34th Annual J.P. Morgan Healthcare Conference

January 11, 2016
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Improving Lives of People with Neurological Diseases

- Multiple Sclerosis
- Parkinson’s disease
- Post-Stroke Walking Deficits
- Epilepsy
- Migraine
2015 Achievements

**AMPYRA 2015 Growth**
- Net sales of $436 Million
- Net sales growth of 19%

**Advanced Late Stage Programs**
- CVT-301 in Parkinson’s disease
- PLUMIAZ in epilepsy
- Dalfampridine in post-stroke

**Initiated CVT-427 Program**
- Completed Phase 1 migraine study

**IP Defense**
- 3 ANDA filer settlements
- PTAB denial of 2 IPR petitions

**rHlgM22 Safety Data in MS**
- Positive Phase 1 safety data
- Second Phase 1 enrolling in acute MS relapses

*Unaudited*
AMPYRA (dalfampridine) for Multiple Sclerosis
Lead Commercial Asset

AMPYRA Annual Sales ($M)

2010 – 2015 CAGR: 27%

$133  $210  $266  $302  $366  $436  $475-$485


*Ten months, Mar – Dec 2010
**Unaudited; subject to audited financials
*** 2016 guidance provided on January 11, 2016
# Clinical Pipeline

<table>
<thead>
<tr>
<th>THERAPY</th>
<th>INDICATION</th>
<th>PHASE 1</th>
<th>PHASE 2</th>
<th>PHASE 3</th>
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<tbody>
<tr>
<td>CVT-301</td>
<td>Parkinson’s Disease</td>
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<tr>
<td>PLUMIAZ™ (diazepam) Nasal Spray</td>
<td>Seizure Clusters</td>
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<tr>
<td>DALFAMPRIDINE</td>
<td>Chronic Post-Stroke Walking Deficits</td>
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<td>CVT-427</td>
<td>Migraine</td>
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<tr>
<td>rHlgM22</td>
<td>MS</td>
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Late Stage Pipeline
Targeting Large Unmet Medical Needs

**Parkinson’s Disease**
- ~350,000 patients in US with OFF periods
- >$500M US peak sales

**Epilepsy**
- ~175,000 patients in US with seizure clusters
- > $200M US peak sales

**Post-Stroke Walking Deficits**
- ~3.5 million stroke survivors in US with mobility issues
- 3 QD prototypes currently in human PK studies
CVT-301 in Parkinson’s Disease
CVT-301 Overview
Phase 3 Study Ongoing

Inhaled Levodopa
• Self-administered, inhaled medication
• Utilizes ARCUS® technology to deliver specific doses of dry powder L-dopa

Positive Phase 2b Efficacy Data
• Results show potential to rapidly treat off periods
• Separation vs. placebo observed at 10 minutes after dosing and was durable for at least an hour
• Clinically important reductions in UPDRS Part III at both tested doses

Phase 2b Safety Profile
• No treatment-associated AEs on lung function
• No serious AEs overall
• Well tolerated; no increase in dyskinesia during at-home use
L-Dopa Pharmacokinetics

Current Oral Standard of Care
Data from Phase 2a in fasted PD patients

CVT-301 Profile
Data from Phase 1 trial in healthy volunteers
Phase 2b Study Achieved Primary Endpoint
UPDRS Part III

Clinically important reductions at both tested doses

Visit 4: CVT-301 35mg or Pbo

- Mean Change in UPDRS Part III
- Pbo: -5.3
- CVT-301: -9.9
- 95% CI: -7.90, -1.30
- p = 0.007

Visit 6: CVT-301 50mg or Pbo

- Mean Change in UPDRS Part III
- Pbo: -3.07
- CVT-301: -10.02
- 95% CI: -10.31, -3.60
- p < 0.001

* Schulman et al, Arch Neurol. 2010;67(1):64-70
Phase 2 Data Presented at MDS 2015
Separation vs. Placebo Observed – 10 Minutes

Visit 6 – CVT-301 50mg dose
Time (minutes)

<table>
<thead>
<tr>
<th>Diff vs Pbo</th>
<th>10 min</th>
<th>20 min</th>
<th>30 min</th>
<th>60 min</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (SEM)</td>
<td>-3.56 (1.62)</td>
<td>-5.68 (2.04)</td>
<td>-8.43 (1.90)</td>
<td>-9.59 (1.83)</td>
</tr>
<tr>
<td>p-value</td>
<td>0.0309</td>
<td>0.0068</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
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</table>

UPDRS Part III Clinically Important Differences (CID)*:
- 2.5pts = Minimal CID
- 5.2pts = Moderate CID
- 10.8pts = Large CID

* Schulman et al, Arch Neurol. 2010;67(1):64-70
## CVT-301 Phase 2b Safety Profile

<table>
<thead>
<tr>
<th>Treatment-Emergent Adverse Event, n (%)</th>
<th>Placebo Group (n=43)</th>
<th>CVT-301 Group (n=43)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dizziness</td>
<td>2 (5)</td>
<td>3 (7)</td>
</tr>
<tr>
<td>Cough</td>
<td>1 (2)</td>
<td>3 (7)</td>
</tr>
<tr>
<td>Nausea</td>
<td>0</td>
<td>3 (7)</td>
</tr>
<tr>
<td>Headache</td>
<td>2 (5)</td>
<td>2 (5)</td>
</tr>
<tr>
<td>Peripheral edema</td>
<td>1 (2)</td>
<td>2 (5)</td>
</tr>
<tr>
<td>Anxiety</td>
<td>0</td>
<td>2 (5)</td>
</tr>
<tr>
<td>Discolored sputum</td>
<td>0</td>
<td>2 (5)</td>
</tr>
</tbody>
</table>

Source: Poster from MDS June 2015
Phase 3 Program – Target NDA Filing 1Q 2017

**Trial 004**
- Multicenter randomized, double-blind, placebo-controlled study
- Three arms (placebo/low dose/high dose)
- ~345 participants

**Duration**
- 12 WEEKS

**Primary Endpoint**
- UPDRS Part III Change @ 30 mins

**Trial 005**
- Multicenter, randomized, safety study compared to an observational control group
- ~365 participants

**Duration**
- 12 MONTHS

**Pulmonary Safety**
CVT-301 U.S. Market Opportunity

Projected U.S. Peak Sales in Excess of $500 million

Source: National Parkinson's Foundation
PLUMIAZ™ (diazepam nasal spray) in Epilepsy
PLUMIAZ Development Overview

Diazepam Nasal Spray for Seizure Clusters

- Unmet need
  - Only approved treatment is rectal gel
- Nasal administration is more practical and socially acceptable

Three Clinical Studies

- Bioavailability: PLUMIAZ vs Diastat
- Long term safety study
- Dose proportionality study expected to begin 1Q16
PLUMIAZ: On Track for 1Q17 NDA Refiling

2.8MM People with Epilepsy (US)

~175K Experience seizure clusters*

Six month review & orphan status

Leverages commercial organization

Potential peak sales of >$200M

*Defined as multiple, distinct seizures that occur over a 24-hour period.

Patients continue to experience seizure clusters even though they are on stable AEDs
Dalfampridine in Chronic Post-Stroke Walking Deficits (PSWD)
Dalfampridine in Development for PSWD

No drug therapy indicated for people with chronic PSWD
- ~7 million people in U.S. have had a stroke
- ~3.5 million have mobility issues

Successful dalfampridine proof-of-concept study

Enrollment in Phase 3 study ongoing; interim analysis in 2016

QD formulation
- Three prototypes currently in Phase 1 PK studies
- Data expected in 1Q 2016
Phase 2 POC Study: Overall Timed Walk Result

- **Placebo**
  - Mean ± SE: 0.1 ft/sec

- **Dalfampridine-ER**
  - Mean ± SE: 0.2 ft/sec

*N=78, p=0.027*

Note: p value from a mixed statistical model with sequence, period, visit and treatment as fixed effects and subject as a random effect.
Percentages of Patients Who Reached Threshold Change from Baseline in Walking Speed by Period

Period 1

Period 2

PBO (n=52)  
D-ER (n=26)

PBO (n=26)  
D-ER (n=49)
Early Stage Pipeline

**CVT-427 (migraine)**
- Phase 1 study complete
- Data to be presented at medical meeting

**rHlgM22 (multiple sclerosis)**
- Phase 1, single ascending dose study in acute MS relapses currently enrolling patients
- Study completion expected 1H17

**Cimaglermin alfa (heart failure)**
- Topline data from second Phase 1 (on clinical hold - Hy’s Law case)
- Safety profile consistent with first Phase 1; inconclusive efficacy data
- Data analyses ongoing; plan to meet with FDA to discuss data/evaluate next steps
2016 Guidance and Milestones
2016 Financial Guidance

**AMPYRA**
$475 – $485 million*

**R&D**
$165 – $175 million

**SG&A**
$195 – $205 million

*U.S. net sales
**Key Clinical Milestones**

<table>
<thead>
<tr>
<th>Event</th>
<th>Date</th>
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<tbody>
<tr>
<td>Single dose PK/safety update Phase 1 CVT-427 in migraine</td>
<td>1Q 2016</td>
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<tr>
<td>Single dose PK results from QD formulation (dalfampridine)</td>
<td>1Q 2016</td>
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<tr>
<td>Interim analysis of dalfampridine Phase 3 post-stroke trial</td>
<td>3Q 2016</td>
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<tr>
<td>Complete CVT-301 Phase 3 in Parkinson’s (LPO)</td>
<td>4Q 2016</td>
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<tr>
<td>File NDA for CVT-301 in Parkinson’s</td>
<td>1Q 2017</td>
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<tr>
<td>File NDA for PLUMIAZ for seizure clusters</td>
<td>1Q 2017</td>
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<tr>
<td>Complete Phase 1 M22 in acute MS relapses</td>
<td>1H 2017</td>
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2016 Priorities

- Advance Pipeline
- Continue to Grow Ampyra
- Business Development