# BioCryst's Oral Factor D Inhibitor, BCX9930, Advancing to Pivotal Trials in PNH Following Successful Proof of Concept Trial

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***—Following doses of 400 mg bid or 500 mg bid of oral BCX9930, 100 percent of treatment-naïve patients and 83 percent of C5 inadequate response patients were transfusion-free—***

***—Mean hemoglobin increased from 8.3 g/dL to 11.8 g/dL in treatment-naïve patients and from 8.9 g/dL to 12.2 g/dL in C5 inadequate response patients, demonstrating control of hemolysis—***

***—Pivotal trials in PNH and proof of concept trials in renal complement-mediated disease expected to begin in 2H 2021 —***

RESEARCH TRIANGLE PARK, N.C., March 22, 2021 (GLOBE NEWSWIRE) -- BioCryst Pharmaceuticals, Inc. (Nasdaq: BCRX) today announced that its oral Factor D inhibitor, BCX9930, significantly increased hemoglobin and reduced transfusions in an ongoing dose-ranging trial in treatment-naïve (no prior treatment with C5 inhibitors) paroxysmal nocturnal hemoglobinuria (PNH) patients, and in PNH patients with an inadequate response to C5 inhibitors. BCX9930 was safe and generally well-tolerated in the trial.

Based on these results, and recent interactions with U.S. and European regulators, the company plans to advance directly into pivotal trials in PNH and proof of concept trials in renal complement-mediated diseases in the second half of 2021.

PNH patients in the trial also experienced reductions in key laboratory biomarkers, such as reticulocyte count, lactate dehydrogenase (LDH) (treatment-naïve patients) and percentage of C3 opsonization (patients with inadequate C5 response) following dosing at 400 mg bid or 500 mg bid.

"The significant reduction in transfusions and increases in hemoglobin seen in this trial with an oral medicine address an unmet need for patients and physicians -- a PNH therapy that can maximize hematological benefit through the control of both intravascular and extravascular hemolysis," said Antonio Risitano, M.D., Ph.D., San Giuseppe Moscati Hospital, Avellino, Italy, and principal investigator of the trial.

"I am very encouraged by these results which may position proximal inhibitors, and in particular this oral anti-Factor D agent, as medications changing the treatment paradigm of PNH, and possibly of other alternative pathway mediated diseases," he added.

**About the Trial**
In the trial, 10 treatment-naïve PNH patients received oral BCX9930 monotherapy and six PNH patients who had an inadequate response on a C5 inhibitor had oral BCX9930 added to their intravenous C5 therapy regimen. Fifteen patients, nine treatment-naïve and six who had an inadequate response on a C5 inhibitor, received BCX9930 at doses of 400 mg bid or 500 mg bid for at least eight weeks. Some patients have now been on study drug for almost a year.

Treatment with BCX9930 at doses of 400 mg bid or 500 mg bid for at least eight weeks resulted in significant improvements in clinical symptoms and laboratory biomarkers of disease in both the treatment-naïve and C5 inadequate-responder cohorts.

- Through their last study visit, 100 percent of treatment-naïve patients and 83 percent of C5 inhibitor inadequate response patients were transfusion-free. Prior to the trial, 22 percent of treatment-naïve patients and 17 percent of C5 inadequate responders were transfusion-free.
- Hemoglobin levels increased by a mean of 3.5 g/dL in treatment-naïve patients and 3.2 g/dL in C5 inhibitor inadequate response patients; at last visit, mean hemoglobin levels were 11.8 g/dL and 12.2 g/dL, respectively.
- Relative red blood cell clone size, a marker of hemolytic control, also increased from 53 to 92 percent in treatment-naïve patients and from 50 to 80 percent in C5 inhibitor inadequate response patients.
- C3 opsonization, a key marker of extravascular hemolysis, declined to less than two percent by the eight-week visit in five of six C5 inadequate response patients following BCX9930 therapy.
- In C5 inhibitor naïve patients, clinical chemistry biomarkers of intravascular hemolysis, including lactate dehydrogenase (LDH), aspartate aminotransferase (AST) and bilirubin, all declined. Mean LDH x ULN declined by 73 percent from 7.5x ULN at baseline to 2.0x ULN.

The most common drug-related treatment-emergent adverse events (TEAEs) were transient headache (in 10 of 16 patients) soon after starting treatment, and a benign drug rash (in six of 16 patients) that resolved in all patients through continued study drug administration. TEAEs of hemolysis occurred in two of 16 patients and resolved without any changes to dosing. There were no discontinuations or drug interruptions due to related adverse events. No safety signals were seen in routine monitoring of adverse events, vital signs, electrocardiograms, or laboratory evaluations of hematology, clinical chemistry, coagulation, or urinalysis.

"The data we are seeing at 400 mg and 500 mg show meaningful disease control in both treatment-naïve and C5 inadequate response patients, and an excellent safety profile. Our goal is to bring an oral monotherapy to patients and we now have the data to rapidly advance an optimal dose into pivotal trials in PNH and proof of concept trials in other complement-mediated diseases," said Dr. Bill Sheridan, chief medical officer of BioCryst.

The U.S. Food and Drug Administration has granted both Fast Track status and Orphan Drug Designation to BCX9930 for PNH.

**Virtual R&D Day Today**
Results from the trial, including slides with additional data and new market research assessing PNH patient demand for an oral therapy, will be presented and discussed at BioCryst's virtual R&D day today from 9:00 am ET to 11:00 am ET, and will be available in the Investors section of BioCryst's website at http://www.biocryst.com. The live video webcast and replay of the virtual R&D day may be accessed at: https://onlinexperiences.com/Launch/QReg/ShowUUID=0108DF33-EA47-4C52-B45E-A49134DC75CF.

**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 Japan for the prevention of HAE attacks in adults and pediatric patients 12 years and older, and under regulatory review for approval in the European Union and United Kingdom. BioCryst has several ongoing development programs including BCX9930, an oral Factor D inhibitor for the treatment of complement-mediated diseases, BCX9250, an ALK-2 inhibitor for the treatment of fibrodysplasia ossificans progressiva, and galidesivir, a potential treatment for Marburg virus disease and Yellow Fever. RAPIVAB® (peramivir injection), a viral neuraminidase inhibitor for the treatment of influenza, has received regulatory approval in the U.S., Canada, Australia, Japan, Taiwan and Korea. Post-marketing commitments for RAPIVAB are 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 BioCryst's plans and expectations for its BCX9930 program. 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; ongoing and future preclinical and clinical development of BCX9930 may not have positive results; BioCryst may not be able to enroll the required number of subjects in planned clinical trials of product candidates; BioCryst may not advance human clinical trials with product candidates as expected; the FDA, EMA, 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; product candidates, if approved, may not achieve market acceptance; BioCryst's ability to successfully commercialize its products and product candidates, 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 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, all of 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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