



## CORRECTION -- BioCryst Reports Positive Results Across Multiple Endpoints in ZENITH-1 Trial of Oral BCX7353 as Acute Therapy for Hereditary Angioedema (HAE) Attacks

September 4, 2018

### —Safety and efficacy data support advancement of 750 mg dose as first oral therapy for acute HAE attacks—

In a release issued under the same headline earlier today by BioCryst Pharmaceuticals, Inc. (NASDAQ:BCRX), please note that in the first line of the table, the values for the change from baseline in VAS score through 4 hours under BCX7353 Treated Attacks and Placebo Treated Attacks are numbers, not percentages as previously published. Please also note a footnote has been added to the end of the table within the release, which notes baseline composite VAS scores for both BCX7353 treated attacks and placebo treated attacks. The corrected release follows:

RESEARCH TRIANGLE PARK, N.C., Sept. 04, 2018 (GLOBE NEWSWIRE) -- [BioCryst Pharmaceuticals, Inc.](#) (NASDAQ:BCRX) today announced initial results from the ZENITH-1 trial showing that a single 750 mg oral dose of BCX7353 was well tolerated and superior to placebo ( $p < 0.05$ ) against the majority of efficacy endpoints evaluated in HAE patients suffering an acute attack. BCX7353 is a novel oral plasma kallikrein inhibitor being developed for both prophylactic and acute treatment of HAE attacks.

In order to guide selection of dose and endpoints for a potential future registration trial for the acute treatment of HAE attacks, ZENITH-1 was designed as an exploratory trial to determine if BCX7353 showed a clinically meaningful benefit on any of several different efficacy endpoints evaluating HAE attack symptom severity.

In the 750 mg dose cohort of the trial, which has completed, 33 patients treated a total of 95 attacks (64 with BCX7353, 31 with placebo). Patients self-treated their HAE attacks on a blinded basis with oral BCX7353 or oral placebo and recorded their symptoms and attack severity using both a Visual Analog Scale (VAS) and a standardized questionnaire. Patients also recorded the time they used any standard-of-care (SOC) acute treatment medicine. BCX7353 was superior to placebo for multiple clinical outcomes, as noted below:

Efficacy Endpoint	BCX7353 Treated Attacks (N=64)	Placebo Treated Attacks (N=31)	Difference	p-value
Change from baseline in VAS score through 4 hours*	-3.9	+3.1	-6.98	0.0024
Proportion of attacks requiring standard of care treatment through 24 hours	29.7%	61.3%	-31.6%	0.0029
Proportion of attacks with no or mild symptoms through 24 hours	64.1%	32.3%	+31.8%	0.0038
Time to standard of care acute attack treatment (median)	>24 hours	14 hours	>+10 hours	0.0043
Proportion of attacks with improved or stable symptoms through 24 hours	64.1%	35.5%	+28.6%	0.0092
Proportion of attacks with improved or stable VAS score through 24 hours	62.5%	35.5%	+27.0%	0.0125
Proportion of attacks with improved or stable symptoms through 4 hours	82.3%	60.0%	+22.3%	0.0192
Proportion of attacks with improved or stable VAS score through 4 hours	67.7%	46.7%	+21.0%	0.0387
Time to stable or improved VAS (median)	1 hour	2 hours	-1 hour	0.0452
Proportion of attacks with no or mild symptoms through 4 hours	69.4%	50.0%	+19.4%	0.0552
Time to $\geq 50\%$ reduction in VAS through 24 hours (median)	8 hours	24 hours	--16 hours	0.0671
Time to initial symptom relief (median)	5.1 hours	19.4 hours	- 14.3 hours	0.0978
Time to almost complete symptom relief (median)	23.1 hours	23.6 hours	-0.5 hours	0.6767
Time to complete symptom relief (median)	35.1 hours	41.3 hour	-6.2 hours	0.8900
* Mean baseline composite VAS scores were 14.0 in BCX7353 treated attacks and 15.0 in placebo treated attacks				

Importantly, compared to placebo, improvement in symptoms and VAS scores was seen as early as one hour after oral BCX7353 dosing, and was sustained through 24 hours. Through 24 hours, SOC medication use was reduced by 31.6 percent after BCX7353 compared with placebo ( $p=0.0029$ ),

and no or mild symptoms were reported in 64.1 percent of attacks treated with BCX7353 compared with 32.3 percent of attacks treated with placebo (p=0.0038).

These and the other clinically meaningful results from ZENITH-1 highlight an attractive profile for patients seeking an oral treatment for acute HAE attacks.

In the ZENITH-1 trial, oral BCX7353 750 mg was generally safe and well tolerated. No serious adverse events were reported in patients receiving BCX7353. There were no grade 3 or 4 adverse events, and no grade 2, 3 or 4 laboratory abnormalities. The most commonly reported adverse events were nasopharyngitis (4/64 attacks treated with BCX7353 vs 1/31 for placebo), diarrhea (3/64 with BCX7353 vs 0/31 for placebo) and headache (3/64 with BCX7353 vs 0/31 for placebo). There were two discontinuations in the trial. One patient discontinued following a BCX7353 dose due to a transient, localized rash and one patient discontinued following a placebo dose due to abdominal pain.

"ZENITH-1 represents a groundbreaking study, as the first clinical trial to demonstrate effective treatment of acute HAE attacks with an oral therapy. The observed effect of BCX7353 within one hour of dosing and the substantial reduction in rescue medication use compared to placebo suggest that BCX7353 has outstanding potential to offer physicians and patients an urgently needed new oral therapy option," said Dr. Hilary Longhurst, honorary consultant immunologist, Addenbrookes Hospital, Cambridge, UK, and principal investigator of the ZENITH-1 trial.

Results from the ongoing evaluation of the 250 mg and 500 mg dose levels of oral BCX7353 in ZENITH-1 are expected in the first quarter of 2019.

"These results from ZENITH-1, combined with the results we saw in APeX-1, are evidence that BCX7353 would be the first safe and effective oral drug for both treating and preventing HAE attacks. We know the HAE community is waiting for an oral option and we look forward to completing APeX-2 and to submitting our applications for product approval to regulatory authorities," said Jon Stonehouse, chief executive officer of BioCryst.

Registration trials for previously approved injectable acute therapies for HAE were conducted in the clinic setting. In these studies, investigational treatment was administered in medical facilities by investigators at least four hours following onset of symptoms. ZENITH-1 is the first controlled clinical trial in the HAE acute therapy setting to assess patient-administered treatment at home, enabling treatment to be given quickly after the onset of symptoms.

"We are thrilled to see such a robust treatment effect with BCX7353 in ZENITH-1, using a modern approach with self-administered therapy. We were able to demonstrate clinically important treatment effects very early after oral dosing, which lasted through 24 hours," said Dr. William Sheridan, chief medical officer of BioCryst.

### **ZENITH-1 Trial Design**

ZENITH-1 is a double-blind, placebo-controlled, randomized, cross-over, dose-ranging trial of oral BCX7353 for acute treatment of angioedema attacks in patients with HAE. ZENITH-1 was designed for compatibility with modern treatment guidelines for at-home self-administered drug administration as early as possible after onset of symptoms. The goals of the trial are to identify activity against clinically meaningful endpoints that the company could use to construct a phase 3 registration trial, to identify the dose or doses the company could advance, and to assess safety and tolerability.

Adults with HAE Type I or II self-administered a dose of blinded study drug for three attacks; two treated with active drug and one with placebo, in a randomized sequence. Subjects were asked to administer blinded study medicine within one hour of onset of symptoms. Subjects were free to use approved prescribed acute medications but were asked to wait at least four hours post-study drug if possible. Patient completed trial diaries to collect information on symptoms, VAS scores and use of SOC medicines prior to dosing and at 1, 2, 3, 4, 8 and 24 hours after study drug administration.

### **About BioCryst Pharmaceuticals**

BioCryst Pharmaceuticals designs, optimizes and develops novel small-molecule medicines that address both common and rare conditions. BioCryst has several ongoing development programs including BCX7353, an oral treatment for hereditary angioedema, galidesivir, a potential treatment for filoviruses, and a preclinical program to develop oral ALK-2 inhibitors for the treatment of fibrodysplasia ossificans progressiva. RAPIVAB® (peramivir injection), a viral neuraminidase inhibitor for the treatment of influenza, is BioCryst's first approved product and has received regulatory approval in the U.S., Canada, Australia, Japan, Taiwan, Korea and the European Union. Post-marketing commitments for RAPIVAB are ongoing. For more information, please visit the Company's website at [www.BioCryst.com](http://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 that 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 BioCryst's 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: that the remaining cohorts of the ongoing ZENITH-1 trial may not be completed as expected; that the current results of the ZENITH-1 trial may not be predictive of future results, including the results of the remaining cohorts of ZENITH-1 and the APeX-2, APeX-S, and APeX-J trials; that developing BCX7353 for acute or prophylactic treatment may take longer or be more expensive than planned or may ultimately be unsuccessful; that producing a commercial formulation of BCX7353 may take longer than expected or may not occur as planned; that the Food and Drug Administration or other regulatory agencies may require additional studies beyond the studies currently planned, may not support trial designs, or may not provide regulatory clearances, which could result in delay of planned clinical trials; that we may never obtain market approval for BCX7353 or that commercialization of BCX7353 may ultimately be unsuccessful. 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 projections and forward-looking statements.

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