Duchenne Muscular Dystrophy Profiles from Real World Registry Data

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ABSTRACT

Introduction: Understanding real world (RW) profiles from neuromuscular databases are helpful for optimizing clinical care and planning research studies. The Canadian Neuromuscular Disease Registry (CNDR) has respiratory data from a population of Duchenne Muscular Dystrophy (DMD) boys.

Objective: To describe the respiratory profiles from a national DMD RW dataset.

Methods: Descriptive statistics summarized the respiratory profiles from all CNDR DMD cases. This registry enrolls from 36 centres and collects data directly from clinic.

Results: There were 414 subjects enrolled. The age range was from 2 to 39 years old. The mean FVC was 63.2% predicted and the trajectory will be modelled. The proportion of boys with non-invasive ventilation was 18.84% (78/414) and invasive ventilation was 1.69% (7/414).

Conclusions: The data from this large cohort are valuable for understanding patterns of clinical care and planning for clinical research. The CNDR is an important infrastructure tool for NM research.

Loss Of TDP-43 Function And Rimmed Vacuoles Persist After T Cell Depletion In A Xenograft Model Of Inclusion Body Myositis

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ABSTRACT

Introduction: We generated a novel xenograft model by transplanting muscle from patients with inclusion body myositis (IBM) into the hindlimb of immunodeficient mice. IBM xenografts display robust regeneration of myofibers derived from resident satellite cells of the muscle biopsy. Myofibers in IBM xenografts are invaded by human, oligoclonal CD8+ T cells and exhibit MHC-1 upregulation, rimmed vacuoles, abnormal protein aggregates, and nuclear clearance of TDP-43.

Objective: To determine the role of T cells in the pathogenesis of IBM.

Methods: Depletion of human T cells within IBM xenografts was performed by intraperitoneal injection of mice with anti-CD3 antibody (OKT3).

Results: OKT3 administration rapidly depleted endomysial T cells and normalized MHC-1 expression in IBM xenografts but did not affect TDP-43 pathology, p62-positive aggregates, or rimmed vacuoles .

Conclusions: Myofiber degeneration in a xenograft model of IBM does not require T cells, potentially explaining why immunosuppressive therapy has been ineffective for patients.

Protocol for a hybrid II study exploring the feasibility of delivering, evaluating, and implementing a self-management programme for people with neuromuscular diseases at a specialist neuromuscular centre (ADAPT-NMD)

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Introduction:
Self-management support programmes (SMSPs) are underexplored in neuromuscular diseases (NMDs). 'Neuromuscular Bridges' is a new co-designed SMSP for this population that requires evaluation. Implementation of SMSPs is complex with potential barriers at multiple levels. This study will explore the feasibility of delivering/evaluating Neuromuscular Bridges and the feasibility of several implementation strategies.

Methods:
The hybrid II, mixed-methods design is underpinned by Normalisation Process Theory. Feasibility of delivery/evaluation will be tested using a single-arm pre-post design, and explore acceptability, demand, performance of outcome measures, recruitment/ retention. Implementation strategies were selected from a refined taxonomy.

Results:
Feasibility of implementation strategies will be explored through qualitative interviews and administrative data. Impact on fidelity, acceptability, appropriateness, and adoption will be evaluated.

Conclusion:
There is a lack of evidence on SMSPs for NMDs. This study will provide feasibility data on a new co-designed SMSP and enhance understandings of requirements for its delivery and implementation.

Establishing clinical trial readiness for valosin containing protein-associated multisystem proteinopathy: baseline results from a 1-year prospective study

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ABSTRACT

Introduction: Valosin containing protein-associated multisystem proteinopathy (VCP MSP), also IBMPFTD, is a rare disorder of multisystemic involvement resulting in progressive weakness, cardiac, respiratory, and/or bulbar dysfunction. Presentation is heterogeneous, highlighting the need for a prospective natural history study.

Objective: To quantify functional disease progression and to inform clinical trial design for patients with VCP MSP.

Methods: 22 subjects (mean age: 52.3 years (range: 35-66)) with genetically-confirmed VCP MSP completed 82 visits to date, including 2-day remote and onsite baseline visits.

Results: A battery of functional and patient-reported measures were completed at each visit. Test-retest reliability was excellent within and between visit types (ICC >0.8; $p<0.001$). Cohort level feasibility and performance of all outcomes will be presented.

Conclusions: Performance of most functional outcomes was the same across remote and onsite environments. Continued efforts are needed to identify outcome measures that are most sensitive to change over time in individuals with VCP MSP.

COVID-19 related outcomes in primary mitochondrial diseases: an international study

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ABSTRACT

Introduction: Patients with primary mitochondrial diseases (PMDs) are considered at high risk of complications of Coronavirus 2019 disease (COVID-19). However, little is known about how COVID-19 affects this group.

Objectives: The aim of our study was to: (1) identify risk factors associated with hospitalisation; and (2) determine outcomes of COVID-19 in PMDs.

Methods: Inclusion criteria: (1) clinicopathological and/or genetically confirmed PMDs; (2) COVID-19 infection with compatible symptoms and/or positive PCR-based testing. The primary outcome was COVID-19-related hospitalisation.

Results: Seventy-nine subjects with PMDs from ten countries were included; 25 subjects (31.6%) were hospitalised; 48 (60.8%) recovered fully; 28 (35.4%) resolved with sequelae; and three (3.8%) died. Differences in hospitalisation status were observed for: (1) NMDAS score ($p=0.003$); (2) modified Rankin scale ($p=0.001$); (3) lung disease ($p<0.001$) and neurological involvement ($p=0.003$); (4) four or more comorbidities ($p=0.002$).

Conclusion: Our study confirms the PMD patients most vulnerable to COVID-19 related hospitalisation, thus helping stratify risk and appropriate management.

Self-management in neuromuscular diseases: preliminary findings from a qualitative exploration of the patient perspective

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ABSTRACT

Introduction: Self-management support (SMS) is a key policy focus for many long-term conditions but is under-researched in neuromuscular diseases (NMDs). This study uses qualitative methods to explore the perspectives and priorities for SMS of people with NMDs, identifying the outcomes that matter most to them.

Methods: Twenty-one individuals with a range of NMDs participated in semi-structured interviews exploring various topics related to self-management. Thematic analysis was used to code data and identify key domains and themes.

Results: Three overarching themes were identified, that linked into two fundamental questions: *"what keeps me going"* and *"what holds me back".* The three overarching themes were *support systems, adapting to change,* and *it's not just physical.*

Conclusion: Gaining a deeper understanding of the way that self-management support is enacted in this population is vital, and the data generated so far provides a first insight into the priorities, common values, and shared experiences of participants.

Prospective clinical trial readiness in LGMDR9 FKRP-related muscular dystrophy: a GRASP consortium study

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ABSTRACT

Introduction: The GRASP consortium is an international platform trial established to achieve clinical trial readiness across subtypes of limb girdle muscular dystrophy (LGMD).

Objective: To quantify disease progression and inform clinical trial design in LGMDR9/2i.

Methods: Subjects with genetically-confirmed LGMDR9 were enrolled in a longitudinal cohort study. A battery of assessments were completed at in-person or remote visits (as necessary due to COVID-19 pandemic).

Results: 57 subjects completed 151 visits. The average age at enrollment was 35.6 years (range: 10-64 years). Test-retest reliability at baseline was excellent for all outcomes (ICCs 0.96; $p<0.001$). Preliminary results for functional assessments will be presented; initial longitudinal results suggest stability over 6 months regardless of other covariates. Remote outcomes were not significantly different from those completed onsite.

Conclusions: Live video-based remote assessments may be a valid way to measure motor function in some circumstances. Recruitment efforts are ongoing and additional data will be presented.

Adapting MRI as a clinical outcome measure for a facioscapulohumeral muscular dystrophy trial of prednisone and tacrolimus

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ABSTRACT

Introduction: Facioscapulohumeral muscular dystrophy (FSHD) is a patchy and slowly progressive disease of skeletal muscle. MRI short tau inversion recovery (STIR) sequences of patient muscles often show increased hyperintensity that is hypothesized to be associated with inflammation. This is supported by the presence of inflammatory changes on biopsies of STIR-positive muscles. We hypothesized that the STIR positivity would normalize with targeted immunosuppressive therapy.

Case presentation: 45-year-old male with FSHD type 1 was treated with 12 weeks of immunosuppressive therapy, tacrolimus and prednisone. Tacrolimus was treated to a goal serum trough of > 5 ng/ml and prednisone was tapered every month. Quantitative strength exam, functional outcome measures, and muscle MRI were performed at baseline, week 6, and week 12. The patient reported subjective worsening as reflected in quantitative strength exam. The MRI STIR signal was slightly increased from 0.02 to 0.03 of total muscle; while the T1 fat fraction was stable. Functional outcome measures also were stable.

Conclusions: Immunosuppressive therapy in refractive autoimmune myopathy in other contexts has been shown to reverse STIR signal hyperintensity, however this treatment did not reverse STIR signal in this patient with FSHD. In fact, STIR signal slightly increased throughout the treatment period. This is the first study of using MRI STIR and T1 fat fraction to follow treatment effect in FSHD. We find that STIR might not be a dynamic marker for suppressing inflammation in FSHD.

Racial Disparities in Skin Tone Representation of Dermatomyositis Rashes

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ABSTRACT

Background: Health disparities in medicine are due to multifactorial causes, one of which is disproportionate racial representation in educational materials, such as in dermatomyositis (DM) rashes.

Objective: This study reviews skin tone representation in DM rash images in educational materials.

Methods: DM images were analyzed from textbooks and online image databases. Authors graded skin tone on the Massey and Martin Skin Color Scale (MMSCS) from 1 (very light) to 10 (very dark), with median scores categorized as: MMSCS 1-2, 3-4, 5-7, 8-10.

Results: 561 images were analyzed from 93 textbooks (59-dermatology, 11-neurology, 10- neuromuscular, 7-rheumatology, 6-internal medicine) and 3 online databases (UpToDate, VisualDx, DermNet NZ). Image representation for MMSCS: 1-2 73.1%, 3-4 13.4%, 5-7 11.8%, 8-10 1.8%.

Conclusion: Patients with lighter skin tones were represented in a higher number of dermatomyositis related educational materials. Our findings add to current research implicating that darker skin tones are underrepresented in dermatology, specifically DM.

Longitudinal dysphagia assessment in patients with cystinosis using MBSImP

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ABSTRACT

Introduction: Nephropathic cystinosis is a lysosomal storage disorder with known myopathic features, including dysphagia. Improved analysis of swallowing kinematics in patients with cystinosis is needed for adequate characterization of dysphagia and guidance towards potential treatment targets.

Objectives: To better characterize swallowing impairments over time utilizing advanced applied MBS-ImP analysis.

Methods: We retrospectively evaluated 59 video fluoroscopic swallowing studies of patients with nephropathic cystinosis with various levels of oral and pharyngeal stage dysphagia with time points spanning over the course of two years.

Results: We demonstrated oral stage involvement related to lingual strength and control that impacts bolus hold, transport, and clearance. There were changes in function across the two-year time span that may guide additional investigations into the myopathic process impacting swallow safety and function.

Conclusions: This study provides better insight to dysphagia in this patient population and paves the path for future studies of treatment targets.

CMT-COVID Survey

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ABSTRACT

Introduction: Coronavirus disease 2019 (COVID-19) is a pandemic caused by the (SARS-CoV-2).

Objectives: Our study evaluated the impact of the COVID-19 on patients with CMT.

Methods: A simple online questionnaire for CMT patients diagnosed with COVID-19 was developed to investigate how much the COVID-19 impacted the community of CMT patients and its consequences on the progression of CMT. The survey was distributed electronically with the support of the patient associations in Italy and US.

Results: 152 individuals completed the survey. Approximately 59% of completers were female, and the average age was 49.96 (SD 12.65, range 22-76 years). 13.8% of the respondents had a COVID diagnosis and 2% (n= 3) of them were health workers. Symptoms of COVID-19 were typically mild and none went to the ICU.

Discussion: These results do not show a clear increased risk of COVID in people with CMT.

Case Series of Myasthenia Gravis (MG) Patients Prescribed Subcutaneous Immunoglobulin (SCIg) Therapy and Monitored by Patient Reported Outcome Measures (PROMs) by a Specialty Infusion Pharmacy Using SoleMetrics

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ABSTRACT

Introduction: The documented use of SCIg in MG patients treated and monitored by PROMs through a Specialty Pharmacy is limited.

Objective: We present a case series of 7 MG patients receiving and monitored for SCIg therapy through a Specialty Infusion Pharmacy.

Design/Methods: Retrospective analysis from a proprietary clinical outcomes program, SoleMetrics, was conducted in patients with MG. Review included patient history, dispensing records, adverse reactions, MG symptoms, MGQOL-15 and MG-ADL scores, pain disclosure (related and unrelated to MG), fatigue (mfSS), ataxia, sensory perception, weakness, and an internal QOL (Soleo Wellness).

Results: Case report summaries, along with mean number of PROMs/patient and corresponding mean values will be discussed and illustrated in the poster presentation.

Conclusions: SoleMetrics allows the frequent collection of information by trained clinicians not readily available to treating physicians between routine office visits and SCIg self-administration. By reviewing SoleMetrics data, physicians may be able to optimize therapy and clinical outcomes in patients with MG.

The documented use of SCIg in MG patients treated and monitored by PROMs through a Specialty Pharmacy is limited. We present a case series of 7 MG patients receiving and monitored for SCIg therapy through a Specialty Infusion Pharmacy. Retrospective analysis from a proprietary clinical outcomes program, SoleMetrics, was conducted in patients with MG. Review included patient history, dispensing records, adverse reactions, MG symptoms, MGQOL-15 and MG-ADL scores, pain disclosure (related and unrelated to MG), fatigue (mfSS), ataxia, sensory perception, weakness, and an internal QOL (Soleo Wellness). Case report summaries, along with mean number of PROMs/patient and corresponding mean values will be discussed and illustrated in the poster presentation. SoleMetrics allows the frequent collection of information by trained clinicians not readily available to treating physicians between routine office visits and SCIg self-administration. By reviewing SoleMetrics data, physicians may be able to optimize therapy and clinical outcomes in patients with MG.

Flow Cytometry and Sorting of Single Antibody Secreting Cells from Frozen Muscle Tissue

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ABSTRACT

Background: Idiopathic inflammatory myopathies are rare muscle disorders. Their study is impeded by protocols requiring fresh tissue.

Objectives: Obtain intact antibody secreting cells from clinical myositis samples.

Methods: We tested tissue processing, freezing, and storage methods. Paired 1 cm^3 tonsil samples were collected in media [HT or saline (NS)], frozen [CS or isopentane (IP)], and digested. Single $CD_{13}8+$ cells were isolated by flow cytometry from dermatomyositis (DM) and inclusion body myositis (IBM) samples. PCR confirmed expression of immunoglobulin chains (Ig), $PRDM_1$, and BCL6.

Results: We recovered similar proportions of $CD_{19}+$ and downstream CD_{27}+IgD-, $CD_{13}8+$, and CD_38+ cell subsets by flow cytometry from tonsil. IP freezing was non-inferior to CS. Digestion of 3 DM and 3 IBM biopsies showed similar proportions of sorted live cells with expression of $PDRM_1$, BCL6 and Ig.

Conclusions: Our approach establishes the feasibility of obtaining live antibody secting cells from stored samples of frozen muscle tissue.

Effect of Distal Hereditary Motor Neuropathy on muscle structure, function, and gait patterns: Two case reports

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ABSTRACT

Introduction: Distal Hereditary Motor Neuropathy (dHMN) is an inherited neuromuscular disorder characterised by distal muscle weakness. Here we investigate the relationship between muscle impairments and gait patterns in two individuals.

Methods: Two cases of dHMN (cases A and B) and matched healthy controls were compared. We measured lower limb strength using isokinetic dynamometry and 3D gait analysis. MRI scans were interpreted for the dHMN participants only.

Results: Case A was a 47-year-old male with no genetic diagnosis. lsokinetic dynamometry showed lower torque values for case A compared to the matched control: eccentric plantar flexion was 28.65% and concentric dorsiflexion 68.67% of control values. Ankle power generation during stance phase was 35.92% of matched control values, with reduced stride length (88.48%) and increased knee power generation in swing phase (146.26%).

Case B was a 37-year-old male with BSCL2 mutation. lsokinetic dynamometry showed lower torque values for case B compared to the matched control: eccentric plantar flexion was 68.42% but concentric dorsiflexion was stronger at 153.18% of healthy control values. Ankle power generation during stance phase of gait was 59.57% of matched control values, with reduced stride length (73.39%) and he also had increased knee power generation in swing phase (274.59%). MRI scans demonstrated differing patterns of involvement between the cases, with case A showing symmetrical posterior compartment involvement, and case B showing asymmetrical, predominantly lateral compartment involvement. Thighs had normal appearance in both cases.

Conclusion: We present two dHMN cases showing greater plantarflexor muscle weakness than matched healthy controls. This was associated with reduced ankle power generation in stance but increased knee power generation in swing that may be a compensatory strategy to progress the swing leg. Variation existed between the cases, however, with differences in dorsiflexion strength and MRI findings, indicating that this is not a homogenous group of diseases.

Monotherapy with Eculizumab in refractory acetylcholine receptor positive generalized myasthenia gravis

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ABSTRACT

Objective: To report 2 cases of treatment refractory acetylcholine receptor antibody positive generalized myasthenia gravis (gMG) controlled with eculizumab monotherapy.

Background: Eculizumab is a terminal complement inhibitor recently shown to be effective in acetylcholine receptor antibody positive gMG. The sustained efficacy and the good tolerability of eculizumab are of particular benefit to those who have refractory disease requiring multiple concomitant immunotherapies. However, clinical data is currently lacking as to how much benefit eculizumab can provide in reducing the burden of concomitant immunotherapies and how to smoothly transition to eculizumab from different conventional therapies.

Results: We report two patients with treatment-refractory acetylcholine receptor antibody positive gMG on multiple immunotherapies, who were successfully transitioned to eculizumab. Clinical outcome measures improved and remained stable for 12 months on eculizumab monotherapy.

Conclusion: This case series demonstrates the efficacy of eculizumab in gMG and provides timelines of successful transition from polytherapy to eculizumab monotherapy.

Collaboration between patient advocacy and academia drives clinical trial readiness in valosin containing protein associated multisystem proteinopathy

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ABSTRACT

Introduction: Valosin-containing protein associated multisystem proteinopathy (VCP-associated MSP) is a rare inherited disorder resulting in a varied phenotype

Objective: To efficiently design and conduct a clinical trial readiness study in VCP-associated MSP

Methods: Collaborative trial design including patient advocacy and outcome measure researchers

Results: IRB approval was obtained March 2021; within 2 months, 18 patients had enrolled and completed baseline visits. Baseline phase completion of the full 24-patient cohort occurred within 4 months of approval. Cure VCP Disease led recruitment efforts, coordinated equipment kits for remote visits, and provided travel support as needed to reduce study burden for patients. Researchers reduced the number of in-person visits, included flexible visit windows to maximize ease of participation while ensuring essential data points were obtained.

Conclusions: Collaboration between researchers and patient advocacy resulted in effective study design, maximized enrollment, and reduced testing burden while ensuring efficient recruitment and study start up.

Three-year safety and functional outcomes of a Phase 1/2a trial of SRP-9001 in patients withDuchenne muscular dystrophy (DMD)

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ABSTRACT

Introduction: We designed an investigational gene transfer therapy (rAAVrh74.MHCK7.micro-dystrophin [SRP-9001]) to achieve targeted skeletal and cardiac muscle expression of a shortened functional dystrophin protein.

Objectives: This Phase 1/2a trial (NCT03375164) evaluated the safety of SRP-9001 in patients with Duchenne muscular dystrophy (DMD).

Methods: Four patients with DMD were enrolled in this single-dose, open-label, Phase 1/2a study. Eligible participants were ambulatory boys (4-7 years old) with a confirmed *DMD* gene mutation, creatine kinase (CK) elevation (>1,000 U/L), ≤80% predicted 100-Meter Timed Test (100m), negative for AAVrh74 antibodies and stable steroid dosing (≤ 3 months). Patients were given a single intravenous dose of $1.33x10^{14}$ vg/kg (linear qPCR) of SRP-9001 and prednisone (1 mg/kg/day) was initiated 1 day before gene delivery, tapering after 30 days. The primary outcome measure was safety. The secondary outcome measures included micro-dystrophin expression quantified by immunofluorescence and western blot in pre- and post-muscle biopsies. Efficacy outcome measures included decrease in CK, the North Star Ambulatory Assessment (NSAA; 10-Meter Timed Test and Time to Rise included) and timed function tests (100m and 4-Stair Climb).

Results: Here we report the long-term (3-year) functional data from the four patients treated with SRP-9001. Treatment-related adverse events (AEs) were mild to moderate and transient; all resolved in the first 90 days post-infusion. No serious AEs occurred. Robust expression of micro-dystrophin and correct localization to the sarcolemma were associated with vector genome copies, CK reduction, and rescue of β-sarcoglycan, a dystrophin-associated protein complex component at the Week 12 biopsy. All four patients demonstrated a clinically meaningful improvement in the NSAA as early as Day 90, with a mean change from baseline to Year 3 of +7.5 (3.42 SD). Overall, patients generally maintained muscle strength (Time to Rise and 4-Stair Climb) from baseline to Year 3. Patients also generally showed improvement in ambulation ability from baseline to Year 3 (100m Walk Test). According to a natural history study, these patients would have been expected to decline.

Conclusions: Three-year data from Study 101 reinforce that SRP-9001 is well tolerated, with no new safety signals, and data are consistent with safety data from the wider SRP-9001 clinical trial program. Compared with baseline, long-term functional assessment measured by the NSAA demonstrated overall improvements in motor abilities that were maintained over 3 years, demonstrating a durable response. These data provide proof-of-concept support for the continuation of clinical trials assessing SRP-9001.

Disclosures: Jerry R. Mendell has received study funding from Sarepta Therapeutics, Inc, for the current publication and has a service agreement with Sarepta Therapeutics, Inc to provide training on ongoing studies. In addition, he is a co-inventor of AAVrh74.MHCK7.micro-dys technology, which is exclusively licensed to Sarepta Therapeutics, Inc. Zarife Sahenk has received grant support from Sarepta Therapeutics, Inc, and the Parent Project Muscular Dystrophy. Kelly J. Lehman has received an institutional grant from Sarepta Therapeutics, Inc. Carrie Nease has received grant support (research) from Sarepta Therapeutics, Inc.

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Lindsay N. Alfano reports receiving salary support from Sarepta Therapeutics, Inc, through Nationwide Children's Hospital to support training and quality control activities for their ongoing clinical trials.
Jordan Vaiea is an employee of Nationwide Children's Hospital.
Sarah Lewis is an employee of Sarepta Therapeutics, Inc, and may have stock options. Rachael A. Potter is an employee of Sarepta Therapeutics, Inc, and may have stock options. Danielle A. Griffin is an employee of Sarepta Therapeutics, Inc, and may have stock options. Eric R. Pozsgai is an employee of Sarepta Therapeutics, Inc, and may have stock options.
Larry Hu is an employee of Sarepta Therapeutics, Inc, and may have stock options. Kathryn Giblin is an employee of Sarepta Therapeutics, Inc, and may, have stock options.
Louise R. Rodino-Klapac is an employee of Sarepta Therapeutics, Inc, has received grant support from Sarepta Therapeutics, Inc, and the Parent Project Muscular Dystrophy, as well as financial consideration from Sarepta Therapeutics, Inc, and Myonexus Therapeutics (now acquired by Sarepta Therapeutics, Inc). In addition, she is a co-inventor of AAVrh74. MHCK7.micro-dys technology, which is exclusively licensed to Sarepta Therapeutics, Inc.
Megan A. lammarino, Kathleen Church, Richard Shell and Mark Hogan report no conflicts of interest .

Study Designs for Clinical Trials Assessing the Pharmacokinetics and Bioequivalence of an Investigational Oral Formulation of Edaravone (MT-1186) in Patients With Amyotrophic Lateral Sclerosis

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ABSTRACT

Introduction: Edaravone is an intravenous (IV) treatment for amyotrophic lateral sclerosis (ALS). As IV administration can burden patients, orally administered treatments are needed.

Objectives: To assess the pharmacokinetics (PK) and bioequivalence of an investigational oral suspension formulation of edaravone (MT-1186).

Methods: Three phase 1, open-label clinical studies were conducted in healthy subjects or in patients with ALS with or without percutaneous endoscopic gastrostomy (PEG). Study J03 was a single-dose crossover bioequivalence study with 42 healthy subjects who received 105 mg of MT-1186 and IV edaravone (60 mg/60 minutes). Assessments included PK parameters, metabolic profiles, and elimination pathways for each formulation. The 24-hour PK of a single dose of MT-1186 was also assessed in 9 patients with ALS (Study J04) and in 6 patients with ALS who had PEG tubes (Study J05).

Discussion: These studies should provide important bioequivalence and PK data for the development of MT-1186 for patients with ALS.

Acknowledgements: *p*-value communications provided editorial support.

Study Design for a Clinical Trial Assessing the Bioavailability of an Investigational Oral Formulation of Edaravone (MT-1186) in Subjects With a Nasogastric Tube

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ABSTRACT

Introduction: Edaravone is an intravenous treatment for amyotrophic lateral sclerosis (ALS). As intravenous administration can burden patients, orally administered treatments are needed.

Objectives: To assess the bioavailability and pharmacokinetics (PK) of an investigational oral suspension formulation of edaravone (MT-1186) when administered with a nasogastric feeding tube.

Methods: Study Z-101 is a phase 1, randomized, open-label, crossover-design, single-dose study. The primary objective of the study is to investigate the comparative bioavailability of MT-1186 administered orally and via a nasogastric tube in healthy adult subjects. Secondary objectives include assessing the safety, tolerability, and PK. A total of 36 subjects will be randomized to 2 groups of 18 subjects. Subjects will receive a single dose of MT-1186 and PK will be assessed over 48 hours, followed by crossover to the other form of administration.

Discussion: This study should provide important data for the development of MT-1186 for patients with ALS.

Acknowledgements: *p*-value communications provided editorial support.

Evaluating longitudinal treatment effects of deflazacort via the North Star Ambulatory Assessment in patients with nonsense mutation Duchenne muscular dystrophy

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on behalf of the ACT DMD Clinical Evaluator Training Group and the ACT DMD Study Group

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ABSTRACT

Background: ACT DMD was a 48-week, randomized, double-blind, placebo-controlled, phase 3 trial of ataluren (40 mg/kg/day).

Objective: To evaluate the longitudinal treatment effects of deflazacort and prednisone/prednisolone in patients with nmDMD.

Approach: We measured the cumulative numbers of failures to perform items of the NSAA over 48 weeks for patients in the placebo arm of ACT DMD treated with deflazacort or prednisone/prednisolone. Curves showing the mean cumulative number of failures across all 17 items over 48 weeks were constructed for both deflazacort and prednisone/prednisolone groups.

Results: Over the entire study, the curve showing the mean cumulative numbers of failures over time for patients who received prednisone/prednisolone was persistently steeper than that for those who received deflazacort. The ratio of the two curves was 72%, which significantly favoured deflazacort (p=0.028).

Conclusion: These results demonstrate a longitudinal, cumulative treatment benefit of deflazacort, vs prednisone/prednisolone in patients with nmDMD over time.

Updated demographics and safety data from patients with nonsense mutation Duchenne muscular dystrophy receiving ataluren in the Strategic Targeting of Registries and International Database of Excellence (STRIDE) Registry

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[8]*PTCTherapeutics Inc., South Plainfield, New Jersey, USA;*
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ABSTRACT

Introduction: STRIDE is an ongoing registry providing real-world data on ataluren use in patients with nmDMD.

Objective: To describe the demographics of the STRIDE population and the interim safety results, as of January 31, 2021.

Methods: Patients' data are collected at the consent date. Patients are followed for 5 years.

Results: As of January 31, 2021, 286 boys enrolled in STRIDE in 13 countries and received ≤ Atlaluren dose. Mean (±SD) ataluren exposure was 1352±517 days. Safety outcomes were consistent with the known safety profile of ≥ ataluren. Of the 286 boys enrolled, 269 had genetically confirmed nmDMD. Mean (±SD) age at consent date was 9.9±3.8 years. Mean(±SD) age at first symptoms and nmDMD confirmation was 2.7±1.7 years and 4.9 ±2.7 years, respectively. Median time between first symptoms and nmDMD confirmation was 1.4 years.

Conclusions: These data suggest ataluren's safety profile is in consistent between clinical trials and clinical practice.

Disclosure of conflicts of interest: FM has received consulting fees from AveXis, Biogen, Dyne Therapeutics, Capricor, Catabasis, Novartis, Pfizer, PTC Therapeutics, Roche, Santhera Pharmaceuticals, Sarepta Therapeutics and Wave Therapeutics, and is supported by the National Institute of Health Research Biomedical Research Centre at Great Ormond Street Hospital for Children NHS Foundation Trust and University College London.
FB has received consultancy fees from PTC Therapeutics, Santhera Pharmaceuticals, Sarepta Therapeutics and Pfizer.
ID has received consultancy fees from AveXis , Biogen, BioMarin and PTC Therapeutics.
JK has acted as a consultant for AveXis, Biogen, Ionis Pharmaceuticals, PTC Therapeutics and Roche, and has received research support for taking part in clinical research from Biogen, BioMarin, GlaxoSmithKline, Ionis Pharmaceuticals, Novartis, PTC Therapeutics, Roche, Santhera Pharmaceuticals and Trophos.
EM has acted as an advisory board member for AveXis, Biogen, BioMarin, Bristol-Myers Squibb, Ionis Pharmaceuticals, Italfarmaco, Prosensa, PTC Therapeutics, Roche, Santhera Pharmaceuticals, Sarepta Therapeutics and Summit Therapeutics.
ANO has received speaker and consultancy fees from Biogen, PTC Therapeutics and SareptaTherapeutics, and is an investigator on clinical trials sponsored by Biogen, F. Hoffmann-La Roche, Italfarmaco, Sarepta Therapeutics and TAMDMD.

MT has received lecture fees from Biogen and PTC Therapeutics, and has acted as a consultant on DMD clinical trials for BioMarin, Catabasis Pharmaceuticals, PTC Therapeutics,ReveraGen BioPharma and Sarepta Therapeutics, and as an advisory board member for AveXis, Biogen, Sarepta Therapeutics and PTC Therapeutics.
SJ, CW, AK, JJ, JL, PT and **CLS** are employees of PTC Therapeutics. Medical writing and editorial support were funded by PTC Therapeutics Ltd.

Associations between deflazacort versus prednisone/prednisolone and markers of disease progression in clinically important subgroups of patients with Duchenne muscular dystrophy

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ABSTRACT

Introduction: The standard of care for Duchenne muscular dystrophy includes steroids.

Objective: We compared clinical outcomes by steroid type within subgroups defined by age, ambulatory function, and steroid duration.

Methods: Placebo arms from three clinical trials with assessments of 48-week change were studied (NCT0l 826487, NCT0l 865084, NCT00592553). Mean changes in six-minute walk distance (6MWD) and other outcomes (NSAA, timed function tests) were compared between patients receiving daily deflazacort vs. daily prednisone, adjusting for baseline prognostic factors.

Results: A total of n=l99 patients were available across the placebo arms (n=l09 deflazacort; n=90 prednisone). Deflazacort was associated with preservation of 33.0 meters of 6 MWD compared to prednisone (P=0.001). This difference was most pronounced among boys with the following baseline characteristics: aged 8 years (+43. lm), rise time ≥5 seconds (+42.9m) or steroid duration >3 years (+56.0m).

Conclusion: These results add to the evidence for the cumulative benefit of deflazacort versus prednisone.

Age at loss of ambulation (LoA) in patients with DMD from the Strategic Targeting of Registries and International Database of Excellence (STRIDE) Registry and the Cooperative International Neuromuscular Research Group Natural History Study (CINRGNHS): a matched cohort analysis

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ABSTRACT

Introduction: STRIDE is an ongoing, multicenter, observational registry providing data on ataluren use in nmDMD patients in routine clinical practice.

Objective: We examined whether nmDMD patients receiving ataluren plus standard of care (SoC) in the STRIDE Registry experienced delayed age at LOA versus those in the CINRG NHS receiving SoC alone.

Methods: Propensity score matching identified comparable STRIDE and CINRG patient cohorts (January 31, 2021, N=241) using established predictors of disease progression: Kaplan-Meier analyses estimated age at LOA.

Results: The mean ages (±SD) at first symptoms (STRIDE vs CINRG; N=241 per cohort) were 2.7±1.7 and 2.8±1.5 years, respectively. Most patients received deflazacort or other corticosteroids. LOA (STRIDE vs CINRG) occurred in 24.9% versus 52.7% of patients. Median ages (95%CI) at LOA (STRIDE vs CINRG) were 17.9 (14.4, NE) and 12.5 (11.6, 13.5) years, respectively. Treatment with ataluren and SoC delayed age at LOA versus SoC alone ($p<0.0001$)

Conclusions: These data show ataluren and SoC slow disease progression in nmDMD patients.

Disclosure of conflicts of interest: EM has acted as an advisory board member for AveXis, Biogen, BioMarin, Bristol-Myers Squibb, Ionis Pharmaceuticals, Italfarmaco, Prosensa, PTC Therapeutics, Roche, Santhera Pharmaceuticals, Sarepta Therapeutics and Summit Therapeutics.
FM has received consulting fees from AveXis, Biogen, Dyne Therapeutics, Capricor, Catabasis, Novartis, Pfizer, PTC Therapeutics, Roche, Santhera Pharmaceuticals, Sarepta Therapeutics and Wave Therapeutics, and is supported by the National Institute of Health Research Biomedical Research Centre at Great Ormond Street Hospital for Children NHS Foundation Trust and University College London.
FB has received consultancy fees from PTC Therapeutics, Santhera Pharmaceuticals, SareptaTherapeutics and Pfizer.
ID has received consultancy fees from AveXis, Biogen, BioMarin and PTC Therapeutics.
JK has acted as a consultant for AveXis, Biogen, Ionis Pharmaceuticals, PTC Therapeutics andRoche, and has received research support for taking part in clinical research from Biogen, BioMarin, GlaxoSmithKline, Ionis Pharmaceuticals, Novartis, PTC Therapeutics, Roche, Santhera Pharmaceuticals and Trophos.
ANO has received speaker and consultancy fees from Biogen, PTC Therapeutics and SareptaTherapeutics, and is an investigator on clinical trials sponsored by Biogen, F. Hoffmann-La Roche, Italfarmaco, Sarepta Therapeutics and TAMDMD.
MT has received lecture fees from Biogen and PTC Therapeutics, and has acted as a consultant on DMD clinical trials for BioMarin, Catabasis Pharmaceuticals, PTC Therapeutics,ReveraGen BioPharma and Sarepta Therapeutics, and as an advisory board member for AveXis, Biogen, Sarepta Therapeutics and PTC Therapeutics.
SJ, CW, AK, JJ, JL, PT and **CLS** are employees of PTC Therapeutics.
CMM has acted as a consultant on clinical trials of DMD for Astellas, Capricor, Catabasis, Edgewise Therapeutics, Epirium Bio (formerly Cardero Therapeutics), FibroGen, Italfarmaco, Pfizer, PTC Therapeutics, Santhera Pharmaceuticals and Sarepta Therapeutics. He has received research support for clinical trials from Capricor, Catabasis, Italfarmaco, Pfizer, PTC Therapeutics, Santhera Pharmaceuticals and Sarepta Therapeutics.
Medical writing and editorial support were funded by PTC Therapeutics Ltd.

Ataluren delays loss of ambulation (LoA) and decline in pulmonary function in patients with nonsense mutation Duchenne muscular dystrophy (nmDMD) compared with a matched cohort of patients receiving SoC alone in the Cooperative International Neuromuscular Research Group Duchenne Natural History Study (CINRG DNHS)

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ABSTRACT

Introduction: Ataluren targets underlying cause of nmDMD, enabling the formation of a full-length dystrophin.

Objective: To evaluate whether nmDMD patients receiving ataluren + standard of care (SoC) experienced a delay in LoA and a slower decline in pulmonary function versus SoC alone in CINRGDNHS.

Methods: Propensity score matching identified Study 019 and CINRGDNHS patients with comparable indicators of disease severity. Kaplan-Meier analyses estimated the age at LoA anddecline in FVC to <60%- or <50%-predicted or <1 L.

Results: Age at LoA was delayed by ~2.5 years in nmDMD patients receiving ataluren compared with CINRGDNHS patients. In non-ambulatory patients, ataluren was associated with a delay in decline to predicted FVC <60% by ~2.5 years and FVC <50% by ~1 year.

Conclusions: Ataluren + SoC delays LoA and may delay pulmonary function decline in nmDMD patients compared with SoC alone, although longer follow-up will be required.

Pulmonary function in patients with Duchenne muscular dystrophy from the Strategic Targeting of Registries and International Database of Excellence (STRIDE) Registry and the Cooperative International Neuromuscular Research Group Natural History Study (CINRG NHS): a matched cohort analysis

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ABSTRACT

Introduction: STRIDE is an ongoing, multicenter, observational registry providing data on ataluren use in nmDMD patients in routine clinical practice.

Objective: We investigated if nmDMD patients receiving ataluren plus standard of care (SoC) in the STRIDE Registry experienced a lesser decline in pulmonary function versus Soc alone in the CINRG

Methods: Propensity score matching identified comparable STRIDE and CINRG patient cohorts (N=241, 31 January 2021) with established predictors of disease progression; Kaplan-Meier analyses estimated ages at % predicted FVC <60% and <30%.

Results: Mean ages(±SD) at first symptoms (STRIDE vs CINRG; N=241 each) were 2.7±1.7 and 2.8±1.5 years, respectively. Median ages(95%CI) at% predicted FVC <60% (STRIDE vs CINRG) were 17.6(16.2,nonestimable) and 15.8(15.1, 16.5) years, respectively. Median ages(95% Cl) at% predicted FVC <30% were nonestimable for STRIDE and 26.4 (20.6, 29.4) years for CINRG (p=0.0085).

Conclusions: These data suggest that ataluren treatment plus SoC slows disease progressionin nmDMD patients.

Disclosure of conflicts of interest: MT has received lecture fees from Biogen and PTC Therapeutics, and has acted as a consultant on DMD clinical trials for BioMarin, Catabasis Pharmaceuticals, PTC Therapeutics,ReveraGen BioPharma and Sarepta Therapeutics, and as an advisory board member for AveXis, Biogen, Sarepta Therapeutics and PTC Therapeutics.
FB has received consultancy fees from PTC Therapeutics, Santhera Pharmaceuticals, SareptaTherapeutics and Pfizer.
ID has received consultancy fees fromAveXis, Biogen, BioMarin and PTC Therapeutics.
JK has acted as a consultant for AveXis, Biogen, Ionis Pharmaceuticals, PTC Therapeutics andRoche, and has received research support for taking part in clinical research from Biogen, BioMarin, GlaxoSmithKline, Ionis Pharmaceuticals, Novartis, PTC Therapeutics, Roche, Santhera Pharmaceuticals and Trophos.

EM has acted as an advisory board member for AveXis, Biogen, BioMarin , Bristol-Myers Squibb, lonis Pharmaceuticals, ltalfarmaco, Prosensa, PTC Therapeutics , Roche, Santhera Pharmaceuticals, Sarepta Therapeutics and Summit Therapeutics.
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ANO has received speaker and consultancy fees from Biogen, PTC Therapeutics and SareptaTherapeutics, and is an investigator on clinical trials sponsored by Biogen, F. Hoffmann-La Roche, ltalfarmaco, Sarepta Therapeutics and TAMDMD.
SJ, CW, AK, JJ, JL, PT and **CLS** are employees of PTC Therapeutics.
CMM has acted as a consultant on clinical trials of DMD for Astellas, Capricor, Catabasis, Edgewise Therapeutics , Epirium Bio (formerly Cardero Therapeutics), FibroGen, ltalfarmaco, Pfizer, PTC Therapeutics, Santhera Pharmaceuticals and Sarepta Therapeutics. He has received research support for clinical trials from Capricor, Catabasis, ltalfarmaco, Pfizer, PTCTherapeutics, Santhera Pharmaceuticals and Sarepta Therapeutics.
Medical writing and editorial support were funded by PTC Therapeutics Ltd.

EFGARTIGIMOD TREATMENT OF PATIENTS WITH GENERALIZED MYASTHENIA GRAVIS DEMONSTRATES IMPROVEMENTS REGARDLESS OF CONCOMITANT IMMUNOSUPPRESSIVE THERAPY OR REFRACTORY VS NON-REFRACTORY STATUS

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ABSTRACT

Introduction: Efgartigimod, a human IgG1 antibody FC-fragment, demonstrated clinical improvement in patients with generalized myasthenia gravis (gMG) by blocking FcRn and decreasing IgG, including pathogenic IgG.

Objective: To assess the efficacy of efgartigimod across subgroups, including concomitant therapies and refractory *vs.* non-refractory status.

Methods: The phase 3 ADAPT study randomized patients with gMG to receive cycles of four weekly infusions of 10 mg/kg efgartigimod or placebo; subsequent treatment cycles initiated according to clinical response. MG-ADL responder status (2-point improvement for 4 consecutive weeks) was assessed across acetylcholinesterase inhibitors (AChE-i), steroids and non-steroidal immunosuppressive (NSIST) use, and refractory vs non-refractory status.

Results: Consistent and statistically significant improvements in MG-ADL responder status were observed in AChR+ patients (n=129) regardless of concomitant NSISTs, steroids, or AChE-i use, and in refractory and non-refractory subgroups.

Conclusions: Efgartigimod demonstrated consistent improvements regardless of refractory and non-refractory status or concomitant background therapies.

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TV Pertinent to MG: Site Pl for clinical trials sponsored by Argenx, Alexion, Ra, and UCB; speaker for Alexion; consultant for Argenx.
VB has received research support from CSL, Grifols, UCB, Bionevia, Shire, and Octapharma.
EB, PU, and LL are argenx employees.
HM has served as a consultant for Alexion Pharmaceuticals, argenx BVBA and Ra Pharmaceuticals,and has received speaker honoraria from the Japan Blood Products Organization and research support from the Ministry of Health, Labour and Welfare, Japan.

CK served as a deputy editor for Neurology and as a consultant for Acceleron Pharma, Inc; Akcea Therapeutics; Alnylam Pharmaceuticals, Inc; Argenx; Biogen; CSL Behring; and Sanofi Genzyme. Dr Karam has received personal compensation for speaking engagements from Akcea Therapeutics; Alnylam Pharmaceuticals, Inc; CSL Behring; and Sanofi Genzyme and research/grant support from Akcea Therapeutics and Sanofi Genzyme.

Safety, β-Sarcoglycan Expression, and Functional Outcomes From Systemic Gene Transfer of rAAVrh74.MHCK7.hSGCB in LGMD 2E/R4

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ABSTRACT

Introduction: Limb-girdle muscular dystrophy type 2E/R4 (LGMD 2E/R4) is caused by mutations in the β-sarcoglycan gene (*SGCB*), resulting in loss of SGCB protein and other components of the dystrophin associated protein complex (DAPC). LGMD 2E/R4 manifests as progressive hip/shoulder muscle weakness and elevated creatine kinase (CK). rAAVrh74. MHCK7.hSGCB (SRP-9003) is an investigational gene transfer therapy for the expression of a codon-optimized, full-length, human SGCB transgene driven by MHCK7, a promoter optimized for skeletal and cardiac muscle expression.

Objectives: To evaluate the safety and efficacy of SRP-9003 in the first-in-human, phase 1/2 genetransfer therapy trial in patients with LGMD 2E/R4 (NCT03652259).

Methods: Six patients aged 4-15 years with *SGCB* mutation (both alleles) received a single SRP-9003 IV infusion: Cohort 1 (n=3), $1.85x10^{13}$ vg/kg dose; Cohort 2 (n=3), $7.41x\ 10^{13}$ vg/kg dose. Prednisone 1 mg/kg/day began 1 day before treatment, tapering after 30-60 days. Endpoints included safety (primary), SGCB expression (secondary), CK level, and functional assessments (North Star Assessment of Limb-girdle Muscular Dystrophies [NSAD], 100-meter timed test (100m, 10m, 4-stair climb, time to rise).

Results: We report Year 2 (Y2; Cohort 1) and Year 1 (Yl; Cohort 2) results. As of January 2021, SRP-9003 was well tolerated with no new safety signals since the previous data cut (July 2020). Adverse events occurred early and were manageable, and included vomiting, dehydration, and elevated liver enzymes, which all resolved. There were no other laboratory abnormalities suggestive of safety concerns, including no decreases in platelets outside the normal range and no clinical complement activation.
Western blot showed robust SGCB expression in muscle biopsies from individual patients at Day 60, and a dose-response in protein expression was observed. SGCB expression was maintained to Y2 (Cohort 1). Immunofluorescence also showed robust SGCB expression post treatment, leading to increased a-, δ- and y-sarcoglycan expression, demonstrating DAPC reconstitution at Day 60 (Cohort 1 and Cohort 2) and at Y2 (Cohort 1). CK decreased by 77% in Cohort 1 (Y2) and 74% in Cohort 2 (Yl) post treatment. SRP- 9003-treated patients showed functional improvements, maintained at Y2 in Cohort 1 (NSAD, +5.7 points; time to rise, -0.6 s; 4-stair climb, -0.3 s; 100m, -2.8 s; 10m, -0.2 s) and Yl in Cohort 2 (NSAD, +4 points; time to rise, -1.1 s; 4-stair climb, -0.4 s; 100m, -7.9 s; 10m, -0.6 s). Post hoc analysis showed improved NSAD outcomes versus untreated natural history cohort (9.2-point difference at Y2; 95% Cl, 3.2-15.1).

Conclusions: These data suggest long-term efficacy of SRP-9003 therapy, supporting advancement ofthe clinical development program.

Funding: This study was funded by Sarepta Therapeutics, Inc.

Disclosures: LRR-K, ERP, SL, DAG, ASM, EK, SN, and XL are or have been employees of Sarepta Therapeutics, Inc, and may own stock in the company. **LPL** received fees from Sarepta Therapeutics, Inc,for licensure of the LGMD natural history data set. **JRM** received financial support from Sarepta Therapeutics, Inc, for the travel to meetings to present any products sponsored by Sarepta. **KJL, KC, NFR, and MAI** have no conflicts to disclose. Product is investigational only.

Part A (Dose-Finding Phase) Results From a Phase 2 Multiple Ascending-Dose Study of SRP-5051, a Peptide-Conjugated PMO, in Patients With DMD Amenable to Exon 51 Skipping

C. Campbell, K. Mathews, M. van de Rijn[2], E. Palatinsky[2], X. Ni[2], N. Sha[2], I. Sehinovych[2], J. Tinsley[2], J. Malhotra[2], H. Phan[3]; on behalf of the MOMENTUM investigators

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[1]University of Iowa, Iowa City, IA, USA;
[2]Sarepta Therapeutics, Inc, Cambridge, MA, USA.. ;
[3]Rare Disease Research, Atlanta, GA, USA

ABSTRACT

Introduction: Peptide-conjugated phosphorodiamidate morpholino oligomers (PPMOs) are a next generation chemistry platform in which a cell-penetrating peptide is conjugated to the PMO backbone, with the goal of increasing tissue penetration, exon skipping, and dystrophin production with less frequent dosing. SRP-5051 is an investigational PPMO designed to skip *DMD* exon 51.

Objectives: To report results from part A dose-finding phase of MOMENTUM (NCT04004065), a phase 2 trial of SRP-5051.

Methods: Patients amenable to exon 51 skipping (aged 7-21 years) received ascending doses of SRP- 5051 (4, 10, 20, or 30 mg/kg) intravenously every 4 weeks. Primary endpoint was safety; other endpoints included exon skipping, dystrophin protein, and pharmacokinetics of each dose.

Results: Eighteen patients were enrolled. At week 12, exon skipping for the 20- and 30-mg/kg cohorts was 2.57% and 10.79%, respectively (versus 0.26% and 1.62% at baseline), and mean dystrophin protein was 3.06% and 6.55% of normal (versus 0.17% and 0.92% at baseline); all patients in these cohorts experienced an increase in exon skipping and dystrophin production. Immunofluorescence results from the 30-mg/kg cohort showed correct localization of dystrophin to the sarcolemma. Overall, 17/18 (94.4%) patients experienced a treatment-emergent adverse event (TEAE); the majority were mild to moderate in severity. Ten (55.6%) patients experienced treatment related TEAEs of hypomagnesemia (including 2 serious cases) prior to the implementation of magnesium monitoring and supplementation; most cases were mild to moderate, asymptomatic, and resolved with supplementation. No other safety concerns were identified.

Conclusions: MOMENTUM Part A results show SRP-5051 increases exon skipping and dystrophin production and that the majority of TEAEs were mild to moderate in severity. All participants from Part A will be invited to enroll in Part B of MOMENTUM.

Funding: This study was funded by Sarepta Therapeutics, Inc.

Disclosures: CC is a site investigator for Acceleron, AMO, Biogen, Biomarin, Cytokinetics, GSK, Pfizer, PTC Therapeutics, Roche, Sarepta, and Wave, and has received research support from Biogen, Genzyme, PTC Therapeutics, and Valerian for investigator-initiated grants. He has received fees for advisory functions from AMO, Biogen, Roche, and PTC Therapeutics, and is a data safety monitoringboard member for Catabasis and Solid. **MvdR, EP, XN, JT, NS, JM, and IS** are or have been employees of Sarepta Therapeutics, Inc, and may own stock in the company. **KM** has received research support as a site Pl from Catabasis, ltalfarmaco, Reata, Retrotope, Santhera, and Sarepta. She also has research support from CDC (U0l D0001248) and FARA and NIH (5 U54 NS053672, U24 NS-10718). **HP** has received grants from the CDC foundation and research support as a site Pl from Catabasis, ltalfarmaco, Pfizer, Santhera, and Sar epta. Products are investigational only.

Safety, Tolerability, and Pharmacokinetics of Eteplirsen in Patients 6-48 Months Old With Duchenne Muscular Dystrophy Amenable to Exon 51 Skipping

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ABSTRACT

Introduction: Eteplirsen is indicated for treatment of exon 51 skip-amenable patients with Duchenne muscular dystrophy (DMD). Previous studies in patients >4 years of age indicate eteplirsen is well tolerated and attenuates pulmonary and ambulatory declines compared with matched natural history cohorts.

Objectives: To evaluate safety, tolerability, and pharmacokinetics of eteplirsen in patients aged 6-48 months, the youngest population in a clinical trial to date of exon 51 skip-amenable patients with DMD (Study 4658-102, NCT03218995).

Methods: In this open-label, multicenter, dose-escalation study, all patients (Cohort 1: aged 24-48 months, n=9; Cohort 2: aged 6 to <24 months, n=6) received ascending doses (2, 4, 10, 20, 30 mg/kg) of once-weekly eteplirsen intravenously over 10 weeks, continuing at 30 mg/kg up to 96 weeks. Endpoints included incidence of adverse events and clinically significant laboratory abnormalities (primary) and pharmacokinetics (secondary).

Results: All patients completed the study (N=15). Average time since diagnosis was 10.5 months, and most (13/15, 86.7%) were not taking corticosteroids. Eteplirsen was well tolerated with no treatment related discontinuations, deaths, or evidence of renal toxicity. Most treatment-emergent adverse events were mild, and the most common were consistent with those commonly seen in pediatric populations (pyrexia, nasopharyngitis, vomiting, cough, diarrhea). Eteplirsen pharmacokinetics were consistent between both cohorts and aligned with expectations based on clinical experience in the older population.

Conclusions: These data contribute to the growing body of evidence supporting eteplirsen use at the approved 30-mg/kg dose by demonstrating its safety, tolerability, and predictable pharmacokinetic profile in patients as young as 6 months.

Funding: This study was funded by Sarepta Therapeutics, Inc.

Disclosures: EM has received consultant fees from Sarepta Therapeutics, Inc. **AMS** has no conflicts todisclose. **LS** has participated on advisory boards for Sarepta Therapeutics, Inc. **ND** has participated on advisory boards for Sarepta Therapeutics, Inc. **HS, LE, WZ, and SU** are employees of Sarepta Therapeutics, Inc, and may own stock/options in the company. **FM** has received consultant fees and speaker honoraria from Sarepta Therapeutics, Inc.

ENDEAVOR: Evaluating the safety and expression of the gene transfer therapy SRP-9001 in Duchenne muscular dystrophy (DMD)

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ABSTRACT

Introduction: rAAVrh74.MHCK7.micro-dystrophin (SRP-9001), an investigational gene transfer therapy, is being developed to achieve targeted skeletal and cardiac muscle expression of a shortened functional micro-dystrophin protein. Initial findings from ongoing Phase 1 and 2 trials in which patients received SRP-9001 clinical process material reported micro-dystrophin expression following gene transfer and suggest the potential for SRP-9001 therapy to provide clinical benefit to people with Duchenne muscular dystrophy (DMD).

Objectives: The aim of ENDEAVOR (Study 103; NCT04626674), an open-label, Phase 1b study, is to assess expression and safety of commercially representative SRP-9001 process material in patients with DMD.

Methods: Trial participants were given a single intravenous dose of $1.33x10^{14}$ vg/kg (linear qPCR) of SRP-9001 commercially representative material. The follow-up period consists of two parts: Part 1, from post infusion through Week 12; and Part 2, post-Week 12 through Week 260. The primary outcome measure is the change from baseline to Week 12 (Part 1) in micro-dystrophin protein expression as measured by western blot (WB). Secondary outcome measures include evaluation of micro-dystrophin expression at Week 12 by immunofluorescence (IF) and safety of SRP-9001 (incidence of adverse events [AEs] or clinically significant abnormalities in vital signs, including electrocardiograms and echocardiograms, up to Week 260). This interim analysis presents results for the first 11 patients enrolled (cut-off date May 2021).

Results: Treatment with SRP-9001 resulted in robust levels of micro-dystrophin protein expression by WB (change from baseline 55.4% of normal, SD=43.4). Expression was localized to the sarcolemma, as shown by IF (change from baseline in PDPF 57.7%, SD=22.2; change from baseline in IF intensity 75.9% of normal, SD=46.4) at Week 12. Micro-dystrophin expression was also associated with vector genome copies (change from baseline 3.9 vcgs, SD=2.4), confirming successful delivery of SRP-9001 to target cells. Safety of the commercially representative SRP-9001 material was consistent with previous experience with SRP-9001. No new safety signals were identified. Seventy-nine treatment-emergent AEs (TEAEs) occurred. As seen in previous studies, vomiting was the most common TEAE (64% of patients). No clinically relevant complement activation was observed. Two patients experienced three treatment-related serious AEs: one patient had increased transaminases that required corticosteroid treatment; one patient experienced both nausea and vomiting that required intravenous treatment. No deaths were observed.

Conclusions: Study 103, the first clinical study using commercially representative SRP-9001 material, provides preliminary evidence that the commercially representative material demonstrates safety and expression consistent with previous studies. The safety profile was consistent with prior studies, with no new safety signals identified.

Disclosures: Craig Zaidman receives research support from Biogen, serves on an advisory board for Biogen Inc, and was a paid consultant for Optum.
Crystal Proud participates on advisory boards and is a consultant for Biogen, Sarepta, AveXis/Novartis Gene Therapies, Genentech/Roche and Scholar Rock. She serves as a speaker for Biogen. She is a Principal investigator of studies sponsored by AveXis/Novartis Gene Therapies, AMO, Astellas, Biogen, CSL Behring, FibroGen, PTC, Pfizer, Sarepta and Scholar Rock.

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Kathryn Giblin is an employee of Sarepta Therapeutics, Inc and may have stock options. Larisa Collins is an employee of Sarepta Therapeutics, Inc and may have stock options. Shufang Wang is an employee of Sarepta Therapeutics, Inc and may have stock option. Sameer Upadhyay is an employee of Sarepta Therapeutics, Inc and may have stock options.Sarah Lewis is an employee of Sarepta Therapeutics, Inc and may have stock options.
Jyoti Malhotra is an employee of Sarepta Therapeutics, Inc and may have stock options. Danielle A. Griffin is an employee of Sarepta Therapeutics, Inc and may have stock options.Rachael A. Potter is an employee of Sarepta Therapeutics, Inc and may have stock options.Maitea Guridi reports no conflicts of interest.
Louise R. Rodino-Klapac is an employee of Sarepta Therapeutics, Inc, has received grant support from Sarepta Therapeutics, Inc and the Parent Project Muscular Dystrophy, as well as financial consideration from Sarepta Therapeutics, Inc and Myonexus Therapeutics (now acquired by Sarepta Therapeutics). In addition, she is a co-inventor of AAVrh74.MHCK7. micro-dys technology, which is exclusively licensed toSarepta Therapeutics, Inc.
Jerry R. Mendell has received study funding from Sarepta Therapeutics, Inc for the current publication and has a service agreement with Sarepta Therapeutics, Inc, to provide training on ongoing studies. In addition, he is a co-inventor of AAVrh74.MHCK7.micro-dys technology, which is exclusively licensed to Sarepta Therapeutics, Inc.

A Phase 2 clinical trial evaluating the safety and efficacy of SRP-9001 for treating patients with Duchenne muscular dystrophy (DMD)

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ABSTRACT

Introduction: rAAVrh74.MHCK7.micro-dystrophin (SRP-9001), an investigational gene transfer therapy, is being developed to achieve targeted skeletal and cardiac muscle expression of a shortened functional micro dystrophin protein. We tested the safety and efficacy of SRP-9001 in a three-part, multicenter, Phase 2 clinical trial (Study 102; NCT03769116). Part 1 is a 48-week, randomized, double-blind, placebo controlled period. Part 2 is a 48-week period in which Part 1 placebo-treated patients receive SRP-9001 (blinded crossover). Part 3 is an open-label follow-up period (up to 212 weeks).

Objectives: We evaluated the safety and efficacy of SRP-9001 in a double-blind, placebo-controlled trial.

Methods: Participants (ambulatory boys 4-7 years old, confirmed *DMD* mutation, stable steroid dosing) received SRP-9001 (n=20) or placebo (n=21). The target dose was $2.0x10^{14}$ vg/kg (supercoiled qPCR, linear plasmid standard equivalent of $1.33x10^{14}$ vg/kg). Randomization was stratified by age (4-5 and 6-7 yearsold). Primary endpoints were change in micro-dystrophin expression (western blot; baseline to Week 12) and change in North Star Ambulatory Assessment (NSAA; baseline to Week 48). Safety endpoints included treatment-emergent adverse events (AEs) and serious AEs.

Results: In Part 1, the primary biological endpoint (change in micro-dystrophin expression) was met. At Week 48, NSAA change from baseline was not statistically different between groups. Pre-specified subgroup analysis of 4- to 5-year olds showed a statistically significant difference in NSAA change between SRP- 9001 and placebo groups (+2.5, P=0.0172). Baseline NSAA score of the 4- to 5-year olds was balanced across arms but was significantly imbalanced in the 6- to 7-year olds. We observed no clinically relevant complement activation. Treatment-related AEs were transient and manageable . Four patients had treatment-related serious AEs, which resolved.

Conclusions: Data suggest a biological effect of SRP-9001 that may be clinically relevant in people with DMD. Results reinforce a favorable benefit-risk profile.

Disclosures: Perry B. Shieh reports being a consultant/independent contractor for AveXis/Novartis Gene Therapies, Biogen Inc, Cytokinetics, and Sarepta Therapeutics, Inc, and receiving grants/research support from AveXis/Novartis Gene Therapies, Biogen Inc, Cytokinetics, lonis Pharmaceuticals, Inc, Sanofi Genzyme, and Sarepta Therapeutics, Inc.
Linda P. Lowes reports receiving salary support from Sarepta Therapeutics, Inc through Nationwide Children's Hospital to support training and quality control activities for their ongoing clinical trials and licensing fees for natural history data.
Natalie F. Reash reports receiving salary support from Sarepta Therapeutics, Inc, for Clinical Evaluatortraining for ongoing and upcoming clinical trials.
Lindsay N. Alfano reports receiving salary support from Sarepta Therapeutics, Inc, through Nationwide Children's Hospital to support training and quality control activities for their ongoing clinical trials.
Rachael A. Potter is an employee of Sarepta Therapeutics, Inc, and may have stock options. Danielle A. Griffin is an employee of Sarepta Therapeutics, Inc, and may have stock options. Sarah Lewis is an employee of Sarepta Therapeutics, Inc, and may have stock options.
Larry Hu is an employee of Sarepta Therapeutics, Inc, and may have stock options.

Sameer Upadhyay is an employee of Sarepta Therapeutics, Inc, and may have stock options.Teji Singh is an employee of Sarepta Therapeutics, Inc, and may have stock options.
Louise R. Rodino-Klapac is an employee of Sarepta Therapeutics, Inc, has received grant support from Sarepta Therapeutics, Inc and the Parent Project Muscular Dystrophy, as well as financial consideration from Sarepta Therapeutics, Inc and Myonexus Therapeutics (now acquired by Sarepta Therapeutics). In addition, she is a co-inventor of AAVrh74. MHCK7.micro-dys technology, which is exclusively licensed to Sarepta Therapeutics, Inc.
Jerry R. Mendell has received study funding from Sarepta Therapeutics, Inc for the current publication and has a service agreement with Sarepta Therapeutics, Inc, to provide training on ongoing studies. In addition, he is a co-inventor of AAVrh74.MHCK7.micro-dys technology, which is exclusively licensed to Sarepta Therapeutics, Inc.
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Megan A. lammarino, Brenna Powers, Jeremy D. Woods, Christy L. Skura, Howard C. Mao, and Loretta A. Staudt report no conflicts of interest.

The impact of the coronavirus 2019 (COVID-19) pandemic on enrollment of patients with chronic demyelinating polyneuropathy (CIDP) in subcutaneous immunoglobulin (SCIg) self administration training

E. Murphy, L. Barrett, C. Vanname*, C. Jackson*, J. Barber, P. Patel, A. Katz

CSL Behring LLC, King of Prussia, PA
Specialty Pharmacy Nursing Network [SPNN] Inc, Sarasota, FL

ABSTRACT

Introduction: SCIg is an FDA approved treatment for adult patients with CIDP. Patients can participate in self-administration training by Specialty Pharmacy Nurse Network (SPNN).

Objective: To assess the impact of the COVID-19 pandemic on enrollment of patients with CIDP in SCIg self-administration training.

Methods: This was a retrospective study utilizing SPNN data of patients with CIDP enrolled in 1-7 training sessions between 5/2018-1/2020 ('2018/19') and 1/2020-1/2021 ('2020').

Results: Overall, 120 patients were referred to SPNN for SCIg training in 2020, compared with 310 in 2018/19. Training discontinuation rates were slightly lower in 2020 compared with 2018/19 (4% vs. 10%, respectively). The majority of patients (84%) continued with in-person training during 2020 (9% virtual and 7% mix of both). Most successfully-trained patients (75%) required 3-4 sessions irrespective of year trained.

Conclusion: Enrollment during the COVID-19 pandemic (2020) was lower compared with 2018/19, and discontinuation rates were slightly lower.

Funding: CSL Behring sponsored this analysis

Risk of CIDP relapse by body mass index (BMI): a sub-analysis from the PATH and open label extension (OLE) studies

Jaclyn Barber, Palak Patel, Michaela Praus*, John-Philip Lawo*, Orel! Mielke*, and Arie Katz

(CSL Behring LLC, King of Prussia, USA; CSL Behring GmbH, Marburg, Germany)*

ABSTRACT

Introduction: Subcutaneous immunoglobulin (SCIg) is an FDA approved maintenance treatment for adult patients with chronic inflammatory demyelinating polyneuropathy (CIDP).

Objective: To evaluate CIDP relapse rates vs body mass index (BMI) in PATH and its open label extension (OLE).

Methods: PATH was a randomized, double-blind study investigating 0.2 and 0.4 g/kg weekly SCIg versus placebo, followed by an OLE. This sub-analysis stratified data by BMI: lean (<25 kg/ m^2), overweight (≥25-<30 kg/ m^2), and obese (≥30 kg/ m^2).

Results: In PATH, relapse rates were lower with SCIg than with placebo across all BMI ranges. In both PATH and its OLE, the relapse risk was lower with 0.4 g/kg than with 0.2 g/kg. In the OLE, no difference was observed in overall relapse rate (no. of relapses/weeks on treatment) between lean,overweight, and obese patients (0.013, 0.013, and 0.016, respectively).

Conclusion: SCIg was effective as a CIDP maintenance therapy across a range of patient BMIs.

Funding: CSL Behring sponsored this study and conducted the analysis

FORCE™ platform delivers exon skipping PMO, leads to durable increases in dystrophin protein in *mdx* mice and is well tolerated in NHPs

Cody A. Desjardins, Reshmii Venkatesan, Emma O'Donnell, John Hall, Ryan Russo, Sean Spring, Kim Tang, John W. Davis II, Tim Weeden, Oxana Beskrovnaya

Waltham, MA

ABSTRACT

Duchenne muscular dystrophy (DMD) is the most common X-linked muscular dystrophy. We developed the FORCE™ platform, which consists of a Fab targeting TfR1, Val-Cit linker, and an exon skipping phosphorodiamidate morpholino oligomer (PMO), to deliver a potentially transformative therapy for patients with DMD.

Approved PMO therapies are limited by poor muscle delivery. We therefore evaluated the potential of FORCE to improve exon skipping and dystrophin expression in mdx model of DMD.

Multiple ascending doses were administered via a single IV dose of FORCE to *mdx* mice. Muscle PMO concentration, exon skipping, and dystrophin protein were measured at multiple timepoints. Tolerability was assessed in nonhuman primates (NHP).

A substantial long-lasting, dose-dependent increase in dystrophin was achieved in *mdx* mice. Our lead candidate was well-tolerated with no dose-limiting toxicities in NHP.

Together our data support the ability of the FORCE platform to deliver exon skipping therapy to patients with DMD.

Development of a standard of care for patients with valosin-containing protein associated multisystem proteinopathy

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ABSTRACT

Valosin-containing protein (VCP) associated multisystem proteinopathy (MSP) is a rare inherited disorder that may result in varying phenotypes including inclusion body myopathy, Paget's disease of bone, and frontotemporal dementia. An international consortium was convened by the patient advocacy organization, Cure VCP Disease, in April 2021 to develop a standard of care for this under diagnosed disease. To achieve this goal, working groups collaborated to generate best evidence recommendations in 10 key areas: genetics and diagnosis, myopathy, frontotemporal dementia, Paget's disease of bone, ALS and CMT, parkinsonism, cardiomyopathy, supportive therapies, pulmonology, nutrition and supplements, and mental health. Timely referral to a specialty neuromuscular center and multidisciplinary team follow up are essential for screening and management of secondary complications. The goal of our consortium was to expedite the time to accurate diagnosis, initiate appropriate therapies for optimal management, and elevate the recommended best practices guidelines for VCP MSP care.

MUSCLE STUDY GROUP

Annual Scientific Meeting

OCTOBER 1-3, 2021

Muscle Study Group

WELCOME!

Welcome! On behalf of your Muscle Study Group, we would like to welcome each of you to the 2021 Muscle Study Group Annual Meeting. It is an exciting time in neuromuscular research as we continue to grow and adapt.

We once again are conducting our meeting virtually given the recent surge of COVID over the summer. We were also shown by our meeting last year a ZOOM conference is an effective way to communicate at a distance. Again, we have set up the meeting for three morning sessions, as all day sessions contribute to ZFS (ZOOM FATIGUE SYNDROME), and our European colleagues need to sleep at some point!

We are excited this year to have more industry involvement than we have ever had. The Shark Tank session was such a success last year we are bringing it back with the opportunity of a $10K grant to the winner!

We also have been encouraging residents to register and have been successful. We want to encourage and stimulate residents to pursue NM Fellowships as this group is our successors to the next generation.

The MSG continues to fund a Neuromuscular Research 2-year fellowship program so at any one time we have a Fellow in the first year and one in the second year. Both our current Fellows will be presenting during the meeting.

As the Co-Chairs of the Muscle Study Group, we would like to thank this year's planning committee for putting together an excellent agenda that covers such a broad range of topics and interests within the neuromuscular field. They have spent much time planning an in-person meeting and then changing course to secure a virtual meeting. Keep a lookout on the MSG website for the 2022 meeting information as next year we are hoping to meet in person in northern Italy.

Best wishes,

Richard J. Barohn, M.D.
Executive Vice Chancellor for Health Affairs, University of Missouri
Co-chair, Muscle Study Group

Prof Michael G. Hanna, M.D.
Director, University College London Institute of Neurology
Co-chair, Muscle Study Group

2021 Planning Committee

Chafic Karam, M.D. // Chair
University of Pennsylvania Health System

James Lilleker, MBChB, Ph.D. // Co-Chair
The University of Manchester

Senda Ajroud-Driss, M.D.
Northwestern University

Richard Barohn, M.D. // MSG Chair
University of Missouri

Laurie Gutmann, M.D.
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Melissa McIntyre, DPT
University of Utah

Colin Quinn, M.D.
University of Pennsylvania Health System

Tracey Willis, MBChB, MMedSci, M.D.
Chester University, UK

Amelia Wilson, DPT
University of Utah Health

AGENDA //
Friday, October 1

MUSCLE STUDY GROUP

James Lilleker, MBChB, Ph.D.; Senda Ajroud-Driss, M.D. // *Moderators*

8:00 - 8:05 A.M. OPENING
Richard J. Barohn, M.D., Prof Michael G. Hanna, M.D.

8:05 - 9:05 A.M. ROBERT C. GRIGGS, M.D. ANNUAL MSG LECTURE: IDIOPATHIC DOES NOT MEAN CRYPTOGENIC: THERAPEUTIC DEVELOPMENT FOR METABOLIC NEUROPATHY
Gordon Smith, M.D. // *Virginia Commonwealth University*

9:10 - 9:25 A.M. IBM INTERNATIONAL GENETICS CONSORTIUM STUDY UPDATE Prof Michael G. Hanna, M.D.

SESSION 1: INFLAMMATORY MYOPATHIES

9:25 - 9:45 A.M. AUTOANTIBODIES IN MYOSITIS
Prof Neil McHugh, MBChB, M.D. // *University of Bath*

9:50 - 10:10 A.M. INTERVENTIONAL STUDIES IN MYOSITIS (IVIG, TOC, RITUX)
Rohit Aggarwal, M.D. // *University of Pittsburgh*

10:15 - 10:35 A.M. RAPAMYCIN STUDY
Prof Olivier Benveniste, M.D., Ph.D. // *AP-HP*

10:37 - 10:50 A.M. BREAK Sponsored by CSL Behring

SESSION 2: FLASH PRESENTATIONS

10:50 - 11:00 A.M. MOLECULAR BIOMARKERS IN MYOTONIC MUSCULAR DYSTROPHY TYPE 2
Paloma Gonzalez-Perez, M.D., Ph.D. //
MSG Fellow, Massachusetts General Hospital

11:02 - 11:12 A.M. CD8 POSITRON EMISSION TOMOGRAPHY (PET/CT) IMAGING WITH 89ZR-DF-IAB22M2C IN PATIENTS WITH INCLUSION BODY MYOSITIS
Colin Quinn, M.D. // *University of Pennsylvania*

11:14 - 11:24 A.M. 10 PS MNEMONIC FOR DX OF IIM
Amir Sabouri, M.D. // *Kaiser Permanente*

11:26 - 11:36 A.M. INFLAMMATORY MYOPATHIES PRESENTING WITH AXIAL WEAKNESS Elie Naddaf, M.D. // *Mayo Clinic*

11:38 - 11:58 A.M. OPTIMIZING CIDP CARE WITH SCIG: PATH OLE AND BEYOND
Mazen Dimachkie, M.D. // *CSL Behring Update*

12:03 - 12:23 P.M. THE ROLES OF AUTOANTIBODIES IN IMMUNE CHECKPOINT INHIBITOR THERAPY: FROM BIOMARKERS TO MEDIATORS OF NEUROLOGICAL SYNDROMES
Karin Hoang Woodman, M.D. // *Argenx Update*

12:28 - 12:48 P.M. FORCETM PLATFORM DELIVERS EXON SKIPPING PMO, LEADS TO DURABLE INCREASES IN DYSTROPHIN PROTEIN IN MDX MICE AND IS WELL TOLERATED IN NHPS
Oxana Beskrovnaya, Ph.D. // *Dyne Therapeutics Update*

12:50 P.M. CLOSING
Richard J. Barohn, M.D., Prof Michael G. Hanna, M.D.

12:50-1:30 P.M. MINGLING TIME (OPTIONAL)
Zoom Rooms: Cigar Mingling Room
CSL Behring Room
Dyne Therapeutics Room
Argenx Room

All times US Central Time

AGENDA //
Saturday, October 2

MUSCLE STUDY GROUP

Chafic Karam, M.D.; Amelia Wilson, DPT // *Moderators*

8:00 - 8:08 A.M. OPENING
Richard J. Barohn, M.D., Prof Michael G. Hanna, M.D.

8:09 - 9:19 A.M. ARIMOCLOMOL IN IBM TRIAL UPDATE
Mazen Dimachkie, M.D. //
University of Kansas Medical Center

SESSION 3: INFLAMMATORY NEUROPATHIES AND OUTCOME MEASURES

8:20 - 8:40 A.M. EXPANDING THE SPECTRUM OF CHRONIC IMMUNE SENSORY POLYRADICULOPATHY: THE CISP-PLUS SYNDROME James Dyck, M.D. // *Mayo Clinic*

8:45 - 9:05 A.M. BIOMARKERS IN CIDP/GBS
Karissa Gable, M.D. // *Duke University Medical Center*

9:05 - 9:25 A.M. 2021 EAN/PNS CIDP GUIDELINES: A FOCUSED REVIEW OF THE NEW DIAGNOSTIC AND TREATMENT GUIDELINES
Jeff Allen, M.D. // *University of Minnesota*

9:30 - 9:50 A.M. OUTCOME MEASURES
Gita Ramdharry, DPT // *University College London*

9:55 - 10:10 A.M. BREAK Sponsored by PTC Pharma

SESSION 4: FLASH PRESENTATIONS

10:10 - 10:25 A.M. POST-TRANSLATIONAL MODIFICATIONS OF DUX4
Renatta Knox, M.D. // *MSG Fellow, Nationwide Children's Hospital*

10:27 - 10:37 A.M. LOSS OF TDP-43 FUNCTION AND RIMMED VACUOLES PERSIST AFTER T CELL DEPLETION IN A XENOGRAFT MODEL OF INCLUSION BODY MYOSITIS
Chiseko Ikenaga, M.D., Ph.D. // *Johns Hopkins University*

10:39 - 10:49 A.M. PROTOCOL FOR A HYBRID II STUDY EXPLORING THE FEASIBILITY OF DELIVERING, EVALUATING, AND IMPLEMENTING A SELF-MANAGEMENT PROGRAMME FOR PEOPLE WITH NEUROMUSCULAR DISEASES AT A SPECIALIST NEUROMUSCULAR CENTRE (ADAPT-NMD)
Louie Lee, BSc (HONS) // *University College London*

10:51 - 11:01 A.M. ESTABLISHING CLINICAL TRIAL READINESS FOR VALOSIN CONTAINING PROTEIN-ASSOCIATED MULTISYSTEM PROTEINOPATHY: BASELINE RESULTS FROM A 1-YEAR PROSPECTIVE STUDY
Megan A. Iammarino, PT, DPT //
Nationwide Children's Hospital

11:03 - 11:13 A.M. COVID-19 RELATED OUTCOMES IN PRIMARY MITOCHONDRIAL DISEASES: AN INTERNATIONAL STUDY
Chiara Pizzamiglio, M.D. // *University College London*

11:15 - 11:25 A.M. SELF-MANAGEMENT IN NEUROMUSCULAR DISEASES: PRELIMINARY FINDINGS FROM A QUALITATIVE EXPLORATION OF THE PATIENT PERSPECTIVE
Louie Lee, BSc (HONS) // *University College London*

11:27 - 11:37 A.M. PROSPECTIVE CLINICAL TRIAL READINESS IN LGMDR9 FKRP-RELATED MUSCULAR DYSTROPHY: A GRASP CONSORTIUM STUDY
Megan A. Iammarino, PT, DPT //
Nationwide Children's Hospital

11:37 - 11:45 A.M. BREAK Sponsored by Argenx

11:45 A.M. - 12:05 P.M. DEFLAZACORT EVIDENCE FOR ITS ROLE IN SLOWING DMD DISEASE Richard A. Able, Jr., Ph.D. //
PTC Therapeutics Inc. Update

12:10 - 12:30 P.M. EXPLORE THE SCIENCE FOR AN APPROVED SPINAL MUSCULAR ATROPHY TREATMENT
Elizabeth Kichula, M.D., Ph.D. // *Genentech Update*

12:35 - 12:37 P.M. SAREPTA THERAPEUTICS SPONSOR INTRODUCTION
Dr. Gilmore O'Neill

12:40 P.M. CLOSING
Richard J. Barohn, M.D., Prof Michael G. Hanna, M.D.

12:40 - 1:30 P.M. MINGLING TIME (OPTIONAL)
Zoom Rooms: Cigar Mingling Room
Genentech Room
PTC Therapeutics Room

All times US Central Time

AGENDA //
Sunday, October 3

MUSCLE STUDY GROUP

James Lilleker, MBChB, Ph.D.; Laurie Gutmann, M.D.; Melissa McIntyre, DPT // *Moderators*

8:00 - 8:05 A.M. OPENING
Richard J. Barohn, M.D., Prof Michael G. Hanna, M.D.

8:05 - 8:15 A.M. NIH SIBM NATURAL HISTORY STUDY TRIAL UPDATE
Tahseen Mozaffar, M.D. // *University of California, Irvine*

8:17 - 8:27 A.M. DUCHENNE MUSCULAR DYSTROPHY RESPIRATORY PROFILES FROM REAL WORLD REGISTRY DATA
Mona Hnaini, M.D. // *Pediatric Neuromuscular Fellow, London Health Science Centre Western University*

SESSION 5: SHARK TANK

8:20 - 9:45 A.M. SHARK TANK SESSIONS
James Lilleker, MBChB, Ph.D. // Moderator
W. David Arnold, M.D.,
Prof Tracey Willis, MBChB, MMedSci, M.D.,
Gita Ramdharry, DPT // *Shark Panel*

THE INNATE IMMUNE SYSTEM IN MYASTHENIA GRAVIS
Katherine Dodd, MBChB MRCP, Ph.D. Student // *University of Manchester, UK*

THE THERAPEUTIC PLAY GYM PILOT STUDY
Jenna Linn Lammers, MSR/PT,CNT, PCS // *University of Florida*

IDENTIFICATION OF NOVEL BIOMARKERS FOR INCLUSION BODY MYOSITIS USING SINGLE-NUCLEI RNA SEQUENCING OF MUSCLE BIOPSIES
Chiseko Ikenaga, M.D., Ph.D. // *Johns Hopkins University School of Medicine*

9:45 - 10:00 A.M. BREAK Sponsored by Genentech

SESSION 6: GENETICS

10:00 - 10:20 A.M. VUS
Tanya Bardkjian, MS, LCGC // *University of Pennsylvania*

10:25 - 10:45 A.M. RESOLUTION OF GENETIC VARIANTS OF UNCERTAIN SIGNIFICANCE USING MUSCLE BIOPSIES
Karra Jones, M.D., Ph.D. // *University of Iowa*

10:50 - 11:10 A.M. GENETIC TESTING IN NEUROMUSCULAR DISORDERS
Shawna Feely, MS, LGC // *University of Iowa*

11:10 - 11:15 A.M. ANNOUNCEMENT OF SHARK TANK AWARD

SESSION 7: FLASH PRESENTATIONS

11:15 - 11:25 A.M. 2020 SHARK TANK AWARD WINNER PRESENTATION: MEND (MEXILETINE VERSUS LAMOTRIGINE IN NON-DYSTROPHIC MYOTONIA)
Dr. Vinojini Vivekanandam, MBBS // *University College London Institute of Neurology*

11:27 - 11:37 A.M. ADAPTING MRI AS A CLINICAL OUTCOME MEASURE FOR A FACIOSCAPULOHUMERAL MUSCULAR DYSTROPHY TRIAL OF PREDNISONE AND TACROLIMUS
Leo Wang, M.D., Ph.D. // *University of Washington*

11:38 - 11:48 A.M. RACIAL DISPARITIES IN SKIN TONE REPRESENTATION OF DERMATOMYOSITIS RASHES
Salman Bhai, M.D. // *University of Texas Southwestern*

11:49 - 11:59 A.M. LONGITUDINAL DYSPHAGIA ASSESSMENT IN PATIENTS WITH CYSTINOSIS USING MBSIMP
Stacey Sullivan, MS, CCC, SLP // *Mass General Hospital*

12:00 - 12:10 P.M. CMT-COVID SURVEY Riccardo Zuccarino, M.D. // *NEMO*

12:11 - 12:21 P.M. CASE SERIES OF MYASTHENIA GRAVIS (MG) PATIENTS PRESCRIBED SUBCUTANEOUS IMMUNOGLOBULIN (SCIG) THERAPY AND MONITORED BY PATIENT REPORTED OUTCOME MEASURES (PROMS) BY A SPECIALTY INFUSION PHARMACY USING SOLEMETRICS
Timothy Walton, MHS, CCRP // *Soleo Health*

12:22 - 12:32 P.M. FLOW CYTOMETRY AND SORTING OF SINGLE ANTIBODY SECRETING CELLS FROM FROZEN MUSCLE TISSUE
Vladimir Liarski, M.D. // *University of Chicago Medicine*

12:33 - 12:43 P.M. EFFECT OF DISTAL HEREDITARY MOTOR NEUROPATHY ON MUSCLE STRUCTURE, FUNCTION, AND GAIT PATTERNS: TWO CASE REPORTS
Aljwhara Alangary, PT, Ph.D. Student // *University College London*

12:44 - 12:54 P.M. MONOTHERAPY WITH ECULIZUMAB IN REFRACTORY ACETYLCHOLINE RECEPTOR POSITIVE GENERALIZED MYASTHENIA GRAVIS Xiaoyang Li, MBBS, M.D. // *University of North Carolina at Chapel Hill*

12:55 P.M. CLOSING
Richard J. Barohn, M.D., Prof Michael G. Hanna, M.D.

1:00 - 1:30 P.M. AFTER HOURS OPEN MINGLING (all welcome to attend)

All times US Central Time

MEETING SUPPORT // Thank You!

MUSCLE STUDY GROUP

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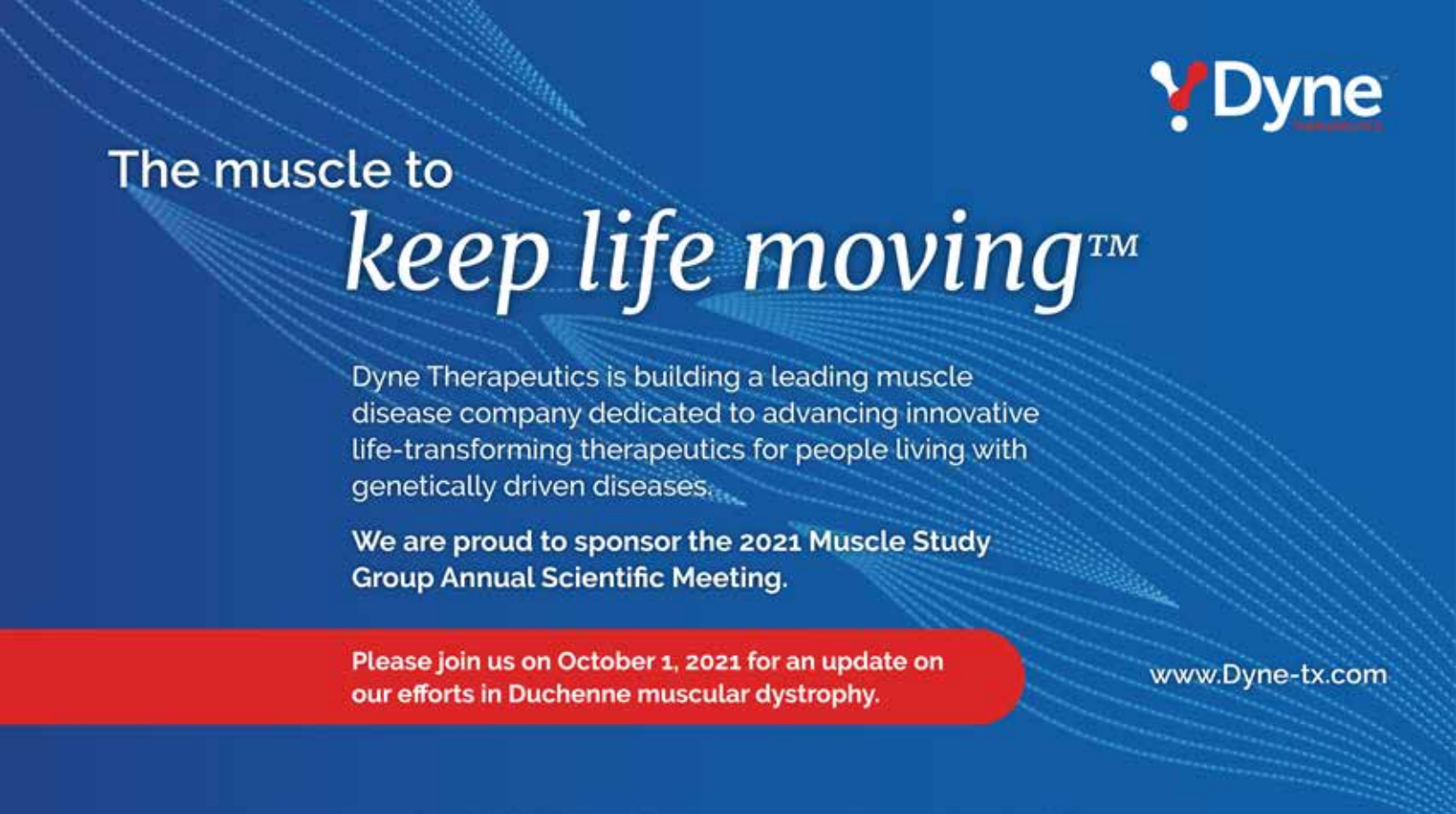
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PTC THERAPEUTICS

~50%

OF PATIENTS WITH GENERALIZED MYASTHENIA GRAVIS (gMG) REMAIN UNCONTROLLED[1]

UP TO **70%** OF PATIENTS

FIND IT CHALLENGING TO DO HOUSEHOLD CHORES[2,3]

33% OF PATIENTS

HAVE DIFFICULTY DRIVING DUE TO ARM WEAKNESS AND VISION PROBLEMS[4]

~40% OF PATIENTS

HAVE DIFFICULTY CHEWING AND SWALLOWING[4]

UNCONTROLLED. UNPREDICTABLE. UNEXPECTED.
Get the facts on uncontrolled disease at **gMGFacts.com**

REFERENCES: 1. Cutter G, et al. *Muscle Nerve*. 2019;60(6):707-715. 2. Nowak RJ. *Neurology Reviews*. March 2018;(Suppl):S1-S4. 3. The CIE. *The cost to patients and the community of Myasthenia Gravis*. Centre for International Economics; November 2013. 4. Twork S, et al. *Health Qual Life Outcomes*. 2010;8:129.

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2022 MSG MEETING //
September 30-October 2

Regina Palace, Stresa, Lake Magiorre, Italy

Our goals are to be the premier neuromuscular clinical and translational research organization and to create an environment to establish the next generation of researchers with your active involvement in the MSG we can accomplish these goals.

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