CVT-301
Phase 3 Program Overview
Movement Disorder Society – Investor Event
June 5, 2017
Forward Looking Statement

THIS PRESENTATION WILL DISCUSS CVT-301, AN INVESTIGATIONAL PRODUCT NOT APPROVED TO TREAT ANY DISEASE

This presentation is subject to risks and uncertainties that could cause actual results to differ materially, including: the ability to realize the benefits anticipated from the Biotie and Civitas transactions, among other reasons because acquired development programs are generally subject to all the risks inherent in the drug development process and our knowledge of the risks specifically relevant to acquired programs generally improves over time; the ability to successfully integrate Biotie's operations and Civitas' operations, respectively, into our operations; we may need to raise additional funds to finance our expanded operations and may not be able to do so on acceptable terms; our ability to successfully market and sell Ampyra (dalfampridine) Extended Release Tablets, 10 mg in the U.S., which will likely be materially adversely affected by the recently announced court decision in our litigation against filers of Abbreviated New Drug Applications (each, an “ANDA”) to market generic versions of Ampyra in the U.S.; third party payers (including governmental agencies) may not reimburse for the use of Ampyra or our other products at acceptable rates or at all and may impose restrictive prior authorization requirements that limit or block prescriptions; the risk of unfavorable results from future studies of Ampyra or from our other research and development programs, including INBRIJA™ (CVT-301, levodopa inhalation powder), or any other acquired or in-licensed programs; we may not be able to complete development of, obtain regulatory approval for, or successfully market INBRIJA, any other products under development, or the products that we acquired with the Biotie transaction; the occurrence of adverse safety events with our products; delays in obtaining or failure to obtain and maintain regulatory approval of or to successfully market Fampyra outside of the U.S. and our dependence on our collaborator Biogen in connection therewith; competition; failure to protect our intellectual property, to defend against the intellectual property claims of others or to obtain third party intellectual property licenses needed for the commercialization of our products; and failure to comply with regulatory requirements could result in adverse action by regulatory agencies.

These and other risks are described in greater detail in our filings with the Securities and Exchange Commission. We may not actually achieve the goals or plans described in our forward-looking statements, and investors should not place undue reliance on these statements. Forward-looking statements made in this presentation are made only as of the date hereof, and we disclaim any intent or obligation to update any forward-looking statements as a result of developments occurring after the date of this presentation.
Ron Cohen, M.D., CEO
Acorda Therapeutics
Guest Speakers

MATTHEW STERN, M.D.
• Professor Emeritus of Neurology, Perelman School of Medicine (University of Pennsylvania)
• Former Director of the Parkinson’s Disease and Movement Disorders Center
• Past President of the International Parkinson and Movement Disorder Society (MDS)
• Co-Founder of the Panorama Patient Network

PETER LeWITT, M.D.
• Professor of Neurology, Wayne State University School of Medicine
• Editor-in-chief of Clinical Neuropharmacology
• Founding member of the Parkinson Study Group
• Past Secretary of the International Parkinson and Movement Disorder Society (MDS)
• Principal investigator: CVT-301-004 study

DONALD GROSSET, M.D.
• Consultant Neurologist, Institute of Neurological Sciences, Queen Elizabeth University Hospital (Glasgow)
• Honorary Professor in Neurology, University of Glasgow
• Chair, Movement Disorder Advisory Group, Association of British Neurologists
• Principal investigator: CVT-301-005 study
Meeting Agenda

• Introduction
  Ron Cohen, M.D., CEO
• OFF Periods in Parkinson’s Disease
  Matt Stern, M.D.
• CVT-301: Rationale
  Rick Batycky, Ph.D., CTO
• CVT-301: Overview of Phase 3 Program
  Burkhard Blank, M.D., CMO
• CVT-301-004 Study Overview
  Peter LeWitt, M.D.
• CVT-301-005 Study Overview
  Donald Grosset, M.D.
• CVT-301 Summary / Closing
  Burkhard Blank, M.D., CMO
• Q&A
Matt Stern, M.D.
OFF Periods in Parkinson's Disease
OFF Periods in PD: Epidemiology

### Prevalence and Incidence of PD in U.S.

<table>
<thead>
<tr>
<th>Prevalence and Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Affects approximately 1 million patients in the United States</td>
</tr>
<tr>
<td>- Prevalence in population &gt;80 years old is 10%</td>
</tr>
<tr>
<td>• Approximately 60,000 new cases/year</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Onset</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Average age of onset is 60 years</td>
</tr>
</tbody>
</table>

Impact of PD Progression and OFF Periods

- PD symptoms become increasingly difficult to control with oral levodopa therapy as the disease progresses.
- OFF periods, defined as re-emergence of PD symptoms, can occur throughout the day and be unexpected.
- Re-emergence of PD symptoms is a major concern for people with PD and can be disruptive.
In a survey of ~3,000 individuals with PD, most experienced at least two OFF periods daily, each with an average duration of 30–60 minutes\(^1\)

OFF periods\(^2,3\) interrupt ability to function throughout the day

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1 The Michael J. Fox Foundation Survey of Parkinson’s Patients’ Off Time Experience, July 2014.
Over time, patients may experience OFF Periods despite being optimized on oral LD and other baseline PD medications.

Patients may experience OFF periods due to wearing off of LD, delayed onset of LD, or an incomplete response.
Oral Levodopa is Highly Effective and the Gold Standard…

At L-dopa therapeutic threshold:

Small change in plasma level

Large change in motor function

300-400 ng/ml can bridge

…but There is Inherent Variability of the Oral Route…

Barriers to getting oral L-dopa to the CNS

Oral levodopa related challenges
• Site specific intestinal active transport
• Competitive amino acid absorption
• First pass metabolism

Parkinson’s related challenges
• Erratic and slowed gastric emptying
• Difficulty swallowing
• Exacerbated food effect

“Variation in levodopa concentration is the determining factor for motor fluctuations.”
- Nyholm, 2002

Error bars represent standard deviations. Source: 001 clinical study
…Exacerbated by Parkinson’s Disease Effects

Barriers to getting oral L-dopa to the CNS

Oral levodopa related challenges
• Site specific intestinal active transport
• Competitive amino acid absorption
• First pass metabolism

Parkinson’s related challenges
• Erratic and slowed gastric emptying
• Difficulty swallowing
• Exacerbated food effect


Delay in Gastric Emptying: Arrow points to a carbidopa tablet remaining intact in a patient’s stomach about 1.5 hours after intake
Rick Batycky, Ph.D
Chief Technology Officer, Acorda
CVT-301 Rationale
The Pulmonary Route Avoids the GI Tract

Potential Benefits of Pulmonary Delivery

- Efficient and rapid path for systemic delivery via the bloodstream
- Bypasses the GI tract
  - Avoids first pass metabolism
  - Increases the amount of available drug to the brain

Unlike oral delivery, pulmonary delivery provides more direct route to CNS

Oral Delivery
- Esophagus
- Stomach
- Intestine
- Liver
- Heart
- Lungs
- Heart
- Brain

Pulmonary
- Lungs
- Heart
- Brain
Acorda’s ARCUS® Platform for LD Delivery

ARCUS® was designed to:

- Deliver large doses
- Achieve high efficiency
- Deliver doses across flow rates


CVT-301 Showed $C_{\text{max}}$ Within 30 Minutes

Source: CVT-301-002 study (conducted in PD patients)

Note: Formulation in 002 used different fill weights as compared to comparable doses in studies 004 or 005; 60 mg and 84 mg doses used in studies 004 and 005 reflect 25 mg and 50 mg equivalent fine particle doses (FPD), respectively

Right: Fasted oral Carbidopa / Levodopa: 25 mg / 100 mg
Phase 2B Results

**CVT-301-003 Study: UPDRS3 Change from Baseline at Week 4 (82.8 mg CVT-301 vs. Placebo)**

- **Mean Change in UPDRS**
  - **CVT V6**
  - **Placebo**

<table>
<thead>
<tr>
<th>Time (minutes)</th>
<th>Diff vs Pbo</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 min</td>
<td>-3.56</td>
<td>0.0309</td>
</tr>
<tr>
<td>20 min</td>
<td>-5.68</td>
<td>0.0068</td>
</tr>
<tr>
<td>30 min</td>
<td>-8.43</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>60 min</td>
<td>-9.59</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

*p Nominal p-values; error bars are standard errors

Note: Formulation in 003 high dose used lower fill weight (82.8 mg) as compared to comparable dose in studies 004 or 005 (84 mg); both formulations reflect 50 mg equivalent fine particle doses
Burkhard Blank, M.D.
Chief Medical Officer, Acorda
CVT-301 Program Overview
CVT-301 - A Comprehensive Development Program

Phase I
- Study 001 (n=26)
- Study 010 (n=24)

Phase II
- Study 002 (n=24)
- Study 003 (n=86)

Phase 3
- Study 004 (n=339)
- Study 005 (n=398)
- Study 004E (n=295, n=42 naïve)

Special Populations
- Study 007 (smokers) (n=56)
- Study 008 (asthmatics) (n=25)
- Study 009 (early morning) (n=36)

Greater than 1,000 subjects studied in the CVT-301 clinical program

Naïve defined as subjects who had never been in a prior CVT-301 study
CVT-301 Phase 3 - Current Status

**Current Status**

**CVT-301-004**  
(n=339)  
- Complete

**CVT-301-004E**  
(n=295)  
- Ongoing  
  - Interim data as of February 10th, 2017  
    - 94 (32%) completed month 6  
    - 44 (15%) completed month 12

**CVT-301-005**  
(n=398)  
- Ongoing  
  - Interim data as of February 10th, 2017  
    - Nearly 100% completed month 9  
    - 187 (46%) completed month 12

**Special Populations**  
CVT-301-007, 008, 009  
(n=117)  
- Complete

**Regulatory Plan**

- Will be submitted complete with initial NDA submission

- Datasets as of February 10th 2017 will comprise the initial NDA submission
- To submit updated interim data at 120 day safety update

- Datasets as of February 10th 2017 will comprise the initial NDA submission
- Complete data to be submitted at 120 day safety update

- Will be submitted complete with initial NDA submission
### Design of Phase 3 Program

<table>
<thead>
<tr>
<th>CVT-301-004</th>
<th>CVT-301-004E (Interim Analysis)</th>
<th>CVT-301-005 (Interim Analysis)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Randomized, double-blind, placebo controlled multicenter (US/Can: 79%, EU*: 21%)</td>
<td>1. Randomized, dose-level blinded, multicenter, uncontrolled (US/Can: 69%, EU*: 31%)</td>
<td>1. Randomized, open-label, multicenter, observational control (US: 7%, EU*: 93%)</td>
</tr>
<tr>
<td>2. 1:1:1 randomization:</td>
<td>2. CVT-301 60 mg and 84 mg doses randomized 1:1</td>
<td>2. CVT-301 84 mg to Observational Cohort, randomized 2:1</td>
</tr>
<tr>
<td>- Dose level 1 (DL1): 60 mg (35 mg FPD)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Dose level 2 (DL2): 84 mg (50 mg FPD)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Sample size: 339</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Randomization stratified for all studies by:
- H&Y in ON state <2.5 vs ≥2.5
- FEV₁ <60% or FEV₁/FVC <70% vs FEV₁ ≥60% and FEV₁/FVC ≥70%

* Including Israel
In CVT-301-004 + 005, North America was predominantly US patients (> 95%); US and Canada represented 67% of CVT-301-004E patients naïve (n=42) to the program, not included in the above
Source: Decision Resources
## Key Inclusion and Exclusion Criteria

**Similar Criteria Used Across the Phase 3 Studies**

<table>
<thead>
<tr>
<th>Inclusion</th>
<th>Exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males/females 30-85 years of age</td>
<td>Dyskinesia interfering with performing study procedures</td>
</tr>
<tr>
<td>Idiopathic PD, H&amp;Y 1-3 in the ON state</td>
<td>Known contraindications to CD/LD</td>
</tr>
<tr>
<td>Daily OFF ≥2 hrs per day (excludes morning OFF)</td>
<td>Undergone deep brain stimulation (DBS)</td>
</tr>
<tr>
<td>CD/LD regimen</td>
<td>History of asthma, COPD, other chronic lung disease*</td>
</tr>
<tr>
<td>PD medications stable ≥4 wks prior to screen**</td>
<td>Concomitant use of apomorphine HCl</td>
</tr>
<tr>
<td>UPDRS 3 ≥25% between ON &amp; OFF at screening</td>
<td></td>
</tr>
<tr>
<td>MMSE ≥25</td>
<td></td>
</tr>
<tr>
<td>Able to perform spirometry in ON &amp; OFF</td>
<td></td>
</tr>
<tr>
<td>Screening lung function tests***</td>
<td></td>
</tr>
</tbody>
</table>

* Within the past 5 years

** Patients on Rytary (CD/LD) required stable medication for ≥6 weeks prior to screen

*** FEV1 ≥ 50% predicted, FEV1/FVC > 60% in ON state
**Baseline Parkinson’s Disease Characteristics**

<table>
<thead>
<tr>
<th>Baseline PD Characteristics</th>
<th>CVT-301-004</th>
<th>CVT-301-005</th>
</tr>
</thead>
<tbody>
<tr>
<td>H&amp;Y ≥ 2.5</td>
<td>35%</td>
<td>53%</td>
</tr>
<tr>
<td>PD Duration</td>
<td>8.3 years</td>
<td>9.3 years</td>
</tr>
<tr>
<td>Baseline LD Dosage</td>
<td>828 mg</td>
<td>808 mg</td>
</tr>
<tr>
<td>Frequency of OFF Periods</td>
<td>3.5</td>
<td>3.7</td>
</tr>
<tr>
<td>Avg OFF Time</td>
<td>5.5 hours</td>
<td>5.6 hours</td>
</tr>
</tbody>
</table>

**Concomitant Medications**

<table>
<thead>
<tr>
<th></th>
<th>CVT-301-004</th>
<th>CVT-301-005</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dopamine agonists</td>
<td>206 (61%)</td>
<td>299 (75%)</td>
</tr>
<tr>
<td>MAO-B inhibitors</td>
<td>122 (36%)</td>
<td>152 (38%)</td>
</tr>
<tr>
<td>Amantadine (and equivalents)</td>
<td>70 (21%)</td>
<td>117 (29%)</td>
</tr>
<tr>
<td>COMT inhibitors</td>
<td>74 (22%)</td>
<td>131 (33%)</td>
</tr>
</tbody>
</table>

Population experienced average of > 3 OFF periods daily in spite of existing levodopa treatment averaging > 800 mg daily

Most patients studied were on multiple Parkinson's disease therapies in addition to levodopa
Peter LeWitt, M.D.
CVT-301-004 Study Overview
CVT-301-004 Study Design

- **3 month study, parallel group design**
  - Patients randomized to CVT-301 (60 mg or 84 mg) or placebo
  - Patients dosed themselves in-clinic while in the OFF state
  - UPDRS3 measurements were conducted in-clinic, in addition to clinician assessed dyskinesia
  - In-clinic visits every month

- **Inhaler and capsules taken home: patient instructed to use CVT-301 as needed**
  - PD diary collected over course of the trial
CVT-301-004 Subject Disposition

- Withdrawal rate (any reason):
  - 60 mg CVT-301: 15%
  - 84 mg CVT-301: 14%
  - Placebo: 13%

- Rate of withdrawal due to AEs:
  - 60 mg CVT-301: 3%
  - 84 mg CVT-301: 5%
  - Placebo: 3%

- Cough:
  - 3 patients out of 227 patients (1.3%) exposed to CVT-301 discontinued due to cough
### CVT-301-004
### Baseline Characteristics

<table>
<thead>
<tr>
<th>Parkinson's Disease Characteristics</th>
<th>CVT-301 60 mg</th>
<th>CVT-301 84 mg</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (yrs)</td>
<td>63.9</td>
<td>63.5</td>
<td>62.6</td>
</tr>
<tr>
<td>Sex (male), %</td>
<td>70.8%</td>
<td>72.8%</td>
<td>76.8%</td>
</tr>
<tr>
<td>H&amp;Y ≥2.5 (More Severe)</td>
<td>34.5%</td>
<td>36.8%</td>
<td>33.9%</td>
</tr>
<tr>
<td>Duration of PD (yrs)</td>
<td>8.7 years</td>
<td>8.0 years</td>
<td>8.1 years</td>
</tr>
<tr>
<td>CD/LD treatment (yrs)</td>
<td>7.1 years</td>
<td>6.3 years</td>
<td>6.8 years</td>
</tr>
<tr>
<td>Daily Levodopa (mg)</td>
<td>822.7</td>
<td>818.6</td>
<td>841.4</td>
</tr>
<tr>
<td>CD/LD (doses)</td>
<td>5.0</td>
<td>5.0</td>
<td>5.2</td>
</tr>
<tr>
<td>Daily OFF Periods incl. AM</td>
<td>3.5</td>
<td>3.6</td>
<td>3.3</td>
</tr>
<tr>
<td>Daily OFF incl. AM (hrs)</td>
<td>5.6</td>
<td>5.4</td>
<td>5.6</td>
</tr>
</tbody>
</table>
CVT-301-004
Hierarchy Order of Endpoints

<table>
<thead>
<tr>
<th>Hierarchy Order</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary Endpoint (UPDRS3 at 30 minutes)</td>
</tr>
<tr>
<td>Responder ON at 60 minutes</td>
</tr>
<tr>
<td>UPDRS3 at 20 minutes</td>
</tr>
<tr>
<td>PGI-C: Improvement</td>
</tr>
<tr>
<td>UPDRS3 at 10 minutes</td>
</tr>
<tr>
<td>OFF Time (diary)</td>
</tr>
<tr>
<td>UPDRS3 at 30 minutes</td>
</tr>
<tr>
<td>Responder ON at 60 minutes</td>
</tr>
<tr>
<td>UPDRS3 at 20 minutes</td>
</tr>
<tr>
<td>PGI-C: Improvement</td>
</tr>
<tr>
<td>UPDRS3 at 10 minutes</td>
</tr>
<tr>
<td>OFF Time (diary)</td>
</tr>
</tbody>
</table>

- Order of hierarchy was set based on likely probability of success
  - Guided by Phase 2b results
CVT-301-004
Primary and Secondary Endpoints

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Step</th>
<th>84 mg vs PBO</th>
<th>60 mg vs PBO</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Δ</td>
<td>Δ</td>
</tr>
<tr>
<td>Change UPDRS 3 at 30 min</td>
<td>1</td>
<td>-3.92</td>
<td>-3.07</td>
</tr>
<tr>
<td>(Primary)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% Responder ON at 60 min</td>
<td>2</td>
<td>21.60</td>
<td>19.50</td>
</tr>
<tr>
<td>Change UPDRS 3 at 20 min</td>
<td>3</td>
<td>-2.55</td>
<td>-1.98</td>
</tr>
<tr>
<td>% Patients improved on PGI-C</td>
<td>4</td>
<td>25.00</td>
<td>15.20</td>
</tr>
<tr>
<td>Change UPDRS 3 at 10 min</td>
<td>5</td>
<td>-2.26</td>
<td>-0.97</td>
</tr>
<tr>
<td>Change PD Diary OFF time</td>
<td>6</td>
<td>-0.01</td>
<td>0.10</td>
</tr>
</tbody>
</table>

** Statistically significant on a nominal and adjusted basis
* Statistically significant on a nominal basis only
Primary Endpoint Achieved
Change from Pre-dose UPDRS 3 30 Min at Week 12

UPDRS3 Least-Squared Mean Change from Baseline

Placebo (N=112)  CVT-301 84 mg (n=114)

-5.91  -9.83

-3.92 p=0.009
CVT-301-004
UPDRS3 Change from Baseline at Week 12: CVT-301 vs. Placebo

- Primary endpoint achieved (84 mg dose vs. placebo at 30 minutes)
- Dose-dependent response observed
- Effect persisted through 60 minutes

Nominal P-values: * p < 0.05, ** p < 0.01, *** p < 0.001
Error bars indicate standard errors; time points staggered for readability; changes vs. placebo represent least squared means changes

<table>
<thead>
<tr>
<th></th>
<th>10 min</th>
<th>20 min</th>
<th>30 min</th>
<th>60 min</th>
</tr>
</thead>
<tbody>
<tr>
<td>Δ 60 mg vs. Pbo:</td>
<td>-0.97</td>
<td>-1.98</td>
<td>-3.07</td>
<td>-3.35</td>
</tr>
<tr>
<td>p-value:</td>
<td>p = 0.387</td>
<td>p = 0.147</td>
<td>p = 0.039*</td>
<td>p = 0.035*</td>
</tr>
<tr>
<td>Δ 84 mg vs. Pbo:</td>
<td>-2.26</td>
<td>-2.55</td>
<td>-3.92</td>
<td>-4.94</td>
</tr>
<tr>
<td>p-value:</td>
<td>p = 0.046*</td>
<td>p = 0.062</td>
<td>p = 0.009**</td>
<td>p = 0.002**</td>
</tr>
</tbody>
</table>
CVT-301-004
Significantly More CVT-301 patients Turned ON vs. Placebo at Week 12

% of Patients who were ON at 60 minutes

- Placebo: 36% (n = 97)
- 60 mg CVT: 56% (n = 99)
- 84 mg CVT: 58% (n = 84)

Nominal P-values: * p < 0.05, ** p < 0.01, *** p < 0.001
Note: Assumes worst case imputation for missing data if visit occurred
Patient global impression of change (PGI-C) at Week 12 consistent with effect on UPDRS3
- 84 mg arm patients experiencing “improvement” or “much improvement” more than double that of placebo
- Improvement correlated with dose

Nominal P-values: * p < 0.05, ** p< 0.01, *** p < 0.001
Note: PGI-C: Nominal p-values represent significance for any improvement in PGI-C over placebo, assuming worst case imputation for missing data if visit occurred
CVT-301-004
Secondary Endpoints: OFF Time at Week 12

Average Daily OFF Time Change from Screening

Placebo
n=97

60 mg CVT-301
n=96

84 mg CVT-301
n=95

-0.48
-0.58
-0.47

LS Means Change in Average Daily OFF Time (Hours) from Screening

Significant OFF time improvement vs. placebo was not observed in CVT-301-004

Note: Error bars indicate standard errors
Post-hoc Analysis - PGI-C Improvement vs. UPDRS 3 Results

Changes in UPDRS 3 at 30 minutes in Patients that Did Improve vs. Patients that Did Not Improve in PGI-C (Week 12, Pooled* Patients)

- Improved
  - Mean UPDRS3 Change from Baseline: -12.1
  - n = 171

- Did not Improve
  - Mean UPDRS3 Change from Baseline: -3.7
  - n = 114

* Pooled includes both arms of CVT-301 and placebo
Note: Post-hoc analysis is hypothesis generating
CVT-301-004
Dyskinesia Reported within 60 min CVT-301 Post-Inhalation (3 mo. Visit)

Most CVT-301 patients reported no dyskinesia: dyskinesia observed was mostly mild
CVT-301-004
Pulmonary Function Tests: FEV$_1$ & DLCO Change From Baseline

Over the course of 3 months, there were no statistically significant differences for CVT-301 vs placebo on either FEV$_1$ or DLCO

Notes: Time points staggered for readability
Error bars represent standard deviations
# CVT-301-004
## Safety: Treatment Emergent Adverse Events

<table>
<thead>
<tr>
<th>Preferred Term, n (%)</th>
<th>Placebo (n=112)</th>
<th>60 mg (n=113)</th>
<th>84 mg (n=114)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cough</td>
<td>2 (1.8%)</td>
<td>17 (15.0%)</td>
<td>17 (14.9%)</td>
</tr>
<tr>
<td>Upper Resp Infection</td>
<td>3 (2.7%)</td>
<td>2 (1.8%)</td>
<td>7 (6.1%)</td>
</tr>
<tr>
<td>Nausea</td>
<td>3 (2.7%)</td>
<td>0</td>
<td>6 (5.3%)</td>
</tr>
<tr>
<td>Sputum discoloured</td>
<td>0</td>
<td>0</td>
<td>6 (5.3%)</td>
</tr>
<tr>
<td>Dyskinesia</td>
<td>0</td>
<td>5 (4.4%)</td>
<td>4 (3.5%)</td>
</tr>
<tr>
<td>Fall</td>
<td>2 (1.8%)</td>
<td>5 (4.4%)</td>
<td>3 (2.6%)</td>
</tr>
<tr>
<td>Nasopharyngitis</td>
<td>2 (1.8%)</td>
<td>2 (1.8%)</td>
<td>3 (2.6%)</td>
</tr>
<tr>
<td>Hallucination</td>
<td>2 (1.8%)</td>
<td>2 (1.8%)</td>
<td>2 (1.8%)</td>
</tr>
<tr>
<td>Headache</td>
<td>0</td>
<td>4 (3.5%)</td>
<td>2 (1.8%)</td>
</tr>
<tr>
<td>Pain in extremity</td>
<td>1 (0.9%)</td>
<td>2 (1.8%)</td>
<td>2 (1.8%)</td>
</tr>
<tr>
<td>Throat irritation</td>
<td>0</td>
<td>8 (7.1%)</td>
<td>1 (0.9%)</td>
</tr>
<tr>
<td>Dizziness</td>
<td>5 (4.5%)</td>
<td>2 (1.8%)</td>
<td>1 (0.9%)</td>
</tr>
<tr>
<td>Back pain</td>
<td>0</td>
<td>4 (3.5%)</td>
<td>1 (0.9%)</td>
</tr>
<tr>
<td>Influenza</td>
<td>0</td>
<td>4 (3.5%)</td>
<td>1 (0.9%)</td>
</tr>
<tr>
<td>Depression</td>
<td>2 (1.8%)</td>
<td>1 (0.9%)</td>
<td>1 (0.9%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1 (0.9%)</td>
<td>2 (1.8%)</td>
<td>1 (0.9%)</td>
</tr>
</tbody>
</table>

- Cough was most common AE for CVT-301
  - Withdrawal due to cough < 2%
  - Most patients reported a single case in the pooled CVT-301 population
  - Majority of cough was mild

- CVT-301 rates of AEs commonly seen with dopaminergic therapies:
  - Nausea < 6%
  - Somnolence < 1%
  - Hypotension < 1%

Treatment emergent adverse events relative to screening visit
• **Study met primary endpoint at 30 minutes**
  – Clinically meaningful* change in UPDRS3 at 30 minutes relative to placebo sustained through 60 minutes
  – Nominally statistically significant at 10 minutes (84 mg dose)
  – Trend (p=0.062) towards improvement at 20 minutes (84 mg dose)

• **Additional secondary endpoints were supportive of primary endpoint result**
  – Statistically significant improvement in ON at 60 minutes (84 mg dose)
  – PGI-C showed nominal significance
  – Diary-recorded OFF time did not show any significant differences

• **Safety profile**
  – 1.3% withdrawal rate due to cough, the most common adverse event
  – Adverse events were mostly mild
  – Mild to no dyskinesia in over 95% of patients in-clinic
  – Discontinuation rates due to adverse events < 6%

Donald Grosset, M.D.
CVT-301-005 Study Overview
CVT-301-005 Study Design

CVT-301-005 was a safety study comparing treatment with CVT-301 (84 mg) to an observational control group of PD patients.

- Observational cohort allows for the comparison to pulmonary function in PD patients (which may decline over time).

- Primary objective was on pulmonary safety out to a year of treatment vs. observational cohort.

- Exploratory efficacy conducted for most endpoints in the active treatment arm only.
CVT-301-005 Patient Disposition

- Screen fail: 105
- Study withdrawal: 69
  - By subject: 26
  - AE: 24
- Randomized: 408
- Safety Population: 398
- 84 mg: 271
- Observational Cohort: 127
- Completed 12 month visit (as of interim analysis): 122 (45%)
- Completed 12 month visit (as of interim analysis): 65 (51%)

- 7.4% of the CVT-301 cohort withdrew due to a treatment-emergent adverse event
- 3 patients withdrew due to cough (1.1%)
- No other AE resulting in withdrawal represented > 1% of the studied population

Note: As of interim analysis, >99% of patients completed 9 month visit.
# CVT-301-005 Baseline Characteristics

<table>
<thead>
<tr>
<th>Parkinson's Disease Characteristics</th>
<th>CVT-301-005</th>
<th>CVT-301-005 84 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (yrs)</td>
<td>64.2</td>
<td>63.6</td>
</tr>
<tr>
<td>Sex (male), %</td>
<td>61.4%</td>
<td>59.4%</td>
</tr>
<tr>
<td>H&amp;Y ≥2.5 (More Severe)</td>
<td>53%</td>
<td>53%</td>
</tr>
<tr>
<td>Duration of PD (yrs)</td>
<td>9.7 years</td>
<td>9.0 years</td>
</tr>
<tr>
<td>CD/LD treatment (yrs)</td>
<td>7.3 years</td>
<td>7.2 years</td>
</tr>
<tr>
<td>Daily Levodopa (mg)</td>
<td>874.1</td>
<td>777.2</td>
</tr>
<tr>
<td>CD/LD (doses)</td>
<td>5.2</td>
<td>5.1</td>
</tr>
<tr>
<td>Daily OFF Periods incl. AM</td>
<td>3.7</td>
<td>3.6</td>
</tr>
<tr>
<td>Daily OFF incl. AM (hrs)</td>
<td>5.7</td>
<td>5.6</td>
</tr>
</tbody>
</table>
Pulmonary function tests were conducted to characterize CVT-301’s effects on lung function compared to the natural course of disease, using commonly used lung function measures:

- FEV1: forced expiratory volume in 1 second
- DLCO: diffusing capacity of the lung for carbon monoxide

Adverse events were also recorded for this long term study:

- CVT-301-005 design included an observational (non-interventional) control, allowing for the monitoring of adverse events out to 1 year
CVT-301-005
Pulmonary Function Tests: FEV₁ & DLCO Change From Baseline

No statistical difference between CVT-301 and observational cohort in FEV₁ or DLCO in CVT-301-005

Notes: Time points staggered for readability
Error bars represent standard deviations
CVT-301-005
Safety: Treatment Emergent Adverse Events

<table>
<thead>
<tr>
<th>Preferred Term, n (%)</th>
<th>Observed Cohort (n=127)</th>
<th>CVT-301 (n=271)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cough</td>
<td>1 (0.8%)</td>
<td>35 (12.9%)</td>
</tr>
<tr>
<td>Nasopharyngitis</td>
<td>6 (4.7%)</td>
<td>17 (6.3%)</td>
</tr>
<tr>
<td>Dyskinesia</td>
<td>4 (3.1%)</td>
<td>15 (5.5%)</td>
</tr>
<tr>
<td>Fall</td>
<td>3 (2.4%)</td>
<td>14 (5.2%)</td>
</tr>
<tr>
<td>Back pain</td>
<td>4 (3.1%)</td>
<td>12 (4.4%)</td>
</tr>
<tr>
<td>Upper respiratory tract infection</td>
<td>3 (2.4%)</td>
<td>12 (4.4%)</td>
</tr>
<tr>
<td>Nausea</td>
<td>1 (0.8%)</td>
<td>10 (3.7%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>3 (2.4%)</td>
<td>9 (3.3%)</td>
</tr>
<tr>
<td>Sputum discolored</td>
<td>0</td>
<td>9 (3.3%)</td>
</tr>
<tr>
<td>Throat irritation</td>
<td>0</td>
<td>9 (3.3%)</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>2 (1.6%)</td>
<td>8 (3.0%)</td>
</tr>
<tr>
<td>Orthostatic Hypotension</td>
<td>3 (2.4%)</td>
<td>7 (2.6%)</td>
</tr>
<tr>
<td>Headache</td>
<td>1 (0.8%)</td>
<td>7 (2.6%)</td>
</tr>
<tr>
<td>Parkinson's disease</td>
<td>4 (3.1%)</td>
<td>6 (2.2%)</td>
</tr>
<tr>
<td>UTI</td>
<td>2 (1.6%)</td>
<td>6 (2.2%)</td>
</tr>
<tr>
<td>Dizziness</td>
<td>1 (0.8%)</td>
<td>6 (2.2%)</td>
</tr>
<tr>
<td>Depression</td>
<td>2 (1.6%)</td>
<td>5 (1.8%)</td>
</tr>
<tr>
<td>Bronchitis</td>
<td>4 (3.1%)</td>
<td>5 (1.8%)</td>
</tr>
<tr>
<td>Insomnia</td>
<td>5 (3.9%)</td>
<td>3 (1.1%)</td>
</tr>
<tr>
<td>Musculoskeletal pain</td>
<td>4 (3.1%)</td>
<td>2 (0.7%)</td>
</tr>
<tr>
<td>Somnolence</td>
<td>1 (0.8%)</td>
<td>0</td>
</tr>
</tbody>
</table>

- Most commonly observed AE was cough
  - Majority of cases (> 90%) were characterized as mild
- CVT-301 rates of AEs commonly seen with dopaminergic therapies:
  - Nausea (3.7%)
  - Orthostatic hypotension (2.6%)
  - Somnolence (0%)
- SAEs reported in 14.9% of patients in the CVT-301 arm versus 10.2% in the observational control
  - UTI most common (1.4%)
  - No other SAEs in the CVT-301 arm observed at >1%
• Pulmonary function was not statistically different from observational cohort out to 12 months using standard lung function measures (FEV1, DLCO) as of the interim analysis

• Cough was the most common adverse event
  – Occurred in 12.9% of CVT-301 84 mg vs. < 1% in the observational control
  – Majority of cases (> 90%) were characterized as mild
  – All other AEs occurred at less than 7% of patients

• Discontinuation due to AE was 7.4%

• Dopaminergic side effect* rates were each < 6% during the study
  – Includes dyskinesia

* Examples include nausea, orthostatic hypotension, somnolence
CVT-301-005 Exploratory Efficacy Measures

• Uncontrolled exploratory efficacy measurements* (only conducted in the CVT-301 arm) also measured in CVT-301-004:
  – UPDRS3
  – Responder ON
  – PGI-C
  – OFF time

* Exploratory analyses are hypothesis generating
CVT-301-005 Exploratory Efficacy
UPDRS3 Change from Baseline Through 52 Weeks

Notes: Time points staggered for readability
Error bars indicate standard errors

CVT-301-005 open label
UPDRS3 change at 52 weeks largely stable as compared to week 4 and week 12 data
Percentage of patients ON at 60 minutes remained at similar levels through 52 weeks

Note: Assumes worst case imputation for missing data if visit occurred
CVT-301-005 Exploratory Efficacy
PGI-C: Improvement

Patient global impression of improvement remains greater than 70% of patients at month 12 and greater than 80% at the 6 month visit

Note: Assumes worst case imputation for missing data if visit occurred; early terminations pooled to the last visit
CVT-301-005 Exploratory Efficacy
OFF Time Reduction at Week 4 and Week 52

**Week 4 Visit**

<table>
<thead>
<tr>
<th>LS Means Change in Average Daily OFF Time (Hours) from Screening</th>
<th>84 mg CVT-301</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n = 262</td>
</tr>
<tr>
<td></td>
<td>-1.36</td>
</tr>
</tbody>
</table>

**Week 52 Visit (Interim Analysis)**

<table>
<thead>
<tr>
<th>LS Means Change in Average Daily OFF Time (Hours) from Screening</th>
<th>84 mg CVT-301</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n = 108</td>
</tr>
<tr>
<td></td>
<td>-1.15</td>
</tr>
</tbody>
</table>

Exploratory OFF time data (open label) showed changes in OFF time of 1.15-1.36 hours from baseline.

Note: Error bars represent standard errors
• No statistically significant differences in lung function tests (FEV$_1$, DLCO) observed for CVT-301 84 mg versus observational control out to 1 year*

• Adverse events were mostly mild, with cough being the most common AE (12.9%)
  – Withdrawals due to cough occurred in three patients (1.1%)

• Over 12 months, exploratory efficacy supportive of results from CVT-301-004

* As of interim analysis
Burkhard Blank, M.D.
Chief Medical Officer, Acorda
Summary and Closing Remarks
Efficacy Data over Time
UPDRS3 Change from Baseline (Studies 003, 004 and 005)

Notes: Intention to Treat population, LS means
Formulation in 003 high dose used lower fill weight (82.8 mg) as compared to comparable dose in studies 004 or 005 (84 mg); both formulations reflect 50 mg equivalent fine particle doses

4 Week Visit
(CVT-301 82.8/84 mg dose shown)

12 Week Visit
(CVT-301 82.8/84 mg dose shown)
CVT-301 Showed Greater Responder ON % Across All Studies

Nominal P-values: * p < 0.05, ** p< 0.01, *** p < 0.001

Notes: Assumes worst case imputation for missing data if visit occurred for 004 and 005

Formulation in 003 high dose used lower fill weight (82.5 mg) as compared to comparable dose in studies 004 or 005 (84 mg); both formulations reflect 50 mg equivalent fine particle doses
PGI-C (Improvement) Across Studies

Consistency in improved and much improved patients across the CVT-301 program

Note: Formulation in 003 high dose used lower fill weight (82.5 mg) as compared to comparable dose in studies 004 or 005 (84 mg); both formulations reflect 50 mg equivalent fine particle doses; early terminations pooled to the last visit.
• CVT-301 averaged 2.3 doses / day in year-long study and 2.0 doses / day over three months

• Total capsules self-administered by patients during treatment:
  – Study 004: 86,295 (3 months)
  – Study 005: 385,175 (12 months)
CVT-301 Phase 3 Program
Overall Summary

- CVT-301 has been studied in over 1000 subjects in multiple clinical trial settings encompassing over 15 countries across the US and EU

- CVT-301’s Study 004 had statistically significant improvements in UPDRS3 at 30 minutes versus placebo with supportive secondary endpoint results at the 84 mg dose:
  - Responder ON at 60 minutes was statistically significant
  - UPDRS3 nominally statistically significant at 10 minutes and 60 minutes with trends observed at 20 minutes
  - PGI-C nominally statistically significant – most of difference vs. placebo in “Improved” and “Much improved” categories

- CVT-301-005 exploratory efficacy also supportive

- Safety profile was consistent across CVT-301-004 and CVT-301-005
  - No statistically significant differences in acute and chronic pulmonary safety as measured by FEV1 or DLCO
  - Cough was the most common AE
  - No concerning dopaminergic AEs