



## **BioCryst Presents New Real-world Data Showing Reduced Attack Rates in Patients with HAE with Normal C1-inhibitor Following Long-term Treatment with ORLADEYO® (berotralstat)**

November 10, 2023

**– Additional analysis from APeX-S showed patients who self-reported HAE attack rates at baseline had a median attack rate of 0 attacks per month across 12-month period –**

RESEARCH TRIANGLE PARK, N.C., Nov. 10, 2023 (GLOBE NEWSWIRE) -- [BioCryst Pharmaceuticals, Inc.](https://www.biocryst.com) (Nasdaq: BCRX) today announced new analyses of real-world use of oral, once-daily ORLADEYO® (berotralstat) leading to a reduction in monthly attack rates in patients with hereditary angioedema (HAE) who have normal C1-inhibitor (C1-INH) level and function.

"There is a significant unmet need among people who live with HAE with normal C1-INH, and identifying optimal treatments has been challenging for these patients. These real-world observations suggest ORLADEYO can have a meaningful impact on the lives of people who have HAE with normal C1-INH. We look forward to continuing to evaluate our oral, once-daily prophylaxis as a treatment option for this subpopulation," said Dr. Ryan Arnold, chief medical officer of BioCryst.

The company also announced a new post-hoc analysis from the APeX-S clinical trial that showed a sustained reduction in HAE attacks compared to patients' self-reported baseline attack rates.

"The ability to compare patients' treatment outcomes with their HAE attack rates at baseline is tremendously helpful to characterize the impact of a prophylactic therapy. While this analysis from APeX-S includes baseline attack rates that were retrospectively self-reported by patients, the findings are consistent with results previously reported from the pivotal APeX-2 trial, that long-term prophylaxis with ORLADEYO leads to a sustained reduction in attack rates and is an important therapeutic option for the prevention of HAE attacks," said H. James Wedner, M.D., professor of medicine in the division of allergy and immunology at the John T. Milliken department of medicine at Washington University School of Medicine.

The data are being presented at the 2023 Annual Scientific Meeting of the American College of Allergy, Asthma & Immunology (ACAAI), which is being held at the Anaheim Convention Center in Anaheim, Calif., from November 9-13, 2023.

### **BioCryst ACAAI 2023 Presentation Highlights**

The presentations at ACAAI include analyses from the APeX-S clinical study and real-world data from patients taking ORLADEYO in the United States. APeX-S was a Phase 2, open label, international study evaluating the safety and effectiveness of ORLADEYO 110 mg once daily (QD) and 150 mg QD in patients with HAE Type I or Type II for up to 96 weeks in the US and 240 weeks in all other countries. The real-world data are analyses from patient-reported results collected in the real-world clinical setting from BioCryst's sole-source pharmacy.

- ***Berotralstat Reduced Attack Rates in Patients with Hereditary Angioedema with Normal C1-Inhibitor: Real-World Outcomes***; ePoster #P082; Friday, November 10, 5:30-5:45 p.m. PT; Monitor #13, Exhibit Hall
  - This analysis assessed patient-reported HAE attack rates for patients with healthcare provider-diagnosed HAE (reflective of an ICD-10 code of D84.1 or T78.3) who have normal C1-INH level and function in the United States and actively received ORLADEYO 110 mg or 150 mg QD at any timepoint between December 16, 2020 and June 15, 2023 (n=302), with data shown for up to 540 days. Data are also reported for a subset of these patients who reported a 90-day baseline attack rate and received ORLADEYO for ≥360 days (n=103). A sizeable number of patients who received another prophylactic treatment for HAE at any time, such as lanadelumab, intravenous and subcutaneous C1-INH and androgens, were included in both cohorts.
  - Patient-reported attack rates were collected by the sole-source pharmacy at baseline and at each refill (approximately every 30 days). The baseline 30-day average was calculated based on each patient's self-reported attack rate for the 90 days prior to initiating ORLADEYO and by dividing that value by three. Monthly attack rates were calculated by taking the average of the reported attacks across each 90-day period.
  - A reduction in HAE attack rates was observed in both cohorts upon initiation of ORLADEYO:
    - At baseline, the median attack rate was 3.00 attacks per month (n=249). Upon initiation of ORLADEYO, median attack rates were reduced to 1.00 at Days 1-90 (n=277) and Days 91-180 (n=232); 1.29 at Days 181-270 (n=174); 1.00 at Days 271-360 (n=143); and 1.50 at Days 361-450 (n=105) and Days 451-540 (n=79), with a median attack rate of ≤1.50 attacks per month across all reporting periods over the entire duration.
    - For patients who reported a 90-day baseline attack rate and received ORLADEYO for ≥360 days (n=103),

the median baseline attack rate was 3.00 attacks per month. Upon initiation of ORLADEYO, median attack rates were reduced to 1.29 at Days 1-90 (n=100); 1.00 at Days 91-180 (n=99); 1.33 at Days 181-270 (n=99); and 1.00 at Days 271-360 (n=101), with a median attack rate of  $\leq 1.33$  attacks per month across all reporting periods over the entire duration.

- This analysis suggests that long-term prophylaxis with ORLADEYO resulted in a reduction in patient-reported monthly attack rates compared to baseline and median patient-reported attack rates remained consistently low in patients with HAE who have normal C1-INH level and function.
- ***Bertralstat Reduced Attack Rates Compared to Baseline in Patients with Hereditary Angioedema in APeX-S;*** ePoster #P064; Saturday, November 11, 12:05-12:20 p.m. PT; Monitor #12, Exhibit Hall
  - This analysis characterized the safety and effectiveness of ORLADEYO 150 mg QD in U.S. patients enrolled in the APeX-S trial who self-reported a baseline attack rate (n=147). Patients were asked to recall the average number of HAE attacks per month (attack rates) they experienced over the six months prior to beginning therapy. Attack rates after beginning therapy were calculated for each patient based on the number of attacks they experienced that met predefined criteria, as specified in the study protocol, and were adjusted for the duration of treatment in each month. Attack rates at baseline were not evaluated according to the predefined criteria used for inclusion in the effectiveness analysis in APeX-S.
  - ORLADEYO was generally well tolerated, and safety was consistent with that of the entire APeX-S population.
  - In patients who reported HAE attack rates at baseline, mean (SEM) attack rates declined from 2.3 (0.29) self-reported attacks per month prior to initiating ORLADEYO treatment to 0.71 (0.12) at Month 1, 0.49 (0.09) at Month 6 and 0.32 (0.10) at Month 12, respectively. A median attack rate of 0 attacks per month was observed for all months across the 12-month period.
  - Patients who were treated with ORLADEYO experienced a sustained reduction in HAE attacks compared to their self-reported baseline attack rates, suggesting a reduction in disease burden and durable treatment effect.

In addition to being displayed in the exhibit hall at the noted times, ePosters are accessible online and on demand to registered attendees on ACAAI's [website](#).

#### **About ORLADEYO® (bertralstat)**

ORLADEYO® (bertralstat) 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® (bertralstat) 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) and in patients taking chronically administered P-glycoprotein (P-gp) or breast cancer resistance protein (BCRP) inhibitors (eg, cyclosporine).

Bertralstat is a substrate of P-gp and BCRP. P-gp inducers (eg, rifampin, St. John's wort) may decrease bertralstat 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](http://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 complement-mediated 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](http://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. 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: the ongoing COVID-19 pandemic, which could create challenges in all aspects of BioCryst's business, including without limitation delays, stoppages, difficulties and increased expenses with respect to BioCryst's and its partners' development, regulatory processes and supply chains, negatively impact BioCryst's ability to access the capital or credit markets to finance its operations, or have the effect of heightening many of the risks described below or in the documents BioCryst files periodically with the Securities and Exchange Commission; BioCryst's ability to successfully implement its commercialization plans for, and to commercialize, ORLADEYO, which could take longer or be more expensive than planned; the commercial viability of ORLADEYO, including its ability to achieve 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; BioCryst's ability to successfully manage its growth and compete effectively; risks related to the international expansion of BioCryst's business; and actual financial results may not be consistent with expectations, including that revenue, operating expenses and cash usage may not be within management's expected ranges. 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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