BioCryst R&D Day Highlights New Diversified Pipeline of First-in-Class/Best-in-Class Therapies with Five Programs Expected in Clinical Development in Next 24 Months

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- ***Company builds on deep structure-based drug design capabilities to add protein therapeutics to pipeline:***
  - ***BCX17725 for Netherton syndrome — entering clinic in 2H 2024***
  - ***Bifunctional fusion protein enabling simultaneous inhibition of multiple complement pathways to better address complex complement-mediated diseases — entering clinic in 2025***
- ***Oral C5 program for generalized myasthenia gravis — entering clinic in 2025***
- ***Combination of avoralstat with SCS Microinjector® from Clearside enables direct delivery into the suprachoroidal space in the eye to treat patients with DME — entering clinic in 2025***

RESEARCH TRIANGLE PARK, N.C., Nov. 03, 2023 (GLOBE NEWSWIRE) -- BioCryst Pharmaceuticals, Inc. (Nasdaq: BCRX) today announced updates from its drug discovery process and additional therapies from its pipeline that the company will highlight at a Research and Development (R&D) Day today at 1:00p ET at the company's Discovery Center of Excellence in Birmingham, Alabama. A live webcast of the event will be available online in the investors section of the company website at www.biocryst.com.

"The success we are achieving with ORLADEYO demonstrates that when we deliver a first-in-class or best-in-class medicine, we can change patients' lives. The focus of our discovery efforts is to leverage our 30-plus years of experience to bring more first-in-class or best-in-class medicines to patients living with complement-mediated and other rare diseases. The team is excited to share our approach, and our expanded pipeline of new programs, at our R&D Day," said Jon Stonehouse, president and chief executive officer of BioCryst.

"We have significantly diversified our pipeline and we continue to be disciplined around decisions to invest further only when a program meets the high bar we have set of first-in-class or best-in-class. We believe the combination of ORLADEYO, our exciting pipeline and our financial strength, position us to continue to make a big difference in patients' lives, and that leads to sustainable growth for years to come," Stonehouse added.

PROGRAM UPDATES AT R&D DAY

BCX17725 — Fusion Protein KLK5 Inhibitor for treatment of Netherton syndrome

Netherton syndrome is a rare, lifelong genetic disorder that often presents in neonates or infancy. The disease is caused by the deficiency of a natural inhibitor (SPINK5) of KLK5, a serine protease responsible for regulating skin shedding. Patients may have red, scaly and inflamed skin and susceptibility to recurrent immune reactions. Netherton syndrome can be life threatening, especially during infancy when patients are vulnerable to dehydration and recurrent infections. Currently, there is no approved treatment for Netherton syndrome.

BCX17725 is a potent and selective investigational fusion protein KLK5 inhibitor designed to provide best-in-class, potentially disease-modifying treatment for people with Netherton syndrome.

At the R&D Day, the company plans to showcase how it applied its structure-guided drug design expertise to create this fusion protein, and share nonclinical data showing distribution of the molecule to the epidermis following intraperitoneal (IP) administration.

The company expects to begin clinical trials of BCX17725 in 2024.

Avoralstat — Plasma kallikrein inhibitor combined with Clearside's SCS Microinjector® for treatment of diabetic macular edema (DME) in patients with sub-optimal response to anti-VEGF therapy

DME is the most common cause of vision loss in individuals with diabetes and at least one-third of patients have persistent DME despite anti-VEGF therapies, which are administered via monthly injection. Data have shown that elevated plasma kallikrein may be a cause of non-response to anti-VEGF therapy.

Delivering avoralstat directly into the suprachoroidal space of the eye with the SCS Microinjector could allow avoralstat to inhibit plasma kallikrein at the sites of edema formation in DME disease, the retinal and choroidal vascular endothelium. Avoralstat has low solubility, which supports evaluation of a suspension depot formulation for ophthalmic injection. With low solubility, the drug could persist in the eye at the site of disease for a long duration, resulting in less frequent injections.

At the R&D Day, the company plans to present nonclinical data showing high levels of avoralstat are maintained in the eye for at least 90 days following suprachoroidal injection.

Avoralstat was previously studied in an oral formulation in a phase 3 trial in patients with HAE. In the HAE clinical trial program in 276 individuals,

avoralstat was safe and well tolerated with an adverse event profile similar to placebo.

The company believes that combining a potent, low-solubility kallikrein inhibitor that has a pre-existing systemic safety database with the only FDA-approved approach to access the suprachoroidal space provides the potential to deliver a best-in-class medicine for DME patients inadequately controlled with anti-VEGF therapy.

The company expects to conduct formulation and nonclinical work in 2024 and begin clinical trials in 2025.

Oral C5 Inhibitor — Treatment of generalized myasthenia gravis (and other complement-mediated diseases)

Generalized myasthenia gravis (gMG) is a chronic autoimmune, neuromuscular disease that causes muscle weakness that worsens after periods of activity. It is caused when autoantibodies (anti-AChR) form that activate the complement system, causing the immune system to attack the neuromuscular junctions, or connections between muscles and nerves.

BioCryst is developing a first-in-class oral C5 inhibitor that could be the first targeted oral therapy with competitive efficacy to currently approved injected and infused anti-C5 therapies, such as eculizumab and ravulizumab. A drug with this profile could enable gMG patients to switch from infused therapy and address their disease earlier in the treatment paradigm.

At the R&D Day, the company plans to show data from the nonclinical program highlighting the potency, selectivity, oral bioavailability and pharmacokinetic parameters of its lead molecule candidates.

The company expects to complete lead optimization in 2024 and begin clinical trials in 2025.

Bifunctional complement inhibitor — simultaneously inhibiting multiple complement pathways to better address complex renal complement-mediated diseases like IgAN and lupus nephritis

BioCryst is developing a bifunctional complement inhibitor anti-C2 monoclonal antibody that also inhibits the alternative pathway. This investigational candidate could be a first-in-class combined inhibitor of the classical, lectin and alternative pathways of the complement system to best treat complex renal complement-mediated diseases like progressive IgAN and lupus nephritis, which are influenced by multiple complement pathways.

At the R&D Day, the company plans to share nonclinical data demonstrating the strong potency and ability of the company's bifunctional monoclonal antibody to inhibit multiple pathways in the complement system.

The company expects to select a lead molecule in 2024 and begin clinical trials in 2025.

Oral C2 Inhibitor — classical and lectin pathway complement inhibitor to treat autoimmune hemolytic anemias, including cold agglutinin disease (CAD) and warm autoimmune hemolytic anemia (wAIHA)

The limited approved options for treating diseases like CAD and wAIHA are injectable or infused. An oral C2 inhibitor from BioCryst would be first-in-class and allow patients to switch from infused therapy and address their disease earlier in the treatment paradigm.

Inhibiting C2 could decrease red cell destruction (hemolysis) in autoimmune hemolytic anemias by blocking the classical and lectin pathways.

At the R&D Day, the company plans to describe the data targets for potency, selectivity and bioavailability of its lead compounds.

The company expects to select a lead molecule in 2025.

BCX10013 — Once-daily, oral Factor D inhibitor for renal complement-mediated diseases

BCX10013 is a potent and selective Factor D inhibitor that, if it achieves comparable or superior efficacy to twice-daily alternative pathway inhibitors in development, would offer a best-in-class profile as the first and only oral alternative pathway inhibitor with once-daily dosing.

At the R&D Day, the company plans to present data from the recently completed 160 mg cohort of its multiple ascending dose healthy volunteer trial which highlights the strength and duration of alternative pathway suppression achieved at this dose level, supporting once-daily clinical dosing.

The company expects to report data from its ongoing proof-of-concept trial in 2024.

ORLADEYO® (berotralstat) — Pediatric formulation for the prevention of HAE attacks in patients 2 to <12 years of age

ORLADEYO, the first oral, once-daily plasma kallikrein inhibitor, is approved in the United States and many global markets for people with HAE age 12 and older. The ongoing APeX-P clinical trial is assessing an oral granule formulation of ORLADEYO in pediatric HAE patients who are 2 to <12 years of age.

Approximately 40 percent of HAE patients have their first attack by five years of age and there are no current targeted oral therapies available for prophylaxis in children <12 years old.

The company expects to submit a U.S. supplemental new drug application for the pediatric use of ORLADEYO in 2025.

2024 R&D Investment Guidance

The company's focus on rigorous best-in-class or first-in-class investment criteria, and the lower investment cost of earlier stage programs, are expected to limit 2024 R&D spending to a total of between $230 million and $240 million across all programs. This represents an increase from projected 2023 R&D spending of $25 million to $35 million, and represents a decrease from R&D spending in 2022 of $13 million to $23 million. These numbers include non-cash stock compensation. At the R&D Day, the company will describe its disciplined approach to capital allocation.

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 BioCryst's plans and expectations for its pipeline development. These statements involve known and unknown risks, uncertainties and other factors which may cause BioCryst's 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 progress its pipeline development plans as described herein; the results of BioCryst's partnerships with third parties may not meet BioCryst's current expectations; ongoing and future preclinical and clinical development of product candidates may take longer and be more expensive than expected and 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 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 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 projections and forward-looking statements.

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