



**DEAR SHAREHOLDER,**

“Resilience is the capacity of a system, enterprise or person to maintain its core purpose and integrity in the face of dramatically changed circumstances,” wrote Andrew Zolli, noted author and social scientist. Like the courageous people fighting devastating diseases like ALS, SMA and heart failure who inspire us with their hope and optimism and who personify resilience every day,

Cytokinetics demonstrated extraordinary resilience in 2017. Despite negative results from our first Phase 3 clinical trial, we rededicated to our fundamental mission and values and advanced and expanded our innovative pipeline of muscle biology directed drug candidates.

In 2017, we suspended development of *tirasemtiv*, our first-generation skeletal muscle activator following review of results from VITALITY-ALS, the Phase 3 clinical trial which evaluated its effects in patients with ALS. We were profoundly disappointed that VITALITY-ALS did not deliver on either its primary or secondary endpoints. However, we believe that data from VITALITY-ALS validate the mechanism of action and that our next-generation skeletal muscle activator, *reldesemtiv* (CK-2127107), may address certain limitations of *tirasemtiv*. Recently published Phase 1 data demonstrate *reldesemtiv* may be more potent and potentially better tolerated than *tirasemtiv*.

Like patients battling diseases of muscle dysfunction, we push forward with renewed hope and resilience. *Reldesemtiv* is the subject of a broad clinical trials program under our collaboration with Astellas. Cytokinetics is conducting neuromuscular trials and Astellas is conducting non-neuromuscular trials. In 2017, we began FORTITUDE-ALS, a Phase 2 clinical trial designed to assess effects on SVC and other measures of muscle function after treatment with *reldesemtiv* in patients living with ALS. We also continued conduct of a Phase 2 clinical trial to assess effects of *reldesemtiv* on multiple measures of muscle function in ambulatory and non-ambulatory patients with SMA. In 2017, Astellas conducted clinical trials of *reldesemtiv* in patients with COPD as well as in elderly adults with limited mobility, in both cases, to assess measures of physical function and exercise stamina. Maintaining muscle strength and endurance are essentials to sustain independence and minimize risks of disability. We and Astellas share a commitment to investigate the potential of *reldesemtiv* to increase healthspan for an aging demographic. We remain enthusiastic about the potential of *reldesemtiv* to increase muscle force, power and the time to muscle fatigue in rare diseases and conditions associated with aging.

Furthermore, we continue to conduct joint research activities with Astellas and expect to advance yet another skeletal muscle activator potential drug candidate into development in 2018.

GALACTIC-HF, the global Phase 3 outcomes clinical trial of *omecamtiv mecarbil*, our cardiac muscle activator, continued to enroll patients in 2017 and is proceeding on schedule. This 8,000-patient clinical trial 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. GALACTIC-HF is being conducted by Amgen in collaboration with Cytokinetics. The first patient was dosed in Japan in 2017 prompting a \$10 million milestone payment from Amgen to Cytokinetics. Additionally, in 2017, we sold to Royalty Pharma a 4.5% royalty on potential worldwide sales of *omecamtiv mecarbil* in a \$100 million transaction. We had previously exercised our option to co-invest \$40 million in the Phase 3 development of *omecamtiv mecarbil* in exchange for an incremental royalty of up to 4% on increasing worldwide sales outside Japan. As such, we gained the right to co-promote *omecamtiv mecarbil* in institutional care settings in North America, with reimbursement by Amgen for certain sales force activities. A joint operating team comprising representatives of both companies will be responsible to plan commercialization activities. Our 2017 deal with Royalty Pharma provided important non-dilutive capital to fund our continuing operations. With Amgen, we also continued joint research activities and recently advanced a next-generation cardiac muscle activator into early development.

2017 was a year that tested our resolve. The enduring power of our science and the benefits of a diversified pipeline strategy came into clear focus during the past year. We now press forward with two first-in-class muscle activators in clinical trials, next-generation compounds proceeding in early development, productive collaborations with Astellas and Amgen, and a reinforced balance sheet, all of which provide a solid foundation on which we are planning for a prosperous future. Like patients with ALS and other diseases of severe muscle dysfunction, we persevere, remain resilient and continue to offer much-needed hope to patients and their caregivers that we aim to serve. We look forward to updating you on our continued progress and remain grateful for your persistent support.

Robert I. Blum  
President and Chief Executive Officer

|   | PRE-CLINICAL                  | PHASE 1                       | PHASE 2 | PHASE 3 |
|---|-------------------------------|-------------------------------|---------|---------|
| <b>SKELETAL MUSCLE</b>                      |                               |                               |         |         |
| <i>Tirasemtiv</i> (ALS)                     | <b>SUSPENDED*</b>             |                               |         |         |
| <i>Reldesemtiv</i> (SMA)                    | <b>ASTELLAS COLLABORATION</b> |                               |         |         |
| <i>Reldesemtiv</i> (COPD)                   | <b>ASTELLAS COLLABORATION</b> |                               |         |         |
| <i>Reldesemtiv</i> (ALS)                    | <b>ASTELLAS COLLABORATION</b> |                               |         |         |
| <i>Reldesemtiv</i> (Frailty)                | <b>ASTELLAS COLLABORATION</b> |                               |         |         |
| Next-Generation FSTA                        |                               | <b>ASTELLAS COLLABORATION</b> |         |         |
| <b>CARDIAC MUSCLE</b>                       |                               |                               |         |         |
| <i>Omeclamtiv Mecarbil</i> (heart failure)  | <b>AMGEN COLLABORATION</b>    |                               |         |         |
| Next-Generation Cardiac Sarcomere Activator |                               | <b>AMGEN COLLABORATION</b>    |         |         |
| Cardiac Sarcomere Directed Compound         |                               | <b>UNPARTNERED</b>            |         |         |
| <b>RESEARCH</b>                             |                               |                               |         |         |
| Next Generation Skeletal Muscle Activators  |                               | <b>ASTELLAS COLLABORATION</b> |         |         |
| Other Muscle Biology Directed Research      |                               |                               |         |         |

\*Astellas Option Outside North America & Europe