CAP-1002 Development in DMD: The HOPE Clinical Trials
Forward-Looking Statements

Statements in this presentation regarding the efficacy, safety, and intended utilization of Capricor's product candidates; the initiation, conduct, size, timing and results of discovery efforts and clinical trials; the pace of enrollment of clinical trials; plans regarding regulatory filings, future research and clinical trials; regulatory developments involving products, including the ability to obtain regulatory approvals or otherwise bring products to market; plans regarding current and future collaborative activities and the ownership of commercial rights; scope, duration, validity and enforceability of intellectual property rights; future royalty streams, expectations with respect to the expected use of proceeds from the recently completed offerings and the anticipated effects of the offerings, and any other statements about Capricor's management team's future expectations, beliefs, goals, plans or prospects constitute forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Any statements that are not statements of historical fact (including statements containing the words "believes," "plans," "could," "anticipates," "expects," "estimates," "should," "target," "will," "would" and similar expressions) should also be considered to be forward-looking statements.

There are a number of important factors that could cause actual results or events to differ materially from those indicated by such forward-looking statements. More information about these and other risks that may impact Capricor's business is set forth in Capricor's Annual Report on Form 10-K for the year ended December 31, 2017 as filed with the Securities and Exchange Commission on March 22, 2018, in its Registration Statement on Form S-3, as filed with the Securities and Exchange Commission on September 28, 2015, together with the prospectus included therein and prospectus supplements thereto and in its Quarterly Report on Form 10-Q for the quarter ended June 30, 2018, as filed with the Securities and Exchange Commission on August 13, 2018. All forward-looking statements in this press release are based on information available to Capricor as of the date hereof, and Capricor assumes no obligation to update these forward-looking statements.
CAP-1002 Background

• CAP-1002 is a biologic product consisting of allogeneic cardiosphere-derived cells (CDCs) derived from donated heart muscle

• CDCs do not act by “stemness” – do not engraft into host tissue

• CDCs act by releasing extracellular vesicles (EVs), or exosomes
  ✓ EVs contain non-coding RNAs and proteins
  ✓ Internalized by target cells
  ✓ Stimulate diverse and lasting changes in cellular behavior

• CAP-1002 has been investigated in several clinical trials and more than 140 human participants
Mechanism of Action

Intravenous CDC delivery

After administration, CDCs are retained in the lungs from where they secrete exosomes and growth factors that can travel through the circulatory system and promote tissue regeneration.
Effects of CDCs in mdx Mouse Model

- Following a single administration of CDCs or vehicle in mdx mice:

**Improved cardiac function**

- Left ventricular ejection fraction markedly improved vs. control
  
  \[ p < 0.05 \] at all timepoints through Week 12

**Increased exercise capacity**

- Exercise performance approximately doubled vs. control
  
  \[ p < 0.005 \] at all timepoints through Week 12

HOPE-Duchenne Trial
HOPE-Duchenne Trial Design

- One time, multi-vessel, intracoronary delivery of 75M cells
- Safety trial with multiple exploratory efficacy endpoints
- Conducted at 3 clinical sites in the United States
- Enrollment population characterized by advanced disease
- Open-label extension for Usual Care group underway

25 Patients
Ages 12+
Stable steroid regimen
LV scar in 4+ segments
EF > 35%

1 x CAP-1002
(75M cells)
n=13

Usual Care
n=12

Endpoints

Safety
TIMI, death,
MACE, CV
hosp., VT, DSA,
cardiac biomarkers

Exploratory Efficacy
Cardiac MRI, PUL,
6MWT, Spirometry,
QOL, DMD
Biomarkers

Baseline | Usual Care | CAP-1002
---|---|---
Age, median yrs. | 17.5 | 18
Wheelchair Use, Always | 58% | 77%
Cardiac Scar, mean % (SD) | 21.4 (10.8) | 17.6 (6.8)
LVEF, mean % (SD) | 48.4 (7.5) | 49.6 (6.7)
Cardiac Muscle: Scar & Wall Thickening

- Cardiac structure and function assessed by cardiac MRI with blinded analysis by core lab
- Scar increased in Usual Care group, but decreased in CAP-1002 group
  - 11.9% group difference in change score at Month 12 (p=0.03)
- Increased regional systolic wall thickening
  - Greatest evidence of improvement seen in inferior wall; similar trend in anterior wall
  - Consistent with natural history of scar progression in DMD

* p-values are based on absolute change from baseline
Skeletal Muscle: PUL Results Indicate Functional Benefit

- Performance of the Upper Limb (PUL) test is a validated instrument in DMD
  - Relates to patients’ ability to perform common activities of daily living
- Trends towards improvement observed throughout follow-up

![Diagram of PUL test items](image)

**Middle + Distal PUL Score**

- **Shoulder Level**: 4 items
  - Lifting upper extremity weights
  - Shoulder height
  - Above shoulder height
- **Middle Level**: 9 items
  - Hand to mouth w/o weights
  - Hand to table
  - Stack light and heavy cans
  - Moving weights on table
  - Remove container lid
  - Lift light and heavy cans
  - Tearing paper
- **Distal Level**: 8 items
  - Tracing a path
  - Supination
  - 3-point grip
  - Push on a light
  - Pick up coins
  - Finger pinch
  - Place fingers on diaphragm
  - Thumb (key) grip

Percentage change from baseline:

- **Week 6**: p=0.20
- **Month 3**: p=0.49
- **Month 6**: p=0.92
- **Month 12**: p=0.66

*Usual Care (N = 11) | CAP-1002 (N = 13)*
Key Conclusions from HOPE Duchenne Trial Results

- CAP-1002 (75M cells) generally safe and well-tolerated
  - Adverse events consistent with an intracoronary infusion procedure
- Early clinical data demonstrated that CAP-1002 benefits both cardiac (scar & thickening) and skeletal (PUL) muscle in DMD
- Sustained benefit likely to require repeat doses
HOPE-2
Duchenne Clinical Trial
• **Design**: Phase 2, randomized, double-blind, placebo-controlled trial

• **Objective**: Evaluate safety and efficacy of CAP-1002 administered every three months in participants with DMD and reduced muscle function

• **Sites**: 10-15 (USA)

• **Open-Label Extension**: If recommended by a DSMB, planning to offer CAP-1002 to participants who were randomized to placebo and completed the trial

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**Endpoints**

**Safety**
1. Respiratory Fx
2. Immune Response
3. Adverse Events
4. Death

**Efficacy**
1. PUL
2. Cardiac MRI
3. Myometry
4. PFTs
5. Biomarkers
6. QOL

**Over 12 months**
- 9 Visits
- 4 Infusions

**CAP-1002 (150M cells)**

**Placebo**

**84 Patients**
Ages 10+
- upper limb strength
- Stable steroid regimen
- EF & FVC > 35%
Trial Site Visits

- 30-day screening period
- 4 IV infusions over 12 months
- No muscle biopsy required
- Interim Analysis performed when half of participants complete Month 6
- Capricor will cover cost of travel for HOPE-2 participant & one travel companion
Key Inclusion Criteria

- Genetic confirmation of DMD
- Reduced upper limb strength as measured by PUL
- Reduced ability to walk/run
- Loss of independent ambulation by 18th birthday
- Systemic glucocorticoids for at least 12 months
  - Stable dose for at least 6 months
  - Weight- and toxicity-based adjustments allowed
Key Exclusion Criteria

- LVEF < 35%
- FVC < 35%
- BMI > 45
- Mutations in DMD gene
  - Exon 44 skip-amenable
  - Deletion in exons 3-7

- FDA-approved DMD exon-skipping therapy if stable dose < 24 months
  - Weight-based dose adjustments allowed
- HGH within 3 months, unless stable dose ≥ 24 months
- Idebenone within 3 months
- Cell therapy product within 12 months
- Investigational product within 6 months
HOPE-2 Trial Open for Enrollment

- **Actively enrolling participants**
- First participant treated in April 2018
- Currently enrolling sites:
  - University of California, Davis | Dr. McDonald
  - University of Utah | Dr. Butterfield
  - Children’s Hospital of Colorado | Dr. Janas
  - Washington Univ., St. Louis | Dr. Connolly
  - Nemours Children’s Hospital | Dr. Finkel
  - Cincinnati Children’s Hospital | Dr. Tian
  - University of Iowa | Dr. Mathews
  - Children’s Hospital of Wisconsin | Dr. Harmelink
- More sites expected in Fall 2018

For more information, visit [hope2trial.com](http://hope2trial.com) or [clinicaltrials.gov](http://clinicaltrials.gov) (NCT03406780)
HOPE-2 Considerations

- Ambulatory & non-ambulatory boys and young men may be eligible
- Long-term eteplirsen use permitted
- Requires 4 intravenous infusions
- Robust travel policy to reduce burden on participants & families
- Open-label extension to offer CAP-1002 to participants randomized to placebo

For questions, email hope-2@capricor.com or call Jennifer Shoskes at (310) 358-3047
Thank You!

HOPE-Duchenne & HOPE-2 Trial participants and their families