



BioCryst Announces Positive Results from APeX-P Trial for ORLADEYO® (berotralstat) in Pediatric Patients with Hereditary Angioedema Aged 2 to <12 Years

February 24, 2025

–Additional real-world studies with ORLADEYO show statistically significant HAE attack rate reductions experienced by patients with C1-INH deficiency and normal C1-INH levels and function–

–Data will be presented in five posters at the 2025 American Academy of Allergy, Asthma & Immunology (AAAAI) / World Allergy Organization (WAO) Joint Congress–

RESEARCH TRIANGLE PARK, N.C., Feb. 24, 2025 (GLOBE NEWSWIRE) -- [BioCryst Pharmaceuticals, Inc.](#) (Nasdaq: BCRX) today announced positive results from an interim analysis of the ongoing APeX-P clinical trial evaluating an oral granule formulation of once-daily ORLADEYO® (berotralstat) in pediatric patients with hereditary angioedema (HAE) aged 2 to <12 years.

"We are pleased to share results from APeX-P, the largest trial to date evaluating a prophylactic therapy for HAE in patients 2 to <12 years old, which will be presented later this week in a late-breaking abstract at the AAAAI / WAO Joint Congress. Importantly, the data show the oral granule formulation of ORLADEYO to be safe and well tolerated in the trial, with early and sustained reductions in monthly attack rates. We remain on track to submit our New Drug Application to the FDA this year, and we look forward to addressing a significant unmet need for children with HAE and their families," said Dr. Helen Thackray, chief research and development officer of BioCryst.

- ***HAE Attack Rates in Pediatric Patients 2 to <12 Years of Age with Prophylactic Berotralstat: Results from Interim Analysis of APeX-P***, Poster #L55

- ORLADEYO was safe and well tolerated in APeX-P, with no new safety signals identified. Adverse events (AEs) were similar across all ages and weights.
- ORLADEYO resulted in early and sustained reductions in monthly attack rates. The median (range) and mean (\pm SEM) monthly attack rates in the standard-of-care period were 0.96 (0–5.0) and 1.5 (\pm 0.2) attacks/month, respectively. After one month of taking ORLADEYO, median and mean monthly attack rates dropped to 0 (0–4.0) and 0.5 (\pm 0.2), and the median monthly attack rate remained at 0 through month 12 (month 12 range: 0–1.7); the mean monthly attack rate at month 12 was 0.3 (\pm 0.1).
- Eighty-three percent of participants experienced symptom onset before six years of age and 90 percent were diagnosed with HAE in the same timeframe.

Methods

- APeX-P consisted of a 12-week standard-of-care treatment period, followed by a subsequent open-label ORLADEYO treatment period lasting up to a total of 144 weeks. The data presented here are from an interim data cut taken at the time 17 participants had completed at least 48 weeks of ORLADEYO treatment.
- Participants (n=29) were placed into four cohorts by body weight at baseline.

"APeX-P was designed to collect pharmacokinetic data to inform appropriate weight ranges and doses for children to match the exposure of ORLADEYO seen in adult patients. This interim analysis shows there is significant potential for an oral, once-daily prophylactic therapy to meaningfully impact the lives of pediatric patients with HAE who are 2 to <12 years of age, especially considering the burden of disease and injectable treatment currently experienced by these patients," said Jolanta Bernatoniene, Paediatric Infectious Disease Department, Bristol Royal Hospital for Children, Bristol, UK.

Real-world evidence with ORLADEYO at 2025 AAAAI / WAO Joint Congress

The company also announced new real-world evidence with ORLADEYO showing statistically significant HAE attack rate reductions experienced by patients with HAE with C1-INH deficiency (HAE Type I/II) and normal C1-INH levels and function (HAE-nl-C1-INH), as well as high satisfaction with treatment after starting ORLADEYO. Research exploring factors that contribute to patients' willingness to switch long-term prophylaxis (LTP) for HAE will also be presented.

Posters #603 and #607 evaluate data collected through BioCryst's sole-source pharmacy that show real-world effectiveness outcomes for individuals with HAE aged 12 and above, both with and without C1-inhibitor deficiency.

"Here, we compare attack rates prior to and following ORLADEYO initiation stratified by baseline attack frequency among patients with C1-inhibitor deficiency and with normal C1-INH level and function, respectively. The results show substantial attack reductions after starting ORLADEYO among most patients with attacks at baseline. For patients with zero attacks at baseline, this is maintained after starting ORLADEYO. We continue to be encouraged by these real-world outcomes that show ORLADEYO is having a meaningful impact on patients regardless of disease activity," said Dr. Donald S. Fong, chief medical officer of BioCryst.

- **Real-World Attack Rates Before and After Berotralstat Initiation Among Patients with Hereditary Angioedema with C1-Inhibitor Deficiency (Type I/II) Stratified by Monthly Baseline HAE Attack Frequency**; Poster #603

- Patients with C1-INH deficiency (n=466) experienced statistically significant, sustained reductions in HAE attack rates after ORLADEYO initiation, regardless of baseline attack frequency.
 - Patients who experienced ≥ 5 baseline attacks/month (n=82) had the largest reductions, with 6.20 fewer attacks/month at 12 months (n=45) and 6.37 fewer attacks/month at 18 months (n=36) (both $p < 0.05$).
 - Patients with 0 attacks/month at baseline (n=128) maintained a low attack rate of 0 attacks/month during follow up; 70 percent had 0 attacks/month at 12 months (n=60) and 85 percent had 0 attacks/month at 18 months (n=40).

- **Real-World Attack Rates Before and After Berotralstat Initiation Among Patients with Hereditary Angioedema without C1-Inhibitor Deficiency (HAE-nl-C1-INH) Stratified by Monthly Baseline HAE Attack Frequency**; Poster #607

- Patients with HAE-nl-C1-INH (n=353) experienced statistically significant, sustained reductions in HAE attack rates after ORLADEYO initiation, regardless of baseline attack frequency.
 - Patients who experienced ≥ 5 baseline attacks/month had mean monthly attack rates decrease by 5.24 at 12 months (n=75) and 4.88 at 18 months (n=53) (both $p < 0.05$).
 - Patients with 0 attacks/month at baseline (n=39) maintained a low attack rate of 0 attacks/month during follow-up; 71 percent had 0 attacks/month at 12 months (n=14) and 70 percent had 0 attacks/month at 18 months (n=10).

Methods

- Data were collected through BioCryst's sole-source pharmacy and included U.S. patients who actively received ORLADEYO from December 15, 2020, to January 8, 2024.
- Patient-reported HAE attack rates were collected at ORLADEYO initiation and each refill (approximately every 30 days).
- Patients were classified into four subgroups based on baseline HAE attack frequency: 0: < 0.5 attacks/month; 1: between ≥ 0.5 and < 1.5 attacks/month; 2–4: between ≥ 1.5 and < 4.5 attacks/month; and ≥ 5 : ≥ 4.5 attacks/month.
- The top two reasons for decrease in sample size across intervals included end of study (i.e., patients reaching the end of the study period, January 8, 2024, without evidence of discontinuation) and ORLADEYO discontinuation (i.e., a gap in supply of ≥ 60 days).

Patient-reported outcomes show willingness to change LTP and improved treatment satisfaction across varying levels of attack frequency and severity after ORLADEYO initiation

Posters #608 and #655 explore two sets of patient-reported insights from online channels about patients' willingness to switch prophylactic therapy for HAE and the impact of ORLADEYO on HAE attack frequency and severity among patients naïve to LTP and those switching from another LTP, respectively.

"We continue to see encouraging patient-reported outcomes in the real-world setting among those who switch to ORLADEYO from another LTP and those who are naïve to LTP. In these posters, we report insights from our ongoing patient-focused research that show patients have a willingness to switch LTP and have less frequent and severe attacks following a switch to ORLADEYO," continued Dr. Fong.

- **Exploring the Role of Disease Burden, Treatment Effectiveness, and Administration Preference on Willingness of Patients With HAE to Change Long-Term Prophylaxis**; Poster #608

- U.S. patients with HAE (n=150) completed an online survey on willingness to switch LTP; participants had a mean age of 47.1, a mean of 26.8 years since diagnosis and 93 percent were on a prophylactic therapy with or without on-demand therapy. Of those on LTP, 92 percent were on injectable therapy.
- Participants' anxiety about taking their LTP, administration preference and treatment burden were leading factors in patients' willingness to switch to a different LTP, including those who preferred oral LTP being more likely to be extremely willing to switch LTP than those with no preference.
- Disease burden, severity and attack control also contributed to participants' willingness to switch their LTP.

- **Patient-Reported Impact of Berotralstat as Long-Term Prophylaxis on Hereditary Angioedema Attack Frequency and Attack Severity**; Poster #655

- U.S. patients with HAE (n=124) who had been treated with ORLADEYO participated in an online discussion and survey about their experiences with ORLADEYO and other HAE therapies; participants had a mean age of 43.2, a mean of 13.4 years since diagnosis and 54 percent had been on ORLADEYO for at least one year.

- o Most participants, including those switching from prior LTP and those who had been on ORLADEYO for less than one year, reported having less frequent and less severe attacks after starting ORLADEYO.
- o All participants were either “extremely satisfied” or “somewhat satisfied” with their initiation of, or transition to, ORLADEYO with respect to HAE attack frequency and severity.

All posters will be on display during the 2025 AAAAI / WAO Joint Congress in the poster hall in the San Diego Convention Center (Ground Level, Hall A) during the poster session on Sunday, March 2 from 9:45-10:45 a.m. PT.

About ORLADEYO® (berotralstat)

ORLADEYO® (berotralstat) is the first and only oral therapy designed specifically to prevent attacks of hereditary angioedema (HAE) in adult and pediatric patients 12 years and older. One capsule of ORLADEYO per day works to prevent HAE attacks by decreasing the activity of plasma kallikrein.

U.S. Indication and Important Safety Information

INDICATION

ORLADEYO® (berotralstat) is a plasma kallikrein inhibitor indicated for prophylaxis to prevent attacks of hereditary angioedema (HAE) in adults and pediatric patients 12 years and older.

Limitations of use

The safety and effectiveness of ORLADEYO for the treatment of acute HAE attacks have not been established. ORLADEYO should not be used for the treatment of acute HAE attacks. Additional doses or dosages of ORLADEYO higher than 150 mg once daily are not recommended due to the potential for QT prolongation.

IMPORTANT SAFETY INFORMATION

An increase in QT prolongation was observed at dosages higher than the recommended 150 mg once-daily dosage and was concentration dependent.

The most common adverse reactions ($\geq 10\%$ and higher than placebo) in patients receiving ORLADEYO were abdominal pain, vomiting, diarrhea, back pain, and gastroesophageal reflux disease.

A reduced dosage of 110 mg taken orally once daily with food is recommended in patients with moderate or severe hepatic impairment (Child-Pugh B or C).

Berotralstat is a substrate of P-glycoprotein (P-gp) and breast cancer resistance protein. P-gp inducers (eg, rifampin, St. John's wort) may decrease berotralstat plasma concentration, leading to reduced efficacy of ORLADEYO. The use of P-gp inducers is not recommended with ORLADEYO.

ORLADEYO at a dose of 150 mg is a moderate inhibitor of CYP2D6 and CYP3A4. For concomitant medications with a narrow therapeutic index that are predominantly metabolized by CYP2D6 or CYP3A4, appropriate monitoring and dose titration is recommended. ORLADEYO at a dose of 300 mg is a P-gp inhibitor. Appropriate monitoring and dose titration is recommended for P-gp substrates (eg, digoxin) when coadministering with ORLADEYO.

The safety and effectiveness of ORLADEYO in pediatric patients <12 years of age have not been established.

There are insufficient data available to inform drug-related risks with ORLADEYO use in pregnancy. There are no data on the presence of berotralstat in human milk, its effects on the breastfed infant, or its effects on milk production.

To report SUSPECTED ADVERSE REACTIONS, contact BioCryst Pharmaceuticals, Inc. at 1-833-633-2279 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please see full [Prescribing Information](#).

About BioCryst Pharmaceuticals

BioCryst Pharmaceuticals is a global biotechnology company with a deep commitment to improving the lives of people living with hereditary angioedema and other rare diseases. BioCryst leverages its expertise in structure-guided drug design to develop first-in-class or best-in-class oral small-molecule and protein therapeutics to target difficult-to-treat diseases. BioCryst has commercialized ORLADEYO® (berotralstat), the first oral, once-daily plasma kallikrein inhibitor, and is advancing a pipeline of small-molecule and protein therapies. For more information, please visit www.biocryst.com or follow us on [LinkedIn](#).

Forward-Looking Statements

This press release contains forward-looking statements, including statements regarding future results, performance or achievements and statements relating to ORLADEYO performance. These statements involve known and unknown risks, uncertainties and other factors which may cause actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. These statements reflect our current views with respect to future events and are based on assumptions and are subject to risks and uncertainties. Given these uncertainties, you should not place undue reliance on these forward-looking statements. Some of the factors that could affect the forward-looking statements contained herein include: BioCryst's ability to successfully implement or maintain its commercialization plans for ORLADEYO; BioCryst's ability to successfully progress its development plans as described herein, including meeting the expected timelines; ongoing and future preclinical and clinical development of product candidates may take longer than expected and may not have positive results; the commercial viability of ORLADEYO, including its ability to achieve sustained market acceptance; the FDA or other applicable regulatory agency may require additional studies beyond the studies planned for products and product candidates, may not provide regulatory clearances which may result in delay of planned clinical trials, may impose certain restrictions, warnings, or other requirements on products and product candidates, may impose a clinical hold with respect to product candidates, or may withhold, delay, or withdraw market approval for products and product candidates; and

BioCryst's ability to successfully manage its growth and compete effectively. Please refer to the documents BioCryst files periodically with the Securities and Exchange Commission, specifically BioCryst's most recent Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, and Current Reports on Form 8-K, which identify important factors that could cause the actual results to differ materially from those contained in BioCryst's forward-looking statements.

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