



BioCryst Announces Approval of Japanese NHI Price Listing of ORLADEYO™ (berotralstat) for Prophylactic Treatment of Hereditary Angioedema

April 14, 2021

—ORLADEYO is the first and only approved prophylactic therapy for HAE in Japan—

—NHI price listing triggers \$15 million milestone payment to BioCryst—

RESEARCH TRIANGLE PARK, N.C., April 14, 2021 (GLOBE NEWSWIRE) -- [BioCryst Pharmaceuticals, Inc.](https://www.biocryst.com) (Nasdaq: BCRX) today announced that the Japanese National Health Insurance System (NHI) has approved the addition of oral, once-daily ORLADEYO™ (berotralstat) to the NHI drug price list on April 21, 2021.

Oral, once-daily ORLADEYO was approved in Japan in January 2021 for prophylactic treatment of hereditary angioedema (HAE) in adults and pediatric patients 12 years and older. ORLADEYO is the first and only prophylactic HAE medication approved in Japan.

ORLADEYO will be commercialized in Japan by BioCryst's partner, Torii Pharmaceutical Co., Ltd. Torii plans to launch ORLADEYO following the NHI drug price listing.

"Our goal is to bring ORLADEYO to HAE patients around the world who want a new oral, once-daily option to prevent their attacks. In Japan, ORLADEYO is the first approved prophylactic HAE medication, which has the potential to significantly impact the lives of HAE patients," said Jon Stonehouse, president and chief executive officer of BioCryst.

The NHI price listing triggers a \$15 million milestone payment from Torii to BioCryst. In addition, BioCryst will receive tiered royalties ranging from 20 percent to 40 percent of Japanese net sales.

BioCryst received Orphan Drug and Sakigake designation for ORLADEYO in Japan. The APeX-J trial in Japan met its primary endpoint ($p=0.003$) of a reduction in HAE attacks from baseline for ORLADEYO 150 mg compared to placebo, and ORLADEYO was safe and generally well-tolerated in the trial. In APeX-2, ORLADEYO also met its primary endpoint ($p<0.001$) for ORLADEYO 150 mg compared to placebo and was safe and generally well-tolerated.

About ORLADEYO™ (berotralstat)

ORLADEYO™ (berotralstat) is the first and only oral therapy designed specifically to prevent attacks of hereditary angioedema (HAE) in adults 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 ($\geq 10\%$ 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 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. 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 ORLADEYO. 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 implement its commercialization plans for, and to commercialize, ORLADEYO, which could take longer or be more expensive than planned; the results of BioCryst's partnerships with Torii and OrphanPacific may not meet BioCryst's current expectations; the commercial viability of ORLADEYO, including its ability to achieve market acceptance, which could impact the amount of any related royalties BioCryst would be entitled to receive from Torii; the FDA, EMA, PMDA 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 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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