BioCryst Presents New Long-term and Real-world Data Demonstrating Sustained Reductions in Hereditary Angioedema Attack Rates and Improvement in Quality of Life with ORLADEYO® (berotralstat)

February 24, 2023

— Final safety and effectiveness analysis from APeX-S showed ORLADEYO 150 mg resulted in a median attack rate of 0.0 attacks per month in 20 of 24 months —

RESEARCH TRIANGLE PARK, N.C., Feb. 24, 2023 (GLOBE NEWSWIRE) -- BioCryst Pharmaceuticals, Inc. (Nasdaq: BCRX) today announced new data from the APeX-S and APeX-2 clinical trials which evaluated oral, once-daily ORLADEYO® (berotralstat) for the prophylactic treatment of hereditary angioedema (HAE) demonstrating sustained reductions in attack rates and improvement in quality of life (QoL) among patients living with HAE, highlighting its profile as a well-tolerated, effective and convenient prophylactic HAE therapeutic option.

The company also announced additional analyses from new real-world data that further demonstrate a meaningful reduction in attack rates experienced by patients on ORLADEYO, in addition to findings from a survey that underscore a significant disease and treatment burden among pediatric HAE patients, as reported by their caregivers.

The data are being presented at the 2023 American Academy of Allergy, Asthma & Immunology (AAAAI) annual meeting, which is being held in San Antonio, Texas, from February 24-27, 2023.

“The final results from the long-term APeX-S study show that ORLADEYO was consistently well-tolerated, with no new safety signals observed, and attack reduction was sustained through 96 weeks. These results are complemented by the analyses from APeX-2, in which clinically meaningful patient-reported improvements in QoL across subgroups was shown at 96 weeks,” said Emel Aygören-Pürsün, M.D., Internal Medicine and Hemostaseology, Division of Oncology, Hematology and Hemostaseology, Department for Children and Adolescents, University Hospital Frankfurt.

“We are excited to report the final results of our ORLADEYO clinical studies, as these new datasets are being reinforced by what we have observed in the real-world use of ORLADEYO. This real-world evidence supports the continued need for an oral, once-daily option for patients and physicians who are seeking control of their HAE attacks,” said Dr. Ryan Arnold, chief medical officer of BioCryst.

BioCryst AAAAI 2023 Presentation Highlights

The posters being presented at AAAAI include analyses from the APeX-2 and APeX-S clinical studies, as well as real-world data from patients taking ORLADEYO in the United States. APeX-2 was a Phase 3, double-blind, placebo-controlled, parallel-group, three-part study evaluating ORLADEYO versus placebo for the prevention of HAE attacks in patients with HAE Type I or Type II. 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.

Overall, treatment-emergent adverse events (TEAEs) reported in APeX-2 and APeX-S were mild and transient, indicating that ORLADEYO was generally well tolerated.

- ***Real-World Outcomes in Patients with Hereditary Angioedema (HAE) Treated with Berotralstat*; Poster #415; Sunday, February 26, 9:45-10:45 am CT**
    - This analysis assessed patient-reported HAE attack rates of HAE Type I or Type II patients on ORLADEYO 110 mg or 150 mg QD for at least 120 days based on review of data from a sole-source pharmacy from December 2020 to May 2022 (n=213). Baseline attack rates were captured by pharmacist progress notes for the previous 90 days prior to initiation of ORLADEYO and converted to a 30-day average for each patient.
    - Overall, attack rates subsequently decreased upon initiation with ORLADEYO and remained consistently low through 360 days on therapy. The median reported attack rate was ≤0.5 attacks/month across all reporting periods through 360 days, and the median reported attack rate was 0.0 in half of the 30-day reporting periods.
    - These real-world findings suggest that ORLADEYO is a durable and effective long-term prophylactic treatment for patients with HAE.
- ***Disease and Treatment Burden of Hereditary Angioedema (HAE) in Pediatric Patients: Assessment by Caregivers*; Poster #417; Sunday, February 26, 9:45-10:45 am CT**
    - This analysis focused on a blinded, cross-sectional study based on results from an online survey of U.S. adults (n=35) who self-reported being the caregiver of pediatric HAE Type I or Type II patients (age 2-12 years old). They were asked to share perceptions of their experiences with disease management, current HAE treatments and the potential impact of an oral HAE treatment in pediatric patients.

- Key findings from the survey included:
  - Only 17 percent of pediatric patients (n=6) were on prophylactic HAE treatment.
  - 40 percent of caregivers (n=14) reported ≥1 attack experienced by the pediatric patient in the past six months.
  - 75 percent of school-age pediatric patients (≥ 5 years old; n=12) who had ≥1 attack missed at least one day of school in the last six months because of HAE and 33 percent missed 6-15 days.
  - Caregivers of pediatric patients who had ≥1 attack not on prophylactic therapy (n=12) most commonly reported infusion requirements (33 percent) and administration inconvenience (25 percent) as reasons why pediatric patients were not on prophylactic therapy.
- These findings demonstrate significant disease and treatment burden experienced by pediatric patients and underscore the need for a more convenient option to help increase adoption of prophylactic treatment for HAE in this patient population.

- ***Long-term HAE Prophylaxis with Berotralstat Is Well Tolerated and Effective: Analysis for the APeX-S Study*; Poster #398; Sunday, February 26, 9:45-10:45 am CT**

  - This analysis characterizes the final safety and effectiveness results of APeX-S through 96 weeks. Patients (n=387) were initially allocated to once-daily ORLADEYO 110 mg or 150 mg until superior efficacy at 150 mg was demonstrated in APeX-2 and patients on the 110 mg dose at that time transitioned to 150 mg (n=100).
  - No new safety signals were observed. Overall, TEAEs were generally mild and transient, indicating that ORLADEYO was generally well tolerated.
  - Clinically meaningful and sustained reductions in HAE attack rates were observed in patients receiving ORLADEYO 150 mg (n=287). In patients who received ORLADEYO 150 mg, a median attack rate of 0.0 attacks/month was observed in 20 of 24 months. Following one month of ORLADEYO treatment, the mean (SEM) adjusted HAE attack rate was 1.1 (0.1). Subsequently, SEM adjusted HAE attack rates declined to 0.9 (0.1) at Month 6, 0.7 (0.1) at Month 12, and 0.8 (0.1) at Month 24.
  - Patients experienced sustained reductions in attacks throughout treatment through 24 months, consistent with previously reported data, further supporting the long-term safety and effectiveness of ORLADEYO.

- ***Berotralstat Improved Quality of Life through 96 Weeks Across Multiple Subgroups of Patients with Hereditary Angioedema*; Poster #426; Sunday, February 26, 9:45-10:45 am CT**

  - This analysis focused on the changes in QoL assessed in APeX-2 using the validated patient-reported Angioedema Quality of Life Questionnaire (AE-QoL), specifically AE-QoL scores in patients randomized to ORLADEYO 150 mg in part 1 of the study through Week 96 in part 3 of the study (n=40).
  - Results were stratified by four baseline characteristics: age (<35 years old, 35-50 years old, >50 years old); sex (male, female); baseline attack rate (<2 attacks/month, ≥2 attacks/month); prior prophylaxis (prior treatment with androgens or C1 esterase inhibitor). Additionally, AE-QoL results were stratified by the presence or absence of gastrointestinal adverse events (GI AEs) in part 1.
  - Mean patient-reported improvements from baseline to Week 96 in total AE-QoL score exceeded the minimal clinically important difference (MCID) value starting at Week 4 and were sustained through Week 96.
  - Improvements were also observed in all domains of the AE-QoL (functioning, fatigue/mood, fear/shame, nutrition) regardless of stratification, with the largest improvement occurring in the functioning domain in almost all stratification groups.
  - These data illustrate that long-term prophylaxis with ORLADEYO led to sustained and clinically meaningful improvements in patient-reported QoL across multiple subgroups after 96 weeks of treatment, and that patients reported improvements in total AE-QoL score and all AE-QoL domains, regardless of the presence or absence of GI AEs.

All posters are available to meeting registrants and will be on display in the poster hall in the Henry B. Gonzalez Convention Center 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) and in patients taking chronically administered P-glycoprotein (P-gp) or breast cancer resistance protein (BCRP) inhibitors (eg, cyclosporine).

Berotralstat is a substrate of P-gp and BCRP. 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 discovers novel, oral, small-molecule medicines that treat rare diseases in which significant unmet medical needs exist and an enzyme plays a key role in the biological pathway of the disease. Oral, once-daily ORLADEYO® (berotralstat) is approved in the United States and many global markets. BioCryst has active programs to develop oral medicines for multiple targets across the complement system, including BCX10013, an oral Factor D inhibitor in clinical development. RAPIVAB® (peramivir injection) is approved in the U.S. and multiple global markets, with post-marketing commitments ongoing. For more information, please visit the company's website at www.biocryst.com.

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 periodically files 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 actual results to differ materially from those contained in BioCryst's forward-looking statements.

BCRXW

Investor Contact:
John Bluth
+1 919 859 7910
jbluth@biocryst.com

Media Contact:
Catherine Collier Kyroulis
+1 917 886 5586
ckyroulis@biocryst.com