In Search of New CNS Therapies

Suven, Inc.

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Suven Vision and Mission

Vision

- In search of new CNS therapies
- Become a leading company focused on treatments for unmet medical needs in Mental Health

Mission

- Health for patients and Value for partners
Suven, Inc., a Delaware Company is wholly owned subsidiary of Suven Life Sciences, India

A clinical-stage biopharmaceutical company focused on the acquisition, development and commercialization of novel therapeutics for the treatment of neurodegenerative disorders

Goal is to be the leading biopharmaceutical company focused on the treatment of dementia, a condition characterized by a significant decline in mental capacity and impaired daily function

Near-term focus is to develop our product candidate **SUVN-502** for the treatment of Alzheimer's disease and other forms of dementia
In Search of New CNS Therapies

Promising Pipeline with Well differentiated Assets

Novel Mechanisms with First-in-Class Potential

Excellent Probability of Clinical and Regulatory Success

Health for Patients – Value for Partners
In Search of New CNS Therapies

Core Research Area - Neuroscience

Focused in Neuroscience, the most challenging area in drug discovery

Alzheimer’s Disease (AD)

Normal Brain  Brain with AD

Schizophrenia

Normal Brain  Schizophrenic

Depression

Normal Brain  Depressed

To discover & develop Differentiated Therapeutics for the treatment of neurodegenerative disorders
In Search of New CNS Therapies

Therapeutic Targets

Alzheimer’s Disease
- Potential to be a symptomatic treatment
  - 5-HT_6_ receptor antagonist
  - Histamine H_3_ receptor inverse agonist
- Potential to be both symptomatic and disease modifying treatment
  - 5-HT_4_ receptor partial agonist
  - M1 receptor positive allosteric modulator

Schizophrenia
- Dopamine D_2_, 5-HT_2A_, SSRI

Depression
- Cholinergic α4β2 antagonist

Pain
- Cannabinoid 2 receptor agonist
## In Search of New CNS Therapies

### NCE Assets for Partnering

<table>
<thead>
<tr>
<th>Candidates</th>
<th>Pre-clinical &amp; GLP Tox</th>
<th>Clinical Phase</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SUVN-502</strong></td>
<td></td>
<td>I, II, III</td>
<td>Cognitive Deficits Associated with Alzheimer's Disease</td>
</tr>
<tr>
<td>5-HT₆ antagonist</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>SUVN-G3031</strong></td>
<td></td>
<td>I, II, III</td>
<td></td>
</tr>
<tr>
<td>H₃ inverse agonist</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>SUVN-D4010</strong></td>
<td></td>
<td>I, II, III</td>
<td></td>
</tr>
<tr>
<td>5-HT₄ agonist</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>SUVN-911</strong></td>
<td></td>
<td>I, II, III</td>
<td>Depression (MDD)</td>
</tr>
<tr>
<td>α4β2 antagonist</td>
<td></td>
<td></td>
<td></td>
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</tbody>
</table>

Potential to address unmet medical needs
SUVN-502 is a safe, potent, selective, orally available, brain penetrant and pure $5-HT_6$ antagonist being developed for the symptomatic treatment of Alzheimer’s disease

**Current Status:** Phase 2A POC study in progress - USA
### 5-HT<sub>6</sub> Antagonists in Clinical Development

<table>
<thead>
<tr>
<th>Company</th>
<th>Compound ID</th>
<th>Indication</th>
<th>Stage of Development</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lundbeck</td>
<td>Lu AE58054 (Idalopirdine)</td>
<td>Alzheimer's Disease</td>
<td>Phase-III</td>
</tr>
<tr>
<td>Roivant Neurosciences</td>
<td>RVT-101 (Intepirdine)</td>
<td>Alzheimer's Disease</td>
<td>Phase-III</td>
</tr>
<tr>
<td>Suven Life Sciences</td>
<td>SUVN-502</td>
<td>Alzheimer's Disease</td>
<td>Phase-II</td>
</tr>
<tr>
<td>Biotie Therapies</td>
<td>SYN120</td>
<td>Parkinson's Disease Dementia</td>
<td>Phase-II</td>
</tr>
</tbody>
</table>
Differentiation from Competitor 5-HT<sub>6</sub> Antagonists (Efficacy)

<table>
<thead>
<tr>
<th></th>
<th>RVT-101 (Intepirdine)</th>
<th>Lu AE58054 (Idalopirdine)</th>
<th>SUVN-502</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standalone treatment</td>
<td>↑ acetylcholine, enhanced procognitive effects</td>
<td>No effects</td>
<td>↑ acetylcholine, enhanced procognitive effects</td>
</tr>
<tr>
<td>In combination with donepezil</td>
<td>↑ acetylcholine, enhanced procognitive effects</td>
<td>↑ acetylcholine, enhanced procognitive effects</td>
<td>↑ acetylcholine, enhanced procognitive effects</td>
</tr>
<tr>
<td>In combination with donepezil and memantine</td>
<td>No reports</td>
<td>No reports</td>
<td>↑ acetylcholine, enhanced procognitive effects</td>
</tr>
</tbody>
</table>

Only compound with preclinical POC in combination with donepezil and memantine
A Well Differentiated Asset

- **Pure 5-HT<sub>6</sub> receptor antagonist** ( >1200 fold selectivity over 5-HT<sub>2A</sub> receptor)
- Superior profile that differentiates from competitor 5-HT<sub>6</sub> antagonists
- Potentiates the preclinical efficacy of current SOC for AD treatment
- No gastrointestinal side effects in aged population (Phase I study)
- No liver toxicity in healthy elderly (Phase I MA study)
- No drug-drug interactions and dose limiting toxicity
- No effect of food, gender and age on pharmacokinetics
- Excellent human pharmacokinetics for once a day treatment
- **Well differentiated Asset and Excellent Probability of Clinical Success**
Rationale for Phase 2 Proof of Concept Study

**SUVN-502**

- **SUVN-502 enhance hippocampal acetylcholine/glutamate release**
- **Donepezil blocks degradation of acetylcholine**
- **Memantine protect neurons from glutamate toxicity**
  - **SUVN-502, Donepezil and Memantine triple combination may have greater efficacy and better tolerability**
Rationale for Phase 2 Proof of Concept Study

SUVN-502 potentiates the neurochemical and electrophysiological effects of donepezil and memantine combination in rats.
Rationale for Phase 2 Proof of Concept Study

Combination of SUVN-502, Donepezil and Memantine is superior to the Combination of Donepezil and Memantine in preclinical animal models.

The effect observed in preclinical species may translate to efficacy in humans.
# Phase 2 Study Design

<table>
<thead>
<tr>
<th>Days</th>
<th>Day -28 to Day -14</th>
<th>Baseline</th>
<th>Week 4</th>
<th>Week 13</th>
<th>Week 26 or Early Term</th>
<th>Week 30 Follow Up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Visits</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>Screening</td>
<td>&lt;----------Double-Blind Treatment Period-------------&gt;</td>
<td>Total ~ 537 Moderate AD subjects</td>
<td>Placebo or SUVN-502 (low and high dose)</td>
<td>All treatments once daily</td>
<td>Single-Blind Placebo</td>
<td></td>
</tr>
</tbody>
</table>

<-----------------------Concomitant Alzheimer’s Disease Therapy----------------------->

Donepezil (10 mg) & Memantine 10 mg twice daily [or Namenda XR (28mg)]
or Namzaric™ (28/10):

**Primary efficacy end point : ADAS – Cog 11**
Phase 2A POC Investigational Plan

US FDA Regulated

Primary Outcome Measure
ADAScog-11

Secondary Outcome Measures
MMSE, CDR-SB, ADCS-ADL, NPI, C-SDD, C-SSRS, Safety and Tolerability

Inclusion Criteria
Moderate Alzheimer's Disease Diagnosed for at least 1 Year and Treatment with Stable Doses of Donepezil and Memantine for 3 Months
First-in-Class Phase-2 in Progress

SUVN-502 + Donepezil + Memantine represents a Promising new approach for the Symptomatic Treatment of Alzheimer’s Disease.
Phase 2A POC Study of SUVN-502

SUVN-502 + Donepezil + Memantine Represents a Promising New Approach for Symptomatic Treatment of Alzheimer’s Disease

Recruiting Sites / Investigators / Patients

SUVN-502 + Donepezil + Memantine Represents a Promising New Approach for Symptomatic Treatment of Alzheimer’s Disease
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SUVN-G3031

Current Status: Phase-1 Completed in USA
Current Status: Phase-1 Completed in USA

- Potent and selective histamine $H_3$ receptor inverse agonist
- Good brain penetration with adequate unbound concentration
- Robust efficacy in animal models with increase in acetylcholine levels
- Potentiates the efficacy of cholinesterase inhibitor in animal models
- No dose limiting toxicity and No sleep related side effects
- Translatable biomarker available for POC study
- Well tolerated with favorable pharmacokinetics for once a day dosing
- Steady state concentrations achieved within 6 days; no sleep related side effects
SUVN-G3031: Best in Class H$_3$ Clinical Candidate

- Well tolerated in humans with dose dependent pharmacokinetics
- Suitable for once a day oral dosing
- Projected human efficacy concentrations achieved at low doses in Phase 1 study
- Phase 2 enabling long term safety studies are currently in progress

Target Engagement in Rats

Object Recognition Task in Rats

No sleep related side effects
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**SUVPN-D4010**

*Current Status: Phase-1 Completed in USA*
SUVN-D4010: Dual Mechanism of Action

**Current Status: Phase-1 Completed in USA**

- Selective *Serotonin-4 receptor (5-HT₄) partial agonist*
- Clean hERG, phospholipidosis and AMES
- Orally bioavailable with good brain penetration
- Good correlation between affinity, free fraction, occupancy and efficacy
- Robust efficacy in animal models
- Potentiates the efficacy of cholinesterase inhibitors in animal models
- Disease modifying effects in animal models
- Translatable biomarker available for POC study
- No effect on ECG in the dog telemetry study
Target Engagement in Rats

Object Recognition Task in Rats

Well tolerated in humans with dose dependent pharmacokinetics in Phase 1 single and multiple ascending dose studies
SUVN-911

Current Status: IND in preparation - USA
SUVN-911 for Major Depressive Disorders (MDD)

**Current Status: IND in preparation - USA**

- Novel, potent and selective $\alpha_4\beta_2$ nAChR antagonist
- Excellent ADME properties with no drug-drug interaction liability
- Robust efficacy in animal models of depression
- Increase in cortical serotonin levels
- Translatable biomarker available for POC study
- Demonstrated good safety margin in preclinical species
- Well protected intellectual property in all major countries
SUVN-911: Key Biology Results

**Target Engagement in Rats**

- **Dominant Submissive Assay in Rats**
- **Week**
- **Feeding time (sec)**

- **% Receptor Occupancy**

- **Dose (mg/kg, p.o.)**

- **Dominant**
- **Submissive**

- **Axes**

- **Legend**

- **Graphs**

- **Points**

- **Bars**

- **Error Bars**

- **Values**

- **Data**

- **Analysis**

- **Conclusion**

- **Addresses major limitations of current MDD therapeutics by offering**
  - Rapid onset of action, No sexual dysfunction and is Procognitive

- **Phase -1 enabling GLP studies completed and IND filing in progress**
In Search of New CNS Therapies

Suven NCE Assets for Partnering

- **SUVN-502** for Cognition in Alzheimer’s Commenced Phase 2A (POC) clinical trial in USA in September 2015 (537 patients)

- **SUVN-G3031** for Cognition in Alzheimer’s Completed Phase 1 Clinical Trial in USA under US-IND

- **SUVN-D4010** for Cognition in Alzheimer’s Completed Phase 1 Clinical Trial in USA under US-IND

- **SUVN-911** for Major Depressive Disorders (MDD) - IND in preparation
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