LATUDA Clinical Development Update

LATUDA Meeting (Tokyo)

January 2011

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Executive Vice President
Clinical Research and Medical Affairs
Sunovion Pharmaceuticals Inc.
Agenda

◆ LATUDA Label Overview
  • Approval timeline
  • Label highlights

◆ Schizophrenia Program
  • Overview of results of PEARL studies
  • Highlights from the PEARL Safety study
  • Ongoing and planned studies in schizophrenia

◆ Bipolar Depression Development Program
  • Overview of PREVAIL program

◆ LATUDA Global Development Plan
Successfully Launch LATUDA and Maximize the Molecule Across Its Lifecycle

LATUDA

- Schizophrenia
- Bipolar
- Depression

Foundational

Expand into Additional Markets
LATUDA US FDA Approval

◆ First atypical antipsychotic to receive a first-cycle US FDA approval

◆ 10 Month Standard FDA Review
  • NDA filed: December 30, 2009
  • FDA Approval: October 28, 2010

◆ One of only 21 products approved by the FDA in 2010
  • The only Psychiatric Products division NME approved in 2010

Source: Bloomberg News
LATUDA Label Highlights

Label Reflects Favorable Product Profile

◆ Indication
  • LATUDA is indicated for the treatment of patients with schizophrenia

◆ Doses
  • 40 or 80 mg/d recommended, no titration needed; once daily with food (350 cal min)

◆ Contraindications/Warnings
  • Contraindicated for hypersensitivity to drug (angioedema case);
    Strong 3A4 blockers (ketoconazole) or inducers (rifampin)
  • Elderly patients with dementia-related psychosis should not be treated with
    atypical antipsychotics like LATUDA
  • No QTc contraindication or warning

◆ Other Highlights
  • Metabolic data – includes short as well as long-term data (24, 36 and 52 week)
    for weight, lipids and glucose
  • Data from PEARL 2 (study 231) on olanzapine is included in the efficacy and
    safety section of the label

Note: Please refer to LATUDA Full Prescribing Information, 2010
LATUDA Label Highlights

Label Includes Substantial Safety and Efficacy Database

◆ 4 efficacy data studies included
  • Phase 2a (006): LATUDA 40 and 120 mg/d
  • Phase 2b (196): LATUDA at 80 mg/d
  • PEARL 1 (229): LATUDA at 80 mg/d
  • PEARL 2 (231): LATUDA at 40 and 120 mg/d and olanzapine

◆ 2,096 patients with schizophrenia exposed to one or more LATUDA doses
  • 1,004 patients treated with LATUDA in short-term placebo-controlled schizophrenia studies (doses 20-120 mg/d)
  • 533 patients treated with LATUDA for ≥24 weeks
  • 238 patients treated with LATUDA for ≥52 weeks
  • 624 patient-years total exposure

Source: LATUDA Full Prescribing Information, 2010
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◆ LATUDA Global Development Plan
## LATUDA Phase 2 and 3 Schizophrenia Trials

<table>
<thead>
<tr>
<th>LATUDA mg/d</th>
<th>N</th>
<th>40 mg</th>
<th>80 mg</th>
<th>120 mg</th>
<th>160 mg</th>
<th>Active Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study 006</td>
<td>149</td>
<td>40</td>
<td>120</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study 196</td>
<td>180</td>
<td>80</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study 229 (PEARL 1)</td>
<td>500</td>
<td>40</td>
<td>80</td>
<td>120</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study 231 (PEARL 2)</td>
<td>478</td>
<td>40</td>
<td>120</td>
<td></td>
<td></td>
<td>Olanz 15</td>
</tr>
<tr>
<td>Study 233 (PEARL 3)</td>
<td>488</td>
<td>80</td>
<td>160</td>
<td></td>
<td></td>
<td>Quet XR 600</td>
</tr>
</tbody>
</table>

LATUDA Phase 2 and 3 Schizophrenia Trials

LATUDA mg/d

| Study 006 | 149 | 40 | 120 |
| Study 196 | 180 | 80 |
| Study 229 (PEARL 1) | 500 | 40 | 80 | 120 |
| Study 231 (PEARL 2) | 478 | 40 | 120 |
| Study 233 (PEARL 3) | 488 | 80 | 160 | Quet XR 600 |
PEARL 2 (Study 231): Study Design

**Open-Label Extension Phase**

**Double-Blind Phase**

- LATUDA 40 mg/d
- LATUDA 120 mg/d
- Olanzapine 15 mg/d (active control)
- Placebo

6 weeks

6 months

Data were analyzed using LOCF analysis

Olanzapine 15 mg/d was included as an active control for assay sensitivity
PEARL 2 Results: PANSS Total (MMRM)

Baseline

Day

Wk

Wk

Wk

Wk

Wk

Wk 6

Endpoint

0

-5

-10

-15

-20

-25

-30

LS Mean Change from Baseline

Placebo (n=114)

120 mg/d LATUDA (n=118)

40 mg/d LATUDA (n=118)

15 mg/d Olanzapine (n=121)

*p<0.05; **p<0.01

H. Meltzer et al. Poster presented at ACNP meeting, December 2009
PEARL 2 Results:
CGI-S (MMRM)

Baseline
Day 4  Wk 1  Wk 2  Wk 3  Wk 4  Wk 5  Wk 6  Endpoint

0.0

-0.5

-1.0

-1.5

LS Mean Change from Baseline

Placebo (n=114)
120 mg/d LATUDA (n=118)
40 mg/d LATUDA (n=119)
15 mg/d Olanzapine (n=122)

*p<0.05; **p<0.01
H. Meltzer et al. Poster presented at ACNP meeting, December 2009
PEARL 2 Results: Weight Change (LOCF)

Mean Change from Baseline (kg)

- Placebo: 0.6 (n=115)
- LATUDA 40 mg/d: 1.0 (n=119)
- LATUDA 120 mg/d: 1.1 (n=118)
- Olz 15 mg/d: 4.2 (n=122)

J. Meyer et al. Poster presented at ACNP meeting, December 2009
PEARL 2 Results: Lipid Profile

LOCOr endpoint values; all subjects fasting per protocol

PEARL 2 Results: Glucose (LOCF)

All subjects fasting per protocol

PEARL 2 Results: Insulin (LOCF)

Placebo LATUDA 40 mg/d LATUDA 120 mg/d Olz 15 mg/d
n=114 n=119 n=115 n=121

Mean Change from Baseline (mg/dL)
-2.4 -3.2 -1.3 5.9

All subjects fasting per protocol
**PEARL 3: Study Design**

**Double-Blind Phase**

- **Short-Term Phase**
  - LATUDA 80 mg/d
  - LATUDA 160 mg/d
  - Placebo
  - Quetiapine XR 600 mg/d

- **6 weeks**

**Double-Blind Extension Phase**

- LATUDA 40-120 mg/d
- Quetiapine XR 200-800 mg/d

12 months

Note: The data for 160 mg/day dose of LATUDA have not yet been submitted to the U.S. Food and Drug Administration. The use of quetiapine XR in the study was for the purpose of establishing assay sensitivity. Quetiapine XR is not marketed in Japan.
## PEARL 3: Subject Disposition

<table>
<thead>
<tr>
<th>Disposition</th>
<th>LATUDA 80 mg/d</th>
<th>LATUDA 160 mg/d</th>
<th>Quet XR 600 mg/d</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Subjects Randomized (n=488)</td>
<td>125</td>
<td>121</td>
<td>120</td>
<td>122</td>
</tr>
<tr>
<td>Discontinuations</td>
<td>36 (29%)</td>
<td>28 (23%)</td>
<td>23 (19%)</td>
<td>48 (39%)</td>
</tr>
<tr>
<td>Insufficient Clinical Response</td>
<td>16 (13%)</td>
<td>12 (10%)</td>
<td>6 (5%)</td>
<td>28 (23%)</td>
</tr>
<tr>
<td>Adverse Event</td>
<td>5 (4%)</td>
<td>4 (3%)</td>
<td>4 (3%)</td>
<td>5 (4%)</td>
</tr>
<tr>
<td>Withdrawal of Consent</td>
<td>12 (10%)</td>
<td>9 (7%)</td>
<td>13 (11%)</td>
<td>14 (11%)</td>
</tr>
<tr>
<td>Lost to Follow-up</td>
<td>1 (&lt;1%)</td>
<td>1 (&lt;1%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Protocol Violation</td>
<td>1 (&lt;1%)</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Administrative</td>
<td>1 (&lt;1%)</td>
<td>2 (2%)</td>
<td>0</td>
<td>1 (&lt;1%)</td>
</tr>
</tbody>
</table>
PEARL 3 Results: PANSS Total (MMRM)

Baseline Day 4 Wk 1 Wk 2 Wk 3 Wk 4 Wk 5 Wk 6 Endpoint
LS Mean Change from Baseline

Placebo (n=120) 80 mg/d LATUDA (n=125) 160 mg/d LATUDA (n=121) 600 mg/d QuetiapineXR (n=116)

PEARL 3 Results:
CGI-S (MMRM)

**A. Loebel et al. Poster presented at ACNP meeting, Dec 8th, 2010.**
PEARL 3 Results: Metabolic

Weight Change

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Mean Change from Baseline (kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>0.1</td>
</tr>
<tr>
<td>LATUDA 80 mg/d</td>
<td>0.6</td>
</tr>
<tr>
<td>LATUDA 160 mg/d</td>
<td>0.6</td>
</tr>
<tr>
<td>Quet XR 600 mg/d</td>
<td>2.1</td>
</tr>
</tbody>
</table>

n=115 n=116 n=113 n=116

Triglycerides

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Median Change from Baseline (mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>-9.0</td>
</tr>
<tr>
<td>LATUDA 80 mg/d</td>
<td>-2.0</td>
</tr>
<tr>
<td>LATUDA 160 mg/d</td>
<td>-9.0</td>
</tr>
<tr>
<td>Quet XR 600 mg/d</td>
<td>8.0</td>
</tr>
</tbody>
</table>

n=111 n=111 n=114 n=106

PEARL 3 Results: Epworth Sleepiness Scale

A. Loebel et al. Poster presented at ACNP meeting, Dec 8th, 2010

**Placebo**
-0.9

**LATUDA 80 mg/d**
-1.1

**LATUDA 160 mg/d**
-0.7

**Quet XR 600 mg/d**
0.6

***p<0.001
PEARL 3: Selected Common AEs for LATUDA and Quetiapine XR

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>LATUDA 80 mg/d (n=125)</th>
<th>LATUDA 160 mg/d (n=121)</th>
<th>Quet XR 600 mg/d (n=119)</th>
<th>Placebo (n=121)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Akathisia</td>
<td>10 (8.0%)</td>
<td>9 (7.4%)</td>
<td>2 (1.7%)</td>
<td>1 (0.8%)</td>
</tr>
<tr>
<td>Nausea</td>
<td>10 (8.0%)</td>
<td>9 (6.6%)</td>
<td>4 (3.4%)</td>
<td>4 (3.3%)</td>
</tr>
<tr>
<td>Parkinsonism</td>
<td>7 (5.6%)</td>
<td>8 (6.6%)</td>
<td>4 (3.4%)</td>
<td>0</td>
</tr>
<tr>
<td>Dizziness</td>
<td>6 (4.8%)</td>
<td>7 (5.8%)</td>
<td>16 (13.4%)</td>
<td>2 (1.7%)</td>
</tr>
<tr>
<td>Somnolence</td>
<td>5 (4.0%)</td>
<td>8 (6.6%)</td>
<td>16 (13.4%)</td>
<td>1 (0.8%)</td>
</tr>
<tr>
<td>Dry Mouth</td>
<td>2 (1.6%)</td>
<td>2 (1.7%)</td>
<td>9 (7.6%)</td>
<td>1 (0.8%)</td>
</tr>
<tr>
<td>Constipation</td>
<td>3 (2.4%)</td>
<td>1 (0.8%)</td>
<td>8 (6.7%)</td>
<td>3 (2.5%)</td>
</tr>
<tr>
<td>Weight Increased</td>
<td>1 (0.8%)</td>
<td>2 (1.7%)</td>
<td>8 (6.7%)</td>
<td>1 (0.8%)</td>
</tr>
</tbody>
</table>
PEARL Safety trial (LTSS: Long Term Safety Study): Study design

- **Screening**
- **Baseline**

**Double-Blind Phase**
- LATUDA 40-120 mg/d (n=400)
- Risperidone 2-6 mg/d (n=200)

**Open-Label Continuation Phase**
- LATUDA 40-120 mg/d

12 months
6 months
LTSS Safety Results: Weight Change (Observed Case)

<table>
<thead>
<tr>
<th></th>
<th>BL</th>
<th>Day 7</th>
<th>Wk 3</th>
<th>Wk 6</th>
<th>Wk 12</th>
<th>Mo 6</th>
<th>Mo 9</th>
<th>Mo 12</th>
</tr>
</thead>
<tbody>
<tr>
<td>LATUDA</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Risperidone</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LATUDA</td>
<td>419</td>
<td>406</td>
<td>359</td>
<td>337</td>
<td>282</td>
<td>216</td>
<td>173</td>
<td>150</td>
</tr>
<tr>
<td>Risperidone</td>
<td>202</td>
<td>196</td>
<td>175</td>
<td>162</td>
<td>135</td>
<td>122</td>
<td>106</td>
<td>98</td>
</tr>
</tbody>
</table>
LTSS Safety Results: Triglycerides (LOCF)

-3.5

LATUDA
n=354

Risperidone
n=169

-1.0

Median Change from Baseline (mg/dL)
LTSS Safety Results: Glucose (LOCF)

**LATUDA**
- Median Change from Baseline (mg/dL): -0.5
- n=354

**Risperidone**
- Median Change from Baseline (mg/dL): 3.0
- n=171

***p= 0.001
LTSS Safety Results: Prolactin (LOCF)

LATUDA
n=378

Risperidone
n=176

Median Change from Baseline (ng/mL)

9.10

**p=0.001
**LTSS: Selected Common AEs for LATUDA and Risperidone**

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>LATUDA (n=419)</th>
<th>Risperidone (n=202)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>16.7 %</td>
<td>10.9 %</td>
</tr>
<tr>
<td>Akathisia</td>
<td>14.3</td>
<td>7.9</td>
</tr>
<tr>
<td>Vomiting</td>
<td>10.0</td>
<td>3.3</td>
</tr>
<tr>
<td>Weight Increased</td>
<td>9.3</td>
<td>19.8</td>
</tr>
<tr>
<td>Somnolence</td>
<td>13.6</td>
<td>17.8</td>
</tr>
<tr>
<td>Psychotic Disorder</td>
<td>5.0</td>
<td>7.4</td>
</tr>
<tr>
<td>Constipation</td>
<td>1.9</td>
<td>6.9</td>
</tr>
<tr>
<td>Dystonia</td>
<td>3.1</td>
<td>5.9</td>
</tr>
<tr>
<td>Parkinsonism</td>
<td>4.3</td>
<td>5.4</td>
</tr>
</tbody>
</table>
Long Term Safety Trial Summary

◆ Discontinuation rate was higher for LATUDA vs. risperidone
  • LATUDA completer rate: 34%
  • Risperidone completer rate: 44%

◆ Effects on weight and glucose for LATUDA suggest benefits from a metabolic risk perspective

◆ Minimal elevation in prolactin in LATUDA-treated patients

◆ Most frequent LATUDA adverse events were nausea, akathisia and vomiting
# Current and Planned LATUDA Studies in Schizophrenia

<table>
<thead>
<tr>
<th>Study</th>
<th>Timing</th>
<th>Purpose</th>
<th>Post-Marketing</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Switch Study in Schizophrenia</strong></td>
<td>Initiated in Q3 2010</td>
<td>Provide info on impact on patients switching from one atypical antipsychotic therapy to LATUDA</td>
<td></td>
</tr>
<tr>
<td><strong>Schizophrenia Maintenance Study</strong></td>
<td>Planned Start Q3 2011</td>
<td>Supports efforts to obtain maintenance claim in label. Requirement for EMA submission</td>
<td>✓</td>
</tr>
<tr>
<td><strong>Low-dose Schizophrenia Study with 20 mg/d</strong></td>
<td>Planned Start Q2 2012</td>
<td>Identify lowest therapeutic dose for LATUDA</td>
<td>✓</td>
</tr>
<tr>
<td><strong>Pediatric (13-17 yrs) PK Study</strong></td>
<td>Planned Start Q3 2011</td>
<td>Supports potential opportunity for US patent extension</td>
<td>✓</td>
</tr>
<tr>
<td><strong>Pediatric (13-17 yrs) Efficacy Study</strong></td>
<td>Planned Start Q2 2012</td>
<td>Supports potential opportunity for US patent extension</td>
<td>✓</td>
</tr>
</tbody>
</table>
LATUDA Switch (Study 289 and 290) in Schizophrenia

Open-Label

Screening

LATUDA 40 mg/d
LATUDA 40 mg/d
LATUDA 40-120 mg/d (n=70)

LATUDA 40 mg/d
LATUDA 80 mg/d
LATUDA 40-120 mg/d (n=70)

LATUDA 80 mg/d
LATUDA 80 mg/d
LATUDA 40-120 mg/d (n=70)

Previous Antipsychotic

50%

0%

7 Days
7 Days
4 Weeks

As of January 17, 2011, enrollment is 60% complete

US only. Patient enrollment ongoing LPI planned: March 2011
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◆ LATUDA Global Development Plan
Bipolar Depression Development Plan: PREVAIL Studies

- PREVAIL: Program to EValuate Antidepressant Impact of LATUDA
- Ongoing global clinical trials for LATUDA in Bipolar Depression will evaluate effectiveness of LATUDA as
  - Monotherapy
  - Adjunct therapy
  - Maintenance therapy
- Lower, flexible dose range of LATUDA – 20 to 120 mg/day
- Short-term 6 weeks and 24 weeks in an open-label extension
- sNDA planned for 1H/2012

<table>
<thead>
<tr>
<th>Study Detail</th>
<th>Timing</th>
</tr>
</thead>
<tbody>
<tr>
<td>PREVAIL 1 – Add-on therapy added to treatment with lithium or divalproex</td>
<td>Initiated in April 2009 – Estimated completion: Q4 2011</td>
</tr>
<tr>
<td>PREVAIL 2 – Monotherapy</td>
<td>Initiated in April 2009 – Estimated completion: Q4 2011</td>
</tr>
<tr>
<td>PREVAIL 3 – Add-on therapy added to treatment with lithium or divalproex</td>
<td>Initiated in December 2010</td>
</tr>
<tr>
<td>PREVAIL Extension</td>
<td>PREVAIL 1, 2, 3 trial participants to enter into 24 week open-label extension</td>
</tr>
</tbody>
</table>
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◆ LATUDA Global Development Plan
LATUDA Global Development Plan

◆ United States
  • Launch in early February 2011 for Schizophrenia
  • Bipolar depression sNDA planned for 1H/2012
  • Other indications under consideration:
    – Bipolar maintenance: study initiation 3rd Q 2011 (12 months to complete)
    – MDD with mixed features: study initiation 2nd Q 2011 (12 months to complete)
  • IM depot formulation in progress – timelines under development

◆ Japan
  • Phase 3 data analysis currently underway

◆ China
  • Expected submitting IND in 2011

◆ Europe
  • Active partnering discussions in process

◆ Canada
  • Expected filing at some point in 2011
Disclaimer Regarding Forward-looking Statements

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