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News Release

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

OSAKA, Japan, March 2, 2026 – Takeda (TSE:4502/NYSE:TAK) ("Takeda") and Protagonist Therapeutics, Inc. (NASDAQ:PTGX) today announced that the U.S. Food and Drug Administration accepted the New Drug Application ("NDA") and granted Priority Review for rusfertide. Please see the attached press release for details.

The impact on Takeda's financial results for the fiscal year ending March 31, 2026 (FY2025), following the acceptance of the NDA, is immaterial.

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News Release

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

- ***Rusfertide Demonstrated Significant Improvements in Hematocrit Control, Phlebotomy Reduction and Patient Reported Outcomes for Patients with Polycythemia Vera in a Pivotal Study***
- ***Submission Primarily Based on Phase 3 VERIFY Study, in Which Rusfertide Plus Standard of Care More Than Doubled Clinical Response Rates, as Well as Four-Year Efficacy and Safety Data from Phase 2 REVIVE/THRIVE Studies***
- ***Prescription Drug User Fee Act (PDUFA) Target Action Date is in the Third Quarter of this Calendar Year***

OSAKA, Japan, CAMBRIDGE, Massachusetts and NEWARK, California, March 2, 2026 – Takeda (TSE:4502/NYSE:TAK) and Protagonist Therapeutics, Inc. ("Protagonist") (NASDAQ:PTGX) today announced that the U.S. Food and Drug Administration (FDA) accepted the New Drug Application (NDA) and granted Priority Review for rusfertide. Rusfertide is an investigational, first-in-class hepcidin mimetic peptide therapeutic for the treatment of adults with polycythemia vera (PV). The FDA has set a Prescription Drug User Fee Act (PDUFA) goal date in the third quarter of this calendar year. In addition to Priority Review, rusfertide has received Breakthrough Therapy designation, Orphan Drug designation and Fast Track designation from the U.S. FDA.

PV is characterized by the overproduction of red blood cells (erythrocytosis), which increases blood viscosity, or thickness, and can result in life threatening thrombotic events. Hematocrit is the ratio of red blood cells to the total amount of blood in the body. Achieving and maintaining controlled hematocrit levels of <45% is the primary treatment goal in PV to prevent thrombotic events and alleviate burdensome symptoms.

"There is an urgent need for innovative treatment options in polycythemia vera, where patients currently face limited therapeutic choices to control their hematocrit and significant symptom burden," said Andy Plump, M.D., Ph.D., president of R&D at Takeda. "The FDA's acceptance of our NDA brings us closer to potentially offering a first-in-class therapy that could meaningfully improve clinical outcomes and quality of life. This milestone is a reflection of our successful partnership with Protagonist and Takeda's unwavering commitment to advancing innovative treatments in hematologic cancers where significant unmet needs persist."

The NDA for rusfertide was primarily based on the positive 32-week primary analysis and 52-week results from the Phase 3 global randomized VERIFY study (NCT05210790), as well as four-year efficacy and safety data from the Phase 2 REVIVE study (NCT04057040) and long-term extension THRIVE study (NCT06033586). In the VERIFY study, rusfertide met the primary endpoint and all four key secondary endpoints. Patients receiving rusfertide plus current standard of care demonstrated a higher

response rate compared to current standard of care. This included hematocrit control, a reduction in phlebotomy requirements and improvement in pre-specified patient reported outcomes of fatigue and symptom burden. Rusfertide was generally well-tolerated through 52 weeks of treatment. The most common treatment-emergent adverse events (AEs) in rusfertide-treated patients were injection site reactions (47.4%), anemia (25.6%) and fatigue (19.6%), which were mainly grade 1 or 2. Serious AEs occurred in 8.1% of overall rusfertide-treated patients.

"Rusfertide exemplifies Protagonist's end-to-end expertise, from exploring a novel hepcidin mimetic mechanism to address unmet needs in polycythemia vera to discovering the peptide and driving its clinical development through NDA filing. We are very pleased with the FDA granting rusfertide priority review and look forward to its potential approval in 2026," said Dinesh V. Patel, Ph.D., Protagonist President and CEO. "We have identified a great partner in Takeda as rusfertide progresses toward this milestone, thereby bringing a successful closure to our more than decade-long journey from concept-to-commercialization."

In January 2024, Protagonist and Takeda entered into a worldwide license and collaboration agreement for rusfertide. Protagonist discovered rusfertide and led its development through Phase 3 studies, with Takeda responsible for implementing the regulatory strategy for the U.S. NDA filing and for leading any future global regulatory filings. Protagonist holds an option to co-commercialize in the U.S. through a 50/50 profit and loss share structure or to opt-out of this structure, providing Takeda with a worldwide license pursuant to the license and collaboration agreement.

About Rusfertide
Rusfertide is a first-in-class investigational subcutaneous treatment that mimics the action of hepcidin, a natural hormone that regulates iron homeostasis and red blood cell production. By targeting the underlying mechanism of iron dysregulation in polycythemia vera, rusfertide aims to reduce excess red blood cell production and help patients achieve sustained hematocrit control. Rusfertide is administered once weekly via subcutaneous self-injection and has been generally well-tolerated in clinical trials to date.

About VERIFY
The Phase 3 VERIFY study (NCT05210790) is an ongoing, three-part, global, randomized, placebo-controlled study evaluating rusfertide in 293 patients with polycythemia vera over a 156-week period, with treatment extension for participants who are continuing to derive benefit from rusfertide beyond the 156-week treatment period. The study is evaluating the efficacy and safety of once-weekly, subcutaneously self-administered rusfertide 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%.

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

About REVIVE and THRIVE
The Phase 2 REVIVE study (NCT04057040) evaluated rusfertide in adult patients with polycythemia vera and consisted of three parts, including 70 patients in the dose-finding Part 1 (28 weeks), 59 patients in the blinded, placebo-controlled, randomized withdrawal Part 2 (13 weeks) and 58 patients in the Part 3

open-label expansion (52 weeks). The THRIVE study (NCT06033586) is an ongoing, open-label extension study evaluating the long-term durability of response and safety profile of rusfertide in patients with polycythemia vera. The study includes 46 patients who previously participated in REVIVE. Patients eligible to transition to the THRIVE study completed the open-label extension portion of REVIVE, ≥12 months of rusfertide therapy and had an end-of-treatment visit. THRIVE is designed to further assess the maintenance of hematocrit control, reduction in the need for therapeutic phlebotomy and overall safety of once-weekly, subcutaneous rusfertide over an additional two-year treatment period.

About Polycythemia Vera (PV)
Polycythemia vera (PV) is 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 <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.

About Protagonist
Protagonist Therapeutics is a discovery through late-stage development biopharmaceutical company. Two novel peptides derived from Protagonist's proprietary discovery platform are currently in advanced Phase 3 clinical development, with NDAs for both ICOTYDE™ (icotrokinra) and rusfertide under review at the FDA. ICOTYDE is a first-in-class investigational targeted oral peptide that selectively blocks the Interleukin-23 receptor ("IL-23R"), which is licensed to Janssen Biotech, Inc., a Johnson & Johnson company. Following ICOTYDE's joint discovery by Protagonist and Johnson & Johnson scientists pursuant to the companies' IL-23R collaboration, Protagonist was primarily responsible for the development of ICOTYDE through Phase 1, with Johnson & Johnson assuming responsibility for development in Phase 2 and beyond.

Rusfertide is a first-in-class hepcidin mimetic peptide that is being co-developed with Takeda Pharmaceuticals pursuant to a worldwide license and collaboration agreement entered in 2024. Protagonist holds an option to co-commercialize rusfertide in the U.S. through a 50/50 profit and loss share structure or can opt-out of this structure. The Company also has a number of preclinical stage drug discovery programs addressing clinically and commercially validated targets, including an oral IL-17 peptide antagonist, obesity dual and triple agonists, an oral hepcidin functional mimetic, and the recently announced IL-4 and amylin programs.

More information on Protagonist, its pipeline drug candidates, and clinical studies can be found on the Company's website at https://www.protagonist-inc.com.

Takeda Important Notice
For the purposes of this notice, “press release” means this document, any oral presentation, any question and answer session and any written or oral material discussed or distributed by Takeda Pharmaceutical Company Limited (“Takeda”) regarding this release. This press release (including any oral briefing and

any question-and-answer in connection with it) is not intended to, and does not constitute, represent or form part of any offer, invitation or solicitation of any offer to purchase, otherwise acquire, subscribe for, exchange, sell or otherwise dispose of, any securities or the solicitation of any vote or approval in any jurisdiction. No shares or other securities are being offered to the public by means of this press release. No offering of securities shall be made in the United States except pursuant to registration under the U.S. Securities Act of 1933, as amended, or an exemption therefrom. This press release is being given (together with any further information which may be provided to the recipient) on the condition that it is for use by the recipient for information purposes only (and not for the evaluation of any investment, acquisition, disposal or any other transaction). Any failure to comply with these restrictions may constitute a violation of applicable securities laws.

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.

Takeda Medical Information

This press release contains information about products that may not be available in all countries, or may be available under different trademarks, for different indications, in different dosages, or in different

strengths. Nothing contained herein should be considered a solicitation, promotion or advertisement for any prescription drugs including the ones under development.

Protagonist Cautionary Note on Forward-Looking Statements
This press release contains forward-looking statements for purposes of the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. Forward-looking statements include statements regarding the potential benefits of rusfertide. In some cases, you can identify these statements by forward-looking words such as "anticipate," "believe," "may," "will," "expect," or the negative or plural of these words or similar expressions. Forward-looking statements are not guarantees of future performance and are subject to risks and uncertainties that could cause actual results and events to differ materially from those anticipated, including, but not limited to, our ability to develop and commercialize our product candidates, our ability to earn milestone payments under our collaboration agreements with Janssen and Takeda, our ability to use and expand our programs to build a pipeline of product candidates, our ability to obtain and maintain regulatory approval of our product candidates, our ability to operate in a competitive industry and compete successfully against competitors that have greater resources than we do, and our ability to obtain and adequately protect intellectual property rights for our product candidates. Additional information concerning these and other risk factors affecting our business can be found in our periodic filings with the Securities and Exchange Commission, including under the heading "Risk Factors" contained in our most recently filed periodic reports on Form 10-K and Form 10-Q filed with the Securities and Exchange Commission. Forward-looking statements are not guarantees of future performance, and our actual results of operations, financial condition, and liquidity, and the development of the industry in which we operate, may differ materially from the forward-looking statements contained in this press release. Any forward-looking statements that we make in this press release speak only as of the date of this press release. We assume no obligation to update our forward-looking statements, whether as a result of new information, future events, or otherwise, after the date of this press release.

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