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Novartis receives FDA approval of Farydak®, the first HDAC inhibitor for patients with multiple myeloma

- *Farydak, an HDAC inhibitor with epigenetic activity, approved in combination for patients who received at least two prior regimens including bortezomib and IMiD*[1]
- *Farydak prolonged median PFS benefit when used with bortezomib and dexamethasone combination versus combination alone (from 6 to 11 months)*[1]
- *Multiple myeloma is an incurable blood cancer and there is an urgent need for new treatments*[2]
- *Farydak is approved under FDA's accelerated approval program; regulatory applications are underway in the EU, Japan and worldwide*

East Hanover, N.J., February 23, 2015 – Novartis announced today that the US Food and Drug Administration (FDA) has approved Farydak® (panobinostat, previously known as LBH589) capsules 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 immunomodulatory (IMiD) agent[1].

"Farydak represents an exciting agent with a new mechanism of action that is part of a promising class of drugs in this setting," said study investigator Paul Richardson, MD, Clinical Program Leader and Director of Clinical Research, Jerome Lipper Multiple Myeloma Center at Dana-Farber Cancer Institute. "Importantly, Farydak has been shown to improve progression-free survival in relapsed multiple myeloma patients who have received at least two prior regimens, including bortezomib and an IMiD, which is an area of particular unmet medical need."

Farydak has been shown to extend the progression-free survival (PFS) benefit of the standard-of-care therapy in this patient population[1]. Farydak is approved under accelerated approval based on PFS[1]. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials. The FDA's accelerated approval program gives patients access to treatments for serious or life-threatening illnesses that provide meaningful therapeutic benefit over existing treatments. The FDA has approved a risk evaluation and mitigation strategy (REMS) for Farydak. The REMS program serves to inform and educate healthcare professionals about the risks that may be associated with Farydak treatment.

This FDA approval is based on efficacy and safety data in a pre-specified subgroup analysis of 193 patients who had received prior treatment with both bortezomib and an IMiD during the Phase III, randomized, double-blind, placebo-controlled, multicenter global registration trial, called PANORAMA-1 (PANobinostat ORAl in Multiple MyelomA)[1]. The trial found that the median PFS benefit increased in Farydak patients who had received prior treatment with both bortezomib and an IMiD (10.6 months; n=94), as

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

compared to the placebo arm (5.8 months; n=99) (hazard ratio=0.52 [95% confidence interval (CI): 0.36, 0.76])[1].

The most common adverse reactions (incidence ≥ 20%) in clinical studies are diarrhea, fatigue, nausea, peripheral edema, decreased appetite, pyrexia and vomiting[1]. The most common non-hematologic laboratory abnormalities (incidence ≥ 40%) are hypophosphatemia, hypokalemia, hyponatremia and increased creatinine[1]. The most common hematologic laboratory abnormalities (incidence ≥ 60%) are thrombocytopenia, lymphopenia, leukopenia, neutropenia and anemia[1]. Farydak can cause fatal and serious toxicities including severe diarrhea and cardiac toxicities. Severe diarrhea occurred in 25% of Farydak-treated patients. Severe and fatal cardiac ischemic events, including severe arrhythmias and ECG changes have occurred in patients receiving Farydak. Serious adverse events (SAEs) occurred in 60% of patients treated with Farydak, bortezomib and dexamethasone compared to 42% of patients in the control arm. The most frequent (≥ 5%) treatment-emergent SAEs reported for patients treated with Farydak were pneumonia (18%), diarrhea (11%), thrombocytopenia (7%), fatigue (6%) and sepsis (6%). Additional serious adverse reactions included hemorrhage, myelosuppression, infections, hepatotoxicity and embryo-fetal toxicity[1].

“Novartis is committed to developing innovative first-in-class therapies for patients who need treatment options,” said Bruno Strigini, President, Novartis Oncology. “Farydak represents a new drug class in multiple myeloma, providing these patients with an important treatment approach for this difficult-to-treat cancer.”

Farydak is the first histone deacetylase (HDAC) inhibitor available to patients with multiple myeloma[3]. As an HDAC inhibitor, its epigenetic activity may help to restore cell function in multiple myeloma[4].

Additional regulatory submissions for Farydak are being reviewed by health authorities worldwide.

About multiple myeloma

Epigenetics is the cell programming that governs gene expression and cell development[3]. In multiple myeloma, the normal epigenetic process is disrupted (also called epigenetic dysregulation) resulting in the growth of cancerous plasma cells, potential resistance to current treatment, and ultimately disease progression[5,6].

Multiple myeloma impacts approximately 81,000 people in the United States[2]. 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 normally[7]. Multiple myeloma is an incurable disease with a high rate of relapse (when the cancer returns) and resistance (when the therapy stops working), despite currently available treatments[2]. It typically occurs in individuals 60 years of age or older, with few cases in individuals younger than 40[8].

Farydak® Important Safety Information

Farydak can cause serious side effects, including diarrhea and heart problems.

Diarrhea is common with Farydak and can be severe. Patients should tell their healthcare provider (HCP) right away if they have abdominal (stomach) cramps, loose stool, diarrhea, or feel like they are becoming dehydrated. HCPs may prescribe medicines to help prevent or treat these side effects. Taking or using stool softeners or laxative medicines may worsen diarrhea, patients should talk to their HCP before taking or using these medicines.

Farydak can cause severe heart problems which can lead to death. Risk of heart problems may be increased with a condition called “long QT syndrome” or other heart problems. Patients should call their HCP and get emergency medical help right away if they have any of the following symptoms of heart problems: chest pain, faster or slower heart beat, palpitations (feel like heart is racing), feel lightheaded or faint, dizziness, blue colored lips, shortness of breath, or swelling in legs.

Farydak can cause severe bleeding which can lead to death. It may take patients longer than usual to stop bleeding while taking Farydak. Patients should tell their HCP right away if they get any of the following signs of bleeding: blood in stools or black stools (look like tar), pink or brown urine, unexpected bleeding or bleeding that is severe or that cannot be controlled, vomit blood or vomit looks like coffee grounds, cough up blood or blood clots, increased bruising, feeling dizzy or weak, confusion, change in speech, or headache that lasts a long time.

Farydak is a prescription medicine used, in combination with bortezomib and dexamethasone, to treat people with a type of cancer called multiple myeloma after at least two other types of treatment have been tried. It is not known if Farydak is safe and effective in children.

Patients should tell their HCP about all of the medicines they take, including prescription and over-the-counter medicines, vitamins and herbal supplements.

Patients should take Farydak exactly as the HCP tells them to take it. The HCP will tell patients how much Farydak to take and when to take it. The HCP may change the dose or stop treatment temporarily if patients experience side effects. Patients should not change the dose or stop taking Farydak without first talking with their HCP.

Patients should avoid eating star fruit, pomegranate or pomegranate juice, and grapefruit or grapefruit juice while taking Farydak. These foods may affect the amount of Farydak in the blood.

Low blood cell counts are common with Farydak and can be severe. Low platelet count (thrombocytopenia) can cause unusual bleeding or bruising under the skin. Low white blood cell count (neutropenia) can cause infections. Low red blood cell count (anemia) may make a patient feel weak, tired, or they may get tired easily, look pale, or feel short of breath.

There is an increased risk of infection while taking Farydak. Patients should contact their HCP right away if they have a fever or have any signs of an infection including sweats or chills, cough, flu-like symptoms, shortness of breath, blood in phlegm, sores on body, warm or painful areas on body, or feeling very tired.

Patients should call their HCP right away with any of the following symptoms of liver problems: feel tired or weak, loss of appetite, dark amber colored urine, upper abdominal pain, yellowing of skin or the white of eyes.

The most common side effects of Farydak include tiredness, nausea, swelling in arms or legs, decreased appetite, fever and vomiting. Patients should tell their HCP if they have any side effect that is bothersome or that does not go away.

Please see full Prescribing Information, including Boxed WARNING, for Farydak® (panobinostat) capsules, at
http://www.pharma.us.novartis.com/info/products/brands/Farydak.jsp.

Outside of the US, Farydak (LBH589) is an investigational agent and has not been approved by regulatory authorities.

Disclaimer

The foregoing release contains forward-looking statements that can be identified by words such as “underway,” “exciting,” “promising,” “committed,” “being reviewed,” “may,” “contingent,” “investigational,” 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 Pharmaceuticals Corporation researches, develops, manufactures and markets innovative prescription drugs used to treat a number of diseases and conditions, including cardiovascular, dermatological, central nervous system, bone disease, cancer, organ transplantation, psychiatry, infectious disease and respiratory. The company's mission is to improve people's lives by pioneering novel healthcare solutions.

Located in East Hanover, New Jersey, Novartis Pharmaceuticals Corporation is an affiliate of Novartis AG, which 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, cost-saving generic pharmaceuticals, preventive vaccines and over-the-counter products. Novartis is the only global company with leading positions in these areas. In 2014, the Group achieved net sales of USD 58 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 130,000 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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