



## DEAR SHAREHOLDER,

Rowing has been described as a symphony of motion. As sport, it is both artful and requires highly orchestrated teamwork, perseverance and synchronous execution. Looking back on 2019, rowing represents a very fitting metaphor for the way your company performed and delivered on key goals.

With four drug candidates advancing in clinical research and another one poised to enter clinical development, we are well positioned to realize our Vision

2025, which foresees our being the leading muscle biology biopharmaceutical company that discovers, develops and commercializes new medicines that may meaningfully improve the lives of patients suffering from diseases of impaired muscle function and weakness. Six key tenets will define our transformation over the next five years: achieving at least two regulatory approvals; building commercial capabilities; generating sustainable product revenues; doubling our development pipeline to ten programs; expanding our discovery platform; and being the science-driven company that people want to join. Cytokinetics' excellence in execution in 2019 laid the foundation for us to accomplish these key objectives by 2025.

Under our collaboration with Amgen, GALACTIC-HF, the Phase 3 cardiovascular outcomes trial of *omecamtiv mecarbil*, our cardiac myosin activator, has completed enrollment of more than 8,200 patients with heart failure and is designed to determine if *omecamtiv mecarbil*, when added to standard of care, can reduce the risk of cardiovascular death or heart failure events in patients with high-risk heart failure. The first interim analysis, designed for potential futility, was conducted in 2019 and the Data Monitoring Committee (DMC) recommended the trial continue without changes to its conduct. Recently, the DMC conducted the second and final planned interim analysis for potential futility and superiority, and recommended the trial continue. We now expect top-line results from GALACTIC-HF in Q4 2020. In 2019, we also started METEORIC-HF, the second Phase 3 clinical trial of *omecamtiv mecarbil*, designed to evaluate the effect of treatment with *omecamtiv mecarbil* on exercise capacity in patients with heart failure. We expect to complete enrollment in this trial this year. This program began at Cytokinetics over 20 years ago and we are now especially hopeful and optimistic for pivotal trial results in 2020.

In 2019, Amgen also began a Phase 1 clinical study of AMG 594, a cardiac troponin activator discovered under our joint research program. Development of AMG 594 may include the evaluation of this novel drug candidate as a potential treatment of patients with heart failure with reduced ejection fraction and other types of heart failure resulting from impaired cardiac contractility. The study is designed to evaluate the safety, tolerability, pharmacokinetics and pharmacodynamics of AMG 594 and we expect to complete a key portion of the study this year as may inform new strategies to extend and expand our collaborative cardiac muscle activator activities.

The economic burden of heart failure is especially challenging, approximating \$31 billion to our healthcare system in the United States alone, and is projected to increase to \$70 billion by 2030. As the prevalence of heart failure is expected to double over the next 10 years, new therapies that can have a meaningfully positive effect on clinical outcomes and healthcare budgets will undoubtedly be welcomed.

In 2019, we unveiled a wholly-owned, independent cardiac myosin inhibitor program for the treatment of hypertrophic cardiomyopathies (HCM), inherited cardiovascular disorders. In obstructive HCM, the heart muscle becomes abnormally thick and obstructs blood flow out of the heart, resulting in chest pain, dizziness, shortness of breath, fainting during physical activity, and even sudden death. There are no approved medical treatments that



directly address the underlying hypercontractility of HCM. In 2019, we presented Phase 1 data supportive of the advancement of our drug candidate, CK-274, into REDWOOD-HCM, a Phase 2 clinical trial in patients with obstructive HCM which recently started and for which we expect preliminary results in 2020. In parallel, we will advance an additional cardiac myosin inhibitor, CK-271, into clinical development to explore other patient populations that may benefit.

Last year, results from FORTITUDE-ALS, the Phase 2 clinical trial of *reldesemtiv*, our fast skeletal muscle troponin activator (FSTA) for the potential treatment of amyotrophic lateral sclerosis (ALS), showed that patients on all dose groups of *reldesemtiv* declined less than patients on placebo for slow vital capacity, a measure of respiratory function, and ALSFRS-R, a measure of disease progression, with larger and clinically meaningful differences emerging over time, despite not meeting statistical significance for the primary efficacy analysis. In 2019, the FDA granted orphan drug designation to *reldesemtiv* for the potential treatment of amyotrophic lateral sclerosis (ALS). Previously *reldesemtiv* was granted orphan drug designation by the FDA and orphan medicinal product designation by the European Medicines Agency for the potential treatment of spinal muscular atrophy (SMA) and more recently for the potential treatment of ALS. This year, we will continue to engage with regulatory and reimbursement authorities to prepare for a potential registration program for *reldesemtiv* in patients with ALS. We also advanced joint research activities and the preclinical development of CK-601, a next-generation FSTA, under our collaboration with Astellas which may open the door on more expanded development.

Our excellence in execution in 2019 positioned us well for what could be a transformative year for Cytokinetics. With multiple drug candidates advancing through development, innovative independent and partnered research and a strong balance sheet, we remain mindful of the unmet needs facing patients with impaired muscle function and are motivated to continue to execute well aligned with our Vision to bring them novel mechanism medicines. We look forward to updating you on our continued progress throughout the year ahead and we continue to be grateful for your persistent support.

Robert I. Blum  
President and Chief Executive Officer