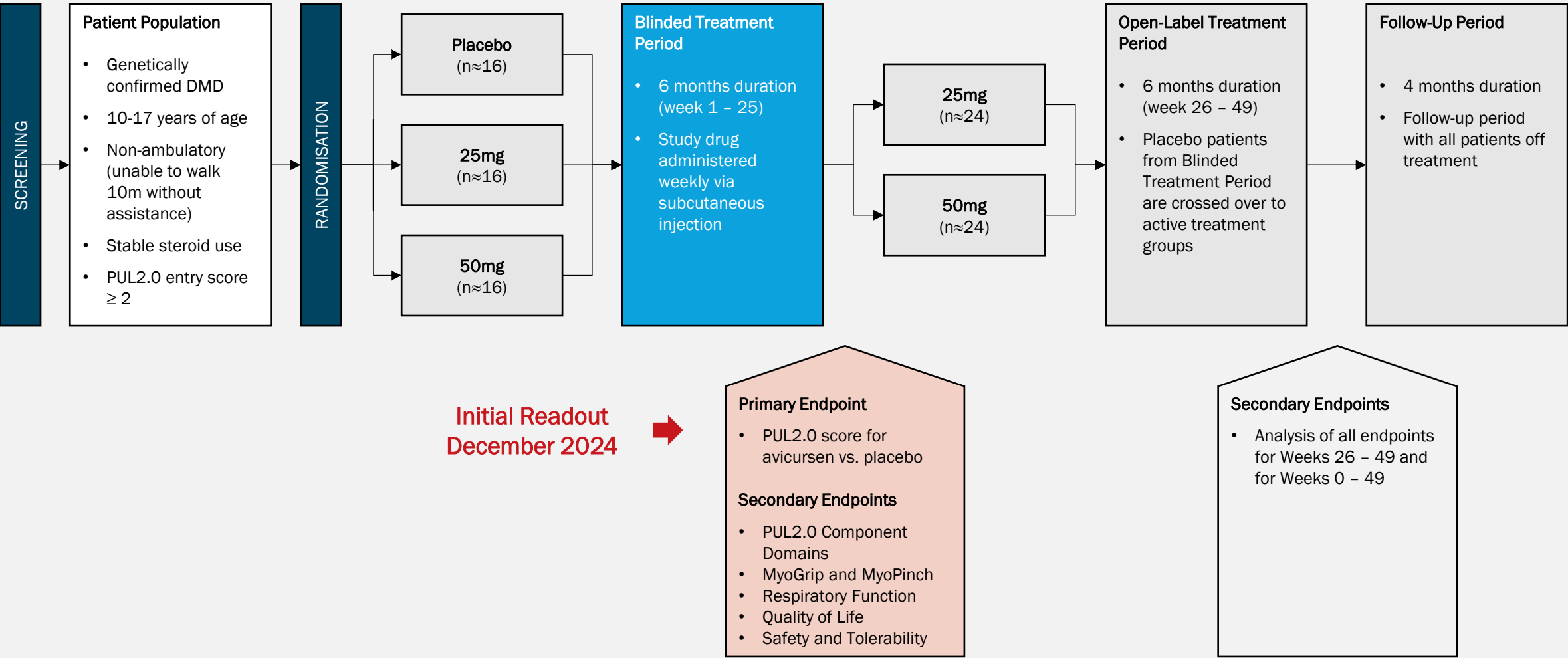
Background

Duchenne muscular dystrophy is an incurable genetic condition that affects approximately 300,000 children and young adults worldwide



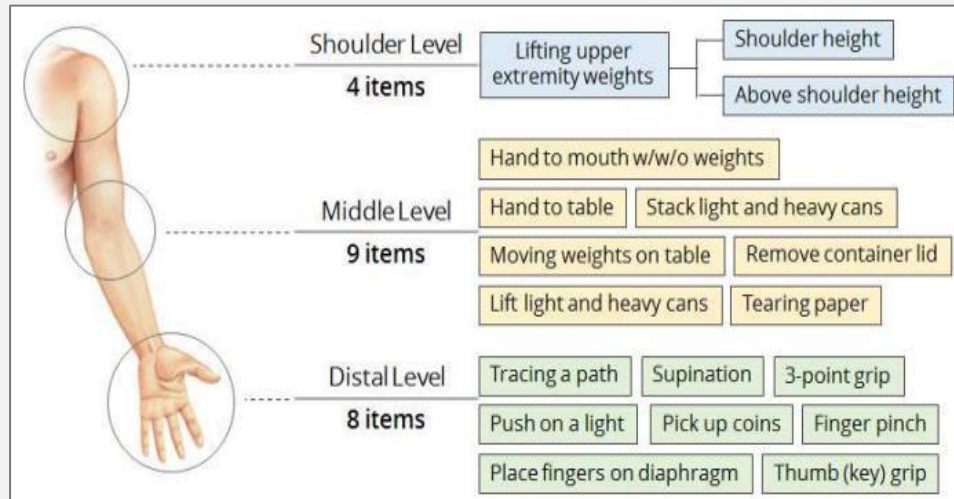
Duchenne muscular dystrophy represents ~50% of MD cases	Incidence is approximately 6 in 100,000 births	DMD also associated with cognitive dysfunction, brittle bones, and other degenerative effects
Usually diagnosed by Age 5	Typically wheelchair-bound by Age 12	Life expectancy 20s

The phase IIb study was designed in three sections, with a placebo-controlled primary read-out at six months to meet regulatory requirements



PUL2.0 is the primary endpoint of the study; MyoGrip and MyoPinch are included as secondary efficacy endpoints

Performance of the Upper Limb Module 2.0 (PUL2.0)

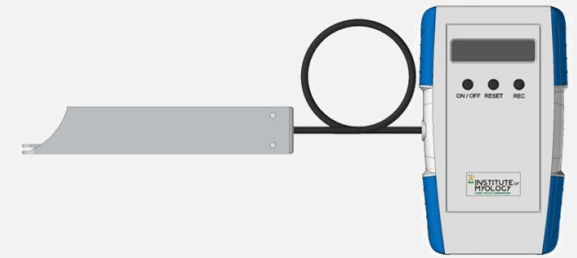


- PUL2.0 is a 'functional endpoint' – it measures the ability of the patient to perform actions relevant to daily life.
- PUL2.0 is an aggregate of three 'domains' or sub-components: upper / shoulder level; middle or elbow level; and distal or wrist level.
- The PUL2.0 assessment is performed in a highly standardised way, typically by a trained clinician or physiotherapist.

MyoGrip and MyoPinch



MyoGrip dynamometer



MyoPinch device

- MyoGrip and MyoPinch are proprietary measurement devices produced by the Institute de Myology in France.
- MyoGrip measures a patient's grip strength (largely a measure of forearm muscles) and MyoPinch measures their pinch strength (largely a measure of hand muscles).
- Assessment is performed by trained personnel and compared to standardised benchmarks for a comparable individual.

Topline Study Data (6-Month Endpoint)

Baseline Characteristics

In general, treatment groups were well-balanced at baseline

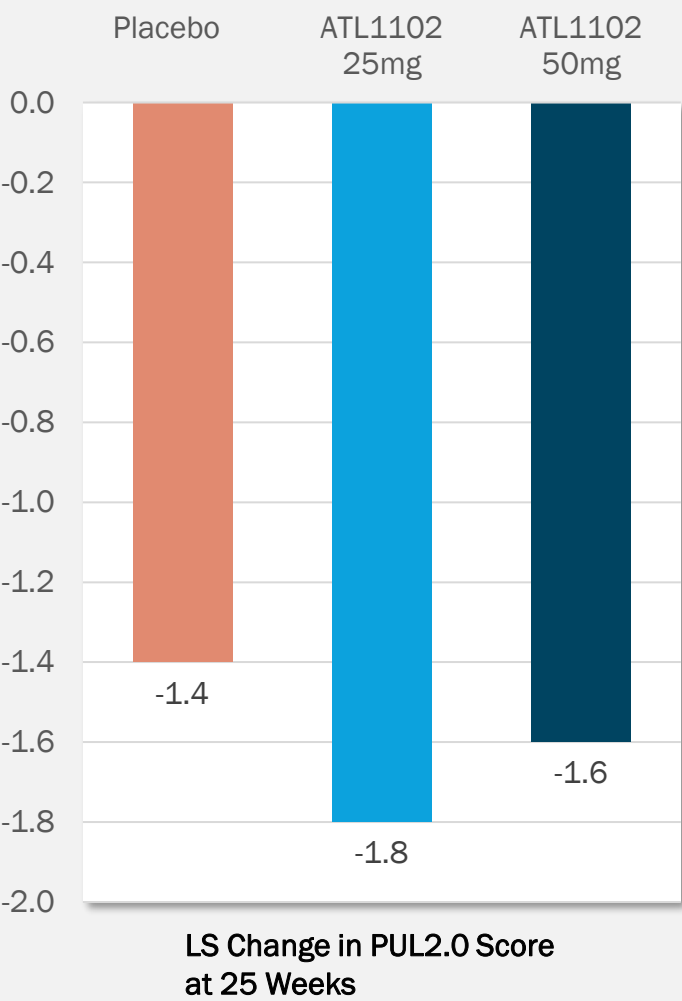
	Placebo	ATL1102 25mg	ATL1102 50mg
Sample size, n	17	16	15
Age, years, mean (SD)	13.6 (2.0)	13.4 (2.8)	12.7 (1.7)
Weight, kg, mean (SD)	58.7 (21.5)	59.2 (18.2)	55.6 (16.1)
Age at Diagnosis, years (SD)	4.4 (2.3)	6.3 (2.9)	6.3 (3.5)
Time since loss of ambulation, years, mean (SD)	1.5 (1.1)	1.7 (1.6)	1.8 (1.2)
Duration of steroid use, years, mean (SE)	8.4 (0.8)	7.0 (0.8)	5.7 (0.8)
PUL 2.0 total score, mean (SD)	28.3 (7.7)	27.3 (6.2)	28.1 (7.3)
PUL 2.0 shoulder domain score, mean (SD)	4.8 (4.0)	4.4 (3.3)	4.9 (3.6)
PUL 2.0 elbow domain score, mean (SD)	12.7 (3.1)	12.1 (3.0)	12.7 (3.0)
PUL 2.0 wrist & hand domain score, mean (SD)	10.8 (1.1)	10.9 (1.2)	11.0 (1.1)
% predicted MyoGrip (dominant hand), mean (SD)	39.7% (18.2)	36.7% (19.0)	38.9% (18.9)
% predicted MyoPinch (dominant hand), mean (SD)	39.3% (14.5)	40.5% (16.6)	39.2% (14.7)

Commentary

- In general, the three arms of the study were well-balanced, with no meaningful differences between them, implying successful randomisation.
- The two ATL1102 groups were, on average, older at diagnosis, but this is substantially driven by a small number of 'outlier' patients. This is unlikely to substantially affect study outcome.
- The placebo group had the longest average duration of steroid use before entering the study, followed by the 25mg group, with the 50mg group having the shortest duration of steroid use. It is possible that this may have slowed decline in the placebo group thus making it more difficult to show a difference. However, this is again unlikely to have definitively shaped the study outcome.

Overall PUL2.0 Measurement at 25 Weeks

No significant difference in the primary endpoint between the three arms of the study



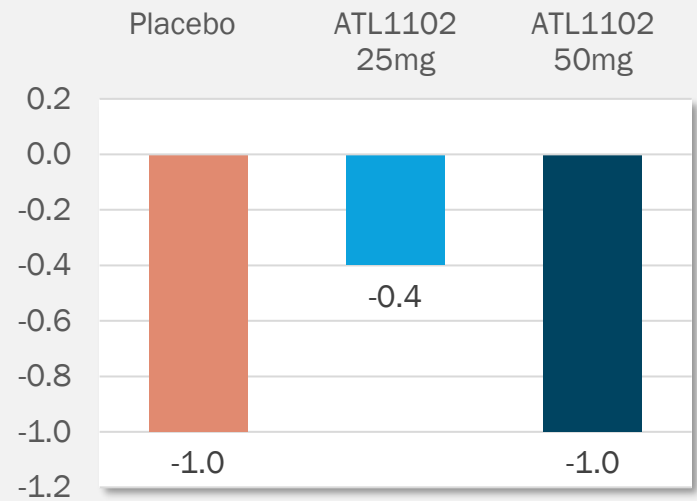
	Placebo	ATL1102 25mg	ATL1102 50mg
ANCOVA Analysis (Primary)			
Change from baseline (95% CI)	-1.4 (-3.3 – 0.4)	-1.8 (-3.7 – 0.0)	-1.6 (-3.6 – 0.5)
Difference vs. placebo (95% CI)		-0.4 (-2.5 – 1.7)	-0.1 (-2.3 – 2.1)
p-value		0.695	0.919
MMRM Analysis (Secondary)			
Change from baseline (95% CI)	-0.9 (-2.3 – 0.5)	-1.4 (-2.9 – 0.0)	-1.0 (-2.5 – 0.5)
Difference vs. placebo (95% CI)		-0.5 (-2.6 – 1.5)	-0.1 (-2.2 – 2.0)
p-value		0.607	0.935

- Commentary
- There was no statistically significant difference between the three arms of the study. Although there were numerical differences in favour of placebo, the *p*-value, which measures the statistical ‘meaningfulness’ of the data was much greater than 0.05, which is considered the threshold for statistical significance. Accordingly, the correct conclusion from this data is that there was no difference between treatment groups on the primary endpoint.
 - The MMRM analysis was a pre-defined secondary assessment and uses a broader range of data to assess treatment effect. The directional trend is very similar to the primary ANCOVA analysis.

PUL2.0 Domains at 25 Weeks

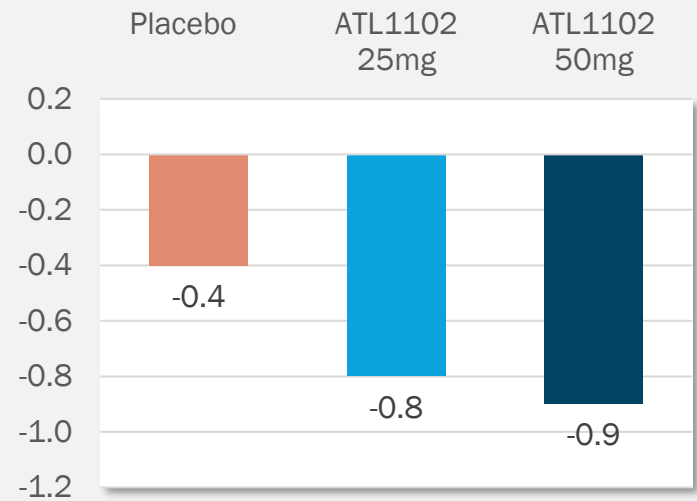
No significant differences between arms in constituent domains of PUL2.0

High-Level Shoulder Domain



	ATL1102 25mg	ATL1102 50mg
Difference vs. Placebo (95% CI)	0.7 (-0.5 - 1.8)	0.0 (-1.2 - 1.3)
p-value	0.274	0.942

Mid-Level Elbow Domain



	ATL1102 25mg	ATL1102 50mg
Difference vs. Placebo (95% CI)	-0.5 (-1.5 - 0.6)	-0.5 (-1.6 - 0.6)
p-value	0.403	0.353

Distal-Level Wrist Domain

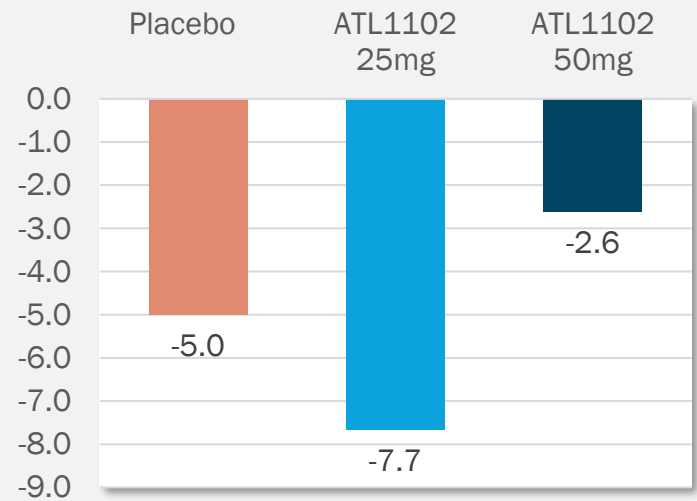


	ATL1102 25mg	ATL1102 50mg
Difference vs. Placebo (95% CI)	-0.3 (-0.8 - 0.3)	0.3 (-0.2 - 0.9)
p-value	0.327	0.243

MyoGrip and MyoPinch

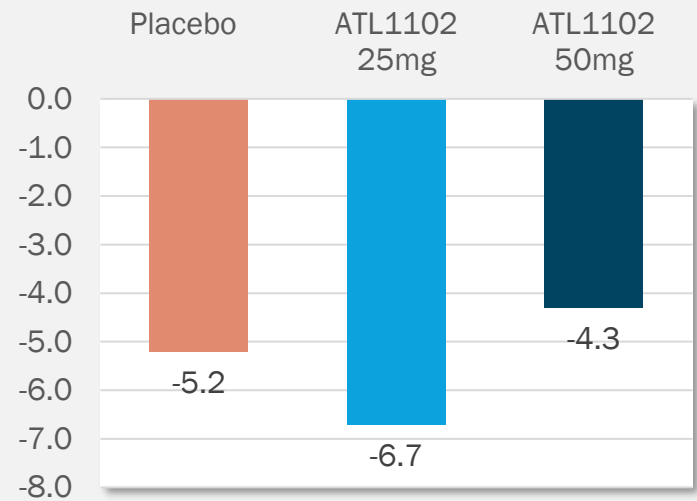
No significant differences between treatment groups on MyoGrip and MyoPinch secondary endpoints

MyoGrip



	ATL1102 25mg	ATL1102 50mg
Difference vs. Placebo (95% CI)	-2.7 (-10.6 – 5.3)	2.4 (-5.8 – 10.6)
p-value	0.502	0.559

MyoPinch



	ATL1102 25mg	ATL1102 50mg
Difference vs. Placebo (95% CI)	-1.5 (-7.2 – 4.3)	1.0 (-5.0 – 6.9)
p-value	0.614	0.740

Commentary

- MyoGrip and MyoPinch secondary efficacy endpoints showed no statistically significant difference between the three arms of the study.
- There was a directional trend toward modest benefit at the 50mg group, but this was non-significant.
- Taken with the distal (hand) domain of the PUL2.0 score, it is possible that there is a slight but non-significant trend to improvement in hand function at the 50mg dose.

Safety Outcomes

ATL1102 was generally safe and well-tolerated

	Placebo	ATL1102 25mg	ATL1102 50mg
Number of Patients, n			
Patients	17	16	15
Discontinuations due to Adverse Events (AEs) (%)			
From Study	0	0	0
From Treatment	0	0	0
Adverse Events, n (%)			
Total	12 (71%)	14 (88%)	13 (87%)
Serious	0 (0%)	3 (19%)	0 (0%)
Severe	0 (0%)	1 (6%)	0 (0%)
Related to Study Treatment	3 (18%)	7 (44%)	10 (67%)

Commentary

- ATL1102 was generally safe and well-tolerated. No patients discontinued either drug treatment or study participation as a result of adverse events.
- There was a dose-dependent trend towards more adverse events that were considered by investigators to be ‘related’ to study treatment, with the 25mg group showing more AEs than placebo and the 50mg group showing more than 25mg. This is, in some respects, encouraging, since it points to the pharmacological activity of the drug.
- The most common adverse events related to study treatment were injection site reactions, which are common with injectable therapies and which were also seen in the prior phase IIa study.

Analysis

Placebo Group Comparison

In general, our placebo group behaved consistently with prior studies of other drugs in similar populations

Placebo Group Behaviour	Fibrogen Pamrevlumab LELANTOS-1	Capricor CAP-1002 HOPE-2	Percheron ATL1102 Phase IIb Study
Sample size, n (placebo group)	40	8 – 12	17
Phase of Development	III	II	IIb
Population	Non-ambulant	Non-ambulant and Late ambulant	Non-ambulant
Age, years (mean)	15.5	14.3	13.6
Decline in PUL2.0 at 6 months	-	-2.1 – -2.3	-1.4
Decline in PUL2.0 at 12 months	-2.1	-3.7	-

Commentary

- The most directly comparable studies are the LELANTOS-1 study of pamrevlumab and the HOPE-2 study of CAP-1002.
- The placebo group in the Percheron study performed roughly in between the Fibrogen and Capricor studies. Patients in the ATL1102 study likely deteriorated a little faster than in LELANTOS-1 and a little slower than in HOPE-2. These differences are not likely to be meaningful. Overall, it appears that the ATL1102 phase IIb study recruited a population that was broadly similar to the population at large.

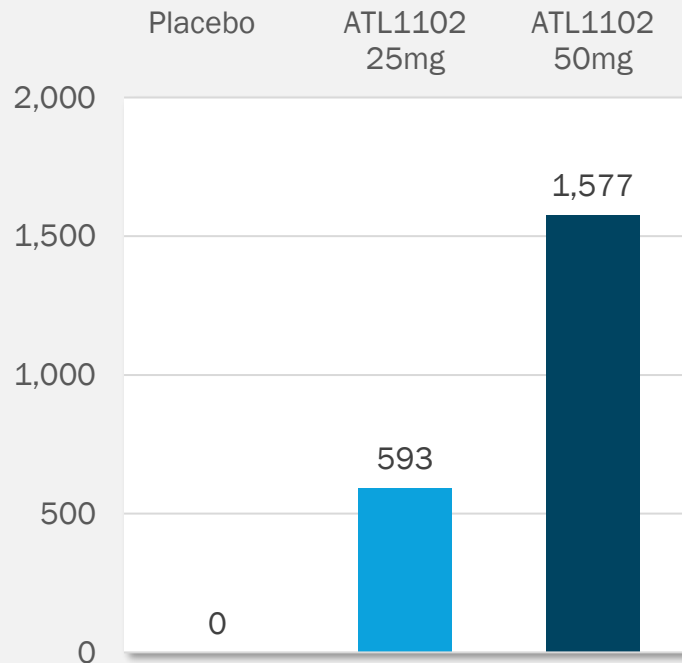
Source: Capricor press releases; Fibrogen presentation to Muscular Dystrophy Association annual meeting, March 2024

Pharmacokinetic – Pharmacodynamic Effects

ATL1102 appears to engage its target in a dose-dependent fashion, causing intended effects in muscle

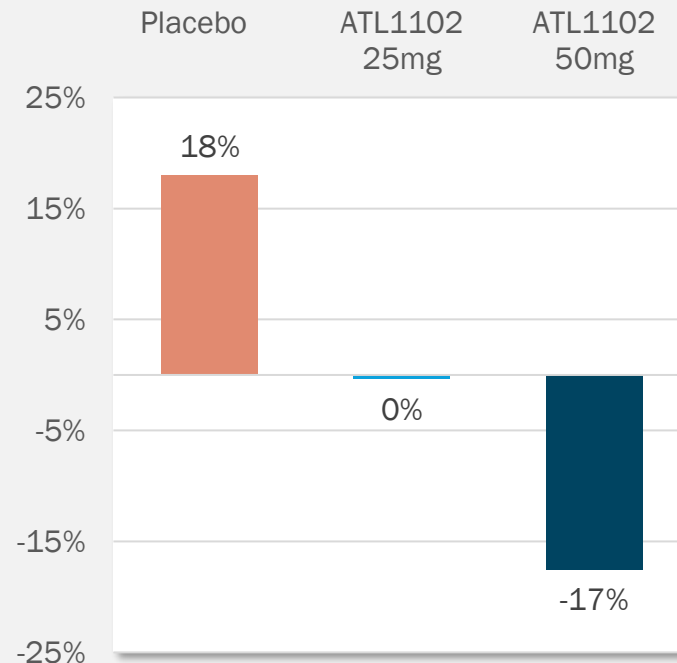
Pharmacokinetics

(ATL1102 Concentration after 2 hrs)



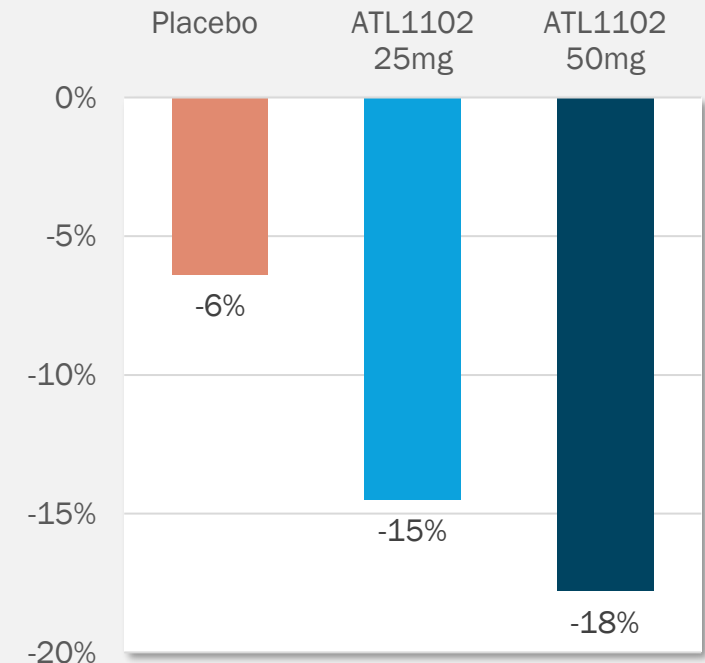
Pharmacodynamics

(CD49d+ T-Cells at wk 22)



Biomarker

(Serum Creatine Kinase at wk 24)



Treatment Effect Beyond Six Months

No evidence of activity in those patients transitioning from placebo to active after six months



Commentary

- It was intended that all patients would complete twelve months of treatment on study. Those originally randomised to placebo would be re-randomised to either 25mg or 50mg of ATL1102.
- Nineteen patients had completed at least 37 weeks of treatment at the time of study termination.
- Of those that transitioned from placebo to ATL1102, there is no convincing signal of a different trajectory to the disease during the second six-month period.
- For those that remained on active drug for the entirety of the study, there is no evidence that the efficacy of the drug improved in the second six-month period.

Comparison Against Phase IIa Study

Comparison Against Phase IIa Study

The phase IIa and IIb studies recruited similar populations

	Phase IIa Study	Phase IIb Study		
	ATL1102 25mg	Placebo	ATL1102 25mg	ATL1102 50mg
Sample size, n	9	17	16	15
Age, years, mean (SD)	14.9 (2.1)	13.6 (2.0)	13.4 (2.8)	12.7 (1.7)
Weight, kg, mean (SD)	52.7 (9.8)	58.7 (21.5)	59.2 (18.2)	55.6 (16.1)
PUL2.0 Score at Baseline, mean (SD)	24.8 (9.6)	28.3 (7.7)	27.3 (6.2)	28.1 (7.3)
Plasma concentration, ng/ml, mean @2 hours after first dose	583	0	593	1,577
Change in CD49d+ T-cells @ wk 24 (IIa) / wk 22 (IIb)	-3.6%	18%	-0.4%	-17.5%
Change in PUL2.0 @ wk 24 (IIa) / wk 25 (IIb)	+0.9	-1.4	-1.8	-1.6
Change in MyoGrip @ wk24 (IIa) / wk 25 (IIb)	-0.7	-2.2	-3.3	-2.1
Change in MyoPinch @ wk24 (IIa) / wk 25 (IIb)	-1.0	-1.5	-3.8	-3.2

Commentary

- The study population in the phase IIb study appears broadly similar to that in the phase IIa study.
- PK and CD49d+ T-cells behaved broadly similarly between the two studies, but clinical efficacy was less in the phase IIb study. This likely reflects the difference between a double-blind, placebo-controlled study and an open-label study.
- Note that MyoGrip and MyoPinch in the phase IIb study are calculated using a slightly different methodology to the earlier slide. This is to allow like-for-like comparison with the way they were calculated in the phase IIa study.

Drugs which appear promising in open label exploratory studies sometimes disappoint in confirmatory randomised controlled studies...

Peer-Reviewed Publication of Pamrevlumab Single-Arm Open-Label Phase II MISSION Study in Non-Ambulant DMD

	MISSION Study
Number of Subjects	21
Change in PUL2.0 at 12 months	-2.0 (-2.9 – -1.1)
Change in PUL2.0 at 24 months	-4.1 (-5.4 – -2.9)
Change in Grip Strength (dominant hand) at 12 months	1.0 (-5.9 – 8.0)
Change in Grip Strength (dominant hand) at 24 months	-2.5 (-9.6 – 4.6)
Change in Forced Vital Capacity (respiratory function) at 12 months	-4.0 (-5.8 – -2.2)
Change in Forced Vital Capacity (respiratory function) at 24 months	-8.2 (-10.3 – -6.0)

FibroGen Press Release of 7 June 2023 Describing Randomised Phase III Study in Non-Ambulant DMD

FibroGen Announces Topline Results from LELANTOS-1 Phase 3 Clinical Study of Pamrevlumab in Non-Ambulatory Patients with Duchenne Muscular Dystrophy

- Study did not meet the primary endpoint
- Pamrevlumab was generally safe and well tolerated
- Topline results from LELANTOS-2 Phase 3 study of pamrevlumab in ambulatory patients with DMD expected 3Q 2023

SAN FRANCISCO, June 07, 2023 (GLOBE NEWSWIRE) – FibroGen, Inc. (NASDAQ: FGEN) today announced topline data from the Phase 3 LELANTOS-1 placebo-controlled trial of pamrevlumab for the treatment of non-ambulatory patients with Duchenne Muscular Dystrophy (DMD) on background corticosteroids. The study did not meet the primary endpoint of Performance of the Upper Limb 2.0 (PUL 2.0) score at week 52 compared to baseline. Pamrevlumab was generally safe and well tolerated and the majority of treatment emergent adverse events were mild or moderate.

Source: [AM Connolly et al. \(2023\) J Neuromusc Dis. 10\(4\):685-699](#); Company press releases

...and even drugs which showed positive data in randomised studies are not guaranteed of success in confirmatory studies

Peer-Reviewed Publication of Puldysa® (Idebanone)
Randomised Phase III DELOS Study in DMD

	Idebanone Group	Placebo Group
Number of Subjects	31	33
Change in Peak Expiratory Flow (respiratory function) at 12 months	-2.6 (-6.7 – -1.5)	-8.8 (-12.7 – -5.0)
	$p = 0.031$	
Number of patients whose Forced Vital Capacity (respiratory function) did non deteriorate over 12 months	15 (48%)	6 (18%)
	$p = 0.011$	

Santhera Press Release of 6 October 2020
Describing Approval Phase III Study in DMD

Santhera to Discontinue Phase 3 SIDEROS Study and Development of Puldysa® in Duchenne Muscular Dystrophy (DMD) and Focus on Vamorolone

Pratteln, Switzerland, October 6, 2020 – Santhera Pharmaceuticals (SIX: SANN) announces the discontinuation of its Phase 3 SIDEROS study with Puldysa® (idebenone) in patients with Duchenne muscular dystrophy (DMD) who are in respiratory decline and receive concomitant glucocorticoid treatment. Data from an interim analysis conducted by the independent Data and Safety Monitoring Board (DSMB) concluded that the study was unlikely to meet its primary endpoint. As a consequence, Santhera will discontinue the study, withdraw the European marketing authorization application and end the global development program for Puldysa. The Company intends to initiate a restructuring plan for the business with a focus on retaining key functions for bringing DMD drug candidate vamorolone to patients and execute on its other pipeline programs.

Source: [GM Buyse et al. \(2015\) Lancet 385\(9979\):1748-1757](#); Company press releases

Conclusions

Conclusions

- There were no indications of manufacturing, storage, or administration defects with the ATL1102 drug product. The study appears to have been conducted substantially in accordance with the protocol.
- The drug is measurable in plasma, causes dose-dependent reductions in CD49d lymphocyte counts, and causes dose-dependent reductions in creatine kinase, a biomarker of muscle inflammation. In simple terms, the drug worked as expected on biological parameters, indicating pharmacological activity.
- These pharmacological effects did not result in clinical efficacy greater than placebo that was measurable with the functional endpoints used in the study (PUL2.0, MyoGrip, MyoPinch).
 - There may be a faint signal of activity in hand function at the 50mg dose, but not at the 25mg dose.
- The placebo group in this study behaved broadly in line with placebo groups in other studies, suggesting that the placebo population was typical and representative.
- Percheron has several hypotheses as to why the study failed:
 1. The drug was pharmacologically active, but the dose was too low for its activity to meaningfully affect the course of the disease.
 2. The drug was pharmacologically active, but inhibition of CD49d+ lymphocytes (the mechanism of action of ATL1102) is not enough to meaningfully affect the course of the disease, and alternative disease mechanisms continued to cause clinical deterioration.
 3. The drug was pharmacologically and clinically active, but the available measurement instruments (PUL2.0, MyoGrip, MyoPinch) were too insensitive to detect a treatment effect of drug versus placebo.
- The ATL1102-treated groups behaved differently in some respects from the prior phase IIa study (where only 25 mg was tested), suggesting lower efficacy than was seen in the IIa study.
 - These differences likely reflect the fact that the prior phase IIa study was a single-arm, open-label study at a single specialist centre, which can magnify apparent efficacy, whereas the phase IIb was a more robust placebo-controlled study at thirteen centres.



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