PRESS RELEASE

New Oral Therapy VENCLYXTO® ▼ (venetoclax) Receives Marketing Authorisation For Patients With Difficult-To-Treat, Chronic Lymphocytic Leukaemia, The Most Common Form Of Adult Leukaemia

- *VENCLYXTO (venetoclax) is the first B-cell lymphoma 2 (BCL-2) inhibitor to be granted a licence in the UK and works differently to all other licensed therapies for chronic lymphocytic leukaemia (CLL)*[1-10]
- *Venetoclax is indicated as a monotherapy for the treatment of CLL in adult patients in the absence of 17p deletion or TP53 mutation who have failed both chemo-immunotherapy and a B-cell receptor (BCR) inhibitor. Venetoclax is also indicated as monotherapy for the treatment of adult CLL patients with these mutations who are either unsuitable for or have failed a BCR inhibitor*[11]
- *One in two CLL patients failing current standards of care could face survival as short as three months.*[12,13,14] *In patients failing on B-cell receptor (BCR) inhibitors, 72% of patients taking venetoclax are yet to have their disease progress after 12 months. In patients with previously treated CLL and 17p deletion, median progression free survival is over 27 months*[11]

Maidenhead, UK, Thursday 8 December, 2016 – AbbVie, a global biopharmaceutical company, today announced that the European Commission (EC) has authorised VENCLYXTO® (venetoclax) as a first-in-class, oral, once-daily medicine that selectively inhibits the function of the BCL-2 protein, restoring the body's ability to trigger cancer cell self-destruction.[1,11] Venetoclax has been granted marketing authorisation as monotherapy for the treatment of chronic lymphocytic leukaemia (CLL) in adult patients in the absence of 17p deletion or TP53 mutation who have failed both chemo-immunotherapy and a B-cell receptor (BCR) inhibitor. Venetoclax is also indicated as monotherapy for the treatment of adult CLL patients in the presence of 17p deletion or TP53 mutation who are either unsuitable for or have failed a BCR inhibitor.[11]

Professor Peter Hillmen, Consultant Haematologist, Leeds Teaching Hospitals NHS Trust and Coordinating Investigator of the venetoclax studies in the UK said, "Venetoclax represents an important new option to offer eligible patients with CLL who have a very poor outcome with conventional therapies. Studies have shown that clinically significant numbers of patients respond to the treatment, with a number of these achieving complete responses. For clinicians, it has been meaningful to observe that some patients are achieving a deeper remission where minimal disease is not detectable on a molecular level, rarely seen in pre-treated patients. These types of clinical advances are bringing us closer than ever to successfully treating these types of cancers."

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CLL is the most common form of leukaemia in adults, affecting the lives of nearly 3,500 people in the UK each year.[15,16] CLL has a highly variable clinical course, with the cancer growing and progressing slowly in some people whereas in others the cancer is more aggressive and treatment is required sooner.[17] The build-up of abnormal/immature lymphocytes compromises patients' ability to ward off infections and attacks on the immune system.[18] Other common symptoms include swollen lymph glands, abdominal discomfort, weight loss, fever and severe fatigue which significantly impacts quality of life.[18]

Despite treatment, the majority of people living with CLL will eventually have their disease recur.[18] In people for whom BCR inhibitors fail, less than half will survive longer than 3 months.[12] While for people who develop or harbor gene mutations, such as 17p deletion or TP53 mutation, treatment is particularly challenging and these are associated with poorer quality of life and a median life expectancy of less than two to three years with current standard-of-care regimens.[19,20]

Nick York, from the CLL Support Association said, "We are pleased about the venetoclax marketing authorisation announcement. This may begin to address a critical unmet need in a difficult-to-treat patient population who have used all available treatment options. At the moment, there is a treatment void for those with hard to treat CLL who are not suitable for treatment with BCR inhibitors or who have relapsed from them. The evidence we have seen so far for venetoclax suggests it can help to extend lives and can potentially play a role in enabling patients, their carers and families to more fully live their lives."

"AbbVie is making significant investment in studying ways to block BCL-2 activity in cancer and with this licence we are very pleased by the opportunity to bring venetoclax to eligible UK patients who have had limited options to date." said Alice Butler, Medical Director, AbbVie UK.

In a Phase 2, two arm study of venetoclax in 64 CLL patients who relapsed or were refractory to BCR inhibitors, the primary endpoint, overall response rate was 67 per cent. Twenty-five per cent of patients achieved minimal residual disease (MRD) negativity in the peripheral blood, including 1 in the bone marrow. MRD was an exploratory endpoint and is defined as <1 CLL cell per 10^4 leukocytes in the sample.[11] At 12 months, 72% per cent of patients were yet to have their disease progress.[11] In a separate Phase 2, single arm study in 107 relapsed/refractory CLL patients with 17p deletion, the primary endpoint, overall response rate was 79 per cent, with 7 per cent in complete remission. In an exploratory endpoint evaluated by investigator assessment, minimal residual disease (MRD) negativity in peripheral blood was achieved in 27.1 per cent (41/158) of patients, including 15 patients who were also MRD negative in the bone marrow.[11] Investigator-assessed median progression free survival was 27.2 months.[11]

The most commonly occurring adverse reactions (≥20%) of any grade in patients receiving venetoclax in clinical trials were neutropenia/neutrophil count decreased, diarrhoea, nausea, anaemia, upper respiratory tract infection, fatigue, hyperphosphataemia, vomiting, and constipation. The most

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frequently reported serious adverse reactions (≥2%) were pneumonia, febrile neutropenia, and tumour lysis syndrome.[11]

Full summary of product characteristics is available at www.medicines.org.uk/emc

▼Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to AbbVie UK Ltd. Please contact ukadverseevents@abbvie.com. With biological medicines, healthcare professionals should report adverse reactions by brand name and batch number.

About VENCLYXTO® (venetoclax)
Venetoclax is an oral B-cell lymphoma-2 (BCL-2) inhibitor. The BCL-2 protein prevents apoptosis (programmed cell death) of some cells, including lymphocytes, and can be overexpressed in some cancer types.[1] Venetoclax, which is given once daily, is designed to selectively inhibit the function of the BCL-2 protein.[1]

Venetoclax is being developed by AbbVie and Genentech, a member of the Roche Group. It is jointly commercialised by the companies in the U.S. and by AbbVie outside of the U.S. Together, the companies are committed to BCL-2 research with venetoclax, which is currently being evaluated in Phase 3 clinical trials for the treatment of relapsed/refractory chronic lymphocytic leukaemia (CLL), along with studies in several other cancers. [21,22,23,24]

The safety of venetoclax is based on pooled data of 296 patients treated with venetoclax in two Phase 2 studies and one Phase 1 study.[11] In all, the studies enrolled patients with previously treated CLL, including 188 patients with 17p deletion and 92 patients who had failed a BCR inhibitor.[11] Patients were treated with venetoclax 400mg monotherapy once daily following a dose-titration schedule. The most commonly occurring adverse reactions (≥20 per cent) of any grade in patients receiving venetoclax were neutropenia/neutrophil count decreased, diarrhoea, nausea, anaemia, upper respiratory tract infection, fatigue, hyperphosphataemia, vomiting and constipation.[11] The most frequently reported serious adverse reactions (≥2 per cent) were pneumonia, febrile neutropenia and tumor lysis syndrome (TLS). Discontinuations due to adverse reactions occurred in 9.1 per cent of patients. Dosage adjustments due to adverse reactions occurred in 11.8 per cent of patients.[11]

TLS is an important identified risk when initiating venetoclax. TLS is caused by rapid killing of cancer cells. In 122 patients with CLL with a 20mg daily starting dose, the rate of TLS was three per cent. No TLS with clinical consequences such as acute renal failure, cardiac arrhythmias or sudden death and/or seizures was observed in these patients.[11] This rate of TLS reflects the use of a dose ramp up, starting with a daily dose of 20mg and increasing over five weeks to a daily dose of 400mg, as well as implementation of specific prophylaxis and monitoring measures during the ramp up phase.

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About AbbVie in Oncology
AbbVie is striving to outsmart cancer by working with scientists, physicians, industry peers, patient advocacy groups and most importantly patients, to discover, develop and provide new therapies that will have a remarkable impact on the lives of people around the world affected by cancer. Our goal is to provide medicines that make a transformational improvement in cancer treatment and outcomes for cancer patients. By exploring and investing in new pathways, technologies and approaches, AbbVie is breaking ground in some of the most widespread and difficult-to-treat cancers. We are also exploring solutions to help patients obtain access to our cancer medicines. With the acquisition of Pharmacyclics in 2015 and Stemcentrx in 2016, and through several collaborations, AbbVie's oncology portfolio consists of marketed medicines and a pipeline containing multiple new molecules being evaluated worldwide in nearly 200 clinical trials in 20 different tumour types.

About AbbVie
AbbVie is a global, research-based biopharmaceutical company formed in 2013 following separation from Abbott Laboratories. The company's mission is to use its expertise, dedicated people and unique approach to innovation to develop and market advanced therapies that address some of the world's most complex and serious diseases. Together with its wholly-owned subsidiary, Pharmacyclics, AbbVie employs more than 28,000 people worldwide and markets medicines in more than 170 countries. For further information on the company and its people, portfolio and commitments, please visit www.abbvie.co.uk.

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References

[1] AbbVie data on file.
[2] European Medicines Agency. Summary of Product Characteristics (Arzerra).
[3] European Medicines Agency. Summary of Product Characteristics (Gazyvaro).
[4] European Medicines Agency. Summary of Product Characteristics (Hizentra).
[5] European Medicines Agency. Summary of Product Characteristics (HyQvia).
[6] European Medicines Agency. Summary of Product Characteristics (Imbruvica).
[7] European Medicines Agency. Summary of Product Characteristics (Kiovig).
[8] European Medicines Agency. Summary of Product Characteristics (Mabthera).
[9] European Medicines Agency. Summary of Product Characteristics (Privigen).

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[10] European Medicines Agency. Summary of Product Characteristics (Zydelig).
[11] VENCLYXTO summary of product characteristics.
[12] Jain PW et al. 'Outcomes of patients with chronic lymphocytic leukemia after discontinuing ibrutinib' in Blood. 2015; 125: 2062-2067.
[13] NCCN clinical practice guidelines in oncology. Non-Hodgkin's Lymphoma. Available at: https://www.nccn.org/about/nhl.pdf Accessed December 2016
[14] Follows GA, et al. BCSH CLL guidelines interim statement. 2015 Available at: http://www.bcshguidelines.com/documents/Interim_statement_CLL_guidelines_version6.pdf Accessed December 2016
[15] Macmillan. What is Chronic Lymphocytic Leukaemia. Available at: http://www.macmillan.org.uk/information-and-support/leukaemia/chronic-lymphocytic/understanding-cancer/about-cll.html Accessed December 2016
[16] Cancer Research UK. Chronic Lymphocytic Leukaemia (C91.1): 2013 Number of New Cases, Crude and European Age-Standardised (AS) Incidence Rates per 100,000 Population, UK Available at http://www.cancerresearchuk.org/sites/default/files/cstream-node/cases_rates_leukaemia_cll_2.pdf Accessed December 2016
[17] Lymphoma Coalition Europe. Chronic Lymphocytic Leukaemia European report. May 2016
[18] American Cancer Society. (2013) Leukemia – Chronic Lymphocytic. Available at: http://www.cancer.org/acs/groups/cid/documents/webcontent/003111-pdf.pdf Accessed December 2016.
[19] Schnaiter A, et al. 17p deletion in chronic lymphocytic leukemia: risk stratification and therapeutic approach. Hematol Oncol Clin N Am. 2013; 27:289-301
[20] Stilgenbauer S, et al. Understanding and managing ultra high-risk chronic lymphocytic leukemia. *Hematology Am Soc Hematol Educ Program*. 2010; 1:481-488.
[21] Clinicaltrials.gov. NCT01889186: A study of the efficacy of ABT-199 in subjects with relapsed or refractory chronic lymphocytic leukemia with the 17p deletion. Accessed December2016.
[22] Clinicaltrials.gov. NCT01994837: A Phase 2 Study of ABT-199 in subjects with Acute Myelogenous Leukemia (AML). Accessed December 2016.
[23] Clinicaltrials.gov. NCT01794520: Study evaluating ABT-199 in subjects with relapsed or refractory Multiple Myeloma. Accessed December 2016.
[24] Clinicaltrials.gov. NCT01328626: A Phase 1 study evaluating the safety and pharmacokinetics of ABT-199 in subjects with relapsed or refractory Chronic Lymphocytic Leukemia and Non-Hodgkin Lymphoma. Accessed December 2016.

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