Novartis Oncology

_A History of Commitment to Breast Cancer_

For more than 20 years, Novartis Oncology has helped pave the way for significant advances in the treatment of patients with breast cancer. The company’s research priorities are determined by patient need and disease understanding. Novartis Oncology’s research strategy is to identify the structure of a tumor and the molecular pathways of the disease to develop targeted medicines that address the unmet medical needs of patients.

Novartis Oncology has advanced the treatment of patients with breast cancer across the disease continuum. In addition to developing medicines that are specifically aimed at breast cancer, Novartis is a leader in seeking to improve outcomes for cancer patients, having brought to market the first medical therapy for the treatment of patients with bone complications associated with advanced malignancies, Aredia® (pamidronate disodium), more than 20 years ago.

Since then, Novartis Oncology has a proven track record of discovering and developing therapies that aim to change the way patients live with various types of cancer. The company’s commitment to breast cancer patients is demonstrated by Femara® (letrozole), Zometa® (zoledronic acid) and Afinitor® (everolimus).

Importantly, open collaborations with research organizations and advocacy groups broaden the scope of the company’s research capabilities and enable us to better understand patient needs and barriers to treatment success to ensure patients have both information and resources to help them better manage their disease.

**Product Portfolio**

Femara is an aromatase inhibitor (AI) used to treat postmenopausal women with hormone-sensitive breast cancer and is the only AI approved for both post-surgery (adjuvant) use and following completion of five years of tamoxifen therapy (extended adjuvant) in postmenopausal women with hormone-sensitive early breast cancer. Femara binds to the aromatase enzyme, blocking the conversion of androgen to estrogen, thereby reducing the amount of estrogen in the body and reducing tumor growth.

Zometa is approved in more than 100 countries (including the member states of the European Union and United States) for the reduction or delay of bone complications in multiple myeloma and across a broad range of metastatic cancers (breast, prostate, lung and other solid tumors) involving bone. In addition, Zometa is indicated to treat hypercalcemia of malignancy (HCM). The efficacy and tolerability profile of Zometa has been established in more than 140 complete or active studies, and through real world use in treating over 4 million patients worldwide.

Afinitor is approved in the EU for the treatment of hormone receptor-positive (HR+), HER2/neu-negative (HER2-) advanced breast cancer (HR+ advanced breast cancer), in combination with exemestane, in postmenopausal women without symptomatic visceral disease after recurrence or progression following a non-steroidal aromatase inhibitor, and it is under regulatory review by additional health authorities worldwide. Afinitor targets the mTOR pathway, which is hyperactivated in many types of cancer cells. mTOR is a protein that acts as an important regulator of tumor cell division, blood vessel growth and cell metabolism. Therapeutic resistance has also been associated with overactivation of the PI3K/AKT/mTOR pathway.

**Pipeline**

Novartis continues to support ongoing investigational trials evaluating Zometa in early breast cancer, and is also researching Afinitor in Phase III trials to evaluate its potential to treat additional advanced breast cancer patient populations, including:
BOLERO-1: a Phase III, randomized, double-blind study of everolimus plus trastuzumab and paclitaxel as a first-line therapy in women with HER2+ advanced breast cancer regardless of ER status. This clinical trial has completed enrollment.

BOLERO-3: a Phase III, randomized, double-blind study of everolimus plus trastuzumab and vinorelbine in women with HER2+ advanced breast cancer previously treated with a taxane and resistant to trastuzumab. This clinical trial has completed enrollment.

Because of the uncertainty of clinical trials, there is no guarantee that everolimus will be approved for use in any of these patient populations.

In addition, the Novartis Oncology pipeline includes several molecular entities with different mechanisms of action targeting pathways – such as mTOR and PI3K – that are involved in the development of multiple tumor types, including breast cancer. These investigational compounds include:

- BEZ235, a dual mTOR/PI3K inhibitor
- Dovitinib (TKI258), a vascular endothelial growth factor receptor and fibroblast growth factor receptor (FGFR) inhibitor
- BKM120, a selective PI3K inhibitor
- AUY922, heat short protein (HSP) 90 inhibitor

Because of the uncertainty of clinical trials, there is no guarantee that any of these compounds will become commercially available.

Access to Medicines
Novartis focuses on improving access to treatments globally. In 2010, Novartis’ access-to-medicine programs, valued at USD 1.5 billion, reached more than 85 million patients around the world.

Novartis Oncology Access programs take a partnership-based approach through locally-tailored patient-centric models. Novartis has created groundbreaking access programs through partnerships with the World Health Organization, other procurement agencies and nongovernmental organizations. Novartis offers discounts and assistance programs to qualifying patients who lack medical insurance or cannot afford treatment.

About Novartis
Novartis 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.novartis.com.

Novartis is on Twitter. Sign up to follow @Novartis at http://twitter.com/novartis.

# # #
About Femara
Femara is a once-daily oral aromatase inhibitor available in more than 100 countries, including the US, major European countries and Japan. It is approved for a number of indications:

- Adjuvant treatment of postmenopausal women with hormone receptor-positive early breast cancer*
- Extended adjuvant treatment of hormone-dependent early breast cancer in postmenopausal women who have had prior standard adjuvant tamoxifen therapy for five years**
- First-line treatment in postmenopausal women with hormone-dependent advanced breast cancer
- Advanced breast cancer in women with natural or artificially induced postmenopausal status after relapse or disease progression who have been treated with antiestrogens
- Pre-operative therapy in postmenopausal women with localized hormone receptor-positive breast cancer which allows subsequent breast-conserving surgery in patients not originally considered suitable for this type of surgery

* Femara is also approved as neo-adjuvant (pre-operative) therapy in Japan, and in some countries for patients with metastatic disease.

** Not all indications are approved in every country.

Important Safety Information about Femara
Femara should not be taken by women who have previously had any unusual or allergic reactions to letrozole or any of its ingredients. Femara should not be taken by women who are pregnant or breastfeeding. Only women who are of postmenopausal endocrine status should take Femara. Patients with severe liver impairment should be monitored closely. The use of Femara in patients with significantly impaired kidney function warrants careful consideration.

The most frequent adverse reactions of Femara are hot flushes, nausea, fatigue and arthralgia. Other common side effects are anorexia, appetite increase, peripheral oedema, headache, dizziness, malaise, vomiting, dyspepsia, constipation, diarrhea, alopecia, increased sweating, rash, myalgia, bone pain, osteoporosis, bone fractures, weight increase, hypercholesterolemia and depression. Other rare, but potentially serious adverse events include leukopenia, cataract, cerebrovascular accident or infarction, thrombophlebitis, pulmonary embolism, arterial thrombosis, general oedema, ischemic cardiovascular disease, angioedema, anaphylactic reaction, hepatitis, toxic epidermal necrolysis and erythema multiforme.

About Zometa (zoledronic acid)
Zometa (zoledronic acid) Injection is indicated for the prevention of skeletal-related events (pathological fractures, spinal compression, radiation or surgery to bone, or tumor-induced hypercalcemia) in patients with multiple myeloma and advanced malignancies involving bone. Zometa, a potent third generation bisphosphonate, is the only bisphosphonate with demonstrated efficacy in reducing or delaying bone complications in multiple myeloma and across a broad range of tumor types such as breast, prostate, lung and renal cell cancers in patients with metastatic disease when administered monthly, as well as in the treatment of hypercalcemia of malignancy (HCM). Zometa is administered to patients as a 4 mg, 15-minute infusion.

Important Safety Information about Zometa
Zometa has been associated with reports of renal insufficiency. Patients should be adequately rehydrated and have their serum creatinine assessed prior to receiving each dose of Zometa. Due to the risk of clinically significant deterioration in renal function, single doses of Zometa should not exceed 4 mg and the duration of infusion should be no less than
15 minutes in 100 ml of diluent. The risk of renal adverse events may be greater in patients with renal insufficiency. Zometa is not recommended for treatment of patients with severe renal impairment. Severe and occasionally incapacitating bone, joint, and/or muscle pain has been reported in patients taking bisphosphonates including Zometa. Caution is advised when Zometa is used in aspirin-sensitive patients, or with aminoglycosides, loop diuretics and other potentially nephrotoxic drugs. Zometa contains the same active ingredient (zoledronic acid) as found in Aclasta. Patients being treated with Zometa should not be treated with Aclasta concomitantly. Zometa should not be used in patients who are pregnant, or plan to become pregnant, or who are breast-feeding.

In clinical trials, the most commonly reported adverse events included flu-like syndrome (fever, arthralgias, myalgias, skeletal pain), fatigue, gastrointestinal reactions, anemia, weakness, cough, dyspnea and edema. Zometa should not be used during pregnancy. Zometa is contraindicated in patients with clinically significant hypersensitivity to zoledronic acid or other bisphosphonates, or any of the excipients in the formulation of Zometa.

Osteonecrosis of the Jaw (ONJ): ONJ has been reported in patients with cancer receiving treatment including bisphosphonates, chemotherapy, and/or corticosteroids. The majority of reported cases have been associated with dental procedures such as tooth extraction. A dental examination with appropriate preventive dentistry should be considered prior to treatment with bisphosphonates in patients with concomitant risk factors. While on treatment, these patients should avoid invasive dental procedures if possible. No data are available to suggest whether discontinuation of bisphosphonate therapy reduces the risk of ONJ in patients requiring dental procedures. A causal relationship between bisphosphonate use and ONJ has not been established.

Please see full Prescribing Information. Approved indications vary by country.

About Afinitor (everolimus)
Afinitor® (everolimus) tablets is approved in more than 80 countries including the United States and throughout the European Union in the oncology settings of advanced renal cell carcinoma following progression on or after vascular endothelial growth factor (VEGF)-targeted therapy, and in the United States and European Union for locally advanced, metastatic or unresectable progressive neuroendocrine tumors of pancreatic origin.

Everolimus is also available from Novartis for use in non-oncology patient populations under the brand names Afinitor® or Votubia®, Certican® and Zortress® and is exclusively licensed to Abbott and sublicensed to Boston Scientific for use in drug-eluting stents.

Indications vary by country and not all indications are available in every country. 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.

Afinitor® Important Safety Information
Afinitor®/Votubia® can cause serious side effects including lung or breathing problems, infections, and renal failure, which can lead to death. Mouth ulcers and mouth sores are common side effects. Afinitor/Votubia can affect blood cell counts, kidney and liver function, and blood sugar and cholesterol levels. Afinitor/Votubia may cause fetal harm in pregnant women. Highly effective contraception is recommended for women of child-bearing potential while receiving Afinitor/Votubia and for up to eight weeks after ending treatment. Women taking Afinitor/Votubia should not breast feed.

The most common adverse drug reactions (incidence ≥15 %) are mouth ulcers, diarrhea, feeling weak or tired, skin problems (such as rash or acne), infections, nausea, swelling of

G-AFI-1046311 7/12
extremities or other parts of the body, loss of appetite, headache, inflammation of lung tissue, abnormal taste, nose bleeds, inflammation of the lining of the digestive system, weight decreased and vomiting. The most common Grade 3-4 adverse drug reactions (incidence ≥2 %) are mouth ulcers, feeling tired, low white blood cells (a type of blood cell that fights infection), diarrhea, infections, inflammation of lung tissue, diabetes and amenorrhea. Cases of hepatitis B reactivation and blood clots in the lung and leg have been reported.

Please see full Prescribing Information. Approved indications vary by country.

# # #