Shelly, diagnosed with ALS in 2013

Cytokinetics

EMPOWERING

MUSCLE

EMPOWERING

LIVES

Forward Looking Statements

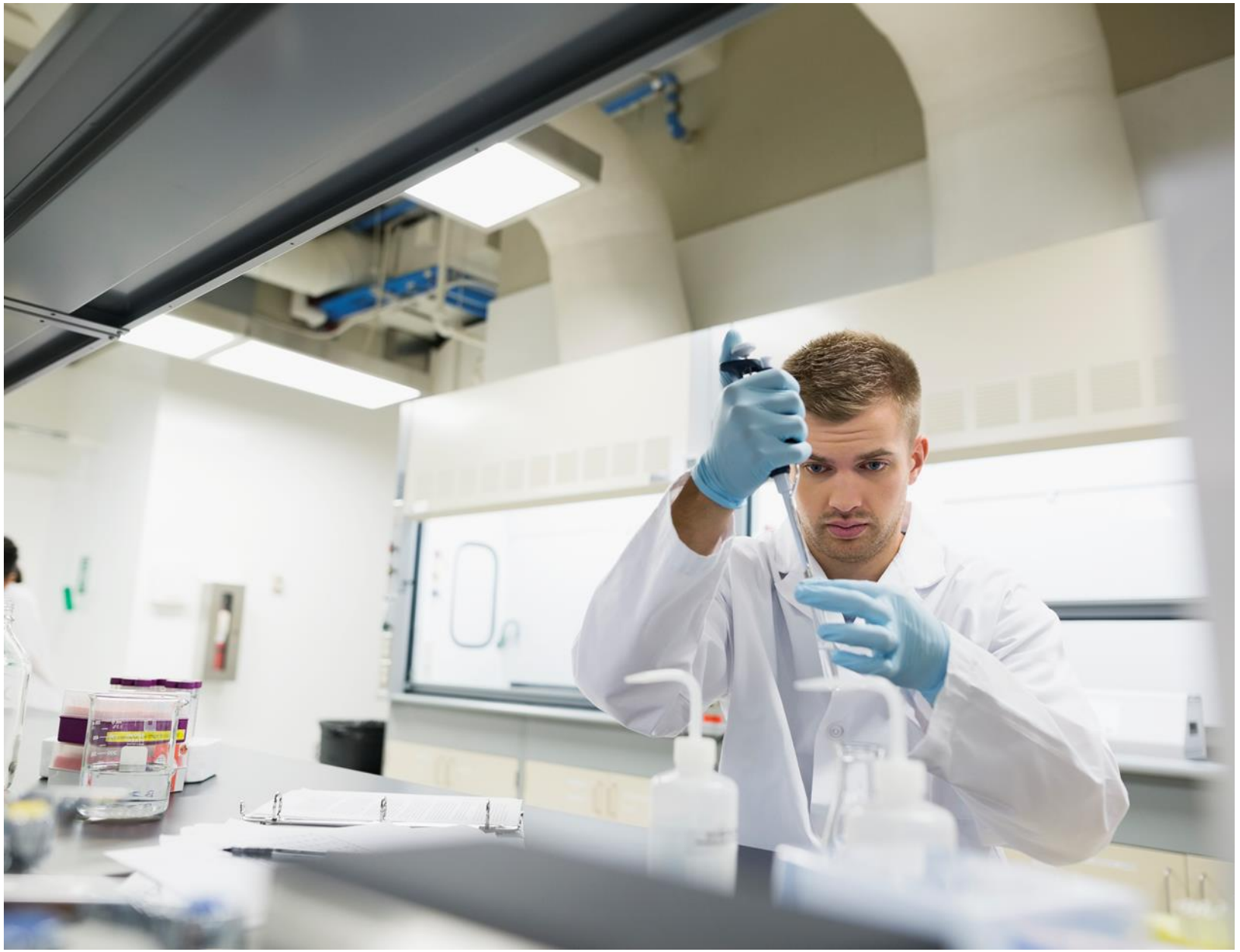
This Presentation contains forward-looking statements for purposes of the Private Securities Litigation Reform Act of 1995 (the "Act"). Cytokinetics disclaims any intent or obligation to update these forward-looking statements, and claims the protection of the Act's Safe Harbor for forward-looking statements. Examples of such statements include, but are not limited to, statements relating to Cytokinetics' and its partners' research and development activities; the design, timing, results, significance and utility of preclinical study results, including Cytokinetics' expectations regarding the timing or results from its clinical trials of *reldesemtiv*, enrollment of patients in GALACTIC-HF and pipeline expansion in 2018; and the properties and potential benefits of *reldesemtiv* and Cytokinetics' other drug candidates. Such statements are based on management's current expectations; but actual results may differ materially due to various risks and uncertainties, including, but not limited to, potential difficulties or delays in the development, testing, regulatory approvals for trial commencement, progression or product sale or manufacturing, or production of Cytokinetics' drug candidates that could slow or prevent clinical development or product approval, including risks that current and past results of clinical trials or preclinical studies may not be indicative of future clinical trial results, patient enrollment for or conduct of clinical trials may be difficult or delayed, Cytokinetics' drug candidates may have adverse side effects or inadequate therapeutic efficacy, the FDA or foreign regulatory agencies may delay or limit Cytokinetics' or its partners' ability to conduct clinical trials, and Cytokinetics may be unable to obtain or maintain patent or trade secret protection for its intellectual property; Astellas' or Amgen's decisions with respect to the design, initiation, conduct, timing and continuation of development activities for *reldesemtiv* or omecamtiv mecarbil, respectively; Cytokinetics may incur unanticipated research, development and other costs or be unable to obtain financing necessary to conduct development of its products; standards of care may change, rendering Cytokinetics' drug candidates obsolete; competitive products or alternative therapies may be developed by others for the treatment of indications Cytokinetics' drug candidates and potential drug candidates may target; and risks and uncertainties relating to the timing and receipt of payments from its partners, including milestones and royalties on future potential product sales under Cytokinetics' collaboration agreements with such partners. For further information regarding these and other risks related to Cytokinetics' business, investors should consult Cytokinetics' filings with the Securities and Exchange Commission.

Our Inspiration

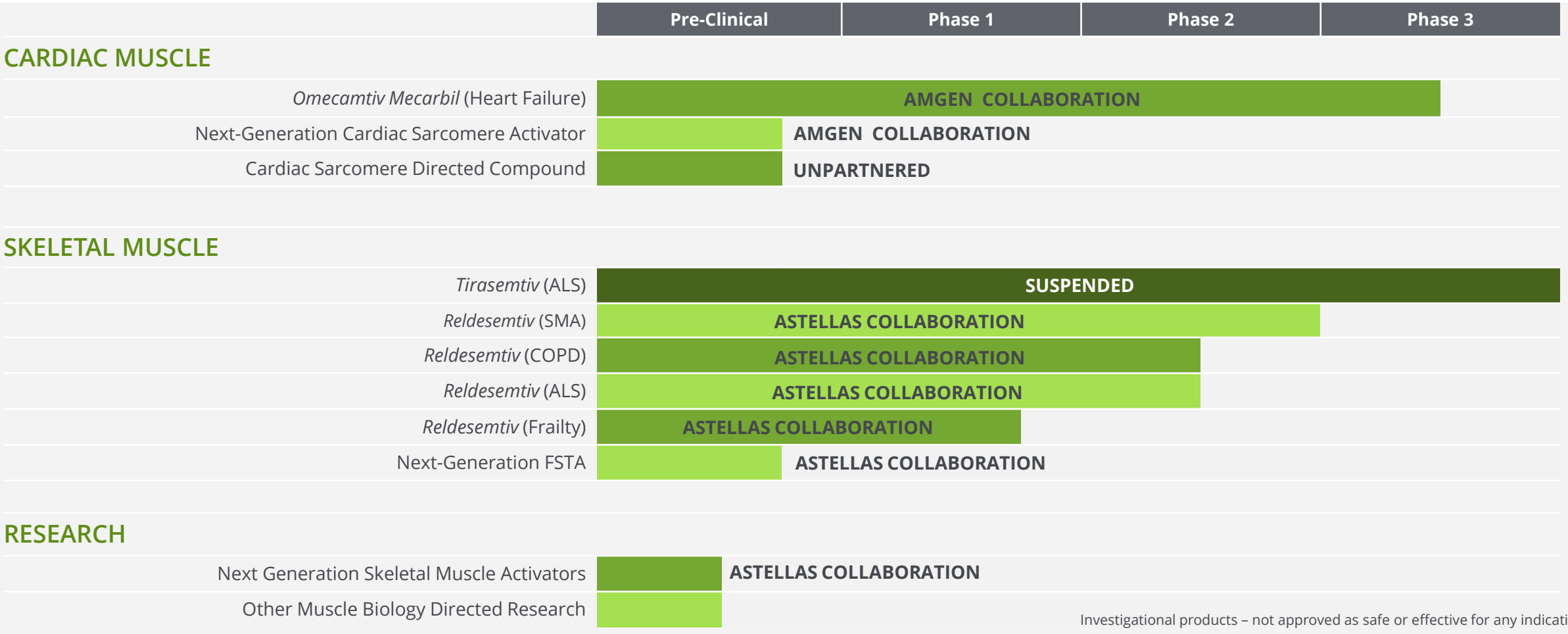
Every day we are motivated by people living with ALS, SMA, heart failure and other diseases of impaired muscle function. They are fighting with spirit, determination and courage. They amaze us. They inspire us. They are our heroes.

POWERED BY

SCIENCE

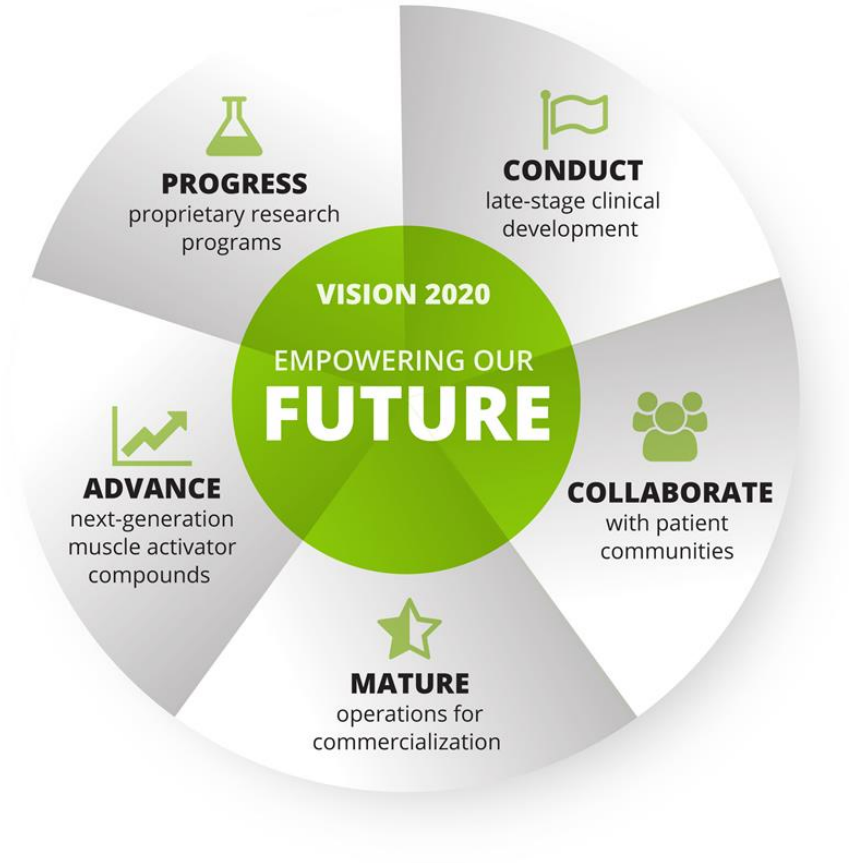


Late-Stage Pipeline of Novel Muscle Biology Compounds



Investigational products – not approved as safe or effective for any indication.

Vision 2020: Five-Year Strategic Roadmap



- **Progress** proprietary research programs focused on muscle contractility, growth and energetics into development under new collaborations
- **Advance** next-generation skeletal and cardiac muscle activator compounds into clinical development by leveraging existing research collaborations
- **Conduct** late-stage clinical development of novel, first-in-class muscle activators for the potential treatment of ALS, SMA, heart failure and other diseases impacting muscle function
- **Collaborate** with patient communities to support the urgent development of new medicines for diseases of impaired muscle function with pressing unmet medical needs
- **Mature** operations to enable development, registration and commercialization of muscle biology drug candidates across North America and Europe

Cytokinetics Business Strategy: Near-Term Validation Drives Long-Term Value

Skeletal Muscle

Reldesemtiv

Next-Gen FSTA

Diseases of Muscle Weakness & Dysfunction

Diseases of Muscle Dysfunction

- ALS
- SMA

Diseases of Aging/Muscle Weakness

- Heart Failure
- COPD
- Frailty
- Other Diseases Associated with Aging

Cardiac Muscle

Omecamtiv Mecarbil

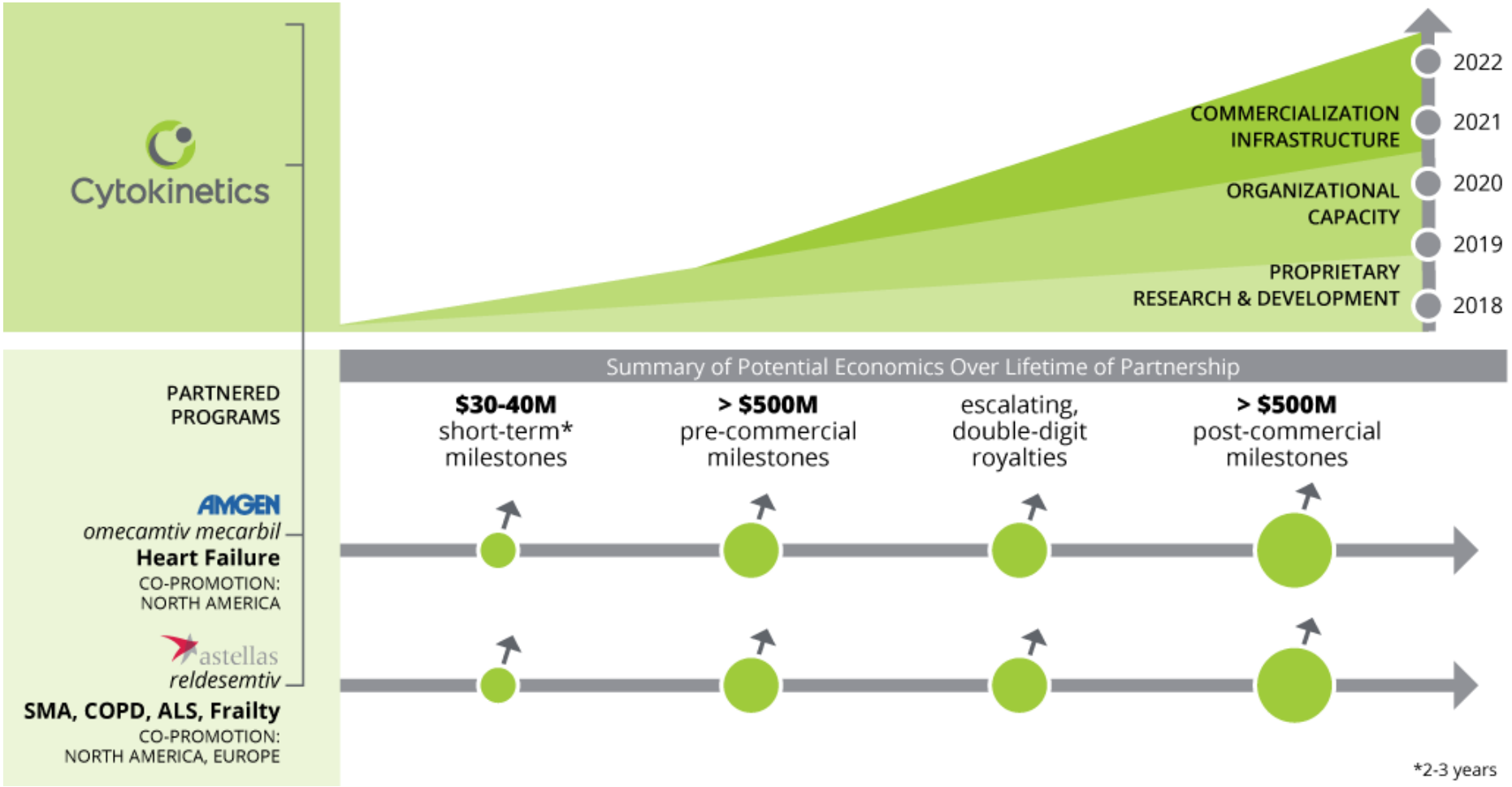
Next-Gen Cardiac Sarcomere Activator

Cardiac Sarcomere Directed Compound

Leverage Validation of Skeletal Muscle Activation in Severe Conditions of Muscle Dysfunction to Drive Expansion to Larger Diseases of Muscle Weakness Associated with Aging

Corporate Development Strategy

Leveraging Partnerships to Fund R&D and Commercialization



Cytokinetics Financing History

Strategic Partners and Institutional Investors Have Committed Approximately Equal Amounts of Capital to Cytokinetics

		Equity	Upfront Cash, Option, and Milestones	R&D Reimbur.	Total
Investors	Private Investors (VCs)	$116M			
	IPO	$94M			
	Public Post-IPO/Other	$414M			
	Total	**$625M**			**$625M**
Strategic Partners & Grants	Astellas	$10M	$130M	$86M[1]	$226M
	Amgen	$43M	$145M	$29M	$217M
	Royalty Pharma	$10M	$90M		$100M
	GSK	$24M	$22M	$33M	$78M
	AstraZeneca			$2M	$2M
	MyoKardia		$0M	$2M	$2M
	Global Blood			$2M	$2M
	Grants (ALS Assoc./ NINDS / other)		$6M		$6M
	Total	**$87M**	**$393M**	**$153M**	**$633M**

Note: Figures above exclude current debt outstanding of $30M.

(1) Includes Astellas' commitment to fund Cytokinetics' conduct of the Phase 2 clinical development of reldesemtiv in ALS (approximately $35.8 million) through 2018

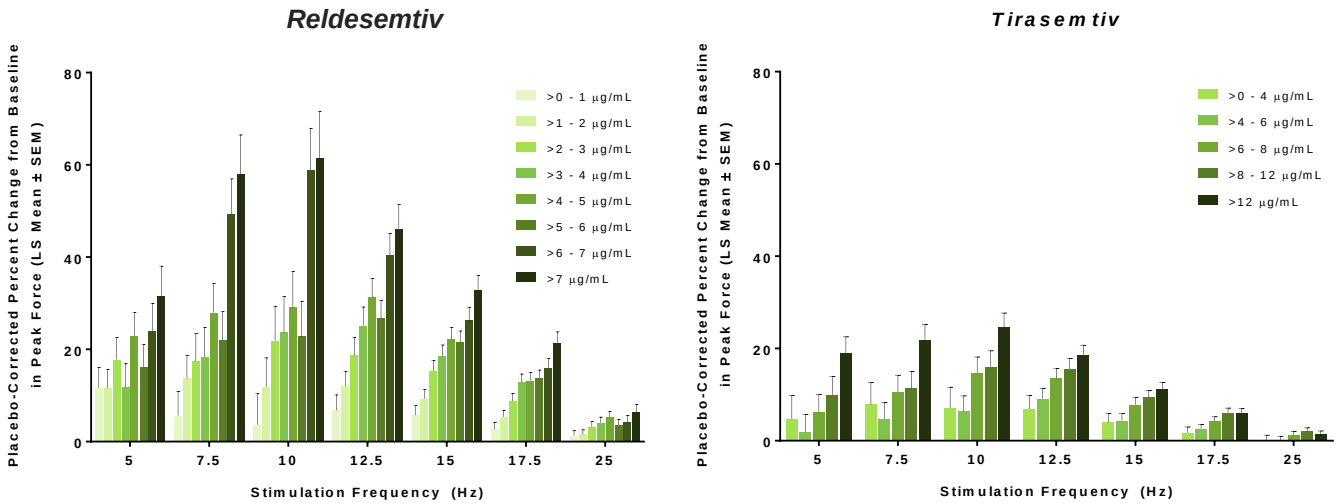
Reldesemtiv
(CK-2127107)

SMA
ALS
COPD
Frailty

Logan, diagnosed with SMA in 2008

Reldesemtiv: Potentially More Potent, Well Tolerated

- *Reldesemtiv* increased the force generated by the tibialis anterior muscle versus placebo in response to nerve stimulation in a dose, plasma concentration, and frequency-dependent manner
- The overall largest increase from baseline in peak force, compared to placebo, was **58.7** (10.2)% (least-squares mean [SE]) at a stimulation frequency of 10 Hz.
- The largest response *tirasemtiv* produced in a comparable study was a **24.5** (3.1)% increase in peak force at 10 Hz
- Single doses of *reldesemtiv* were well-tolerated in healthy volunteers at doses up to 4000 mg. No SAEs were reported, AEs were mild or moderate



Results from Three Phase 1 Studies of *Reldesemtiv* Published in *Muscle & Nerve*

Andrews JA, Miller TM, Vijayakumar V, Stoltz R, James JK, Meng L, Wolff AA, Malik FI. CK-2127107 amplifies skeletal muscle response to nerve activation in humans. *Muscle & Nerve*. 2017 Nov 18.

Reldesemtiv: Phase 1 Clinical Trials Program

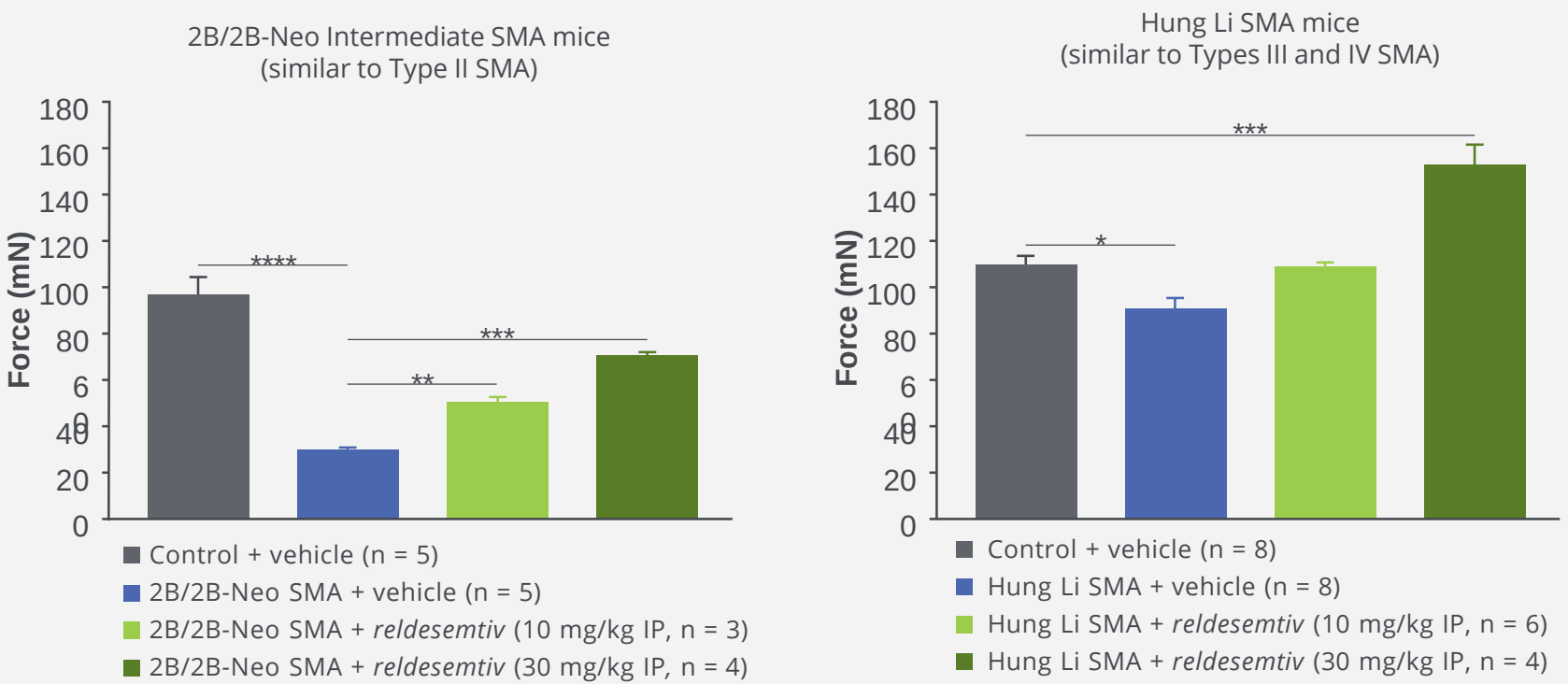
POPULATION (STUDY #)	N	FORM	TRIAL OBJECTIVE	RESULTS	STATUS
Healthy Subjects (CY 5011)	35	Oral	Assess safety and tolerability; Evaluate pharmacokinetics (increasing single doses)	Achieved highest planned dose; No emerging pattern of adverse events; Well tolerated	**Announced Feb 2010**
Healthy Subjects (CY 5012)	24	Oral	Assess safety, tolerability and pharmacokinetics in healthy young and elderly (multiple dose)	10-day course of either 300 mg or 500 mg twice daily was well tolerated by young and older Plasma concentrations achieved steady state; no age-related differences in PK	**Announced Jan 2010**
Healthy Subjects (CY 5013)	16	Oral	Assess pharmacodynamic effects	Statistically significant increases (versus placebo) in peak force; Well tolerated	**Announced Jan 2010**
Healthy Subjects (CY 5014)	24	Oral	Assess pharmacokinetics of two different physical forms of API in suspension	Well tolerated at 300 mg and 1000 mg; physical form selected	**Announced Oct 2011**
Healthy Subjects (CY 5015)	24	Oral	Assess pharmacokinetics of a tablet formulation; fed vs. fasted	Well tolerated at 250 mg, 500 mg and 1000 mg Tablet appropriate for use in potential future clinical trials	**Announced Dec 2010**

>100 Subjects; 5 Phase 1 Clinical Trials

Well Characterized Safety, Tolerability, PK/PD

Improved Muscle Function in Mouse Models of SMA

30 Hz Stimulation Force Response



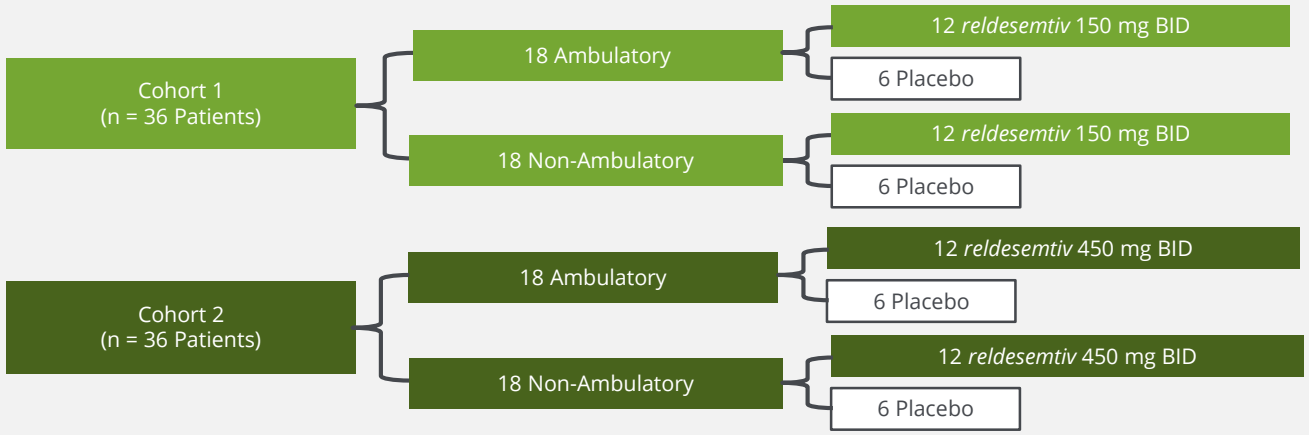
*P < 0.05, **P < 0.01, ***P < 0.001, ****P < 0.0001 vs. respective control
IP, intraperitoneal

Doses of *reldesemtiv* increased isometric force in situ in response to sub-tetanic nerve stimulation in mouse models, suggesting *reldesemtiv* may be viable to improve muscle function in SMA

Reldesemtiv: Four Trials with Data in 2018

SMA

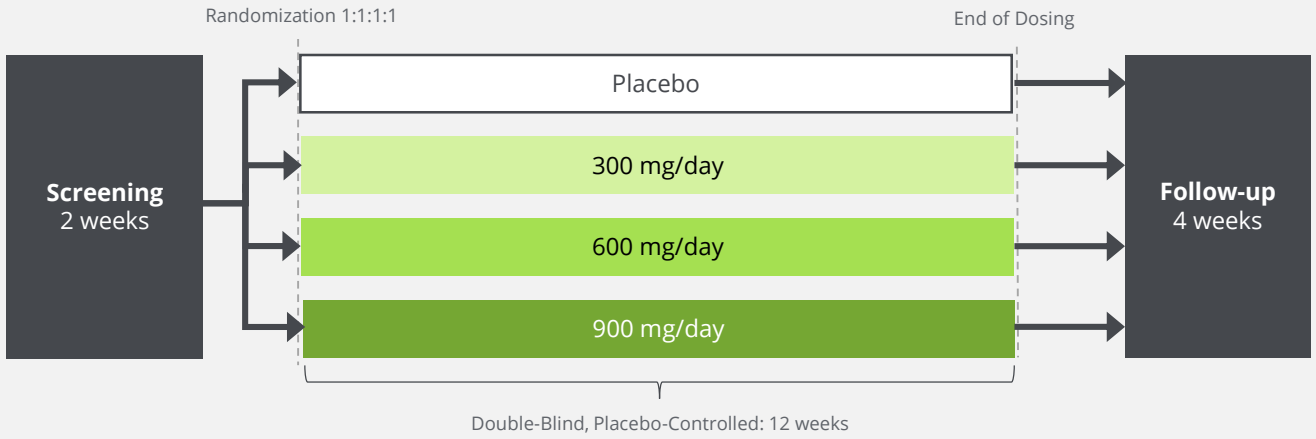
A severe, genetic, neuromuscular disease that manifests in various degrees of severity as progressive muscle weakness resulting in respiratory and mobility impairment



Phase 2 – CY 5021
Hypothesis generating study enrolling 72 people with Type II-IV SMA over 8 weeks. Study includes two dose cohorts, stratified by ambulatory versus non-ambulatory status, randomized 2:1 to receive *reldesemtiv* or placebo 2 times daily.

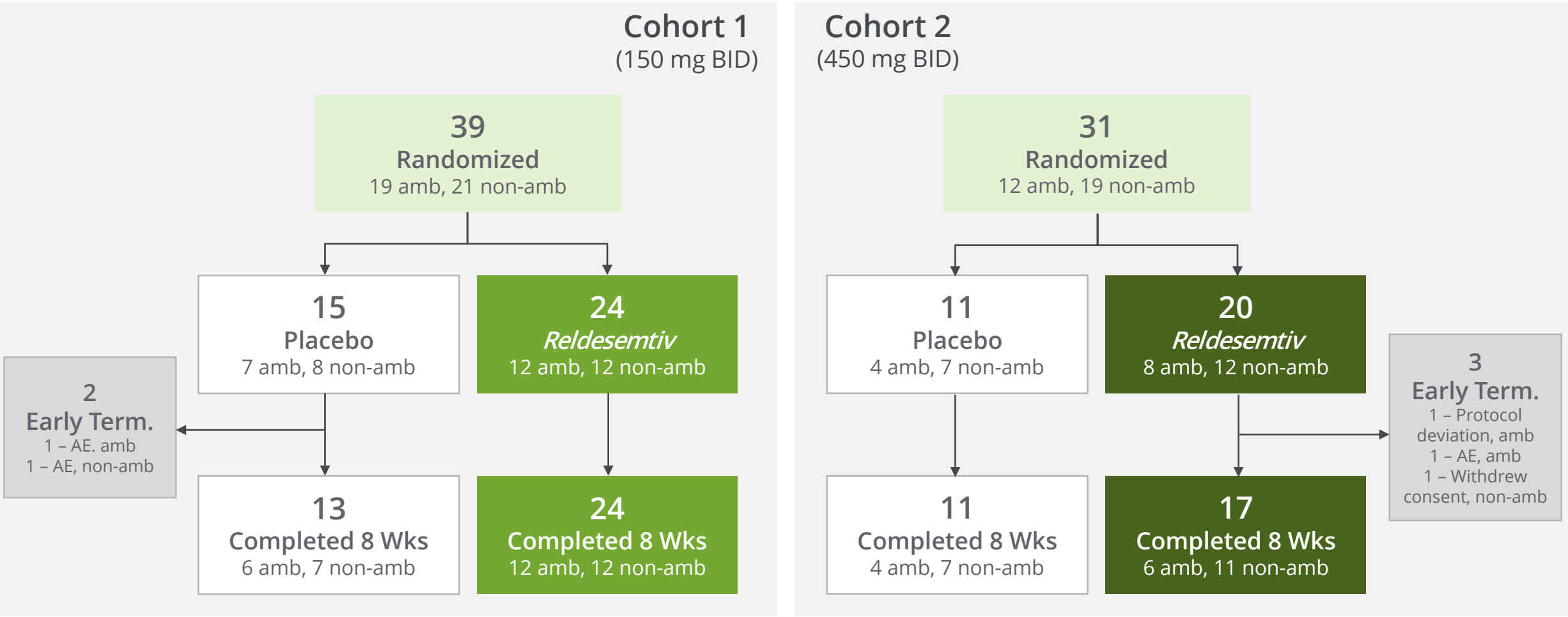
ALS

Progressive, degenerative neuromuscular disease that affects the nerve cells in the brain and spinal cord



Phase 2 – FORTITUDE-ALS
Parallel group, dose ranging study enrolling 450 patients with ALS in the US and Canada, evaluating change from baseline in the percent predicted slow vital capacity (SVC) at 12 weeks of treatment with *reldesemtiv* or placebo

CY 5021: Patient Disposition



CY 5021: Demographics & Baseline Characteristics

Demographics

	Placebo (N=27)	150 mg BID (N=26)	450 mg BID (N=17)
Age, years, mean (SD)	28.5 (16.03)	27.8 (11.96)	32.6 (17.92)
Age < 18 years, n (%)	8 (30.8%)	7 (29.2%)	5 (25.0%)
Male, n (%)	15 (57.7%)	14 (58.3%)	12 (60.0%)
Caucasian, n (%)	22 (84.6%)	23 (95.8%)	18 (90.0%)
BMI, mean (SD)	24.3 (7.39)	25.4 (9.24)	25.1 (5.52)
SMA Type II, n (%)	2 (7.7%)	3 (12.5%)	1 (5.0%)
SMA Type III, n (%)	24 (92.3%)	21 (87.5%)	19 (95.0%)
Ambulatory, n (%)	11 (42.3%)	12 (50.0%)	8 (40.0%)

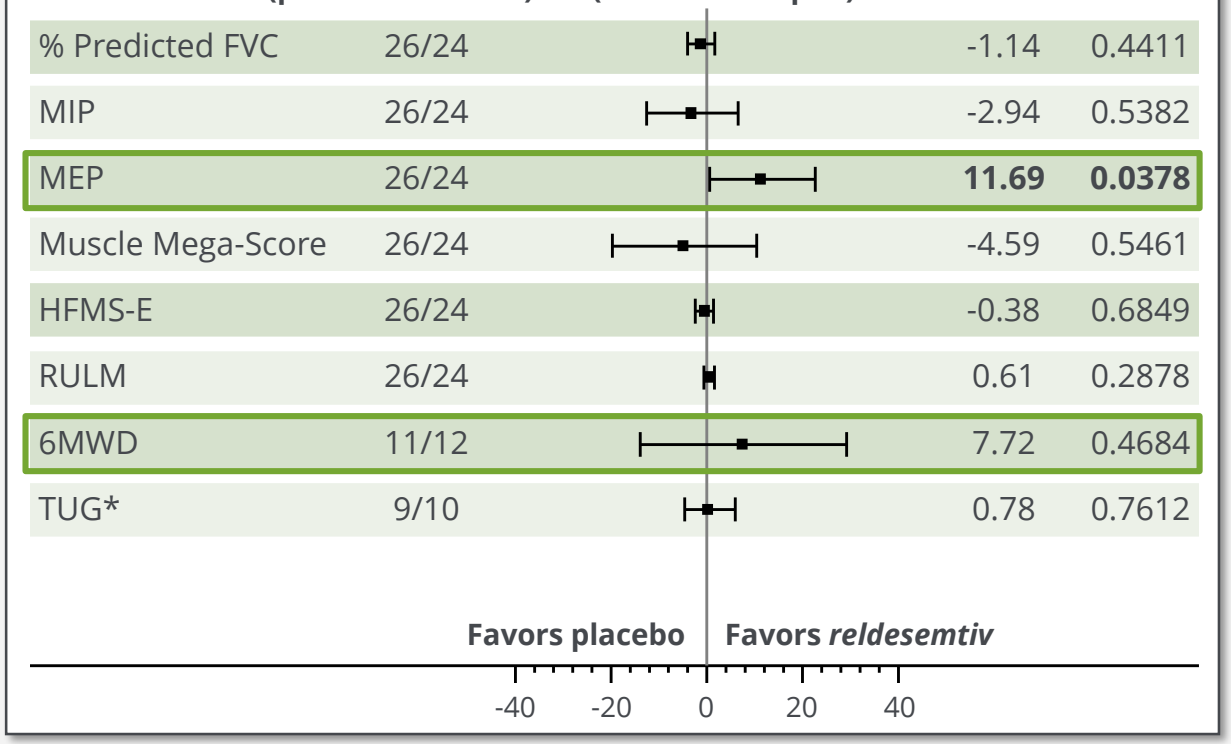
Baseline Characteristics

mean (SD)	Placebo (N=27)	150 mg BID (N=26)	450 mg BID (N=17)
% Predicted FVC	84.4 (22.39)	83.1 (22.05)	85.9 (21.21)
MEP (cm H2O)	86.5 (36.87)	94.0 (43.44)	88.9 (47.68)
MIP (cm H2O)	-106 (38.45)	-109 (44.18)	-101 (43.15)
HFMS-E Score	30.6 (16.60)	36.0 (17.17)	30.4 (16.25)
RULM Total Score	31.0 (8.74)	34.8 (7.90)	33.7 (8.00)
Timed Up and Go (sec)	21.5 (11.00)	15.7 (6.52)	22.8 (16.05)
Six Minute Walk (meter)	240.1 (111.8)	316.6 (68.96)	311.0 (107.3)
SMA-HI Total Score	33.1 (19.91)	NA	39.7 (17.11)

CY 5021: Change from Baseline at Week 8
All Participants

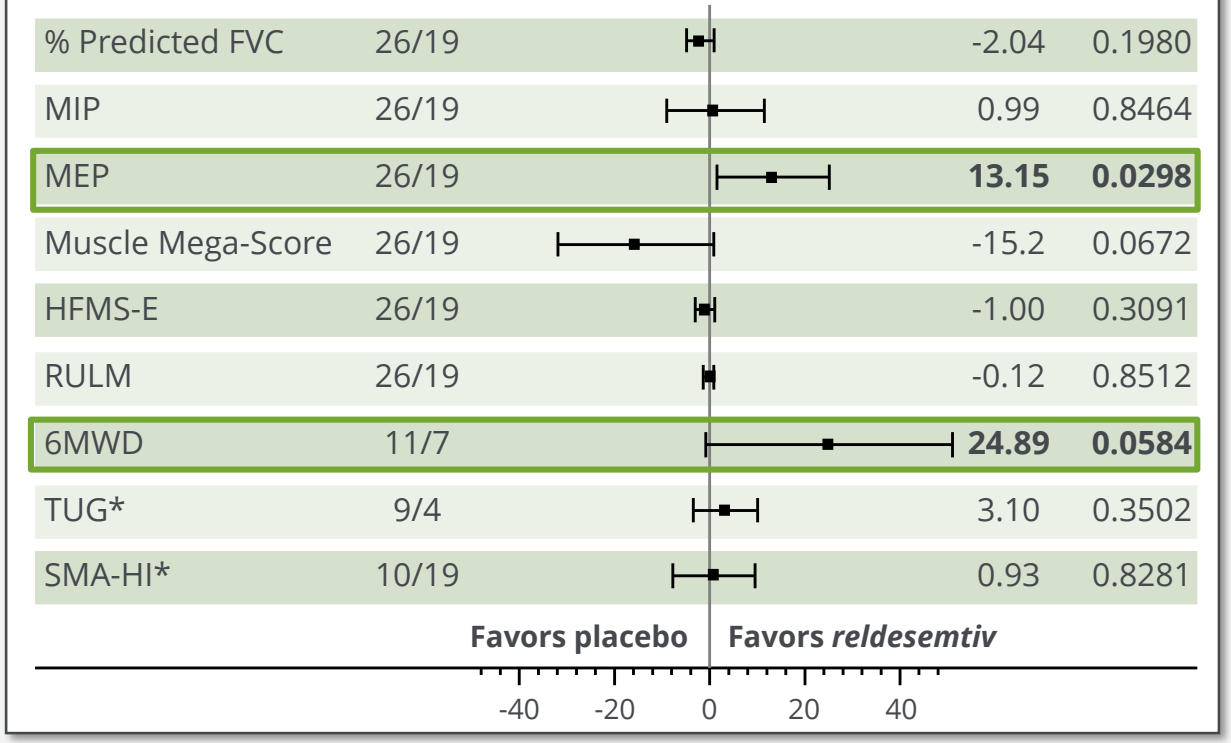
150 mg BID vs. Placebo

	No. of Patients (pbo / *reldesemtiv*)	Estimate	*P* value
% Predicted FVC	26/24	-1.14	0.4411
MIP	26/24	-2.94	0.5382
MEP	26/24	**11.69**	**0.0378**
Muscle Mega-Score	26/24	-4.59	0.5461
HFMS-E	26/24	-0.38	0.6849
RULM	26/24	0.61	0.2878
6MWD	11/12	7.72	0.4684
TUG*	9/10	0.78	0.7612



450 mg BID vs. Placebo

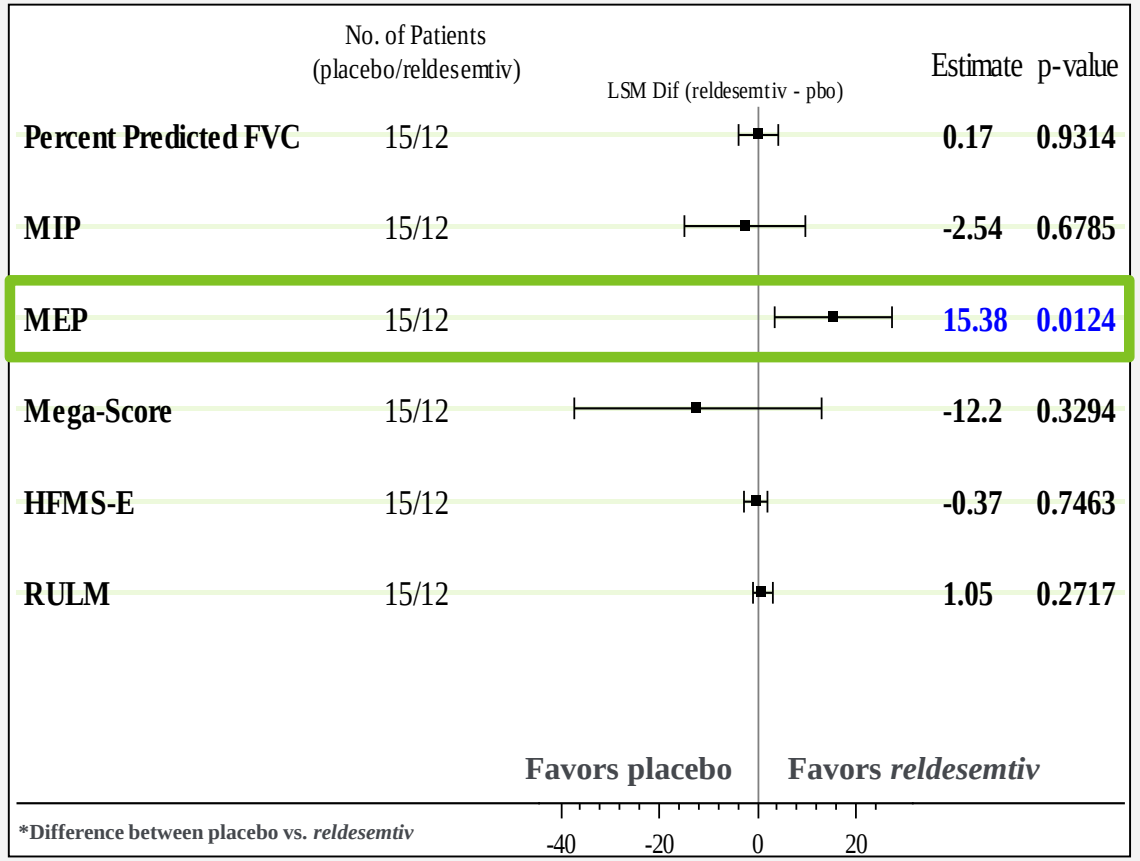
	No. of Patients (pbo / *reldesemtiv*)	Estimate	*P* value
% Predicted FVC	26/19	-2.04	0.1980
MIP	26/19	0.99	0.8464
MEP	26/19	**13.15**	**0.0298**
Muscle Mega-Score	26/19	-15.2	0.0672
HFMS-E	26/19	-1.00	0.3091
RULM	26/19	-0.12	0.8512
6MWD	11/7	**24.89**	**0.0584**
TUG*	9/4	3.10	0.3502
SMA-HI*	10/19	0.93	0.8281



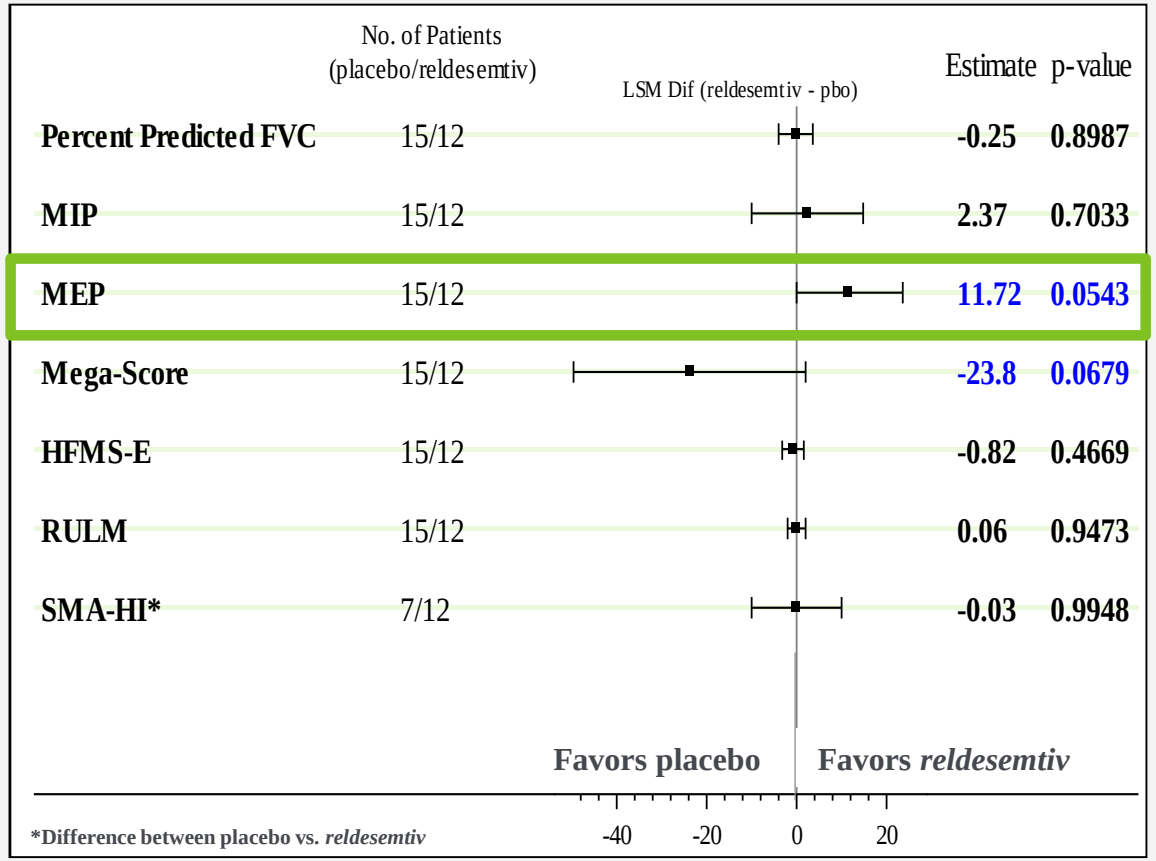
*Difference between placebo vs. *reldesemtiv*
pbo, placebo; LSM, least squares mean

CY 5021: Change from Baseline at Week 8 Non-Ambulatory Participants

150 mg BID vs. Placebo

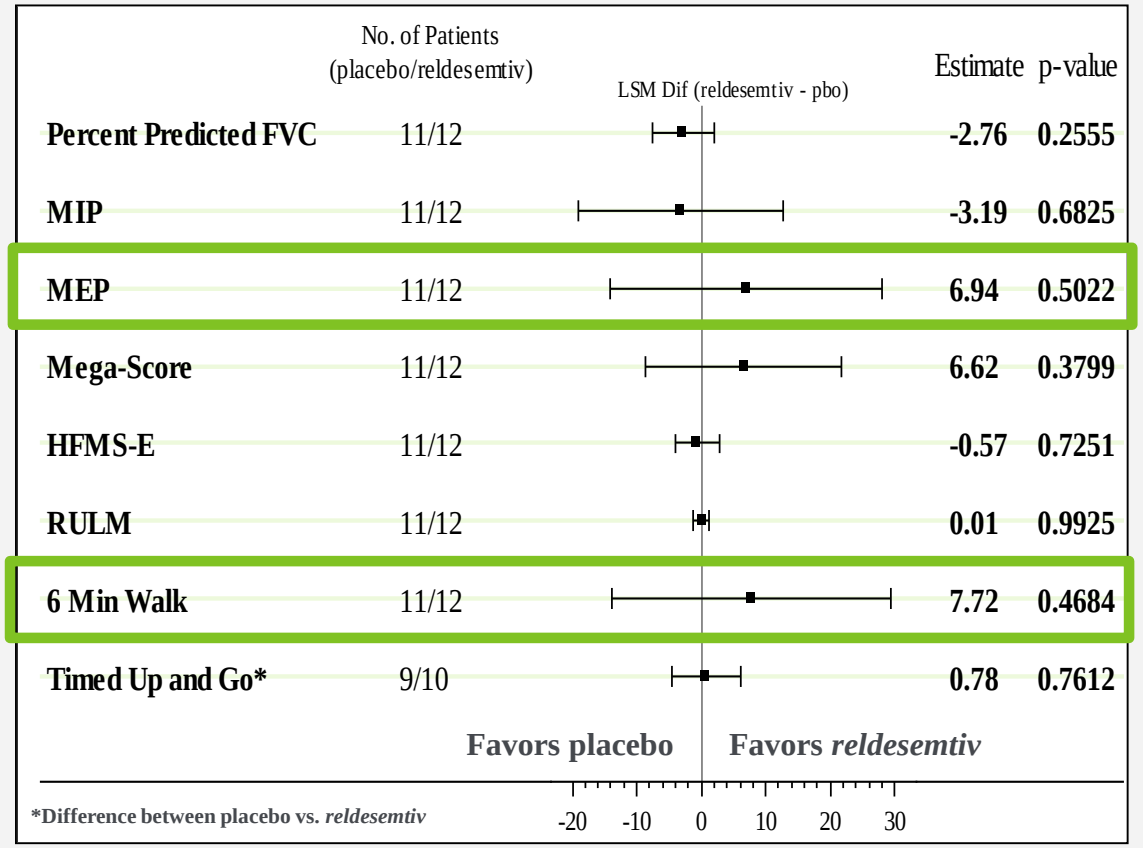


450 mg BID vs. Placebo

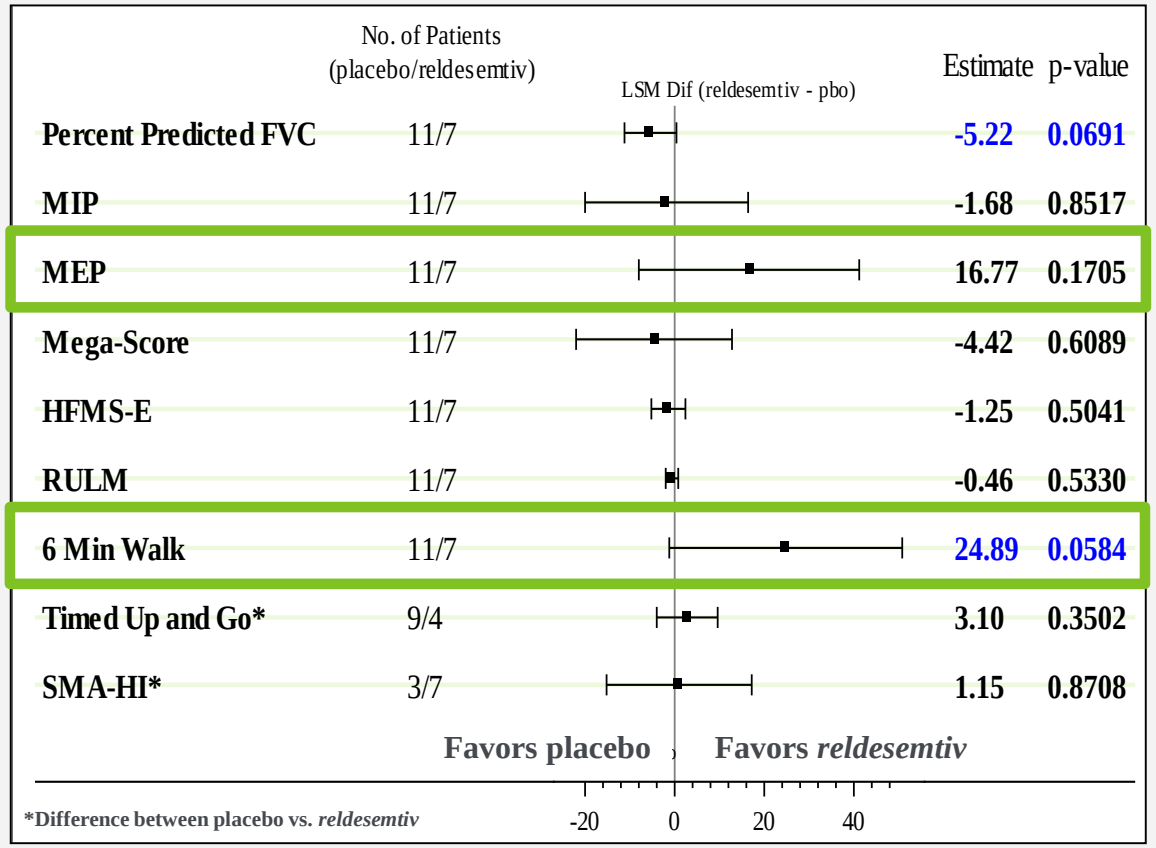


CY 5021: Change from Baseline at Week 8 Ambulatory Participants

150 mg BID vs. Placebo

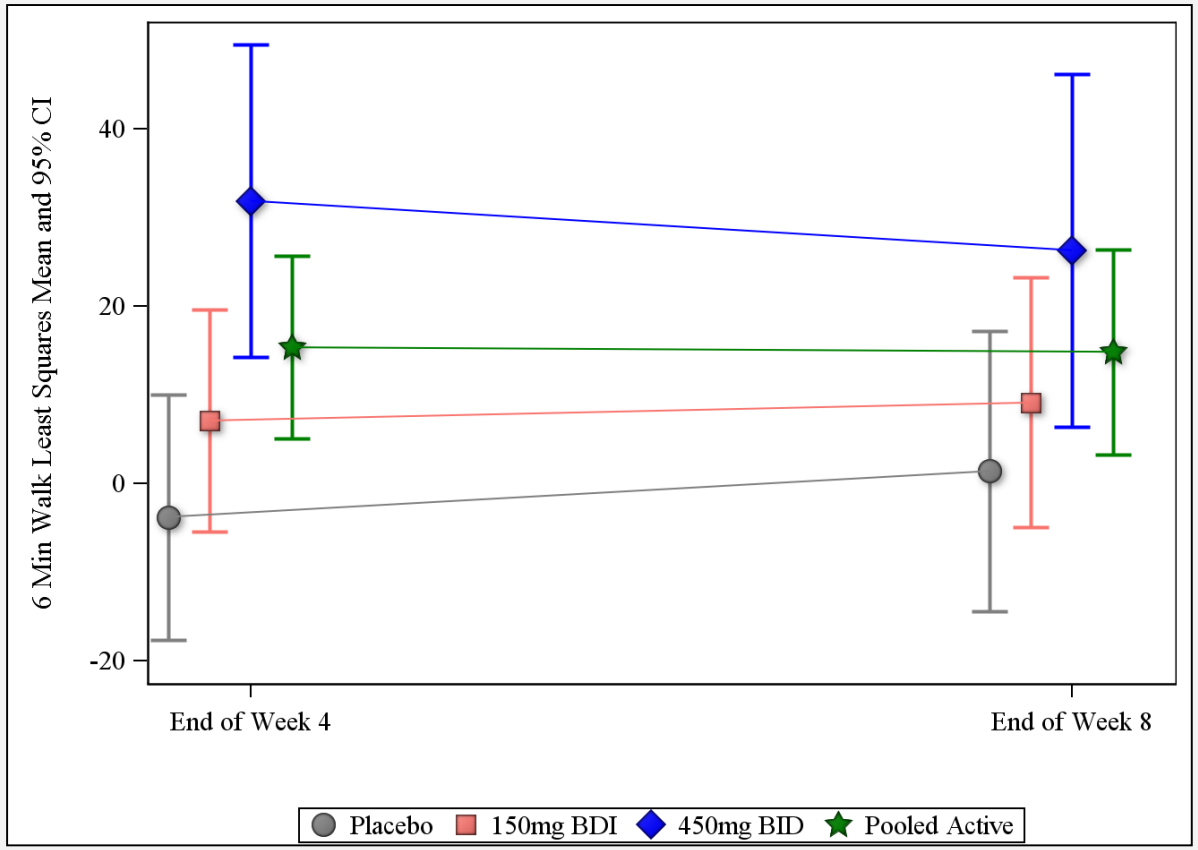


450 mg BID vs. Placebo

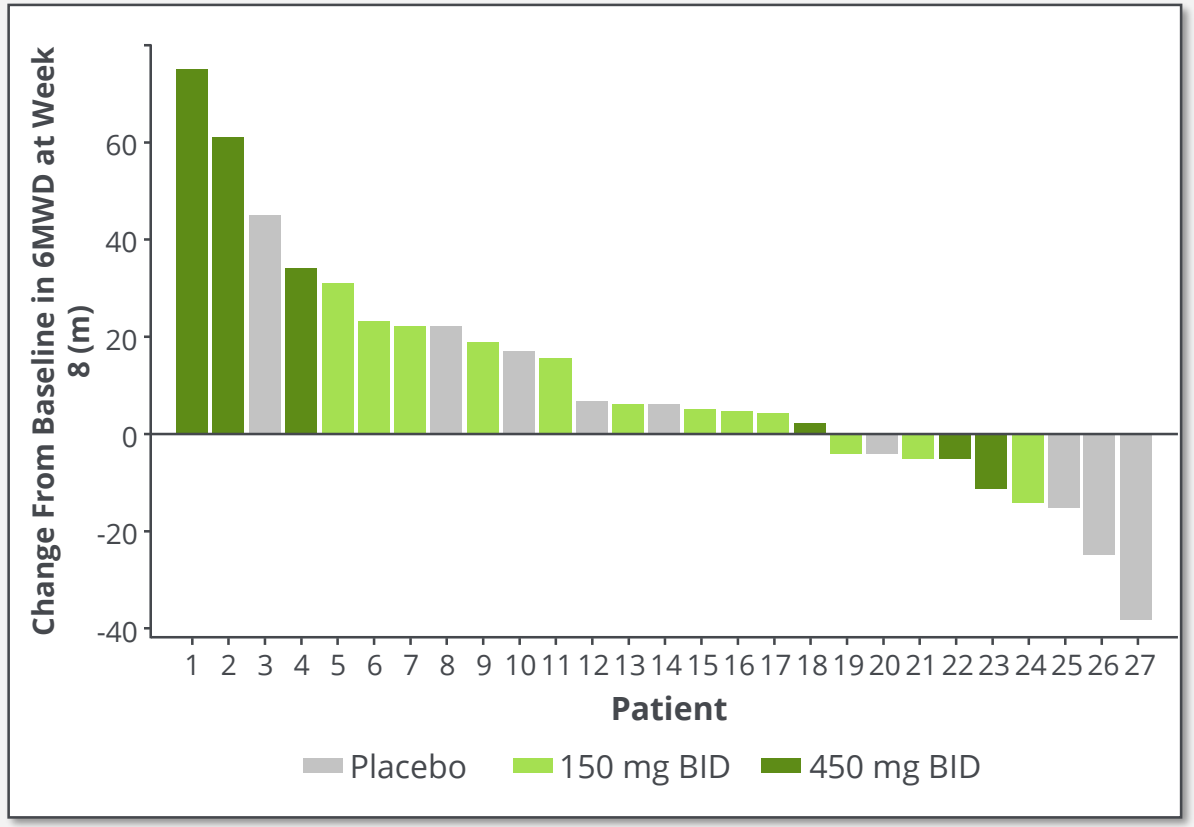


CY 5021: Dose-Dependent Increase in 6MWD

Change from Baseline Over Time

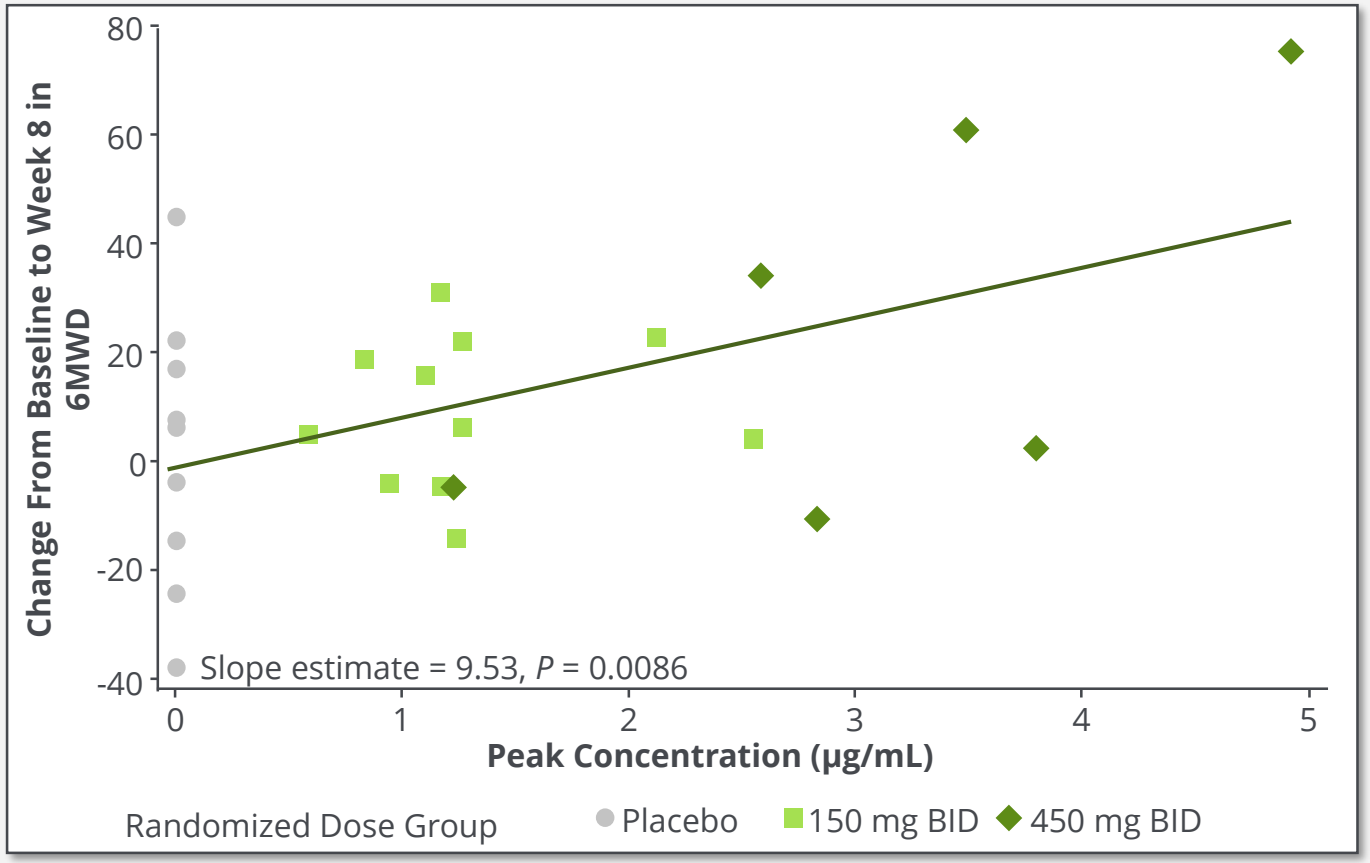


Change from Baseline at Week 8



CY 5021: Concentration-Dependent Increase in 6MWD

6 Minute Walk Change from Baseline at Week 8 versus C_{max}



C_{max}, maximum concentration
Data Transfer on 24MAY18

CY 5021: Adverse Events

Treatment-Emergent Adverse Events (≥ 2 Patients on *Reldesemtiv*)

Preferred Term, n (%)	Placebo (N=26)	150 mg BID (N=24)	450 mg BID (N=20)	All Active Doses (N=44)	Overall (N=70)
Patients with AEs	24 (92.3%)	20 (83.3%)	17 (85.0%)	37 (84.1%)	61 (87.1%)
Headache	5 (19.2%)	6 (25.0%)	5 (25.0%)	11 (25.0%)	16 (22.9%)
Constipation	0	3 (12.5%)	2 (10.0%)	5 (11.4%)	5 (7.14%)
Nausea	5 (19.2%)	3 (12.5%)	2 (10.0%)	5 (11.4%)	10 (14.3%)
Fatigue	4 (15.4%)	2 (8.33%)	2 (10.0%)	4 (9.09%)	8 (11.4%)
Diarrhoea	2 (7.69%)	2 (8.33%)	1 (5.00%)	3 (6.82%)	5 (7.14%)
Dyspepsia	0	2 (8.33%)	1 (5.00%)	3 (6.82%)	3 (4.29%)
Nasopharyngitis	3 (11.5%)	3 (12.5%)	0	3 (6.82%)	6 (8.57%)
Abdominal pain upper	1 (3.85%)	2 (8.33%)	0	2 (4.55%)	3 (4.29%)
Blood creatine phosphokinase increased	0	0	2 (10.0%)	2 (4.55%)	2 (2.86%)
Contusion	0	2 (8.33%)	0	2 (4.55%)	2 (2.86%)
Decreased appetite	1 (3.85%)	1 (4.17%)	1 (5.00%)	2 (4.55%)	3 (4.29%)
Fall	3 (11.5%)	1 (4.17%)	1 (5.00%)	2 (4.55%)	5 (7.14%)
Hypoaesthesia	0	1 (4.17%)	1 (5.00%)	2 (4.55%)	2 (2.86%)
Respiratory tract congestion	0	2 (8.33%)	0	2 (4.55%)	2 (2.86%)
Respiratory tract infection	0	1 (4.17%)	1 (5.00%)	2 (4.55%)	2 (2.86%)
Skin abrasion	0	0	2 (10.0%)	2 (4.55%)	2 (2.86%)
Upper respiratory tract infection	4 (15.4%)	0	2 (10.0%)	2 (4.55%)	6 (8.57%)

Adverse Events Resulting in Early Treatment Termination

Preferred Term, n (%)	Placebo (N=26)	150 mg BID (N=24)	450 mg BID (N=20)
Patients with AEs	2(7.69%)	0	1(5.00%)
Blood creatine phosphokinase increased	0	0	1(5.00%)
Asthenia	1(3.85%)	0	0
Gait disturbance	1(3.85%)	0	0
Muscular weakness	1(3.85%)	0	0

CY 5021: Potential Clinical Benefit of *Reldesemtiv* in SMA

- Treatment with *reldesemtiv* in CY 5021 showed potentially clinically beneficial effects in adolescent and adult patients with SMA as evidenced primarily by increases vs. placebo in:
  - Six Minute Walk Distance
  - Maximal Expiratory Pressure
- Data from CY 5021 support the evaluation of higher doses of *reldesemtiv* in future clinical trials in SMA given:
  - No efficacy plateau was demonstrated
  - No dose-limiting safety or tolerability issues were observed
  - Exposures were below those that were well tolerated and associated with increased pharmacodynamic activity in Phase 1, possibly due to a change in drug formulation

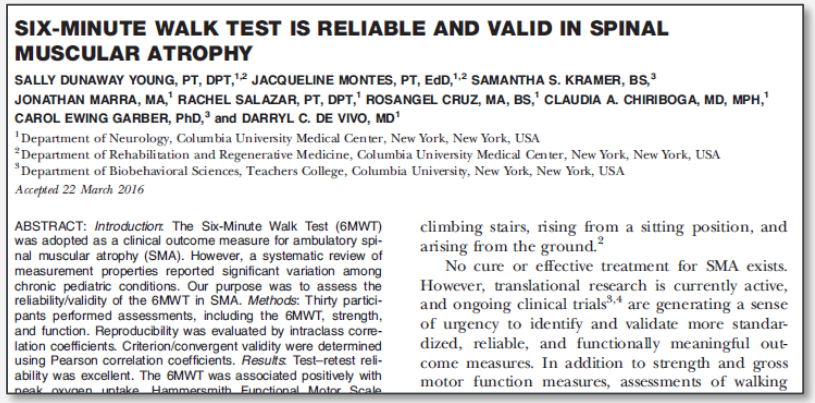
This hypothesis-generating study provides the first data indicating that a muscle-directed therapy, namely the FSTA, *reldesemtiv*, may be clinically beneficial in patients with SMA

6MWD is Validated, Approvable Endpoint

Drug Name	Disease	Duration of Treatment (weeks)	Study Size	Improvement in 6MWD compared to placebo (meters)	Indication	6MWD in Label
ALDURAZYME (laronidase)	MPS I Hurler/Hurler-Scheie	26	45	38 (p = 0.07)	Increase walking capacity	Yes
ELAPRASE (idursulfase)	MPS II Hunter syndrome	53	64	35 (p = 0.01)	Increase walking capacity	Yes
VIMIZIM (elosulfase)	MPS IVA Morquio A syndrome	24	176	22.5 (p = 0.017)	Treat MPS IVA	Yes
LUMIZYME (alglucosidase alpha)	GAA deficiency Pompe Disease	78	90	28 (p=0.06)	Pompe Disease	Yes
TRACLEER (bosentan)	Pulmonary Hypertension	213	16	35 (low dose), 54 (high dose) (p = 0.01, 0.0001)	Increase exercise ability	Yes
LETAIRIS (ambrisentan)	Pulmonary Hypertension	201	12	27 (low dose), 39 (high dose) (p = 0.008, <0.001)	Increase exercise ability	Yes

6 Minute Walk Distance Used as Endpoint in Clinical Trials Outside of SMA and Included in Labels

6MWD is Reliable, Valid Outcome Measure



SIX-MINUTE WALK TEST IS RELIABLE AND VALID IN SPINAL MUSCULAR ATROPHY

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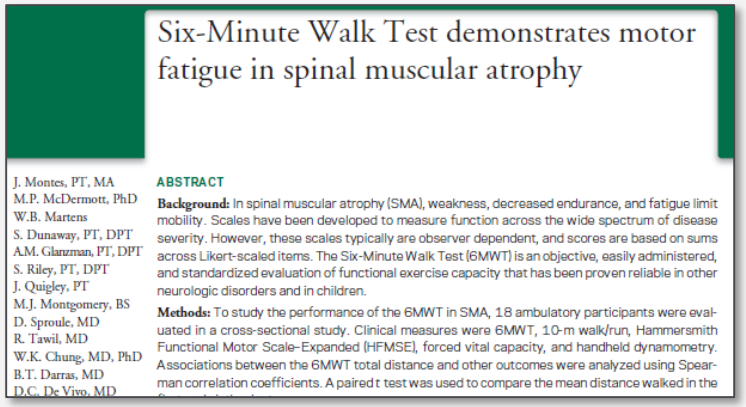
Accepted 22 March 2016

ABSTRACT: *Introduction*: The Six-Minute Walk Test (6MWT) was adopted as a clinical outcome measure for ambulatory spinal muscular atrophy (SMA). However, a systematic review of measurement properties reported significant variation among chronic pediatric conditions. Our purpose was to assess the reliability/validity of the 6MWT in SMA. *Methods*: Thirty participants performed assessments, including the 6MWT, strength, and function. Reproducibility was evaluated by intraclass correlation coefficients. Criterion/convergent validity were determined using Pearson correlation coefficients. *Results*: Test–retest reliability was excellent. The 6MWT was associated positively with peak oxygen uptake, Hammersmith Functional Motor Scale climbing stairs, rising from a sitting position, and arising from the ground.[2]

No cure or effective treatment for SMA exists. However, translational research is currently active, and ongoing clinical trials[3,4] are generating a sense of urgency to identify and validate more standardized, reliable, and functionally meaningful outcome measures. In addition to strength and gross motor function measures, assessments of walking

- **Systematic 22 study review** of reproducibility and validity of 6MWT showed:
  - Premier outcome measure in ambulatory SMA **captures disease severity, demonstrates all of the required measurement properties,** confirms **reliability and validity** of the 6MWT in ambulatory SMA patients
  - supports acceptance of the 6MWT as **a valuable outcome measure for ambulatory SMA** and the **primary endpoint of choice**

Dunaway Young, S., Montes, J., Kramer, S.S., Marra, J., Salazar, R., Cruz, R., Chiriboga, C.A., Garber, C.E. and De Vivo, D.C.. Six-minute walk test is reliable and valid in spinal muscular atrophy. *Muscle & nerve.* 2016 May 13.



Six-Minute Walk Test demonstrates motor fatigue in spinal muscular atrophy

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M.P. McDermott, PhD
W.B. Martens
S. Dunaway, PT, DPT
A.M. Glanzman, PT, DPT
S. Riley, PT, DPT
J. Quigley, PT
M.J. Montgomery, BS
D. Sproule, MD
R. Tawil, MD
W.K. Chung, MD, PhD
B.T. Darras, MD
D.C. De Vivo, MD

ABSTRACT

Background: In spinal muscular atrophy (SMA), weakness, decreased endurance, and fatigue limit mobility. Scales have been developed to measure function across the wide spectrum of disease severity. However, these scales typically are observer dependent, and scores are based on sums across Likert-scaled items. The Six-Minute Walk Test (6MWT) is an objective, easily administered, and standardized evaluation of functional exercise capacity that has been proven reliable in other neurologic disorders and in children.

Methods: To study the performance of the 6MWT in SMA, 18 ambulatory participants were evaluated in a cross-sectional study. Clinical measures were 6MWT, 10-m walk/run, Hammersmith Functional Motor Scale-Expanded (HFMSE), forced vital capacity, and handheld dynamometry. Associations between the 6MWT total distance and other outcomes were analyzed using Spearman correlation coefficients. A paired t test was used to compare the mean distance walked in the

- Cross-sectional study of 18 ambulatory participants showed:
  - 6MWT **correlates with established outcome measures** and is sensitive to fatigue-related changes
  - Assessments of walking ability and endurance are direct measures of functional mobility and considered **inherently clinically meaningful**
  - 6MWT has been **accepted by regulatory agencies as a clinically meaningful endpoint**

Montes J, McDermott MP, Martens WB, Dunaway S, Glanzman AM, Riley S, Quigley J, Montgomery MJ, Sproule D, Tawil R, Chung WK. Six-Minute Walk Test demonstrates motor fatigue in spinal muscular atrophy. *Neurology.* 2010, Mar 9.

Patient Commentary

I remember feeling like I was **gliding through the airport with ease**, not worried about having to stop 10 times between security and my gate. I didn't have to stop at all, and felt incredible as I moved through the airport with confidence.

I remember increased leg strength and stability, and I **felt more confident and able** to step off and on to curbs. I feel like my musculature changed too. I could see a stronger calf muscle for example. And walking longer distances was huge.

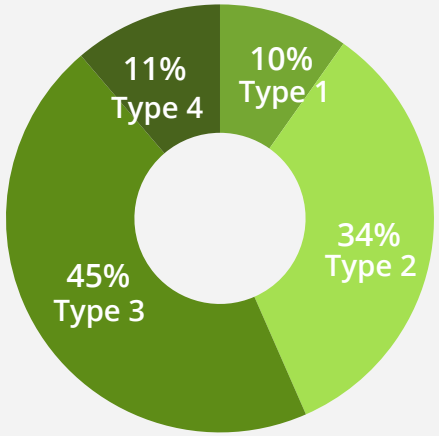
I needed to rake maple leaves out of our backyard and I was able to complete the entire process of raking. While I was fatigued from the task, it seemed like I was **able to recover faster** and **did not have the residual pain or stiffness** the next day. Prior to being on the drug I could complete the task, but would normally break it into smaller tasks with breaks in-between (sometimes a day or more) and would be very fatigued and had residual pain and stiffness.

Patients who received *reldesemtiv* in CY 5021 reported feeling stronger, less fatigued, and more confident in their functional ability

Growing Population of Ambulatory Patients

- **Clinical Manifestation:**
  - **Type 2** patients have delayed motor milestones; Most advanced milestone achieved is sitting unsupported. These children suffer from general weakness
  - **Type 3** patients can usually stand and walk but have increasingly limited mobility. They have difficulties running, climbing steps or rising from a chair, depending the severity of the disease
  - **Type 4** patients have similar symptoms to type 3s. Patients are typically able to walk but can no longer run

SMA Prevalence (US)



~10,000 living SMA patients

Life Expectancy	
Type 1	4 Years
Type 2	30 Years
Type 3	78 Years
Type 4	78 Years

2018: ~3,500-5,000 Ambulatory SMA patients

2023: Potentially up to 10,000 Ambulatory SMA patients*

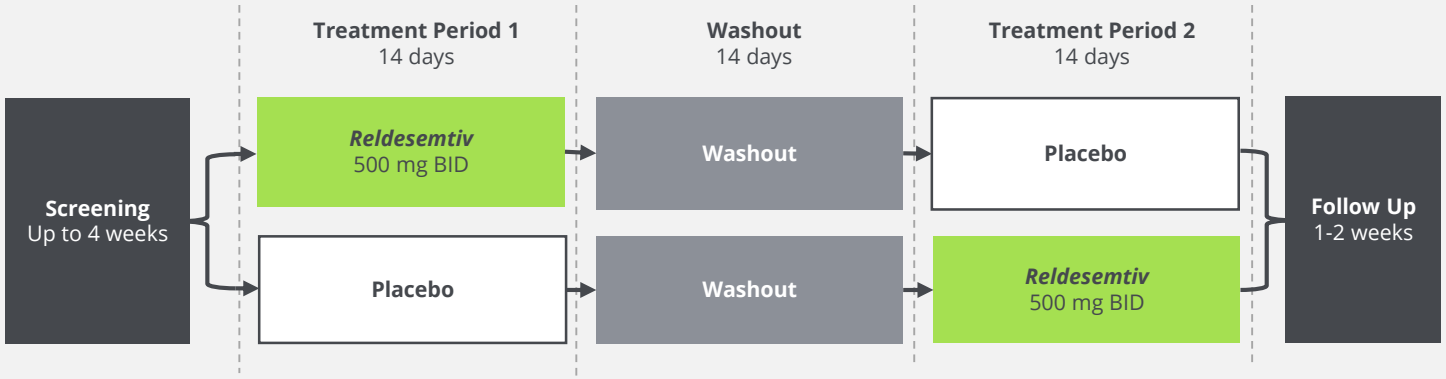
*Assuming advent of genetically directed therapies alter Type 1 and Type 2 phenotype

Source: Proprietary market research and company estimates

Reldesemtiv: Four Trials with Data in 2018

COPD

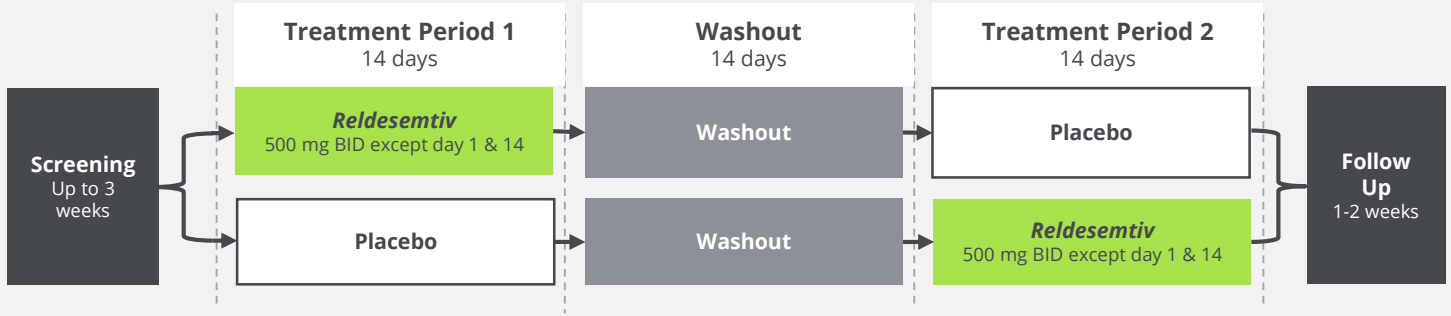
Progressive obstructive lung disease, and 3rd leading cause of death in the US behind cancer and heart disease



Phase 2 Trial
Two-period crossover study enrolling 40 patients with COPD to evaluate effect of *reldesemtiv* on exercise tolerance, assessed as change from period baseline (Day 14) in Constant Work Rate (CWR) endurance time over two weeks. Study includes 2 weeks of treatment with *reldesemtiv* (or placebo), 2 week washout, 2 weeks of placebo (or *reldesemtiv*)

Frailty

Up to 25% of older adults experience limitations in mobility, meaning higher rates of morbidity, mortality and hospitalizations, plus higher costs



Phase 1b Trial
Two-period crossover study of 60 elderly adults with limited mobility in US to evaluate effect of *reldesemtiv* on skeletal muscle fatigue, assessed as change from baseline versus 14 days of treatment in sum of peak torque during isokinetic knee extensions. 2 periods of 2 weeks of treatment with *reldesemtiv* (or placebo) separated by a 2 week washout period

Astellas Collaboration

Original Deal: 2013
Expanded to include SMA: 2014
Expanded to Include ALS: 2016
>$200M in Upfront Payments/R&D Sponsorship

- Collaborative research program on next-generation skeletal muscle activators through 2019 (under Astellas' sponsorship)
- Development of *reldesemtiv* in non-neuromuscular and neuromuscular indications (e.g., SMA and ALS)
- Cytokinetics conducts Phase II clinical trials of *reldesemtiv* in SMA and ALS (at Astellas' expense)
- Astellas primarily responsible for development; Cytokinetics' option to co-fund (e.g., SMA) and co-funding obligation (e.g., ALS)
- Cytokinetics has option to conduct early-stage development for certain indications at its expense, subject to reimbursement

Astellas to commercialize products subject to Cytokinetics' option to co-promote for neuromuscular indications in US, Canada, and Europe; **Cytokinetics** has the option to co-promote for all other indications in the US and Canada

Astellas will reimburse Cytokinetics for certain expenses associated with co-promotion activities

Cytokinetics eligible to receive over $600 mm in pre-commercialization and commercialization milestones plus royalties, which are increased for co-funded products

Reldesemtiv: 2018 Milestones

Expect Data from Three Mid-Stage Trials in 2H 2018

Ongoing trials in COPD, ALS and Elderly Adults with Limited Mobility

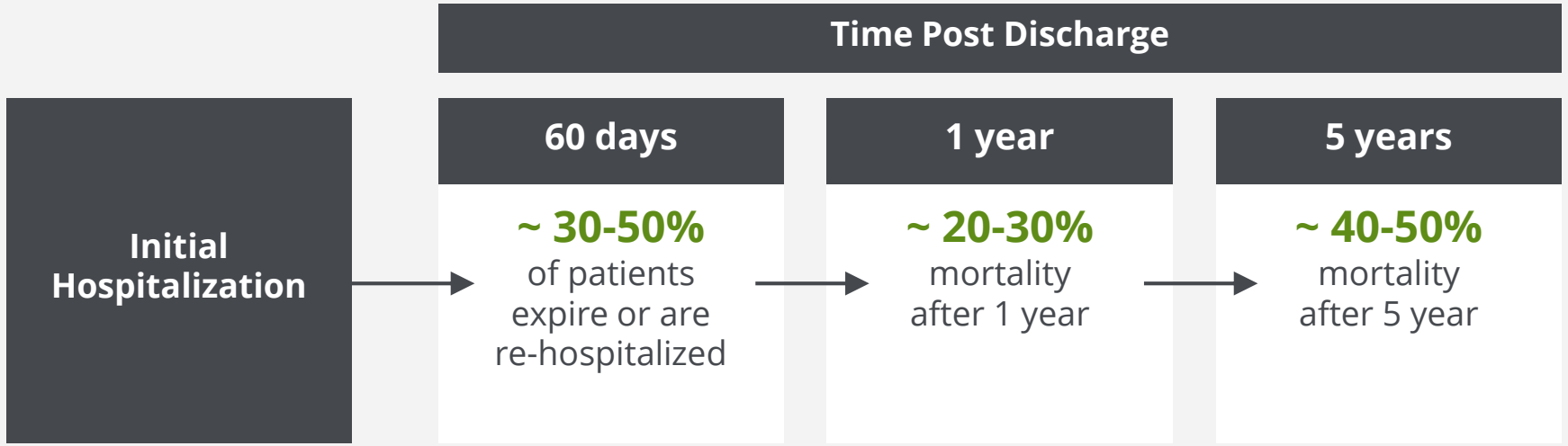
Omecamtiv Mecarbil

Heart Failure

Tomas, diagnosed with Heart Failure in 2014

High Mortality and Hospital Readmission Rates

Poor Outcomes in Patients Hospitalized with Heart Failure



Acute heart failure is the most frequent cause of hospitalization in people > 65

> 1 million hospitalizations with primary diagnosis of heart failure annually in US

Adams et al. Am Heart J 2006; 149:209-16
Dickstein et al. Eur Heart J 2008;29:2388-442
Chen et al. JAMA 2011;306:1669-78

Loehr et al. Am J Cardiol 2008;101:1016-22
Roer et al. Circulation 2012;125:32-220

Significant Unmet Need Exists To Address Mortality And Hospital Readmission

Unmet Need for HFrEF

Reduction in mortality & hospital visits	Physicians say Entresto has prolonged survival, decreased hospital visits, but still **see need for other therapies that reduce mortality**
Drugs that do not affect renal function	Most physicians recognize negative effect therapies such as aldosterone antagonists have **on renal function**
Drugs that do not affect BP	BP often limiting factor for up titration and therapy initiation; Need efficacious drugs **that do not result in hypotension**
Drugs with molecular targets & inotropic agents	Need drugs that target **novel/more specific molecular targets**; Need targets other than the neurohormonal pathway; Need for inotropic drugs as support agents
Disease modifying therapies	Need therapies **that offer contractile support** Increased EF most frequently mentioned desired measure
Drugs that increase QoL	Patient management will improve **with drugs that increase QoL;** Patient QoL decreases as they lose the ability to perform daily tasks

Proprietary Market Research Suggests Need for Novel Therapy

Omecamtiv Mecarbil

Effects Observed in Pre-Clinical and Clinical Studies

- Increased duration of systole
- Increased stroke volume
- Ca — No increase in myocyte calcium
- Decreased heart rate
- No change in blood pressure
- O_2 — No increase in oxygen consumption
- No change in rate of contraction

Omecamtiv Mecarbil: Phase 1 Clinical Trials Program

Study #	N	Form	Trial Objectives	Results	Status
Healthy Volunteers* (CY 1111)	**34**	**IV**	Safety and Tolerability MTD / Plasma Concentration	PK: Linear, Dose Proportional Echo: Dose and concentration dependent increases in cardiac function Safety: Well- tolerated up to MTD	Announced 2006
Healthy Volunteers (CY 1011)	**10**	**IV Oral**	Oral Bioavailability	100% Bioavailability No first-pass hepatic metabolism	Announced 2006
Healthy Volunteers (CY 1016)	**12**		Modified Release Pharmacokinetics	Prototype selected	Announced June 2008
Healthy Volunteers (CY 1015)	**32**	**Oral**	Single dose to multi-dose Pharmacokinetics	Dose-proportionality No gender differences	Announced June 2008
Healthy Volunteers (CY 1013)	**24**	**Oral**	Drug/Drug Interaction	Absence of metabolism by CYPs 3A4 and 2D6 had minimal effect on *omecamtiv mecarbil* pharmacokinetics	Announced Dec 2008
Healthy Volunteers (AMG 20090727)	**65**	**Oral**	Modified Release Pharmacokinetics	MR formulations selected for study in Ph2	Completed 2012
Healthy Volunteers (AMG 2009229)	**14**	**IV Oral**	ADME Mass balance and metabolite ID	No metabolites in plasma No significant new metabolites identified	Completed 2012
Renal Patients (AMG 20080676)	**12**	**Oral**	Safety and Tolerability Pharmacokinetics	No clinically meaningful differences in *omecamtiv mecarbil* pharmacokinetics in patients undergoing hemodialysis	Completed 2013
Healthy Volunteers (CY 1211)	**36**	**Oral**	Safety and Tolerability Pharmacokinetics Japanese vs. Caucasian	No meaningful differences between Japanese and Caucasian volunteers relating to safety and pharmacokinetics	Completed 2014

>200 Subjects; 9 Phase 1 Clinical Trials

Well Characterized Safety, Tolerability, PK/PD

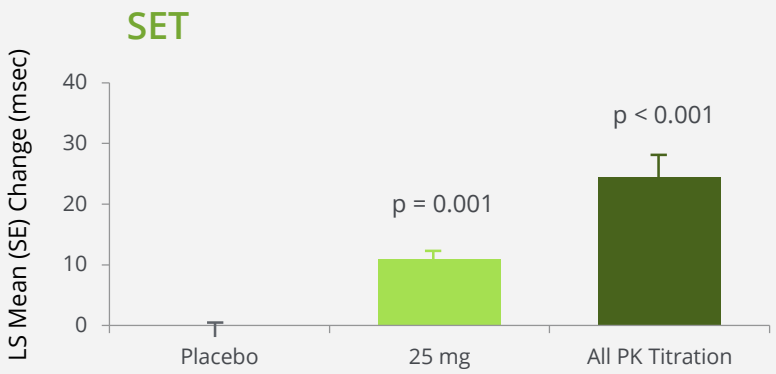
Omecamtiv Mecarbil: Phase 2 Clinical Trials Program

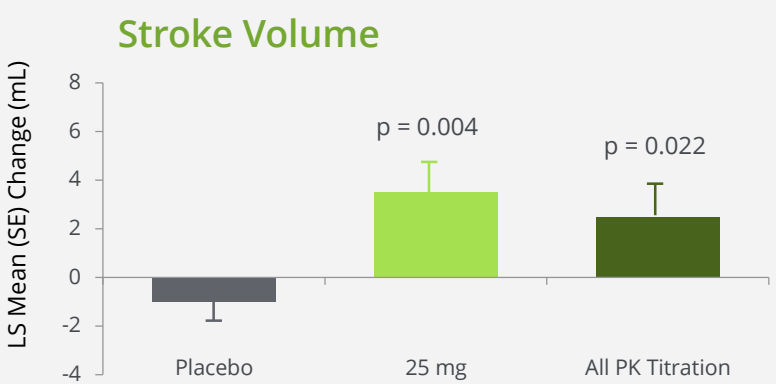
Study #	N	Form	Trial Objectives	Results	Status
Stable Heart Failure (CY 1121)**	**45**	**IV**	Safety and tolerability, PK/PD dose-response	Safety: Well-tolerated; cardiac ischemia noted at higher exposures Statistically significant increases: Stroke Volume, Fractional Shortening, Systolic Ejection Time, Ejection Fraction	Announced Mar 2009
Ischemic Cardiomyopathy (CY 1221)	**94**	**IV Oral**	Safety	Findings supported progression into Phase IIb	Announced June 2009
ATOMIC-AHF	**606**	**IV**	Safety and tolerability, PK/PD, potential efficacy	Safety: Overall SAE profile and tolerability similar to placebo PK: Similar to healthy volunteers and stable HF patients PD: Systolic ejection time significantly increased consistent with MOA Efficacy: Primary endpoint of dyspnea response not met; nominally significant dose- and concentration-related trends in dyspnea response observed	Announced Sept 2013
COSMIC-HF	**520**	**Oral**	Safety and tolerability, PK/PD	Safety: AE's, including SAE's, appeared to be comparable to placebo PK: PK-based dose titration adequately controlled patient exposure; resulted in statistically significant decreases in cardiac dimensions and heart rate in dose-titration group PD: Statistically significant improvements in measures of cardiac function - systolic ejection time, stroke volume and N-terminal-pro-brain-natriuretic peptide	Announced Oct 2015

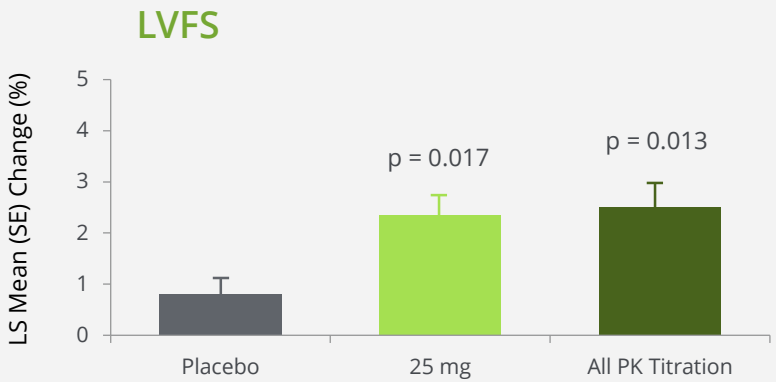
>1000 Subjects; 4 Phase 2 Clinical Trials

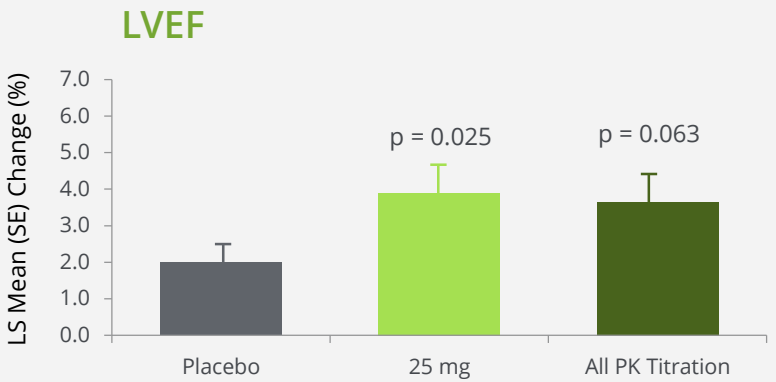
Pharmacodynamic Effects

Dose-dependent Increases in Cardiac Performance





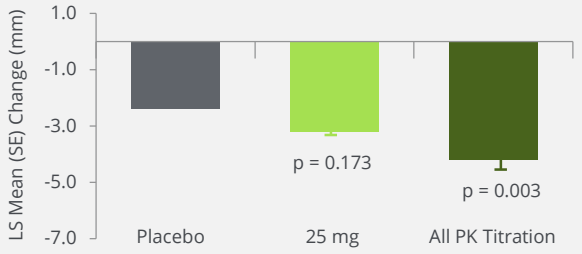




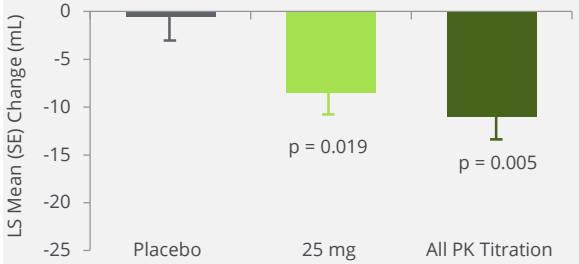
LVEF, left ventricular ejection fraction; LVFS, left ventricular fractional shortening; SE, standard error; SET, systolic ejection time

Reductions in Heart Volume & Dimensions, as well as Heart Rate & Biomarker of Wall Stress

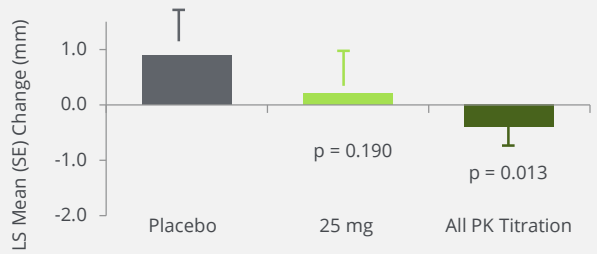
LVESD



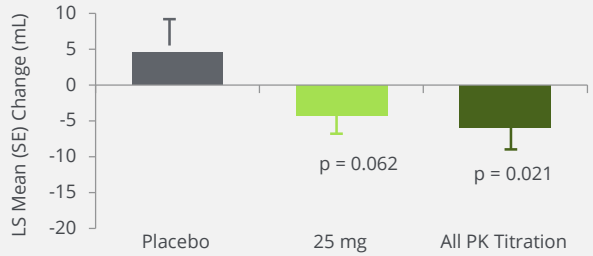
LVESV



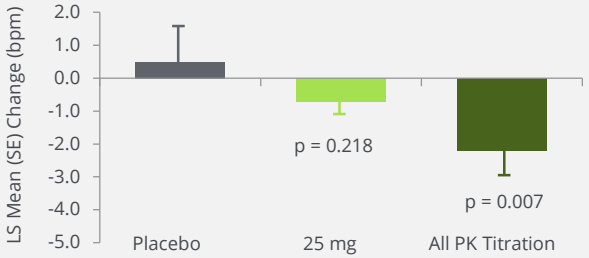
LVEDD



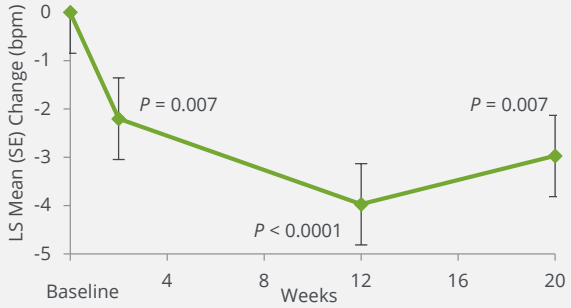
LVEDV



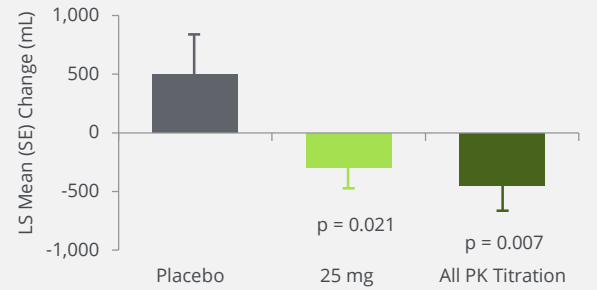
Heart Rate



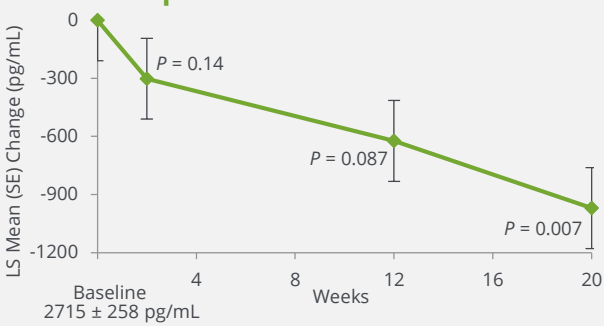
Heart Rate



NT-proBNP



NT-proBNP



LVESD left ventricular end systolic diameter LVEDD left ventricular end diastolic diameter
LVESV left ventricular end systolic volume LVEDV left ventricular end diastolic volume

Phase 3 Outcomes Trial Approaching 50% Enrollment

GALACTIC-HF

Study Overview

- Enrolling 8,000 patients at 900 sites in 35 countries

Primary endpoint

- Composite of time to CV death or first HF event*, whichever occurs first

Secondary endpoints

- Time to CV death
- Change in Kansas City Cardiomyopathy Questionnaire Total Symptoms Score (KCCQ TSS) from baseline to Week 24
- Time to first HF hospitalization
- Time to all-cause death

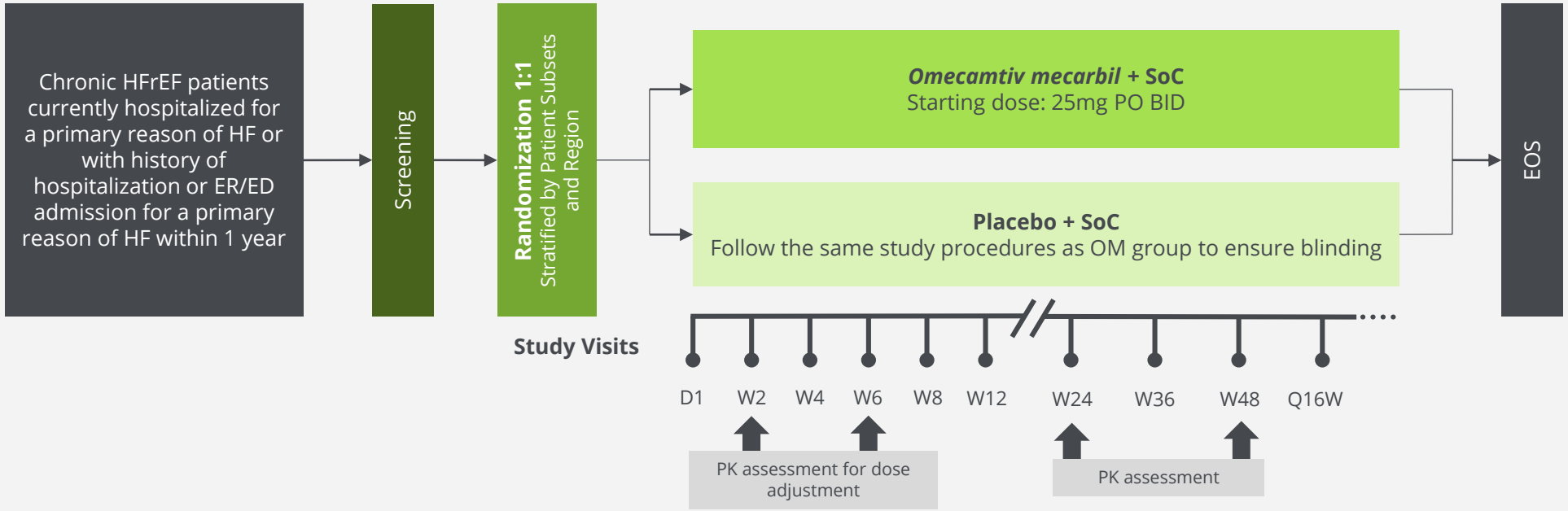
*An HF event defined as the presentation of the subject for an urgent, unscheduled clinic/office/ED visit, or hospital admission, with a primary diagnosis of HF, where the patient exhibits new or worsening symptoms of HF on presentation, has objective evidence of new or worsening HF, and receives initiation or intensification of treatment specifically for HF (Hicks et al, 2015). Changes to oral diuretic therapy do not qualify as initiation or intensification of treatment.

Global **A**pproach to **L**owering **A**dverse **C**ardiac Outcomes **T**hrough **I**mproving **C**ontractility in **H**eart **F**ailure

Design Overview

GALACTIC-HF

2 years enrollment, approx. 4 years total follow-up/study period



~8000 patients randomized 1:1 to *omecamtiv mecarbil* versus placebo, stratified by inpatient versus outpatient at randomization

Omecamtiv mecarbil started at 25 mg BID: PK-guided dose optimization to one of 3 target doses (25, 37.5, 50mg BID)

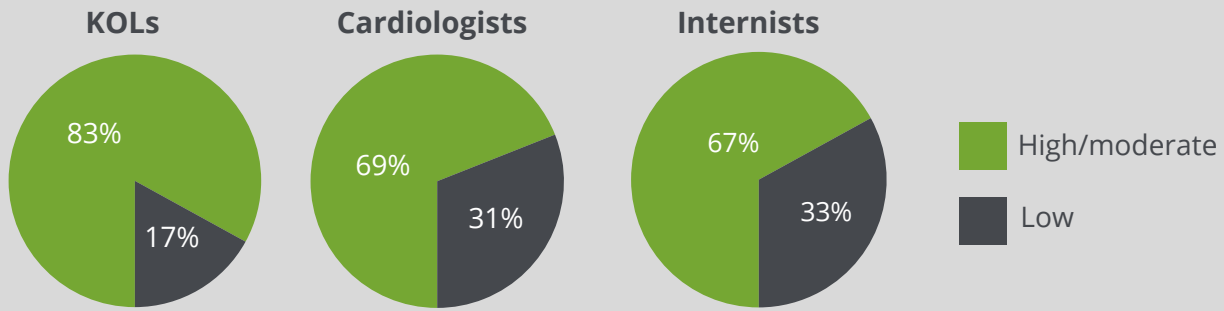
Event-driven; patients will be followed indefinitely until CV death events have accumulated (90% powered for CV Mortality)

Second Phase 3 Clinical Trial of *Omecamtiv Mecarbil*

- Cytokinetics and Amgen finalizing plans for second Phase 3 trial of *omecamtiv mecarbil*
- The trial is intended to evaluate its potential effect on exercise performance
- Regulatory and feasibility assessments in 2018

- Increased exercise capacity has positive influence on physicians' perception of *omecamtiv mecarbil* because it addresses unmet need and improves QOL*

Impact of Increased Exercise Performance on Physician Perception



*proprietary research

Second Phase 3 Trial of *Omecamtiv Mecarbil* to be Conducted by Cytokinetics Concurrent with GALACTIC-HF and at Amgen's Expense

Amgen Collaboration

Purchase Option: 2006
Exercise Option Ex-Japan: 2009
Expanded to Include Japan/Purchase Equity: 2013
Received >$200M over 11 Years

Amgen responsible for development and commercialization subject to Cytokinetics' participation rights*

Cytokinetics can earn over $650 mm in milestone payments

*Servier has a sub-license from Amgen to commercialize *omecamtiv mecarbil* in Europe and certain other countries.

COMMERCIALIZATION:

- Cytokinetics may receive escalating double-digit royalties
- Cytokinetics to co-fund Phase 3 development program
- Co-fund enables co-promote NA
- Cytokinetics reimbursed for certain sales force activities

Royalty Pharma Agreement

Paid $100M for 4.5% royalty on worldwide sales of *omecamtiv mecarbil*: 2017

- Royalty rate may increase up to additional 1% associated with timing of US approval
- Cytokinetics agreed to exercise option to co-invest $40 mm in Ph 3 development program in exchange for up to incremental 4% royalty on increasing worldwide sales outside of Japan
- Cytokinetics retains right to receive >$600 mm in additional potential milestone payments and escalating double-digit royalties that may exceed 20% on tiered worldwide sales outside Japan; lower royalty rate in Japan

Cytokinetics gains right to co-promote *omecamtiv mecarbil* in institutional care settings in North America, with reimbursement from Amgen for certain sales force activities

Joint commercial operating team responsible for commercialization program

Omecamtiv Mecarbil: 2018 Milestones

Expect to Complete Enrollment in GALACTIC-HF Within One Year

Expect to Finalize Preparations for the Second Phase 3 Trial of *Omecamtiv Mecarbil*

Estimate 2-3 Years to Complete GALACTIC-HF

Expect Results From Both Trials in Similar Timeframe

CORPORATE

PROFILE

Q1 2018 Condensed Balance Sheet

	3/31/2018 (in millions)
Presentation	
Cash and investments	$255.5
Other assets	$24.4
Total assets	$279.9
Long term debt	$32.0
Liability related to sale of future royalties	$108.7
Other liabilities	$39.6
Total liabilities	$180.3
Working capital	$233.7
Accumulated deficit	-$658.3
Stockholders' Equity	$99.6
Shares outstanding	54.2
Fully diluted shares outstanding	65.3

2018 Financial Guidance

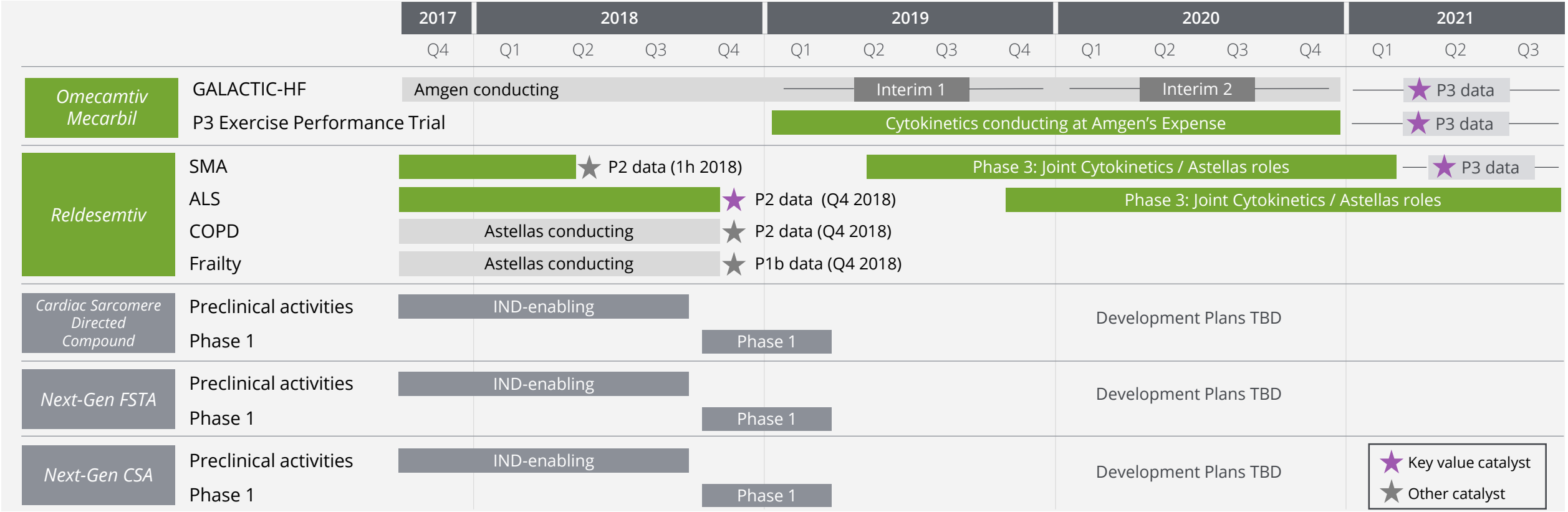
	(in millions)
Cash Revenue	**$17 - 23**
Cash Operating Expenses	**$105 - 115**
Net	**~$100**

Over 24 Months of Cash Based on 2018 Guidance

Capitalization Table

	3/31/18 (in millions)
Shares Oustanding	**54.2**
2004 Incentive Plan	10.6
2015 Employee Stock Purchase Plan and Warrants	0.5
Fully Diluted Shares Outstanding	**65.3**

Current Cash Builds Bridge to Future Milestones



Several Value-driving Catalysts in the Pipeline Leading to Results from GALACTIC-HF in 2021

2018 Milestones

Programs Advancing in Mid to Late-Stage Clinical Trials

Reldesemtiv

Expect Data from Three
Mid-Stage Trials In 2H 2018

Omecamtiv Mecarbil

Expect to Complete Enrollment in GALACTIC-HF Within
Approximately One Year

Research

Expect to advance one development compound under our collaborations with Amgen and Astellas to Phase 1 in 2018
Expect to advance cardiac sarcomere directed compound into Phase 1 in 2018

Shelly, diagnosed with ALS in 2013

THANK YOU

Cytokinetics

APPENDIX

Phase 3 Clinical Trial of *Tirasemtiv* Did Not Meet Primary or Secondary Endpoints

Study Overview

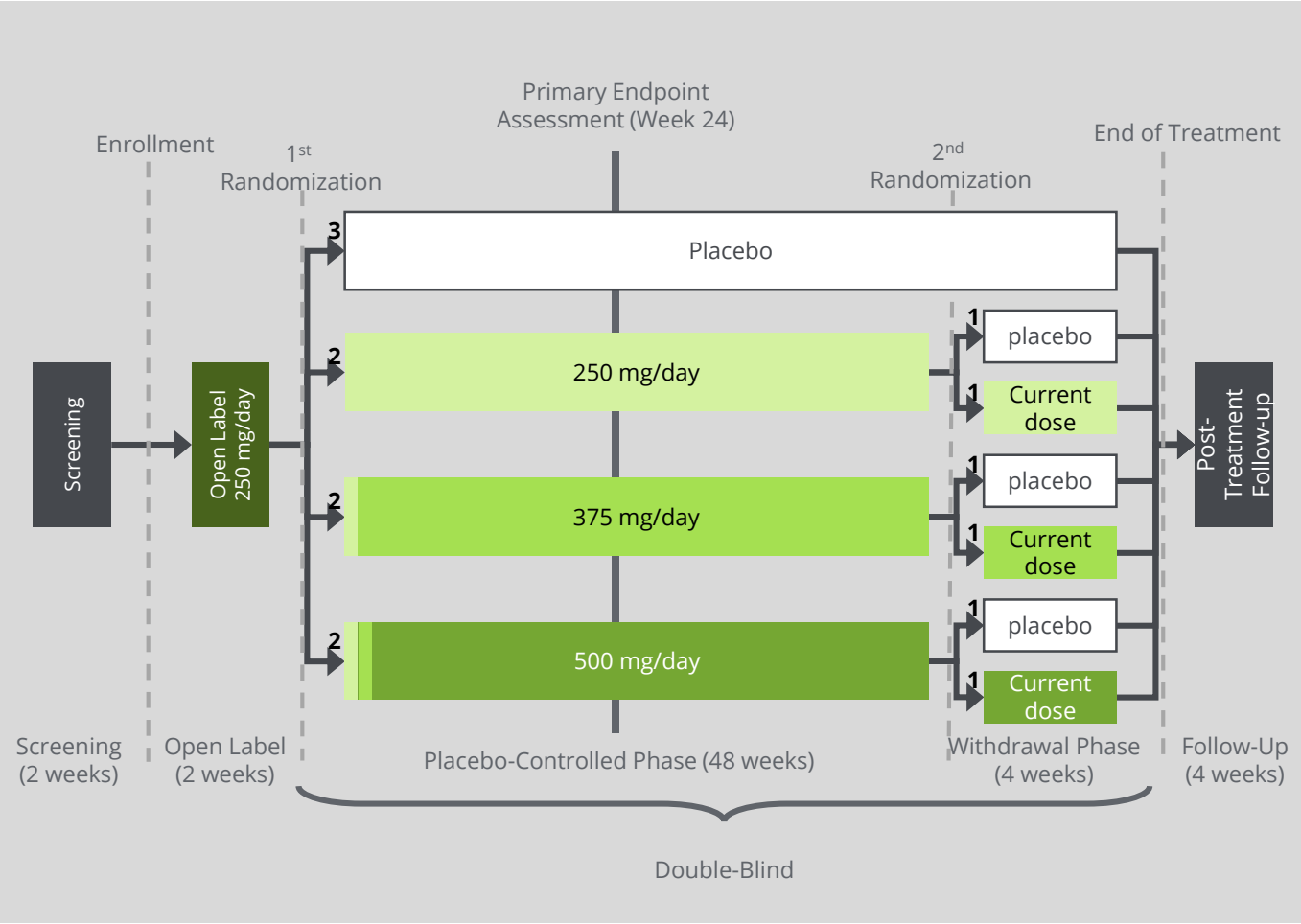
- Enrolled over 700 patients in 11 countries

Primary endpoint

- Change from baseline in slow vital capacity (SVC) at 24 weeks

Secondary endpoints

- Change from baseline in the ALSFRS-R score of the three respiratory items of the ALSFRS-R (i.e., the sum of items 10, 11 and 12) at 48 weeks
- Slope of mega-score of muscle strength at 48 weeks
- Time to the first occurrence of a decline from baseline in percent predicted SVC ≥20 percentage points or the onset of respiratory insufficiency or death at 48 weeks
- Time to the first occurrence of a decline in SVC to ≤50% predicted or the onset of respiratory insufficiency or death at 48 weeks
- Change from baseline in the ALSFRS-R total score at 48 weeks
- Time to the first use of mechanical ventilatory assistance or death



Baseline Characteristics

Demographic	Placebo (N=188)	All *Tirasemtiv* (N=373)	p-value
Age [years; mean (SD)]	55.9 (10.6)	56.8 (10.0)	0.29
Age <65 [n (%)]	143 (76.1)	291 (78.0)	0.61
Male [n (%)]	123 (65.4)	263 (70.5)	0.30
Riluzole user [n (%)]	141 (75.0)	281 (75.3)	0.84
Weight [kg, mean (SD)]	80.7 (15.7)	81.1 (14.8)	0.71
BMI [kg/m^2, mean (SD)]	27.3 (4.3)	27.2 (4.1)	0.81
Months from Diagnosis [mean (SD)]	8.1 (6.0)	7.4 (5.6)	0.19
Months from 1st Symptom [mean (SD)]	21.5 (16.2)	20.0 (12.9)	0.39
Bulbar Onset [n (%)]	31 (16.5)	54 (14.5)	0.53
ALSFRS-R Total Score [mean (SD)]	38.3 (5.1)	38.1 (5.3)	0.68
ALSFRS-R Respiratory Domain Score [mean (SD)]	11.6 (0.8)	11.5 (0.9)	0.23
SVC (%Predicted) [mean (SD)]	90.7 (16.5)	90.4 (15.3)	0.85

Primary Endpoint Analysis

Multiple Imputation Mixed Model for Repeated Measures

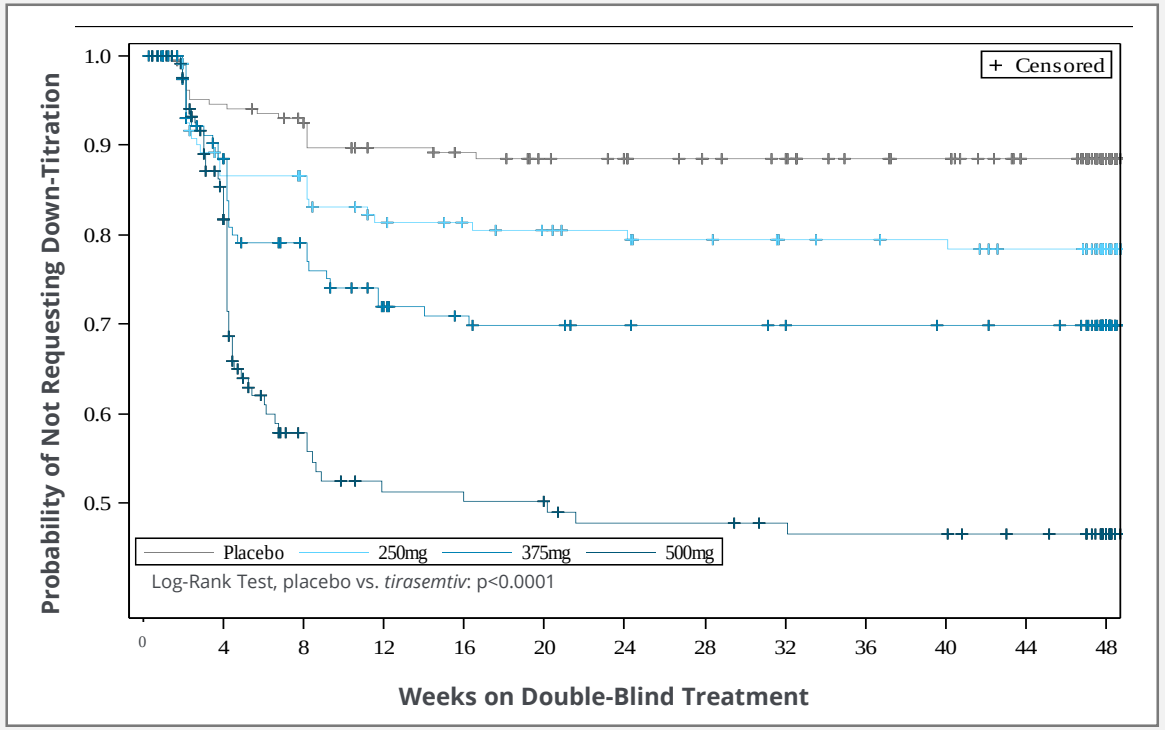
	Placebo	*Tirasemtiv* Overall	*Tirasemtiv* 250 mg*	*Tirasemtiv* 375 mg*	*Tirasemtiv* 500 mg*
Randomized and received Rx (N)	188	373	126	125	122
SVC measured at Week 24 (N)	169	286	106	92	88
Least squares (LS) means (95% CI)	-14.4 (-16.8, -11.9)	-13.4 (-15.3, -11.6)	-12.6 (-15.6, -9.67)	-13.7 (-16.9, -10.6)	-13.9 (-17.3, -10.5)
LS mean difference from placebo (95% CI)		0.92 (-2.13, 3.96)	1.71 (-2.09, 5.50)	0.61 (-3.36, 4.58)	0.43 (-3.71,4.57)
p-value		0.5552	0.3782	0.7625	0.8394

*randomized dose group

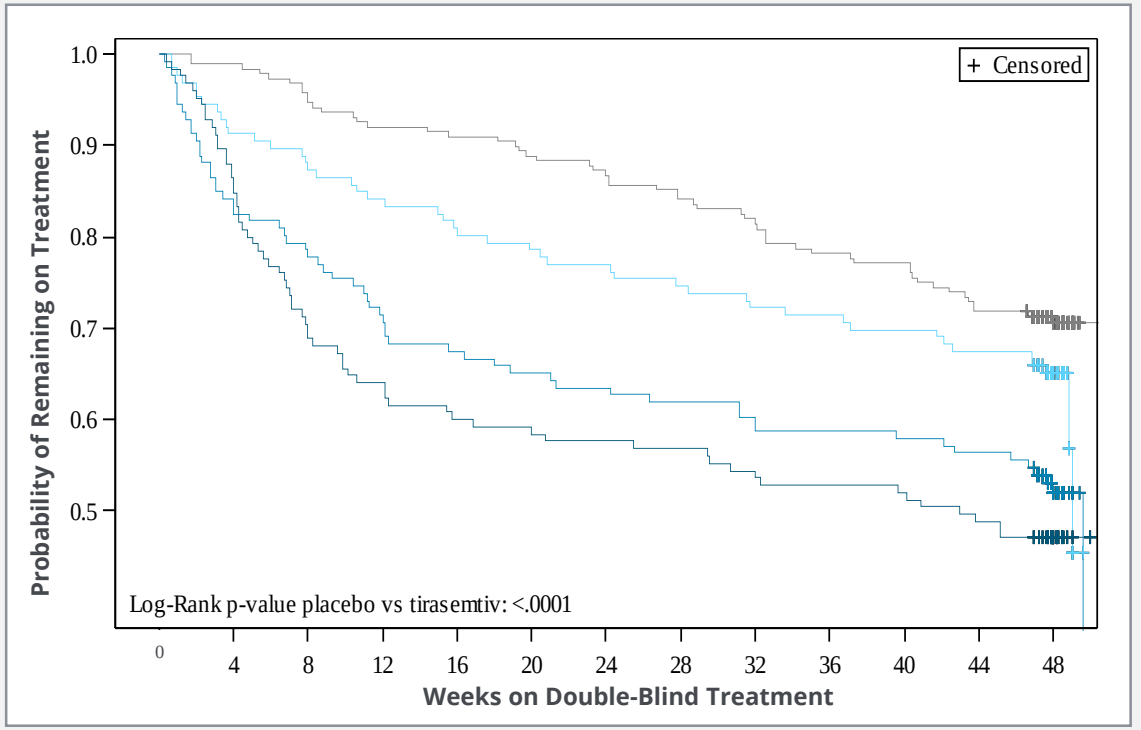
Change from Baseline in Percent Predicted SVC at Week 24

Down-Titration & Early Termination

Time to Down-Titration



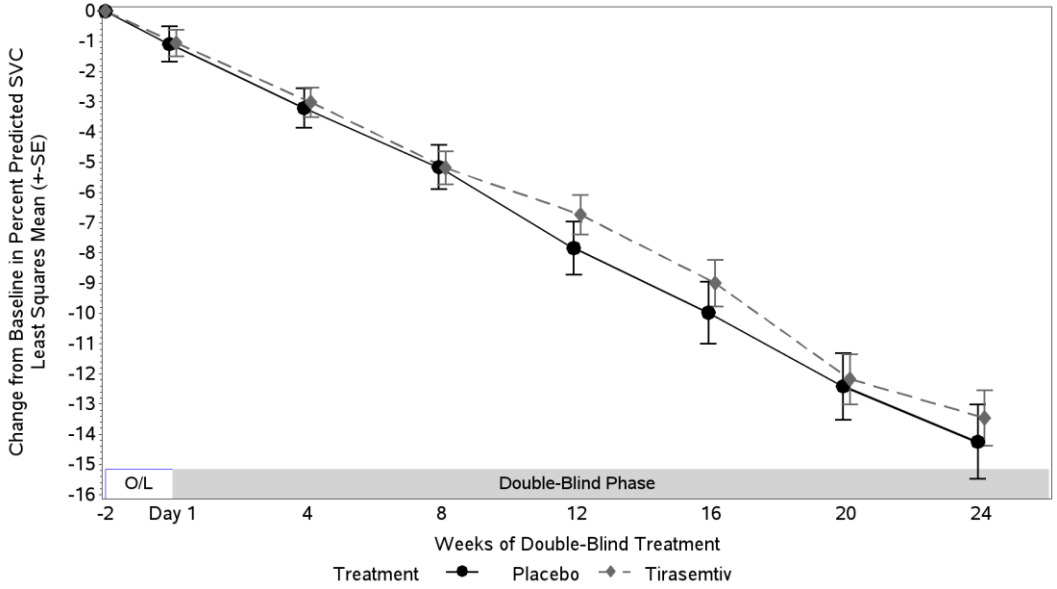
Early Termination from Treatment



Change from Baseline in % Predicted SVC

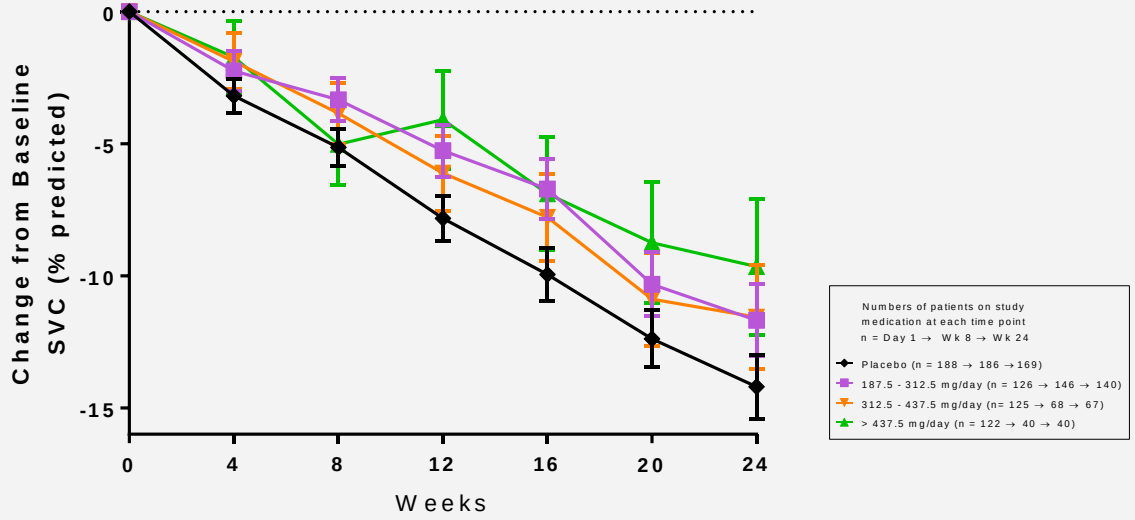
Change from Baseline in Percent Predicted SVC at Week 24

Intent to Treat Analysis



Change from Baseline in Percent Predicted SVC by Dose

Per Protocol Analysis



Change in SVC Week 24	Placebo	187.5 – 312.5 mg/day	312.5 – 437.5 mg/day	> 437.5 mg/day
LS mean (percentage points)	-14.23	-11.68	-11.56	-9.65
LS mean difference from placebo (percentage points)		2.55	2.67	4.57
p-value		0.160	0.247	0.107

AEs in 48 Weeks of the Double-Blind Phase

Preferred Term	Placebo (N=188)	All *Tirasemtiv* (N=377)	Difference *Tirasemtiv* - Placebo
Patients with any AE, n (%)	182 (96.8%)	375 (99.5%)	2.7%
AEs more frequent on *tirasemtiv*			
Dizziness	45 (23.9%)	158 (41.9%)	18.0%
Weight decreased	40 (21.3%)	110 (29.2%)	7.9%
Insomnia	25 (13.3%)	78 (20.7%)	7.4%
Fatigue	61 (32.4%)	147 (39.0%)	6.6%
Nausea	30 (16.0%)	84 (22.3%)	6.3%
Muscular weakness	58 (30.9%)	128 (34.0%)	3.1%
AEs more frequent on placebo			
Dyspnea	35 (18.6%)	57 (15.1%)	-3.5%
Contusion	34 (18.1%)	56 (14.9%)	-3.2%
Muscle spasms	34 (18.1%)	58 (15.4%)	-2.7%
Nasopharyngitis	30 (16.0%)	51 (13.5%)	-2.5%
Constipation	40 (21.3%)	72 (19.1%)	-2.2%
Headache	28 (14.9%)	53 (14.1%)	-0.8%
Dysphagia	33 (17.6%)	66 (17.5%)	-0.1%

SAEs were similar between patients who received *tirasemtiv* or placebo, but more patients discontinued double-blind treatment on *tirasemtiv* than on placebo primarily due to non-serious adverse events related to tolerability

Conclusions

- VITALITY-ALS did not meet its primary or secondary endpoints, in large part because of poor tolerability of the drug
- In patients who remained on *tirasemtiv*, there is evidence of an effect on SVC, with the highest effect in patients on 500 mg daily
- There were trends toward a positive effect of *tirasemtiv* on SVC in patients who remained on treatment at any dose
- Fast skeletal muscle troponin activation remains a viable therapeutic strategy in patients with ALS