Long Term Safety and Efficacy of CAP-1002 in late-stage patients with DMD:

A New Treatment Approach to Target Skeletal and Cardiac Muscle Pathogenesis (24-Month Data from HOPE-2-OLE Study)

WMS World Muscle Society

POSTER: LBP13

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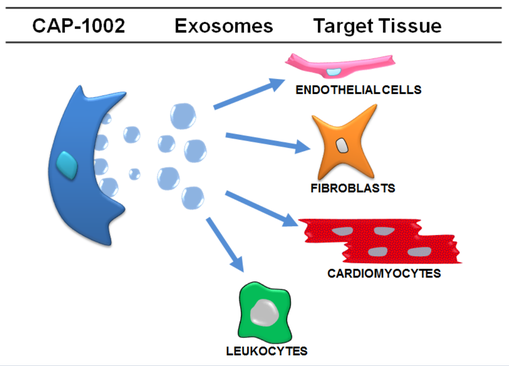
Capricor

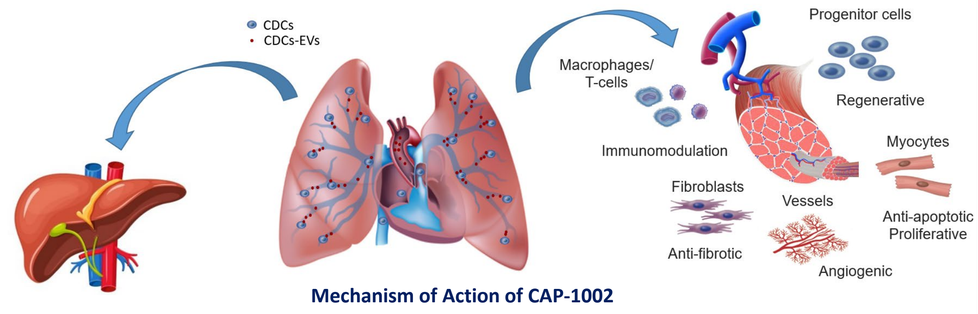
BACKGROUND AND MECHANISM OF ACTIONS

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.

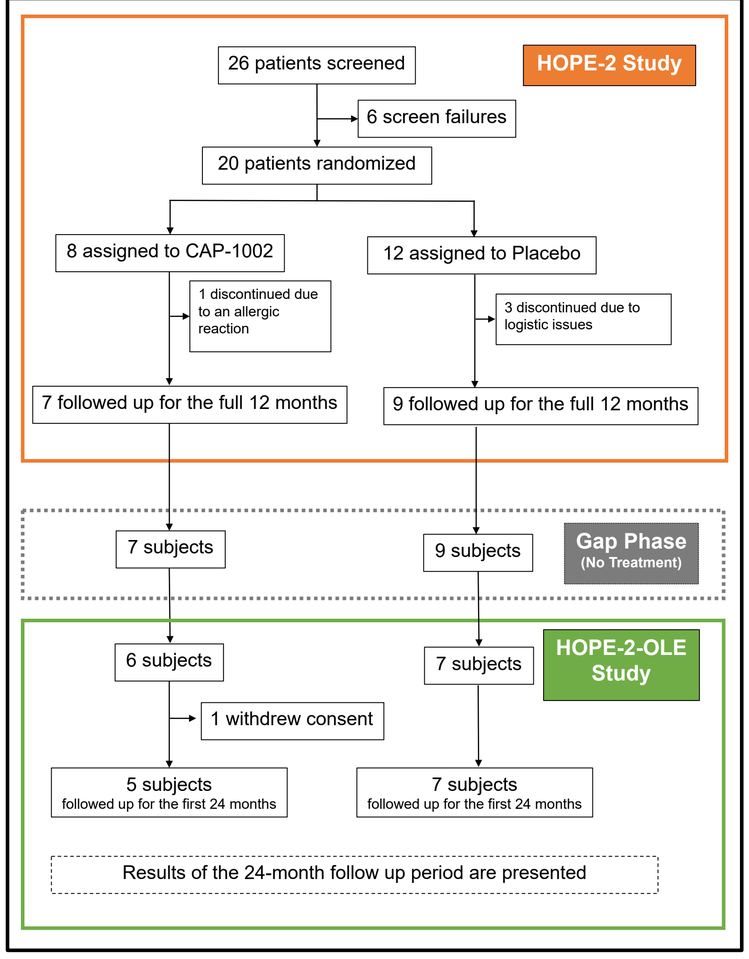
As CAP-1002 is a cell-based therapy, and the formulation contains excipients such as DMSO, immunologic and hypersensitivity reactions to the product are possible. Hence, a pre-treatment regimen was implemented to reduce potential allergic reactions.





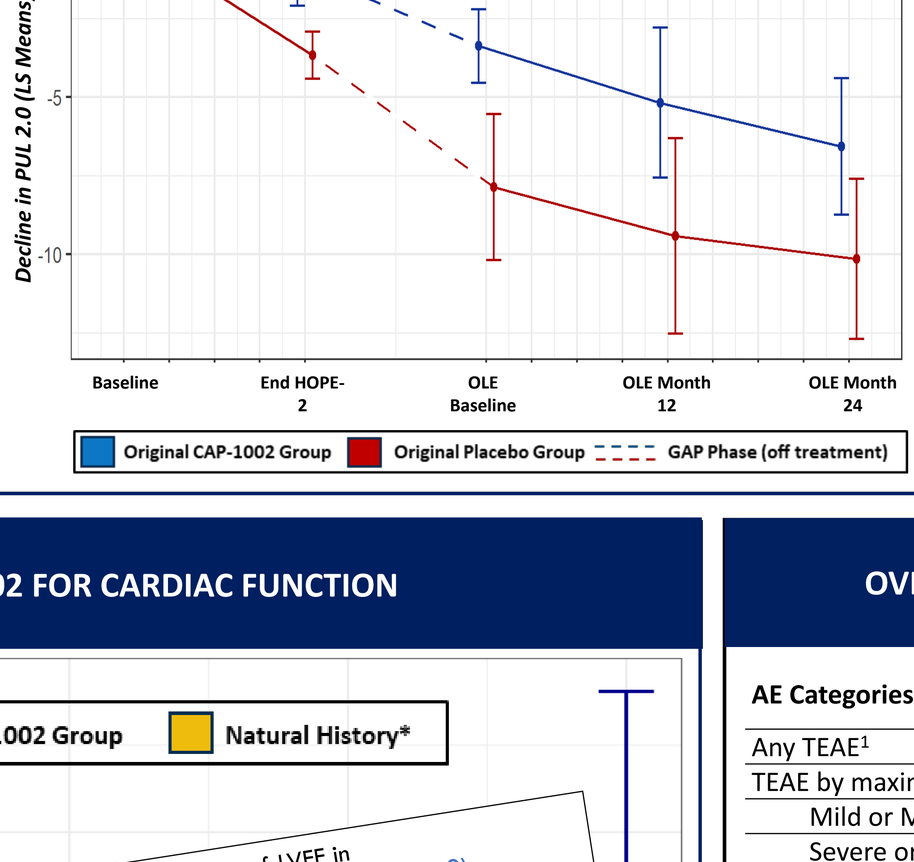
Mechanism of Action of CAP-1002

OVERVIEW OF HOPE-2 AND OLE SUBJECT ENROLLMENT

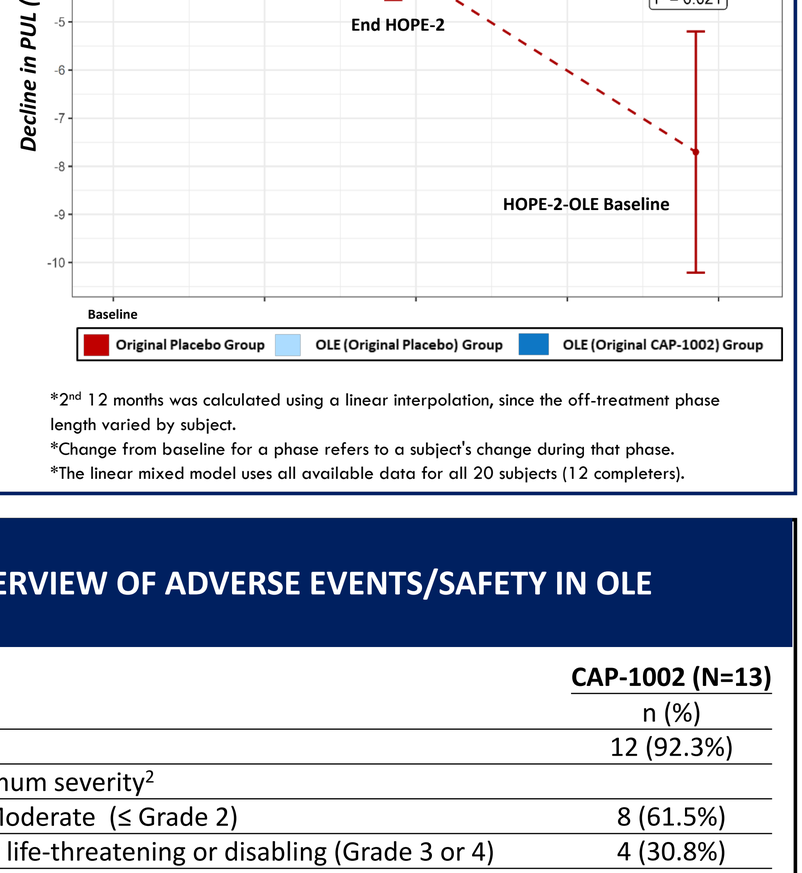


THE RESULTS FROM THE 24-MONTH HOPE-2-OLE STUDY FURTHER STRENGTHENED THE PREVIOUSLY REPORTED RESULTS FROM HOPE-2

- HOPE 2 randomized controlled study shows statistically significant difference in patients treated with CAP-1002 vs Placebo. (Δ 1.8 pts, p=0.040)
- GAP period shows a slower progression rate in patients who were previously treated with CAP-1002 vs Placebo
- Patients regardless of original treatment group in HOPE 2 show a similar rate of decline (~2.8 pts over 2 years) when on long term treatment (8 doses [24 months] of HOPE-2-OLE)
- Data is indicative of CAP-1002's disease modifying potential and supports earlier treatment in patients with DMD



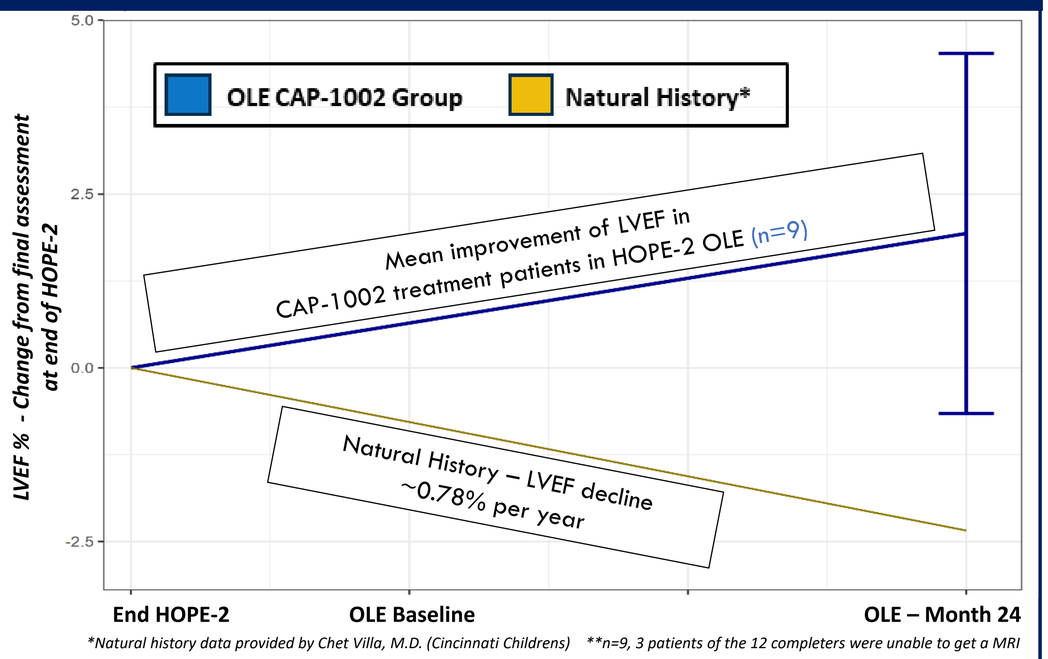
The mean PUL 2.0 decline after 24 months of treatment with CAP-1002 in the HOPE-2-OLE was 2.8 points versus a 7.7 point mean decline observed over 24 months in the HOPE-2 placebo patients that went untreated for 24 months during combined 12-month placebo + gap phase (Δ=4.9 points, p=0.021). The average rate of decline in CAP-1002 treated patients showed an attenuation of disease progression by 64%.



*2nd 12 months was calculated using a linear interpolation, since the off-treatment phase length varied by subject.
*Change from baseline for a phase refers to a subject's change during that phase.
*The linear mixed model uses all available data for all 20 subjects (12 completers).

POTENTIAL BENEFIT OF CAP-1002 FOR CARDIAC FUNCTION

- Cardiomyopathy is prevalent in DMD and is a leading cause of death in patients with DMD. Stabilization or improvement of cardiac function is a meaningful result of treatment intervention.
- Natural History data shows a mean decline in LVEF percentages by ~0.78% annually.
- Measurement of cardiac function (left ventricular ejection fraction; LVEF%) by cMRI in the HOPE2-OLE at the 24-month timepoint, showed benefit in LVEF% in 6 out of 9 (67%) patients when compared LVEF% measured ~3 years prior at the end of HOPE-2.
- There was correlation with PUL v2.0 and LVEF (r=0.75, p=0.02)



*Natural history data provided by Chet Villa, M.D. (Cincinnati Childrens) **n=9, 3 patients of the 12 completers were unable to get a MRI

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)	8 (61.5%)
Severe or life-threatening or disabling (Grade 3 or 4)	4 (30.8%)
Death	0
TEAE related to IP or administration procedure[3]	9 (69.2%)
TEAE related to IP[3]	8 (61.5%)
TEAE related to administration procedure	7 (53.8%)
Any SAE related to IP or administration procedure	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 95 TEAEs occurred by Month 24 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 and continues to maintain a favorable risk/benefit profile in HOPE-2-OLE.
- CAP-1002 demonstrates novel, clinically meaningful, and cumulative preservation of upper limb function by potentially modifying the underlying DMD disease.
- Potential benefit of the long-term treatment with CAP-1002 is observed by maintaining or improving left ventricular ejection fraction.
- Ongoing long-term open-label extension studies appear to confirm the potential therapeutic durability and established safety of CAP-1002 beyond 24 months for the treatment of skeletal and cardiac myopathy in DMD.

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)

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