DATA UPDATE

Post hoc analysis: **AISRS Total Score data based on prior stimulant use in adults with ADHD**

This article is sponsored by Supernus Pharmaceuticals

INDICATION

Qelbree is indicated for the treatment of ADHD in adults and pediatric patients 6 years and older.

IMPORTANT SAFETY INFORMATION

WARNING: SUICIDAL THOUGHTS AND BEHAVIORS

In clinical studies, higher rates of suicidal thoughts and behaviors were reported in patients with ADHD treated with Qelbree than in patients treated with placebo. Closely monitor all Qelbree-treated patients for clinical worsening and for emergence of suicidal thoughts and behaviors.

Please see full Important Safety Information on page 4.

Qelbree is a first-line, FDA-approved, nonstimulant treatment option for adults and pediatric patients 6 years and older with ADHD.[1]

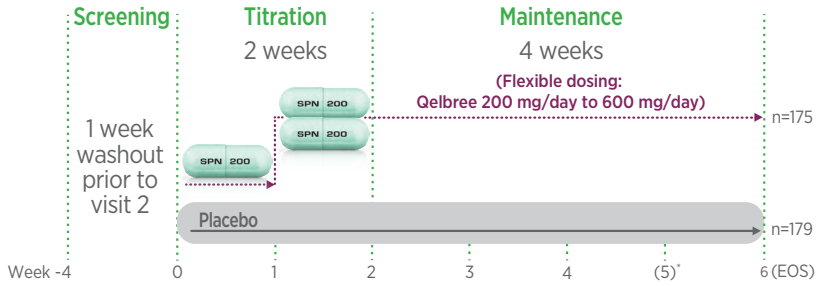
This is the first nonstimulant ADHD treatment option to be approved for adults (18 years and older) in 20 years.[1]

Four clinical studies evaluated the efficacy and safety of Qelbree for ADHD treatment in patients 6 years and older.[1,2]

Qelbree phase III adult trial (P306) designed to assess efficacy and safety of Qelbree in adults with ADHD[1,2]

Figure 1

- **Adults Ages 18 to 65 Years**
  (November 2019 to October 2020)
- **Primary Endpoint**
  Change from baseline to EOS in AISRS Total Score
- **Key Secondary Endpoint**
  Change from baseline to EOS in CGI-S score



Capsules shown are not actual size.

Qelbree phase III adult trial study design and methodology[1,2]

The adult phase III pivotal trial (Figure 1) was a randomized, double-blind, placebo-controlled trial designed to evaluate the safety and efficacy of Qelbree 200 mg/day to 600 mg/day in adults (18 to 65 years of age) with ADHD. Eligible subjects were randomized 1:1 to either the Qelbree or matched placebo arms. Subjects in the Qelbree arm received 200 mg/day of Qelbree during the first week and 400 mg/day of Qelbree during the second week. At study visits from week 3 through week 6, the investigators adjusted the doses, either increasing or decreasing them, based on the subject's clinical response and tolerability. The primary efficacy endpoint was CFB at EOS (week 6) in the AISRS Total Score. The key secondary endpoint was CFB at EOS in the CGI-S score. Additional secondary outcomes were measured.

*No study visit was scheduled/performed at week 5.

Abbreviations: ADHD, attention-deficit/hyperactivity disorder; HCP, healthcare professional.AISRS, Adult Investigator Symptom Rating Scale; CFB, change from baseline; CGI-S, Clinical Global Impression-Severity; EOS, end of study; FDA, Food and Drug Administration.

CONTRAINDICATIONS

- Concomitant administration of a monoamine oxidase inhibitor (MAOI), or dosing within 14 days after discontinuing an MAOI, because of an increased risk of hypertensive crisis
- Concomitant administration of sensitive CYP1A2 substrates or CYP1A2 substrates with a narrow therapeutic range

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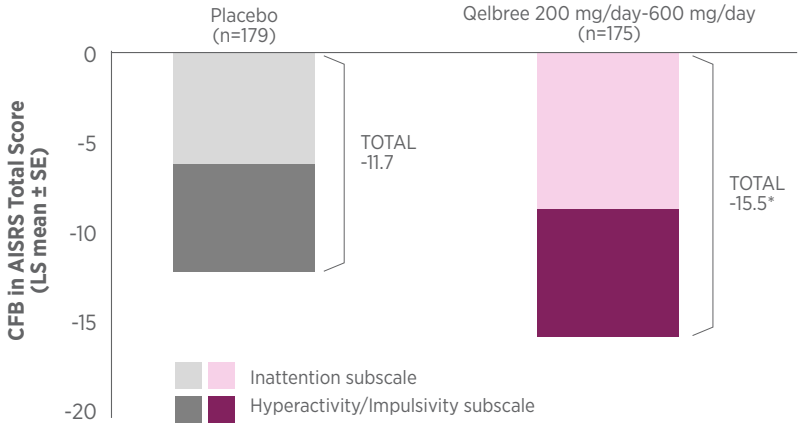
Qelbree phase III adult trial results[1]

Qelbree met the primary endpoint (change from baseline in the AISRS Total Score at EOS) in the adult phase III pivotal trial. The LS mean (±SE) change from baseline in AISRS Total Score at EOS was -15.5 (±0.91) in the Qelbree group and -11.7 (±0.90) in the placebo group (*P*=.004; Figure 2). Qelbree delivered significant symptom score reductions in the AISRS Total Score, which measures both inattention and hyperactivity/impulsivity symptoms in adults. The change from baseline (reduction) in the CGI-S score was statistically significantly greater in adults treated with Qelbree than in adults taking placebo.

Qelbree phase III study designed to assess efficacy and safety of Qelbree in adults with ADHD[1]

Figure 2

Primary endpoint: AISRS Total Score[1,2]



Secondary endpoint[1]
The change from baseline (reduction) in the CGI-S score was statistically significantly greater in adults treated with Qelbree than in adults taking placebo.

Mean baseline AISRS Total Score: placebo=37.6; Qelbree=38.5.[1]

*$P<0.05$ vs placebo.

Qelbree safety profile in adults: most common AEs[1,2]

Figure 3

	AEs Occurring in ≥5% of Patients and ≥2 Times More Frequent than Placebo[1]	
AE, n (%)	Placebo (n=183)	Qelbree (n=189)
Insomnia†	13 (7%)	46 (23%)
Headache†	13 (7%)	32 (17%)
Fatigue	6 (3%)	23 (12%)
Nausea	5 (3%)	23 (12%)
Decreased appetite	5 (3%)	19 (10%)
Dry mouth	4 (2%)	18 (10%)
Somnolence†	4 (2%)	11 (6%)
Constipation	2 (1%)	11 (6%)

†The following items were combined:
- **Somnolence:** somnolence, lethargy, sedation
- **Headache:** headache, migraine, migraine with aura, tension headache
- **Insomnia:** initial insomnia, insomnia, middle insomnia, poor quality sleep, sleep disorder, terminal insomnia

Discontinuation rates due to AEs[1,2]
- Qelbree: 9%
- Placebo: 5%

- The most common adverse reactions associated with discontinuation were fatigue, insomnia, constipation, and headache[1,2]

Abbreviation: AEs, adverse events; LS-mean, least squares mean; SE, standard error.

IMPORTANT SAFETY INFORMATION

- *Suicidal thoughts and behaviors*: Closely monitor all Qelbree-treated patients for clinical worsening and emergence of suicidal thoughts and behaviors, especially during the initial few months of drug therapy and at times of dosage changes

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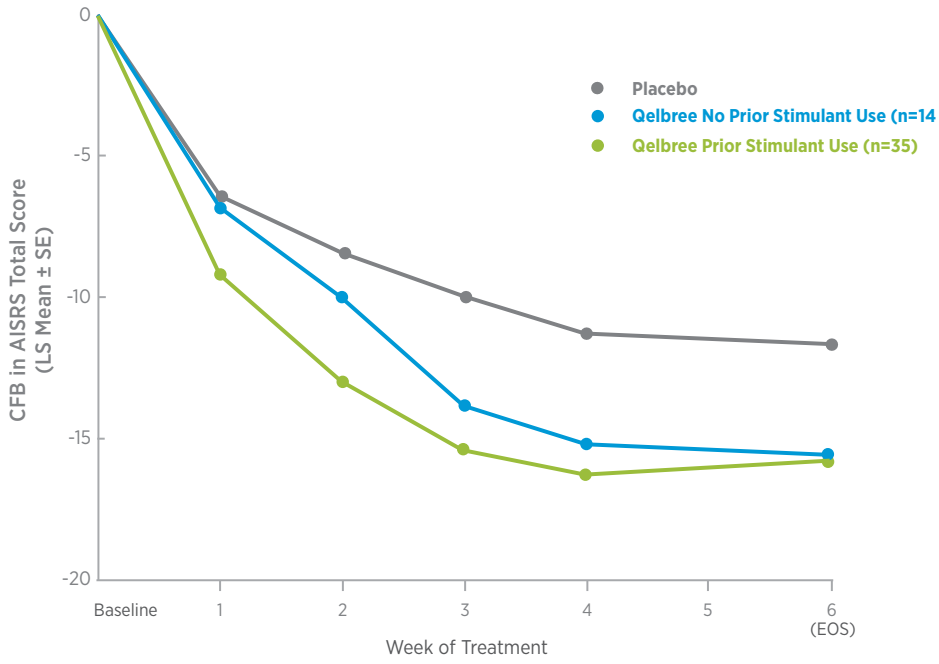
Post hoc analysis: AISRS Total Score data based on prior stimulant use in adults with ADHD

- Methodology: A post hoc analysis was conducted using phase III trial results (P306) in adults with ADHD. Participants were stratified based on prior history of reported stimulant use (using medication history at enrollment)[2]
  - Participants using stimulants at the screening visit underwent a ≥1-week washout period before randomization[2]
- CFB in the AISRS Total Score was analyzed in the prior stimulant user and nonuser groups using MMRM approach[2]
- Data were analyzed first for Qelbree-treated subjects with vs without a prior history of stimulant use. Data were then analyzed to evaluate placebo-subtracted treatment differences between stimulant users vs nonusers. The primary objective of the analysis was to evaluate the response to Qelbree based on history of prior stimulant use[2]

AISRS EOS Total Score data based on prior stimulant use[2]

Figure 4



- Participants randomized to Qelbree: AISRS Total Scores at EOS were not statistically different regardless of prior stimulant use[2]

This analysis was limited by its post hoc nature, including lack of an *a priori* power analysis, and the small sample size of the prior stimulant user group. These data are descriptive and conclusions cannot be drawn.[2]

Abbreviation: MMRM, mixed model repeated measure.

IMPORTANT SAFETY INFORMATION

- *Heart rate, blood pressure increases*: Qelbree can cause an increase in diastolic blood pressure and heart rate. Assess these measures prior to starting therapy, following increases in dosage, and periodically during therapy

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WARNINGS & PRECAUTIONS

- *Suicidal thoughts and behaviors*: Closely monitor all Qelbree-treated patients for clinical worsening and emergence of suicidal thoughts and behaviors, especially during the initial few months of drug therapy, and at times of dosage changes
- *Heart rate, blood pressure increases*: Qelbree can cause an increase in diastolic blood pressure and heart rate. Assess these measures prior to starting therapy, following increases in dosage, and periodically during therapy
- *Activation of mania or hypomania*: Noradrenergic drugs may induce a manic or mixed episode in patients with bipolar disorder. Prior to initiating treatment with Qelbree, screen patients to determine if they are at risk for bipolar disorder. Screening should include a detailed psychiatric history, including a personal or family history of suicide, bipolar disorder, and depression
- *Somnolence and fatigue*: Patients should not perform activities requiring mental alertness, such as operating a motor vehicle or hazardous machinery, due to potential somnolence (including sedation or lethargy) and fatigue, until they know how they will be affected by Qelbree

ADVERSE REACTIONS

The most common adverse reactions (≥5% and at least twice the rate of placebo for any dose) in patients 6 to 17 years were somnolence, decreased appetite, fatigue, nausea, vomiting, insomnia, and irritability, and in adults, insomnia, headache, somnolence, fatigue, nausea, decreased appetite, dry mouth, and constipation.

PREGNANCY

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to Qelbree during pregnancy. Healthcare providers are encouraged to register patients by calling the National Pregnancy Registry for Psychiatric Medications at 1-866-961-2388 or by visiting www.womensmentalhealth.org/preg.

REFERENCES: 1. Qelbree [package insert]. Rockville, MD: Supernus Pharmaceuticals, Inc. **2.** Data on file, Supernus Pharmaceuticals.

Please see full Prescribing Information, including Boxed Warning.