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Phase 3, Randomized, Double-Blind, Placebo-Controlled Study (P301) Assessing Efficacy and Safety of Extended-Release Viloxazine in Children with ADHD

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ABSTRACT: Study Objective: SPN-812 (extended-release viloxazine) is a structurally distinct, bicyclic, Serotonin Norepinephrine Modulating Agent (SNMA) in development as a treatment for attention-deficit/hyperactivity disorder (ADHD) in children and adolescents. This Phase 3, randomized, double-blind study (P301) evaluated the efficacy and safety of once-daily SPN-812 at doses of 100 and 200 mg compared to placebo in children ages 6-11yrs with ADHD.

METHOD: Inclusion criteria required subjects have a confirmed Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5) ADHD diagnosis, ADHD-Rating Scale-5 (ADHD-RS-5) score ≥28, a Clinical Global Impression-Severity score ≥4, and be free of ADHD medication ≥1 week before randomization. This investigation was conducted at 34 study sites in the United States. Subjects (N=477) were randomized 1:1:1 to placebo:100 mg SPN-812:200 mg SPN-812. The 6-week treatment period included up to 1 week of titration and 5 weeks of maintenance (intent-to-treat population: N=460; placebo=155, 100 mg=147, 200 mg=158). The primary efficacy endpoint was the change from baseline (CFB) at end of study (EOS) in ADHD-RS-5 total score. Key secondary endpoints included Clinical Global Impression-Improvement (CGI-I) scores at EOS, and CFB at EOS in Conners 3-Parent Short Form (Conners 3-PS) Composite T-score and in Weiss Functional Impairment Rating Scale-Parent Version (WFIRS-P) total average score. Safety assessments included adverse events (AEs), laboratory tests, vital signs, physical exams, electrocardiograms, and the Columbia-Suicide Severity Rating Scale.

RESULTS: Compared to placebo, a significantly greater improvement in ADHD-RS-5 total score was observed in the 100 mg and 200 mg SPN-812 treatment groups beginning at week 1 (p=0.0004, p=0.0244; respectively) through EOS (p=0.0004, p<0.0001; respectively). Significant improvement at EOS for both 100 mg and 200 mg SPN-812 compared to placebo was also observed in CGI-I score (p=0.0020, p<0.0001; respectively), Connors 3-PS Composite T-score (p=0.0003, p=0.0002; respectively), and in WFIRS-P total average score (p=0.0019, p=0.0002, respectively). The most common (≥5%) treatment-related AEs reported were somnolence, decreased appetite, and headache.

CONCLUSIONS: In this study, SPN-812 at 100 mg and 200 mg doses met the primary and secondary objectives with statistical significance. AE-related dropouts were ≤5%, indicating SPN-812 treatment was well tolerated. This study is an encore of a poster presentation at the 2019 Annual Meeting of the American Academy of Child and Adolescent Psychiatry (AACAP).

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A Phase 3, Randomized, Double-Blind, Placebo-Controlled Study (P302): Efficacy and Safety of Extended-Release Viloxazine in Adolescents with ADHD

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ABSTRACT: Study Objective: SPN-812 (extended-release viloxazine) is a structurally distinct, bicyclic, Serotonin Norepinephrine Modulating Agent (SNMA) in development as a treatment for attention-deficit/hyperactivity disorder (ADHD) in children and adolescents. This Phase 3, randomized, double-blind study (P302) evaluated the efficacy and safety of once-daily SPN-812 at doses of 200 and 400 mg compared to placebo in adolescents ages 12-17yrs with ADHD.

METHOD: Inclusion criteria required subjects have a confirmed Diagnostic and Statistical Manual of Mental

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Disorders, 5th edition (DSM-5) ADHD diagnosis, ADHD-Rating Scale-5 (ADHD-RS-5) score ≥28, Clinical Global Impression-Severity score ≥4, and be free of ADHD medication ≥1 week before randomization. This investigation was conducted at 34 study sites in the United States. Subjects (N=310) were randomized 1:1:1 to placebo:200 mg SPN-812:400 mg SPN-812. The treatment period included up to 1 week of titration and 5 weeks of maintenance (intent-to-treat population: N=301; placebo=104, 200 mg=94, 400 mg=103). The primary efficacy endpoint was change from baseline (CFB) at end of study (EOS) in ADHD-RS-5 total score. Key secondary endpoints included Clinical Global Impression-Improvement (CGI-I) score at EOS, and CFB at EOS in Conners 3-Parent Short Form (Conners 3-PS) Composite T-score and Weiss Functional Impairment Rating Scale-Parent Form (WFIRS-P) total average score. Safety assessments included adverse events (AEs), laboratory tests, vital signs, physical exams, electrocardiograms, and the Columbia-Suicide Severity Rating Scale.

RESULTS: Compared to placebo, a significantly greater improvement in ADHD-RS-5 total score was observed in the 200 mg and 400 mg SPN-812 treatment group at EOS (p=0.0232, p=0.0091; respectively). Significant improvement in CGI-I score at EOS for both 200 mg and 400 mg SPN-812 compared to placebo was also observed (p=0.0042, p=0.0003; respectively). No significant change was observed at either dose compared to placebo in the Conners 3-PS Composite T-score (p=0.6854, p=0.0518; respectively), or the WFIRS-P total average score (p=0.2062, p=0.0519; respectively). The most common (≥5%) treatment-related AEs were somnolence, decreased appetite, fatigue, headache, and nausea.

CONCLUSIONS: In this study, SPN-812 met the primary objective for both the 200 and 400 mg doses, and a key secondary objective (CGI-I) for both the 200 and 400 mg doses. AE-related dropouts were ≤5%, indicating SPN-812 treatment was well tolerated.

This study is an encore of a poster presentation at the 2019 Annual Meeting of the American Academy of Child and Adolescent Psychiatry (AACAP).

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Phase 3, Randomized, Double-Blind, Placebo-Controlled Study (P303) Assessing Efficacy and Safety of Extended-Release Viloxazine in Children with ADHD

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ABSTRACT: Study Objective: SPN-812 (extended-release viloxazine) is a structurally distinct, bicyclic, Serotonin Norepinephrine Modulating Agent (SNMA) in development as a treatment for attention-deficit/hyperactivity disorder (ADHD) in children and adolescents. This Phase 3, randomized, double-blind study (P303) evaluated the efficacy and safety of once-daily SPN-812 at doses of 200 and 400 mg compared to placebo in children ages 6-11yrs with ADHD.

METHOD: Inclusion criteria required subjects have a confirmed Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5) ADHD diagnosis, ADHD-Rating Scale-5 (ADHD-RS-5) score ≥28, Clinical Global Impression-Severity score ≥4, and be free of ADHD medication ≥1 week before randomization. Subjects were enrolled at 31 study sites in the United States. Subjects (N=313) were randomized 1:1:1 to placebo:200 mg SPN-812:400 mg SPN-812. Treatment included up to 3 weeks of titration and 5 weeks of maintenance (intent-to-treat population: N=301; placebo=97, 200 mg=107, 400 mg=97). The primary efficacy endpoint was change from baseline (CFB) at end of study (EOS) in ADHD-RS-5 total score. Key secondary endpoints included Clinical Global Impression-Improvement (CGI-I) score at EOS, and CFB at EOS in Conners 3-Parent Short Form (Conners 3-PS) Composite T-score and in Weiss Functional Impairment Rating Scale-Parent Form (WFIRS-P) total average score. Safety assessments included adverse events (AEs) among other measures.

RESULTS: Compared to placebo, a significantly greater improvement in ADHD-RS-5 total score was observed in the 200 mg and 400 mg SPN-812 treatment group at EOS (p=0.0038, p=0.0063; respectively). Significant improvement in CGI-I score at EOS for both 200 mg and 400 mg SPN-812 was also observed (p=0.0028, p=0.0099; respectively). Significant improvement was observed for the 200 mg SPN-812 dose compared to placebo in the Conners 3-PS Composite T-score (p=0.0064), but not for the 400 mg dose (p=0.0917). No significant improvement was observed in either

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