**Background**

**CK-2127107 Activates the Fast Skeletal Muscle Troponin Complex**

CK-2127107, a selective fast skeletal muscle troponin activator, slows the rate of calcium release from troponin C, sensitizing the sarcomere to calcium and increasing fast skeletal muscle contractility.

**Results**

**Study Objectives**

- To evaluate the safety and tolerability
- To determine potential pharmacodynamic effects
- To evaluate the pharmacokinetics

**Sequential dose escalation, randomized, double blind placebo controlled study**

- Cohort 1: 150 mg bid compared to placebo
- Cohort 2: 450 mg bid (proposed) compared to placebo
- At end of cohort 1, safety, tolerability and pharmacodynamics reviewed to establish dose for Cohort 2

**Patient Population**

- Patients 12 years of age and older
- Genetically confirmed spinal muscular atrophy Types II, III, or IV
- 72 patients equally divided between ambulatory and non-ambulatory status

**Studying the Potential Treatment of Spinal Muscular Atrophy**

**Study Design**

Sequential dose escalation, randomized, double blind placebo controlled study

- Dosing: 8 weeks
- Screening: up to 3 weeks
- Follow-Up: 4 weeks after last dose

- 72 patients equally divided between ambulatory and non-ambulatory status
- Genetically confirmed spinal muscular atrophy Types II, III, or IV
- Patients 12 years of age and older

**Phase I Clinical Trials Program**

**Study**

- **Study 1**: Investigates safety and tolerability; Evaluate pharmacokinetics, (Increasing single dose)
- **Study 2**: Investigates safety, tolerability and pharmacodynamics in healthy, young and elderly (multiple dose)
- **Study 3**: Investigates pharmacodynamic effects
- **Study 4**: Investigates pharmacokinetics of two different physical forms of API in subjects
- **Study 5**: Investigates pharmacokinetics of a stable formulation

**Results**

- **Study 1**: Achieved highest planned dose; No emerging pattern of adverse events; Statistically significant increases (versus placebo) in peak force; Well tolerated
- **Study 2**: 16-day courses of either 300 mg or 500 mg twice daily were well tolerated by young and older subjects; Plasma concentrations achieved steady state; No age-related differences in PK
- **Study 3**: Well tolerated at 300 mg and 1000 mg; Physical form selected
- **Study 4**: Well tolerated at 250 mg, 500 mg and 1000 mg; Tablet appropriate for use in potential future clinical trials
- **Study 5**: Tablet appropriate for use in potential future clinical trials

**Conclusion**

Based on safety, pharmacokinetics, and pharmacodynamics findings in Phase 1 studies, a Phase 2a clinical trial of CK-2127107 is currently enrolling patients in the US.

**Disclosures**

S Rudnicki J Andrews, F Malik, A Wolff are employees of Cytokinetics, Inc. J Day has served as a consultant to Cytokinetics.