Supernus Pharmaceuticals

SPN-812 Phase III Topline Data

Investor Webcast – December 2018

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SPN-812

Novel Non-Stimulant ADHD Product Candidate

- Viloxazine hydrochloride
  - Norepinephrine reuptake inhibitor, selective serotonin activity
  - New Chemical Entity (NCE) with five year market exclusivity
  - Previously marketed outside the U.S. as an antidepressant
- Building strong IP with expirations from 2029-2033
- Clinical data point to a well-differentiated ADHD product
- Targeted NDA filing 2H 2019, and if approved, launch 2H 2020

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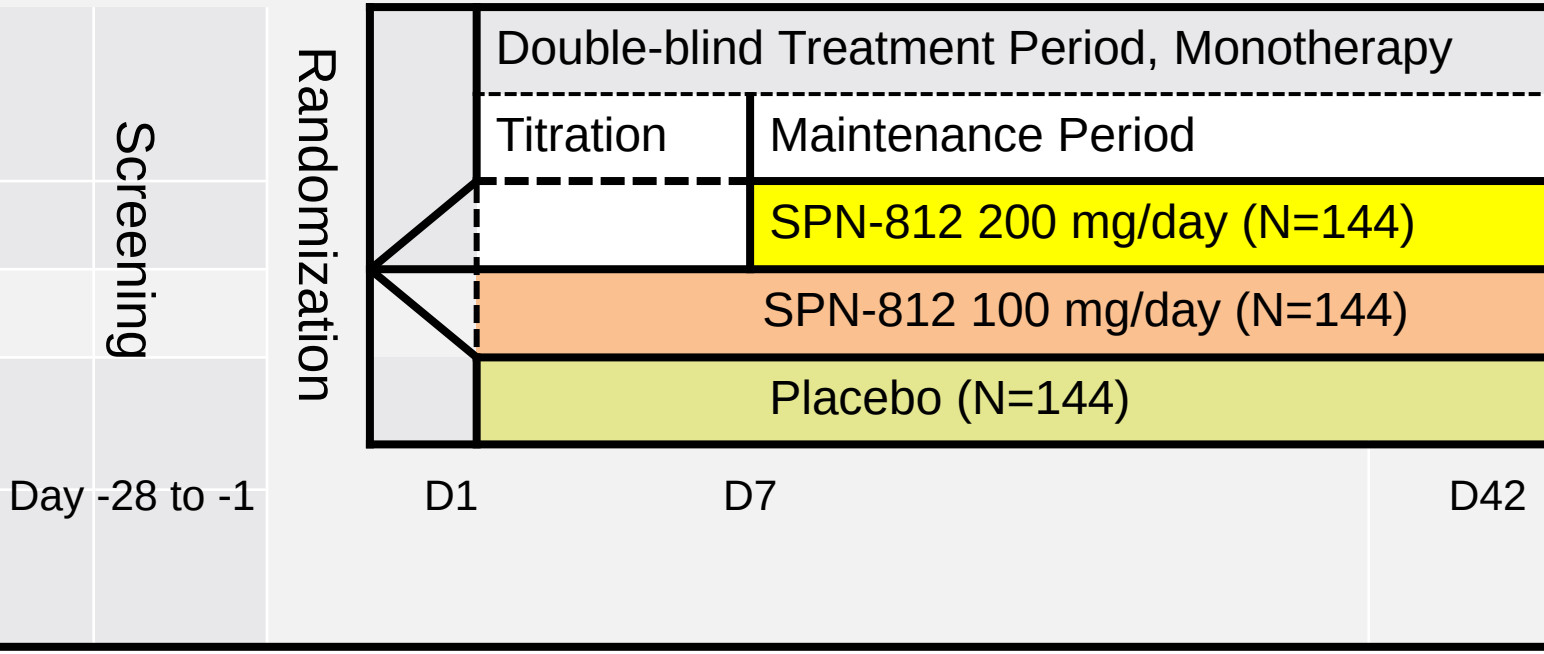
SPN-812
Phase III Studies Status

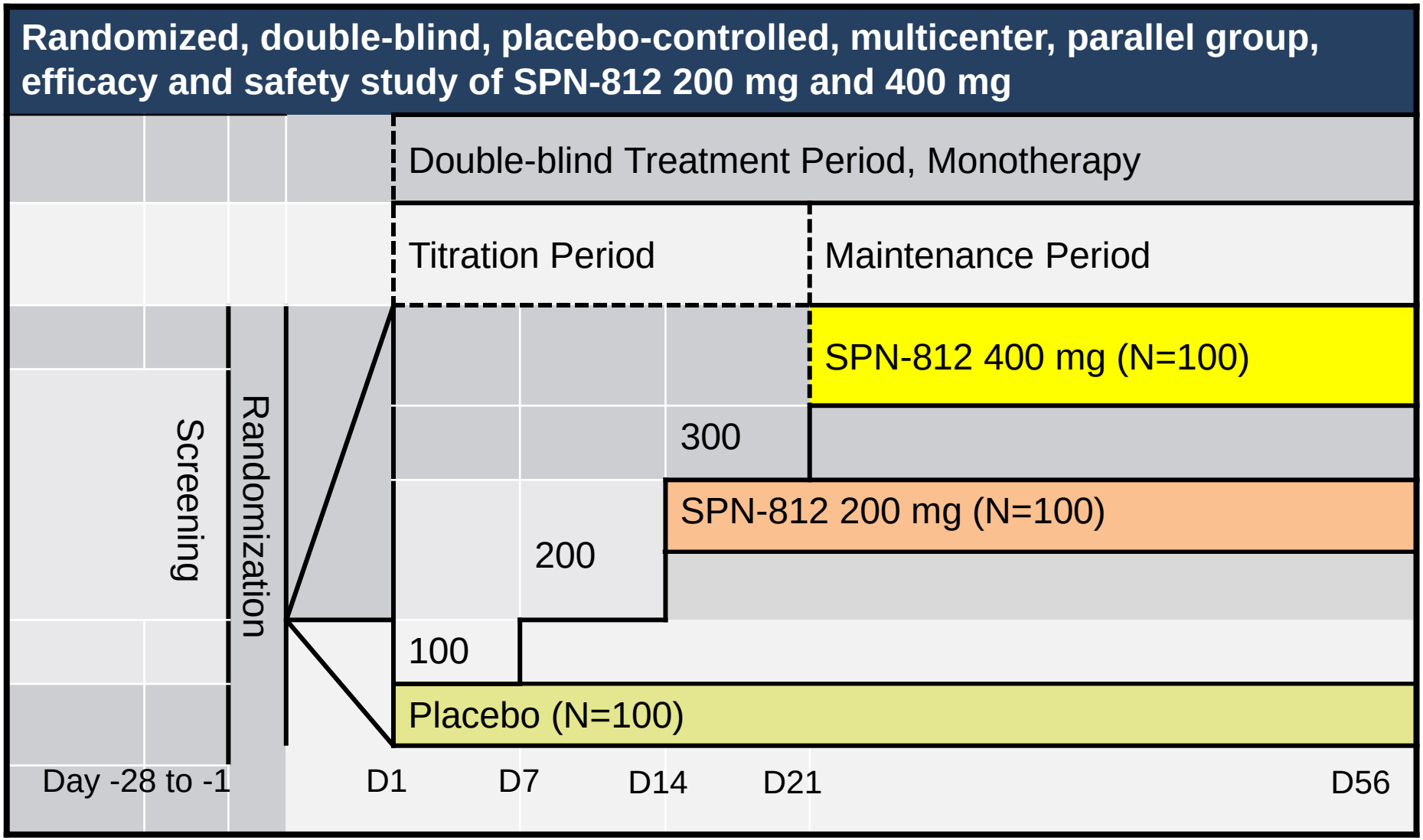
	P301 N = 477	P303 N = 313	P302 N = 300	P304 N = 300
ADHD Patients	6-11 years	6-11 years	12-17 years	12-17 years
Daily Doses	100mg 200mg	200mg 400mg	200mg 400mg	400mg 600mg
Status	Completed	Completed	Topline Data December 2018	Topline Data 1Q 2019

SPN-812 P301 Phase III Study Design

Randomized, double-blind, placebo-controlled, multicenter, parallel group, efficacy and safety study of SPN-812 100 mg and 200 mg



SPN-812 P303 Phase III Study Design



SPN-812 P301/303 Phase III Studies Design

- Primary Endpoint
  - Change from baseline on the ADHD-RS-5 scale compared to placebo
- Secondary Endpoints
  - Clinical Global Impression - Improvement (CGI-I) scale
  - Conners 3rd edition - parent, composite T-score
  - Weiss Functional Impairment Rating Scale - parent report (WFIRS-P)
- Evaluate safety & tolerability

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SPN-812 P301/303 Topline Results

Executive Summary

- Two positive phase III trials in children 6-11 years old
  - Met primary endpoint with robust statistical significance
    - P-values ranging from <0.0001 to 0.0121
  - Sensitivity analysis confirms primary analysis
- Both trials showed strong efficacy on Hyperactivity and Inattention subscales
- Larger P301 study showed fast onset of action
  - Statistical significance as early as one week for 100mg and 200mg
  - Sustained statistical significance through the end of study (week 6)
  - P303 study shows a supportive trend

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SPN-812 P301/303 Topline Results
Executive Summary

- P301 met all secondary endpoints
  - P303 met the CGI-I secondary endpoint
- Both trials showed favorable tolerability and safety profile
  - Low incidence of AE's across all doses (100mg, 200mg and 400mg)
- Overall, AE's are mild leading to very low discontinuation rates
  - Discontinuation rates due to AE's of 2.2% – 4.8%
  - Placebo-adjusted discontinuation rates of 0.9% - 1.9%

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SPN-812 P301 Study Topline Results

SPN-812 P301: Met Primary Endpoint

Primary Analysis of ADHD-RS-5 based on MMRM (ITT Population)

Visit	Statistics	Placebo (N=155)	100 mg (N=147)	200 mg (N=158)
Baseline	Mean	43.6	45.0	44.0
Week 6 (EOS)	LS Mean	-10.9	-16.6	-17.7
	Effect Size		0.54	0.57
	p-value		**0.0004**	**<.0001**

MMRM = Mixed Model for Repeated Measure ITT = Intent to Treat EOS = End of study
Effect size in Phase IIb study ranged from 0.46 to 0.63

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SPN-812 P301: Met Primary Endpoint

Efficacy Starting in Week 1

Visit	Statistics	Placebo (N=155)	100 mg (N=147)	200 mg (N=158)
Baseline	Mean	43.6	45.0	44.0
Week 1	LS Mean	-5.8	-9.5	-8.1
	p-value		0.0004	0.0244
Week 2	LS Mean	-7.9	-12.6	-12.3
	p-value		<.0001	0.0001
Week 3	LS Mean	-9.9	-15.4	-15.7
	p-value		<.0001	<.0001
Week 4	LS Mean	-11.2	-17.0	-17.7
	p-value		<.0001	<.0001
Week 5	LS Mean	-11.9	-17.3	-18.4
	p-value		0.0006	<.0001
Week 6 (EOS)	LS Mean	-10.9	-16.6	-17.7
	p-value		**0.0004**	**<.0001**

MMRM = Mixed Model for Repeated Measure ITT = Intent to Treat EOS = End of study

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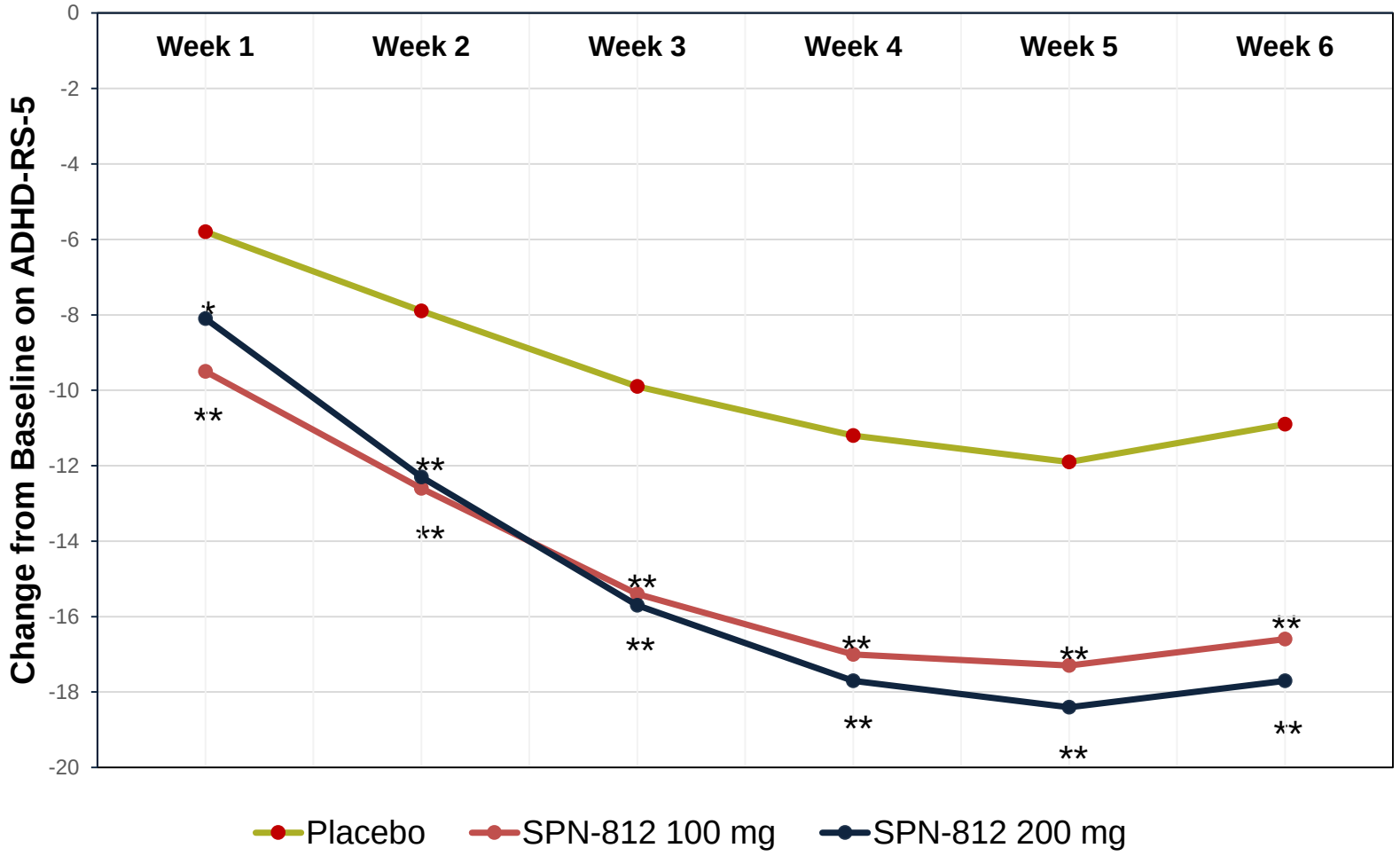
SPN-812 P301 – Efficacy Starting in Week 1

LS Mean Change from Baseline over Time – MMRM (ITT Population)



* $p \leq 0.05$ ** $p \leq 0.01$ MMRM = Mixed Model for Repeated Measure ITT = Intent to Treat

SPN-812 P301: Met Primary Endpoint

Sensitivity Analysis of ADHD-RS-5 based on ANCOVA at Week 6 (EOS) Confirms Primary Analysis (ITT Population)

Visit	Statistics	Placebo (N=155)	100 mg (N=147)	200 mg (N=158)
Baseline	Mean	43.6	45.0	44.0
Week 6 (EOS)	LS Mean	-11.1	-16.5	-17.8
	p-value		**0.0008**	**<.0001**

ANCOVA = Analysis of Covariance
ITT = Intent to Treat EOS = End of study

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SPN-812 P301: Met Secondary Endpoint

Analysis of Observed Global Improvement Score (CGI-I) at Week 6 (EOS)

Visit	Statistics	Placebo (N=155)	100 mg (N=147)	200 mg (N=158)
Baseline	Mean	4.8	4.8	4.8
Week 6 (EOS)	LS Mean	3.1	2.7	2.6
	p-value		**0.0020**	**<.0001**

EOS = End of study

SPN-812 P301: Met Secondary Endpoint

Analysis of Change from Baseline at Week 6 (EOS) in Composite T-score for Conners 3 - Parent Reported Scores

Visit	Statistics	Placebo (N=155)	100 mg (N=147)	200 mg (N=158)
Baseline	Mean	75.9	77.4	75.5
Week 6 (EOS)	LS Mean	-4.8	-9.1	-9.5
	p-value		**0.0004**	**<.0001**

EOS = End of study

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SPN-812 P301: Met Secondary Endpoint

Analysis of Change from Baseline at Week 6 (EOS) in WFIRS-P

Visit	Statistics	Placebo (N=155)	100 mg (N=147)	200 mg (N=158)
Baseline	Mean	1.08	1.15	1.10
Week 6 (EOS)	LS Mean	-0.22	-0.36	-0.39
	p-value		**0.0019**	**0.0002**

EOS = End of study
WFIRS-P = Weiss Functional Impairment Rating Scale - Parent Report

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SPN-812 P301
Significant Reduction in Hyperactivity and Inattention

Analysis in ADHD-RS-5 Inattention and Hyperactivity/Impulsivity Subscales

Visit	Statistics	Placebo (N=155)	100 mg (N=147)	200 mg (N=158)
ADHD-RS-5 Hyperactivity/Impulsivity				
Baseline	Mean	21.1	22.2	21.1
Week 6 (EOS)	LS Mean	-5.5	-8.0	-8.7
	p-value		**0.0026**	**<.0001**
ADHD-RS-5 Inattention				
Baseline	Mean	22.5	22.8	22.9
Week 6 (EOS)	LS Mean	-5.7	-8.6	-9.2
	p-value		**0.0006**	**<.0001**

EOS = End of study

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SPN-812 P301
Well Tolerated

Number (%) of Patients Reporting Common AEs (≥ 5% and greater than placebo)

	Placebo (N=159)	100 mg (N=154)	200 mg (N=161)	Overall SPN-812 (N=315)
Somnolence	3 (1.9)	16 (10.4)	15 (9.3)	31 (9.8)
Headache	6 (3.8)	15 (9.7)	16 (9.9)	31 (9.8)
Decreased appetite	0	8 (5.2)	14 (8.7)	22 (7.0)
Sedation	0	3 (1.9)	9 (5.6)	12 (3.8)
Vomiting	3 (1.9)	7 (4.5)	8 (5.0)	15 (4.8)
Discontinuation Due to AE's	**2 (1.3)**	**5 (3.2)**	**2 (1.2)**	**7 (2.2)**

SPN-812 P301
Well Tolerated

Number (%) of Patients - Treatment Related AEs with ≥ 5% incidence

	Placebo (N=159)	100 mg (N=154)	200 mg (N=161)	Overall SPN-812 (N=315)
Somnolence	3 (1.9)	14 (9.1)	14 (8.7)	28 (8.9)
Headache	3 (1.9)	7 (4.5)	10 (6.2)	17 (5.4)
Decreased appetite	0	7 (4.5)	12 (7.5)	19 (6.0)

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SPN-812 P303 Study Topline Results

SPN-812 P303: Met Primary Endpoint

Primary Analysis of ADHD-RS-5 Total Score based on MMRM (ITT Population)

Visit	Statistics	Placebo (N=97)	200 mg (N=107)	400 mg (N=97)
Baseline	Mean	43.5	43.8	45.0
Week 8 (EOS)	LS Mean	-11.7	-17.6	-17.5
	Effect Size		0.46	0.49
	p-value		**0.0038**	**0.0063**

MMRM = Mixed Model for Repeated Measure ITT = Intent to Treat EOS = End of study
Effect size in Phase IIb study ranged from 0.46 to 0.63

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SPN-812 P303: Met Primary Endpoint

Efficacy Starting in Week 1 but not statistically significant

Primary Analysis of ADHD-RS-5 Total Score based on MMRM (ITT Population)

Visit	Statistics	Placebo (N=97)	200 mg (N=107)	400 mg (N=97)
Baseline	Mean	43.5	43.8	45.0
Week 1	LS Mean	-5.0	-7.9	-6.7
	p-value		0.0268*	0.2058
Week 2	LS Mean	-8.4	-11.6	-10.9
	p-value		0.0398*	0.1141
Week 3	LS Mean	-10.6	-13.7	-13.7
	p-value		0.0668	0.0742
Week 4	LS Mean	-11.8	-14.7	-15.3
	p-value		0.1182	0.0585

*Note: Though the “p-value” is 0.0268 for the 200 mg dose, the outcome is not statistically significant because the 400 mg dose was not statistically significant at the same time point

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SPN-812 P303: Met Primary Endpoint

Efficacy Starting in Week 1 but not statistically significant

Primary Analysis of ADHD-RS-5 Total Score based on MMRM (ITT Population)

Visit	Statistics	Placebo (N=97)	200 mg (N=107)	400 mg (N=97)
Week 5	LS Mean	-11.6	-17.6	-16.5
	p-value		0.0015	0.0114
Week 6	LS Mean	-12.4	-17.7	-17.7
	p-value		0.0050	0.0057
Week 7	LS Mean	-12.9	-18.6	-17.3
	p-value		0.0045	0.0325
Week 8 (EOS)	LS Mean	-11.7	-17.6	-17.5
	p-value		**0.0038**	**0.0063**

EOS = End of study

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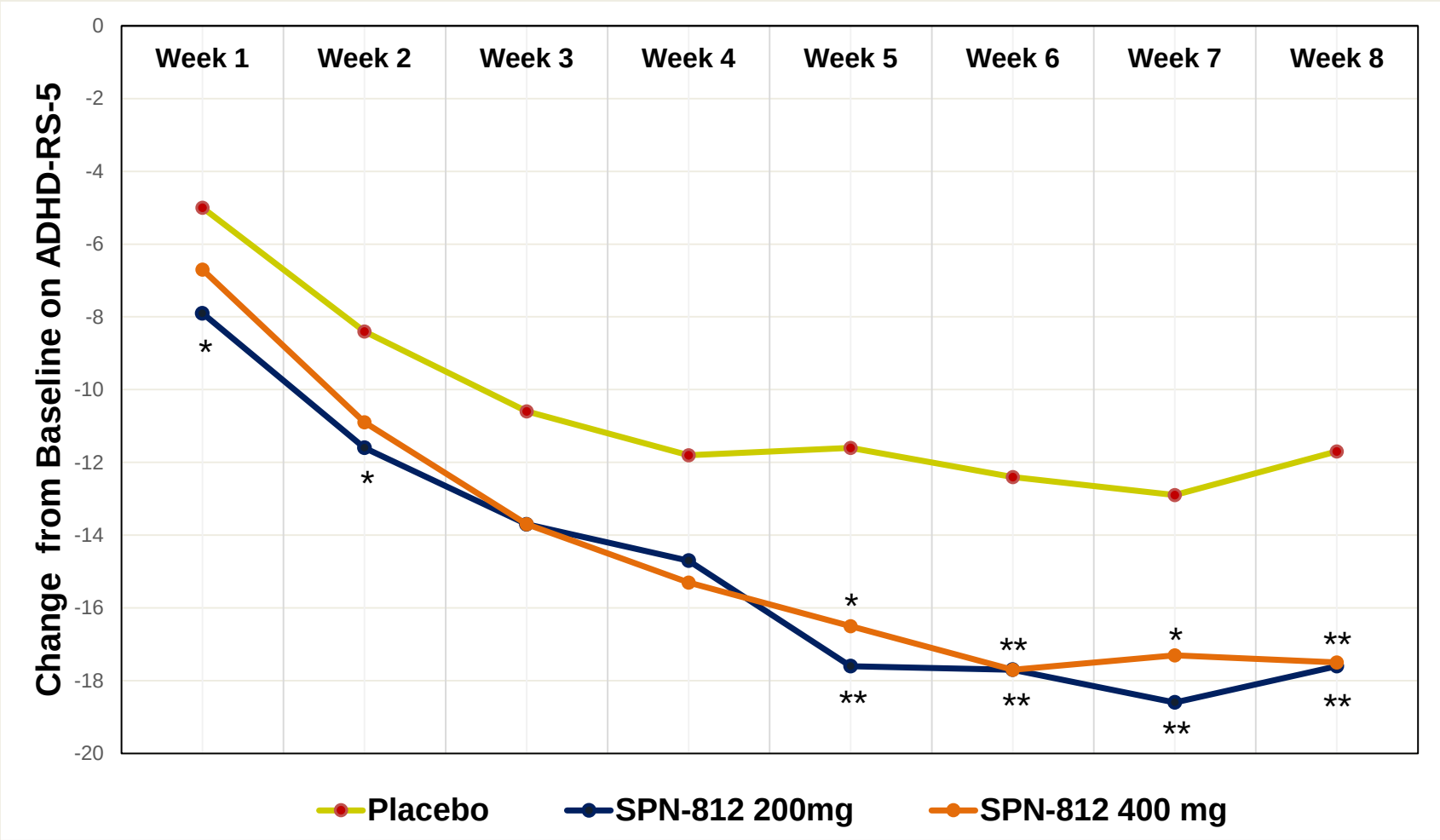
SPN-812 P303 – Efficacy By Week

LS Mean Change from Baseline over Time – MMRM (ITT Population)



* p≤ 0.05; **p≤ 0.01 MMRM = Mixed Model for Repeated Measure ITT = Intent to Treat

SPN-812 P303: Met Primary Endpoint

Sensitivity Analysis of ADHD-RS-5 based on ANCOVA at Week 8 (EOS) (ITT Population)

Visit	Statistics	Placebo (N=97)	200 mg (N=107)	400 mg (N=97)
Baseline	Mean	43.5	43.8	45.0
Week 8 (EOS)	LS Mean	-11.3	-17.0	-16.6
	p-value		**0.0058**	**0.0121**

ANCOVA = Analysis of Covariance
ITT = Intent to Treat EOS = End of study

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SPN-812 P303: Met Secondary Endpoint

Analysis of Observed Global Improvement Score (CGI-I) at Week 8 (EOS)

Visit	Statistics	Placebo (N=97)	200 mg (N=107)	400 mg (N=97)
Baseline	Mean	4.8	4.8	4.8
Week 8 (EOS)	LS Mean	3.1	2.6	2.6
	p-value		**0.0028**	**0.0099**

EOS = End of study

SPN-812 P303
Significant Reduction in Hyperactivity and Inattention

Analysis in ADHD-RS-5 Inattention and Hyperactivity/Impulsivity Subscales

Visit	Statistics	Placebo (N=97)	200 mg (N=107)	400 mg (N=97)
ADHD-RS-5 Hyperactivity/Impulsivity				
Baseline	Mean	21.0	21.2	22.0
Week 8 (EOS)	LS Mean	-5.1	-8.4	-8.3
	p-value		**0.0020**	**0.0039**
ADHD-RS-5 Inattention				
Baseline	Mean	22.5	22.6	23.0
Week 8 (EOS)	LS Mean	-6.2	-8.9	-8.6
	p-value		**0.0087**	**0.0248**

EOS = End of study

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SPN-812 P303
Well Tolerated

Number (%) of Patients Reporting Common AEs (≥ 5% and greater than placebo)

	Placebo (N=103)	200 mg (N=107)	400 mg (N=100)	Overall SPN-812 (N=207)
Somnolence	2 (1.9)	16 (15.0)	14 (14.0)	30 (14.5)
Decreased appetite	0	10 (9.3)	9 (9.0)	19 (9.2)
Fatigue	5 (4.9)	10 (9.3)	9 (9.0)	19 (9.2)
Headache	5 (4.9)	13 (12.1)	6 (6.0)	19 (9.2)
Vomiting	1 (1.0)	1 (0.9)	7 (7.0)	8 (3.9)
Upper abdominal pain	3 (2.9)	6 (5.6)	6 (6.0)	12 (5.8)
Insomnia	1 (1.0)	7 (6.5)	3 (3.0)	10 (4.8)
Irritability	3 (2.9)	3 (2.8)	6 (6.0)	9 (4.3)
Cough	0	6 (5.6)	0	6 (2.9)
Discontinuation Due to AE's	**3 (2.9)**	**6 (5.6)**	**4 (4.0)**	**10 (4.8)**

SPN-812 P303
Well Tolerated

Number (%) of Patients - Treatment Related AEs with ≥ 5% incidence

	Placebo (N=103)	200 mg (N=107)	400 mg (N=100)	Overall SPN-812 (N=207)
Somnolence	1 (1.0)	15 (14.0)	14 (14.0)	29 (14.0)
Decreased appetite	0	8 (7.5)	8 (8.0)	16 (7.7)
Fatigue	4 (3.9)	7 (6.5)	5 (5.0)	12 (5.8)
Headache	1 (1.0)	9 (8.4)	5 (5.0)	14 (6.8)
Upper abdominal pain	2 (1.9)	4 (3.7)	6 (6.0)	10 (4.8)

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SPN-812 P301/303 Topline Results
Executive Summary

- Two positive phase III trials in children 6-11 years old
- Clinical data point to a well-differentiated ADHD product
  - Strong efficacy with robust statistical significance
    - Efficacy on both Hyperactivity and Inattention
  - Fast onset of action
    - Works as early as the first week
  - Very well tolerated
- Data on the P302 adolescent trial before year-end
- Data on the P304 adolescent trial in 1Q 2019
- Targeted NDA filing 2H 2019, and if approved, launch 2H 2020

Supernus® Pharmaceuticals

Positioned For Continued Strong Growth

Growth Potential for Existing Products

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

Innovative Late Stage Portfolio in Psychiatry

SPN-812	Well Differentiated Novel Non-Stimulant
SPN-810	First Product to be Developed for Impulsive Aggression
SPN-604	Novel Product for Bipolar Disorder

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