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CLINICAL REVIEW OF ROPEGINTERFERON ALFA-2B SUGGESTS AMENDED DOSING SCHEDULE MAY SUPPORT IMPROVED CLINICAL OUTCOMES IN POLYCYTHEMIA VERA

Review of studies published in Frontiers in Oncology *highlights dosing considerations that may help more patients achieve earlier complete hematological response*

February 2, 2023, Burlington, MA – PharmaEssentia USA Corporation, a subsidiary of PharmaEssentia Corporation (TPEx:6446), a global biopharmaceutical innovator based in Taiwan leveraging deep expertise and proven scientific principles to deliver new biologics in hematology and oncology, today announced the publication of a review of clinical literature in the journal, *Frontiers in Oncology.* The research indicates that an amended dosing schedule, with higher initial dose and faster dose titration of ropeginterferon alfa-2b (marketed as BESREMi®), may correlate to earlier complete hematological response (CHR) in polycythemia vera (PV) in adults. The analysis titled, *"An alternative dosing strategy for ropeginterferon alfa-2b may help improve outcomes in myeloproliferative neoplasms: An overview of previous and ongoing studies with perspectives on the future,"* was co-authored by PharmaEssentia researchers.

"This publication delves into the critical connection between an accelerated dosing regimen for ropeginterferon alfa-2b and the key efficacy, safety and tolerability outcomes we aim to achieve for our patients," said John Mascarenhas, M.D., Director of the Adult Leukemia Program and Leader of Clinical Investigation within the Myeloproliferative Disorders Program at Mount Sinai and study author. "The data from these clinical and investigational studies suggest that a higher starting dose and faster titration could be an appropriate approach to attain clinical outcomes earlier while minimizing the risk of thrombosis and hemorrhage in patients with PV."

PV is the most common myeloproliferative neoplasm (MPN) and a long-term, potentially life-threatening disease with limited treatment options. Recent clinical investigations suggest the potential for rapid titration and higher starting doses to benefit those with PV.[1]

The publication highlights the findings from multiple studies supporting the efficacy, safety and tolerability of a 250-350-500 mcg titration dosing regimen of ropeginterferon alfa-2b:

- A compassionate use program (CUP) study in Taiwan (n=14; hydroxyurea and/or anagrelide resistance or intolerance patients) resulted in a CHR rate of 73% at 52 weeks vs 51% observed in a study with a slower titration method. No new safety signals were detected.
- Interim results from an ongoing, Phase 2, single-arm study in Chinese PV patients (n=49; resistant or intolerant to hydroxyurea) showed that amended dosing achieved a CHR rate of 52% at Week 24 compared to 43% at Week 52 observed in PROUD-PV. Treatment-related Grade ≥3 adverse events (AEs) were reported in five patients (10.2%).
- Data from an investigator-initiated trial in Korea (n=45; hydroxyurea naïve or pre-treated PV patients) indicated higher hematologic and molecular responses at 6 months. Dose reductions were required in 4.4% of patients and the majority of AEs were Grade 1 or 2 with no treatment-related serious AEs reported.

Across the studies, ropeginterferon alfa-2b was generally well-tolerated. No thromboembolic complications have been reported with the accelerated titration regimen in PV. Rather, the review authors indicate that it is reasonable to believe that the accelerated dosing regimen may potentially minimize the risk of thrombosis and hemorrhage associated with an under-dosing during dose titrations.

“As more clinicians gain familiarity with BESREMi®, we want to support treatment goals by ensuring patients can effectively achieve and maintain their target clinical and molecular responses, as this may help reduce the risk of disease progression over time,” said Raymond Urbanski, M.D., Ph.D., Senior Vice President and U.S. Head of Clinical Development and Medical Affairs. “This latest research will help support more informed dialogue among physicians regarding their patients with PV.”

PharmaEssentia is interested in the attributes of the amended dosing approach with ropeginterferon alfa-2b that may extend into related MPNs with unmet needs such as essential thrombocythemia (ET) and pre-fibrotic primary myelofibrosis (pMF). Several planned or ongoing Phase 3 clinical trials will further evaluate this regimen of ropeginterferon alfa-2b in ET (SURPASS and EXCEED trials) and PV (ECLIPSE trial). Plans for a Phase 3 clinical trial in pMF are also underway.

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About Polycythemia Vera (PV)

Polycythemia vera (PV) is a cancer originating from a disease-initiating stem cell in the bone marrow resulting in a chronic increase of red blood cells, white blood cells, and platelets. PV may result in cardiovascular complications such as thrombosis and embolism, and often transforms to secondary myelofibrosis or leukemia. While the molecular mechanism underlying PV is still subject of intense research, current results point to a set of acquired mutations, the most important being a mutant form of JAK2.[2]

About BESREMi® (ropeginterferon alfa-2b-njft)

BESREMi is an innovative monopegylated, long-acting interferon. With its unique pegylation technology, BESREMi has a long duration of activity in the body and is aimed to be administered once every two weeks (or every four weeks with hematological stability for at least one year), allowing flexible dosing that helps meet the individual needs of patients.

BESREMi has orphan drug designation for the treatment of polycythemia vera (PV) in adults in the United States. The product was approved by the European Medicines Agency (EMA) in 2019, in the United States in 2021, and has recently received approval in Taiwan and South Korea. The drug candidate was invented by PharmaEssentia and is manufactured in the company’s Taichung plant, which was cGMP certified by TFDA in 2017 and by EMA in January 2018. PharmaEssentia retains full global intellectual property rights for the product in all indications.

Indication

BESREMi is indicated for the treatment of adults with polycythemia vera.

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Important Safety Information

WARNING: RISK OF SERIOUS DISORDERS

Interferon alfa products may cause or aggravate fatal or life-threatening neuropsychiatric, autoimmune, ischemic, and infectious disorders. Patients should be monitored closely with periodic clinical and laboratory evaluations. Therapy should be withdrawn in patients with persistently severe or worsening signs or symptoms of these conditions. In many, but not all cases, these disorders resolve after stopping therapy.

CONTRAINDICATIONS

- Existence of, or history of severe psychiatric disorders, particularly severe depression, suicidal ideation, or suicide attempt
- Hypersensitivity to interferons including interferon alfa-2b or any of the inactive ingredients of BESREMi.
- Moderate (Child-Pugh B) or severe (Child-Pugh C) hepatic impairment
- History or presence of active serious or untreated autoimmune disease
- Immunosuppressed transplant recipients

WARNINGS AND PRECAUTIONS

- Depression and Suicide: Life-threatening or fatal neuropsychiatric reactions have occurred in patients receiving interferon alfa-2b products, including BESREMi. These reactions may occur in patients with and without previous psychiatric illness.

  Other central nervous system effects, including suicidal ideation, attempted suicide, aggression, bipolar disorder, mania and confusion have been observed with other interferon alfa products.

  Closely monitor patients for any symptoms of psychiatric disorders and consider psychiatric consultation and treatment if such symptoms emerge. If psychiatric symptoms worsen, it is recommended to discontinue BESREMi therapy.

- Endocrine Toxicity: These toxicities may include worsening hypothyroidism and hyperthyroidism. Do not use BESREMi in patients with active serious or untreated endocrine disorders associated with autoimmune disease. Evaluate thyroid function in patients who develop symptoms suggestive of thyroid disease during BESREMi therapy. Discontinue BESREMi in patients who develop endocrine disorders that cannot be adequately managed during treatment with BESREMi.

- Cardiovascular Toxicity: Toxicities may include cardiomyopathy, myocardial infarction, atrial fibrillation and coronary artery ischemia. Patients with a history of cardiovascular disorders should be closely monitored for cardiovascular toxicity during BESREMi therapy. Avoid use of BESREMi in patients with severe or unstable cardiovascular disease, (e.g., uncontrolled hypertension, congestive heart failure (≥ NYHA class 2), serious cardiac arrhythmia, significant coronary artery stenosis, unstable angina) or recent stroke or myocardial infarction.

- Decreased Peripheral Blood Counts: These toxicities may include thrombocytopenia (increasing the risk of bleeding), anemia, and leukopenia (increasing the risk of infection).

Monitor complete blood counts at baseline, during titration and every 3-6 months during the maintenance phase. Monitor patients for signs and symptoms of infection or bleeding.

- Hypersensitivity Reactions: Toxicities may include serious, acute hypersensitivity reactions (e.g., urticaria, angioedema, bronchoconstriction, anaphylaxis). If such reactions occur, discontinue BESREMi and institute appropriate medical therapy immediately. Transient rashes may not necessitate interruption of treatment.
- Pancreatitis: Pancreatitis has occurred in 2.2% of patients receiving BESREMi. Symptoms may include nausea, vomiting, upper abdominal pain, bloating, and fever. Patients may experience elevated lipase, amylase, white blood cell count, or altered renal/hepatic function. Interrupt BESREMi treatment in patients with possible pancreatitis and evaluate promptly. Consider discontinuation of BESREMi in patients with confirmed pancreatitis.
- Colitis: Fatal and serious ulcerative or hemorrhagic/ischemic colitis have occurred in patients receiving interferon alfa products, some cases starting as early as 12 weeks after start of treatment. Symptoms may include abdominal pain, bloody diarrhea, and fever. Discontinue BESREMi in patients who develop these signs or symptoms. Colitis may resolve within 1 to 3 weeks of stopping treatment.
- Pulmonary Toxicity: Pulmonary toxicity may manifest as dyspnea, pulmonary infiltrates, pneumonia, bronchiolitis obliterans, interstitial pneumonitis, pulmonary hypertension, and sarcoidosis. Some events have resulted in respiratory failure or death. Discontinue BESREMi in patients who develop pulmonary infiltrates or pulmonary function impairment.
- Ophthalmologic Toxicity: These toxicities may include severe eye disorders such as retinopathy, retinal hemorrhage, retinal exudates, retinal detachment and retinal artery or vein occlusion which may result in blindness. During BESREMi therapy, 23% of patients were identified with an eye disorder. Eyes disorders ≥5% included cataract (6%) and dry eye (5%). Advise patients to have eye examinations before and during BESREMi therapy, specifically in those patients with a retinopathy-associated disease such as diabetes mellitus or hypertension. Evaluate eye symptoms promptly. Discontinue BESREMi in patients who develop new or worsening eye disorders.
- Hyperlipidemia: Elevated triglycerides may result in pancreatitis. Monitor serum triglycerides before BESREMi treatment and intermittently during therapy and manage when elevated. Consider discontinuation of BESREMi in patients with persistently, markedly elevated triglycerides.
- Hepatotoxicity: These toxicities may include increases in serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma-glutamyl transferase (GGT) and bilirubin. Liver enzyme elevations have also been reported in patients after long-term BESREMi therapy. Monitor liver enzymes and hepatic function at baseline and during BESREMi treatment. Discontinue BESREMi in patients who develop evidence of hepatic decompensation (characterized by jaundice, ascites, hepatic encephalopathy, hepatorenal syndrome or variceal hemorrhage) during treatment.
- Renal Toxicity: Monitor serum creatinine at baseline and during therapy. Avoid use of BESREMi in patients with eGFR <30 mL/min. Discontinue BESREMi if severe renal impairment develops during treatment.
- Dental and Periodontal Toxicity: These toxicities may include dental and periodontal disorders, which may lead to loss of teeth. In addition, dry mouth could have a damaging

effect on teeth and mucous membranes of the mouth during long-term treatment with BESREMi. Patients should have good oral hygiene and regular dental examinations.

- Dermatologic Toxicity: These toxicities have included skin rash, pruritus, alopecia, erythema, psoriasis, xeroderma, dermatitis acneiform, hyperkeratosis, and hyperhidrosis. Consider discontinuation of BESREMi if clinically significant dermatologic toxicity occurs.
- Driving and Operating Machinery: BESREMi may impact the ability to drive and use machinery. Patients should not drive or use heavy machinery until they know how BESREMi affects their abilities. Patients who experience dizziness, somnolence or hallucination during BESREMi therapy should avoid driving or using machinery.
- Embryo-Fetal Toxicity: Based on the mechanism of action, BESREMi can cause fetal harm when administered to a pregnant woman. Pregnancy testing is recommended in females of reproductive potential prior to treatment with BESREMi. Advise females of reproductive potential to use an effective method of contraception during treatment with BESREMi and for at least 8 weeks after the final dose.

ADVERSE REACTIONS

The most common adverse reactions reported in > 40% of patients in the PEGINVERA study (n=51) were influenza-like illness, arthralgia, fatigue, pruritis, nasopharyngitis, and musculoskeletal pain. In the pooled safety population (n=178), the most common adverse reactions greater than 10%, were liver enzyme elevations (20%), leukopenia (20%), thrombocytopenia (19%), arthralgia (13%), fatigue (12%), myalgia (11%), and influenza-like illness (11%).

DRUG INTERACTIONS

Patients on BESREMi who are receiving concomitant drugs which are CYP450 substrates with a narrow therapeutic index should be monitored to inform the need for dosage modification for these concomitant drugs. Avoid use with myelosuppressive agents and monitor patients receiving the combination for effects of excessive myelosuppression. Avoid use with narcotics, hypnotics or sedatives and monitor patients receiving the combination for effects of excessive CNS toxicity.

USE IN SPECIFIC POPULATIONS

- Pregnancy: Based on mechanism of action and the role of interferon alfa in pregnancy and fetal development, BESREMi may cause fetal harm and should be assumed to have abortifacient potential when administered to a pregnant woman. There are adverse effects on maternal and fetal outcomes associated with polycythemia vera in pregnancy. Advise pregnant women of the potential risk to a fetus.
- Lactation: There are no data on the presence of BESREMi in human or animal milk, the effects on the breastfed child, or the effects on milk production. Because of the potential for serious adverse reactions in breastfed children from BESREMi, advise women not to breastfeed during treatment and for 8 weeks after the final dose.
- Females of Reproductive Potential: BESREMi may cause embryo-fetal harm when administered to a pregnant woman. Pregnancy testing prior to BESREMi treatment is recommended for females of reproductive potential. Advise female patients of reproductive

potential to use effective contraception during treatment with BESREMi and for at least 8 weeks after the final dose.

- Pediatric Use: Safety and effectiveness in pediatric patients have not been established.
- Geriatric Use: In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function and of concomitant disease or other therapy.

Please see accompanying full Prescribing Information, including Boxed Warning.

About PharmaEssentia

PharmaEssentia (TPEx: 6446), headquartered in Taipei, Taiwan, is a global and rapidly growing biopharmaceutical innovator. Leveraging deep expertise and proven scientific principles, PharmaEssentia aims to deliver effective new biologics for challenging diseases in the areas of hematology and oncology, with one approved product and a diversifying pipeline. Founded in 2003 by a team of Taiwanese-American executives and renowned scientists from U.S. biotechnology and pharmaceutical companies, today PharmaEssentia is expanding its global presence with operations in the U.S., Japan, China, and Korea, along with a world-class biologics production facility in Taichung, Taiwan.

For more information about PharmaEssentia USA, visit the website, LinkedIn or Twitter.

Forward Looking Statement

This press release may contain forward looking statements, including statements regarding the clinical benefits to be derived from ropeginterferon alfa-2b, the commercial opportunity and competitive positioning, new indications or labeling for ropeginterferon alfa-2b, and any business prospects for ropeginterferon alfa-2b. For those statements, we claim the protection of the safe harbor for forward-looking statements contained in the Private Securities Litigation Reform Act of 1995 and similar legislation and regulations under Taiwanese law. These forward-looking statements are based on management expectations and assumptions as of the date of this press release, and actual results may differ materially from those in these forward looking statements as a result of various factors. These factors include risks and uncertainties related to the initiation, timing, progress and results of our research and development programs, preclinical studies, clinical trials, and regulatory submissions. We do not undertake to update any of these forward-looking statements to reflect events or circumstances that occur after the date hereof.

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[1] Qin A, Urbanski R, et al. An Alternative Dosing Strategy for Ropeginterferon alfa-2b may Help Improve Outcomes in Myeloproliferative Neoplasms: An Overview of Previous and Ongoing studies with Perspectives on the Future. *Front. Oncol.* (2023) 13; doi:10.3389/fonc.2023.1109866.

[2] Cerquozzi S, Tefferi A. Blast Transformation and Fibrotic Progression in Polycythemia Vera and Essential Thrombocythemia: A Literature Review of Incidence and Risk Factors. *Blood Cancer J* (2015) 5, e366; doi:10.1038/bcj.2015.95.