

## ADHD (child and adolescent) – Non-Stimulant Medication

A Phase 3, Multicenter, Randomized, Double-blind, Placebo-controlled Trial to Determine the Efficacy and Safety of Once Daily Centanafadine Capsules for the Treatment of Children With Attention-deficit/Hyperactivity Disorder

With a rollover option for patients that complete one of the parent studies.

A Phase 3, Multicenter, Open-label, Long-term (52 weeks) Trial Evaluating the Long-term Safety and Tolerability of Once Daily Centanafadine Capsules in Children and Adolescents with Attention-deficit/Hyperactivity Disorder

<b>Protocol</b>	405-201-00016 / 00017 / 00021
<b>Ideal Patient Profile</b>	Child or adolescent with a <i>primary</i> diagnosis of ADHD
<b>Study Duration</b>	Parent study approximately 10 weeks; Extension study 52 weeks
<b>Visit Schedule</b>	Parent study weekly; Extension study every 6 weeks
<b>Reimbursement</b>	Parent study \$416; Extension study \$624 (\$1040 total)
<b>Key Inclusions:</b>	
<b>Age</b>	Child 6 – 12 years of age; Adolescent 13 – 17 years of age
<b>Indication</b>	ADHD
<b>Severity Level</b>	ADHD-RS-5 raw score $\geq 28$
<b>Lifestyle Requirements</b>	Subjects must agree to restrictions of medications and lifestyle described in the protocol
<b>Key Exclusions:</b>	
<b>Psychological Conditions</b>	Co-morbid diagnosis of a psychological disorder (Tourette's, GAD, Panic Disorder, Conduct Disorder, Psychosis, PTSD, Bipolar Disorder ASD, ODD, Obsessive-Compulsive Disorder, MDD or eating disorders in adolescents)
<b>Therapeutic Drug History</b>	No suitable therapeutic benefit has been derived from adequate courses of 2 classes of therapy during the subject's lifetime, in the investigator's opinion
<b>Suicide Risk</b>	Risk of suicide as measured by the C-SSRS
<b>Cognitive Capacity</b>	IQ $\leq 70$
<b>Physical Condition</b>	BMI $\geq 40$ or $\leq 5^{\text{th}}$ percentile for age and gender
<b>Other Medical Conditions</b>	<ul style="list-style-type: none"> <li>• History of seizures</li> <li>• A diagnosis of T1DB or unstable T2DB</li> </ul>
<b>Blood Pressure and ECG</b>	<ul style="list-style-type: none"> <li>• 6 – 8 years of age: resting, supine SBP <math>\geq 126</math> or DBP <math>\geq 80</math></li> <li>• 9 – 17 years of age: resting supine SBP <math>\geq 130</math> or DBP <math>\geq 80</math></li> <li>• QTcF <math>\geq 450</math></li> </ul>
<b>Labs</b>	<ul style="list-style-type: none"> <li>• Abnormal results for hematology</li> <li>• AST/ALT <math>&gt; 2x</math> ULN</li> <li>• HbA1c <math>\geq 6.5\%</math></li> <li>• CPK <math>\geq 2x</math> ULN (unless otherwise approved by the medical monitor)</li> <li>• Abnormal free T4</li> </ul>
<b>Drug Screen</b>	Positive drug or alcohol test at screening (marijuana may be allowed at the discretion of the medical monitor)