EMPOWERING MUSCLE
EMPOWERING LIVES

Sarcomere Directed Therapies

John, diagnosed with heart failure
Jillian, diagnosed with HCM
Chuck, diagnosed with ALS
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 the clinical trials of omecamtiv mecarbil, reldesemtiv and CK-274; projections regarding growing prevalence, low survival rates and market opportunity in heart failure; Cytokinetics’ commercial readiness for omecamtiv mecarbil; Cytokinetics’ ability to earn and receive milestone payments; the timing and results of clinical trials of AMG 594 and CK-274; the timing of any potential commercial launch of our product candidates, if approved; commercial opportunities for our product candidates; Cytokinetics’ cash runway and 2019 financial guidance; interactions with the FDA; the properties, potential benefits and commercial potential of CK-274, omecamtiv mecarbil, AMG 594, 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 MISSION

To bring forward new medicines to improve the healthspan of people with devastating cardiovascular and neuromuscular diseases of impaired muscle function.
Heart Failure: Growing Prevalence and Low Survival Rates

6 million people have heart failure in the United States

Prevalence Expected to Increase by 46% from 2012 – 2030

Number of cases (M)

<table>
<thead>
<tr>
<th>Year</th>
<th>Cases (M)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2012</td>
<td>5.7</td>
</tr>
<tr>
<td>2030</td>
<td>8.3</td>
</tr>
</tbody>
</table>

+46%


HF Survival Rates Worse than Some Prevalent Cancers

Mamas et al. Eur J Heart Fail. 2017 Sep;19(9):1095-104
High Mortality and Hospital Readmission Rates

Acute heart failure is the most frequent cause of hospitalization in people > 65\(^1,2\)

1 of 2 hospitalized HF patients are readmitted within 6 months\(^5\)

- **Initial Hospitalization**
  - \(<1\) month post-discharge\(^4,6\)
  - 24% readmitted

- **60 days post-discharge\(^7\)**
  - \(~25\) - 50% of patients expire or are re-hospitalized

- **1 year post-discharge\(^7,9\)**
  - \(~20\) - 30% mortality after 1 year

- **<6 months post-discharge\(^5\)**
  - 44% readmitted

- **<12 months post-discharge\(^3,10\)**
  - 66% readmitted

- **5 years post-discharge\(^3,7,8\)**
  - \(~40\) - 50% mortality after 5 years

2. Chen et al. JAMA 2011;306:1669-78
High Economic Burden of Heart Failure
Heart failure costs ~$123 billion annually, representing 33% of total Medicare budget

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

1. Milliman Analysis of Medicare 5% Sample 2011-2012 (2012 index year, 2011 look back year)
2. 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
Significant Unmet Need in HFrEF

Proprietary market research suggests need for novel therapy

Market research suggests need for novel therapy
Physicians say newly approved therapies have 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 that enhance cardiac performance
Need drugs that target novel/more specific molecular targets
Need targets other than the neurohormonal pathway;

Disease modifying therapies
Need drugs that safely enhance contractility
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
Significant Unmet Need in HCM

**Current therapies do not target underlying disease**

**HCM is an inherited cardiovascular disease**
- 1 in 500 have genetic mutation
- 1 in 3200 have HCM
- Subset of patients have progressive symptoms, atrial fibrillation, stroke, sudden death

**Surgical intervention not permanent solution**
- Invasive therapy to reduce septal thickness is effective
- Surgical myectomy or percutaneous ablation

**Current medical therapy does not target underlying disease**
- Indirect mechanisms of action with systemic side effects
- Variable efficacy, often inadequate

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Pipeline of Novel Muscle-Directed Drug Candidates

**CARDIAC MUSCLE**
- **Omecamtiv Mecarbil** (Heart Failure)
- **CK-274** (HCM)
- **CK-271**
- **AMG 594** (Heart Failure, other)

**SKELETAL MUSCLE**
- **Reldesemtiv**
- **CK-601**
- **Additional Skeletal Muscle Activators**

**OTHER**
- **Muscle Biology Directed Research**

Investigational products – not approved as safe or effective for any indication.
Sarcomere Directed Drug Development

CARDIAC MUSCLE

Omecamtiv Mecarbil
AMG 594, CK-274, CK-271
The sarcomere is a molecular structure found in skeletal and cardiac muscle that enables cardiac myocytes to contract and generate force.

**Sarcomere Directed Drug Development**

**Cardiac muscle**

- **Actin**
- **Tropomyosin**
- **Thin filament**
- **Thick filament**
- **Myosin**
  - Head
  - Lever arm
- **Calcium**
- **Troponin**
- **ATP**

**Activate**
- Omecamtiv
- Mecarbil (Cardiac)

**Inhibit**
- CK-274 (Cardiac)
- CK-271 (Cardiac)

**Troponin**
- Activate AMG 594 (Cardiac)
Omecamtiv Mecarbil: Novel Mechanism Approach

Current Treatments
- Block SNS and RAAS*
  - ACE inhibitor (ACEI)
  - Angiotensin-receptor blocker (ARB)
  - Aldosterone antagonist
  - Beta blocker

* SNS = Sympathetic Nervous System
RAAS = Renin-Angiotensin-Aldosterone System

Left ventricular systolic dysfunction
Perceived reduction in circulating volume and pressure

Omecamtiv Mecarbil
- Selective cardiac myosin activator designed to improve heart muscle performance and increase the pumping function of the heart.
Omecamtiv Mecarbil: Robust Clinical Trials Program

Over 10,000 patient-years of exposure to omecamtiv mecarbil

**Phase 1 Studies**
- 11
- Subjects Enrolled: 324
- Well characterized safety, tolerability and PK/PD data

**Phase 2 Studies**
- 7
- Subjects Enrolled: 1,414
- COSMIC-HF showed statistically significant improvements in measures of cardiac function
Dose-Dependent Increases in Cardiac Performance
Pharmacodynamic results from COSMIC-HF

**Dose-Dependent Increases in Cardiac Performance**

**Pharmacodynamic results from COSMIC-HF**

**SET**
- Placebo
- 25 mg
- All PK Titration

**LVFS**
- Placebo
- 25 mg
- All PK Titration

**Stroke Volume**
- Placebo
- 25 mg
- All PK Titration

**LVEF**
- Placebo
- 25 mg
- All PK Titration

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 in COSMIC-HF

LVESV left ventricular end systolic volume; LVEDV left ventricular end diastolic volume
All p values are nominal without multiplicity adjustment
Neutral or Improved Measures of Diastolic Function

Improved systolic function with no negative impact on diastolic function

**E/e’**

- Placebo: 0
- 25 mg Fixed Dose: -1.5
- PK Titration: 0.7

*p* = 0.6718

**IVRT**

- Placebo: -5
- 25 mg Fixed Dose: 0
- PK Titration: 5

*p* < 0.0001

**TR Velocity**

- Placebo: 0
- 25 mg Fixed Dose: -20
- PK Titration: -5

*p* = 0.9767

**Diastolic Filling Time**

- Placebo: 10
- 25 mg Fixed Dose: 0
- PK Titration: -15

*p* = 0.877

IVRT = isovolumic relaxation time
TR = tricuspid regurgitation
Prognostic Implications: NT-proBNP and Remodeling

Studies demonstrate correlation with cardiovascular outcomes

Patients in PARADIGM-HF who had significant reductions in NT-proBNP had lower rates of CV death or heart failure hospitalization\(^1\)

Meta-analysis of drug/device therapies demonstrated association between LV remodeling and longer-term effects on mortality in patients with LVD\(^2\)

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1. Zile et al. JACC 2016; 68(22): 2425-2436
Troponins: Small Increases, Unrelated to Exposures of *Omecamtiv Mecarbil*

Baseline troponin levels were above the diagnostic limit for myocardial infarction (0.04 ng/mL) for >50% of patients in ATOMIC-AHF and ~25% in COSMIC-HF.

### Troponin Levels

<table>
<thead>
<tr>
<th></th>
<th>ATOMIC-AHF</th>
<th>Pooled Placebo</th>
<th>OM Cohort 1</th>
<th>OM Cohort 2</th>
<th>OM Cohort 3</th>
</tr>
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<tbody>
<tr>
<td><strong>Median (ng/mL)</strong></td>
<td>0.044</td>
<td>0.060</td>
<td>0.044</td>
<td>0.056</td>
<td></td>
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<tr>
<td><strong>COSMIC-HF</strong></td>
<td>Placebo</td>
<td>25 mg BID</td>
<td>All PK Titration</td>
<td>All OM</td>
<td></td>
</tr>
<tr>
<td><strong>Median (ng/mL)</strong></td>
<td>0.025</td>
<td>0.022</td>
<td>0.025</td>
<td>0.022</td>
<td></td>
</tr>
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Pivotal Phase 3 Trial Completed Enrollment

GALACTIC-HF continuing following first planned interim analysis

Second interim analyses expected in Q1 2020, following accrual of 2/3 of targeted 1,590 CV deaths

Overview

Enrolled 8,256 patients at ~1,000 sites in 35 countries

Primary Endpoint

Composite of time to cardiovascular (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
• High risk patients enrolled from inpatient and outpatient settings
  • Patients enrolled from time of hospitalization to within 1 year of discharge
  • Approximately 25% of patients were hospitalized at randomization
• Designed to provide 90% statistical power to assess risk of CV death
  • Accrual of 1,590 CV deaths provides 90% power to detect hazard ratio of 0.8 for CV death
  • Primary composite endpoint expected to have >99% statistical power
Chronic HFrEF patients currently hospitalized for a primary reason of HF or with history of hospitalization or ER/ED admission for a primary reason of HF within 1 year.

Omecamtiv mecarbil + SoC
Starting dose: 25mg PO BID

Placebo + SoC
Follow the same study procedures as OM group to ensure blinding

Study Visits:
- D1
- W2
- W4
- W6
- W8
- W12
- W24
- W36
- W48
- Q16W

PK assessment for dose adjustment

PK assessment
Second Phase 3 Clinical Trial Underway

Investigating effect of **omecamtiv mecarbil** on exercise tolerance

Trial will enroll patients in 9 countries in North America and Europe

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**Primary Endpoint**

Change in peak VO2 on CPET from baseline to Week 20

**Second Endpoints**

- Change in total workload during CPET from baseline to Week 20
- Change in ventilatory efficiency (VE/VO2 slope) during CPET from baseline to Week 20
- Change in average daily activity units measured over 2 weeks from baseline to Week 18-20

**Exploratory Endpoints**

- Change from baseline to Week 20 in oxygen uptake efficiency slope (VO2/logVE slope), ventilatory threshold (by the V-slope method), VO2 recovery kinetics, percent predicted pVO2, and exercise duration
- Change from baseline in average daily activity units at Week 6-8 and Week 12-14
- Change from baseline in KCCQ Total Symptom Score and sub-domains from baseline to Week 20

**Key Design Points**

- Designed to enroll approximately 270 patients
- 20 weeks of treatment
- 90% power
- Patients must:
  - Have LVEF ≤35 percent
  - Be New York Heart Association (NYHA) heart failure class II or III
  - Have reduced exercise capacity compared to age matched controls
- Patients randomized 2:1 to **omecamtiv mecarbil**
- Starting dose at 25 mg twice daily, titrated to 25, 37.5 or 50 mg twice daily based on the same PK-guided dosing regimen used in GALACTIC-HF

VO2 = Oxygen Uptake; CPET = Cardio-Pulmonary Exercise Testing; VE = Ventilatory Efficiency
Subjects with chronic HFrEF and reduced exercise capacity

Study Visits
- Screen
- W-2
- D1
- W2
- W4
- W6
- W8
- W14
- W20
- W24

Omecamtiv mecarbil + SoC
Starting dose 25mg BID; titrated by PK to 25, 37.5 or 50 mg BID

Placebo + SoC
“Titrated” to maintain study blind

- Screening
- CPET
- Echocardiogram*
- Dose Adjustment
- OM Concentration
- Actigraphy

*Screening echocardiogram is not required if an appropriate LVEF assessment has been performed within one year
Omecamtiv Mecarbil: Pivotal Phase 3 Results Q4 2020

<table>
<thead>
<tr>
<th>Event Date</th>
<th>Event Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>July 1999</td>
<td>First Cardiac Sarcomere Screen</td>
</tr>
<tr>
<td>Dec 2000</td>
<td>First POC Isolated Hearts and in vivo</td>
</tr>
<tr>
<td>Aug 2004</td>
<td>CK-1827452 First Synthesized</td>
</tr>
<tr>
<td>Jan 2005</td>
<td>CK-1827452 Candidate Selection</td>
</tr>
<tr>
<td>July 2005</td>
<td>First CTA/Regulatory Filing</td>
</tr>
<tr>
<td>Aug 2005 – Apr 2006</td>
<td>Phase 1 CY 1111</td>
</tr>
<tr>
<td>Mar 2007 – Feb 2009</td>
<td>Phase 2 CY 1121</td>
</tr>
<tr>
<td>May 2009</td>
<td>Amgen Option Agreement</td>
</tr>
<tr>
<td>May 2009</td>
<td>Amgen Exercises Option</td>
</tr>
<tr>
<td>Jan 2013</td>
<td>Initiate COSMIC-AHF</td>
</tr>
<tr>
<td>Dec 2016</td>
<td>Initiate GALACTIC-HF</td>
</tr>
<tr>
<td>Feb 2019</td>
<td>Initiate METEORIC-HF</td>
</tr>
</tbody>
</table>
Commercial Opportunity for New Heart Failure Therapy

2019 sales exceeded $1.5B; Analysts expect $3-5B in peak annual sales

<table>
<thead>
<tr>
<th>Year</th>
<th>Q1</th>
<th>Q2</th>
<th>Q3</th>
<th>Q4</th>
</tr>
</thead>
<tbody>
<tr>
<td>2017</td>
<td>84</td>
<td>110</td>
<td>128</td>
<td>185</td>
</tr>
<tr>
<td>2018</td>
<td>200</td>
<td>239</td>
<td>271</td>
<td>318</td>
</tr>
<tr>
<td>2019</td>
<td>357</td>
<td>421</td>
<td>430</td>
<td>518</td>
</tr>
</tbody>
</table>

*As with all products in Phase 3, the product profile achieved by omecamtiv mecarbil in GALACTIC-HF is required to provide a better understanding of the expected revenue.

Source: Novartis public quarterly results presentations

![Entresto® Global Product Sales (M)](chart)
Commercial Readiness for Omecamtiv Mecarbil

Multiple workstreams in progress to prepare for successful commercial launch

- Educate heart failure market
- Assess impact for value proposition
- Determine areas of differentiation for HCPs
- Cultivate advocacy for heart failure patients
Collaborations & Agreements

Amgen Collaboration

Purchase Option: 2006
Exercise Option Ex-Japan: 2009
Expanded to Include Japan/Purchase Equity: 2013
Received >$220M over 13 Years

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

Cytokinetics could earn over $600 mm in milestone payments

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

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

Royalty Monetization

Royalty Pharma paid $100M for 4.5% royalty on worldwide sales of\(\text{omecamtiv mearcarbil}^{\text{2017}}\)

Cytokinetics gains right to co-promote \(\text{omecamtiv mearcarbil}\), if approved, 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 co-invest $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
AMG 594: Cardiac Troponin Activator

Advancing through Phase 1: Potential for HFrEF and other indications

• Intended to improve ventricular systolic function in patients with heart failure
• Preclinical results support the potential for best-in-class safety and efficacy
• Projected once daily dosing
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
- Safety and tolerability: AEs, laboratories, cardiac markers, ECGs
- Pharmacokinetics: $C_{\text{max}}$, $T_{\text{max}}$, AUC
- Pharmacodynamics: LVEF, LVFS, LVOT-VTI, SET

Endpoints
- Safety and tolerability
- Pharmacokinetics
- Pharmacodynamics

AMG 594: Nested SAD and MAD in Healthy Subjects
Potential treatments for patients with HCM

- Discovered by company scientists independent of collaborations
- Selective allosteric inhibitor of cardiac myosin
- Potential \textit{in vivo} pharmacodynamic advantages related to distinctive binding site
- No inhibition of smooth muscle myosin observed
- Clear pharmacokinetic/pharmacodynamic (PK/PD) relationship observed
- Projected once daily dosing to reach steady state rapidly in patients
- Shallow dose response curve translated to favorable therapeutic window in healthy volunteers
CK-274 was well tolerated in healthy participants: no SAEs*

SAD Pharmacokinetics Appeared Generally Dose Proportional

Steady-State Appeared Evident After 14 Days of Dosing

*No SAEs and no clinically meaningful changes in vital signs, ECGs, or laboratory tests

Data points represent mean ± standard error of the mean

Cmax = maximum drug plasma concentration; AUC = area under the plasma concentration curve; SAD = single ascending dose; d = day; qd = once daily
**Cytokinetics**

**CY 6011: MAD Pharmacokinetic Parameters**

**PK Parameter, Geometric Mean (%CV)***

<table>
<thead>
<tr>
<th>Dose (n)</th>
<th>5 mg (6)</th>
<th>7.5 mg (6)</th>
<th>10 mg (6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$C_{\text{max}}$ (ng/mL)</td>
<td>69 (23.2%)</td>
<td>148 (39.5%)</td>
<td>141 (19.7%)</td>
</tr>
<tr>
<td>$t_{\text{max}}$ (h)</td>
<td>2.75 (1.5–4)</td>
<td>1.0 (0.5–5)</td>
<td>2.5 (0.5–3)</td>
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<tr>
<td>AUG24 (ng•h/mL)</td>
<td>1,321 (23.0%)</td>
<td>2,518 (25.8%)</td>
<td>2,631 (22.8%)</td>
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<td>79.7 (14.1)</td>
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<tr>
<td>AR</td>
<td>4.71</td>
<td>4.5</td>
<td>4.79</td>
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</table>

*Except data for $t_{\text{max}}$ shown as median (minimum–maximum), and $t_{\frac{1}{2}}$ shown as the arithmetic mean (standard deviation).

AR (accumulation ratio) calculated as $(\text{AUC}_{24\text{ on Day 14 or 17}}) / (\text{AUC}_{24\text{ on Day 1}})$.

%CV = percent coefficient of variation; $C_{\text{max}}$ = maximum plasma concentration; AUG$_{24}$ = area under the plasma concentration curve; MAD = multiple ascending dose; $t_{\frac{1}{2}}$ = apparent plasma terminal elimination half-life; $t_{\text{max}}$ = time to maximum observed plasma concentration.

**Shallow Exposure-Response Relationship Observed Preclinically Appears to Have Translated to Humans, May Enable Flexible Dose Optimization in Humans**

Graphs show LVEF as a function of exposure; data points represent observed values in dogs and humans.

Decrease in LVEF as function of exposure is similar in humans and dogs.

**PK/PD Relationship of CK-274 for Ejection Fraction (LVEF)**

**Half-Life of CK-274 at Steady-State was ~81 hours (3.4 days) On Average**

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<td>79.7 (14.1)</td>
</tr>
<tr>
<td>AR</td>
<td>4.71</td>
<td>4.5</td>
<td>4.79</td>
</tr>
</tbody>
</table>

*Except data for $t_{\text{max}}$ shown as median (minimum–maximum), and $t_{\frac{1}{2}}$ shown as the arithmetic mean (standard deviation).

AR (accumulation ratio) calculated as $(\text{AUC}_{24\text{ on Day 14 or 17}}) / (\text{AUC}_{24\text{ on Day 1}})$.

%CV = percent coefficient of variation; $C_{\text{max}}$ = maximum plasma concentration; AUG$_{24}$ = area under the plasma concentration curve; MAD = multiple ascending dose; $t_{\frac{1}{2}}$ = apparent plasma terminal elimination half-life; $t_{\text{max}}$ = time to maximum observed plasma concentration.

**Shallow Exposure-Response Relationship Observed Preclinically Appears to Have Translated to Humans, May Enable Flexible Dose Optimization in Humans**

Graphs show LVEF as a function of exposure; data points represent observed values in dogs and humans.

Decrease in LVEF as function of exposure is similar in humans and dogs.

**PK/PD Relationship of CK-274 for Ejection Fraction (LVEF)**

**CY 6011: MAD Pharmacokinetic Parameters**

**PK Parameter, Geometric Mean (%CV)***

<table>
<thead>
<tr>
<th>Dose (n)</th>
<th>5 mg (6)</th>
<th>7.5 mg (6)</th>
<th>10 mg (6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$C_{\text{max}}$ (ng/mL)</td>
<td>69 (23.2%)</td>
<td>148 (39.5%)</td>
<td>141 (19.7%)</td>
</tr>
<tr>
<td>$t_{\text{max}}$ (h)</td>
<td>2.75 (1.5–4)</td>
<td>1.0 (0.5–5)</td>
<td>2.5 (0.5–3)</td>
</tr>
<tr>
<td>AUG$_{24}$ (ng•h/mL)</td>
<td>1,321 (23.0%)</td>
<td>2,518 (25.8%)</td>
<td>2,631 (22.8%)</td>
</tr>
<tr>
<td>$t_{\frac{1}{2}}$ (h)</td>
<td>86.3 (11.9)</td>
<td>76.9 (14.5)</td>
<td>79.7 (14.1)</td>
</tr>
<tr>
<td>AR</td>
<td>4.71</td>
<td>4.5</td>
<td>4.79</td>
</tr>
</tbody>
</table>

*Except data for $t_{\text{max}}$ shown as median (minimum–maximum), and $t_{\frac{1}{2}}$ shown as the arithmetic mean (standard deviation).

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%CV = percent coefficient of variation; $C_{\text{max}}$ = maximum plasma concentration; AUG$_{24}$ = area under the plasma concentration curve; MAD = multiple ascending dose; $t_{\frac{1}{2}}$ = apparent plasma terminal elimination half-life; $t_{\text{max}}$ = time to maximum observed plasma concentration.

**Shallow Exposure-Response Relationship Observed Preclinically Appears to Have Translated to Humans, May Enable Flexible Dose Optimization in Humans**

Graphs show LVEF as a function of exposure; data points represent observed values in dogs and humans.

Decrease in LVEF as function of exposure is similar in humans and dogs.

**PK/PD Relationship of CK-274 for Ejection Fraction (LVEF)**
Patients with symptomatic oHCM, and resting or provoked LVOT gradient ≥ 50 mmHg

Study Visits
- Screening
- W-1
- D1
- W2
- W4
- W6
- W9
- W10
- W12
- W14

Ambulatory Cardiac Monitoring
- Screen
- W-1
- D1
- W2
- W4
- W6
- W9
- W10
- W12
- W14

Dose Titration

Phase 2 Clinical Trial Design

Phase 2 clinical trial open to enrollment

CK-3773274 + SoC

Placebo + SoC

End of Study
CK-274: Clinical Development Plan for HCM

**Phase 1**
- Safety, PK & PD
- SAD & MAD Healthy Volunteers
- Safe & tolerated dose with desired PD effects

**Phase 2**
- Proof of Concept, Dose Finding
- oHCM patients
  - Placebo Controlled
  - Echocardiography Endpoints
- Improved LVOT gradient

**Phase 3**
- Pivotal Studies
- oHCM patients
  - Exercise Endpoint (peak VO2)

- NDA: Potential for approval based on a single Ph3 study with an exercise endpoint

- Extension study
  - Long-term safety & efficacy

- Proof of activity in nHCM pts
- Pivotal study in nHCM

- IND Filed

**CK-274: Clinical Development Plan for HCM**
Opportunity to Tap Intersection of HF & HCM Centers

**Situation**
- 49% account overlap between HF & HCM treatment centers represents:
  - 94% of total claim volume (923K of 980K claims)

**Opportunity**
- Total of 2,000 treatment centers represent key targets for cross selling sales force
- ~50% of addressable target accounts for *omecamtiv mecarbil* include HCM claims

---

**High HF Prevalence Aligns with HCM COEs**

---

1. Some accounts have listed Charges ($) and unlisted number of Claims or Primary Diagnoses (accounts with <11 "Total # of Claims" or "# Primary Diagnoses" are blank due to privacy). For these accounts with charges >$100K, number of Claims or Primary Diagnoses have been updated to an average of 5.
Sarcomere Directed Drug Development

SKELETAL MUSCLE

Reldesemtiv
CK-601
The sarcomere is a molecular structure found in skeletal and cardiac muscle that enables skeletal myocytes to contract and generate force.
Significant Unmet Need in ALS

**No approved muscle directed therapies**

- **Average 3-5 year mortality**
- **Current therapies provide modest benefit**
- **Initial symptoms include: limb weakness, slurred speech, swallowing issues**
- **Average age at diagnosis is 55-65**
- **Death most commonly due to respiratory failure**

---

### Prevalence*

- **U.S.**: 25,000
- **Germany**: 5,700
- **U.K.**: 4,300
- **France**: 4,300

### Incidence*

- **U.S.**: 6,300
- **Germany**: 1,600
- **France**: 1,200
- **U.K.**: 1,200

---

*Cytokinetics estimates based on proprietary market research
Source: NIH National Institute of Neurological Disorders and Stroke, ALS Fact Sheet
Parallel group, dose ranging study enrolled 458 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.

Phase 2 Clinical Trial in ALS

Results presented at American Academy of Neurology 2019

Double-Blind, Placebo-Controlled: 12 weeks

- Placebo (n = 110)
- 150 mg BID (n = 110)
- 300 mg BID (n = 110)
- 450 mg BID (n = 110)

Follow-up 4 weeks

Screening 2 weeks

Randomization 1:1:1:1

End of Dosing

Results presented at American Academy of Neurology 2019
Primary Endpoint: SVC
Change from baseline in percent predicted SVC at week 12

*Based on Mixed Model for Repeated Measures (MMRM) with the contrasts of (-5, -1, 3, 3) for placebo, relədesemtiv 150 mg, 300 mg and 450 mg BID, respectively

Primary Analysis*

P = 0.11 for weighted dose-response relationship

**Percent Predicted SVC Change From Baseline at Week 12 (95% CI)**

<table>
<thead>
<tr>
<th>Dose Level</th>
<th>Percent Predicted SVC Change</th>
<th>CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>-6.46</td>
<td></td>
</tr>
<tr>
<td>150 mg BID</td>
<td>-4.97</td>
<td></td>
</tr>
<tr>
<td>300 mg BID</td>
<td>-4.62</td>
<td></td>
</tr>
<tr>
<td>450 mg BID</td>
<td>-4.58</td>
<td></td>
</tr>
</tbody>
</table>
Change From Baseline: All Active vs Placebo*

Results support progression to potential Phase 3 clinical trial

<table>
<thead>
<tr>
<th>Study Treatment</th>
<th>LS Mean (SE) Difference in Change of % Predicted SVC From Baseline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>-2.5 (1.1)</td>
</tr>
<tr>
<td>All Active</td>
<td>-5.0 (1.0)</td>
</tr>
</tbody>
</table>

*post hoc analysis

FORTITUDE-ALS did not achieve statistical significance, but patients on all dose groups of reldesemtiv declined less than patients on placebo.

Relative reduction of **27%** in decline of percent predicted SVC compared with placebo.

---

<table>
<thead>
<tr>
<th>Study Treatment</th>
<th>LS Mean (SE) Difference in Change of % Predicted ALSFRS-R From Baseline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>0.9 (0.3)</td>
</tr>
<tr>
<td>All Active</td>
<td>1.7 (1.1)</td>
</tr>
</tbody>
</table>

Relative reduction of **25%** in drop of ALSFRS-R compared to placebo.
## Subgroup Analyses*

### Percent Predicted SVC

<table>
<thead>
<tr>
<th>Percent predicted SVC at baseline</th>
<th>No. of Patients (pbo/reldesemtiv)</th>
<th>LSM Difference (95% Cl)</th>
<th>Estimate</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;80</td>
<td>38/102</td>
<td>1.037 0.5935</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥80</td>
<td>52/187</td>
<td>2.135 0.0834</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ALSFRS-R total score at baseline</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;Median (38.0)</td>
<td>43/118</td>
<td>2.886 0.141</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥Median (38.0)</td>
<td>47/171</td>
<td>0.451 0.7146</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ALSAQ-5 total score at baseline</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;150</td>
<td>49/159</td>
<td>0.568 0.6689</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥150</td>
<td>41/130</td>
<td>3.489 0.0287</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anatomic site of disease onset</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Limb</td>
<td>73/234</td>
<td>2.309 0.0448</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bulbar</td>
<td>17/55</td>
<td>-0.027 0.9923</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time since ALS symptom onset</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;2 Years</td>
<td>50/188</td>
<td>0.530 0.7211</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥2 Years</td>
<td>40/101</td>
<td>3.640 0.0094</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time since ALS diagnosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;1 Year</td>
<td>65/210</td>
<td>0.819 0.5263</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥1 Year</td>
<td>25/79</td>
<td>4.237 0.0172</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;6 Months</td>
<td>39/130</td>
<td>1.230 0.4538</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥6 Months</td>
<td>51/159</td>
<td>2.285 0.1024</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-study rate of disease progression (ALSFRS-R total score reduction per month)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1st tertile ≤(0.3667)</td>
<td>29/107</td>
<td>0.663 0.6361</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2nd tertile &gt; (0.3667) - (0.6673)</td>
<td>35/94</td>
<td>2.960 0.0976</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3rd tertile (0.6673)</td>
<td>26/88</td>
<td>1.620 0.4597</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*FORTITUDE-ALS did not achieve statistical significance, but patients on all dose groups of reldesemtiv declined less than patients on placebo

### ALSFRS-R Total Score

<table>
<thead>
<tr>
<th>Percent predicted SVC at baseline</th>
<th>No. of Patients (pbo/reldesemtiv)</th>
<th>LSM Difference (95% Cl)</th>
<th>Estimate</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;80</td>
<td>43/109</td>
<td>1.588 0.0089</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥80</td>
<td>57/196</td>
<td>0.264 0.5296</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ALSFRS-R total score at baseline</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;Median (38.0)</td>
<td>48/129</td>
<td>1.107 0.0585</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥Median (38.0)</td>
<td>52/176</td>
<td>0.685 0.0987</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ALSAQ-5 total score at baseline</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;150</td>
<td>52/164</td>
<td>0.266 0.5025</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥150</td>
<td>48/141</td>
<td>1.598 0.0055</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anatomic site of disease onset</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Limb</td>
<td>80/245</td>
<td>0.872 0.0279</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bulbar</td>
<td>20/60</td>
<td>0.861 0.2194</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time since ALS symptom onset</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;2 Years</td>
<td>56/199</td>
<td>1.422 0.0025</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥2 Years</td>
<td>44/106</td>
<td>0.475 0.3439</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time since ALS diagnosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;1 Year</td>
<td>71/225</td>
<td>1.123 0.0101</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥1 Year</td>
<td>29/80</td>
<td>0.359 0.5350</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;6 Months</td>
<td>42/137</td>
<td>1.359 0.0154</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥6 Months</td>
<td>58/168</td>
<td>0.566 0.1920</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-study rate of disease progression (ALSFRS-R total score reduction per month)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1st tertile ≤(0.3667)</td>
<td>32/110</td>
<td>0.389 0.4298</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2nd tertile &gt; (0.3667) - (0.6673)</td>
<td>38/99</td>
<td>0.987 0.0665</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3rd tertile (0.6673)</td>
<td>30/96</td>
<td>1.733 0.0177</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Note:** Favors Placebo indicates a trend where patients on placebo showed greater decline compared to those on reldesemtiv.
Post-Hoc Analyses Inform Potential Path Forward

**Change From Baseline in ALSFRS-R by Progressor Tertiles**

![Graph showing the change from baseline in ALSFRS-R by progressor tertiles. The graph includes lines for SP reldesemtiv combined (n=117), SP placebo (n=35), MP + FP reldesemtiv combined (n=227), and MP + FP placebo (n=79). The treatment difference is 1.15, P = 0.0112.]

**Probability of No New DME* Over Time With Treatment With Reledesemtiv**

DME (Durable Medical Equipment): Manual wheelchair, power wheelchair, NIV, Augmentative Language Device, PEG

![Graph showing the probability of no new DME over time with treatment with reledesemtiv. The graph includes data points for all active and placebo groups, indicating patients on reledesemtiv had significantly lower risk (38%) of agreeing to receive DME compared to placebo.]

*DME*
Sarcomere Directed Therapies

CORPORATE PROFILE
Our vision is to be the leading muscle biology biopharma company that meaningfully improves the lives of patients with diseases of impaired muscle function through access to our pioneering medicines.

- Achieve regulatory approvals for at least two drugs arising from our pipeline
- Build commercial capabilities to market and sell our medicines reflective of their innovation and value
- Generate sustainable and growing revenues from product sales
- Double our development pipeline to include ten therapeutic programs
- Expand our discovery platform to muscle energetics, growth and metabolism
- Be the science-driven company people want to join and partner with

As always, we will support disease advocacy groups elevating the patient voice and live by our values of integrity, fairness and compassion in all that we do.

VISION 2025
Leading with Science, Delivering for Patients
### Cytokineti cs Financing History

<table>
<thead>
<tr>
<th>Financing</th>
<th>Equity</th>
<th>Upfront Cash, Option, &amp; Milestones</th>
<th>R&amp;D Reimbursement</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Private Investors (VCs)</td>
<td>$116</td>
<td></td>
<td></td>
<td>$116</td>
</tr>
<tr>
<td>IPO</td>
<td>$94</td>
<td></td>
<td></td>
<td>$94</td>
</tr>
<tr>
<td>Public Post-IPO/Other</td>
<td>$420</td>
<td></td>
<td></td>
<td>$420</td>
</tr>
<tr>
<td>Term Loan</td>
<td>$45</td>
<td></td>
<td></td>
<td>$45</td>
</tr>
<tr>
<td>Convertible Debt (net)*</td>
<td>$120.5</td>
<td></td>
<td></td>
<td>$120.5</td>
</tr>
<tr>
<td></td>
<td>$165.5</td>
<td>$630</td>
<td></td>
<td>$795.5</td>
</tr>
</tbody>
</table>

**Investors**

- Astellas: $10, $130, $92, $232
- Amgen: $43, $145, $40, $228
- Royalty Pharma: $10, $90, - , $100
- GSK: $24, $22, $33, $79
- AstraZeneca: - , - , $2, $2
- MyoKardia: - , - , $2, $2
- Global Blood: - , - , $2, $2
- Grants (ALS Assoc/NINDS/other): - , $6, - , $6

**Strategic Partners & Grants**

- $87, $393, $171, $651

---

*Net of fees and expenses

Capital raised: combination of strategic partners and investors
### Balance Sheet & Financial Guidance

**Ended 2019 with 2-3 years of cash based on 2019 guidance***

#### Q3 2019 Condensed Balance Sheet
As of 9/30/19

<table>
<thead>
<tr>
<th></th>
<th>in millions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Cash and investments</td>
<td>$166.0</td>
</tr>
<tr>
<td>Other assets</td>
<td>$21.4</td>
</tr>
<tr>
<td><strong>Total Assets</strong></td>
<td><strong>$187.4</strong></td>
</tr>
<tr>
<td>Debt</td>
<td>$44.8</td>
</tr>
<tr>
<td>Liability related to sale of future royalties</td>
<td>$137.7</td>
</tr>
<tr>
<td>Other liabilities</td>
<td>$24.8</td>
</tr>
<tr>
<td><strong>Total Liabilities</strong></td>
<td><strong>$207.3</strong></td>
</tr>
<tr>
<td>Working capital</td>
<td>$155.0</td>
</tr>
<tr>
<td>Accumulated deficit</td>
<td>-$834.4</td>
</tr>
<tr>
<td>Stockholders' Equity (Deficit)</td>
<td>-$19.9</td>
</tr>
<tr>
<td><strong>Basic Shares Outstanding</strong></td>
<td><strong>58.6</strong></td>
</tr>
</tbody>
</table>

*Q3 balance sheet doesn't include $120M raised in convertible debt financing in Q4 2019*

#### 2019 Financial Guidance

<table>
<thead>
<tr>
<th></th>
<th>in millions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cash Revenue</td>
<td>$28 – 32</td>
</tr>
<tr>
<td>Cash Operating Expenses</td>
<td>$110 – 115</td>
</tr>
<tr>
<td><strong>Net</strong></td>
<td>~ $90</td>
</tr>
</tbody>
</table>

---

*OVERVIEW  CARCIIAC CANDIDATES  SKELETAL CANDIDATES  CORPORATE PROFILE*
Upcoming 2020 Milestones

- Expect Second Interim Analyses from **GALACTIC-HF** in Q1
- Expect Topline Results from **GALACTIC-HF** in Q4
- Complete Enrollment in **METEORIC-HF**
- Conduct Commercial Readiness & Develop Co-Promotion Plan for **Omecamtiv Mecarbil**
- Conduct **REDWOOD-HCM**
- File IND and Initiate Phase 1 Study of **CK-271** in 1H
- Complete Phase 1 SAD/MAD Study of **AMG 594** in 2H
- Prepare for Potential Phase 3 Clinical Trial of **Reldesemtiv** in Patients with ALS
- Advance **CK-601** in IND-Enabling Studies
THANK YOU

John, diagnosed with heart failure

Jillian, diagnosed with HCM

Chuck, diagnosed with ALS

Sarcomere Directed Therapies