CLINICAL TRIAL PROTOCOL

A PHASE 2, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL EVALUATING THE SAFETY AND EFFICACY OF INTRAVENOUS DELIVERY OF ALLOGENEIC CARDIOSPHERE-DERIVED CELLS IN SUBJECTS WITH DUCHENNE MUSCULAR DYSTROPHY (HOPE-2)

Protocol Number:	CAP-1002-DMD-02
Trial Phase:	Phase 2
Product Name:	CAP-1002 Allogeneic Cardiosphere-Derived Cells
IND Number:	[redacted]
Indication:	Duchenne Muscular Dystrophy
Sponsor:	Capricor, Inc. 8840 Wilshire Blvd., 2nd Floor Beverly Hills, CA 90211
Sponsor Contact:	[redacted]
Original:	20-Oct-2017
Amendment 1.0:	01-Dec-2017
Amendment 2.0:	28-Feb-2018
Amendment 3.0:	09-Jul-2018
Amendment 4.0:	17-Jan-2019
Amendment 5.0:	27-Sep-2019

INVESTIGATOR'S AGREEMENT

Trial Title:	A Phase 2, Randomized, Double-Blind, Placebo-Controlled Trial Evaluating the Safety and Efficacy of Intravenous Delivery of Allogeneic Cardiosphere-Derived Cells in Subjects with Duchenne Muscular Dystrophy
Short Title:	Halt myOPathy progrEssion in Duchenne (HOPE-2)
Protocol Number:	CAP-1002-DMD-02
Amendment 5.0:	27-Sep-2019

I have read this clinical trial protocol and agree to conduct the trial according to the investigational plan. I agree to maintain the confidentiality of all information received or developed in connection with this protocol.

_____

Printed Name of Investigator

_____

Signature of Investigator

_____

Date

SPONSOR APPROVAL

Trial Title:	A Phase 2, Randomized, Double-Blind, Placebo-Controlled Trial Evaluating the Safety and Efficacy of Intravenous Delivery of Allogeneic Cardiosphere-Derived Cells in Subjects with Duchenne Muscular Dystrophy (HOPE-2)
Protocol Number:	CAP-1002-DMD-02
Amendment 5.0:	27-Sep-2019

The clinical trial protocol was subject to critical review and quality assurance and has been approved by Capricor.

PROCEDURES IN CASE OF EMERGENCY

Table 1: Emergency Contact Information

Role in Trial	Name	Address and Telephone Number
[redacted]	[redacted]	Capricor, Inc. 8840 Wilshire Blvd., 2nd Floor Beverly Hills, CA 90211 Tel: [redacted] Email: [redacted]
[redacted]	[redacted],	Capricor, Inc. 8840 Wilshire Blvd., 2nd Floor Beverly Hills, CA 90211 Tel: [redacted] Email: [redacted]
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2. SYNOPSIS

Name of Sponsor: Capricor, Inc.	
Name of Investigational Product: CAP-1002 Allogeneic Cardiosphere-Derived Cells	
Name of Active Ingredient: Cardiosphere-Derived Cells	
IND Number: [redacted]	
Title of Trial: A Phase 2, Randomized, Double-Blind, Placebo-Controlled Trial Evaluating the Safety and Efficacy of Intravenous Delivery of Allogeneic Cardiosphere-Derived Cells in Subjects with Duchenne Muscular Dystrophy	
Trial Name: Halt myOPathy progrEssion (HOPE-2)	
Trial Centers: Up to 15 (USA)	
National Principal Investigator: [redacted] **Principal Investigators:** This is a multi-center trial with multiple Principal Investigators.	
Study Period: Approximately 24 months	**Phase of Development:** 2
Objectives: *Primary*: Evaluate the safety and efficacy of intravenous (IV) CAP-1002 administered every three months in subjects with Duchenne muscular dystrophy (DMD) and impaired skeletal muscle function *Secondary*: Evaluate the impact of repeated IV administrations of CAP-1002 on exploratory efficacy assessments of skeletal and cardiac muscle function, and quality of life	
Methodology: This Phase 2, multi-center, randomized, double-blind, placebo-controlled trial will assess the safety and efficacy of allogeneic cardiosphere-derived cells (CDCs), or CAP-1002, administered as four IV infusions, one every three months, for the treatment of subjects with DMD. Subjects with a clinical diagnosis of DMD confirmed by genetic testing and evidence of skeletal muscle impairment will undergo a battery of tests and procedures during a 30-day screening period to determine eligibility based on protocol inclusion and exclusion criteria. Eligible subjects will be prospectively randomized in stratified permuted blocks to CAP-1002 or placebo (1:1 ratio). To allow sufficient time for delivery of Investigational Product (IP), subjects must be randomized approximately 7 days in advance of their first IV infusion of Investigational Product (IP) on Day 1. Randomization will be stratified by site and entry item score of the Performance of the Upper Limb 1.2 (PUL). Subjects will undergo baseline safety and efficacy assessments (Table 3) prior to the first infusion of IP (CAP-1002 or placebo). Administration of IP (Day 1) should occur within a maximum of 14 days following randomization; if a delay of more than 14 days between randomization and IP administration is unavoidable, a conversation between the Investigator and Medical Monitor should occur to determine the need for repeat assessments prior to infusion. Subjects who are not randomized may be re-screened at the discretion of the Investigator.	

Subjects will complete study assessments at Screening; Baseline (≤ 2 days prior to Day 1); Day 1; Weeks 4 and 6 (±7 days, each); Month 3 (±14 days), Month 4.5 (±14 days), and Months 6, 9, and 12 (±14 days, each).

All IV infusions will be conducted in an outpatient setting at the investigative site on Day 1 and Months 3, 6, and 9. Prior to each IP infusion, medications will be administered to the subject as determined by the Investigator based on the pre-treatment guidelines provided by Capricor and/or institutional protocols to minimize the risk of potential severe allergic reactions such as anaphylaxis. Subjects will be observed in the outpatient setting for at least two hours post infusion and then discharged the same day if medically cleared by the site Investigator. As part of these visits, subjects will complete a safety phone call 14 days (±3 days) after each IP infusion, and if clinically indicated, an unscheduled in-person visit will be performed at the investigative site with targeted assessments based on presentation of signs and symptoms.

Blood samples for donor-specific antibody (DSA) testing will be collected at Baseline, Week 4, 14-30 days prior to the IP infusions scheduled for the Month 3, 6 and 9 visits, and Month 12. Blood collections for clinical laboratory and DSA testing at Week 4and pre-dose DSA testing at Months 3, 6, and 9 will occur either at the investigative site or remotely at a designated central laboratory patient service center. Blood collection for biomarker and exploratory biomarker testing at Week 6 and Month 4.5 will be conducted for those subjects who are able to travel to the investigative site.

If trial evidence suggests an appropriate risk/benefit profile of CAP-1002, Capricor, upon the recommendation of the Data Safety Monitoring Board (DSMB), will introduce an open-label extension study to offer CAP-1002 to subjects who were randomized to placebo and completed the 12-month follow-up period of the original trial.

The ***primary safety endpoints*** include the incidence of the following <u>from baseline through the 12-month timepoint</u>:

- Acute respiratory decompensation within 2 hours following IP administration
- Hypersensitivity reaction
  - Hypersensitivity reaction is defined as a clinical syndrome including, but not limited to, fever, leukocytosis, or rash with onset ≤ 2 hours post infusion and lasting < 24 hours, in the absence of clinical signs of concomitant infection.
- All-cause mortality
- Serious adverse events
- Treatment-emergent adverse events related to IP or administration procedure
- Immune sensitization syndrome
  - Immune sensitization syndrome shall be defined as: (a) clinical signs and symptoms consistent with systemic inflammation (e.g., fever, leukocytosis, rash, or arthralgia) with onset ≥ 24 hours post infusion and the absence of clinical signs of concomitant infection, **<u>AND</u>** (b) elevation of anti-human leukocyte antigen (HLA) antibodies against the donor cells (i.e., DSAs), detected ≤ 30 days following onset of syndrome, of (i) ≥ 2000 mean fluorescent intensity (MFI) if baseline MFI ≤ 1000, or (ii) ≥ 2 times baseline otherwise

The ***primary efficacy endpoint*** is change from baseline to the 12-month timepoint in functional capacity as assessed by the mid-level (elbow) dimension of the PUL 1.2.

The ***secondary safety endpoint*** is the incidence and severity of all adverse events through the 12-month timepoint.

The ***secondary efficacy endpoints*** include the change from baseline for the following:

- Mid-level (elbow) dimension of the PUL 1.2 at Months 3, 6, and 9 *(Month 12 is the primary endpoint)*
- Regional systolic left ventricular (LV) wall thickening as assessed by cardiac magnetic resonance imaging (MRI) at Months 6 and 12

The ***exploratory efficacy endpoints*** include the change from baseline to each assessment timepoint for the following assessments:

- All subjects
  - High-level (shoulder) dimension of the PUL 1.2
  - High-level (shoulder) dimension of the PUL 2.0
  - Mid-level (elbow) dimension of the PUL 2.0
  - Distal-level (wrist and hand) dimension of the PUL 1.2
  - Distal-level (wrist and hand) dimension of the PUL 2.0
  - Grip strength
  - Key and tip-to-tip pinch strength
  - Elbow flexion strength
  - Slow vital capacity (SVC), forced expiratory volume in one second (FEV_1), forced vital capacity (FVC), peak expiratory flow (PEF), maximum inspiratory pressure (MIP), maximum expiratory pressure (MEP), peak cough flow (PCF), and inspiratory flow reserve (IFR)
  - LV structure and function as assessed by cardiac MRI including ejection fraction, end-diastolic volume, end-systolic volume, stroke volume, regional wall thickness, and circumferential strain
  - Biomarkers may include those for muscle inflammation (osteopontin); systemic inflammation (interleukin 1 beta [IL-1ß], IL-2, -6 and -10; tumor necrosis factor alpha [TNF-α] and C-X-C motif chemokine 10 [CXCL10]; muscle damage (troponin I [cardiac, fast skeletal, slow skeletal], troponin T, creatine kinase MM isoenzyme [CK-MM], creatine kinase MB isoenzyme [CK-MB], creatine kinase [total], creatine phosphate, and creatinine); and muscle regeneration (myostatin and follistatin)
  - DMD Upper Limb Patient-Reported Outcome Measures (DMD UL-PROM)
  - Pediatric Outcomes Data Collection Instrument (PODCI)

- DMD Lifetime Mobility Scale (DMD-LMS)
- Resource utilization including the incidence of hospitalizations for orthopedic injury or surgery, pulmonary infections, and antibiotic usage

- Ambulatory subjects only
  - 10-Meter Walk/Run Time (10MWRT)
  - Incidence of loss of ambulation (defined by 10MWRT > 30 seconds)
  - North Star Ambulatory Assessment (NSAA)

Oversight of the trial will be provided by the blinded trial Steering Committee, an independent, unblinded DSMB, and an independent, blinded Clinical Events Committee (CEC) that will adjudicate all potential primary safety endpoints.

Number of Subjects: Twenty (20) subjects will be randomized in the trial.

Diagnosis and Main Criteria for Inclusion: Subjects with DMD and evidence of skeletal muscle impairment will be evaluated for eligibility to participate in the trial.

Inclusion Criteria Assessed within 30 Days Prior to Randomization Unless Otherwise Noted:

1. Male subjects at least 10 years of age at time of consent
2. Willing and able to provide informed consent to participate in the trial if ≥ 18 years of age, and assent with parental or guardian informed consent if < 18 years of age
3. Diagnosis of DMD based on clinical and phenotypic manifestations consistent with DMD (e.g., family history of DMD, elevated creatine kinase, dystrophin muscle biopsy, calf pseudohypertrophy, Gowers' sign, and gait impairment before 7 years of age) with confirmatory genetic testing performed at a Clinical Laboratory Improvement Amendments (CLIA)-certified laboratory. *See exclusion criteria 4 and 5 for mutation-specific exclusions.*
4. Performance of the Upper Limb entry item score 2-5
5. If ambulatory, 10-meter walk/run velocity < 1 meter/second
6. Loss of independent ambulation by 18th birthday (standing unassisted or ability to take, at most, several steps independently is not considered ambulation)
7. Receiving standard of care therapy at an experienced, multidisciplinary, DMD center as evidenced by regular cardiac and pulmonary monitoring, systemic glucocorticoid treatment, and at-home range of motion exercises
8. Treatment with a systemic glucocorticoid is required for at least 12 months prior to randomization. The dose must remain stable for at least 6 months prior to randomization with the exception of either weight-based dose adjustment or a decrease in steroid dose of ≤ 10% for toxicity. For patients on chronic deflazacort, treatment with an equivalent dose of prednisone or prednisolone for a period of ≤ 30 days to bridge lack of availability of deflazacort during the 6 months prior to randomization is acceptable
9. Current and up-to-date immunizations according to children and adolescent Centers for Disease Control immunization schedule, unless contraindicated, including the following: meningococcal

and meningococcal B; tetanus, diphtheria & acellular pertussis (Tdap); and pneumococcal polysaccharide vaccinations

10. Adequate venous access for parenteral IP infusions and routine blood collections in the judgement of the Investigator
11. Assessed by the Investigator as willing and able to comply with the requirements of the trial

Exclusion Criteria Assessed within 30 Days Prior to Randomization Unless Otherwise Indicated:

1. Left ventricular ejection fraction (LVEF) < 35%
2. Elbow-flexion contractures > 30° in both extremities
3. Body mass index (BMI) > 45
4. Documentation of exon 44 skip-amenable mutation(s) in the dystrophin gene *(see Appendix 1 for comprehensive list of mutations)*
5. Documentation of dystrophin deletion mutation(s) encompassing and limited to exons 3-7
6. Percent predicted FVC (FVC%p) < 35%
7. Inability to perform consistent FVC measurements within ±15% during paired testing at screening
8. Risk of near-term respiratory decompensation in the judgment of the investigator, *or* the need for initiation of non-invasive ventilator support as defined by serum bicarbonate ≥ 29 mmol/L at screening
9. History of non DMD-related chronic respiratory disease requiring ongoing or intermittent treatment including, but not limited to, asthma, bronchitis, and tuberculosis
10. Acute respiratory illness within 30 days prior to screening
11. Initiation of non-invasive ventilation within 30 days prior to screening, or the anticipated need to initiate non-invasive ventilation within the 12 months following screening
12. Planned or anticipated thoracic or spinal surgery within the 12 months following randomization
13. Planned or anticipated lower extremity surgery within the 12 months following randomization, if ambulatory
14. Known hypersensitivity to dimethyl sulfoxide (DMSO) or bovine products
15. Initiation of treatment with metformin or insulin within 3 months prior to randomization
16. Initiation of treatment with an FDA-approved exon skipping therapy for the treatment of DMD within 24 months prior to randomization or dose adjustments to the therapy within 12 months prior to randomization with the exception of weight-based dose adjustments
17. Treatment with human growth hormone (HGH) within 3 months prior to randomization, unless on a stable dose (as determined by the site PI) for at least 24 months prior to randomization
18. Treatment with idebenone within 3 months prior to randomization
19. Treatment with a cell therapy product within 12 months prior to randomization

20. Treatment with an investigational product within 6 months prior to randomization
21. History, or current use, of drugs or alcohol that could impair their ability to comply with participation in the trial
22. Inability to comply with the investigational plan and follow-up visit schedule for any reason, in the judgment of the investigator

Investigational Product, Dosage and Mode of Administration: [redacted] Subjects assigned to CAP-1002 will receive a total dose of 150 million CDCs per administration.

Duration of Treatment: CAP-1002 (150 million CDCs) or placebo is administered once every 3 months for a total of 4 administrations.

Duration of Trial: All subjects will be followed until 12 months post Day 1.

Criteria for evaluation:

Efficacy

The following efficacy outcome measures will be performed at Months 3, 6, 9 and 12 unless otherwise specified:

- Skeletal muscle function: PUL (1.2 and 2.0), grip strength, key and tip-to-tip pinch strength, elbow flexion strength, and, if ambulatory, NSAA
- Pulmonary function: SVC, FVC, FEV_1, PEF, MIP, MEP, PCF, and IFR

- Cardiac function and structure at Month 6 and 12 only: cardiac MRI (LV ejection fraction, end-diastolic volume, end-systolic volume, stroke volume, regional systolic wall thickening, regional wall thickness, and circumferential strain)
- Quality of Life (QOL): DMD Upper Limb Patient-Reported Outcome Measures, Pediatric Outcomes Data Collection Instrument, and DMD Lifetime Mobility Scale
- Biomarker analysis at Week 6, Month 3, Month 4.5[1], and Months 6, 9, and 12 may include:
  - *Muscle inflammation*: osteopontin
  - *Systemic inflammation*: IL-1β, IL-2, IL-6, IL-10, TNF-α, and CXCL10
  - *Muscle damage*: troponin I (cardiac, fast skeletal, slow skeletal), troponin T, CK-MM, CK-MB, creatine kinase (total), creatine phosphate, and creatinine
  - *Muscle regeneration*: myostatin and follistatin
  - Additional serum collection reserved for future biomarker analyses (i.e., exploratory biomarkers)

Safety

Safety assessments at Week 4 and Months 3, 6, 9 and 12, unless otherwise indicated, will include the following: vital signs, height, weight, physical examination, 12-lead ECG, adverse events, DSA assessment, and clinical laboratory testing (serum chemistry, hematology, and urinalysis). Adverse events and concomitant medications will also be collected during each 14-day post-infusion safety phone call, or if clinically indicated, an unscheduled in-person visit will be performed at the investigative site with targeted assessments based on presentation of signs and symptoms of subject.

Other

The medical resource utilization pharmacoeconomic analysis will explore all-cause hospitalizations, hospitalizations for orthopedic injury/surgery or pulmonary infections, and antibiotic usage. Billing information will not be collected; rather, standardized, composite or bundled costings of national averages will be used in the analysis.

Statistical Methods:

The statistical test for the primary efficacy endpoint will be two-sided and will be conducted using 0.05 significance levels. The detailed description of the trial statistical methods is provided in the Statistical Analysis Plan (SAP).

Sample Size

The trial will randomize 20 subjects. [redacted]

[1] Biomarker and exploratory biomarker testing at Week 6 and Month 4.5 will be conducted only for those subjects who are able to travel to the investigative site.

[redacted]

Analysis Populations

The following analysis populations will be defined for the trial:

Safety Population: Subjects who begin an infusion of IP. Safety endpoints for subjects will be summarized and analyzed according to the treatment actually received.

Intent-to-Treat (ITT) Population: Subjects who were randomized. Subjects will be summarized and analyzed in the treatment group to which they were randomized.

Modified Intent-to-Treat (mITT) Population: For each efficacy parameter, the mITT population will include subjects in the ITT population who have a baseline observation (i.e., mITT populations are parameter-specific). Subjects will be summarized and analyzed in the treatment group to which they were randomized.

Per Protocol Population: Subjects who received IP with no deviations/violations that could significantly impact the completeness, accuracy and/or reliability of the trial data. The list of subjects in the per protocol population will be compiled prior to database lock.

Interim Analysis for Futility

An interim analysis was performed based on data collected for the twenty treated subjects and submitted to the DSMB for review. The DSMB made a recommendation to continue the trial as originally designed. After review of the DSMB recommendation, the Sponsor decided to continue trial follow-up for the currently enrolled subjects but to terminate further enrollment in the trial. No additional interim analyses are planned.

Safety Analysis

Safety parameters will be evaluated using the safety population. The incidence of adverse events and any serious adverse events will be summarized by event types and the proportion of subjects with those events. There are no formal tests of hypotheses associated with the primary safety endpoint.

Efficacy Analysis

The primary efficacy endpoint will be evaluated in the ITT population, with possible supportive analyses in the mITT and PP populations. Comparisons between treatment groups on efficacy endpoints will be done using repeated measures linear models. Other analyses may also be done using appropriate parametric or non-parametric methods, depending on distributions of the data and whether or not model assumptions are met. An algorithm detailing the decision-making process for performing the primary efficacy analysis, in light of features of the data that cannot be known until the data are observed (e.g., outliers), will be detailed in the SAP.

Pharmacoeconomic Analysis

The pharmacoeconomic analysis will be done using the safety population.

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4. LIST OF ABBREVIATIONS AND DEFINITIONS OF TERMS

The following abbreviations and specialist terms are used in this trial protocol.

Table 2: Abbreviations and Specialist Terms

Term	Explanation
%p	Percent Predicted
10MWR	10-Meter Walk/Run
10MWRT	10-Meter Walk/Run Time
6MWT	Six-Minute Walk Test
ACEi	angiotensin-converting enzyme inhibitor
AE	Adverse Event
ALT	Alanine Aminotransferase
AST	Aspartate Aminotransferase
BMI	Body Mass Index
BUN	Blood Urea Nitrogen
C	Celsius
CBC	Complete Blood Count
CDC	Cardiosphere-Derived Cells
CEC	Clinical Events Committee
CFR	Code of Federal Regulations
CK-MB	Creatine kinase MB Isoenzyme
CK-MM	Creatine kinase MM Isoenzyme
CLIA	Clinical Laboratory Improvement Amendments
CRF	Case Report Form
CRO	Clinical Research Organization
CT	Computerized Tomography

Term	Explanation
CXCL10	C-X-C Motif Chemokine 10
DCM	Dilated Cardiomyopathy
DMD	Duchenne Muscular Dystrophy
DMD UL-PROM	DMD Upper Limb Patient-Reported Outcome Measures
DMD-LMS	DMD Lifetime Mobility Scale
DMSO	Dimethyl Sulfoxide
DSA	Donor-Specific Antibody
DSMB	Data Safety Monitoring Board
ECG	Electrocardiogram
EDC	Electronic Data Capture
ESR	Expedited Safety Report
ET	Early Termination
FDA	U.S. Food and Drug Administration
FEV_1	Forced Expiratory Volume in 1 Second
FVC	Force Vital Capacity
GCP	Good Clinical Practice
GMP	Good Manufacturing Practice
HED	Human Equivalent Dose
HEENT	Head, Eyes, Ears, Nose, and Throat
HFrEF	Heart Failure with Reduced Ejection Fraction
HGH	Human Growth Hormone

Term	Explanation
Term	**Explanation**
HIPAA	Health Insurance Portability and Accountability Act
HLA	Human Leukocyte Antigen
[redacted]	[redacted]
IB	Investigator's Brochure
ICH	International Conference of Harmonisation
IFR	Inspiratory Flow Reserve
IL	Interleukin
IND	Investigational New Drug Application
IP	Investigational Product
IRB	Institutional Review Board
ITT	Intent-to-Treat
IV	Intravenous
IWRS	Interactive Web Response System
L	Liter
LDH	Lactate Dehydrogenase
LGE	Late Gadolinium Enhancement
LV	Left Ventricle / Left Ventricular
LVEDV	Left Ventricular End-Diastolic Volume
LVEF	Left Ventricular Ejection Fraction
LVESV	Left Ventricular End-Systolic Volume
M	Million
MACE	Major Adverse Cardiac Event
MCB	Master Cell Bank

Term	Explanation
Term	**Explanation**
MedDRA	Medical Dictionary for Regulatory Activities
MEP	Mean Expiratory Pressure
MFI	Mean Fluorescence Intensity
MHC	Major Histocompatibility Complex
MI	Myocardial Infarction
MIP	Mean Inspiratory Pressure
mITT	Modified Intent-to-Treat
mL	Milliliter
MOP	Manual of Procedures
MRI	Magnetic Resonance Image
MSC	Mesenchymal Stem Cells
NSAA	North Star Ambulatory Assessment
OAE	Other Adverse Events
p.r.n.	As Needed
PCF	Peak Cough Flow
PE	Physical Exam
PEF	Peak Expiratory Flow
PFT	Pulmonary Function Test
PI	Principal Investigator
PODCI	Pediatric Outcomes Data Collection Instrument
PP	Per Protocol
PROM	Patient-Reported Outcome Measure
PT	Preferred Term

Term	Explanation
PUL	Performance of the Upper Limb
QOL	Quality of Life
RBC	Red Blood Cell
RV	Residual Volume
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SD	Standard Deviation
SOC	System Organ Class
SpO_2	Peripheral Capillary Hemoglobin Oxygen Saturation
SUSAR	Serious, Unexpected Suspected Adverse Reaction

Term	Explanation
SVC	Slow Vital Capacity
Tdap	Tetanus, Diphtheria, and Acellular Pertussis
TEAE	Treatment-Emergent Adverse Events
TIMI	Thrombolysis in Myocardial Infarction
TLC	Total Lung Capacity
TNF-α	Tumor Necrosis Factor Alpha
v/v	Volume to Volume
WBC	White Blood Cell
WHO-DD	World Health Organization Drug Dictionary

5. INTRODUCTION

5.1. Background

Duchenne muscular dystrophy (DMD) is a severe, X-linked, progressive disease affecting approximately one in 3,600 to 9,200 male births (Mah et al., 2014). It is caused by mutations in the dystrophin gene resulting in the absence of or non-functional dystrophin protein (Hoffman et al., 1988).

Dystrophin is a cytoplasmic protein encoded by the *dmd* gene, which links cytoskeletal actin filaments to membrane proteins. The dystrophin protein acts as a shock absorber during muscle fiber contraction by linking the actin of the contractile apparatus to the layer of connective tissue that surrounds each muscle fiber (Koenig et al., 1988; Fairclough et al., 2013; Aartsma-Rus et al., 2016).

Due to the lack of dystrophin, the connection between the actin cytoskeleton and connective tissue is lost, inducing excessive membrane fragility and permeability, dysregulation of calcium homeostasis, and oxidative damage, which results in muscle cell necrosis and a chronic inflammatory state. Initially, muscle necrosis is followed by regeneration, but with age, the regenerative ability of myofibers is lost and muscle fibers are gradually replaced by connective and adipose tissue. It has been postulated that chronic injury and regeneration induce satellite cell exhaustion. Recent studies suggest that the absence of dystrophin in satellite cells impairs their ability to divide properly, thus reducing the generation of myogenic progenitors that are needed for proper muscle regeneration (Dumont et al., 2015). As a consequence, muscle function is lost (Muntoni et al., 2003; Deconinck and Dan, 2007; Falzarano et al., 2015).

DMD occurs in early childhood, with degeneration occurring progressively in the skeletal musculature and ultimately in the heart and respiratory muscles, resulting in premature death (Hendriksen et al., 2015). Progressive weakness and muscle atrophy caused by degenerating muscle fibers begins in the lower extremities and pelvis before spreading into the upper extremities. Other symptoms include loss of some reflexes, a waddling gait, frequent falls, difficulty when rising from a sitting or lying position or when climbing stairs, changes to overall posture, and impaired breathing. Many children precipitously lose the ability to run or jump. The atrophied muscles, in particular the calf muscles, and less commonly, muscles in the buttocks, shoulders, and arms, may be enlarged by an accumulation of fat and connective tissue, causing them to look larger and healthier than they actually are ("pseudohypertrophy"). Bone thinning and scoliosis are common. Ultimately, a wheelchair becomes necessary, in most cases between 12 to15 years of age (Henricson et al., 2013).

As the disease progresses, the muscles in the diaphragm that assist in breathing and coughing become weaker. Affected individuals experience breathing difficulties, respiratory infections, and swallowing problems. Almost all DMD patients will develop cardiomyopathy (Aartsma-Rus et al., 2016). Pneumonia, compounded by cardiac involvement, is the most frequent cause of death, which typically occurs in the late teens or early 20s. However, improvements in multidisciplinary care, in particular respiratory care and various forms of assisted ventilation, have extended the life expectancy; numerous individuals with DMD now survive into their 30s, and some even into their 40s (Emery, 2002; Bushby et al., 2010; Bushby et al., 2010).

No pharmacologic or biological therapies proven to stop or reverse the progression of DMD have been approved in the US. Disease management consists primarily of preventive measures as well as active interventions to address the primary and secondary aspects of the disorder.

[redacted]

a total of 4 severe events, including 2 subjects (16.7%) in the usual care group (1 subject with

[redacted]

5.4. Risks and Benefits

[redacted]

[redacted]

Based on these data, the benefit-risk balance for CAP-1002 is considered favorable and warrants additional clinical investigation.

5.5. Trial Rationale

CAP-1002 is intended to be used as a therapeutic to improve the morbidities associated with DMD and thus improve or prevent decline in muscle function through its composite immune-modulatory, anti-fibrotic, and regenerative mechanisms of action. [redacted] CAP-1002 can have systemic effects, including benefits on skeletal function (as assessed by mid-level PUL) compared to usual care control subjects. This clinical evidence suggests that CAP-1002 has the potential to address unmet medical needs for patients with DMD. [redacted]

5.6. Dose Justification

5.6.1. Dosing Interval

Data [redacted] shows a maintenance of benefit in PUL with CAP-1002 treatment up to 3 months post dose that then wanes by 6 months. This observation that some benefits of a CAP-1002 dose may be transient inspired the plan for a repeat administration regimen in the proposed clinical trial, with doses re-administered every 3 months. [redacted]

5.6.2. Dose Selection

The 150M dose selected for testing in the proposed clinical trial was chosen [redacted] Thus, 150M was selected as a dose below the anticipated maximum tolerated dose and in the anticipated effective dose range. Notably, the dose [redacted] already demonstrated preliminary efficacy via intracoronary administration [redacted] and would be expected to be similarly efficacious via intravenous administration, given what is known about cell biodistribution and engraftment post infusion by either route.

Cell biodistribution by intracoronary and intravenous infusion was previously studied [redacted] and the proposed 150M CAP-1002 dose can be expected to be equally or possibly more efficacious.

[redacted] These collective data suggest that intravenous infusion of CAP-1002 doses of 150M should be reasonably safe in humans. These data also help define the safety assessments planned for the proposed clinical trial.

5.6.3. Repeat Administrations

The other element of safety relevant for the proposed clinical trial and related to the planned dosing regimen, is the potential for an immune response to the allogeneic product, planned for repeated administrations. Several lines of evidence suggest that repeat administration of CAP-1002 should have low immunotoxicity risk in humans. [redacted] In fact, equivalent primary (i.e., after a first dose) and secondary (i.e. after a second dose) efficacy benefits (i.e., improvements in LVEF) were observed using allogeneic and syngeneic CDCs in this study. Furthermore, there was no evidence of an increased cellular or humoral immune memory response using allogenic compared to syngeneic CDCs.

[redacted]

[redacted] Further information about the allergic reactions is found in the Investigator's Brochure and Section 13.2.1.3.

These collective data suggest that repeat administration of CAP-1002 should be reasonably safe in humans. However, the risk of severe allergic reactions should be minimized by administration of medications that will be determined by the Investigator based on the pre-treatment guidelines provided by Capricor (Section 21.2) and/or institutional protocols.

5.7. Trial Population

The target population for this trial includes pediatric and adult males with a diagnosis of DMD, evidence of skeletal muscle impairment regardless of ambulatory status, and on a stable regimen of systemic glucocorticoids (see Inclusion Criterion 8 for additional details regarding stable regimen of systemic glucocorticoids).

6. TRIAL OBJECTIVES AND PURPOSE

6.1. Primary Objective

The primary objective of this trial is to evaluate the safety and efficacy of intravenous CAP-1002 administered every three months in subjects with DMD and impaired skeletal muscle function.

6.2. Secondary Objectives

The secondary objective of this trial is to evaluate the impact of repeated IV administrations of CAP-1002 on exploratory efficacy assessments of skeletal and cardiac muscle function, and quality of life.

7. INVESTIGATIONAL PLAN

7.1. Overall Trial Design

This Phase 2, multi-center, randomized, double-blind, placebo-controlled trial will assess the safety and efficacy of allogeneic CDCs, or CAP-1002, administered as four IV infusions, one every three months, for the treatment of subjects with DMD. Subjects with a clinical diagnosis of DMD confirmed by genetic testing and evidence of skeletal muscle impairment will undergo a battery of tests and procedures during a 30-day screening period to determine eligibility based on protocol inclusion and exclusion criteria.

Eligible subjects will be prospectively randomized in stratified permuted blocks to CAP-1002 or placebo (1:1 ratio) approximately 7 days prior to the first IV infusion of IP on Day 1. Randomization will be stratified by site and entry item score of the PUL 1.2 module. Subjects will undergo baseline safety and efficacy assessments (Table 3) prior to the first infusion of IP (CAP-1002 or placebo). Administration of IP (Day 1) should occur within a maximum of 14 days following randomization; if a delay of more than 14 days between randomization and IP administration is unavoidable, a conversation between the Investigator and Medical Monitor should occur to determine the need for repeat assessments prior to infusion. Subjects that are not randomized may be re-screened at the discretion of the Investigator.

Subjects will complete study assessments at Screening; Baseline (≤ 2 days prior to Day 1); Day 1; Weeks 4 (±7 days); and Months 3,6, 9, and 12 (±14 days, each). If the subject can travel to the investigative site, blood samples will be collected at Week 6 (±7 days) and Month 4.5 (±14 days).

All IV infusions will be conducted in an outpatient setting at the investigative site on Day 1 and Months 3, 6, and 9. Prior to each IP infusion, medication(s) will be administered to the subject as determined by the Investigator based on the pre-treatment guidelines (see Section 21.2) and/or institutional protocols to minimize the risk of potential severe allergic reactions such as anaphylaxis. Subjects will be observed in the outpatient setting for at least two hours post infusion and then discharged the same day if medically cleared by the site Investigator. As part of these visits, subjects will complete a safety phone call 14 days (±3 days) after each IP infusion, and if clinically indicated, an unscheduled in-person visit will be performed at the investigative site with targeted assessments based on presentation of signs and symptoms.

Blood samples for DSA testing will be collected at Baseline, Week 4, 14-30 days prior to the IP infusions scheduled for the Month 3, 6 and 9 visits, and Month 12. Blood collections for clinical laboratory and DSA testing at Week 4 and pre-dose DSA testing at Months 3, 6, and 9 will occur either at the investigative site or remotely at a designated central laboratory patient service center. Blood collection for biomarker and exploratory biomarker testing at Week 6 and Month 4.5 will be conducted for those subjects who are able to travel to the investigative site.

If trial evidence suggests an appropriate risk/benefit profile of CAP-1002, Capricor, upon the recommendation of the Data Safety Monitoring Board (DSMB), may introduce an open-label extension study to offer CAP-1002 to subjects who were randomized to placebo and completed the 12-month follow-up period of the original trial.

7.2. Trial Endpoints

7.2.1. Primary Endpoints

The ***primary safety endpoints*** include the incidence of the following from baseline through the 12-month timepoint:

- Acute respiratory decompensation within 2 hours following IP administration
- Hypersensitivity reaction
  - Hypersensitivity reaction is defined as a clinical syndrome including, but not limited to, fever, leukocytosis, or rash with onset ≤ 2 hours post infusion and lasting < 24 hours, in the absence of clinical signs of concomitant infection.
- All-cause mortality
- Serious adverse events
- Treatment-emergent adverse events related to IP or administration procedure
- Immune sensitization syndrome
  - Immune sensitization syndrome shall be defined as: (a) clinical signs and symptoms consistent with systemic inflammation (e.g., fever, leukocytosis, rash or arthralgia) with onset ≥ 24 hours post infusion and the absence of clinical signs of concomitant infection, **AND** (b) elevation of anti-human leukocyte antigen (HLA) antibodies against the donor cells (i.e., DSAs), detected ≤ 30 days following onset of syndrome, of (i) ≥ 2000 MFI if baseline MFI ≤ 1000, or (ii) ≥ 2 times baseline otherwise

The ***primary efficacy endpoint*** is change from baseline to the 12-month timepoint in functional capacity as assessed by the mid-level (elbow) dimension of the PUL 1.2.

7.2.2. Secondary Endpoints

The ***secondary safety endpoint*** is the incidence and severity of all adverse events through the 12-month timepoint.

The ***secondary efficacy endpoints*** include the change from baseline for the following:

- Mid-level (elbow) dimension of the PUL 1.2 at Months 3, 6, and 9 *(Month 12 is the primary endpoint)*
- Regional systolic left ventricular wall thickening as assessed by cardiac MRI at Months 6 and 12

7.2.3. Exploratory Endpoints

The ***exploratory efficacy endpoints*** include the change from baseline to each assessment timepoint for the following assessments:

- All subjects
  - High-level (shoulder) dimension of the PUL 1.2

  - High-level (shoulder) dimension of the PUL 2.0
  - Mid-level (elbow) dimension of the PUL 2.0
  - Distal-level (wrist and hand) dimension of the PUL 1.2
  - Distal-level (wrist and hand) dimension of the PUL 2.0
  - Grip strength
  - Key and tip-to-tip pinch strength
  - Elbow flexion strength
  - Slow vital capacity (SVC), forced expiratory volume in one second (FEV_1), forced vital capacity (FVC), peak expiratory flow (PEF), maximum inspiratory pressure (MIP), maximum expiratory pressure (MEP), peak cough flow (PCF), and inspiratory flow reserve (IFR)
  - Left ventricular structure and function as assessed by cardiac MRI including ejection fraction, end-diastolic volume, end-systolic volume, stroke volume, regional wall thickness, and circumferential strain
  - Biomarkers may include those for muscle inflammation (osteopontin); systemic inflammation (interleukin 1 beta [IL-1ß], IL-2, -6 and -10; tumor necrosis factor alpha [TNF-α] and C-X-C motif chemokine 10 [CXCL10]; muscle damage (troponin I [cardiac, fast skeletal, slow skeletal], troponin T, creatine kinase MM isoenzyme [CK-MM], creatine kinase MB isoenzyme [CK-MB], creatine kinase [total], creatine phosphate, and creatinine); and muscle regeneration (myostatin and follistatin)
  - DMD Upper Limb Patient-Reported Outcome Measures (DMD UL-PROM)
  - Pediatric Outcomes Data Collection Instrument (PODCI)
  - DMD Lifetime Mobility Scale (DMD-LMS)
  - Resource utilization including the incidence of hospitalizations for orthopedic injury or surgery, pulmonary infections, and antibiotic usage

- Ambulatory subjects only
  - 10-Meter Walk/Run Time (10MWRT)
  - Incidence of loss of ambulation (defined by 10MWRT > 30 seconds)
  - North Star Ambulatory Assessment (NSAA)

7.3. Number of Subjects

The trial will enroll a total of 20 evaluable subjects. [redacted].

7.4. Treatment Assignment

Subjects will be prospectively randomized in stratified permuted blocks in a 1:1 allocation to intravenous infusion of either CAP-1002 or placebo. See Section 9.4 for additional details related to randomization.

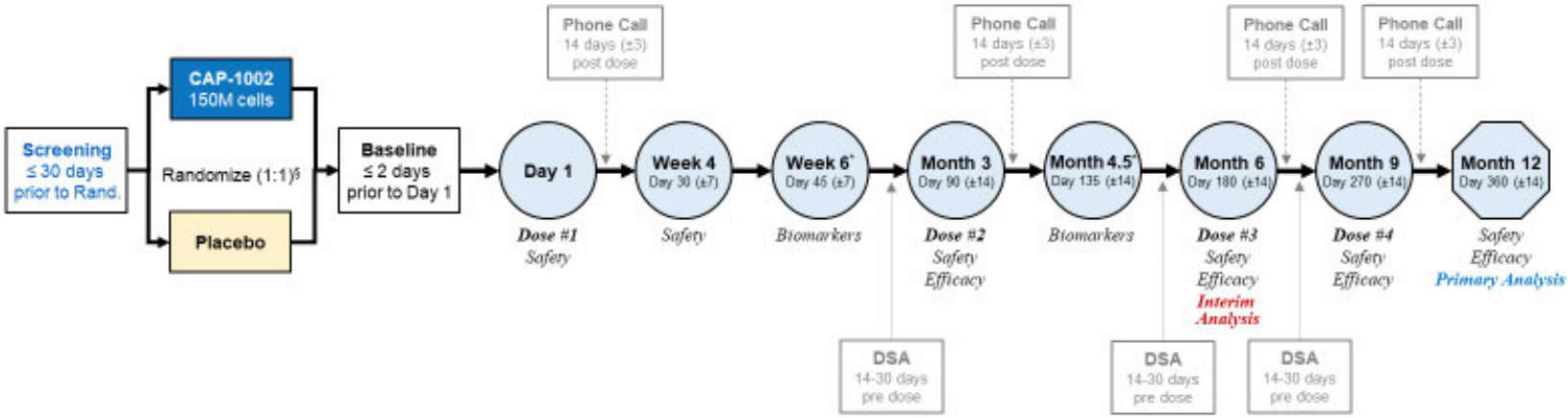
7.5. Dose Adjustment Criteria

There are no planned dose adjustments. Should an acute toxicity arise during the infusion (e.g., hypersensitivity reaction, pulmonary decompensation, etc.), the infusion should be terminated immediately, and the actual total dose administered recorded. Any decision about re-challenging in a subsequent infusion should be made after discussions with the Investigator, Medical Monitor, Data Safety Monitoring Board (DSMB), and other medical experts that may be required to make an informed decision.

7.6. Criteria for Trial Termination

The trial may be terminated at any time and for any reason, including, but not limited to, a recommendation by the DSMB for safety reasons, an action by the FDA, or decision by Capricor.

Figure 1: Trial Design



§ Approximately 7 days prior to Day 1
* Only completed for subjects that are able to travel to the investigative site

Table 3: Schedule of Assessments

Procedure / Event [1]	**Screening**	**Baseline**	**Day 1**		**Week 4**	**Week 6**	**Month 3**			**Month 4.5**	**Month 6**			**Month 9**			**Mo 12 / ET**[2]
Trial Day (Visit Window)	*≤ 30 d prior to Rand.*	*≤ 2 d prior to Day 1*	*1 d*	*14 d (±3) post Inf #1*	*30 d (±7)*	*45 d (±7)*	*14-30 days pre Inf #2*	*90 d (±14)*	*14d (±3) post Inf #2*	*135 d (±14)*	*14-30 days pre Inf #3*	*180 d (±14)*	*14d (±3) post Inf #3*	*14-30 days pre Inf #4*	*270 d (±14)*	*14d (±3) post Inf #4*	*360 d (±14)*
Intravenous Infusion #			*#1*					*#2*				*#3*			*#4*		
Informed Consent / Assent	X																
Demographics	X																
Medical History	X																
Eligibility Assessment	X																
Randomization [3]	X																
Medical Status Questionnaire [4]	X	X						X				X			X		X
Prior & Concomitant Medications	X	X	X	X				X	X			X	X		X	X	X
Adverse Events[5]	X	X	X	X				X	X			X	X		X	X	X
IP Intravenous Infusion [6]			X					X				X			X		
Post-Infusion Safety Call [7]				X					X				X			X	
DMD Upper Limb PROM	X	X						X				X			X		X
PODCI	X	X						X				X			X		X
DMD Lifetime Mobility Scale	X	X						X				X			X		X
Vital Signs	X	X	X					X				X			X		X
Height / Ulna Length [8]	X	X						X				X			X		X
Weight	X	X	X					X				X			X		X
Physical Examination	X											X					X
12-Lead ECG		X						X				X			X		X
Pulmonary Function Testing [9]	X2	X						X				X			X		X

Procedure / Event [1]	**Screening**	**Baseline**	**Day 1**		**Week 4**	**Week 6**	**Month 3**			**Month 4.5**	**Month 6**			**Month 9**			**Mo 12 / ET**[2]
Trial Day (Visit Window)	*≤ 30 d prior to Rand.*	*≤ 2 d prior to Day 1*	*1 d*	*14 d (±3) post Inf #1*	*30 d (±7)*	*45 d (±7)*	*14-30 days pre Inf #2*	*90 d (±14)*	*14d (±3) post Inf #2*	*135 d (±14)*	*14-30 days pre Inf #3*	*180 d (±14)*	*14d (±3) post Inf #3*	*14-30 days pre Inf #4*	*270 d (±14)*	*14d (±3) post Inf #4*	*360 d (±14)*
PUL 1.2 and 2.0	X	X						X				X			X		X
Grip Strength	X	X						X				X			X		X
Pinch Strength (Key and Tip)	X	X						X				X			X		X
Elbow Flexion Strength	X	X						X				X			X		X
NSAA *(ambulatory subjects only)*	X	X						X				X			X		X
PSC Lab Collection [10]					X		X				X			X			
Serum Chemistry [11 12]	X	X			X			X				X			X		X
Hematology [11 13]	X	X			X			X				X			X		X
Urinalysis [11 14]	X	X			X			X				X			X		X
DMD Genetic Testing [11 15]	X																
HLA Typing [11]		X															
Donor-Specific Antibodies [11]		X			X		X				X			X			X
Biomarkers 16[17]		X				X		X		X		X			X		X
Exploratory Biomarkers [16 18]		X				X		X		X		X			X		X
Cardiac MRI [19]	X											X					X

Gray-shaded columns indicate visits that may be performed at either the investigative site or remotely at a designated central laboratory patient service center (see footnote #9)

[1] Sites will complete assessments in the following sequence: 1) QOL (DMD UL-PROM, PODCI, and DMD-LMS), 2) safety and other trial assessments, excluding blood and urine collections (e.g., vital signs, height, weight, 12-lead electrocardiogram [ECG], etc.), 3) pulmonary function testing (PFT), 4) PUL 1.2 and 2.0, 5) grip strength, 6) pinch strength (key and tip-to-tip), 7) elbow flexion strength, 8) NSAA (if ambulatory), 9) blood and urine collections, 10) cardiac MRI (if applicable), and 11) IP Infusion (if applicable). All efforts must be made for the same clinical evaluator to complete assessments for the same subject at the same time of day throughout the trial (preferably in the morning).

[2] All attempts must be made to perform the trial assessments indicated for the Month 12 visit (i.e., final comprehensive visit) for subjects that decide to early terminate from the trial before completion and after starting at least one IP infusion.

[3] Subjects must will be randomized between approximately 7 days in advance of their first IP infusion on Day 1. This lead time is to ensure adequate IP shipping times (see IP Manual for shipping specifications). Randomization will be stratified by site and entry item score of the PUL1.2 at screening. Administration of IP on Day 1 should occur within a maximum of 14 days following randomization; if a delay of more than 14 days between randomization and IP administration is unavoidable, a conversation between the Investigator and Medical Monitor should occur to determine the need for repeat assessments prior to infusion. Subjects that are not randomized may be re-screened at the discretion of the Investigator.

[4] Updates regarding frequency of wheelchair use, transition to wheelchair full time, ventilatory support, and frequency of falls.

[5] A blood sample for tryptase should be obtained within 3 hours of the onset of allergic signs or symptoms, and a second red top tube should be drawn within 3 hours of a severe allergic reaction, and frozen at -20°C, for other future analyses.

[6] All IP infusions will be conducted in an outpatient setting at the investigative site. Prior to each IP infusion, medications will be administered to the subject as determined by the Investigator based on the pre-treatment guidelines provided by Capricor and/or institutional protocols to minimize the risk of potential severe allergic reactions such as anaphylaxis. Subjects will be observed for at least 2 hours post infusion, including pulse oximetry monitoring for at least 30 minutes post infusion. Sites will observe local institutional policies related to parenteral infusions and post-infusion monitoring.

[7] A safety phone call will be performed 14 days (±3 days) after each IP infusion, and if clinically indicated, an unscheduled in-person visit will be performed at the investigative site with targeted assessments based on presentation of signs and symptoms.

[8] Ulna length will be measured in all subjects. Standing height will be measured if a subject is capable. If standing height cannot be measured, height will be calculated using a measurement of ulna length per Section 13.1.2.

[9] Paired forced-maneuver testing will be performed on Screening Day 1 and Day 2 (approximately 24 hours between testing sessions) to confirm acceptable FVC variance (exclusion criterion 7). PFT testing sequence: SVC, forced maneuver (FEV_1/FVC/PEF), MIP, MEP, PCF, and IFR.

[10] Blood collections for clinical laboratory and DSA testing at Week 4 and pre-dose DSA testing at Months 3, 6, and 9 will occur either at the investigative site or remotely at a designated central laboratory patient service center.

[11] Blood and urine samples will be collected using trial-specific laboratory kits, and then shipped to and tested at a central laboratory. Required sample collection for a visit may occur on multiple days; if the visit includes an IP infusion, sample collections should occur prior to IP administration. Baseline blood samples may be collected on Day 1 prior to IP administration to reduce number of venipunctures.

[12] Basic metabolic panel (Glucose, Sodium, Potassium, Chloride, Bicarbonate, BUN, Creatinine, Calcium), comprehensive hepatic panel (Albumin, Alkaline Phosphatase, Total Protein, ALT, AST, GGT, Direct Bilirubin, Total Bilirubin).

[13] CBC with WBC differential, hemoglobin, hematocrit and platelet count

[14] Appearance, bilirubin, color, nitrite, occult blood, pH, protein, specific gravity, glucose, ketones, RBC, and WBC. If required, microscopic analysis of sediment will be performed and reported per occurrence

[15] DMD genetic testing will be available at screening for subjects who have not previously completed genetic testing or whose historical genetic results were not performed at a CLIA-certified laboratory as determined by an Investigator. The turn-around time for final results may exceed the 30-day screening window; allow 29-49 days for receipt of final test results.

[16] Week 6 and Month 4.5 blood samples will only be collected at the investigative site. [17] Biomarkers may include those of muscle inflammation (osteopontin); systemic inflammation (IL-1ß, IL-2, IL-6, IL-10, TNF-α, CXCL10); muscle damage (troponin I [cardiac, fast skeletal, slow skeletal], troponin T, CK-MM, CK-MB, creatine kinase [total], creatine phosphate, and creatinine); and muscle regeneration (myostatin and follistatin).

[18] Collected only if separate informed consent and/or assent provided

[19] Subjects will undergo cardiac MRI if they are physically capable as determined by an Investigator. Subjects that cannot complete a cardiac MRI as part of the trial will complete an echocardiogram at screening using the site's local equipment, acquisition protocol, and evaluation procedures. The reported LVEF from a local interpretation, whether it's measured via cardiac MRI or echocardiogram, will be used to assess eligibility (exclusion criterion 1).

8. SELECTION AND WITHDRAWAL OF SUBJECTS

Subjects who meet all inclusion criteria and no exclusion criteria will be eligible for randomization in the trial.

8.1. Subject Inclusion Criteria

Inclusion criteria will be assessed within 30 days prior to randomization unless otherwise noted:

1. Male subjects at least 10 years of age at time of consent
2. Willing and able to provide informed consent to participate in the trial if ≥ 18 years of age, and assent with parental or guardian informed consent if < 18 years of age
3. Diagnosis of DMD based on clinical and phenotypic manifestations consistent with DMD (e.g., family history of DMD, elevated creatine kinase, dystrophin muscle biopsy, calf pseudohypertrophy, Gowers' sign, and gait impairment before 7 years of age) with confirmatory genetic testing performed at a Clinical Laboratory Improvement Amendments (CLIA)-certified laboratory. *See exclusion criteria 4 and 5 for mutation-specific exclusions.*
4. Performance of the Upper Limb entry item score 2-5
5. If ambulatory, 10-meter walk/run velocity < 1 meter/second
6. Loss of independent ambulation by 18th birthday (standing unassisted or ability to take, at most, several steps independently is not considered ambulation)
7. Receiving standard of care therapy at an experienced, multidisciplinary, DMD center as evidenced by regular cardiac and pulmonary monitoring, systemic glucocorticoid treatment, and at-home range of motion exercises
8. Treatment with a systemic glucocorticoid is required for at least 12 months prior to randomization. The dose must remain stable for at least 6 months prior to randomization with the exception of either weight-based dose adjustment or a decrease in steroid dose of ≤ 10% for toxicity. For patients on chronic deflazacort, treatment with an equivalent dose of prednisone or prednisolone for a period of ≤ 30 days to bridge lack of availability of deflazacort during the 6 months prior to randomization is acceptable
9. Current and up-to-date immunizations according to children and adolescent Centers for Disease Control immunization schedule, unless contraindicated, including the following: meningococcal and meningococcal B; tetanus, diphtheria & acellular pertussis (Tdap); and pneumococcal polysaccharide vaccinations
10. Adequate venous access for parenteral IP infusions and routine blood collections in the judgement of the Investigator
11. Assessed by the Investigator as willing and able to comply with the requirements of the trial

8.2. Subject Exclusion Criteria

Exclusion criteria will be assessed within 30 days prior to randomization unless otherwise indicated:

1. Left ventricular ejection fraction (LVEF) < 35%
2. Elbow-flexion contractures > 30° in both extremities
3. Body mass index (BMI) > 45
4. Documentation of exon 44 skip-amenable mutation(s) in the dystrophin gene *(see Appendix 1 for comprehensive list of mutations)*
5. Documentation of dystrophin deletion mutation(s) encompassing and limited to exons 3-7
6. Percent predicted FVC (FVC%p) < 35%
7. Inability to perform consistent FVC measurement within ±15% during paired testing at screening
8. Risk of near-term respiratory decompensation in the judgment of the investigator, *or* the need for initiation of non-invasive ventilator support as defined by serum bicarbonate ≥ 29 mmol/L at screening
9. History of non DMD-related chronic respiratory disease requiring ongoing or intermittent treatment, including, but not limited to, asthma, bronchitis, and tuberculosis
10. Acute respiratory illness within 30 days prior to screening
11. Initiation of non-invasive ventilation within 30 days prior to screening, or the anticipated need to initiate non-invasive ventilation within the 12 months following screening
12. Planned or anticipated thoracic or spinal surgery within the 12 months following randomization
13. Planned or anticipated lower extremity surgery within the 12 months following randomization, if ambulatory
14. Known hypersensitivity to dimethyl sulfoxide (DMSO) or bovine products
15. Initiation of treatment with metformin or insulin within 3 months prior to randomization
16. Initiation of treatment with an FDA-approved exon skipping therapy for the treatment of DMD within 24 months prior to randomization or dose adjustments to the therapy within 12 months prior to randomization with the exception of weight-based dose adjustments.
17. Treatment with human growth hormone (HGH) within 3 months prior to randomization, unless on a stable dose (as determined by the site PI) for at least 24 months prior to randomization
18. Treatment with idebenone within 3 months prior to randomization
19. Treatment with a cell therapy product within 12 months prior to randomization
20. Treatment with an investigational product within 6 months prior to randomization

21. History, or current use, of drugs or alcohol that could impair their ability to comply with participation in the trial
22. Inability to comply with the investigational plan and follow-up visit schedule for any reason, in the judgment of the investigator

8.3. Screen Failures

Any subject who provides written informed consent/assent and is ultimately not randomized for whatever reason will be classified as a screen failure. All subjects, including screen failures, must be accounted for in the clinical database.

Screen failures may be re-screened at the discretion of the Investigator using the originally assigned screening number.

8.4. Subject Withdrawal Criteria

Every effort will be made to have each randomized subject complete all elements of the trial. If a subject has started at least one IP infusion and withdraws prior to trial completion, all attempts must be made to perform the trial assessments indicated for the Month 12 visit (i.e., final comprehensive visit).

Criteria for withdrawal from trial participation include the following reasons:

- A subject may withdraw his consent at any time without prejudice to his care.
- At the discretion of the Investigator, the subject may be withdrawn from the trial for lack of adherence to the investigational plan.
- A subject may be withdrawn from the trial for an acute reaction to IP or other safety issue that prevents repeat infusions. In this instance, the subject should be followed on schedule until completion of assessments through the Month 12 visit or for at least 3 months post last IP infusion and then complete a final comprehensive visit.

9. TREATMENT OF SUBJECTS

9.1. Description of Investigational Product

CAP-1002 consists of allogeneic cardiosphere-derived cells or CDCs in a cryogenic cell preservation solution. [redacted] Two units of CAP-1002 comprise a single dose of 150 million CDCs for intravenous infusion. Placebo is configured and provided in the same manner.

[redacted].

9.2. Concomitant Medications

Refer to exclusion criteria for medications/therapies that exclude a subject from randomization.

All efforts should be made to maintain the same DMD medication regimen throughout the course of the trial. This should be discussed with the subject's primary medical doctor and caregivers at the outset of the trial and during the trial follow-up period.

9.3. Treatment Compliance

IP will be administered in a licensed infusion center, or other appropriate unit according to a site's institutional standards, by appropriately trained medical personnel who will document the actual volume administered at each infusion.

9.4. Randomization

Subjects who meet all enrollment criteria will be prospectively randomized in stratified permuted blocks to CAP-1002 or placebo (1:1 ratio) via an interactive web-based response system (IWRS) accessed directly by site personnel who have been delegated this responsibility by the Principal Investigator. Randomization will be stratified by site and entry item score of the PUL 1.2 at Screening. Subjects will be randomized approximately 7 days in advance of their first IP infusion on Day 1. This lead time is to ensure adequate IP shipping time (see IP Manual for shipping specifications). The central randomization will be generated in SAS or comparable software using permuted random block sizes held in confidence by the statistician preparing the master randomization list.

9.5. Blinding

Following the prespecified interim analysis, designated Capricor personnel became unblinded to subject treatment assignments and to cumulative aggregate results.

Site personnel and trial subjects, staff members at clinical research organizations (CROs), core laboratory personnel, and Clinical Event Committee (CEC) members will remain blinded to subject treatment assignments until follow-ups have been completed on the currently enrolled subjects. This is a double-blind, placebo-controlled trial. IP will be prepared for IV infusion by site personnel who have been appropriately delegated by the Principal Investigator. The IP syringes once prepared will appear identical for both treatment groups. However, an investigational pharmacist may be able to differentiate CAP-1002 from placebo based on the opacity of the thawed concentrate observed during IP preparation. For this reason, the investigational pharmacists will have limited interaction with the blinded investigative site personnel.

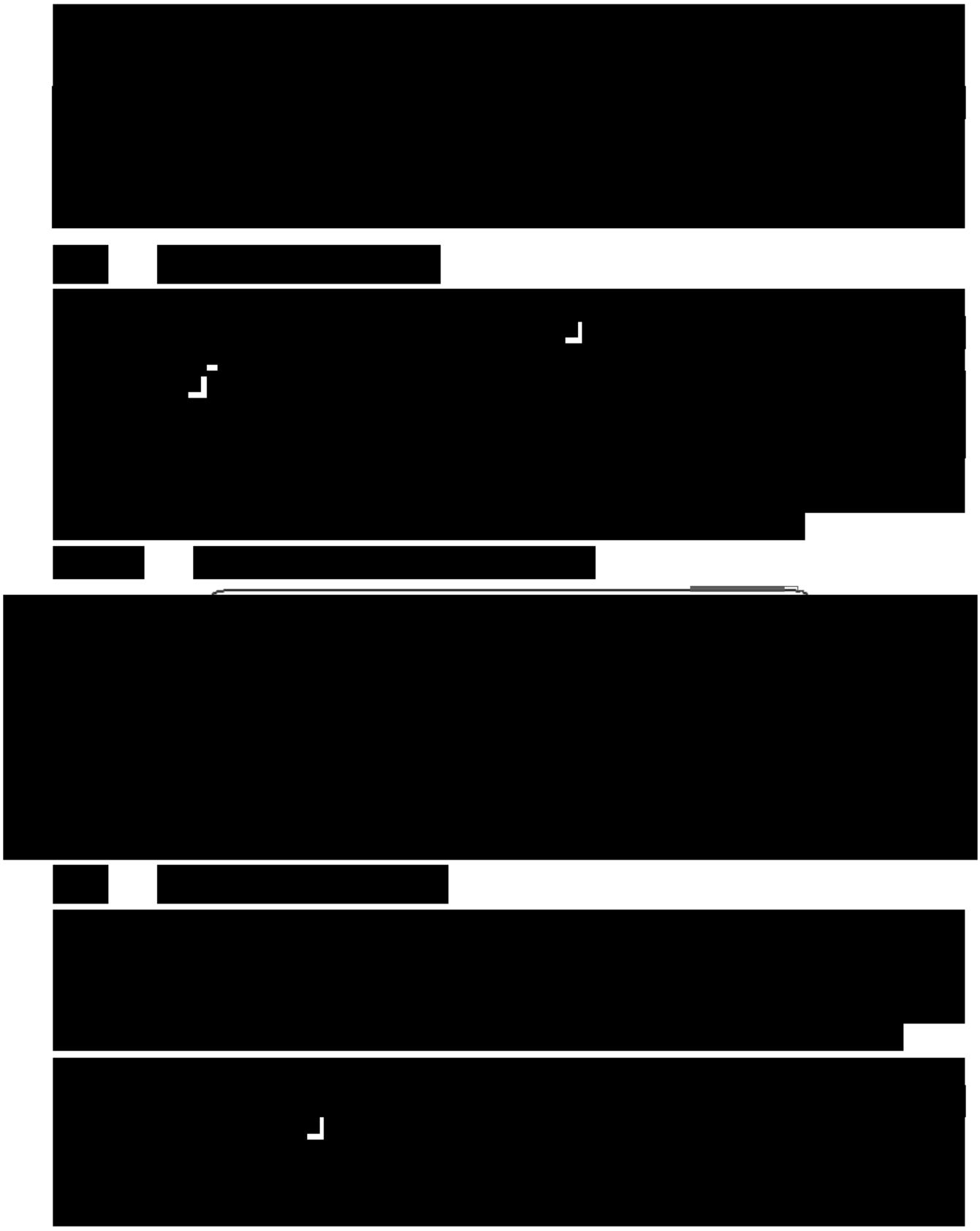
Please refer to Section 9.6 for more information related to emergency unblinding of the investigational product.

9.6. Emergency Unblinding of Investigational Product

To maintain the overall scientific integrity of the clinical trial, further unblinding or code breaks should occur only in exceptional circumstances when knowledge of the actual treatment is absolutely essential for further management and treatment of the subject. Subject safety must always be the first consideration in making such a determination. Investigators are encouraged to discuss with the Medical Monitor prior to unblinding. In case of an emergency, the Investigator has the sole responsibility for determining if unblinding of a subject's treatment assignment is warranted. If unblinding is deemed to be necessary, the Investigator should use the mechanism for emergency unblinding through the IWRS. If a subject's treatment assignment is unblinded, Capricor must be notified within 24 hours after breaking the blind. The date and reason that the blind was broken must be recorded in the source documentation and case report form, as applicable. The Investigator is encouraged to maintain the blind as much as possible. Knowledge of the actual allocation can generally be limited and not disclosed to the subject and/or other trial personnel including personnel at other investigative sites, monitors, or other personnel involved in the trial; nor should there be any written or verbal disclosure of the code in any corresponding subject documents. Unblinding should not necessarily be a reason for termination from the trial.

10. INVESTIGATIONAL PRODUCT MATERIALS AND MANAGEMENT

Detailed investigational product information can be found in the Investigator's Brochure (IB) and the Investigational Product Manual. Below and elsewhere in the protocol, reference is made to an investigational pharmacist which is typically a person licensed to dispense prescription medication usually within a special unit of the institutional pharmacy that handles all investigational products. CAP-1002 is a cell-based investigational product, therefore the chain of custody and responsibility for preparation of the investigational product may reside within another institutional department or unit, such as a center for cellular therapy or human cellular therapy laboratory or similar name, in which case "investigational pharmacy" shall mean the special center, laboratory or unit within the institution designated to handle all cell-based therapies and "investigational pharmacist or other designee" shall mean the person delegated by the Principal Investigator as having the role in receiving, storing and preparing the investigational product (CAP-1002 or placebo) who may not be a licensed pharmacist.



[redacted]

The total dose per infusion is 150 million CDCs or placebo. [redacted]

[redacted]

[redacted]

[redacted]

Upon arrival to the designated place of infusion, the subject identification is confirmed.

10.6. Discontinuation of Medications Prior to Infusion

If clinically acceptable in the judgement of the Investigator, beta blockers and angiotensin-converting enzyme inhibitors (ACEi) should not be administered on the day of infusion. Furthermore, since all subjects who are pre-treated with glucocorticoids, as determined by the site PI as part of their pre-medications, will likely start pre-treatment with glucocorticoids beginning 12 – 14 hours prior to infusion (see Section 21.2), their standing steroid medications schedule may need to be adjusted. Specifically, standing glucocorticoids should not be administered in the setting of glucocorticoid pre-treatment within 24 hours prior to the time of scheduled infusion or on the day of the IP infusion.

10.7. Administration

All investigational product (IP; CAP-1002 or placebo) delivery will be conducted in an outpatient setting at the investigative site on Day 1 and Months 3, 6, and 9. Subjects must complete all other trial assessments prior to IP infusion, excluding those related to the IP infusion (e.g., post-infusion

monitoring). [redacted] Prior to each infusion, it is recommended that site personnel meet to discuss the logistics for that specific infusion.

Capricor requires that subjects be treated prior to each IP infusion with medications to minimize the risk of potential severe allergic reaction. It is strongly encouraged that pre-medication be administered according to the guidelines in Section 21.2, however, investigative sites may use institutional protocols established for anaphylaxis prevention should they be at least physiologically comparable to the guidelines in Section 21.2. [redacted]

[redacted]

10.8. Post-Infusion Monitoring

Subjects will remain in the outpatient setting for at least 2 hours post infusion for observation, for longer should that be warranted in the judgement of the treating clinician. Investigative sites will observe their local institutional policies for post parenteral infusion monitoring. The subject's pulse oximetry (SpO_2) will be monitored for at least 30 minutes post infusion. A site Investigator will assess the subject for adverse events and approve his discharge the same day if medically cleared.

10.9. 14-Day Post-Infusion Monitoring

Subjects will complete a safety, follow-up phone call 14 days (±3 days) after each IP infusion to document subject-reported AEs and new concomitant medications.

If clinically indicated, an unscheduled in-person visit will be performed at the investigative site with targeted assessments based on presentation of signs and symptoms of the subject.

10.10. Accountability

Good Clinical Practice (GCP) and FDA regulations assign responsibility for investigational product accountability at the trial site with the Principal Investigator. In order to maintain the blind, the Investigator should elect to delegate this responsibility to the investigational pharmacist who is under the supervision of the Investigator.

The site must maintain a record of IP received, prepared, administered and returned/destroyed. Therefore, IP accountability must be maintained throughout the trial to show clear product traceability at all times. Details regarding IP accountability will include dates, quantities, batch/serial numbers, expiration dates if applicable, storage conditions and the unique code numbers assigned to the Investigational Product and subjects. IP accountability must adequately document that the subjects were provided the correct treatment assignment and reconcile all investigational product received from Capricor's drug depot.

10.11. Handling and Disposal

All IP materials will be disposed following each IP infusion. Site personnel will follow institutional policies on the proper disposal of containers and disposables coming into contact with the IP. Generally, disposal like other biohazard red-bag trash that is ultimately incinerated should be sufficient to meet local institutional policies and any other regulations or laws.

11. ASSESSMENT OF EFFICACY

Assessments to evaluate efficacy will be performed at trial visits as indicated in Table 3.

11.1. Sequence of Assessments

To the best of the site's ability, subjects should complete assessments in the following sequence and at the same time of day throughout the trial (preferably in the morning). Assessments must be completed prior to IP infusion (if applicable).

- Quality of Life
  - DMD Upper Limb Function Patient-Reported Outcome Measures (DMD UL-PROM)
  - Pediatric Outcomes Data Collection Instrument (PODCI)
  - DMD Lifetime Mobility Scale (DMD-LMS)
- Safety and other trial assessments, excluding blood and urine collections (e.g., vital signs, height, weight, 12-lead ECG, etc.)
- Pulmonary function testing
- Performance of Upper Limb 1.2 and 2.0
- Grip strength
- Key and tip-to-tip pinch strength
- Elbow flexion strength
- North Star Ambulatory Assessment (ambulatory subjects only)
- Blood and urine collections
- Cardiac MRI

11.2. Efficacy Assessment Training

Site personnel must complete trial-specific training prior to conducting efficacy assessments for the trial. Standardization and consistency are essential. All efforts must be made to have the same clinical evaluators conduct the PFT; PUL; grip, pinch, and elbow flexion strength; and NSAA assessments, and the same imaging technologist conduct the cardiac MRI for a subject throughout the duration of the trial. The clinical evaluator performing the functional assessments with the subject should not administer the QOL of questionnaires to the subject. Additional details regarding training requirements can be found in Section 17.1 and the trial's Manual of Procedures (MOP).

11.3. Performance of the Upper Limb

The Performance of the Upper Limb was designed specifically for assessing upper limb function in ambulant and non-ambulant DMD patients (Pane et al., 2014). All the tasks included in the PUL were selected to address patient prioritized activities of daily living that are typical regardless of age, including preschool children. The PUL includes an entry item to define the starting functional

testing level for a subject. The remaining PUL items are divided into three regional dimensions: high-level (shoulder), mid-level (elbow), and distal-level (wrist and hand). Trial subjects will complete testing in both the 1.2 and 2.0 modules in the same preferred arm throughout the course of the trial when PUL testing is required.

Elbow contractures will be measured in each arm of a subject prior to the start of PUL testing at each visit that requires testing.

PUL equipment will be standardized across investigative sites and provided by Capricor. Additional details regarding the PUL requirements can be found in the trial's MOP and Clinical Evaluator Binder.

11.4. Pulmonary Function Testing

Pulmonary function testing (PFT) in this trial will measure slow vital capacity (SVC), forced vital capacity (FVC), forced expiratory volume in one second (FEV_1), peak expiratory flow (PEF), maximum inspiratory pressure (MIP), maximum expiratory pressure (MEP), peak cough flow (PCF), and inspiratory flow reserve (IFR). PFTs will be performed using equipment that meets or exceeds the minimal performance recommendations of the American Thoracic Society/European Respiratory Society and that will be provided by a centralized core lab.

Site personnel must complete competency testing on a volunteer prior to conducting PFTs with a trial subject.

Subjects will complete PFTs in the seated position prior to any other functional outcome measurements (i.e., PUL 1.2 & 2.0, NSAA, grip, pinch, and elbow flexion strength, and cardiac MRI). Every effort should be made to complete a subject's PFTs at approximately the same time in the morning at each trial visit. Additional details regarding each PFT technique and requirements are included in the Site Manual provided by the core lab. This manual should be followed for all pulmonary function testing.

11.4.1. Slow Vital Capacity

SVC maneuvers will be performed prior to spirometry (forced maneuvers) because of the potential for muscular fatigue and volume history effects.

Subjects will perform at least three acceptable SVC maneuvers (with no more than five total attempts) until the highest SVC is no more than 0.150 L greater than the next highest measurement. The largest acceptable SVC value will be reported.

11.4.2. Spirometry

At least three acceptable spirometry efforts (with no more than five attempts) will be obtained for FEV_1, FVC, and PEF determinations. Acceptable forced maneuvers will have a satisfactory start of test and end of test (i.e., a plateau in the volume-time curve) and be free from artifacts due to cough, early termination, poor effort, obstructed mouthpiece, equipment malfunction, or other reasons.

Quality control standards will be implemented within a testing session. The largest FEV_1, FVC, and PEF from the 3 acceptable efforts will be reported, even if they do not come from the same

effort. The two largest accepted FVC values should be within ± 15% of each other. Additionally, the two largest accepted PEF values should be within ± 15% of each other.

Subjects will complete paired spirometry testing at screening to confirm acceptable variance in FVC (exclusion criterion 7). Testing will occur on Screening Day 1 and Screening Day 2 separated by approximately 24 hours.

11.4.3. Maximal Inspiratory & Expiratory Pressures

Maximal inspiratory pressure (MIP) and maximal expiratory mouth pressure (MEP) are simple tests in which patients generate as much inspiratory or expiratory pressure as possible against a blocked mouthpiece. Because lung volume cannot change significantly during measurement, results are to a large extent independent of the properties of the lungs. They are general tests of neuromuscular function of the combined diaphragm, abdominal, intercostal, and accessory muscles (Evans and Whitelaw, 2009).

Subjects will perform the MIP maneuvers (from residual volume (RV)) first, and the MEP maneuvers (from total lung capacity (TLC)) second.

There must be at least 3 acceptable maneuvers from a maximum of five per session.

The two largest accepted values should be within ± 15% of each other.

Subjects will sustain maximal efforts for a total of 3-4 seconds until a plateau in pressure is achieved for at least 1.5 seconds.

Site personnel must carefully judge outlier efforts, which need to be eliminated if the pressure reading showed no gradual increase to the plateau value, suggesting a sharp peak value.

11.4.4. Peak Cough Flow

Subjects will perform at least three cough maneuvers (with no more than five total attempts) from TLC for PCF determination. Site personnel must evaluate each maneuver to determine if it meets acceptability criteria. The largest, acceptable PCF value will be reported.

11.4.5. Inspiratory Flow Reserve

Subjects will perform at least three maximum inspiratory flow-volume maneuvers (with no more than five total attempts). From stable tidal breathing, subjects will expire to RV and then inspire to TLC with maximum effort. Site personnel must evaluate each maneuver to determine if it meets acceptability criteria. The largest, acceptable inspiratory flow reserve value will be reported.

11.5. Strength Testing

Strength testing will be performed using standardized equipment that will be provided by Capricor. All subjects will complete grip, pinch (tip and key), elbow flexion strength testing, regardless of ambulatory status, on the same side throughout the duration of the trial. Additional details regarding the strength testing requirements can be found in the trial's MOP and Clinical Evaluator Binder.

11.5.1. Grip Strength

Subjects will complete grip strength testing in the same hand throughout the course of the trial. Subjects will provide maximal voluntary isometric contractions for at least three seconds. A subject will perform contractions until the highest observed value from a valid effort is within 10% of the next, highest valid effort. Subjects will perform no more than five efforts. The greatest value from a valid effort, regardless of reproducibility, will be captured.

11.5.2. Pinch Strength

All subjects will complete "tip-to-tip" and "key" pinch strength testing, regardless of ambulatory status, using the same hand throughout the duration of the trial. A subject will perform pinch assessments for a given testing position (i.e., "tip-to-tip" or "key") until the highest observed value from a valid effort is within 10% of the next, highest valid effort but, not exceeding five efforts. The greatest value from a valid effort for a testing position, regardless of reproducibility, will be captured.

11.5.3. Elbow Flexion Strength

All subjects will complete elbow flexion strength testing on the same side throughout the duration of the trial. A subject will perform the isometric maneuver until the highest observed value from a valid effort is within 10% of the next, highest valid effort up to a maximum of five efforts. The greatest value from a valid effort, regardless of reproducibility, will be captured.

11.6. North Star Ambulatory Assessment

The NSAA is a functional scale designed specifically for ambulatory patients with DMD. Only ambulatory subjects – defined as those able to complete the 10MWR without assistance – will complete the NSAA. The scale is composed of 17 items that range from the 10MWR to rise from floor. Each item will be graded on a 3-point scale. The 10MWRT will be measured and recorded during each testing session. Additional details regarding the NSAA testing requirements can be found in the trial's MOP.

11.7. Cardiac MRI

Subjects will undergo cardiac MRI at the Screening, Month 6 and Month 12 visits (or, Early Termination Visit) if they are physically capable as determined by an Investigator. Subjects that complete the cardiac MRI will have sufficient attention span, ability to maintain a breath-hold, lack significant contractures that would otherwise make lying flat difficult, and fit properly within the MRI scanner.

A subject's screening cardiac MRI case will require evaluation by a site's radiologist using institutional procedures. The reported LVEF from the local interpretation will be used to assess eligibility (exclusion criterion 1).

It is anticipated that the duration of each MRI session will be 30-45 minutes. Acquisition parameters and techniques are specified in the MRI Imaging Manual. The site-based MRI technologists will be trained and certified in the common acquisition protocol prior to initiation of enrollment at each site. All trial images and applicable imaging data will be sent to and centrally read at an independent, central, imaging core by DMD cardiovascular MRI and imaging experts.

Subjects that cannot complete a cardiac MRI as part of the trial will complete an echocardiogram at screening using the site's local equipment, acquisition protocol, and evaluation procedures. The reported LVEF from the local interpretation will be used to assess eligibility (exclusion criterion 1).

11.8. Quality of Life Assessments

Site personnel must complete trial-specific training prior to administering the QOL questionnaires to a trial subject and parent/caretaker. Clinical evaluators that perform functional evaluations (e.g., PUL, PFTs, NSAA, and grip, pinch, and elbow flexion strength) are not to perform the QOL assessments. All subjects, regardless of ambulatory status, are to complete QOL assessments at trial visits per Table 3.

11.8.1. DMD Upper Limb PROM

The DMD Upper Limb Patient-Reported Outcome Measures (DMD UL-PROM) evaluates the perception of upper limb function in children and young males with DMD. The questionnaire consists of 32 items that cover four domains of activities of daily living: 1) food, 2) self-care, 3) household and environment, and 4) leisure and communication. The subject or parent/caretaker, if required, will evaluate the perceived difficulty in performing the activity on a three-level scale: cannot do, can do with difficulty, or can do easily.

11.8.2. DMD Lifetime Mobility Scale

The Duchenne Muscular Dystrophy Lifetime Mobility Scale (DMD-LMS) is comprised of three sub-domains: 1) walking and moving, 2) transfers and trunk stability, and 3) carrying, moving, and handling objects. Each subdomain is scored out of 100 points. The questionnaire, completed separately by both the trial subject and parent/caretaker, facilitates patient-reported outcomes of function that can be combined with clinically-relative milestones specific to patients with DMD.

11.8.3. Pediatric Outcomes Data Collection Instrument

The PODCI is designed to assess a subject's overall health, pain and ability to participate in normal daily activities, as well as in more vigorous activities associated with young people. Eight scales offer a broad view of the physical, mental, and attitudinal condition for the young subject, as well as their treatment expectations.

Separate subject and parent/caretaker PODCI questionnaires have been validated for pediatric (ages 2-11 years) and adolescent (ages 11-18 years) subjects. The subject and parent/caretaker must complete the questionnaires *independently* of one another. All prompts must be answered per the questionnaire's instructions. Document all reasons for refusals and non-compliance.

11.9. Biomarkers

The following biomarkers will be collected using standardized kits and may be batch tested at a designated central laboratory:

- Muscle inflammation: osteopontin
- Systemic inflammation: IL-1β, IL-2, IL-6, IL-10, TNF-α, and CXCL10

- Muscle damage: troponin I (cardiac, fast skeletal, slow skeletal), troponin T, CK-MM, CK-MB, creatine kinase (total), creatine phosphate, and creatinine
- Muscle regeneration: myostatin and follistatin

The date of each collection will be captured. Reference the Laboratory Manual for additional details regarding the collection, processing, storage, and shipping of biomarker samples.

11.10. Exploratory Biomarkers

For subjects who provide separate consent and/or assent, blood samples for clinical research into exploratory biomarkers that have not been pre-identified will be collected, processed, and shipped to central laboratory for storage and/or analysis (including any future analysis). The date and time of collection will be captured. Reference the Laboratory Manual for additional details regarding the collection, processing, storage, and shipping of biomarker samples.

12. OTHER TRIAL ASSESSMENTS

Other trial assessments will be performed as indicated in Table 3.

12.1. Demographics & Baseline Characteristics

For all subjects screened, date of birth, ethnicity, race, and dystrophin mutation type and analytical method will be captured.

12.2. Medical Status Questionnaire

Subjects will be evaluated for the following at screening and throughout the course of the trial:

- Frequency of manual/power wheelchair use
- Age permanently transitioned to a wheelchair full time
- Ventilatory support
- Frequency of falls

Changes in ambulatory status (i.e., transition from ambulatory to non-ambulatory) will be evaluated by a subject's performance in the 10MWR as part of the NSAA.

12.3. Medical History

Relevant and significant medical/surgical history will be collected at Screening and updated at Baseline.

12.4. Prior and Concomitant Medications

All medications taken within one month prior to the screening visit through trial completion will be captured. Medications will be reviewed at each trial visit and any medication changes, including new and discontinuations, will be recorded.

For each medication, generic name, indication, dose, frequency, route, and starting and stopping dates/times (if applicable) will be collected. The trade name of the medication is to be reported for combination therapies (e.g., Alka-Seltzer, Advair, etc.).

12.5. Planned Medical/Surgical Procedures

Data associated with any elective medical and/or surgical procedure (e.g., wisdom tooth extraction) that is not the result of an adverse event will also be captured.

For each procedure, the type of procedure, indication, and start date/time will be recorded. Any administered medication(s) related to the planned medical/surgical procedure(s) will be captured as a concomitant medication.

12.6. DMD Genetic Mutation Testing

DMD genetic testing will be available at screening for subjects who have not previously completed genetic testing or whose historical genetic results were not performed at a CLIA-certified laboratory as determined by an Investigator. The need for genetic testing should be assessed early

in the screening process, and if required, initial screening should be limited to genetic testing only since the turn-around time for final results may exceed the normal 30-day screening window.

Blood samples for DMD genetic testing will be collected and analyzed at a CLIA-certified central laboratory. Allow 29 to 49 days for receipt of test results.

13. ASSESSMENT OF SAFETY

13.1. Safety Parameters

Safety assessments will be performed as indicated in Table 3.

13.1.1. Vital Signs

Heart rate, systolic and diastolic blood pressure, respiratory rate, body temperature, and blood oxygen saturation (SpO_2) will be measured after the subject has rested for approximately 5 minutes and before performing ECG and spirometry testing. A single set of values will be captured.

A subject's SpO_2 will be monitored for at least 30 minutes following each IP infusion (see Section 10.8).

Vital signs will be performed using equipment provided by investigative sites that has been properly calibrated per institutional guidelines.

13.1.2. Weight and Height

Weight, ulna length, and standing height measurements will be performed.

Investigative sites will make every effort to perform a weight measurement without the subject's wheelchair or other assistive device (e.g., walker), if applicable.

Ulna length will be measured in all subjects. Standing height will be measured if a subject is capable. If standing height cannot be measured, height will be calculated using the subject's ulna length (Gauld et al., 2004). It is critical to reduce variability in ulna length and standing height measurements across investigative sites. Therefore, site personnel must complete trial-specific training prior to measuring a subject's ulna length and standing height.

Table 5: Height Calculation from Ulna Length

Height (cm) = [4.605 x Ulna Length (cm)] + [1.308 x Age (years)] + 28.003

Centimeter and year entries must include decimal places. If a subject is 18 years or older, enter "18" in the formula for age.

13.1.3. Physical Examination

The physical exam (PE) is not considered a standard of care assessment as the examiner will be assessing for research events. Therefore, the physical exam is to be conducted only by an Investigator, or designated site personnel (e.g., nurse practitioners, physician assistants, research fellows) listed on the Delegation of Authority Log.

The physical examination will be a review of the major organ systems including: general appearance, HEENT, lymphatic, respiratory, cardiovascular, chest, abdomen, gastrointestinal, and musculoskeletal.

Clinically significant findings prior to investigational product administration are to be captured as medical history.

Clinically significant findings after the start of investigational product administration are captured and reported as AEs, if they meet the definition of an AE per Section 13.2.1.

13.1.4. Electrocardiogram (ECG)

All ECG measurements will be obtained in the supine position with standardized equipment that meet institutional standards for clinical use. Site personnel must complete trial-specific training prior to ECG measurements. A 12-lead ECG measurement and rhythm strip (10 seconds) will be obtained after measurement of vital signs and before spirometry testing.

The Investigator, a designated Sub-Investigator, or other appropriately trained site personnel will be responsible for performing 12-lead ECG assessments. The Investigator must provide his/her dated signature on the original paper tracing, attesting to the authenticity of the ECG machine interpretation, or their over-read and reinterpretation.

ECG data will be electronically transmitted to an independent cardiologist, contracted by Capricor, and evaluated. The independent cardiologist, blinded to treatment assignment, will conduct an over-read of the ECG measurements required for the trial. Investigative sites will receive a report with the independent cardiologist's ECG interpretations that must be reviewed, signed, and dated by an Investigator.

13.1.5. Immunologic Assessments

Serum for DSA testing and whole blood for HLA typing will be collected at each site at baseline, and then shipped to a central laboratory for analysis (See Laboratory Manual for shipping instructions).

DSA collections at the Week 4 (±7 days) visit and 14-30 days prior to the planned date of the second, third, and fourth IP infusions will be assessed to determine MCB lot compatibility. These follow-up collections will occur either at the investigative site or remotely at a designated central laboratory patient service center.

DSA samples may also be collected in the setting of clinical suspicion of immune sensitization syndrome in the judgment of the Investigator. See Section 7.2.1 for additional details regarding immune sensitization syndrome as a safety endpoint.

13.1.6. Clinical Laboratory Assessments

All blood samples are to be collected following the standard institutional procedures for blood and urine collection and submitted to a central laboratory for analysis.

Instructions on collection, processing, storage and shipping the samples to the central laboratory are located in the Laboratory Manual.

13.1.6.1. Hematology

Hematological testing will include complete blood count (CBC) with white blood cell (WBC) differential, hemoglobin, hematocrit and platelet count

13.1.6.2. Serum Chemistry

Serum chemistry testing will include: basic metabolic panel (Glucose, Sodium, Potassium, Chloride, Bicarbonate, BUN, Creatinine, Calcium), comprehensive hepatic panel (Albumin, Alkaline Phosphatase, Total Protein, ALT, AST, GGT, Direct Bilirubin, Total Bilirubin), and Creatine Kinase

13.1.6.3. Urinalysis

Analytes that will be tested include: appearance, bilirubin, color, nitrite, occult blood, pH, protein, specific gravity, glucose, ketones, red blood cell (RBC), and WBC. If required, microscopic analysis of sediment will be performed and reported per occurrence.

13.2. Adverse and Serious Adverse Events

13.2.1. Definition of Adverse Events

13.2.1.1. Adverse Event (AE)

An AE is any untoward medical occurrence associated with the use of a drug in humans, whether or not considered drug related. It may be indicated by physical sign, symptom, clinically significant laboratory abnormalities, and/or disease temporally associated with a medical (investigational) treatment, procedure, or product, whether or not related to the medical (investigational treatment, procedure or product. This definition includes intercurrent illnesses or injuries, exacerbation of pre-existing conditions, or events occurring due to abuse or overdose.

Any condition that was pre-existing is not an adverse event unless there is a change in the nature, severity, or degree of the condition.

Clinical laboratory abnormalities are considered AEs when deemed clinically significant by the Investigator and/or lead to a change in the subject's functional status.

An AE does not include:

- Medical or surgical procedures (e.g., colonoscopy, biopsy). The medical condition that leads to the procedure is an AE.
- Social or convenience hospital admissions where an untoward medical occurrence did not occur.
- Day-to-day fluctuations of pre-existing disease or conditions present or detected at the start of the trial that do not worsen.
- The disease/disorder being studied or expected progression, signs, or symptoms of the disease/disorder being studied unless more severe than expected for the subject's condition.

All Investigators conducting investigative studies supported by Capricor must report both expected and unexpected SAEs to Capricor, or designee, and their individual Institutional Review Board (IRB) in compliance with their institutional policies. Please see Section 13.2.4 or further details on event reporting.

13.2.1.2. Serious Adverse Event (SAE)

An AE is considered "serious" if, in the view of either the Investigator or Capricor, it results in any of the following outcomes:

- Death
- Life-threatening adverse event
- Inpatient hospitalization or prolongation of existing hospitalization
- Persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions
- Congenital anomaly/birth defect

Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered serious when, based upon appropriate medical judgment, they may jeopardize the subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition.

Examples of such medical events include bronchospasm requiring intensive treatment in an emergency room or at home, blood dyscrasias, or convulsions that do not result in inpatient hospitalization, or the development of drug dependency or drug abuse.

Complications that occur during a hospitalization are AEs. When the hospitalization is prolonged due to the complication or the complication fulfills any other serious criteria, the event is reported as an SAE. Hospitalization for elective treatment of a pre-existing condition that did not worsen from baseline is not considered an SAE.

13.2.1.3. Expected Adverse Events

There is some risk of developing transient DSA with the CAP-1002 allogeneic product. All subjects will be monitored during the trial for immune sensitization as outlined in Table 3.

Other risks of the infusion procedure include those risks that are possible with the intravenous administration. These include risks related to infection, bleeding, pain, and bruising and/or hematoma at the vascular access site(s).

13.2.1.4. Unexpected Adverse Events

An AE is considered "unexpected" if it is not listed in the Investigator's Brochure or is not listed at the specificity or severity that has been observed, if the Investigator's Brochure is not required or available, or if it is not consistent with the risk information described in the general investigational plan or elsewhere in the current application.

"Unexpected," as used in this definition, also refers to adverse events or suspected adverse reactions that are mentioned in the Investigator's Brochure as occurring with a class of drugs or as anticipated from the pharmacological properties of the drug, but are not specifically mentioned as occurring with the particular drug under investigation.

Expedited reporting is required for serious unexpected AEs as discussed in Section 13.2.4.

13.2.1.5. Other Adverse Event (OAE)

OAEs will be identified by the Medical Monitor during the evaluation of safety data for the planned interim analysis and Clinical Study Report. Significant adverse events of particular clinical importance, other than SAEs and those AEs leading to discontinuation of the subject from the trial, will be classified as OAEs.

For each OAE, a narrative may be written and included in the Clinical Study Report.

13.2.2. Relationship to Investigational Product

The Investigator will assess the relationship (causality) of an AE to the investigational product and administration procedure.

Causality will be defined as follows:

- ***Probable***: adverse events that, after careful medical evaluation, are considered with a high degree of certainty to be related to the investigational product or administration procedure. The following characteristics will apply:
  - A reasonable temporal relationship exists between the event and the investigational product or administration procedure, and
  - The event is a known reaction to the investigational product or administration procedure, which cannot be explained by an alternative etiology commonly occurring in the population/individual.
- ***Possible***: adverse events that, after careful medical evaluation, do not meet the criteria for a probable relationship to the investigational product or administration procedure, but for which a connection has reasonable certainty. The following characteristics apply:
  - The event occurs after exposure to the investigational product or administration procedure, and

- The event is not a known reaction to the investigational product or administration procedure, but cannot be explained by a commonly occurring alternative etiology, or
- In the absence of a temporal relationship, the event cannot reasonably be explained by an alternative etiology.

- ***Unlikely***: adverse events that, after careful medical evaluation, do not meet the criteria for possible or probable relationship to investigational product or administration procedure and for which a connection is unlikely. The following characteristics will apply:
  - The event does not follow a reasonable temporal sequence from administration of the investigational product or administration procedure, or
  - May be explained by commonly occurring alternative etiology in the population/individual, or
  - May have been produced by environmental factors, and there is no apparent pattern of response to the investigational product or administration procedure.

An adverse event will be reported as "related" when causality is evaluated by an Investigator as probably or possibly related to the investigational product and/or the administration procedure. Related adverse events indicate a potential cause-and-effect relationship between the investigational product and/or administration procedure and the occurrence of the adverse event.

An adverse event will be reported as "unrelated" when causality is evaluated by an Investigator as unlikely related to the investigational product and/or administration procedure by the Investigator. Unrelated adverse events indicate no relationship between the occurrence of the adverse event and the investigational product and/or administration procedure.

13.2.3. Recording Adverse Events

Investigators will monitor all subjects for AEs during the trial and establish a diagnosis for an event based on signs, symptoms, and/or other clinical information. It is important to distinguish that individual signs and symptoms of the event are not adverse events and should not be reported.

For each AE, the Investigator will evaluate the causality and severity, report the action taken and event outcome and disclose whether or not it caused the subject to discontinue trial participation.

The following severity scale will be used as a guideline to differentiate the severity of adverse events:

- **Mild (Grade 1)**: Transient or mild discomfort; no limitation in activity; no medical intervention/therapy required
- **Moderate (Grade 2)**: Mild to moderate limitation in activity – some assistance may be needed; no or minimal medical intervention/therapy required
- **Severe (Grade 3)**: Marked limitation in activity, some assistance usually required; medical intervention/therapy required and often requiring hospitalization or prolongation of hospitalization

- **Life-Threatening or Disabling (Grade 4):** Extreme limitation in activity, significant assistance required; significant medical intervention/therapy required; hospitalization, prolongation of hospitalization, or hospice care
- **Fatal (Grade 5)**

An AE that is assessed as severe should not be confused with an SAE. Severity is a category utilized for rating the intensity of an event. An event is described as "serious" when it meets one of the pre-defined outcomes noted in Section 13.2.1.2. Both an AE and SAE can be assessed as severe. However, an AE of severe intensity may not meet SAE definition requirements.

13.2.4. Reporting Adverse Events

All adverse events are collected from the time of signing informed consent for trial participation until completion of 12 months or early termination, whichever occurs first. All AEs occurring after the initiation of the IV catheter placement for the initial dose of IP will be considered treatment emergent. Any ongoing adverse event that has not been resolved at the time of trial completion or early termination for a subject will be marked as ongoing on the adverse event case report form (CRF).

All AEs will be entered into the electronic data capture (EDC) system by trained site personnel at the investigative site.

Expected and unexpected SAEs must be reported to Capricor and entered into the EDC system within 24 hours of discovery of the event. For events that do not have complete information available at the time of initial report, the investigative site will submit all available information at the time of the submission. All SAE Report Forms must be signed by an Investigator and submitted with available source documentation. All source documentation must be de-identified prior to submission.

Should access to the EDC system be unavailable, SAEs and subsequent follow-up information must be reported to Capricor, or designee, via:

- Email: [redacted]
- Fax: [redacted]

All SAEs must be reported to the respective IRB in accordance with the investigative site's policies. Copies of the submission will be collected by Capricor.

All SAEs will be reported to the DSMB at least semi-annually, or more frequently at the discretion of the Medical Monitor.

Capricor will promptly upon discovery, report serious and unexpected adverse events for which there is a reasonable possibility that the investigative therapy (i.e. administration product and/or investigative product) caused the events, to the Food and Drug Administration (FDA) in accordance with 21 CFR 312.32 regulations and ICH E2A guidelines.

For trials conducted under an investigational new drug (IND) application, FDA regulations require reporting of any serious suspected adverse reaction that is unexpected according to the current Investigator's Brochure. A serious adverse reaction is defined as any adverse event for which there is a reasonable possibility that the drug/biologic caused the AE. For the purposes of IND safety reporting, "reasonable possibility" means there is evidence to suggest a causal relationship

between the drug/biologic and the adverse event. Serious, unexpected suspected adverse reactions (SUSARs) are SAEs that are unexpected and are possibly or probably related to participation in the research. Expedited reporting is required for all SUSARs. Capricor will send an IND Safety Report to the FDA within 7 calendar days of receipt for fatal/life-threatening events, and within 15 calendar days of receipt for non-fatal/non-life-threatening events that qualify for expedited reporting.

13.2.5. Pregnancy Reporting

Should a female be impregnated by a trial subject, investigative sites are required to notify Capricor within 24 hours of learning about the pregnancy. The investigative site will receive the Pregnancy Reporting Form to complete and submit to Capricor, or designee.

All pregnancies will be followed until the pregnancy outcome is known. In addition, pregnancies that are ongoing at the time of trial completion will be followed until the outcome is known. The investigative site is responsible for outcome reporting via the Pregnancy Reporting Form, including spontaneous or voluntary termination, details of birth, and the presence or absence of any birth defects, congenital abnormalities, or maternal and newborn complications.

The pregnancy is not an adverse event for the male subject unless there is a suspicion that the investigational product interfered with the effectiveness of a contraceptive medication.

13.2.6. Adverse Event Follow-up

All AEs are followed by the investigative site until an outcome is known or the subject's participation in the trial concludes at either 12 months or early termination, whichever occurs first.

The investigative site is expected to review all ongoing AEs at each visit. AEs are followed until resolution or until no further changes in the event are expected (i.e., the point at which a subject experiencing an AE is treated successfully and stabilized even though he may continue to experience lingering sequelae that may never resolve), or it is agreed that further follow-up of the event is not warranted (e.g., non-serious, IP unrelated, ongoing at final visit).

For SAEs that were incomplete or ongoing at the time of initial submission, the investigative site is required to submit follow-up SAE Report Forms when event information is available to the research site personnel and/or an outcome is known.

14. STATISTICS

14.1. General Considerations

The objectives of the trial are to evaluate the safety and efficacy of intravenous infusions of CAP-1002 administered in four doses at 3-month intervals in subjects with DMD and impairment of skeletal muscle function. All statistical tests will be two-sided with 0.05 significance levels. The detailed description of the trial statistical methods is provided in the Statistical Analysis Plan (SAP). Any deviations from the SAP will be described and justified in the final Clinical Study Report.

14.2. Sample Size

This trial will be limited to a total of 20 randomized subjects.

14.3. Analysis Population

The following analysis populations will be defined for the trial:

Safety Population: Subjects who received IP. Safety endpoints for subjects will be summarized and analyzed according to the treatment actually received.

Intent-to-Treat (ITT) Population: Subjects who were randomized. Subjects will be summarized and analyzed in the treatment group to which they were randomized.

Modified Intent-to-Treat (mITT) Population: For each efficacy parameter, the mITT population will include subjects in the ITT population who have at least a baseline observation (i.e., mITT populations are parameter-specific). Subjects will be summarized and analyzed in the treatment group to which they were randomized.

Per Protocol Population: Subjects who received IP with no protocol deviations/violations that could significantly impact the completeness, accuracy and/or reliability of the trial data. The list of subjects in the per protocol population will be compiled prior to database lock.

14.4. Safety Analysis

Safety parameters will be listed, summarized and, if applicable, analyzed for the safety population. There are no formal tests of hypotheses associated with the evaluation of safety endpoints.

14.4.1. Safety Endpoints

The incidence of the following events through the 12-month timepoint will be **primary safety endpoints**:

- Acute respiratory decompensation within 2 hours following IP administration
- Hypersensitivity reaction
- All-cause mortality
- Serious adverse events
- Treatment-emergent adverse events related to IP or administration procedure

- Immune sensitization syndrome

The incidence and severity of all AEs will be evaluated as the **secondary safety endpoint**.

Treatment groups will be summarized and compared by the incidence of each event type and by the subject event rate. Safety during the study will be monitored by the independent, unblinded DSMB. See Section 13.2 for more detail on AE data collection and processing.

14.4.2. Adverse Events

Directly observed and spontaneously reported AEs will be recorded from time of signing informed consent (SAEs only) through the end of the trial. AEs will be coded using MedDRA® (Medical Dictionary for Regulatory Activities), in which each reported event is mapped to a Preferred Term (PT) and a System Organ Class (SOC). A treatment-emergent AE (TEAE) will be defined as an AE that was not present prior to the initiation of line placement procedure for the IP infusion or was present but worsened in intensity or frequency. All reported AEs will be listed. Both TEAEs and non-TEAEs will be summarized, overall and by severity and relationship to the IP and IP administration procedure. For each SOC and PT within SOCs, the numbers and percentages of subjects reporting an event as well as the number of events that were reported will be calculated. Deaths, AEs that resulted in trial discontinuation, SAEs, and AEs within 24 hours of IP administration will be listed and summarized separately.

14.4.3. Medications

Prescription, over-the-counter, and alternative medication use will be coded to drug class, preferred drug name, and generic/trade drug name using the World Health Organization drug dictionary (WHO-DD). Medications that were stopped before the start of the IP administration procedure will be considered “pre-treatment.” All other medications will be considered “concomitant.” Medications that were started or ongoing at the time the IP administration procedure was started will be considered “baseline” (a subset of “concomitant”). All reported medications will be listed. Frequencies and percentages of subjects reporting or receiving each medication will be summarized by WHO-DD drug class and preferred name within drug class. Pre-treatment and baseline medications will be summarized separately. Separate listings and summaries will also be done for cardiac medications and for glucocorticoids.

14.4.4. Clinical Laboratory Evaluations

Laboratory evaluations will be listed and summarized by visit within each panel (e.g., chemistry, hematology, etc.). Summary tables will show means of observed values and changes from baseline for observations on a continuous scale and distributions of categorical observations. Shift tables may be produced that show frequencies and percentages of subjects that shift from one out-of-range category at baseline to another out-of-range category at subsequent visits.

14.4.5. Donor-Specific Antibodies

Donor, donor profile, allele, and MFI will by listed by HLA and visit. Subject HLA profiles will be provided in a separate listing.

DSA data will be analyzed in the context of immune sensitization syndrome should there be an occurrence.

14.4.6. Physical Examination

Observed status (e.g., normal, abnormal) and changes from baseline in body system-specific physical examination findings will be summarized by visit within each body system.

14.4.7. 12-Lead ECG, Vital Signs, and Weight

Observed values and changes from baseline will be summarized by visit.

14.5. Efficacy Analysis

The primary efficacy endpoint will be evaluated in the ITT population, with supportive analyses in the mITT and PP populations. Secondary and exploratory efficacy endpoints will be evaluated in the PP population.

14.5.1. Primary Efficacy Endpoint

The primary efficacy endpoint is change from baseline to Month 12 in the mid-level (elbow) dimension of the PUL 1.2. The hypothesis set to be tested is:

$$H_o: \mu_c - \mu_p = 0$$

$$H_a: \mu_c - \mu_p \neq 0$$

where μ_c and μ_p are population mean absolute changes from baseline in CAP-1002- and placebo-treated patients, respectively.

14.5.2. Secondary Efficacy Endpoints

Supportive secondary efficacy endpoints will be change from baseline in:

- Mid-level (elbow) PUL1.2 at Months 3, 6, and 9;
- Regional systolic LV wall thickening at Months 6 and 12

14.5.3. Exploratory Efficacy Endpoints

Exploratory efficacy endpoints will be change from baseline in:

- High-level (shoulder) dimension of the PUL 1.2 at Months 3, 6, 9, and 12;
- High-level (shoulder) dimensions of the PUL 2.0 at Months 3, 6, 9, and 12;
- Mid-level (elbow) dimensions of the PUL 2.0 at Months 3, 6, 9, and 12;
- Distal-level (wrist and hand) dimensions of the PUL 1.2 at Months 3, 6, 9, and 12;
- Distal-level (wrist and hand) dimensions of the PUL 2.0 at Months 3, 6, 9, and 12;
- Grip strength, absolute and percent predicted, at Months 3, 6, 9, and 12;
- Tip-to-tip pinch strength, absolute and percent predicted at Months 3, 6, 9, and 12;
- Key pinch strength, absolute and percent predicted at Months 3, 6, 9, and 12;
- Elbow flexion strength, absolute and percent predicted, at Months 3, 6, 9, and 12;
- DMD UL-PROM at Months 3, 6, 9, and 12;

- PODCI scales (subject and parent) at Months 3, 6, 9, and 12;
- DMD-LMS at Months 3, 6, 9, and 12;
- NSAA at Months 3, 6, 9, and 12;
- 10MWRT at Months 3, 6, 9, and 12;
- Incidence of loss of ambulation (10MWRT > 30 seconds) at Months 3, 6, 9, and 12;
- Pulmonary function tests (absolute and percent predicted [if available]) at Months 3, 6, 9, and 12;
- LV structure and function as assessed by cardiac MRI at Months 6 and 12;
- Biomarkers, which may include osteopontin, IL-1ß, IL-2, IL-6, IL-10, TNF-α, CXCL10, troponin I (cardiac, fast skeletal, slow skeletal), troponin T, CK-MM, CK-MB, creatine kinase (total), creatine phosphate, creatinine, myostatin, and follistatin at Months 3, 6, 9, and 12;
- Resource utilization, including hospitalizations for orthopedic injury or surgery and for pulmonary infections, over the course of the trial.

14.6. Statistical Methods

Comparisons between treatment groups on efficacy endpoints will be done using repeated measures linear models. Other analyses may also be done using appropriate parametric or non-parametric methods, depending on distributions of the data and whether or not model assumptions are met. An algorithm detailing the decision-making process for performing the primary efficacy analysis, in light of features of the data that cannot be known until the data are observed (e.g., outliers), will be detailed in the SAP.

14.6.1. Multiplicity

Trial-wise type 1 error is controlled at the 0.05 level by declaring a primary efficacy endpoint. All other efficacy parameters are either supportive secondary or exploratory endpoints and there will be no adjustment for multiple analyses.

14.6.2. Missing Data

Subject-level listings will present data as reported. Missing or partially missing dates that are required for date-dependent definitions (eg, treatment-emergent AEs, concomitant medications) will be assumed to be the most conservative date possible. For example, an AE with a completely missing start date will be considered treatment-emergent; similarly, an AE that started the same month and year as IP administration but with missing start day will be considered treatment-emergent.

Multiple imputation methods will be used for missing observations for the primary efficacy endpoint, if required to prevent subjects from being excluded entirely from analysis.

14.6.3. Interim Analysis for Futility

The pre-specified interim analysis was performed. Following the interim analysis, further enrollment in the trial was terminated. No further interim analyses are planned.

15. TRIAL OVERSIGHT

15.1. Steering Committee

The Steering Committee will provide the overall scientific direction for the trial. The responsibilities of the Steering Committee are to: (a) maintain contact with trial Investigators to ensure high quality data collection; (b) approve and implement major protocol changes; (c) collaborate in data analysis, interpretations, and publications; (d) establish criteria for authorship on all manuscripts, publications and presentations that arise from the trial.

15.2. Clinical Events Committee (CEC)

The purpose of CEC adjudication is to provide consistent and unbiased adjudication of clinical outcomes and specified events through the independent review of source documentation. The charge of the CEC is to review source documents and to adjudicate the classifications of all potential primary safety endpoint events. Sites will be provided instructions in the MOP on how to collect and submit event information required for CEC review. The CEC will remain blinded to subject treatment assignments. The individuals that serve on the committee will be appointed by Capricor, are independent from all other trial activities, and are not affiliated with any investigative site. The committee will consist of, at a minimum, a neurologist and pulmonologist with experience in treating patients with DMD. Additional experts in immunology will be consultants to the committee as necessary. The frequency of CEC meetings is detailed in the CEC Charter.

15.3. Data Safety Monitoring Board

To meet the trial's ethical responsibility to its subjects, an independent Data Safety Monitoring Board will monitor results during the trial. The board consists of physicians and biostatistician(s) appointed by Capricor, who have no formal involvement or conflict of interest with the Investigators, investigative sites, subjects, or Capricor. The DSMB will act in a senior advisory capacity to Capricor regarding data and safety matters throughout the duration of the trial. The board will meet on a periodic basis according to the DSMB charter to monitor the available information regarding safety, efficacy, and quality of trial conduct. The DSMB will communicate their recommendations directly to Capricor. The investigative sites will have no contact with the members of DSMB and no voting member of the committee may participate in the trial as an Investigator.

16. SOURCE DATA AND TRIAL DOCUMENTS

16.1. Electronic Data Capture

All trial data will be entered into the EDC system. Site personnel requiring access will have their own Login/Password. Access to trial information will be based on individual roles and responsibilities. The application employs fine-grained role-based access control for data entry, viewing and reporting options. All trial data will be transmitted over an encrypted SSL (Secure Sockets Layer) connection that requires user authentication.

This application is designed to be in full compliance with the International Conference on Harmonization and Good Clinical Practices (ICH-GCP), the FDA's CFR 21 Part 11 Electronic Record and Electronic Signatures, the FDA's "Guidance: Computerized Systems Used in Clinical Studies," and Health Insurance Portability and Accountability Act (HIPAA).

EDC supports efficient data collection and management and facilitates rapid data closure. A strong advantage of web-based design is that Capricor, or designee, has immediate access to the data from all investigative sites so that queries can be generated and distributed to the sites in real-time and the frequency of missing data can be reduced.

16.2. Trial Monitoring

In accordance with 21 CFR 312.56, ICH- GCP, and local regulations, trial monitors will periodically complete on-site monitoring of data with a focus on safety, trial endpoints, data completion, data outliers and data integrity. Trial monitors will schedule an on-site visit with a site coordinator for an appropriate duration based on the scope of data anticipated to be collected. Prior to the visit, a confirmation letter will be sent to the investigative site, which will include a listing of which CRFs and source documents will be reviewed.

Site coordinators are to have all source documents up to date and easily accessible to a monitor.

During an on-site monitoring visit, trial monitors are to:

- Track the overall monitoring process including data collected and entered, visit schedules, and subject screening and enrollment.
- Verify and ensure compliance with the protocol according to GCP and HIPAA requirements.
- Ensure that appropriate data corrections are made, dated, explained, and initialed by the Investigator or representative.
- Assess the impact of any personnel changes on the investigative site's ability to conduct the trial.
- Verify a minimum of the following data points for all subjects: date of birth, signed informed consent, eligibility criteria, medical history, date of enrollment, serious AEs, and mortalities.
- Perform review of informed consent process and review documentation of informed consent for completeness and correctness.

- Perform on-site validation checks of recoded data by reviewing source documents to determine whether the data reported in the EDC system are complete and accurate. Source documents include medical charts, screening records and/or logs, research procedure records and/or files, and other trial related notes.
- Monitor subject safety by verifying that any AE, therapy modification, or concomitant medications are reported in accordance with the protocol.
- Determine whether all AEs, protocol deviations, and protocol violations are appropriately reported within the required time periods according to applicable regulatory requirements as outlined in the protocol and by regulatory agencies.
- Verify that any missed visits, tests, and examinations that were not performed, as well as trial withdrawals and/or dropouts are explained and clearly reported.
- Inform the site PI about any deviations from or violations of the trial protocol, GCP and/or regulatory requirements in order for appropriate actions to be taken to prevent recurrence of the deviation and/or violation.
- Infor the Investigator of any major data entry error, delays in data entry, omissions, or eligibility requirement errors.
- Verify that regulatory documentation is accurate, complete, current, and properly maintained.
- Very that PI oversight of trial conduct is documented via signature or initials and date on documentation regarding eligibility, AEs, and abnormal laboratory values.

The monitor may also inspect the investigative site's facilities to verify that proper space for study documents, equipment and investigational product is available.

A debriefing meeting with the PI, site coordinator(s), and the Monitor to review any notable findings will be scheduled toward the end of the on-site visit. The monitor will submit a written monitoring visit report to Capricor and send a follow-up letter with findings to the PI. The report and letter will include a summary of documentation reviewed by the monitor, any significant findings, AEs, protocol deviations and violations, missing regulatory documents and actions taken, to be taken or recommended to ensure compliance. The report and letter will include a list of action items. Investigative sites are expected to complete the list of actions items within 30 days of receipt.

16.2.1. Source Document Requirements

It is highly recommended that the investigative site uses the CRFs and schedule of assessments (Table 3) to develop a plan for identifying and standardizing where source documentation for data verification will be collected across all trial participants at their site. As part of trial start-up and prior to first enrollment, investigative sites are encouraged to conduct a gap analysis to identify any data points that are not routinely documented in the medical record.

The medical record is the gold standard for source documentation. However, Capricor understands that there may be data points required for this trial that are not collected as routine practice at the investigative site in the medical record for this patient population. Investigative sites may use the provided source document worksheets or create source documents for the purposes of collecting

source data that are not included in the medical record. It is important to remember that "source" documentation is where the information is first recorded.

The investigative site must ensure that all subject source documentation is complete, orderly, and stored in a secure location. For electronic records, the investigative site should abide by the institutional policies for the storage of private health information (PHI). For any paper records containing any PHI, the investigative sites must ensure that the files are double-locked, that is, in a locked filing cabinet within a locked office or suite.

All source documentation is to be de-identified of all unique patient and hospital identifiers by the investigative site prior to review or submission to Capricor or their designee.

16.3. Audits and Inspections

Authorized representatives of Capricor, a regulatory authority, an Independent Ethics Committee or an Institutional Review Board may visit the site to perform audits or inspections, including source data verification. The purpose of a Capricor audit or inspection is to systematically and independently examine all trial-related activities and documents to determine whether these activities were conducted, and data were recorded, analyzed, and accurately reported according to the protocol, Good Clinical Practice guidelines of the International Conference on Harmonization, and any applicable regulatory requirements. The Investigator should contact Capricor immediately if contacted by a regulatory agency about an inspection.

16.4. Retention of Records

The investigative sites must maintain all documentation relating to the trial for a period of two years after the last marketing application approval, or if not approved, two years following the discontinuance of the test article for investigation. If it becomes necessary for Capricor or the Regulatory Authority to review any documentation relating to the trial, the Investigator must permit access to such records.

17. QUALITY CONTROL AND QUALITY ASSURANCE

Capricor will implement and maintain quality control and quality assurance procedures to ensure compliance with the protocol, Good Clinical Practices, and all applicable regulatory requirements, and may conduct a quality assurance audit(s). Please see Section 16.3 for more details regarding the audit process.

17.1. Qualifications and Trainings

A representative of Capricor, or designee, will visit the investigative site to determine adequacy of the facilities and discuss the feasibility of conducting the trial.

Clinical Investigators will be physicians with expertise in the clinical care of patients with DMD in a multi-disciplinary clinical setting that includes neuromuscular medicine, pulmonary, cardiology, and physical therapy.

Each investigative site MRI lab involved in image acquisition for this trial will be certified by the MRI core lab in accordance with the MRI Imaging Manual.

Each investigative site pulmonary function testing lab involved in conducting pulmonary function testing for this trial will be certified by the Pulmonary Function Core Lab as detailed in the Manual of Procedures.

Investigative site personnel delegated to perform the ECG assessment will be certified to perform and transmit the assessment by a centralized vendor.

All Investigators and coordinators will be trained by Capricor, or designee, in the specifics of the protocol, investigational product and administration procedure at the site initiation visit in advance of the first subject enrollment. The Investigators and coordinators will also undergo a separate training to gain familiarity with the electronic data capture system.

17.2. Good Clinical Practices (GCP)

All Investigators, coordinators and other site personnel involved in care of trial subjects, and/or research data collection must provide certification that they have successfully completed their institutionally required GCP or other Human Subject Protection courses. Please refer to Section 6.2 of the Manual of Procedures for specific details regarding certification requirements.

17.3. HIPAA or Other Privacy Training

All Investigators and coordinators must provide documentation that they have successfully completed the institutional requirements to ensure subject rights, privacy and security under HIPAA.

17.4. Site Initiation

IRB approval and the clinical trial agreement between the investigative site and Capricor must be signed and executed prior to the site initiation. Additionally, the completed Form FDA 1572, applicable CVs and other regulatory documents must be on file with Capricor prior to site initiation. A representative from Capricor, or designee, will conduct a site initiation prior to enrollment of the first subject. Investigators, study coordinator(s), investigational pharmacist(s),

infusion suite personnel, clinical evaluator(s), MRI technologist(s), and laboratory personnel will be required to attend the initiation. All other site personnel who may be involved in the trial will be encouraged to attend.

17.5. Protocol Deviations

Efforts to maximize adherence to the protocol will be made through careful and comprehensive training, review of trial data collected via the EDC, and routine communication with all site Investigators.

All protocol deviations and violations are to be documented and captured in the EDC. The investigative site is responsible for reporting deviations and violations to the IRB per the IRB's reporting guidelines. Capricor will ensure reporting to the proper local and federal regulatory authorities in accordance with all applicable federal and local regulations.

Capricor will determine the course of action based on the severity of the deviation or violation. These may include but are not limited to, withdrawal of the subject, additional training at the site, additional site monitoring, and/or other appropriate courses of action. In addition, the Medical Monitor and biostatistician will review the circumstances of each deviation and violation (in a blinded fashion) to determine whether data can reasonably be included in any trial analyses.

18. ETHICS

18.1. Ethics Review

Investigative sites are required to follow their institutional guidelines for obtaining initial approval by the IRB and for submitting continuing reviews to the IRB. Subject enrollment at an investigative site will not commence until initial IRB approval documentation has been received and reviewed by Capricor. The composition and conduct of this committee must conform to the United States CFR and ICH E6.

The informed consent must be reapproved in accordance with the investigative site's IRB policies or at least annually.

Capricor will provide the investigative sites with DSMB approval letters, serious adverse drug reactions and any other applicable correspondences during the trial. Investigative sites are to follow their institutional policies for reporting these correspondences and documents to their IRB.

All IRB approvals and all materials approved/acknowledged by the IRB for this trial, including the subject consent/assent form, recruitment materials, or safety event notifications, must be maintained by the Investigator and made available for inspection.

18.2. Ethical Conduct of the Trial

The trial will be performed in accordance with ethical principles that have their origin in the Declaration of Helsinki and are consistent with ICH/Good Clinical Practice, and applicable regulatory requirements. Please reference Section 17 further information.

In accordance with FDA regulatory requirements, 21 CFR 54.4, the Investigators at each site will be required to complete a financial disclosure form provided by Capricor prior to participation in the trial. Each Investigator shall provide Capricor sufficient accurate financial information to allow Capricor to submit complete and accurate certification or disclosure statements (Forms 3454 and/or 3455) as required by the FDA regulations. Investigators shall promptly update this information if any relevant changes occur in the course of the trial or for 1 year following completion of the trial

18.3. Written Informed Consent and Assent

The Investigator is responsible for ensuring that the informed consent process is conducted and documented appropriately by trained site personnel. A signed informed consent, which has been approved by Capricor and the individual site IRB, is required for trial participation. The consent form must incorporate a clinical research authorization for use and disclosure of private health information and a release of medical information that authorizes release of medical records to the trial Investigators, monitors, and Capricor. The Investigator, or designated and qualified individual, will provide a thorough explanation of objectives, subject responsibilities, risks and benefits of the trial, and will fully address all concerns raised by the subject and/or legal guardian. After all issues have been adequately resolved, and the Investigator confirms that the subject has been fully consented, the subject or his legal guardian will be asked to sign the informed consent. The consent process must be documented in the medical chart and a signed copy of the consent and/or assent must be given to the subject and/or legal guardian.

18.3.1. Obtaining Informed Consent and Assent

The Investigators at each center will ensure that the subject and legal guardian (applicable only if the subject is < 18 years of age) are given full and adequate oral and written information about the nature, purpose, possible risk and benefit of the trial. The subject and legal guardian must also be notified that they are free to discontinue from the trial at any time. The subject and legal guardian should be given the opportunity to ask questions and allowed time to consider the information provided.

The subject must sign and date the informed consent form prior to performing any trial procedures. If the subject is < 18 years of age, the subject must sign and date the assent form and a legal guardian must sign and date the informed consent form prior to performing any trial procedures. Specific requirements and guidelines for providing assent will be determined by the investigative site's IRB.

18.4. Subject Confidentiality

Confidentiality of all subject records will be maintained according to HIPAA guidelines. Investigators, investigative site IRBs, Capricor, CEC, and the FDA may review source documentation for enrolled subjects as necessary, but all unique patient and hospital identifiers will be removed prior to review. If the results of this trial are published, the data will be presented in aggregate, with all subject identifiers removed.

19. PUBLICATION POLICY

Recognizing the importance of communicating clinical trial results to the public and the medical and scientific communities in an accurate and complete manner, the first publication of the trial, to include results from all of the investigative centers in a multi-center publication, will be authored by the lead or national Principal Investigator, and/or other designees assigned by the Steering Committee, for publication in a peer-reviewed scientific journal. All participating Investigators, key site personnel, committees and committee members will be listed in an appendix as part of the main manuscript.

An individual Investigator has the right to publish his/her data after the multi-center publication, unless no such multi-center publication is so published before the first anniversary of the finalization of the multi-center database, in which case the Investigator may publish or submit for publication a manuscript without further delay according to the terms and conditions in the Clinical Trial Agreement.

Additional manuscripts targeting exploratory endpoints or other endpoints or data not included in the first multi-center publication are anticipated and encouraged. In such cases, the Investigator(s) should submit ideas for these additional manuscripts to the Steering Committee that will serve as the clearing house to approve topics, ensure that activity between the Investigator(s) in analyzing the data is coordinated, prioritize data analyses and help determine authorship.

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21. APPENDICES

21.1. Appendix I: Exon 44-Skip Amenable Dystrophin Mutations

Deletions to the following exons of the dystrophin gene are amenable to exon-44 skipping (den Dunnen J.T., 2014; White and den Dunnen, 2006; Aartsma-Rus et al., 2006; Aartsma-Rus, 2014):

10-43	24-43	34-43	45
11-43	25-43	35-43	45-54
13-43	26-43	36-43	45-56
14-43	27-43	37-43	45-62
15-43	28-43	38-43	
16-43	29-43	39-43	
17-43	30-43	40-43	
19-43	31-43	41-43	
21-43	32-43	42-43	
23-43	33-43	43	

21.2. Appendix II: Pre-Infusion Guidance for Minimizing Risk of Potential Severe Hypersensitivity Reaction

As discussed in Section 10.6, Capricor requires treatment of all subjects prior to each IP infusion to minimize the risk of a potential severe allergic reaction. It is strongly encouraged that pre-medication be administered according to the guidelines in Table 6 including the administration of high dose steroids, H1 and H2 blockers; however, investigative sites may use institutional protocols established for anaphylaxis prevention should they be at least physiologically comparable to the guidelines below.

Final decisions regarding the medication(s), dose(s) administered, and route(s) of administration are to be determined by the Investigator taking into consideration the subject's medical history. For any pre-treatment medication administered, the FDA approved label should be reviewed for information on potential side effects and/or drug interactions and followed for detailed instructions on weight-based dosing.

Of note, for subjects routinely treated with beta blocker and ACEi, the doses of both should be held on the day of infusion, if clinically acceptable in the judgment of the site Investigator. Furthermore, it is recommended that the standing steroid doses should be held if the planned schedule is within 24 hours of the time of scheduled infusion of IP. This is because glucocorticoids will likely be administered as part of the pre-medications beginning 12 – 14 hours prior to infusion of IP.

21.3. Summary of Changes – Amendment 1.0

The following table presents a complete list of content changes in the protocol amendment. To avoid redundancy, the "sections affected" column does not list the protocol synopsis as an affected section. For changes shown verbatim, **deleted text** is show in strikethrough font, and *new text* is shown in *red italicized font*.

Description of Change	Rationale / Justification	Sections Affected
Study Assessments		
[redacted]		
Statistical Analysis		
[redacted]		
Eligibility Criteria		
[redacted]		

Description of Change	Rationale / Justification	Sections Affected
[redacted]		
[redacted]		
Concomitant Medications		
[redacted]		
[redacted]		
[redacted]		
Clarifications / Corrections		
[redacted]		
[redacted]		
[redacted]		
[redacted]		
[redacted]		
[redacted]		

Description of Change	Rationale / Justification	Sections Affected
[redacted]		
[redacted]		
[redacted]		
[redacted]		
[redacted]		
[redacted]		
[redacted]		
[redacted]		
[redacted]		
[redacted]		

21.4. Summary of Changes – Amendment 2.0

The following table presents a complete list of content changes in the protocol amendment. To avoid redundancy, the "sections affected" column does not list the protocol synopsis as an affected section. For changes shown verbatim, **deleted text** is show in strikethrough font, and *new text* is shown in *red italicized font*.

Description of Change	Rationale / Justification	Sections Affected
Eligibility Criteria		
[redacted]		
[redacted]		
Study Assessments		
[redacted]		
[redacted]		

Description of Change	Rationale / Justification	Sections Affected
DMD genetic testing duration may		
Investigational Product		

Description of Change	Rationale / Justification	Sections Affected
[redacted]	[redacted]	
[redacted]	[redacted]	[redacted]
Safety and Pharmacovigilance		
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]

Description of Change	Rationale / Justification	Sections Affected
[redacted]		
Statistics		
[redacted]		
Clarifications / Corrections		
[redacted]		
[redacted]		

21.5. Summary of Changes – Amendment 3.0

The following table presents a complete list of content changes in the protocol amendment. The Sections Affected column lists out the sections affected in the main body of the protocol; however, most of these changes also impact the synopsis. Changes from the previous version of the protocol are indicated as **deleted text** in strikethrough font and *new text* in *red italicized font*.

Description of Change	Rationale / Justification	Section(s) Affected
Introduction		
[redacted]	[redacted]	[redacted]
Exploratory Endpoints		
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
Study Assessments		
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]

Description of Change	Rationale / Justification	Section(s) Affected
[redacted]		

Description of Change	Rationale / Justification	Section(s) Affected
[redacted]		
[redacted]		[redacted]
[redacted]		[redacted]
[redacted]		[redacted]
[redacted]		[redacted]
[redacted]		[redacted]
[redacted]		[redacted]
[redacted]		[redacted]
[redacted]		[redacted]

Description of Change	Rationale / Justification	Section(s) Affected
[redacted]		
[redacted]		
[redacted]		
Eligibility Criteria		
[redacted]		
[redacted]		
[redacted]		

Description of Change	Rationale / Justification	Section(s) Affected
[redacted]		
[redacted]		
[redacted]		
[redacted]		
Safety and Pharmacovigilance		
[redacted]		
Investigational Product		
[redacted]		
[redacted]		

Description of Change	Rationale / Justification	Section(s) Affected
[redacted]		
[redacted]		
[redacted]	[redacted]	[redacted]
Statistical Analyses		
[redacted]		
[redacted]		

21.6. Summary of Changes – Amendment 4.0

The following table presents a complete list of content changes in the protocol amendment. The Sections Affected column lists out the sections affected in the main body of the protocol; however, most of these changes also impact the synopsis. Changes from the previous version of the protocol are indicated as **deleted text** in strikethrough font and *new text* in *red italicized font*.

Description of Change	Rationale / Justification	Section(s) Affected
Introduction & Background		
[redacted]	[redacted]	
[redacted]	[redacted]	
[redacted]	[redacted]	

Description of Change	Rationale / Justification	Section(s) Affected
[redacted]		
Investigational Plan		
[redacted]		
[redacted]		
[redacted]		
[redacted]		

Description of Change	Rationale / Justification	Section(s) Affected
[redacted]		
[redacted]		[redacted]
[redacted]		[redacted]
[redacted]		
[redacted]		
[redacted]		
[redacted]		
[redacted]		
[redacted]		
Eligibility Criteria		
[redacted]	[redacted]	[redacted]

Description of Change	Rationale / Justification	Section(s) Affected
[redacted]	[redacted]	
[redacted]	[redacted]	[redacted]
[redacted]		
[redacted]	[redacted]	[redacted]
Investigational Product		
[redacted]	[redacted]	

Description of Change	Rationale / Justification	Section(s) Affected
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]

Description of Change	Rationale / Justification	Section(s) Affected
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	
[redacted]	[redacted]	
[redacted]	[redacted]	
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
Study Assessments		
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]

Description of Change	Rationale / Justification	Section(s) Affected
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	
[redacted]	[redacted]	[redacted]
Safety and Pharmacovigilance		
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
Clarifications / Corrections		
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]

Description of Change	Rationale / Justification	Section(s) Affected
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]

Description of Change	Rationale / Justification	Section(s) Affected
[redacted]	[redacted]	[redacted]

21.7. Summary of Changes – Amendment 5.0

The following table presents a complete list of content changes in the protocol amendment. The Sections Affected column lists out the sections affected in the main body of the protocol; however, most of these changes also impact the synopsis. Changes from the previous version of the protocol are indicated as **deleted text** in strikethrough font and *new text* in *red italicized font*.

Description of Change	Rationale / Justification	Section(s) Affected
Investigational Plan		
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]

Description of Change	Rationale / Justification	Section(s) Affected
[redacted]		
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
Safety and Pharmacovigilance		
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]

Description of Change	Rationale / Justification	Section(s) Affected
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
A [redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
Statistics		
[redacted]	[redacted]	[redacted]

Description of Change	Rationale / Justification	Section(s) Affected
[redacted]		
[redacted]	[redacted]	[redacted]

Description of Change	Rationale / Justification	Section(s) Affected
[redacted]		
Clarifications / Corrections		
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]