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Novartis Drug Afinitor® Helps Women With Advanced Breast Cancer Live Significantly Longer Without Their Disease Progressing

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- -- Everolimus combined with hormonal therapy more than doubled time without tumor growth and reduced risk of progression by 57% vs hormonal therapy alone(1)
- -- Study shows everolimus significantly enhances benefit from hormonal therapy, representing important advance for women with postmenopausal ER+ breast cancer(1,2)
- -- Worldwide regulatory filings planned by the end of 2011 based on these data, marking the first submission for everolimus in breast cancer

EAST HANOVER, N.J., Sept. 25, 2011 /PRNewswire/ -- A pivotal Phase III study shows Afinitor® (everolimus) tablets plus exemestane, a hormonal therapy, more than doubled the time women lived without tumor growth (progression-free survival; PFS) and significantly reduced the risk of cancer progression by 57% versus exemestane alone in patients with advanced breast cancer(1).

"Everolimus is the first drug to show significant efficacy when combined with hormonal therapy in women with ER+HER2- advanced breast cancer, where there continues to be a critical unmet need," said Herve Hoppenot, President, Novartis Oncology. "The magnitude of benefit seen in these patients, despite their resistance to previous hormonal therapies, shows everolimus represents a potential important new treatment approach."

BOLERO-2 (Breast cancer trials of OraL EveROlimus-2) examined the safety and efficacy of everolimus in combination with exemestane versus exemestane alone in postmenopausal women with ER+HER2- advanced breast cancer who recurred or progressed while on or following previous treatment with hormonal therapies, letrozole or anastrozole(1). Findings from the trial will be presented today during a Presidential Symposium at the 2011 European Multidisciplinary Cancer Congress in Stockholm, Sweden.

At a pre-planned analysis, the trial met its primary endpoint of PFS showing treatment with everolimus improved PFS to 6.9 months compared to 2.8 months (hazard ratio 0.43 [95% confidence interval (CI): 0.35 to 0.54]; p<0.0001) by local investigator assessment. This significant improvement was consistent across all subgroups including number of prior therapies, presence of visceral disease, bone metastases and prior use of chemotherapy(1).

Hormonal therapy remains the cornerstone of treatment for women with advanced breast cancer but most women with metastatic disease do not respond to initial treatment with hormonal therapy, and almost all initial responders develop resistance(2,3). Additionally, life expectancy is significantly shortened due to the worsening of the disease(3).

Everolimus targets mTOR in cancer cells, a protein that acts as an important regulator of tumor cell division, blood vessel growth and cell metabolism(4). Resistance to hormonal therapy in breast cancer has been associated with over-activation of the mTOR pathway(3).

Data from BOLERO-2 support worldwide regulatory submissions, which are planned by the end of 2011.

Additional data from BOLERO-2 will be presented at upcoming medical congresses this year.

Worldwide, there are approximately 220,000 newly diagnosed cases of ER+HER2- advanced breast cancer each year(5,6). Everolimus is also being investigated for the treatment of patients with HER2+ advanced breast cancer(7,8).

About BOLERO-2

BOLERO-2 is a Phase III, randomized, double-blind, placebo-controlled, multicenter study. The trial was conducted at 189 sites worldwide and enrolled 724 patients(1). Patients who met the study criteria were randomized (2:1) to receive either everolimus 10 mg/day orally (n= 485), or placebo, plus oral exemestane 25 mg/day (n=239)(1).

The primary endpoint was PFS based on local investigator radiology assessment. Additional analysis by an independent central radiology review committee showed everolimus extended PFS to 10.6 months compared to 4.1 months (hazard ratio 0.36; [95% CI: 0.27 to 0.47]; p<0.0001). Other endpoints include overall survival, overall response rate, safety, patient reported outcome, clinical benefit rate and changes in markers of bone metabolism(1). These data are being evaluated and will be submitted for publication or presentation in a peer-reviewed forum.

The side effects observed were consistent with those previously reported with everolimus with the most common grade 3 or 4 adverse events including stomatitis (7.7%), anemia (5.8%), dyspnea (3.9%), hyperglycemia (4.3%), fatigue (3.7%), non-infectious pneumonitis (3.1%) and increase in liver enzymes (3.1%) (1).

About everolimus

In the US, Afinitor® (everolimus) tablets is approved for the treatment of progressive neuroendocrine tumors of pancreatic origin (pNET) in patients with unresectable, locally advanced or metastatic disease and for the treatment of patients with advanced renal cell carcinoma (RCC) after failure of treatment with sunitinib or sorafenib. The US Food and Drug Administration (FDA) determined that the safety and effectiveness of Afinitor in the treatment of patients with carcinoid tumors have not been established.

Afinitor is also approved in the US to treat patients with SEGA associated with TS who require therapeutic intervention but are not candidates for curative surgical resection. The effectiveness of everolimus is based on an analysis of change in SEGA volume. Clinical benefit such as improvement in disease-related symptoms or increase in overall survival has not been shown.

In the US, everolimus is available from Novartis in different dosage strengths and for different uses in non-oncology patient populations under the trade name Zortress®. Everolimus is exclusively licensed to Abbott and sublicensed to Boston Scientific for use in drug-eluting stents.

Not all indications are available in every country. Access to everolimus outside of the approved indications has been carefully controlled and monitored in clinical trials designed to better understand the potential benefits and risks of the compound. As an investigational compound, the safety and efficacy profile of everolimus has not yet been established outside the approved indications. Because of the uncertainty of clinical trials, there is no guarantee that everolimus will become commercially available for additional indications anywhere else in the world.

Important Safety Information for Afinitor (everolimus) tablets

Patients should not take Afinitor if they are allergic to Afinitor or to any of its ingredients. Patients should tell

their healthcare provider before taking Afinitor if they are allergic to sirolimus (Rapamune®#) or temsirolimus (Torisel®#).

Afinitor can cause serious side effects including lung or breathing problems, infections and kidney failure, which can lead to death. If patients experience these serious side effects, they may need to stop taking Afinitor for a while or use a lower dose. Patients should tell their healthcare provider right away if they have any of these symptoms: new or worsening cough, shortness of breath, chest pain, difficulty breathing or wheezing.

Afinitor may make patients more likely to develop an infection, such as pneumonia, or a bacterial, fungal or viral infection. Viral infections may include reactivation of hepatitis B in people who have had hepatitis B in the past. In some people these infections may be severe, and can even lead to death. Patients may need to be treated as soon as possible. Patients should tell their healthcare provider right away if they have a temperature of 100.5 degrees F or above, chills or do not feel well. Symptoms of hepatitis B or infection may include the following: fever, skin rash, joint pain and inflammation, tiredness, loss of appetite, nausea, pale stool or dark urine, yellowing of the skin or pain in the upper right side.

Afinitor can cause mouth ulcers and sores, which are the most frequently occurring side effects occurring in approximately 44%-70% advanced kidney cancer and advanced pancreatic NET patients taking Afinitor. Eighty-six percent of patients taking Afinitor for SEGA developed mouth ulcers/sores. Patients should tell their healthcare provider if they have pain, discomfort or open sores in their mouth. Their healthcare provider may tell them to use a special mouthwash or mouth gel that does not contain alcohol or peroxide.

Afinitor may cause kidney failure. In some people this may be severe and can even lead to death. Patients should have tests to check their kidney function before and during their treatment with Afinitor.

Patients will have regular blood tests before they start and as needed during their treatment with Afinitor. These tests will include tests to check the patient's blood cell count, kidney and liver function and blood sugar levels. Patients who receive Afinitor for the treatment of SEGA will need regular blood tests to measure how much Afinitor is in their blood since this will help their doctor decide how much Afinitor they need to take.

Afinitor may affect the way other medicines work, and other medicines can affect how Afinitor works. Using Afinitor with other medicines can cause serious side effects. Patients should tell their healthcare provider about all of the medicines they take, including prescription and non-prescription medicines, vitamins and herbal supplements such as: St. John's Wort, and medicine for fungal infections, bacterial infections, tuberculosis, seizures, HIV-AIDS, heart conditions or high blood pressure and medicines that suppress their immune system. Patients should not drink grapefruit juice or eat grapefruit during their treatment with Afinitor as it may make the amount of Afinitor in their blood increase to a harmful level.

Patients should not take Afinitor tablets which are broken or crushed. Patients should not chew or crush the tablets.

The amount of Afinitor in the blood was increased in patients who had liver problems. Patients should tell their healthcare provider about all their medical conditions, including if they have or have had liver problems, diabetes or high blood sugar, high cholesterol levels, infections, hepatitis B or other medical conditions.

Patients should tell their healthcare provider if they are scheduled to receive any vaccinations. Patients should not receive a live vaccine or be around people who have recently received a live vaccine during treatment with Afinitor.

It is not known if Afinitor will harm an unborn baby. Women should use effective birth control while using Afinitor and for eight weeks after stopping treatment.

Common side effects of Afinitor in patients with advanced pancreatic neuroendocrine tumors include mouth ulcers, rash, diarrhea, swelling of arms, hands, feet, ankles, face or other parts of the body, abdominal pain, nausea, fever and headache. Common side effects of Afinitor in patients with advanced kidney cancer include mouth ulcers, infections, feeling weak or tired, cough and diarrhea. Common side effects of Afinitor in patients with SEGA include mouth ulcers, infections of the respiratory tract, sinuses and ears and fever.

Please see full Prescribing Information for Afinitor.

Disclaimer

The foregoing release contains forward-looking statements that can be identified by terminology such as "planned," "will," "potential," "ongoing," or similar expressions, or by express or implied discussions regarding potential new indications or labeling for everolimus or regarding potential future revenues from everolimus. You should not place undue reliance on these statements. Such forward-looking statements reflect the current views of management regarding future events, and involve known and unknown risks, uncertainties and other factors that may cause actual results with everolimus to be materially different from any future results, performance or achievements expressed or implied by such statements. There can be no guarantee that everolimus 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 everolimus will achieve any particular levels of revenue in the future. In particular, management's expectations regarding everolimus could be affected by, among other things, unexpected regulatory actions or delays or government regulation generally; unexpected clinical trial results, including unexpected new clinical data and unexpected additional analysis of existing clinical data; the company's ability to obtain or maintain patent or other proprietary intellectual property protection; government, industry and general public pricing pressures; competition in general; the impact that the foregoing factors could have on the values attributed to the Novartis Group's assets and liabilities as recorded in the Group's consolidated balance sheet, and other risks and factors referred to in Novartis AG's current Form 20-F on file with the US Securities and Exchange Commission. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual results may vary materially from those anticipated, believed, estimated or expected. 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

Located in East Hanover, New Jersey, Novartis Pharmaceuticals Corporation is an affiliate of Novartis AG, which provides healthcare solutions that address the evolving needs of patients and societies. Focused solely on healthcare, Novartis offers a diversified portfolio to best meet these needs: innovative medicines, eye care, cost-saving generic pharmaceuticals, consumer health products, preventive vaccines and diagnostic tools. Novartis is the only company with leading positions in these areas. In 2010, the Group's continuing operations achieved net sales of USD 50.6 billion, while approximately USD 9.1 billion (USD 8.1 billion excluding impairment and amortization charges) was invested in R&D throughout the Group. Headquartered in Basel, Switzerland, Novartis Group companies employ approximately 121,000 full-time-equivalent associates and operate in more than 140 countries around the world. For more information, please visit http://www.us.novartis.com.

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