Developing a Sublingual Formulation of Apomorphine to Rapidly Convert Parkinson’s Patients from OFF to ON State

Analyst & Investor Day
New York, NY
July 19, 2016

www.cynapsus.ca
Analyst & Investor Day
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Kristen Galfetti
Vice President, Investor Relations
Cynapsus Therapeutics
Forward Looking Statements

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Meeting Agenda & Speakers

• Welcome
  • Kristen Galfetti, VP Investor Relations
• Introduction
  • Anthony Giovinazzo, President & CEO
• APL-130277 Development Plan
  • Albert Agro, Chief Medical Officer
• Landscape / Unmet Medical Need / Global Experience with SC Apomorphine
  • C. Warren Olanow
• EU Experience with On-Demand Apomorphine
  • Fabrizio Stocchi
• Commercial Opportunity / Commercial Preparedness / Corporate Update
  • Anthony Giovinazzo, President & CEO
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### Seasoned and Experienced Senior Management Team

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<thead>
<tr>
<th>Name</th>
<th>Position</th>
<th>Experience</th>
</tr>
</thead>
</table>
| **Anthony Giovinazzo, MBA, President & CEO, Director** | • 22+ years CNS experience (Parkinson’s, Alzheimer’s, Pain, Anxiety), including clinical development, IP protection, licensing and M&A  
• Led the turnaround strategy for Cynapsus from 2009; the U.S. IPO in 2015; raised gross proceeds of US$ 72.5 million  
• Is one of three original inventors of the Cynapsus APL-130277 technology  
• In addition, 16 years international tax and investment banking experience with deep knowledge of capital markets  
• MBA from IMD (Switzerland), Leadership and Strategy in Pharmaceuticals and Biotech Program (Harvard)  
• C.Dir, and A.C.C. from The Directors College |
| **Dr. Thierry Bilbault, PhD, Chief Scientific Officer & EVP CMC** | • 20+ years senior management experience with global large pharmaceutical companies  
• 50+ product launches internationally, including over 10 U.S. New Drug Applications; 10+ years thin film expertise  
• Held senior executive positions at Galderma, Novartis, Pfizer and Alcon Laboratories  
• MS in Biological Engineering from CUST Engineering (Clermont-Ferrand, France), and Ph.D. in Molecular and Cellular Biology from Clermont-Ferrand II (Clermont-Ferrand, France) |
| **Dr. Albert Agro, PhD, Chief Medical Officer** | • 18+ years CNS and Parkinson’s clinical development, New Drug Applications and approvals  
• Held scientific and executive positions at TransTech Pharma, Axon, Boehringer Ingelheim and Bayer  
• Ph.D. from the Department of Medicine at McMaster University |
| **Andrew Williams, MBA, Chief Operating Officer and Chief Financial Officer** | • 17+ years finance, operations and consulting, 10 yrs. working in CNS (Parkinson’s and Pain)  
• Co-founded Cynapsus in 2004; led the Canadian IPO transaction in 2006 and the U.S. IPO in 2015; responsible for public company operations from 2006 to present  
• BAH from Queen’s University and MBA from Richard Ivey School of Business |
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Anthony Giovinazzo
President & CEO
Cynapsus Therapeutics
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Clinical Experts

C. Warren Olanow, M.D., FRCPC
- Past Henry P. and Georgette Goldschmidt Professor and Chairman of the Department of Neurology at the Mount Sinai School of Medicine in New York City and is presently Professor Emeritus in the Department of Neurology and in the Department of Neuroscience at this institution
- Medical degree from the University of Toronto, performed neurology training at the New York Neurological Institute at Columbia Presbyterian Medical Center at Columbia University
- Post-graduate studies in neuroanatomy at Columbia University
- Served on the faculties of McGill University, Duke University, and the University of South Florida
- Author of more than 500 peer-reviewed articles primarily related to Parkinson’s disease and neurodegeneration
- Past President of the Movement Disorder Society, Past President of International Society of Motor Disturbances and Past Treasurer of the American Neurological Association

Fabrizio Stocchi, M.D., Ph.D.,
- Professor of Neurology and Director of the Parkinson’s disease and Movement Disorders Research Centre at the Institute for Research and Medical Care, IRCCS San Raffaele, Rome, Italy
- Scientific Advisor of the Institute for Parkinson’s Disease Research in Vicenza
- Awarded MD from the University of L’Aquila and his Ph.D from the University of Catania
- Research activities have centered on neuropharmacology in the field of movement disorders and neurodegenerative diseases
- Multiple publications including books and papers on the genetics, clinical diagnosis, characterization and treatment of Parkinson’s disease, as well as in preclinical research into the disease
- Active member of 11 societies, including the Movement Disorder Society, the European Clinical Neuropharmacology Society and the European Federation Neurological Society
APL-130277: A New Hope for Patients with Parkinson’s Disease

• Cynapsus is developing APL-130277, a sublingual formulation of apomorphine
  • A patented bi-layer sublingual thin film formulated to maximize drug permeability while optimizing film disintegration properties / residence time, stability and buccal tissue compatibility
  • Rapidly converts Parkinson's disease patients from OFF to ON
  • Potentially better alternative to subcutaneous (SC) apomorphine
  • Section 505(b)(2) regulatory pathway

• Phase 3 pivotal program underway
  • Positive Phase 2 results demonstrated rapid, clinically meaningful improvements in motor function
  • NDA Filing expected in the first half of 2017

• Targeting a significant unmet need with a sizeable market
• Strong issued and pending intellectual property

(1) As assessed by Movement Disorder Society Unified Parkinson’s Disease Rating Scale (MDS-UPDRS) Part III scores
Thin Film Strip Manufacturing Program

- APL-130277 drug layer designed to provide mechanical properties to facilitate manufacturability, drug stability, rapid drug diffusion and optimal time under the tongue for desired bioavailability
- Buffer layer ensures rapid and complete neutralization of acid generation following drug absorption while providing additional drug permeability
- CMC program encompasses robust pharmaceutical development dossier including the Phase 3 clinical and registration batches produced on commercial manufacturing and packaging equipment

**Ongoing CMC activities include ICH stability studies to generate no less than 12 months data from registration batches at filing**
Apomorphine: Only Drug Approved to Convert PD Patients from OFF to ON\(^{(1)}\)

Notes: Apomorphine change in MDS-UPDRS is from OFF to ON, whereas the change in MDS-UPDRS for CVT-301 is from partial OFF to ON. APL-130277 preliminary data taken from drug titration phase of CTH-300 clinical trial as reported July 18, 2016. \textit{Values not placebo adjusted.}\n
Apomorphine is approved in the U.S., Europe and Japan.

\(^{(1)}\) BioExcel Report - Investment and Partnering Decision Support; * Cynapsus Therapeutics Inc.
APL-130277: Potential Distinguishable PK Driven Attributes

- Technology imbedded in the thin film system, likely to lower or eliminate irritation
- More rounded and lower C-max than SC Apomorphine, potentially resulting in muted AE profile
- Sufficient drug in plasma to convert to ON (i.e., more than 2.6 to 3.0 ng/ml)
- Rounded PK also displays extended shoulder, potentially resulting in a longer duration than the SC injection

(1) APL-130277 Phase 1 Clinical Trial Results (CTH-103)
Recent and Anticipated Milestones and Estimated Timeline

- **Q2 2016** – Posters at the American Academy of Neurology Meeting in Vancouver, British Columbia
- **Q2 2016** - Meet with European Medicines Agency
- **H2 2016** - Thorough QT study to commence
- **Q4 2016** - European registration study to commence
- **Late Q3 2016 / Early Q4 2016** - Top-line data from CTH-300 Phase 3 efficacy study
- **H1 2017** - Top-line data from CTH-301 Phase 3 safety study
- **H1 2017** - File New Drug Application with U.S. FDA
- **H1 2017** – Commence preparations for EU dossier
- **Late 2017/Early 2018** – Estimated U.S. approval and product launch
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APL-130277 Clinical Program

Albert Agro, Ph.D.
Chief Medical Officer
Cynapsus Therapeutics
APL-130277 Development Roadmap

(1) Timing is based on currently available information and is subject to risks and uncertainties. See “Risk Factors” in the Company’s Form 10-Q for the quarter ended March 31, 2016 filed with the United States Securities and Exchange Commission on May 11, 2016.
APL-130277 Clinical Program
CTH-300 Dose Titration Results
CTH-300: Pivotal Efficacy Study
On Demand Management of OFF Episodes

Trial Overview:
• Enrolment closed June 30, 2016
• Patients entering dose titration: 102
• Planned randomization: 80
• 38 centres in North America
• First Patient In: June 2015
• Dose Titration Phase Data: July 2016
• Top Line Data: Late Q3 / Early Q4

Monthly in-office visits and at-home diary-based assessments will be recorded for all types of OFF and secondary endpoints

Dose Titration Phase (DTP)

12-week primary endpoint, key secondary endpoint

50% Randomized to Placebo

50% Randomized to APL-130277
CTH-300: Titration Phase Change in MDS-UPDRS Part III\textsuperscript{(1)} (Responders)

**Highlights**

- Rapid onset to effect
- Robust peak effect
- Duration of effect

\textsuperscript{(1)} These Phase 3 dose titration results are only a snap shot and the final data and results from the Phase 3 study, when released, could differ from such results.
CTH-300: Titration Phase Patients Turning ON

- Patients entering DTP who turned fully ON with treatment: 83%
- Patients who turned fully ON:
  - 78% within 30 minutes
  - 38% within 15 minutes
- Median Dose Turning to fully ON: 20mg
- Onset of Clinical Benefit as assessed by Patient: 5 to 12 minutes

(1) These Phase 3 dose titration results are only a snap shot and the final data and results from the Phase 3 study, when released, could differ from such results.
## CTH-300 Safety Data: Dose Titration Phase

### Common Adverse Events: Percentage of Patients\(^{(1)}\)

<table>
<thead>
<tr>
<th>Event</th>
<th>Any AE</th>
<th>Mild AE</th>
<th>Moderate AE</th>
<th>Severe AE</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=92</td>
<td>N (%)</td>
<td>N (%)</td>
<td>N (%)</td>
<td>N (%)</td>
</tr>
<tr>
<td>Nausea</td>
<td>15 (16)</td>
<td>12 (13)</td>
<td>2 (2)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Dizziness</td>
<td>7 (8)</td>
<td>4 (4)</td>
<td>3 (3)</td>
<td>0</td>
</tr>
<tr>
<td>Somnolence</td>
<td>4 (4)</td>
<td>3 (3)</td>
<td>1 (1)</td>
<td>0</td>
</tr>
<tr>
<td>Yawning</td>
<td>3 (3)</td>
<td>3 (3)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Vomiting</td>
<td>2 (2)</td>
<td>1 (1)</td>
<td>1 (1)</td>
<td>0</td>
</tr>
<tr>
<td>Symptomatic Hypotension</td>
<td>1 (1)</td>
<td>1 (1)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Stomatitis/irritation</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

### Highlights
- Reduced nausea
- Favourable tolerability
- No local irritation

\(^{(1)}\) These Phase 3 dose titration results are only a snapshot and the final data and results from the Phase 3 study, when released, could differ from such results
CTH-300: Safety Overview and Discontinuations During Dose Titration Phase(1)

- Percentage of Patients with AEs: 37%
- Total Discontinuations: 16
- Consent Withdrawal: 2
- Discontinuations due to AEs:
  - Nausea: 2
  - Somnolence: 1
  - Headache: 1
  - Pre-syncope: 1
- Number of patients who did not turn ON at 35mg: 9

(1) These Phase 3 dose titration results are only a snapshot and the final data and results from the Phase 3 study, when released, could differ from such results.
The study intends to show the superiority of APL-130277 compared with placebo.

CTH-300 study is well powered to demonstrate statistical significant reduction in MDS-UPDRS Part III with 80 patients randomized.
CTH-300: DTP Conclusions\(^{(1)}\)

- APL-130277 was well tolerated
- ALP-130277 demonstrated a robust improvement in motor function
- APL-103277 turned a significant number of patients from OFF to ON

\(^{(1)}\) These Phase 3 dose titration results are only a snap shot and the final data and results from the Phase 3 study, when released, could differ from such results
CTH-301 Safety Study Design

**Trial Overview:**
- N=up to 200 Patients with 6-months safety data
- ~66 Centres in North America & UK
- Patients completing CTH-300 are eligible to rollover into CTH-301
- First Patient In = September 2015
- Top Line Data = H1 2017

**Primary Endpoint:**
- Safety
  - ECG, Oral Tolerability, AE’s

**Secondary Endpoints:**
- Percent of OFF Episodes resolved at home
- Time to ON at home
- Mean change from baseline in MDS-UPDRS Part III at 15, 30, 45, 60, 90 minutes post dose
- Percent of patients ON at 30 minutes
- Duration of ON
- Activities of Daily Living (MDS-UPDRS Part II)
- Quality of Life (PDQ-39)
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European Clinical Program Overview

Albert Agro, Ph.D.
Chief Medical Officer
EMA Advice Summary Based on Recent Meetings

• Expect to conduct an active comparator study with SC apomorphine

• Plan to randomize up to 80 patients in a 4-week open label crossover study

• Will assess functional endpoints rather than scale-based endpoints, including the duration of ON, preference and ease-of-use of APL-130277, the use of patient diaries, and tolerability of APL-130277

• The effect of apomorphine is well-established and the benefit of a sub-lingual application is apparent

• Agree that anti-emetic use should be limited during the study

Based on current trial timing, the European clinical trial is expected to commence in the fourth quarter of 2016
CTH-302: Current European Clinical Trial Plan

Part A
Dose Titration

Dual Titration

Randomization

Part B
Open Label, Crossover

SC repeated dosing
Washout
APL-130277 repeated dosing

28 Days
7 Days
28 Days

APL-130277 repeated dosing
Washout
SC repeated dosing

Dosing 56 Days
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C. Warren Olanow, M.D.
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Fabrizio Stocchi, M.D., Ph.D.
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Anthony Giovinazzo
President & CEO
APL-130277 Addresses Significant Unmet Need and Large Patient Population Looking for Convenient and Efficacious Therapy

The OFF Market is Large with Prevalence of PD Increasing

Today

>1mm PD patients in U.S. (1)

600,000 PD Patients suffer OFF episodes (2)

Patients that suffer at least one OFF episode per day (3)

Assumptions Underlying Our Addressable Market

- ~60% of PD patients suffer morning OFF episodes (2)
- Cynapsus believes nearly all patients that suffer morning OFF episodes suffer other types of OFF episodes

- Of addressable population of ~400,000 patients:
  - ~20% are considered mild (experiencing one OFF episode per day)
  - ~55% are moderate (experiencing two OFF episodes per day)
  - ~25% are advanced (experiencing three or more OFF episodes per day)

Commercialization Strategy

- ~100 targeted sales representatives expected to focus on high-prescribing general neurologists and ~1,200 movement disorder specialists in the U.S.
- Potential for ex-U.S. development/commercial partner(s)

- If 30% of addressable patients use APL-130277 for morning OFF, an estimated 48 million strips would be used annually
- If 50% of these patients use an additional strip daily, 72 million strips would be used annually
- If 25% use a third strip, 84 million strips would be used annually

Addressable Market (3):

~400K patients
(~40% of PD Patients in the U.S.)

Recent Michael J. Fox Foundation Survey of 3,000 Parkinson’s patients found that 90% suffer OFF episodes and that 65% suffer at least 2 hours OFF daily

(1) CIA World Fact Book, deLau LM, Breteler MM (June 2009) “Epidemiology of Parkinson’s Disease”
(2) Rizos A et. al. “Characterizing motor and non-motor aspects of early-morning off periods in Parkinson’s disease: An international multicenter study,” 2014
(3) Estimates are based on management beliefs and publicly available research. See “Risk Factors - The market for our product candidate may not be as large as we expect” in the Company’s Form 10-Q for the quarter ended March 31, 2016 filed with the U.S. Securities and Exchange Commission on May 11, 2016.
High Level of Awareness of Off Episodes Among PD Patients

~92% of PD patients report experiencing OFF episodes at least once per day

Patients experience an average of 2 episodes per day, with severe impairment patients experiencing twice as many episodes (2.8/day) as mild impairment (1.4/day) patients.

(1) Campbell Alliance Primary Research – Parkinson’s Patients and Caregivers Nov 2015; n=120
Considerable Under-Representation of OFF Incidence by Physicians \(^{(1)}\)

**Physician Underrepresentation Factor**

- 1.16
- 1.80
- 1.97

Better communication between physicians and patients and increased physician education will be necessary to raise physician awareness of the frequency OFF episodes.

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\( (1) \) Campbell Alliance Primary Research 120 PD patients and 102 HCPs, Nov 2015
US Commercialization Activities (2016 and 2017)

In 2016 and 2017 we will begin to finalize our launch approach:

1. Develop APL-130277 Positioning, Messaging, and Branding
2. Conduct Detailed Tactical Planning
3. Finalize APL-130277 Pricing Strategy
4. Build Or Acquire Commercial Infrastructure
Expect to Enter Market with Approximately 100 to 125 Sales Representatives

Field Force Sizing Algorithm Under High Frequency Model

Prescribing Universe
- 8,664 Neuros
- 61,581 PCPs/Other

Target Universe
- 3,475 Neuros
- 1,218 PCPs/Other

High Frequency
- 94,543 calls
- 866 call cap

Approximately 100 to 125 Reps
EU Commercial Preparation

• Ongoing contact with key opinion leaders in Europe
• Advice sought from EMA
• Inclusion of Health Economic endpoints in CTH-300, CTH-301, CTH-302
• Comparator trial against Apo-Go with superiority as endpoint
• EU Physician survey complete
• EU Payer advisory board held
Financial Position (as of March 31, 2016)
Stock symbols: Nasdaq (CYNA), TSX (CTH)

- USD $68.6 million

Share Capital
- 12,309,366 common shares
- 3,096,506 warrants
- 1,045,085 options
- 16,450,957 Total (Fully Diluted)

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<th>Number of Warrants</th>
<th>Exercise Price CAD$/Share</th>
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<th>Gross Proceeds If Exercised CAD$</th>
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<td>2,317,784</td>
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<td>30,038,481</td>
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</tbody>
</table>

**CAD$ 37,300,784**
~USD $30,000,000

(1) Subject to certain exceptions, warrants are cancellable if not exercised within 30 days notice from Cynapsus that the stock price has been ≥ the trigger price for 20 consecutive trading days.
MonoSol Rx Intellectual Property Licensing Agreement

Strategic Worldwide IP Licensing Agreement signed in April 2016

- MonoSol Rx has key issued industry-leading patents and pending patent applications as well as significant expertise and know-how in film technology
- Agreement includes a license to 31 granted US patents, 45 foreign granted patents, and numerous pending applications
- Bolsters IP estate surrounding APL-130277, including potential to list additional patents in the Orange Book
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