# Supernus Pharmaceuticals

## SPN-812 Phase IIb Topline Data

### Investor Webcast – October 11, 2016

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# SPN-812: Novel Non-Stimulant ADHD Product

- Viloxazine hydrochloride
  - Norepinephrine reuptake inhibitor
- Once-daily oral extended-release product
- New Chemical Entity (NCE)
  - Five year market exclusivity
  - Previously marketed outside the US as an antidepressant
- Building strong IP portfolio with expirations from 2029-2033
  - API, formulation, novel use
- Emerging clinical profile points to a well differentiated ADHD product
  - A highly effective non-stimulant with a tolerable side effect profile



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# SPN-812 Phase IIb Design

- **Objectives:**
  - Assess effect of SPN-812 ER in reducing symptoms of ADHD in children aged 6-12 years
  - Evaluate safety and tolerability of SPN-812 ER in children with ADHD
- **Primary Endpoint**:
  - Change from baseline to End of Study in the ADHD-RS-IV total score
- **Secondary Endpoints**:
  - Assess effect of SPN-812 ER on:
    - Clinical Global Impression – Improvement Scale (CGI-I) and
    - Clinical Global Impression – Severity Scale (CGI-S)



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# SPN-812 Phase IIb Design

- **Design:**
  - Double-blind, placebo-controlled, multicenter
  - Dose-ranging study; 5-arm, parallel-group
  - Monotherapy
- **Randomization:**
  - Randomized in a ratio of 1:2 of placebo to each of the active treatment arms (100/200/300/400 mg)
  - 222 subjects randomized
- **Study Duration:**
  - 3 weeks titration (100mg/week), 5 weeks treatment
  - Rollover to Open-Label Extension Study



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# Three SPN-812 Doses Met Primary Endpoint

## Primary Analysis
## Change from baseline in ADHD-RS-IV Total Score (ITT Population with LOCF)

| Statistics | 400 mg N=44 | 300 mg N=47 | 200 mg N=46 | 100 mg N=45 | Placebo N=24 | |
|---|---|---|---|---|---|---|
| LS Mean | -19.0 | -18.6 | -18.4 | -16.7 | -10.5 | End of Study |
| Effect Size | 0.63 | 0.60 | 0.55 | 0.46 | | |
| **P-value** | **0.021*** | **0.027*** | **0.031*** | **0.089** | | |
| * At end of study all SPN-812 doses except the 100 mg dose are statistically significant compared to placebo at α = 0.05 level. | | | | | | |

ITT = Intent To Treat
LOCF = Last Observation Carried Forward



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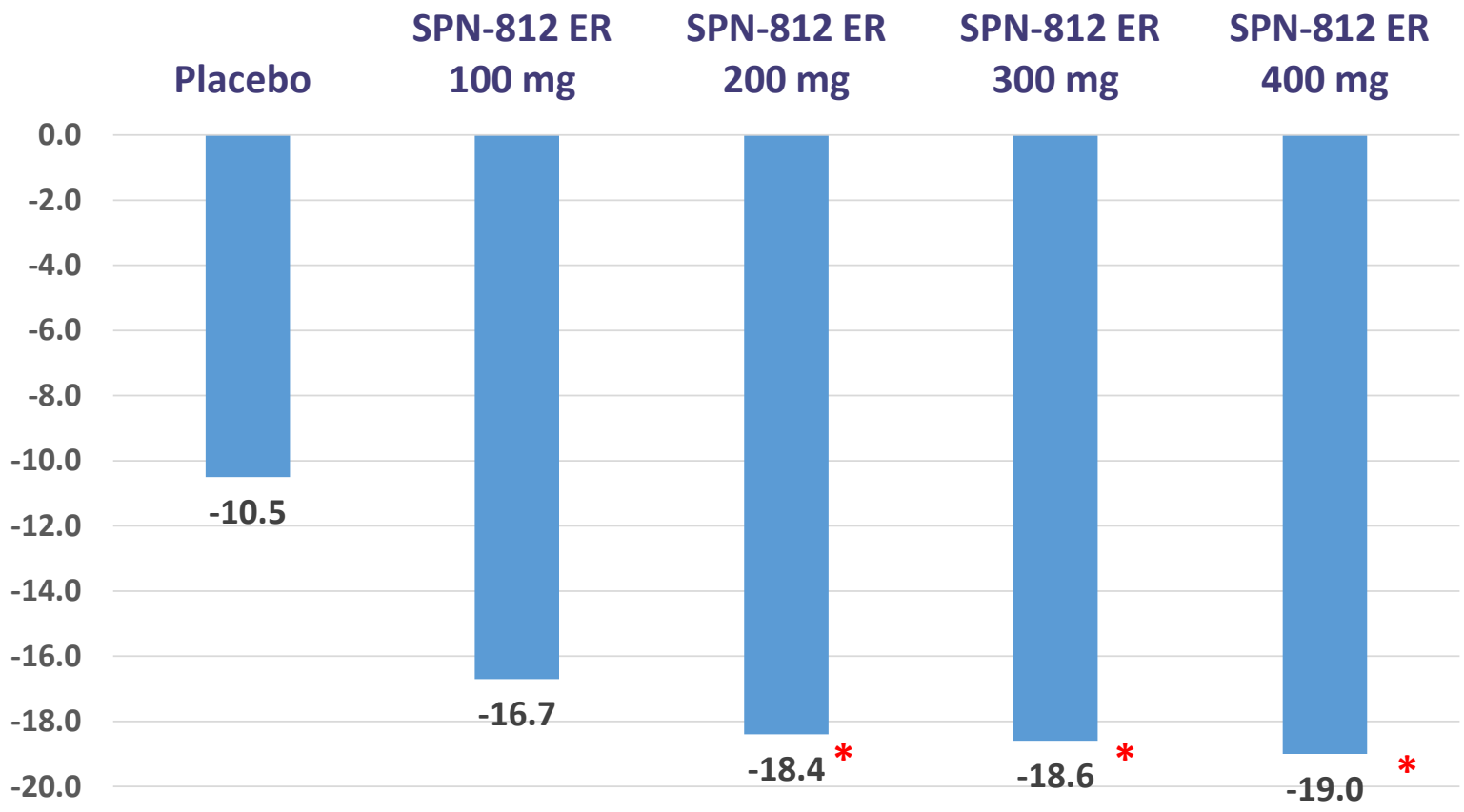
# LS Means of Change from Baseline in ADHD-RS-IV Score




*P-value <0.05



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# All SPN-812 Doses Met Primary Endpoint

## Sensitivity Analysis
## Change from baseline in ADHD-RS-IV Total Score (PP Population)

| Statistics | 400 mg N=32 | 300 mg N=34 | 200 mg N=29 | 100 mg N=35 | Placebo N=19 | |
|---|---|---|---|---|---|---|
| LS Mean | -23.3 | -19.2 | -20.7 | -18.3 | -9.4 | End of Study |
| **P-value** | **0.001*** | **0.017*** | **0.008*** | **0.028*** | | |

* At end of study, all SPN-812 doses are statistically significant compared to placebo at α = 0.05 level.

PP = Per Protocol



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# Three SPN-812 Doses Met CGI-S Secondary Endpoint

## Analysis of Secondary Endpoints, CGI-I and CGI-S (ITT Population with LOCF)

| Statistics | 400 mg N=44 | 300 mg N=47 | 200 mg N=46 | 100 mg N=45 | Placebo N=24 |
|---|---|---|---|---|---|
| **Change from baseline to End of Study in CGI-S** | | | | | |
| LS Mean | -1.7 | -1.6 | -1.5 | -1.4 | -0.8 |
| **P-value** | **0.014*** | **0.015*** | **0.031*** | 0.071 | |
| **Observed CGI-I at End of Study** | | | | | |
| LS Mean | 2.4 | 2.2 | 2.6 | 2.6 | 3.0 |
| **P-value** | 0.055 | **0.009*** | 0.138 | 0.131 | |

ITT = Intent To Treat
LOCF = Last Observation Carried Forward
CGI-I = Clinical Global Impression Improvement
CGI-S = Clinical Global Impression Severity
*Statistical significance at α = 0.05 level.



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# SPN-812 Was Well Tolerated

| Percentage of Patients with Related AEs, >5% | | SPN-812 ER | | | |
|---|---|---|---|---|---|
| **Adverse Event (AE)** | Placebo N=24 | 100 mg N=48 | 200 mg N=48 | 300 mg N=48 | 400 mg N=49 |
| **Somnolence** | 0 | 14.6 | 20.8 | 20.8 | 24.5 |
| **Decreased appetite** | 8.3 | 10.4 | 12.5 | 8.3 | 16.3 |
| **Headache** | 0 | 4.2 | 10.4 | 6.3 | 12.2 |
| **Insomnia** | 0 | 6.3 | 4.2 | 6.3 | 6.3 |
| **Nausea** | 0 | 4.2 | 2.1 | 8.3 | 4.1 |
| **Fatigue** | 0 | 4.2 | 4.2 | 2.1 | 10.2 |
| **Irritability** | 0 | 2.1 | 8.3 | 4.2 | 2.0 |
| **Weight decreased** | 0 | 0 | 0 | 0 | 8.3 |
| | | | | | |
| **Discontinuations Due to AEs** | 0 | 8.3 | 6.3 | 2.1 | 10.2 |



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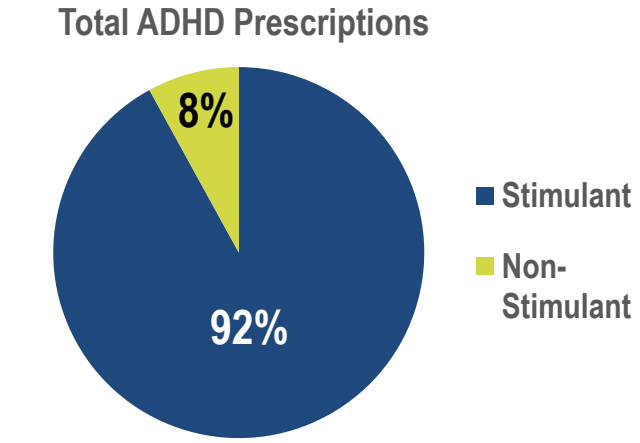
# SPN-812: Novel Non-Stimulant ADHD Product

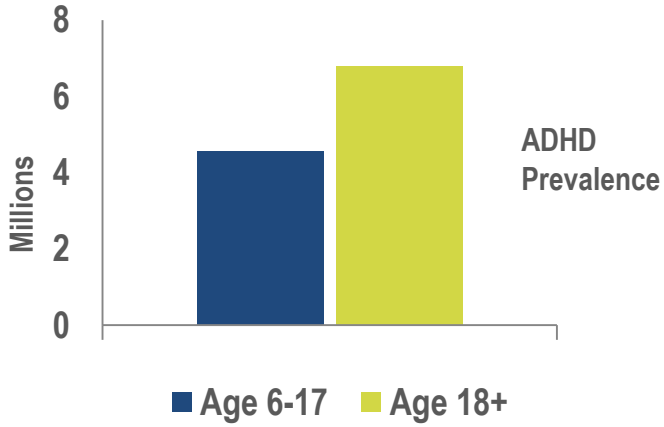
**Market Opportunity**
**$2.5B**

**Completed Phase IIa and Phase IIb studies in ADHD**

**Demonstrated safety and efficacy in adults and children**

**2017** **Phase III studies**




ADHD Prescriptions per SHA TRx data, December 2014
Centers for Disease Control "Trends in the Parent-Report of Health Care Provider-Diagnosed and Medicated ADHD: United States, 2003–2011; WebMD; Datamonitor



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# Positioned For Continued Strong Growth

## Strong Portfolio in Neurology

Potential Peak Sales for Oxtellar XR® and Trokendi XR® >$500M

## Innovative Late Stage Portfolio in Psychiatry

SPN-812 : Highly Effective and Well Tolerated Non-Stimulant

SPN-810 : The First Treatment for Impulsive Aggression



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