

## ACALABRUTINIB GRANTED BREAKTHROUGH THERAPY DESIGNATION BY US FDA FOR THE TREATMENT OF PATIENTS WITH MANTLE CELL LYMPHOMA

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AstraZeneca and its haematology research and development centre of excellence, Acerta Pharma, today announced that the US Food and Drug Administration (FDA) has granted Breakthrough Therapy Designation for acalabrutinib for the treatment of patients with mantle cell lymphoma (MCL) who have received at least one prior therapy. Acalabrutinib is a highly-selective, potent Bruton tyrosine kinase (BTK) inhibitor in development for the treatment of multiple B-cell cancers.

The Breakthrough Therapy Designation is designed to expedite the development and regulatory review of new medicines that are intended to treat a serious condition and that have shown encouraging early clinical results, which demonstrate substantial improvement on a clinically-significant endpoint over available medicines and when there is significant unmet medical need.

Sean Bohan, Executive Vice President, Global Medicines Development and Chief Medical Officer at AstraZeneca, said: “New treatments are urgently needed for people with mantle cell lymphoma who relapse or do not respond to therapy. Breakthrough Therapy Designation for acalabrutinib will help us bring this potential medicine to appropriate patients as quickly as possible.”

The FDA granted Breakthrough Therapy Designation based on the totality of clinical data from the acalabrutinib development programme, including data from the Phase II ACE-LY-004 clinical trial in patients with relapsed or refractory MCL.

Flavia Borellini, PhD, Acerta Pharma Chief Executive Officer, said: “This is an exciting regulatory milestone for our work in haematology. Acalabrutinib is a potent, irreversible BTK inhibitor with a high degree of specificity for its target. If approved, it could be a clinically-meaningful treatment option for patients with this devastating disease.”

This is the fifth Breakthrough Therapy Designation that AstraZeneca has received from the FDA for an oncology medicine since 2014 and the first for the Company in haematology. The acalabrutinib development programme includes both monotherapy and combination therapies for a broad range of blood cancers and solid tumours.

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### NOTES TO EDITORS

#### About mantle cell lymphoma (MCL)

Mantle cell lymphoma (MCL) is an aggressive B-cell non-Hodgkin lymphoma (NHL) with poor prognosis.<sup>i,ii,iii,iv</sup> MCL accounts for approximately 3% to 6% of new NHL cases in Western countries each year, with an annual incidence of 0.5 per 100,000 persons and an

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estimated prevalence of 3.5/100,000.<sup>ii,v</sup> The median age at diagnosis is 68 years, with a 3:1 male predominance.<sup>ii</sup>

### About acalabrutinib

Acalabrutinib is a highly selective, potent, covalent inhibitor of Bruton tyrosine kinase (BTK) with minimal off-target activity observed in pre-clinical trials.<sup>vi,vii,viii</sup> This potential new medicine is in development for the treatment of multiple B-cell and other cancers. The acalabrutinib development programme includes both monotherapy and combination therapy strategies in chronic lymphocytic leukaemia (CLL), MCL, Waldenström macroglobulinemia (WM), follicular lymphoma, diffuse large B-cell lymphoma, and multiple myeloma, as well as monotherapy and combination trials in solid tumours. In total, more than 25 acalabrutinib clinical trials with more than 2,000 patients are underway or have completed. Acalabrutinib was granted Orphan Drug Designation by the FDA for the treatment of patients with MCL in September 2015 and by the European Commission in March 2016 for the treatment of patients with CLL, MCL and WM. Acalabrutinib is a potential new medicine not approved for any current use.

### About Acerta Pharma

Acerta Pharma, a member of the AstraZeneca Group, is creating novel selective therapies intended for the treatment of cancer and autoimmune diseases. AstraZeneca acquired a majority stake interest in Acerta Pharma, which serves as AstraZeneca's haematology research and development centre of excellence. For more information, please visit [www.acerta-pharma.com](http://www.acerta-pharma.com).

### About AstraZeneca in Oncology

AstraZeneca has a deep-rooted heritage in Oncology and offers a quickly growing portfolio of new medicines that have the potential to transform patients' lives and the Company's future. With at least six new medicines to be launched between 2014 and 2020 and a broad pipeline of small molecules and biologics in development, we are committed to advance New Oncology as one of AstraZeneca's five Growth Platforms focused on lung, ovarian, breast and blood cancers. In addition to our core capabilities, we actively pursue innovative partnerships and investments that accelerate the delivery of our strategy, as illustrated by our investment in Acerta Pharma in haematology.

By harnessing the power of four scientific platforms -- Immuno-oncology, Tumour Drivers and Resistance, DNA Damage Response and Antibody Drug Conjugates -- and by championing the development of personalised combinations, AstraZeneca has the vision to redefine cancer treatment and one day eliminate cancer as a cause of death.

### About AstraZeneca

AstraZeneca is a global, science-led biopharmaceutical company that focuses on the discovery, development and commercialisation of prescription medicines, primarily for the treatment of diseases in three main therapy areas - Oncology, Cardiovascular & Metabolic Diseases and Respiratory. The Company also is selectively active in the areas of autoimmunity, neuroscience and infection. AstraZeneca operates in over 100 countries and its innovative medicines are used by millions of patients worldwide. For more information, please visit [www.astrazeneca.com](http://www.astrazeneca.com) and follow us on Twitter @AstraZeneca.

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<sup>i</sup> Leukemia & Lymphoma Society. Mantle Cell Lymphoma Facts.

[https://www.lls.org/sites/default/files/file\\_assets/mantlecelllymphoma.pdf](https://www.lls.org/sites/default/files/file_assets/mantlecelllymphoma.pdf) Accessed June 2017

<sup>ii</sup> Cheah CY, Seymour JF, Wang M. Mantle Cell Lymphoma. *Journal of Clinical Oncology* 34, no. 11 (April 2016) 1256-1269.

<sup>iii</sup> Hoster E, Klapper W et al. Confirmation of the Mantle-Cell Lymphoma International Prognostic Index in Randomized Trials of the European Mantle-Cell Lymphoma Network. *Journal of Clinical Oncology* 2014;32:1338-1346.

<sup>iv</sup> Dreyling M, Ferrero S. The role of targeted treatment in mantle cell lymphoma: is transplant dead or alive? *Haematologica* 2016 Volume 101(2):104-114

<sup>v</sup> Orphanet Report Series. Prevalence and incidence of rare diseases: Bibliographic data. Number 2 March 2016.

<sup>vi</sup> Covey T, Barf T, Gulrajani M, Krantz F, van Lith B, Bibikova E, et al. Abstract 2596: ACP-196: a novel covalent Bruton's tyrosine kinase (Btk) inhibitor with improved selectivity and in vivo target coverage in chronic lymphocytic leukemia (CLL) patients. *Cancer Res.* 2015;75(15 Supplement):2596.

<sup>vii</sup> Byrd JC, Harrington B, O'Brien S, Jones JA, Schuh A, Devereux S, et al. Acalabrutinib (ACP-196) in relapsed chronic lymphocytic leukemia. *N Engl J Med.* 2016;374(4):323–32.

<sup>viii</sup> Harrington BK, Gulrajani M, Covey T, Kaptein A, Van Lith B, Izumi R, et al. ACP-196 is a second generation inhibitor of Bruton tyrosine kinase (BTK) with enhanced target specificity. *Blood.* 2015;126(23):2908.