(LSVP.13)

Human Cardiosphere-Derived Cell Therapy in Duchenne Muscular Dystrophy:
A New Treatment Approach to Target Skeletal and Cardiac Muscle Pathogenesis
(12-Month Data from HOPE-2-OLE Study)

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Capricor Therapeutics™

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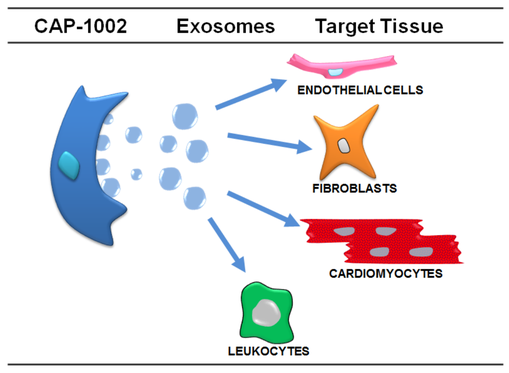
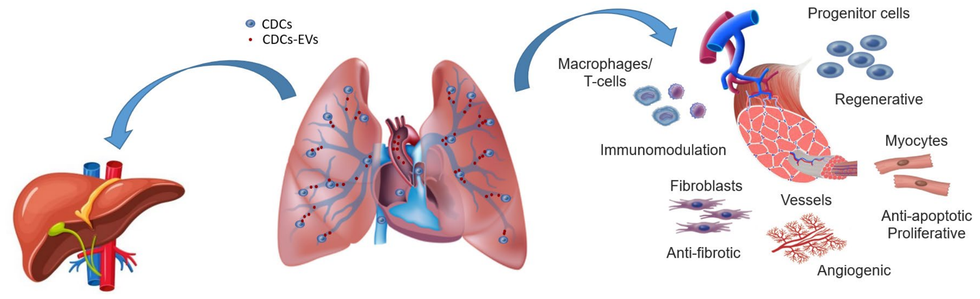
Background and Mechanism of Actions

CAP-1002 is an investigational cell-based product that has been evaluated in more than 200 volunteers, showing promising clinical outcomes for the treatment of DMD and cardiac disease secondary to DMD in multiple clinical trials, including the HOPE-2 study and its open-label extension study (HOPE-2-OLE, or in short, OLE).

CAP-1002 promotes release of extracellular vesicles, or exosomes, and growth factors through the circulatory system. The mechanism of action of CAP-1002 is its composite ability to be immunomodulatory, anti-fibrotic, and pro-regenerative.

As CAP-1002 is a cell-based therapy, and the formulation contains excipients such as DMSO, immunologic and hypersensitivity reactions to the product are possible. Hence, a pre-treatment regimen was implemented to reduce potential allergic reactions.





Mechanism of Action of CAP-1002

Overview of HOPE-2 and OLE Studies

HOPE-2 (12-month Study Period)

A Phase 2, randomized, double-blind, placebo-controlled trial to evaluate the safety and efficacy of CAP-1002 vs Placebo (1:1 ratio) in subjects with DMD and impaired skeletal muscle function.

CAP-1002 was given once every 3 months via IV infusion for 4 doses.

Primary endpoint: Change from baseline at Month 12 in the mid-level (elbow) dimension of PUL 1.2. Note: the advance version of PUL 2.0 was also measured.

Key Inclusion Criteria:

1. > 10 years of age
2. Diagnosis of DMD and confirmation via genetic testing
3. PUL score of 2-5
4. 10 MWR <1 meter/second
5. Prior steroids for ≥ 12 months

Key Exclusion Criteria:

1. LVEF < 35%; BMI > 45
2. Elbow-flexion contractures > 30°
3. Exon 44 mutation and Exon 3 through 7 deletion
4. Known allergic reaction to Investigational Product

Results of HOPE-2

Twenty (20) DMD patients were followed up during the 12-month study period (CAP-1002: n=8; Placebo: n=12). The analysis for the PUL 1.2 mid-level dimension in patients treated with CAP-1002 showed a mean 12-month change from baseline favoring CAP-1002 over Placebo (Δ=2.6 points, p=0.014). This finding represents a clinically relevant and statistically significant 71% of slowing in loss of upper limb function with CAP-1002.

The encouraging clinical outcomes led to initiation of the open-label phase study (HOPE-2-OLE).

Gap Phase

Subjects were off treatment for approximately one year following HOPE-2 prior to entering the OLE Study due to the COVID Pandemic

HOPE-2-OLE Study

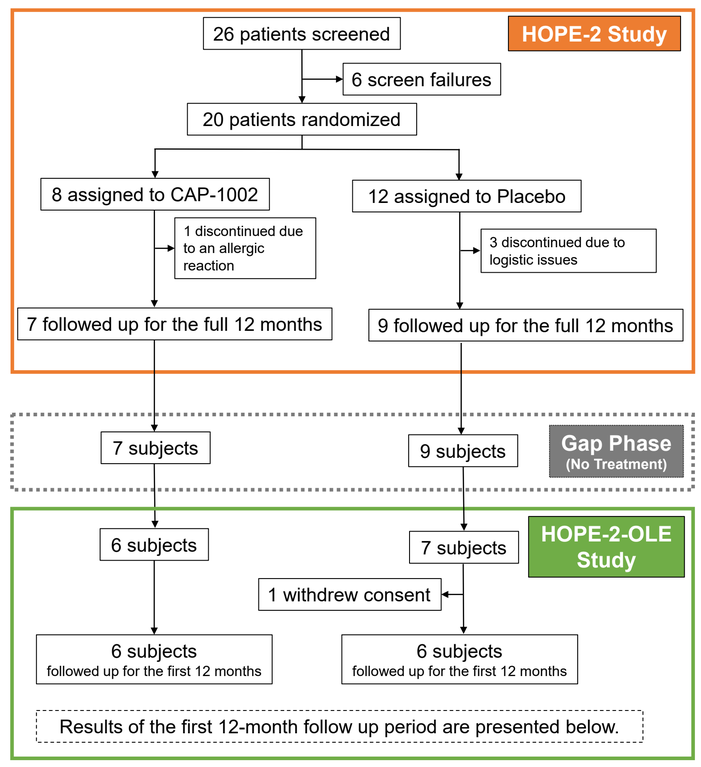
All enrolled subjects were scheduled to receive 4 IV administrations of CAP-1002, once every 3 months, at Month 12. The study is ongoing beyond 12 months.

Primary endpoint: Change from baseline at Month 12 in full PUL 2.0 (high-level + mid-level + distal level dimensions)

Key Inclusion Criteria:
1. Completion of a 12-month follow up in the HOPE-2 study

Key Exclusion Criteria:
1. Known allergic reaction to Investigational Product

Overview of HOPE-2 and OLE Subject Enrollment



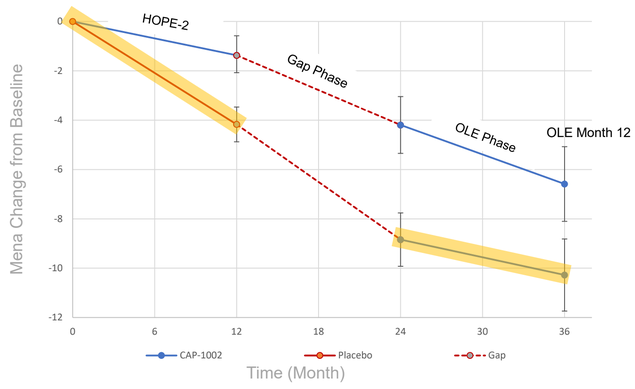
The results from HOPE-2-OLE further strengthened the previously reported results from HOPE-2

Treatment Differences in One Year of HOPE-2-OLE Study

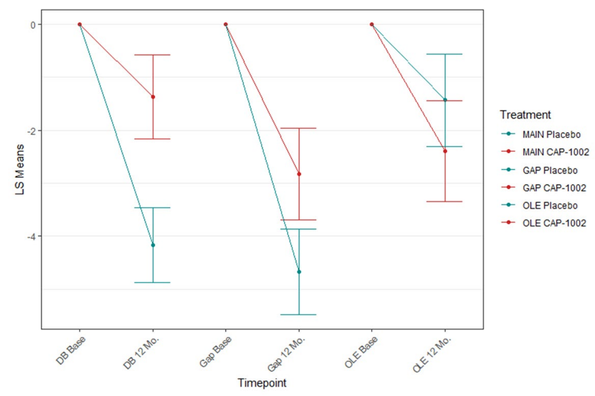
PUL 2.0	Change (Δ) from Baseline	p-value
OLE (n=12) vs. HOPE-2 Placebo Group (n=9)	2.3	0.015
OLE (n=12) vs. HOPE-2 Placebo in the Gap Phase (n=9)	2.8	0.006

- A significant difference in slowing of disease progression was found in the HOPE-2 Placebo group ***after*** starting CAP-1002 in the OLE study versus while they were on placebo in the HOPE-2 study (Δ=2.74 points, p=0.014). A significant difference was also observed in ***all*** subjects on CAP-1002 in the OLE study compared to the Placebo group in the HOPE-2 study (Δ=2.31 points, p=0.015).
- Overall, the slowing of disease progression in OLE is comparable to the slowing of disease progression seen in HOPE-2 study.

HOPE-2-OLE Modeled Decline as Reflected by PUL 2.0 Scores Over Time (Pooled OLE)

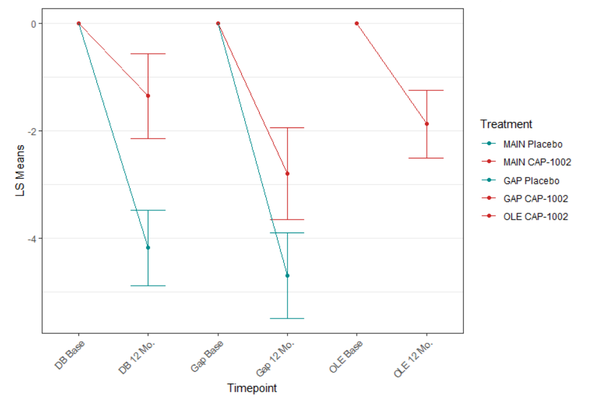


HOPE-2-OLE Treatment Differences as Reflected by PUL 2.0 Scores Compared to Baseline (Un-combined OLE subjects)



Effect	ESTIMATE	STDERR	TVALUE	PVALUE
DB CAP-1002 vs. DB Placebo	2.7996	1.0611	2.6384	0.0096
OLE Placebo vs. DB Placebo	2.7387	1.0924	2.5071	0.0138
OLE Placebo vs. GAP Placebo	3.2386	1.1472	2.8230	0.0057

HOPE-2-OLE Treatment Differences as Reflected by PUL 2.0 Scores Compared to Baseline (Combined OLE subjects)



Effect	ESTIMATE	STDERR	TVALUE	PVALUE
DB CAP-1002 vs. DB Placebo	2.8292	1.0494	2.6959	0.0082
OLE vs. DB Placebo	2.3064	0.9280	2.4853	0.0145
OLE vs. GAP Placebo	2.8203	0.9969	2.8292	0.0056

Reference

McDonald, CM, Marbán E, Hendrix S, Hogan N, Smith RR, Eagle M, et al. Repeated intravenous cardiosphere-derived cell therapy in late-stage Duchenne Muscular Dystrophy (HOPE-2): A multicentre, randomised, double-blind, placebo-controlled, phase 2 trial. The Lancet, 2022; 399(10329), 1049–1058.

The Lancet (McDonald et al, 2022)

Acknowledgement

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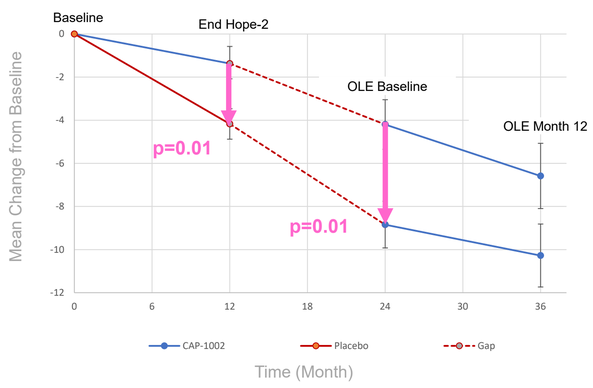
CAP-1002 slows decline of upper limb functionality by potentially modifying disease

- The significant difference in PUL 2.0 scores between groups (CAP-1002 vs Placebo) in HOPE-2 (p=0.01) was maintained at the end of the Gap Phase (p=0.01 without baseline covariate).
- A non-inferiority analysis of disease-progression slopes in the Gap Phase showed no convergence.

HOPE-2-OLE Modeled Decline as Reflected by PUL 2.0 Scores Over Time



Overview of Adverse Events/Safety in OLE

AE Categories	CAP-1002 (N=13) n (%)
Any TEAE[1]	12 (92.3)
TEAE by maximum severity[2]	
Mild or Moderate (≤ Grade 2)	10 (77)
Severe or life-threatening or disabling (Grade 3 or 4)	2 (15)
Death	0
TEAE related to IP or administration procedure[3]	10 (77)
TEAE related to IP[3]	8 (61.5)
TEAE related to administration procedure	7 (53.8)
Any SAE[4]	0
Other Events of Special Interest (Acute respiratory decomposition within 2 hours following IP administration and Hypersensitivity reaction)	0

AE: adverse event; IP: investigational product; IV: intravenous; TEAE: treatment-emergent adverse event defined as an AE occurring after the initiation of the IV catheter placement for the initial dose of IP.
[1] A total of 60 TEAEs occurred at Month 12 in HOPE-2-OLE.
[2] Each Subject is counted once by the worst severity. AEs with missing severity are counted as "severe".
[3] Each Subject is counted once by the greatest relationship to IP or administration procedure, ie, "probable or possible". AEs with missing relatedness to the IP or IP administration will be considered to have "possible" relatedness. A total of 23 events were considered as related to IP, and 21 related to administration procedure.
[4] AEs with missing seriousness are counted as "serious".

Conclusions

- CAP-1002 was well-tolerated without new safety signals identified in HOPE-2-OLE.
- CAP-1002 demonstrates novel, clinically meaningful, and cumulative preservation of upper limb function by potentially modifying the underlying DMD disease.
- Ongoing long-term open-label extension studies appear to confirm the potential therapeutic durability and established safety of CAP-1002 beyond 12 months for the treatment of skeletal myopathy in DMD.

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