Analyst & Investor Event
Wednesday, May 2, 2007
The Colonnade Hotel
Boston, MA

Fampridine-SR Phase 3 MS Data Presentation
A Phase 3, Multi-center Trial of Oral, Sustained-release Fampridine (4-aminopyridine) in Multiple Sclerosis

Andrew D. Goodman¹, Steven R. Schwid¹, Theodore Brown², Lauren Krupp³, Randall Schapiro⁴, Lawrence Marinucci⁵, Ron Cohen⁵, and Andrew Blight⁵

¹ University of Rochester, Rochester, NY
² Evergreen Medical Center, Seattle, WA
³ SUNY-Stony Brook, Stony Brook, NY
⁴ Minneapolis Clinic of Neurology, Minneapolis, MN
⁵ Acorda Therapeutics, Hawthorne, NY

Funding: Acorda Therapeutics

Disclosures: Drs. Goodman, Krupp, and Shapiro have been consultants to Acorda. Mr. Marinucci, Drs. Cohen and Blight are employees and hold equity in Acorda.
Investigators*

Barry Arnason-University of Chicago
Francois Bethoux-Cleveland Clinic Foundation
Christopher Bever-Maryland Center for MS
James Bowen-University of Washington
Dennis Dietrich-Advanced Neurology Specialists
Robert Naismith-Washington University
Norman Kachuck-USC, Keck Sch. Of Medicine
Lauren Krupp-SUNY- Stony Brook
Thomas Leist-Thomas Jefferson University
John Lindsey-University of Texas, Houston
Fred Lublin-Mt.Sinai School of Medicine, NY
Michele Mass-Oregon Health & Science Univ.
Daniel McGowan-Foothills Medical Center
Marshall Keilson-Maimonides Medical Center
Mary Ann Picone-Gimbel MS Center
Kotttil Rammohan-Ohio State Univ. MS Center
Randall Schapiro-Minneapolis Clinic of Neurology
Steven Schwid-University of Rochester
Theodore Brown-MS Center at Evergreen
Ben Thrower-Shepherd Center
Timothy Vollmer-Barrow Neurology Clinic
Mark S. Freedman-Ottawa Hospital General Campus
Thomas Scott-Allegheny General Hospital
Hillel Panitch-Fletcher Allen Health Care
Joel Oger-University of British Columbia
David Mattson-Indiana University
Keith Edwards-Neurological Research Center, Inc.
Christine Short-QEI Health Sciences Center
Mark Agius-University of California at Davis
Omar Khan-Wayne State University
Colleen O'Connell-River Valley Health
Mitchell Freedman-Raleigh Neurology Associate

*by Center # (33 centers in US and Canada)
Overview

• Phase 3, double-blind, placebo-controlled, study of sustained-release fampridine (4-aminopyridine)
• Potassium channel blocker, affects neural conduction
• Previous trials have indicated potential functional benefits
• Current study focused on ambulatory function and lower extremity strength
Efficacy Measures

- Timed 25 Foot Walk
- 12 Item MS Walking Scale (MSWS-12)
- Lower Extremity Manual Muscle Test
- Ashworth score for spasticity
- Clinician Global Impression
- Subject Global Impression

Safety Measures

- Physical examination
- Vital signs
- ECG
- Laboratory tests
- Adverse events
- Drug plasma concentration
Key Inclusion and Exclusion Criteria

**Inclusion:**
- Able to complete the Timed 25 ft Walk at screening within 8 - 45 seconds (average of two trials)
- Stable disease and stable concomitant medication (including immunomodulators)

**Exclusion:**
- History of seizure
- Previously treated with fampridine
- MS exacerbation within 60 days of screening
Study Design

- **Screening**
- **Fampridine-SR 10 mg b.i.d.** (3:1 randomization)
- **Placebo**
- **2 week placebo run-in**
- **14-week stable dose**
- **2 week follow-up**
A *Timed Walk Responder* is a subject whose walking speed on at least 3 of the 4 “on drug” visits is faster than the *fastest* speed during any of the 5 “off drug” visits.
### Patient Disposition

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>Fampridine</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patients Randomized</strong></td>
<td>72</td>
<td>229</td>
<td>301</td>
</tr>
<tr>
<td><strong>ITT Population</strong></td>
<td>72</td>
<td>224</td>
<td>296</td>
</tr>
<tr>
<td><strong>Completed</strong></td>
<td>71 (99%)</td>
<td>212 (93%)</td>
<td>283</td>
</tr>
<tr>
<td><strong>Discontinued</strong></td>
<td>1 (1.4%)</td>
<td>17 (7.4%)</td>
<td>18</td>
</tr>
<tr>
<td><strong>Adverse event</strong></td>
<td>0</td>
<td>11# (4.8%)</td>
<td>11</td>
</tr>
</tbody>
</table>

*# 3 events started before double blind period*
Baseline Demographics

(Safety population)

<table>
<thead>
<tr>
<th></th>
<th>Placebo N=72</th>
<th>Fampridine N=228</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>29 (40.3%)</td>
<td>66 (28.9%)</td>
<td>0.093</td>
</tr>
<tr>
<td>Female</td>
<td>43 (59.7%)</td>
<td>162 (71.1%)</td>
<td></td>
</tr>
<tr>
<td><strong>Mean Age (SD)</strong></td>
<td>50.9 (8.88)</td>
<td>51.5 (8.72)</td>
<td>0.500</td>
</tr>
<tr>
<td><strong>MS Course</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Relapsing-remitting</td>
<td>21 (29.2%)</td>
<td>62 (27.2%)</td>
<td>0.555</td>
</tr>
<tr>
<td>Primary-progressive</td>
<td>14 (19.4%)</td>
<td>31 (13.6%)</td>
<td></td>
</tr>
<tr>
<td>Secondary-progressive</td>
<td>35 (48.6%)</td>
<td>125 (54.8%)</td>
<td></td>
</tr>
<tr>
<td>Progressive relapsing</td>
<td>2 (2.8%)</td>
<td>10 (4.4%)</td>
<td></td>
</tr>
<tr>
<td><strong>Mean EDSS (SD)</strong></td>
<td>5.76 (1.071)</td>
<td>5.77 (1.008)</td>
<td>0.892</td>
</tr>
</tbody>
</table>
## Baseline Efficacy Variables

(ITT population)

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>Fampridine</th>
<th>p - value</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>72</td>
<td>224</td>
<td></td>
</tr>
<tr>
<td>Walking speed (ft/sec)</td>
<td>2.07</td>
<td>2.05</td>
<td>0.853</td>
</tr>
<tr>
<td>LEMMT Score</td>
<td>3.97</td>
<td>4.06</td>
<td>0.245</td>
</tr>
<tr>
<td>Ashworth Score</td>
<td>0.95</td>
<td>0.90</td>
<td>0.718</td>
</tr>
<tr>
<td>MSWS-12 Score</td>
<td>68.5</td>
<td>70.7</td>
<td>0.472</td>
</tr>
<tr>
<td>SGI Score</td>
<td>4.67</td>
<td>4.59</td>
<td>0.460</td>
</tr>
</tbody>
</table>
Primary Endpoint: Timed Walk
Response Analysis (ITT population)

<table>
<thead>
<tr>
<th></th>
<th>Responders (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo (N=72)</td>
<td>8.3%</td>
</tr>
<tr>
<td>Fampridine (N=224)</td>
<td>34.8%</td>
</tr>
</tbody>
</table>

P < 0.0001
**Mean Change in Walking Speed**

(ITT population)

<table>
<thead>
<tr>
<th></th>
<th>Day 14</th>
<th>Day 42</th>
<th>Day 70</th>
<th>Day 98</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo (N=72)</td>
<td><img src="image" alt="Graph" /></td>
<td><img src="image" alt="Graph" /></td>
<td><img src="image" alt="Graph" /></td>
<td><img src="image" alt="Graph" /></td>
</tr>
<tr>
<td>Famp. Non-responders (N=146)</td>
<td><img src="image" alt="Graph" /></td>
<td><img src="image" alt="Graph" /></td>
<td><img src="image" alt="Graph" /></td>
<td><img src="image" alt="Graph" /></td>
</tr>
<tr>
<td>Famp. Responders (N=78)</td>
<td><img src="image" alt="Graph" /></td>
<td><img src="image" alt="Graph" /></td>
<td><img src="image" alt="Graph" /></td>
<td><img src="image" alt="Graph" /></td>
</tr>
</tbody>
</table>

* * * *

* p<0.0001 vs. placebo  # p<0.01 vs. placebo
MSWS-12* – Validation of Response Criterion (ITT population)

(Response mean favored drug over placebo for all 12 questions)

## Secondary Validation of Response Criterion

<table>
<thead>
<tr>
<th></th>
<th>Non-Responders</th>
<th>Responders</th>
<th>p - value</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>212</td>
<td>84</td>
<td></td>
</tr>
<tr>
<td>Avg. SGI Score*, Mean (SD)</td>
<td>4.43 (1.03)</td>
<td>4.88 (0.90)</td>
<td>0.0010</td>
</tr>
<tr>
<td>CGI Score#, Mean (SD)</td>
<td>3.74 (0.75)</td>
<td>3.28 (0.87)</td>
<td>&lt; 0.0001</td>
</tr>
</tbody>
</table>

*SGI score averaged over double-blind visits, 1 = “terrible”, 7 = “delighted”

*CGI score assigned at the last double-blind visit, 1 = very much improved, 7 = very much worse
Lower Extremity Strength (LEMMT) (ITT population)

Placebo (N=72) F Non-Res (N=146) F Res (N=78)

Change LEMMT Score (mean ± 95% CI)

p = 0.0002

p = 0.046
Direct Comparison of Fampridine vs. Placebo Groups (ITT population)

- Improvement in walking speed ($p = 0.0004$)
- Improvement in LEMMT score ($p = 0.0029$)
- Improvement in Ashworth score ($p = 0.021$)
Most Frequent Adverse Events

<table>
<thead>
<tr>
<th>Event</th>
<th>Placebo</th>
<th>Fampridine-SR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Falls</td>
<td>15.3%</td>
<td>15.8%</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>13.9%</td>
<td>13.6%</td>
</tr>
<tr>
<td>Dizziness</td>
<td>5.6%</td>
<td>8.3%</td>
</tr>
<tr>
<td>Insomnia</td>
<td>4.2%</td>
<td>8.3%</td>
</tr>
<tr>
<td>Fatigue</td>
<td>2.8%</td>
<td>6.1%</td>
</tr>
<tr>
<td>Nausea</td>
<td>4.2%</td>
<td>6.1%</td>
</tr>
<tr>
<td>Upper respiratory infection</td>
<td>9.7%</td>
<td>6.1%</td>
</tr>
<tr>
<td>Asthenia</td>
<td>5.6%</td>
<td>5.7%</td>
</tr>
<tr>
<td>Back pain</td>
<td>0.0%</td>
<td>5.7%</td>
</tr>
<tr>
<td>Balance disorder</td>
<td>2.8%</td>
<td>5.7%</td>
</tr>
<tr>
<td>Headache</td>
<td>5.6%</td>
<td>5.7%</td>
</tr>
</tbody>
</table>
Adverse Events Leading to Discontinuation

**Beginning prior to treatment:**
- Throat tightness
- Dyspepsia
- Hepatitis C

**Treatment-emergent:**
- Influenza *
- Sepsis, with seizure *
- Ankle fracture
- Balance disorder
- Confusional state
- Dizziness/balance disorder
- Headache
- Anxiety *

*Serious Adverse Event
Serious Adverse Events

Double-blind period (14 weeks)
- Angina pectoris
- Colitis
- Influenza#
- Sepsis, with seizure #@
- UTI (2)
- Viral infection
- Neck injury
- Pelvic fracture
- Musculoskeletal stiffness
- Osteonecrosis

- Breast cancer
- MS exacerbation
- Syncope
- Anxiety #@
- Deep vein thrombosis

Post-treatment (4 weeks)
- Wound infection
- Foot fracture
- Surgery

# Led to discontinuation  @ Possibly or Probably related
Conclusions

• Significantly more consistent walking responders in the fampridine-treated group
• Consistent timed-walk response is clinically meaningful (MSWS-12, SGI, CGI)
• >20% average improvement in walking speed
• Benefit maintained throughout the 14 weeks of treatment
• Fampridine safety experience in line with previous studies
Additional Data
Response Rate and MS Course Type

<table>
<thead>
<tr>
<th>Course Type</th>
<th>Response Rate</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>R-R</td>
<td>N = 62</td>
<td></td>
</tr>
<tr>
<td>P-P</td>
<td></td>
<td>N = 31</td>
</tr>
<tr>
<td>S-P</td>
<td></td>
<td>N = 125</td>
</tr>
<tr>
<td>P-R</td>
<td></td>
<td>N = 10</td>
</tr>
</tbody>
</table>
Comparison of MS-F202 and MS-F203
Timed Walk Responders

Note: The p-values (versus placebo) are Bonferroni-adjusted.
Consistent Improvement in Walking Speed

**MS-F202**

- **Placebo (N=47)**
- **Fampridine-SR Responders (N=58)**

**Mean Percent Change**

- Week 2: 25%
- Week 6: 30%
- Week 10: 25%
- Week 14: 20%

*p* < 0.001

**MS-F203**

- **Placebo (N=72)**
- **Fampridine-SR Responders (N=78)**

**Mean Percent Change**

- Week 2: 30%
- Week 6: 25%
- Week 10: 20%
- Week 14: 15%

*p* < 0.001
Change in MSWS-12 Score (Mean, SEM)

* Excludes seven non-responders with no MSWS-12 responses
Average Change from Baseline in LEMMT

**MS-F202**
- Placebo (N=47)
- F Non-Res (N=98)
- F Res (N=58)

**MS-F203**
- Placebo (N=72)
- F Non-Res (N=146)
- F Res (N=78)

Average Change in LEMMT Score:
- MS-F202: Placebo < 0.001, F Non-Res < 0.001, F Res < 0.001
- MS-F203: Placebo < 0.001, F Non-Res = 0.046, F Res < 0.001
Return to Baseline
Two Week Follow-up Visit

Change from baseline walking speed

No significant differences between groups
Four Week Follow-up Visit

Change from baseline walking speed

Placebo (N=69)  FNR (N=138)  FR (N=77)

No significant differences between groups
Recent Walking Speed Publications
Walking speed and distance

Creange A, Serre I, Audrey D, Nineb A, Boerio D, Moreau T, Maison P and Sindefi-Sep R.

Walking capacities in multiple sclerosis measured by global positioning system odometer.


Best* correlation for maximum observed walking distance (using GPS monitor) was with walking speed on the Timed 10 Meter Walk ($r^2 = 0.75$).

*relative to EDSS, MSWS-12, and time to walk 10 m.
Creange, et al., 2007

$r^2 = 0.75$
$p < 0.0001$
Clinical impact of change

Kragt JJ, van der Linden FAH, Nielsen JM, Uitdehaag BMJ and Polman CH.
Clinical impact of 20% worsening on Timed 25-foot Walk and 9-hole Peg Test in multiple sclerosis.
*Multiple Sclerosis* 2006;12:594-598.

Showed significant effect of 20% worsening of Timed 25 Foot Walk on the Guys Neurological Disability Scale, a measure of patient-perceived daily life disability.

Confirmed that a 20% change in T25FW is clinically meaningful.
Walking speed and daily activity

Fahey MC, Corben LA, Collins V, Churchyard AJ and Delatycki MB.

The 25-foot walk velocity accurately measures real world ambulation in Friedreich ataxia.


Conclude that the velocity measured over 25 feet is representative of mobility (in Friedreich ataxia) as assessed using daily step counts, % time spent active, and steps taken in 1 and 60 minutes.
Speaker Biographies

Ron Cohen, M.D.
President and Chief Executive Officer
Acorda Therapeutics

Ron Cohen, M.D. is President, CEO, and founder of Acorda Therapeutics, Inc. a biotechnology company developing therapies for spinal cord injury, multiple sclerosis and other disorders of the central nervous system. Dr. Cohen previously was a principal in the startup of Advanced Tissue Sciences, Inc., a biotechnology company engaged in the growth of human organ tissues for transplantation uses. Dr. Cohen received his B.A. degree with honors in Psychology from Princeton University, and his M.D. from the Columbia College of Physicians & Surgeons. He completed a residency in Internal Medicine at the University of Virginia Medical Center, and is Board Certified in Internal Medicine. Dr. Cohen is Chairman Emeritus and a Director of the Board of the New York Biotechnology Association, and serves on the Emerging Company Section of the Board of the Biotechnology Industry Organization (BIO) and the Columbia Presbyterian Health Sciences Clinical Care Center.

Andrew R. Blight, Ph.D.
Chief Scientific Officer
Acorda Therapeutics

Andrew R. Blight, Ph.D. has been Chief Scientific Officer of Acorda Therapeutics since January 2004 and previously served as Executive Vice President, Research and Development from 2000 to 2004, and Vice President from 1998 to 2000. Prior to joining Acorda, Dr. Blight spent approximately six years as Professor and Director of the Neurosurgery Research Laboratory at the University of North Carolina at Chapel Hill. Dr. Blight held prior academic positions at Purdue University and New York University. Dr. Blight is a leader in SCI pathophysiology research and has made several important contributions to the field, particularly on the role of demyelination in SCI. He also pioneered the therapeutic application of 4-AP in SCI animal models and in human clinical trials. Dr. Blight is a member of the editorial board of the Journal of Neurotrauma and has served as a member of the NIH NSDA review committee. He was previously Secretary, Treasurer, and Vice President of the National Neurotrauma Society. He has published over 100 original articles in books and in peer-reviewed journals and is an internationally acknowledged authority in multiple sclerosis and related disorders. He is also an internationally recognized expert in the field of SCI, and has made several important contributions to this field.

Lauren B. Krupp, M.D.
Professor of Neurology and Psychology
Stony Brook University

Lauren Krupp, M.D. received her medical degree from the Albert Einstein College of Medicine, completed her neurology residency at Albert Einstein and Montefiore Medical Center, and then completed additional fellowship training at the Neuroimmunology/Multiple Sclerosis Branch of the National Institutes of Health. She is currently a Fellow of the American Academy of Neurology. She is currently a Professor of Neurology and Psychology at the State University of New York at Stony Brook and Medical Center and specializes in multiple sclerosis. She is the director of the Pediatric MS Center at Stony Brook (the first and only pediatric MS center in the United States), and co-directs the adult MS Center at Stony Brook. She is currently a member of the National Multiple Sclerosis Society and serves as a member of the NIH NSDA review committee. She has published over 100 original articles in books and in peer-reviewed journals and is an internationally recognized authority in multiple sclerosis and related disorders. He is also an internationally acknowledged authority in the field of SCI, and has made several important contributions to this field.

Mark J. Tullman, M.D.
Director, Columbia University Multiple Sclerosis Clinical Care Center

Mark J. Tullman, M.D. is currently an Assistant Professor of Neurology and Director of the Multiple Sclerosis Clinical Care Center of Columbia University Medical Center. He received his medical degree from the Albert Einstein College of Medicine, completed his internal medicine residency at the Albert Einstein College of Medicine, and then completed his neurology residency and multiple sclerosis fellowship at the Mount Sinai School of Medicine. He became a member of the University of Virginia Medical Center and then completed his fellowship in multiple sclerosis at the National Institutes of Health. He is currently a member of the National Multiple Sclerosis Society and serves as a member of the NIH NSDA review committee. He has published over 100 original articles in books and in peer-reviewed journals and is an internationally acknowledged authority in the field of SCI, and has made several important contributions to this field.

Ron Cohen, M.D.
President and Chief Executive Officer
Acorda Therapeutics


