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Novartis data at EHA show increased PFS benefit of Farydak® in new subgroup of patients with previously treated multiple myeloma

- *Panobinostat combination more than doubled median PFS benefit by 7.8 months in patients who received ≥2 prior lines of therapy, including bortezomib and IMiD[1]*
- *Multiple myeloma is an incurable cancer of the plasma cells, a type of white blood cell in the bone marrow; impacts about 1 to 5 in every 100,000 people globally[2,3]*
- *Farydak received FDA approval in February and is the first HDAC inhibitor with epigenetic activity for patients with previously treated multiple myeloma[4,5]*

Basel, June 12, 2015 – Novartis today presented results from a pivotal Phase III clinical trial exploratory subgroup analysis showing a 7.8-month improvement in median progression-free survival (PFS) when using Farydak® (panobinostat, previously known as LBH589) in combination with bortezomib* and dexamethasone in patients with relapsed or relapsed and refractory multiple myeloma who had received two or more prior regimens, including bortezomib and an immunomodulatory agent (IMiD)[1]. Findings are being presented in an oral session at the 20th Congress of the European Hematology Association (EHA) in Vienna.

"I am encouraged by these results because they show that therapy with Farydak, in combination with bortezomib and dexamethasone, translates into a meaningful prolongation in progression-free survival (by 7.8 months) for multiple myeloma patients previously treated with IMiDs and bortezomib who received 2 or more prior regimens," said study investigator Jesús San Miguel, MD, Director of Clinical and Translational Medicine, Clínica Universidad de Navarra, Pamplona, Spain. "These data also provide physicians with a better understanding of the clinical use of Farydak, a histone deacetylase inhibitor, a promising new drug class for this difficult-to-treat patient population with a high unmet need."

These data are from a subgroup analysis of 147 patients with relapsed or relapsed and refractory multiple myeloma who had received two or more prior regimens, including bortezomib and an IMiD, in the Phase III, randomized, double-blind, placebo-controlled, multicenter global registration trial called PANORAMA-1 (PANobinostat ORAl in Multiple MyelomA). This subgroup excluded patients who received only one prior regimen. The analysis showed that in this subgroup, median PFS increased to 12.5 months in the panobinostat-treatment arm compared to 4.7 months in the placebo plus bortezomib and dexamethasone arm (hazard ratio=0.47 [95% confidence interval (CI), 0.31-0.72]). Treatment with panobinostat in combination with bortezomib and dexamethasone when compared to the placebo arm also led to an increase in complete/near complete response rates (21.9% versus 8.1%) and overall response rate (58.9% versus 39.2%)[1].

Common grade 3/4 non-hematologic adverse events (AEs) in the panobinostat-treatment arm compared to the placebo arm for this subgroup included diarrhea (33.3% versus 15.1%), asthenia/fatigue (26.4% versus 13.7%) and peripheral neuropathy (16.7%

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

versus 6.8%). The most common grade 3/4 hematologic laboratory abnormalities in the panobinostat-treatment arm compared to the placebo arm were thrombocytopenia (68.1% versus 44.4%), lymphopenia (48.6% versus 49.3%) and neutropenia (40.3% versus 16.4%). The percentage of on-treatment deaths in the panobinostat-treatment arm compared to the placebo arm in this subgroup was similar (6.9% versus 6.8%)[1].

“These findings, which follow the recent FDA approval of Farydak, provide clinicians with additional evidence on the value of this new treatment to help optimize the management of multiple myeloma," said Bruno Strigini, President, Novartis Oncology. “Multiple myeloma is often complicated because patients who stop responding or become resistant to therapies have limited treatment options. Therefore, these patients may benefit from therapies like Farydak.”

Panobinostat, in combination with bortezomib and dexamethasone, was approved as Farydak by the US Food and Drug Administration (FDA) in February 2015 for the treatment of patients with multiple myeloma who have received at least two prior regimens, including bortezomib and an IMiD[4]. This indication is approved under accelerated approval based on PFS reported in a separate analysis of 193 patients in the PANORAMA-1 trial. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials. 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. Farydak is the first histone deacetylase (HDAC) inhibitor available to patients with multiple myeloma[5]. As an HDAC inhibitor, its epigenetic activity may help to restore cell function in multiple myeloma[6].

About PANORAMA-1 subgroup analysis

PANORAMA-1 (PANobinostat ORAl in Multiple MyelomA) is a Phase III, randomized, double-blind, placebo-controlled, multicenter global registration trial of 768 patients in 215 clinical trial sites evaluating panobinostat in combination with bortezomib and dexamethasone against placebo plus bortezomib and dexamethasone in patients with relapsed or relapsed and refractory multiple myeloma. In the exploratory study presented at EHA, a subgroup of 147 patients with relapsed or relapsed and refractory multiple myeloma who received two or more prior regimens, including bortezomib and an IMiD, were analyzed for outcomes and safety. This subgroup excluded patients who received only one prior regimen[1].

The primary endpoint of the trial was PFS. Data on overall survival, the key secondary endpoint of the trial, are not yet mature. Other secondary endpoints include overall response rate, duration of response, and safety[1].

About multiple myeloma

Epigenetics is the cell programming that governs gene expression and cell development[5]. 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[7,8].

Multiple myeloma impacts approximately 1 to 5 in every 100,000 people globally[3]. 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[9]. 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[10].

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

Farydak has been approved for use in the US and Chile; elsewhere, 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 "encouraged," "promising," "may," "contingent," "investigational," or similar terms, or by express or implied discussions regarding potential new indications or labeling 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 submitted or approved for sale in any additional markets, 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, the uncertainties inherent in research and development, including unexpected clinical trial results and additional analysis of existing clinical data; unexpected regulatory actions or delays or government regulation generally; 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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