BioCryst Presents New Real-world Data Showing Rapid, Substantial and Sustained HAE Attack Rate Reductions After Beginning ORLADEYO® (berotralstat) Treatment

February 23, 2024

RESEARCH TRIANGLE PARK, N.C., Feb. 23, 2024 (GLOBE NEWSWIRE) -- BioCryst Pharmaceuticals, Inc. (Nasdaq: BCRX) today announced new analyses of real-world use of oral, once-daily ORLADEYO® (berotralstat) that showed patients who initiated ORLADEYO experienced rapid, substantial and sustained reductions in attack rates through 18 months of treatment regardless of the severity of their disease, their history of prior prophylaxis or their C1-inhibitor (C1-INH) level and function.

The data are being presented in five posters at the 2024 American Academy of Allergy, Asthma & Immunology (AAAAI) annual meeting, which is being held at the Walter E. Washington Convention Center in Washington, D.C., from February 23-26, 2024.

"These additional analyses of real-world use of ORLADEYO show that any person living with HAE has the potential to experience a rapid, substantial and sustained reduction in their monthly attack rate with ORLADEYO. From patients who live with severe disease to well-controlled patients and those who have a history of being treated with other long-term prophylaxis that carry a therapeutic burden, these data demonstrate that once patients begin oral, once-daily ORLADEYO, they can experience attack control over the duration of their treatment," said Jonathan Bernstein, M.D., professor of medicine, department of internal medicine, division of allergy & immunology at the University of Cincinnati and partner of the Bernstein Allergy Group and Bernstein Clinical Research Center.

Rapid, Substantial and Sustained HAE Attack Rate Reduction After Beginning ORLADEYO Across Multiple Patient Types

Three posters (#012; #008; #281) highlight data collected through BioCryst's sole-source pharmacy that show real-world effectiveness outcomes for patients aged 12 and above with HAE who initiated ORLADEYO in the United States. These analyses present the overall attack rate progression and attack rate progression stratified by severity (i.e., number of attacks at baseline), prior prophylaxis and C1-INH level and function.

"We are continuing to see strong disease control with ORLADEYO in the real world, including in patients with HAE who report differing baseline disease severities. These findings further demonstrate that ORLADEYO can help maintain disease control in patients with lower baseline attack rates and further reduce attack rates in patients with more active disease. We continue to be encouraged by the consistent, building body of real-world evidence demonstrating the significant benefit that our oral, once-daily prophylactic therapy can provide to people living with HAE," said Dr. Ryan Arnold, chief medical officer of BioCryst.

Berotralstat Prophylaxis Reduces HAE Attack Rates Regardless of Baseline Attacks: Real-World Outcomes; Poster #012; Friday, February 23, 3:15-4:15 p.m. ET

- Patients with C1-INH deficiency who received long-term prophylaxis with ORLADEYO achieved rapid reduction in patient-reported monthly HAE attack rates from baseline, regardless of the severity of their disease (n=335).
- Median attack rates decreased below baseline (1.33 median monthly attack rate) in the first 90 days of ORLADEYO treatment and remained below baseline across all additional 90-day intervals for up to 18 months (540 days) (0.50 median monthly attack rate).
- Additionally, when stratified by baseline attacks, median monthly attack rates decreased and remained below baseline for up to 540 days on ORLADEYO regardless of their attack rate at baseline. This was observed across patients who reported a 90-day baseline of 0 attacks (0 attacks/month at all time points except for 0.33 at Days 271-360) to those who reported a 90-day baseline of ≥10 attacks (>3.33 attacks/month at baseline to 1.58 attacks/month at Days 1-90, concluding at 1.50 attacks/month at Days 451-540).

Consistently Low Hereditary Angioedema Attack Rates with Berotralstat Regardless of Prior Prophylaxis: Real-World Outcomes; Poster #008; Friday, February 23, 3:15-4:15 p.m. ET

- Patients who initiated ORLADEYO and were previously on at least one other prophylactic therapy at some point during their lifetime (n=216) also experienced rapid, substantial and sustained reductions in HAE attack rates regardless of prior prophylactic therapy, including lanadelumab, subcutaneous (SC) C1-INH and androgens.
- Of note, the median monthly attack rate for patients who were previously treated with lanadelumab decreased from 1.00 at baseline (n=66) to 0.33 at Days 1-90 (n=71) after initiating ORLADEYO and remained below baseline through Days 451-540 (0.50; n=21).

Real-World Effectiveness of Berotralstat in HAE With and Without C1-Inhibitor Deficiency*; Poster #281; Saturday, February 24, 9:45-10:45 a.m. ET*

- Similarly, a reduction in monthly HAE attack rates was observed in patients with HAE who have normal C1-INH level and function (n=302) and those with C1-INH deficiency (n=402) upon initiating ORLADEYO.

- Patients with normal C1-INH had a median attack rate at baseline of 3.00 attacks/month (n=249), which was reduced to 1.00 at Days 1-90 (n=277) and remained below baseline through Days 451-540 (1.50; n=79), while patients with C1-INH deficiency had a median attack rate at baseline of 1.33 attacks/month (n=335), which was reduced to and remained at 0.50 through Days 451-540 (n=119).

Methods

- These posters highlight outcomes collected through BioCryst's sole-source pharmacy and include patients who actively received ORLADEYO 110 or 150 mg QD from December 16, 2020 to June 15, 2023.
- Patient-reported attack rates were collected 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.
- Not all patients reported a baseline attack rate or attack rates during each 90-day period.

Real-world Data from French Cohorts Support Safety, Effectiveness and Adherence to ORLADEYO

Two additional posters (#028; #023) highlight findings from real-world studies in patients with HAE aged 12 and above in France, including an observational study (BeroLife) and the ongoing prospective MATCH study (Monitoring HAE Treatment Compliance by the community pHarmacist).

"These new findings from the BeroLife and MATCH studies indicate an association between adherence to therapy and effectiveness of ORLADEYO. Of note, the results from MATCH show that the number of patients who had high adherence to ORLADEYO after one month of treatment was comparable to the adherence rate among patients who take medications for chronic diseases in France, but this number increased the longer they remained on treatment. Additionally, patients who participated in these studies had a low discontinuation rate, which supports our previously reported findings that the longer patients remain on ORLADEYO, the better their outcomes are," continued Dr. Ryan Arnold.

Assessment of the Tolerability and Effectiveness of Berotralstat for Long-term Prophylaxis in Hereditary Angioedema: BeroLife Study Interim Analysis; Poster #028; Friday, February 23, 3:15-4:15 p.m. ET

- An interim analysis that shows long-term prophylaxis with ORLADEYO was generally well tolerated and safety was consistent with what has previously been reported from clinical trials. Only 15.6 percent (n=10) experienced a drug-related treatment-emergent adverse event (TEAE), and fewer than 10 percent discontinued ORLADEYO due to a TEAE (n=6).
- From an effectiveness standpoint, this analysis shows a decrease in HAE attack rates among patients, the majority of whom had already been treated with previous long-term prophylaxis such as attenuated androgens, tranexamic acid and lanadelumab, which is consistent with what was observed in clinical trials with long-term prophylaxis with ORLADEYO. Final data from the BeroLife study are expected later this year.

Evaluation of Adherence to Berotralstat in Patients with Hereditary Angioedema: A Prospective Survey in Community Pharmacies; Poster #023; Friday, February 23, 3:15-4:15 p.m. ET

- An association between adherence and effectiveness of ORLADEYO was observed when taken by patients who received follow-up engagements from a pharmacist each month for six months (n=23).
- No association was found between adherence to ORLADEYO and the incidence of adverse events. Additionally, no serious drug-related TEAEs occurred and only 12.8 percent of patients (n=6) discontinued treatment during the study.

Methods

- The BeroLife study assesses the safety and effectiveness of ORLADEYO 150 mg QD in a French cohort of patients ages 12 years and older with HAE Type I or Type II (n=64). Data were collected by 18 physician investigators associated with the Reference Centre for Angioedema (CREAK) Expert Network in France from November 2021 to May 2023.
- The MATCH study assesses the impact of monthly follow-up and therapeutic monitoring by community pharmacists in France on patient adherence to ORLADEYO 150 mg QD (n=47). Adherence is measured using the 8-item Morisky Medication Adherence Scale (MMAS-8), a validated method of determining adherence to treatment through a self-reported measurement of medication-taking behavior.

All posters are available to meeting registrants and will be on display in the poster hall in the Walter E. Washington Convention Center (Level 2, Hall D) during the meeting.

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 (≥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 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 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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