Takeda Receives U.S. FDA Approval of MIMRYLO™ (rusfertide), Marking a Potential Shift in the Treatment Paradigm for Polycythemia Vera

- ***MIMRYLO, a First-in-Class Medicine with a Unique Mechanism of Action, is Approved for the Treatment of Erythrocytosis in Adults with Polycythemia Vera (PV)***
- ***MIMRYLO Has Been Shown to Maintain Hematocrit Control, the Primary Treatment Goal in PV, as Well as Reduce Phlebotomy Burden and Improve Fatigue***
- ***Approval Supported by Phase 3 VERIFY Results Showing 76.9% of Patients Achieved Clinical Response During Weeks 20-32***

OSAKA, Japan and CAMBRIDGE, Massachusetts, August 28, 2026 – Takeda (TSE:4502/NYSE:TAK) announced U.S. Food and Drug Administration (FDA) approval of the New Drug Application (NDA)* for MIMRYLO™ (rusfertide) for the treatment of erythrocytosis in adults with polycythemia vera (PV), a blood cancer.

MIMRYLO is a first-in-class hepcidin mimetic designed to regulate iron distribution in the body and red blood cell overproduction to control hematocrit levels, which is the ratio of red blood cells to the total amount of blood in the body. Maintaining controlled hematocrit levels below 45% is the primary treatment goal in PV.[1]

“For patients living with PV, uncontrolled hematocrit can have serious consequences, including an elevated risk of life-threatening thrombotic events," said Andrew T. Kuykendall, M.D., VERIFY lead investigator and Associate Member in the Department of Hematology at Moffitt Cancer Center. “Current treatments, such as phlebotomy, leave a significant gap for too many patients and can pose challenges to daily life and routines. The approval of MIMRYLO offers clinicians and patients a novel, first-in-class therapy that targets erythrocytosis, which drives excess red blood cell production in PV. The strength and consistency of the VERIFY data give me real confidence in MIMRYLO’s potential to advance how we treat PV in everyday practice and to maintain hematocrit control.”

Uncontrolled Hematocrit is a Challenge in the Treatment of PV

Affecting approximately 90,000 people in the U.S., PV is characterized by the overproduction of red blood cells (erythrocytosis), leading to elevated hematocrit which can increase blood viscosity, or thickness.[2,3] This has the potential to result in life-threatening thrombotic events, including stroke, deep vein thrombosis and pulmonary embolism.[4] Maintaining hematocrit levels consistently below 45% can prevent thrombotic events and alleviate burdensome symptoms, including severe fatigue, pruritus (itching), difficulty concentrating and night sweats.[4] An estimated 78% of patients still experience uncontrolled hematocrit with current standard of care, including phlebotomy and cytoreductive therapies.[5] Patients with PV experiencing uncontrolled hematocrit have a four times higher risk of cardiovascular death or major cardiovascular events.[4]

“People living with PV often experience complex and invisible symptoms, from extreme fatigue to the emotional strain of living with a chronic blood cancer,” said Kapila Viges, Chief Executive Officer, MPN Research Foundation. “At the same time, we know that every patient’s experience with PV is different, underscoring the need to continue to listen closely to the community to understand what matters most. There remains a need for treatments that better address these daily challenges. This meaningful approval reflects important progress and brings forward a new treatment option in a disease where patients have long needed innovation and more choices. We are encouraged by MIMRYLO’s potential to help patients meet their treatment goals.”

MIMRYLO is a First-In-Class Treatment Option for Adults with PV

The approval was supported by data from the global randomized Phase 3 VERIFY study (NCT05210790) that included 293 patients with PV, showing that MIMRYLO met all efficacy endpoints and demonstrated a favorable

safety profile. In the study, patients receiving MIMRYLO plus current standard of care demonstrated a higher response rate compared to placebo plus current standard of care. This included hematocrit control, a reduction in the need for phlebotomy and improvement in fatigue as measured by PROMIS Fatigue Short Form 8a.

MIMRYLO was generally well-tolerated through 52 weeks of treatment in the VERIFY trial. The most common treatment-emergent adverse events in MIMRYLO-treated patients were injection site reactions and anemia. Learn more about the Phase 3 data results here.

"The approval of MIMRYLO underscores the strength of Takeda's late-stage pipeline and our focus on developing genuinely differentiated therapies for patients who are urgently waiting for new options," said Julie Kim, President and Chief Executive Officer, Takeda. "We are at an important inflection point as we prepare to deliver three new medicines, which have the potential to drive our future growth and are a reflection of our commitment to advancing innovation that doesn't just add to the treatment landscape, but reshapes it. We are grateful to the patients, care partners, advocates and investigators who helped make this approval possible."

The open-label extension of the VERIFY trial is ongoing and Takeda will share further findings at upcoming medical conferences. Takeda is working with regulators outside of the U.S. to potentially bring MIMRYLO to more patients worldwide.

This approval does not result in any changes to Takeda's consolidated financial forecast for the fiscal year ending March 31, 2027 (FY2026).

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

- **New or Worsening Thrombocytosis:** MIMRYLO may increase platelet counts in patients with PV. Platelet counts generally plateaued on treatment by Week 8. After initiating MIMRYLO and during dose modifications, monitor CBC every 2 to 4 weeks or as clinically indicated. Platelet elevations associated with MIMRYLO may require cytoreductive therapy initiation, modification, or MIMRYLO dose modifications or discontinuation.
- **Injection-Site Reactions:** Injection site reactions (including Grade 3 reactions) have been reported in patients treated with MIMRYLO. The most common injection site reactions reported were erythema, pruritus, pain, and swelling. Use ice, topical corticosteroid creams, antihistamines or analgesics, as needed, to treat injection site pain and swelling.
- **Embryo-Fetal Toxicity:** Based on findings from animal reproduction studies, MIMRYLO may cause fetal harm when administered to a pregnant woman. Advise patients to stop taking MIMRYLO if they become pregnant.

ADVERSE REACTIONS

The most common (>15%) adverse reactions were injection site reactions (56%) and anemia (16%).

USE IN SPECIFIC POPULATIONS

- **Lactation:** Because of the potential for serious adverse reactions in the breastfed child, including impaired iron absorption, advise patients not to breastfeed during treatment with MIMRYLO and for 30 days after the final treatment.

- **Females and Males of Reproductive Potential**
  - **Pregnancy Testing:** Prior to initiating MIMRYLO, pregnancy testing is recommended for females of reproductive potential.
  - **Contraception:** Advise female patients of reproductive potential to use effective contraception during treatment with MIMRYLO and for at least 30 days after the final dose of MIMRYLO.

To report SUSPECTED ADVERSE REACTIONS, contact Takeda Pharmaceuticals at 1-844-662-8532 or the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please see MIMRYLO (rusfertide) full Prescribing Information.

About MIMRYLO™
MIMRYLO™ is a first-in-class subcutaneous treatment that mimics the action of hepcidin, a natural hormone that regulates iron homeostasis and erythrocytosis. By targeting the underlying mechanism of iron dysregulation in polycythemia vera, MIMRYLO aims to reduce excess red blood cell production and help patients maintain hematocrit control. MIMRYLO is administered once weekly via subcutaneous injection and has been generally well-tolerated in clinical trials to date. Protagonist discovered MIMRYLO and led its development through Phase 3. Takeda now has exclusive global development and commercialization rights for MIMRYLO.

About VERIFY
The Phase 3 VERIFY study (NCT05210790) is an ongoing, three-part, global, randomized, placebo-controlled study evaluating MIMRYLO in 293 patients with polycythemia vera over a 156-week period, with treatment extension for participants who are continuing to derive benefit from MIMRYLO beyond the 156-week treatment period. The study is evaluating the efficacy and safety of once-weekly, subcutaneously self-administered MIMRYLO in patients with uncontrolled hematocrit who are phlebotomy-dependent despite current standard of care treatment, which could include phlebotomy, hydroxyurea, interferon and/or ruxolitinib.

The primary endpoint of the study was the proportion of patients achieving a response during Weeks 20-32, which was defined as the absence of "phlebotomy eligibility." To meet phlebotomy eligibility, patients in the study were required to have: confirmed hematocrit ≥45% that was ≥3% higher than their baseline hematocrit value, or hematocrit ≥48%. Key secondary endpoints evaluated at Week 32 included mean number of phlebotomies, proportion of patients maintaining hematocrit <45%, mean change in fatigue score as measured by PROMIS Fatigue Short Form 8a and total symptom burden as measured by Myelofibrosis Symptom Assessment Form (MFSAF) Version 4.0.

All patients have completed their participation in the randomized, placebo-controlled portion of the study evaluating the efficacy and safety of MIMRYLO plus current standard of care versus placebo plus current standard of care and are now in the open-label portions of the study.

About Polycythemia Vera (PV)
Polycythemia vera (PV) is a chronic blood cancer characterized by the overproduction of red blood cells (erythrocytosis), which increases blood viscosity, or thickness, and can result in life threatening thrombotic events such as stroke, deep vein thrombosis and pulmonary embolism. Hematocrit is the ratio of red blood cells to the total amount of blood in the body. Achieving and maintaining controlled hematocrit levels of less than 45% is the primary treatment goal in PV to prevent thrombotic events and alleviate burdensome symptoms, including severe fatigue, difficulty in concentrating, night sweats and pruritus.

About Takeda
Takeda is focused on creating better health for people and a brighter future for the world. We aim to discover and deliver life-transforming treatments in our core therapeutic and business areas, including gastrointestinal and inflammation, rare diseases, plasma-derived therapies, oncology, neuroscience and vaccines. Together with our partners, we aim to improve the patient experience and advance a new frontier of treatment options through our dynamic and diverse pipeline. As a leading values-based, R&D-driven biopharmaceutical company headquartered in Japan, we are guided by our commitment to patients, our people and the planet. Our employees in approximately 80 countries and regions are driven by our purpose and are grounded in the values that have defined us for more than two centuries. For more information, visit www.takeda.com.

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The companies in which Takeda directly and indirectly owns investments are separate entities. In this press release, "Takeda" is sometimes used for convenience where references are made to Takeda and its subsidiaries in general. Likewise, the words "we", "us" and "our" are also used to refer to subsidiaries in general or to those who work for them. These expressions are also used where no useful purpose is served by identifying the particular company or companies.

Takeda Forward-Looking Statements
This press release and any materials distributed in connection with this press release may contain forward-looking statements, beliefs or opinions regarding Takeda's future business, future position and results of operations, including estimates, forecasts, targets and plans for Takeda. Without limitation, forward-looking statements often include words such as "targets", "plans", "believes", "hopes", "continues", "expects", "aims", "intends", "ensures", "will", "may", "should", "would", "could", "anticipates", "estimates", "projects", "forecasts", "outlook" or similar expressions or the negative thereof. These forward-looking statements are based on assumptions about many important factors, including the following, which could cause actual results to differ materially from those expressed or implied by the forward-looking statements: the economic circumstances surrounding Takeda's global business, including general economic conditions in Japan and the United States and with respect to international trade relations; competitive pressures and developments; changes to applicable laws and regulations, including drug pricing, tax, tariff and other trade-related rules; challenges inherent in new product development, including uncertainty of clinical success and decisions of regulatory authorities and the timing thereof; uncertainty of commercial success for new and existing products; manufacturing difficulties or delays; fluctuations in interest and currency exchange rates; claims or concerns regarding the safety or efficacy of marketed products or product candidates; the impact of health crises, like the novel coronavirus pandemic; the success of our environmental sustainability efforts, in enabling us to reduce our greenhouse gas emissions or meet our other environmental goals; the extent to which our efforts to increase

efficiency, productivity or cost-savings, such as the integration of digital technologies, including artificial intelligence, in our business or other initiatives to restructure our operations will lead to the expected benefits; and other factors identified in Takeda's most recent Annual Report on Form 20-F and Takeda's other reports filed with the U.S. Securities and Exchange Commission, available on Takeda's website at: https://www.takeda.com/investors/sec-filings-and-security-reports/ or at https://www.sec.gov/. Takeda does not undertake to update any of the forward-looking statements contained in this press release or any other forward-looking statements it may make, except as required by law or stock exchange rule. Past performance is not an indicator of future results and the results or statements of Takeda in this press release may not be indicative of, and are not an estimate, forecast, guarantee or projection of Takeda's future results.

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*Takeda and Protagonist Announce U.S. Food and Drug Administration Accepts New Drug Application and Grants Priority Review for Rusfertide as a Potential First-in-Class Therapy for Polycythemia Vera

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