News Release

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FOR IMMEDIATE RELEASE

Takeda receives clearance from the European Commission for the proposed acquisition of Shire plc

Osaka, Japan, November 20, 2018 --- Takeda Pharmaceutical Company Limited ("**Takeda**") announces that it has received clearance from the European Commission (the "**EC**") for the proposed acquisition of Shire plc ("**Shire**") announced on May 8, 2018 (the "**Acquisition**").

The EC's approval is conditional on Takeda and Shire fulfilling commitments given to the EC in connection with the clearance. Specifically, in relation to the future potential overlap in the area of inflammatory bowel diseases between Takeda's marketed product Entyvio (vedolizumab) and Shire's pipeline compound SHP647, Takeda and Shire have committed to divest the pipeline compound SHP647 and certain associated rights. The divestment of SHP647 and certain associated rights is not a condition to the completion of the Acquisition.

SHP647 is an exciting pipeline compound and Takeda expects the asset to attract interest from a number of potential buyers. Takeda remains committed to Entyvio, which has been granted marketing authorization in more than 60 countries and is the cornerstone of Takeda's diverse specialty gastrointestinal portfolio.

"We are very pleased to have secured clearance from the European Commission, the final regulatory approval required to proceed with our acquisition of Shire," said Christophe Weber, President and Chief Executive Officer of Takeda. "We are another step closer to creating a global, values-based, R&D-driven biopharmaceutical leader, and after several months of constructive dialogue, we are optimistic that our shareholders recognize the significant long-term value creation potential of this powerful combination."

The Acquisition has now received clearances from the European Commission, the United States Federal Trade Commission, the Japan Fair Trade Commission, the State Administration for Market Regulation in China and the Brazilian Administrative Council for Economic Defense, among other regulatory authorities.

As announced on November 12, 2018, Takeda has published a circular containing a notice of its decision to hold an Extraordinary General Meeting of Shareholders (the "**EGM**") to vote on the necessary matters relating to the proposed Acquisition. The EGM is to be convened at 10:00 a.m. (Tokyo time) on December 5, 2018 at INTEX Osaka, Hall 6B Zone.

Takeda also confirms its previously announced expectation that, subject to receiving the necessary shareholder approvals and sanction of the scheme of arrangement by the Jersey court, completion of the Acquisition will take place on January 8, 2019. Further announcements will be made as appropriate.

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About Entyvio® (vedolizumab)
Vedolizumab is a gut-selective biologic and is approved as an intravenous (IV) formulation.[1] It is a humanized monoclonal antibody designed to specifically antagonize the alpha4beta7 integrin, inhibiting the binding of alpha4beta7 integrin to intestinal mucosal addressin cell adhesion molecule 1 (MAdCAM-1), but not vascular cell adhesion molecule 1 (VCAM-1).[2] MAdCAM-1 is preferentially expressed on blood vessels and lymph nodes of the gastrointestinal tract.[3] The alpha4beta7 integrin is expressed on a subset of circulating white blood cells. These cells have been shown to play a role in mediating the inflammatory process in ulcerative colitis (UC) and Crohn's disease (CD).[4] [5] By inhibiting alpha4beta7 integrin, vedolizumab may limit the ability of certain white blood cells to infiltrate gut tissues.

Vedolizumab IV is approved for the treatment of adult patients with moderately to severely active UC and CD, who have had an inadequate response with, lost response to, or were intolerant to either conventional therapy or a tumor necrosis factor-alpha (TNFα) antagonist. Vedolizumab IV has been granted marketing authorization in over 60 countries, including the United States and European Union, with over 200,000 patient years of exposure to date.[6]

Therapeutic Indications

Ulcerative colitis
Vedolizumab is indicated for the treatment of adult patients with moderately to severely active ulcerative colitis who have had an inadequate response with, lost response to, or were intolerant to either conventional

therapy or a tumor necrosis factor-alpha (TNFα) antagonist.

Crohn's disease

Vedolizumab is indicated for the treatment of adult patients with moderately to severely active Crohn's disease who have had an inadequate response with, lost response to, or were intolerant to either conventional therapy or a tumor necrosis factor-alpha (TNFα) antagonist.

Important Safety Information

Contraindications

Hypersensitivity to the active substance or to any of the excipients.

Special warnings and special precautions for use

Vedolizumab should be administered by a healthcare professional equipped to manage hypersensitivity reactions, including anaphylaxis, if they occur. Appropriate monitoring and medical support measures should be available for immediate use when administering vedolizumab. Observe all patients during infusion and until the infusion is complete.

Infusion-related reactions

In clinical studies, infusion-related reactions (IRR) and hypersensitivity reactions have been reported, with the majority being mild to moderate in severity. If a severe IRR, anaphylactic reaction, or other severe reaction occurs, administration of vedolizumab must be discontinued immediately and appropriate treatment initiated (e.g., epinephrine and antihistamines). If a mild to moderate IRR occurs, the infusion rate can be slowed or interrupted and appropriate treatment initiated (e.g., epinephrine and antihistamines). Once the mild or moderate IRR subsides, continue the infusion. Physicians should consider pre-treatment (e.g., with antihistamine, hydrocortisone and/or paracetamol) prior to the next infusion for patients with a history of mild to moderate IRR to vedolizumab, in order to minimize their risks.

Infections

Vedolizumab is a gut-selective integrin antagonist with no identified systemic immunosuppressive activity. Physicians should be aware of the potential increased risk of opportunistic infections or infections for which the gut is a defensive barrier. Vedolizumab treatment is not to be initiated in patients with active, severe infections such as tuberculosis, sepsis, cytomegalovirus, listeriosis, and opportunistic infections until the infections are controlled, and physicians should consider withholding treatment in patients who develop a severe infection while on chronic treatment with vedolizumab. Caution should be exercised when considering the use of vedolizumab in patients with a controlled chronic severe infection or a history of recurring severe infections. Patients should be monitored closely for infections before, during and after treatment. Before starting treatment with vedolizumab, screening for tuberculosis may be considered according to local practice. Some integrin antagonists and some systemic immunosuppressive agents have been associated with progressive multifocal leukoencephalopathy (PML), which is a rare and often fatal opportunistic infection caused by the John Cunningham (JC) virus. By binding to the α4β7 integrin expressed on gut-homing lymphocytes, vedolizumab exerts an immunosuppressive effect on the gut. Although no systemic immunosuppressive effect was noted in healthy subjects, the effects on systemic immune system function in patients with inflammatory bowel disease are not known. Healthcare professionals should monitor patients on vedolizumab for any new onset or worsening of neurological signs and symptoms, and consider neurological referral if they occur. If PML is suspected, treatment with

vedolizumab must be withheld; if confirmed, treatment must be permanently discontinued. Typical signs and symptoms associated with PML are diverse, progress over days to weeks, and include progressive weakness on one side of the body, clumsiness of limbs, disturbance of vision, and changes in thinking, memory, and orientation leading to confusion and personality changes. The progression of deficits usually leads to death or severe disability over weeks or months.

Malignancies
The risk of malignancy is increased in patients with ulcerative colitis and Crohn's disease. Immunomodulatory medicinal products may increase the risk of malignancy.

Prior and concurrent use of biological products
No vedolizumab clinical trial data are available for patients previously treated with natalizumab. Caution should be exercised when considering the use of vedolizumab in these patients. No clinical trial data for concomitant use of vedolizumab with biologic immunosuppressants are available. Therefore, the use of vedolizumab in such patients is not recommended.

Vaccinations
Prior to initiating treatment with vedolizumab all patients should be brought up to date with all recommended immunizations. Patients receiving vedolizumab may receive non-live vaccines (e.g., subunit or inactivated vaccines) and may receive live vaccines only if the benefits outweigh the risks.

Adverse reactions include: nasopharyngitis, headache, arthralgia, upper respiratory tract infection, bronchitis, influenza, sinusitis, cough, oropharyngeal pain, nausea, rash, pruritus, back pain, pain in extremities, pyrexia, and fatigue.

Please consult with your local regulatory agency for approved labeling in your country.

For U.S. audiences, please see the full Prescribing Information including Medication Guide for ENTYVIO®.[7]
For EU audiences, please see the Summary of Product Characteristics (SmPC) for ENTYVIO®.

Takeda's Commitment to Gastroenterology
Gastrointestinal (GI) diseases can be complex, debilitating and life-changing. Recognizing this unmet need, Takeda and our collaboration partners have focused on improving the lives of patients through the delivery of innovative medicines and dedicated patient disease support programs for over 25 years. Takeda aspires to advance how patients manage their disease. Additionally, Takeda is leading in areas of gastroenterology associated with high unmet need, such as inflammatory bowel disease, acid-related diseases and motility disorders. Our GI Research & Development team is also exploring solutions in celiac disease and liver diseases, as well as scientific advancements through microbiome therapies.

About Takeda Pharmaceutical Company Limited
Takeda Pharmaceutical Company Limited (TSE: 4502) is a global, research and development-driven pharmaceutical company committed to bringing better health and a brighter future to patients by translating science into life-changing medicines. Takeda focuses its R&D efforts on oncology, gastroenterology and neuroscience therapeutic areas plus vaccines. Takeda conducts R&D both internally and with partners to stay at the leading edge of innovation.

Innovative products, especially in oncology and gastroenterology, as well as Takeda's presence in emerging markets, are currently fueling the growth of Takeda. Approximately 30,000 Takeda employees are committed to improving quality of life for patients, working with Takeda's partners in health care in more than 70 countries. For more information, visit https://www.takeda.com/newsroom/.

Additional Information

This Announcement is provided for information purposes only. It is not intended to and does not constitute, or form part of, an offer, invitation or the solicitation of an 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, pursuant to the Acquisition or otherwise nor will there be any sale, issuance, exchange or transfer of securities of Shire or Takeda pursuant to the Acquisition or otherwise in any jurisdiction in contravention of applicable law.

Forward Looking Statements

This Announcement contains certain statements about Takeda and Shire that are or may be forward looking statements, including with respect to a possible combination involving Takeda and Shire. All statements other than statements of historical facts included in this Announcement may be forward looking statements. Without limitation, forward looking statements often include words such as "targets", "plans", "believes", "hopes", "continues", "expects", "aims", "intends", "will", "may", "should", "would", "could", "anticipates", "estimates", "projects" or words or terms of similar substance or the negative thereof. By their nature, forward-looking statements involve risk and uncertainty, because they relate to events and depend on circumstances that will occur in the future and the factors described in the context of such forward-looking statements in this Announcement could cause actual results and developments to differ materially from those expressed in or implied by such forward-looking statements. Such risks and uncertainties include, but are not limited to, the possibility that a possible combination will not be pursued or consummated, failure to obtain necessary regulatory approvals or to satisfy any of the other conditions to the possible combination if it is pursued, adverse effects on the market price of Takeda's ordinary shares and on Takeda's or Shire's operating results because of a failure to complete the possible combination, failure to realise the expected benefits of the possible combination, negative effects relating to the announcement of the possible combination or any further announcements relating to the possible combination or the consummation of the possible combination on the market price of Takeda's or Shire's ordinary shares, significant transaction costs and/or unknown liabilities, general economic and business conditions that affect the combined companies following the consummation of the possible combination, changes in global, political, economic, business, competitive, market and regulatory forces, future exchange and interest rates, changes in tax laws, regulations, rates and policies, future business combinations or disposals and competitive developments. Although it is believed that the expectations reflected in such forward-looking statements are reasonable, no assurance can be given that such expectations will prove to have been correct and you are therefore cautioned not to place undue reliance on these forward-looking statements which speak only as at the date of this Announcement.

Additional risk factors that may affect future results are contained in Shire's most recent Annual Report on Form 10-K and in Shire's subsequent Quarterly Reports on Form 10-Q, in each case including those risks outlined in 'ITEM1A: Risk Factors', and in Shire's subsequent reports on Form 8-K and other Securities and Exchange Commission filings (available at www.Shire.com and www.sec.gov), the contents of which are not incorporated by reference into, nor do they form part of, this Announcement. These risk factors expressly

qualify all forward-looking statements contained in this Announcement and should also be considered by the reader.

All forward-looking statements attributable to Takeda or Shire or any person acting on either company's behalf are expressly qualified in their entirety by this cautionary statement. Readers are cautioned not to place undue reliance on these forward-looking statements that speak only as of the date hereof. Except to the extent otherwise required by applicable law, neither Takeda nor Shire undertake any obligation to update or revise forward-looking statements, whether as a result of new information, future events or otherwise.

No profit forecasts or estimates

Unless expressly stated otherwise, nothing in this Announcement (including any statement of estimated synergies) is intended as a profit forecast or estimate for any period and no statement in this Announcement should be interpreted to mean that earnings or earnings per share or dividend per share for Takeda or Shire, as appropriate, for the current or future financial years would necessarily match or exceed the historical published earnings or earnings per share or dividend per share for Takeda or Shire, as appropriate.

Medical information

This Announcement contains information about products that may not be available and 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.

Publication on Website

In accordance with Rule 26.1 of the Code, a copy of this Announcement will be made available (subject to certain restrictions relating to persons resident in restricted jurisdictions) on Takeda's website at www.takeda.com/investors/offer-for-shire by no later than 12 noon (London time) on November 21, 2018. The content of the website referred to in this Announcement is not incorporated into and does not form part of this Announcement.

Disclosure requirements of the Code

Under Rule 8.3(a) of the Code, any person who is interested in 1% or more of any class of relevant securities of an offeree company or of any securities exchange offeror (being any offeror other than an offeror in respect of which it has been announced that its offer is, or is likely to be, solely in cash) must make an Opening Position Disclosure following the commencement of the offer period and, if later, following the announcement in which any securities exchange offeror is first identified. An Opening Position Disclosure must contain details of the person's interests and short positions in, and rights to subscribe for, any relevant securities of each of (i) the offeree company and (ii) any securities exchange offeror(s). An Opening Position Disclosure by a person to whom Rule 8.3(a) applies must be made by no later than 3.30 pm (London time) on the 10th business day following the commencement of the offer period and, if appropriate, by no later than 3.30 pm (London time) on the 10th business day following the announcement in which any securities exchange offeror is first identified. Relevant persons who deal in the relevant securities of the offeree company or of a securities exchange offeror prior to the deadline for making an Opening Position Disclosure must instead make a Dealing Disclosure.

Under Rule 8.3(b) of the Code, any person who is, or becomes, interested in 1% or more of any class of relevant securities of the offeree company or of any securities exchange offeror must make a Dealing Disclosure if the person deals in any relevant securities of the offeree company or of any securities exchange

offeror. A Dealing Disclosure must contain details of the dealing concerned and of the person's interests and short positions in, and rights to subscribe for, any relevant securities of each of (i) the offeree company and (ii) any securities exchange offeror(s), save to the extent that these details have previously been disclosed under Rule 8. A Dealing Disclosure by a person to whom Rule 8.3(b) applies must be made by no later than 3.30 pm (London time) on the business day following the date of the relevant dealing.

If two or more persons act together pursuant to an agreement or understanding, whether formal or informal, to acquire or control an interest in relevant securities of an offeree company or a securities exchange offeror, they will be deemed to be a single person for the purpose of Rule 8.3.

Opening Position Disclosures must also be made by the offeree company and by any offeror and Dealing Disclosures must also be made by the offeree company, by any offeror and by any persons acting in concert with any of them (see Rules 8.1, 8.2 and 8.4).

Details of the offeree and offeror companies in respect of whose relevant securities Opening Position Disclosures and Dealing Disclosures must be made can be found in the Disclosure Table on the Panel's website at www.thetakeoverpanel.org.uk, including details of the number of relevant securities in issue, when the offer period commenced and when any offeror was first identified. You should contact the Panel's Market Surveillance Unit on +44 (0)20 7638 0129 if you are in any doubt as to whether you are required to make an Opening Position Disclosure or a Dealing Disclosure.

[1] Entyvio® Summary of Product Characteristics. March 2018.

[2] Soler D, Chapman T, Yang LL, et al. The binding specificity and selective antagonism of vedolizumab, an anti-α4β7 integrin therapeutic antibody in development for inflammatory bowel diseases. J Pharmacol Exp Ther. 2009;330:864-875.

[3] Briskin M, Winsor-Hines D, Shyjan A, et al. Human mucosal addressin cell adhesion molecule-1 is preferentially expressed in intestinal tract and associated lymphoid tissue. Am J Pathol. 1997;151:97 110.

[4] Eksteen B, Liaskou E, Adams DH. Lymphocyte homing and its roles in the pathogenesis of IBD. Inflamm Bowel Dis. 2008;14:1298 1312.

[5] Wyant T, Fedyk E, Abhyankar B. An overview of the mechanism of action of the monoclonal antibody vedolizumab. J Crohns Colitis. 2016;10:1437-1444.

[6] Takeda. 2018. Data on file.

[7] Entyvio (vedolizumab) Prescribing Information. February 2018.

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