









EMPOWERING

MUSCLE

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LIVES

Forward Looking Statements

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Our Mission

We are developing potential medicines to improve the healthspan of people with devastating cardiovascular and neuromuscular diseases of impaired muscle function.

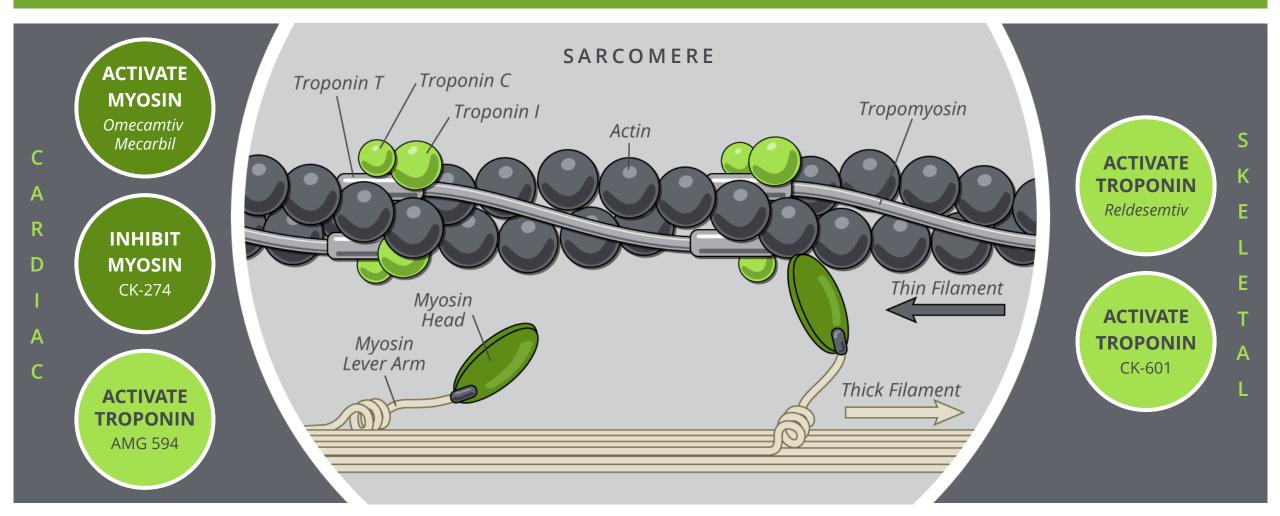


SCIENCE



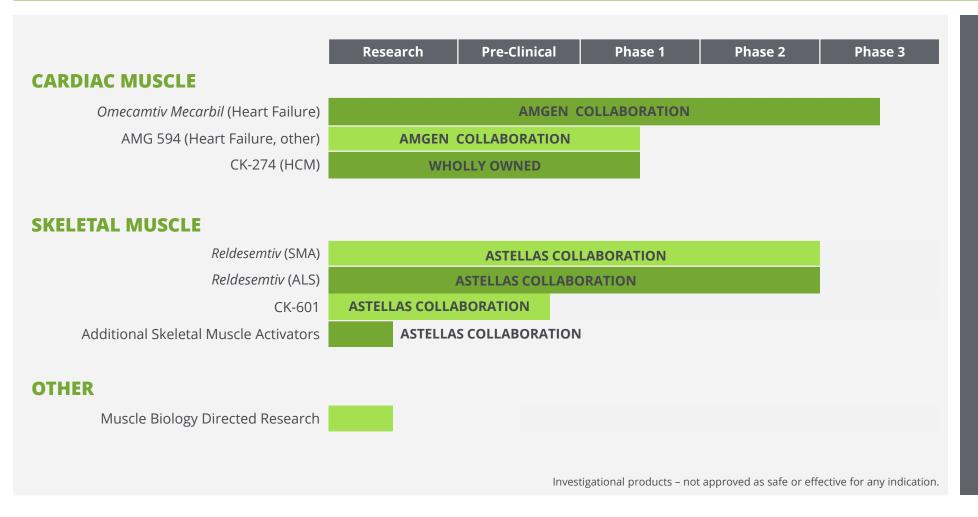


Sarcomere-Directed Research





Pipeline of Novel Muscle-Directed Compounds



Eligible for >\$600M in precommercial milestone
payments & >\$600M in
sales-based milestone
payments & royalties that
can exceed >20% under
deals with Amgen &
Astellas

>24 months cash



Upcoming Milestones

GALACTIC-HF
in 1H 2019

Data Expected from Phase 1
Study
of **CK-274**in Q3 2019

from **FORTITUDE-ALS**& Discussing Next Steps
with Astellas

Continue Enrollment in **METEORIC-HF** through 2019

Continue to Conduct Phase 1
Study
of **AMG 594**through 2019





CARDIAC MUSCLE

Omecamtiv Mecarbil AMG 594 CK-274

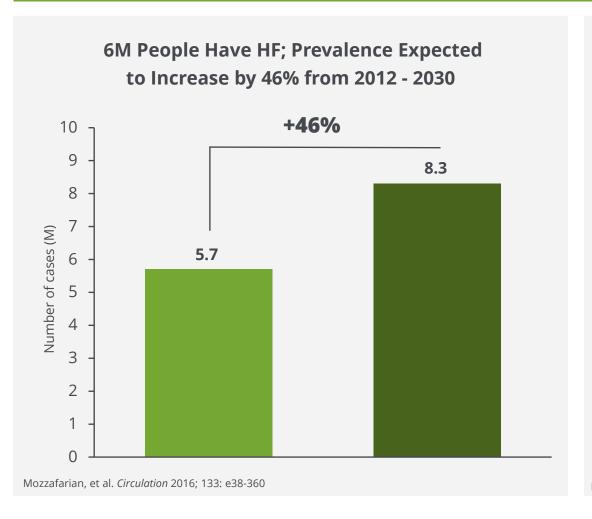
OVERVIEW



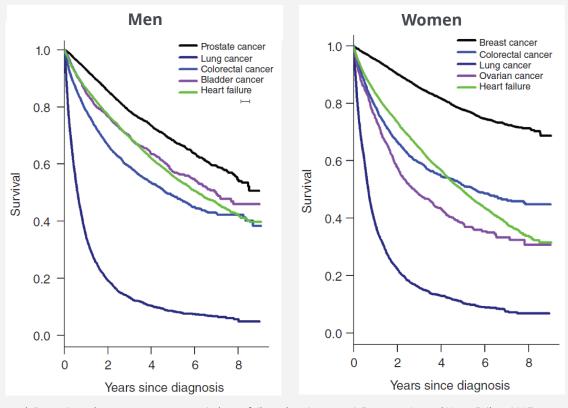




Heart Failure: Growing Prevalence and Low Survival Rate



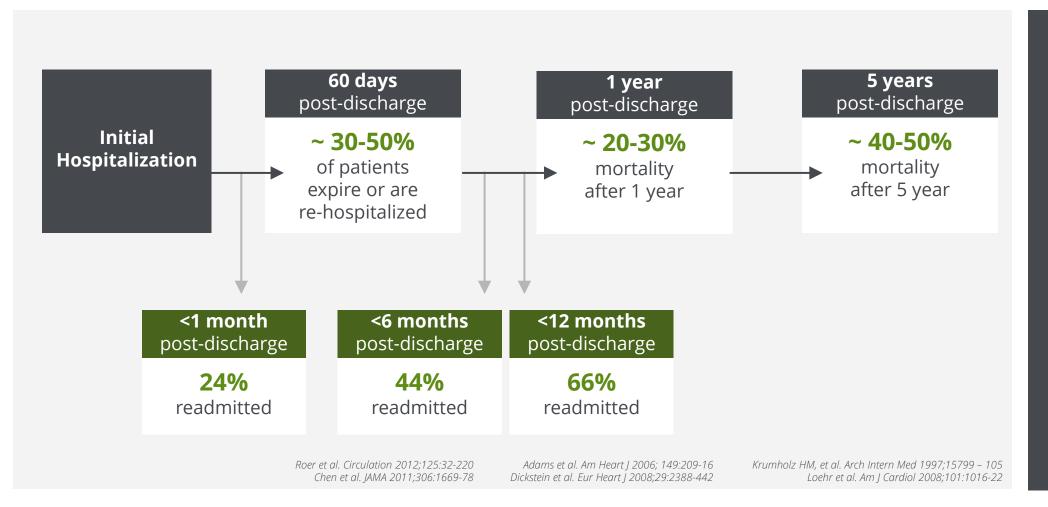
HF Survival Rates Worse than Some Prevalent Cancers



Mamas MA, et al. Do patients have worse outcomes in heart failure than in cancer? European Journal Heart Failure 2017



High Mortality and Hospital Readmission Rates



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

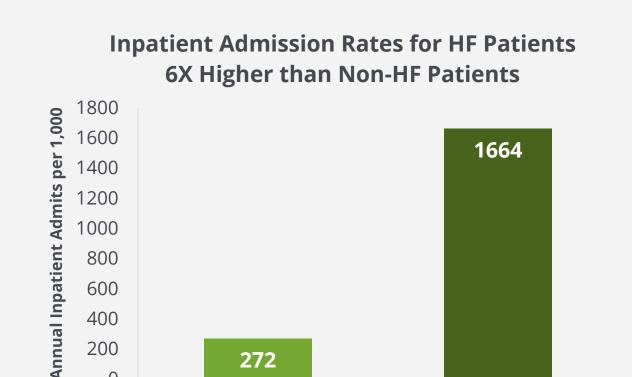
1 of 2 hospitalized HF patients are readmitted within 6 months



High Economic Burden of Heart Failure

Heart failure costs ~\$123 billion annually, which represents 33% of total Medicare budget

Heart failure is the most frequent diagnosis for hospitalized Medicare patients in the US



Source: Milliman Analysis of Medicare 5% Sample 2011-2012 (2012 index year, 2011 look back year) Source: Milliman Analysis of Medicare 5% Sample (2014 index year, 2013 look back year) and Office of the Actuary 2016 Board of Trustees Report. The costs only include Part A & B costs.

272

Non-Heart Failure



Heart Failure

200

Heart Failure: Many Phenotypes with Unmet Need

Decreased Cardiac Contractility

Increased/Preserved Cardiac Contractility

Heart Failure with Reduced Ejection Fraction (HFrEF)

Genetic Dilated Cardiomyopathy

Pulmonary Hypertension with Right Ventricular Heart Failure



Non-obstructive Hypertrophic Cardiomyopathy (nHCM)

Obstructive Hypertrophic Cardiomyopathy (oHCM)

Heart Failure with Preserved
Ejection Fraction
(certain HFpEF subsets)



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: Clinical Trials Program

11Phase 1 Studies

324
Subjects Enrolled

Well characterized safety, tolerability, PK/PD

Robust Clinical Trials Program **7**Phase 2 Studies

1,414
Subjects Enrolled

cosmic-HF showed statistically significant improvements in measures of cardiac function

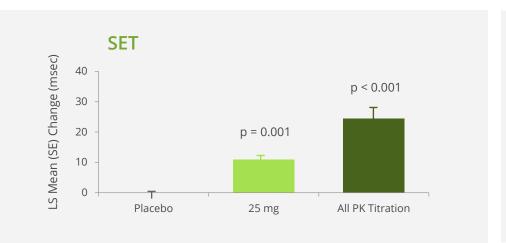


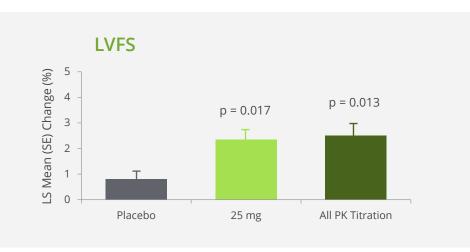


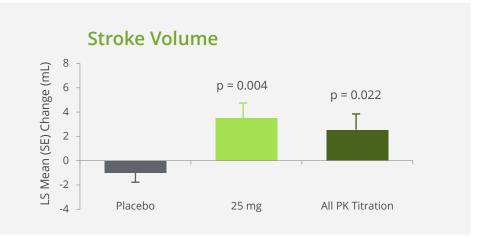
Dose-Dependent Increases in Cardiac Output

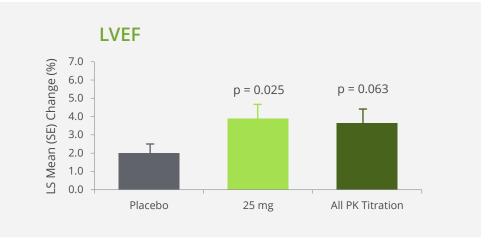
Pharmacodynamic
Effects with
Omecamtiv Mecarbil

LVEF, left ventricular ejection fraction; LVFS, left ventricular fractional shortening; SE, standard error; SET, systolic ejection time; all p values are nominal without multiplicity adjustment.









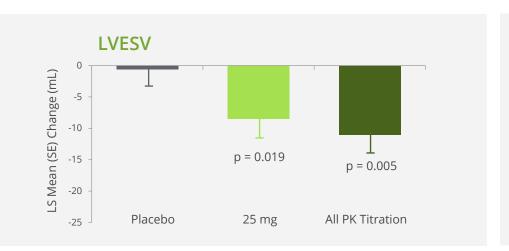




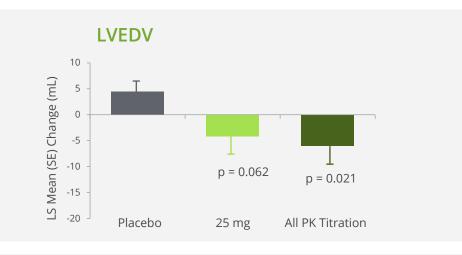
Decreases in Physiology & Cardiac Risk

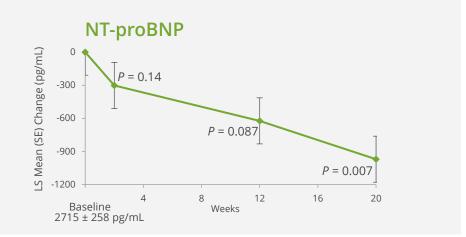
Reductions in Heart
Volume, Oxygen
Demand & Wall
Stress

LVESV left ventricular end systolic volume LVEDV left ventricular end diastolic volume All p values are nominal without multiplicity adjustment













Phase 3 Trial Has Enrolled >7,000 Patients

GALACTIC-HF
Continuing
Following Planned
Interim Analysis
Conducted by DMC

Second Interim
Analysis Expected
in 1H 2020

Study Overview

Enrolling 8,000 patients at ~1,000 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.

Key Design Points

- Dose optimization based on trough concentration of omecamtiv mecarbil at 2 weeks and 6 weeks
 - Starting Dose = 25 mg BID
 - Escalation (or not) at Week 4 to 37.5 mg or 50 mg BID based on plasma concentration of *omecamtiv* mecarbil at Week 2
 - Recheck at Week 6, adjust dose downward if necessary
- Enroll patients from time of hospitalization to within 1 year of discharge
 - In-hospital enrollment target is approximately 25% of total enrollment
 - Stratify on randomization setting
- Event driven with 90% power based on secondary endpoint of CV Death







Second Phase 3 Trial Underway

Primary endpoint

Change in peak VO₂ on CPET from baseline to Week 20

Secondary endpoints

- Change in total workload during CPET from baseline to Week 20
- Change in ventilatory efficiency (V_E/VCO₂ slope) during CPET from baseline to Week 20
- Change in the average daily activity units measured over a 2 weeks from baseline to Week 18-20

Exploratory Endpoints

- Change from baseline to Week 20 in oxygen uptake efficiency slope ($VO_2/logV_E$ slope), ventilatory threshold (by the V-slope method), VO_2 recovery kinetics, percent predicted p VO_2 , and exercise duration
- Change from baseline in the average daily activity units at Week 6-8 and at Week 12-14
- Change from baseline in the KCCQ Total Symptom Score and its sub-domains from baseline to Week 20

 VO_2 = Oxygen Uptake; CPET = Cardio-Pulmonary Exercise Testing; V_E = Ventilatory Efficiency

Multicenter Exercise Tolerance
Evaluation of *Omecamtiv Mecarbil*Related to Increased Contractility in
Heart Failure

9 Countries in North America & Europe

METEORIC-HF Steering Committee:

Greg Lewis (Co-lead, US)

Michael Felker (Co-lead, US)

John Teerlink (US)

David Whellan (US)

Justin Ezekowitz (Canada)

Adriaan Voors (Netherlands)

Alain Cohen-Solal (France)

Piotr Ponikowski (Poland)

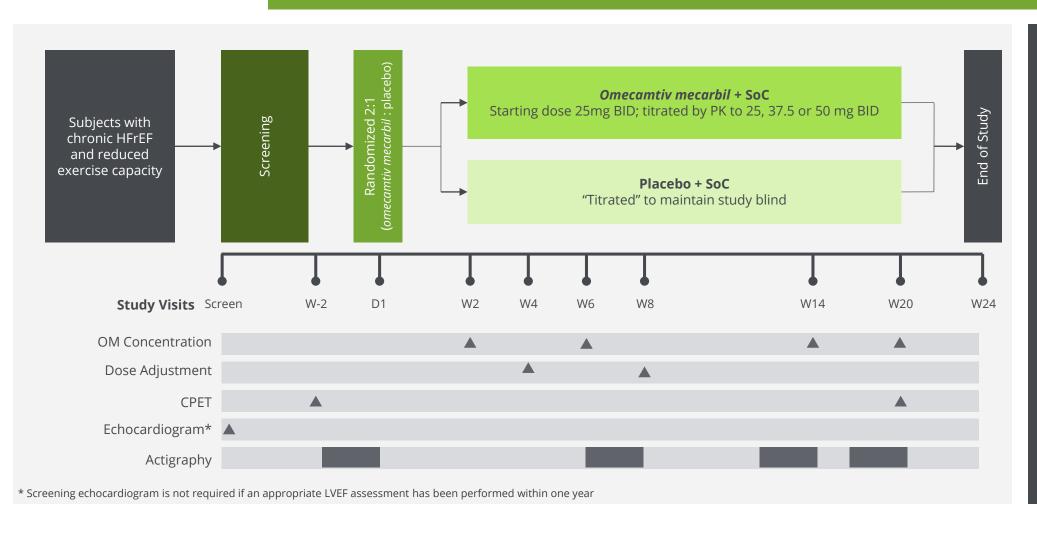
Michael Böhm (Germany)

Marco Metra (Italy)





Trial Overview



~270 subjects 90% power

5 months of treatment (same as COSMIC-HF)

Dose titration of omecamtiv mecarbil same as

GALACTIC-HF



Collaborations & Agreements

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 \$600 mm in milestone payments

*Servier has a sub-license from Amgen to commercialize *omecantiv 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

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

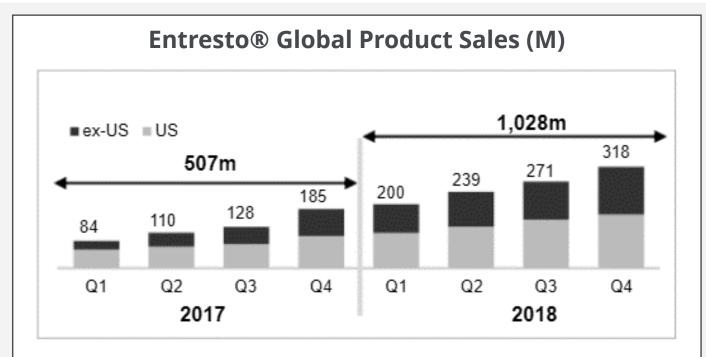
Joint commercial operating team responsible for commercialization program

- Royalty rate may increase up to additional 1% associated with timing of US approval
- Cytokinetics agreed to exercise option to coinvest \$40M 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 >\$600M 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





Commercial Opportunity for New Heart Failure Therapy



- USD 318m (+76% cc) Q4 sales
- Blockbuster in 2018 and doubling sales vs. 2017

Source: Novartis Q4 and FY18 results presentation, January 2019

*As with all products in P3, the product profile achieved by omecamtiv mecarbil in GALACTIC-HF is required to provide a better understanding of the expected revenue.

"Entresto has the potential for more than \$3 billion annual sales in its current usage, for reduced ejection fraction heart failure in patients whose heart muscles do not contract effectively."

Paul Hudson, head of Novartis
Pharmaceuticals Unit, Reuters,
January 2018



AMG 594: Next-Gen Cardiac Sarcomere Activator

Decreased Cardiac Contractility

Heart Failure with Reduced Ejection Fraction (HFrEF)

Genetic Dilated Cardiomyopathy

Pulmonary
Hypertension with
Right Ventricular
Heart Failure

Amgen & Cytokinetics are considering the Phase 2 clinical trials program

AMG 594 is an oral, small molecule cardiac troponin activator

- Intended to improve ventricular systolic function in patients with heart failure
- Selected from >1.5 million compounds in >80 distinct series
- Preclinical results support the potential for best-in-class safety and efficacy
- Projected once daily dosing

Cytokinetics and Amgen are advancing AMG 594 into clinical development

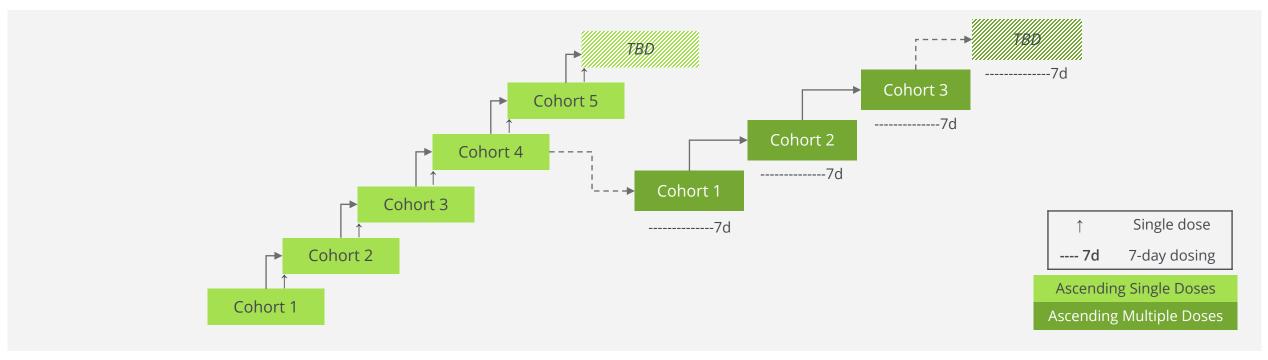
- IND filed
- Early clinical trials will assess the safety and tolerability of AMG 594. as well as its potential to enhance ventricular contraction

AMG 594 is a Next-Generation Cardiac Sarcomere Activator for the Potential Treatment of Patients with Heart Failure

Potential Applications of AMG 594 for Patients with Distinct Types of Ventricular Dysfunction and Heart Failure are Under Discussion



AMG 594: Nested SAD and MAD in Healthy Subjects



Randomized, placebo-controlled, double-blind, multi-part, single center study

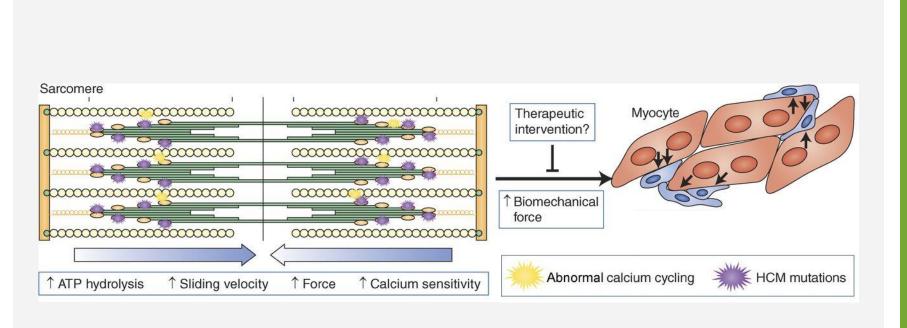
- Part 1: 5 ascending single oral doses (SAD)
- Part 2: 3 ascending multiple oral doses (MAD)
- ~64 healthy subjects overall

Objectives	Endpoints			
Safety and tolerability	AEs, laboratories, cardiac markers, ECGs			
Pharmacokinetics	C _{max} , T _{max} , AUC			
Pharmacodynamics	LVEF, LVFS, LVOT-VTI, SET			



HCM: Lack of Therapy Targeting Underlying Disease Biology

HCM is a Disease of the Sarcomere



Current Medical Therapy:

- Indirect mechanisms of action with systemic side effects
- Variable efficacy, often inadequate
- Treatment failure means resorting to surgical myomectomy or percutaneous ablation

Teekakirikul et al., JCB 2012



CK-274: Therapeutic Hypothesis

Targeted Oral Therapy Addressing Disease Etiology May Improve Symptoms, Exercise Capacity, and Slow Disease Progression

A cardiac sarcomere inhibitor may counteract the pathologic effects of mutations in the sarcomere that lead to HCM

- Hyperdynamic contraction and obstruction of blood flow out of the LV
- Cardiac hypertrophy, small LV cavity, small stroke volume
- Impaired relaxation and high LV filling pressures





CK-274: Potentially Best-in-Class Cardiac Myosin Inhibitor

- Favorable pharmacokinetic / pharmacodynamic properties and other candidate selection criteria
 - Selective allosteric inhibitor of cardiac myosin
 - In vivo pharmacodynamic advantages related to distinctive binding
 - No inhibition of smooth muscle myosin
 - Favorable ADME properties with no CYP inhibition or CYP induction
 - Good oral bioavailability across pre-clinical species
 - Excellent permeability without efflux
 - Clear pharmacokinetic/pharmacodynamic (PK/PD) relationship
 - Projected once daily dosing to reach steady state rapidly in patients
 - Shallow dose response curve may translate to favorable therapeutic window in patients and broaden clinical utility

Discovered by Company Scientists Independent of Collaborations

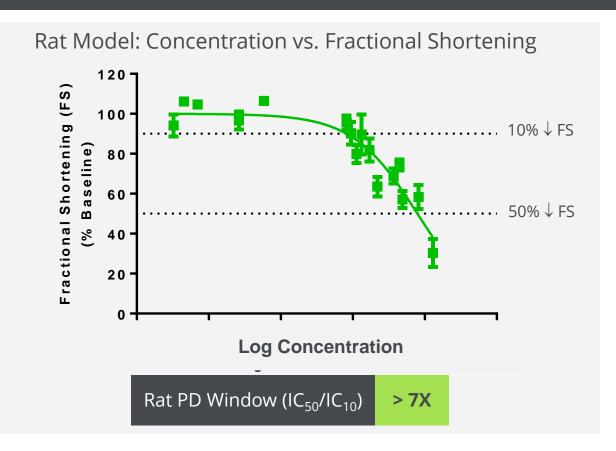
Selected from Multiple Potential Development Candidates (PDCs)

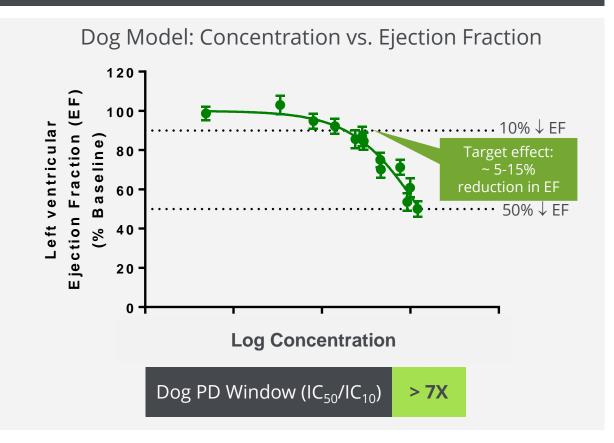




CK-274: Wide PD Window in Rat and Dog Models

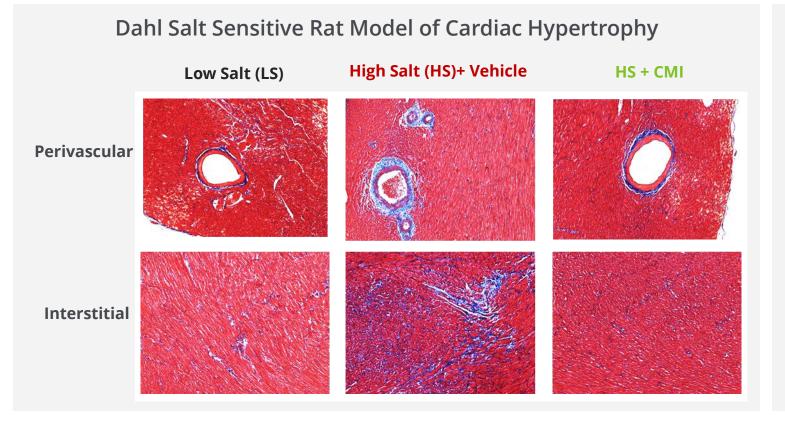
Shallow exposure-response relationship of CK-274 in rats and dogs

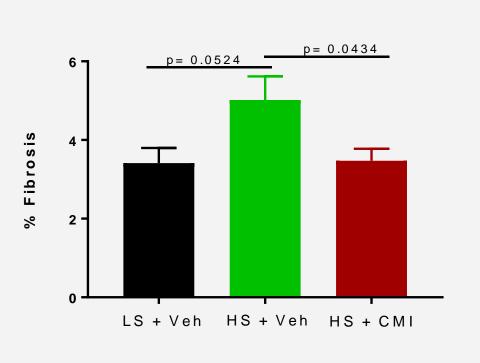






Cardiac Myosin Inhibitor in Model of Cardiac Hypertrophy

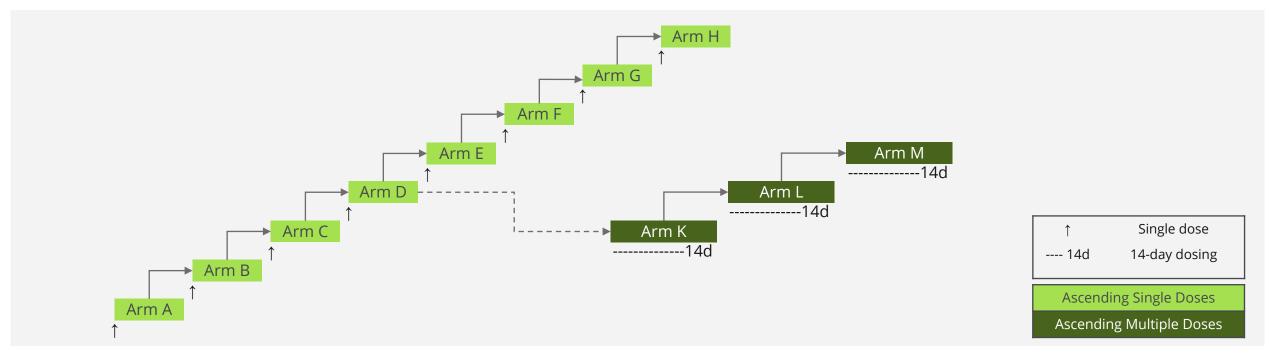




Significant Decrease in Perivascular and Interstitial Fibrosis



CK-274: Nested SAD and MAD in Healthy Subjects



Randomized, placebo-controlled, double-blind, multi-part, single center study in ~96 healthy subjects

- Part 1: 8 ascending single oral doses (SAD)
- Part 2: 3 ascending multiple oral doses (MAD)

Objectives	Endpoints
Safety and tolerability	AEs, SAEs, LVEF
Pharmacokinetics	C_{max} , T_{max} , AUC, t_{y_2} , other
PK-PD Relationship	LVEF, LVFS, LVOT-VTI, other



CK-274: Clinical Development Plan for HCM

Phase 1 Phase 2 Phase 3 Proof of Concept, Dose Finding **Pivotal Studies** Safety, PK & PD Safe & tolerated NDA: Potential for approval Improved LVOT dose with desired based on a single Ph3 study gradient PD effects with an exercise endpoint SAD & MAD **oHCM** patients **oHCM** patients Placebo Controlled Healthy Exercise Endpoint (peak VO2) **Echocardiography Endpoints** Volunteers **NDA IND Filed Extension study** Long-term safety & efficacy Proof of activity in nHCM pts Pivotal study in nHCM



Cardiac Muscle: Upcoming Milestones

Continue enrollment in METEORIC-HF through 2019

Complete Patient Enrollment in GALACTIC-HF in 1H

Expect Data from Phase 1 Study of CK-274 in Q3

Continue to conduct Phase 1 study of AMG 594 through 2019



SKELETAL MUSCLE

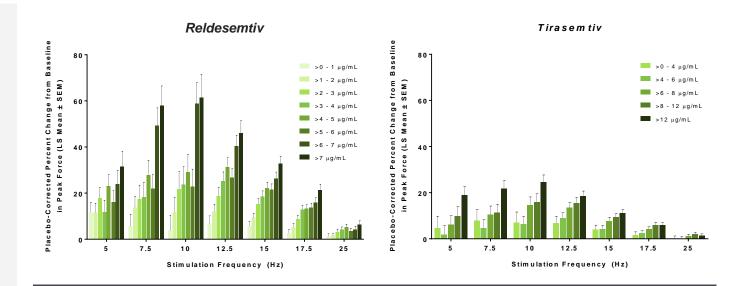
Reldesemtiv





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

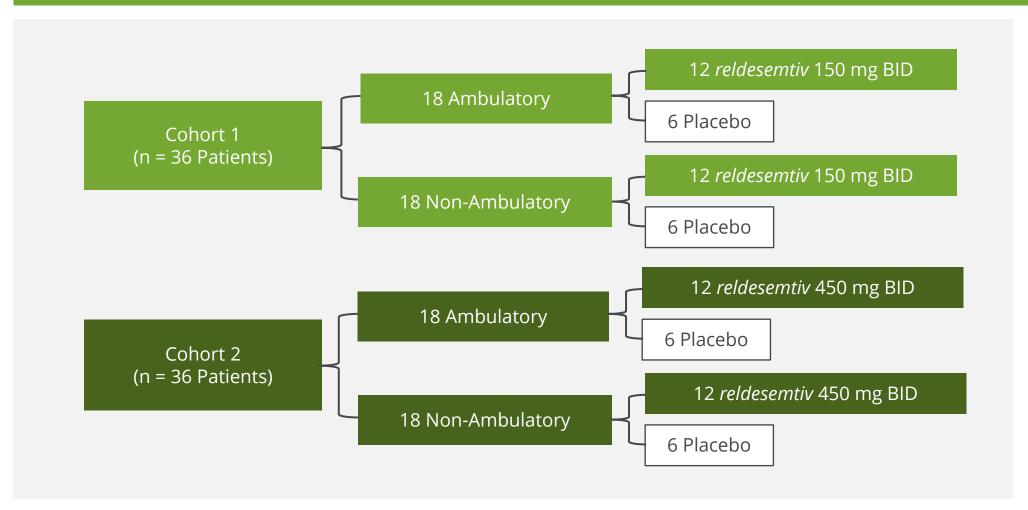


Results from Three Phase 1 Studies of *Reldesemtiv* Published in *Muscle & Nerve*

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



CY 5021: Phase 2 Clinical Trial in SMA



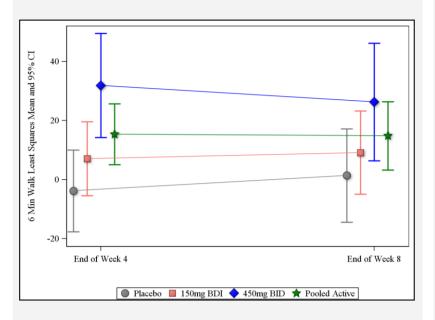
Hypothesis generating study enrolled 70 people with Type II-IV SMA over 8 weeks. Study included two dose cohorts, stratified by ambulatory versus non-ambulatory status, randomized 2:1 to receive *reldesemtiv* or placebo 2 times daily



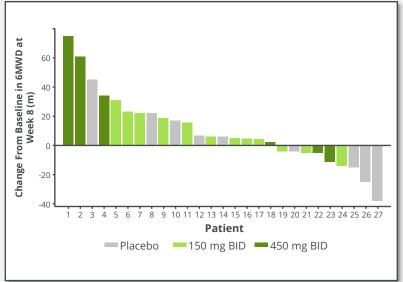
CY 5021: Increases in 6MWD

Dose-Dependent Increases in 6MWD

Change from Baseline Over Time

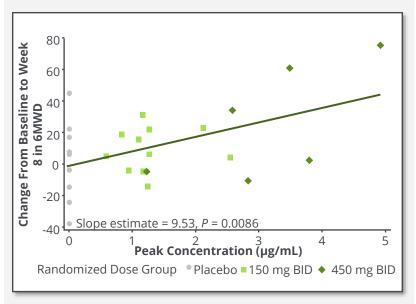


Change from Baseline at Week 8



Concentration-Dependent Increases in 6MWD

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



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



6MWD is Validated, Approvable Endpoint

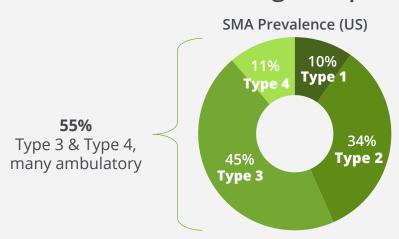
Drug Name	Disease	Duration of Treatment (weeks)	Study Size	Improvement in 6MWD compared to placebo (meters)	Indication	6MWD in Label
ALDURAZYME (laronidase)	MPS I Hurler/Hurler-Scheie	26	45	38 (p = 0.07)	Increase walking capacity	Yes
ELAPRASE (idursulfase)	MPS II Hunter syndrome	53	64	35 (p = 0.01)	Increase 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



Growing Population of Ambulatory Patients

~10,000 living SMA patients



- Type 1, Life Expectancy 1 Year: Severe muscle weakness, limited mobility, many physical challenges
- **Type 2, Life Expectancy 30 Years:** Delayed motor milestones, can typically sit up unsupported, unable to walk, general weakness
- Type 3, Life Expectancy 78 Years: Usually can walk but have increasingly limited mobility. Depending on severity, may have difficulty running, climbing steps
- **Type 4, Life Expectancy 78 Years:** Mild motor impairment, progressive muscle weakness later in life. Typically able to walk but not run



"I think we could benefit patients with a number of different levels of capability of SMA by **complementing** *reldesemtiv* **on top of these different gene-modifying treatments**. So it's not just improving 6MWD for patients who are ambulatory, I'm very excited about the possibility that we can increase the function of patients with all levels of ability."

-John Day, M.D., Ph.D., Professor of Neurology and Pediatrics (Genetics), Stanford University Medical Center

2018

~3,500-5,000 ambulatory SMA patients

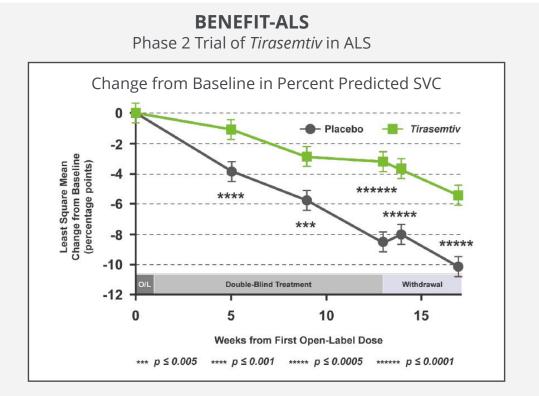
2023

Potentially up to **10,000** ambulatory SMA patients*

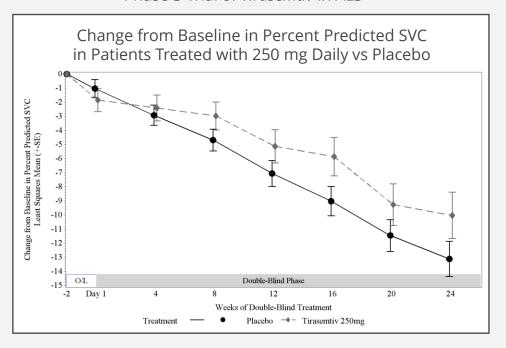
*Assuming advent of genetically directed therapies alter Type 1 and Type 2 phenotype Source: Proprietary market research and company estimates



Previous Studies Demonstrate Slowing Decline of SVC



VITALITY-ALSPhase 3 Trial of *Tirasemtiv* in ALS



Use of a FSTA Slowed the Decline of SVC in Multiple Clinical Trials





Phase 2 Clinical Trial in ALS



Functional
Outcomes in a
Randomized
Trial of
Investigational
Treatment with CK-107
to Understand
Decline in
Endpoints in
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



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 copromote 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 copromotion activities Cytokinetics eligible to receive over \$600 mm in pre-commercialization and commercialization milestones plus royalties, which are increased for cofunded products



Skeletal Muscle: Upcoming Milestone

Continuing to Evaluate Results from FORTITUDE-ALS

Discussing Next Steps in Development Program with Astellas



CORPORATE PROFILE





Vision 2020: Five-Year Strategic Roadmap

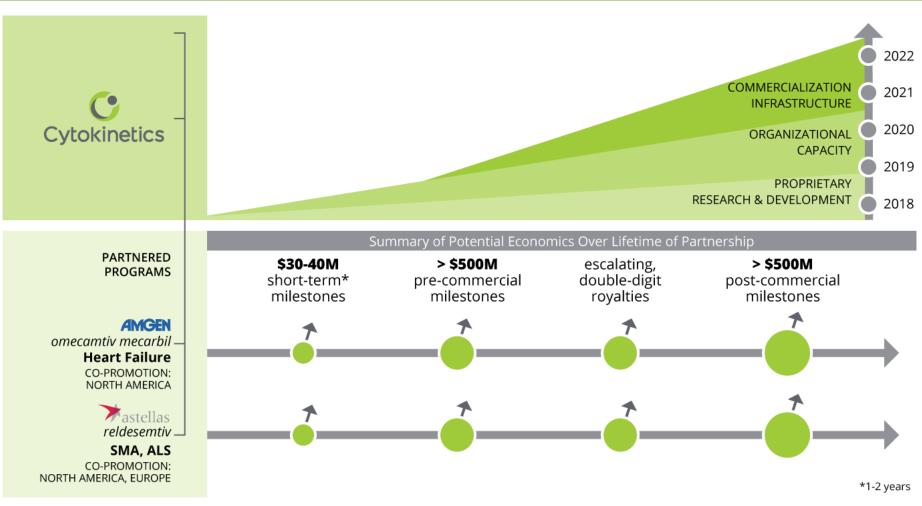


- Progress proprietary research programs focused on muscle contractility, growth and energetics into development under new collaborations
- Advance next-generation skeletal and cardiac muscle activator compounds into clinical development by leveraging existing research collaborations
- Conduct late-stage 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



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	\$420M			
	Total	\$630M			\$630M
Strategic Partners & Grants	Astellas	\$10M	\$130M	\$81M	\$221M
	Amgen	\$43M	\$145M	\$31M	\$219M
	Royalty Pharma	\$10M	\$90M		\$100M
	GSK	\$24M	\$22M	\$33M	\$78M
	AstraZeneca			\$2M	\$2M
	MyoKardia			\$2M	\$2M
	Global Blood			\$2M	\$2M
	Grants (ALS Assoc / NINDS / other)		\$6M		\$6M
				\$143M	\$631M

Note: Figures above exclude current debt outstanding of \$43M.



Q1 2019 Condensed Balance Sheet

	3/31/19 (in millions)
Cash and investments Other assets	\$176.2 \$22.0
Total assets	\$198.6
Debt	\$42.6
Liability related to sale of future royalties	\$127.3
Other liabilities	\$25.3
Total liabilities	\$195.2
Working capital	\$160.1
Accumulated deficit	-\$772.7
Stockholders' Equity	\$3.4
Shares outstanding	55.5
Fully diluted shares outstanding	64.9



2019 Financial Guidance

(in millions)

Cash Revenue

\$28 - 32

Cash Operating Expenses

\$110 - 115

Net

~\$90

Over 24 Months of Cash Based on 2019 Guidance

Financial guidance confirmed on May 9, 2019 earnings call



Capitalization Table

	3/31/19 (in millions)
Shares Oustanding	55.5
2004 Incentive Plan	9.0
2015 Employee Stock Purchase Plan and Warrants	0.4
Fully Diluted Shares Outstanding	64.9



Upcoming Milestones

Complete Enrollment in GALACTIC-HF in 1H 2019

Data Expected from Phase 1
Study
of **CK-274**in Q3 2019

from **FORTITUDE-ALS**& Discussing Next Steps
with Astellas

in **METEORIC-HF** through 2019 Continue to Conduct Phase 1
Study
of **AMG 594**through 2019















THANK YOU