

MEDIA RELEASE • COMMUNIQUE AUX MEDIAS • MEDIENMITTEILUNG**Novartis drug Farydak[®] recommended by CHMP for EU approval to treat multiple myeloma, providing patients a new mechanism of action**

- *Farydak (panobinostat) combination improved PFS by 7.8 months for patients who received ≥ 2 prior regimens including bortezomib and an IMiD¹*
- *Farydak would be the first HDAC inhibitor with epigenetic activity to treat multiple myeloma^{2,3}*
- *CHMP positive opinion marks a key milestone toward panobinostat availability in the EU, aligning with recent US FDA approval*

Basel, June 26, 2015 – The Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) adopted a positive opinion for Farydak[®] (panobinostat, previously known as LBH589) capsules, in combination with bortezomib* and dexamethasone, for the treatment of adult patients with relapsed and/or refractory multiple myeloma who have received at least two prior regimens including bortezomib and an immunomodulatory agent (IMiD). If approved in the EU, panobinostat will be first in its class of anticancer agents available to these patients¹.

Multiple myeloma is a cancer of the plasma cells, a type of white blood cell present in the bone marrow, and affects approximately 84,000 people in Europe^{4,5}. Panobinostat is the first histone deacetylase (HDAC) inhibitor to show efficacy in multiple myeloma². As an HDAC inhibitor, its epigenetic activity may help restore cell function in patients with multiple myeloma³.

“Panobinostat is the first and only HDAC inhibitor recommended by the CHMP for the treatment of patients living with multiple myeloma who have progressed after standard-of-care therapy with bortezomib and an IMiD,” said Alessandro Riva, MD, Global Head of Oncology Development and Medical Affairs, Novartis Oncology. “We are pleased with the positive CHMP opinion on panobinostat for previously treated patients because it brings us one step closer to providing a new treatment option for patients in need in Europe.”

The CHMP recommendation is based on efficacy and safety data in a subgroup analysis of 147 patients who had received at least two prior regimens, including bortezomib and an IMiD, during the Phase III, randomized, double-blind, placebo-controlled, multicenter global registration trial, called PANORAMA-1 (PANobinostat ORAI in Multiple MyelomA), evaluating panobinostat in combination with bortezomib and dexamethasone against bortezomib and dexamethasone alone in patients with relapsed and/or relapsed and refractory multiple myeloma. The trial found that the median progression-free survival (PFS) benefit increased in panobinostat patients who had received prior treatment with both bortezomib and an IMiD (12.5 months; n=73), as compared to the placebo arm (4.7 months; n=74) (hazard ratio=0.47 [95% confidence interval (CI): 0.31, 0.72])⁶.

*Trade name Velcade[®] registered to Millennium Pharmaceuticals, Inc.

The most common non hematological adverse reactions included diarrhea, fatigue, nausea and vomiting. Treatment-emergent hematological toxicities included thrombocytopenia, anemia, neutropenia and lymphopenia. QTc prolongation of >480 and <500 msec was recorded in 1.3% of patients and change from baseline of >60 msec was observed in 0.8% of patients. No patients had an absolute QTc prolongation of >500 msec. Cardiac events (most frequently atrial fibrillation, tachycardia, palpitation and sinus tachycardia) were reported in 17.6% of the panobinostat-treated patients versus 9.8% of placebo-treated patients and syncope events were reported in 6.0% versus 2.4%. Discontinuation due to adverse events (AEs), regardless of causality, was observed in 36.2% of patients. The most common AEs leading to treatment discontinuation were diarrhea (4.5%), asthenia and fatigue (2.9% each) and pneumonia (1.3%). On treatment deaths not due to the study indication (multiple myeloma) were reported in 6.8% of panobinostat-treated patients versus 3.2% of placebo-treated patients⁶.

In the EU, the European Commission generally follows the recommendation of the CHMP and delivers its final decision within three months of the CHMP recommendation. The decision will be applicable to all 28 EU member states plus Iceland, Norway and Liechtenstein. Additional regulatory submissions for panobinostat are being reviewed by health authorities worldwide. Panobinostat in combination with bortezomib and dexamethasone was approved in the US in February 2015 and Chile in May 2015 under brand name Farydak[®] for the treatment of patients with multiple myeloma who have received at least two prior regimens, including bortezomib and an IMiD. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials⁷.

About multiple myeloma

Multiple myeloma impacts approximately 84,000 people in Europe⁵. Multiple myeloma is a cancer of the plasma cells, a kind of white blood cell present in bone marrow—the soft, blood-producing tissue that fills the center of most bones. The cancer is caused by the production and growth of abnormal cells within the plasma, which multiply and build up in the bone marrow, pushing out healthy cells and preventing them from functioning normally⁴. Multiple myeloma is an incurable disease with a high rate of relapse (when the cancer returns) and resistance (when the therapy stops working)⁸. Standard-of-care regimens of proteasome inhibitors and IMiDs are often used to treat multiple myeloma, but most patients will stop responding to these treatments creating an unmet need for new options with novel mechanisms of action^{8,9,10}. Multiple myeloma typically occurs in individuals 60 years of age or older, with few cases in individuals younger than 40¹¹.

About the PANORAMA Clinical Trial Program

PANORAMA-1 (PANobinostat ORAI in Multiple MyelomA) is a Phase III randomized, double-blind, placebo-controlled, multicenter global registration trial to evaluate panobinostat in combination with bortezomib and dexamethasone against bortezomib and dexamethasone alone in patients with relapsed or relapsed and refractory multiple myeloma who failed on at least one prior treatment. The study of 768 patients took place in 215 clinical trial sites worldwide making it the largest global registration trial for multiple myeloma to date. The primary endpoint of the trial was PFS. Data for overall survival, the key secondary endpoint of the trial, are not yet mature. Other secondary endpoints include overall response rate, duration of response and safety¹².

About Farydak[®]

Panobinostat is approved as Farydak[®] in the US and Chile in combination with bortezomib and dexamethasone for the treatment of patients with multiple myeloma who have received at least two prior regimens, including bortezomib and an IMiD⁷. Farydak, an HDAC inhibitor, has an impact on epigenetics and may help restore cell function in patients with multiple myeloma.

Additional regulatory submissions for Farydak are being reviewed by health authorities worldwide. The safety and efficacy profile of panobinostat has not yet been established

outside the approved indications. Because of the uncertainty of clinical trials, there is no guarantee that panobinostat will become commercially available for additional indications anywhere else in the world.

Disclaimer

The foregoing release contains forward-looking statements that can be identified by words such as “recommended,” “would,” “positive opinion,” “will,” “recommendation,” “may,” “being reviewed,” “yet,” or similar terms, or by express or implied discussions regarding potential future marketing approvals for Farydak, or regarding potential future revenues from Farydak. You should not place undue reliance on these statements. Such forward-looking statements are based on the current beliefs and expectations of management regarding future events, and are subject to significant known and unknown risks and uncertainties. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual results may vary materially from those set forth in the forward-looking statements. There can be no guarantee that Farydak will be approved for sale in any market where it has been submitted, or at any particular time. Neither can there be any guarantee that Farydak will be submitted or approved for any additional indications or labeling in any market, or at any particular time. Nor can there be any guarantee that Farydak will be commercially successful in the future. Continued approval of Farydak in the approved indication may be contingent upon verification and description of clinical benefit in confirmatory trials. In particular, management’s expectations regarding Farydak could be affected by, among other things, unexpected regulatory actions or delays or government regulation generally; the uncertainties inherent in research and development, including unexpected clinical trial results and additional analysis of existing clinical data; the company’s ability to obtain or maintain proprietary intellectual property protection; general economic and industry conditions; global trends toward health care cost containment, including ongoing pricing pressures; unexpected manufacturing issues, and other risks and factors referred to in Novartis AG’s current Form 20-F on file with the US Securities and Exchange Commission. Novartis is providing the information in this press release as of this date and does not undertake any obligation to update any forward-looking statements contained in this press release as a result of new information, future events or otherwise.

About Novartis

Novartis provides innovative healthcare solutions that address the evolving needs of patients and societies. Headquartered in Basel, Switzerland, Novartis offers a diversified portfolio to best meet these needs: innovative medicines, eye care and cost-saving generic pharmaceuticals. Novartis is the only global company with leading positions in these areas. In 2014, the Group achieved net sales of USD 58.0 billion, while R&D throughout the Group amounted to approximately USD 9.9 billion (USD 9.6 billion excluding impairment and amortization charges). Novartis Group companies employ approximately 120,000 full-time-equivalent associates. Novartis products are available in more than 180 countries around the world. For more information, please visit <http://www.novartis.com>.

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