FDA approves Novartis drug Odomzo® (sonidegib) for locally advanced basal cell carcinoma (laBCC), a form of skin cancer

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- - Approval is based on pivotal Phase II study in which objective response rate (ORR) in patients with laBCC was 58%; responses were durable(1)
- - Basal cell carcinoma, the most common form of skin cancer, can be highly disfiguring at advanced stages(2)
- - Odomzo adds to company's expanding portfolio of targeted treatments for skin cancer

EAST HANOVER, N.J., July 24, 2015 /PRNewswire/ -- Novartis today announced the US Food and Drug Administration (FDA) has approved Odomzo® (sonidegib, formerly LDE225) 200 mg capsules for the treatment of adult patients with locally advanced basal cell carcinoma (laBCC) that has recurred following surgery or radiation therapy, or those who are not candidates for surgery or radiation therapy.

"The FDA approval of Odomzo offers a new and non-invasive treatment option for a potentially devastating disease that is hard to treat and can be disfiguring," said Bruno Strigini, President, Novartis Oncology. "Odomzo is an important addition to our growing portfolio of targeted treatments for advanced skin cancers and underscores our commitment to developing and bringing to market new options for patients."

The Odomzo approval was based on the demonstration of a durable objective response rate (ORR) in an international, multi-center, double-blind, randomized, two-arm, non-comparative trial in patients with laBCC not amenable to local therapy or metastatic basal cell carcinoma (mBCC).[1]

Patients with laBCC treated with Odomzo 200 mg (n=66) were followed for at least 12 months unless discontinued earlier. The ORR was 58% (95% confidence interval: 45, 70), consisting of 5% (n=3) complete responses (CR) and 53% (n=35) partial responses (PR). A pre-specified sensitivity analysis using an alternative definition for CR, defined as at least a PR according to MRI and/or photography and no evidence of tumor on biopsy of residual lesion, yielded a CR rate of 20%.[1] Among the 38 patients with an objective response, 31 patients (82%) have ongoing responses ranging from at least 1.9 to 18.6 months and the median duration of response has not been reached.[1]

The most serious risks of Odomzo are embryofetal toxicity and musculoskeletal adverse reactions including rhabdomyolysis. Musculoskeletal adverse reactions, which may be accompanied by serum creatine kinase (CK) elevations, may occur with Odomzo and other drugs which inhibit the hedgehog pathway. The incidence of musculoskeletal adverse reactions in patients with laBCC treated with Odomzo 200 mg was 68%, with 9% reported as grade 3 or 4. Adverse reactions occurring in more than 10% of patients treated with Odomzo 200 mg were muscle spasms, alopecia, dysgeusia, fatigue, nausea, musculoskeletal pain, diarrhea, decreased weight, decreased appetite, myalgia, abdominal pain, headache, pain, vomiting, and pruritus. The most frequent grade 3 and 4 laboratory abnormalities occurring in at least 5% of patients were serum creatine kinase (CK) elevation and lipase elevation.[1]

About the BOLT Clinical Trial

Data from the Phase II, randomized, double-blind multicenter BOLT (Basal cell carcinoma Outcomes in LDE225 Trial) formed the basis of the FDA's approval. The primary endpoint was ORR of patients treated with Odomzo 200 mg and 800 mg, defined as the proportion of patients with confirmed complete or partial tumor response, or shrinkage, as measured by a central review committee. There was no evidence of better ORR among patients with laBCC randomized to receive Odomzo 800 mg daily.[1]

The evaluation of tumor response was based on a composite assessment of modified Response Evaluation Criteria in Solid Tumors (mRECIST) that integrated tumor measurements obtained by radiographic assessments of target lesions (per RECIST 1.1), digital clinical photography (World Health Organization (WHO) adapted criteria), and histopathology assessments (via punch biopsies). All modalities used must have demonstrated absence of tumor to achieve a composite assessment of CR.[1]

Please visit http://www.pharma.us.novartis.com/product/pi/pdf/odomzo.pdf for Odomzo full Prescribing Information.

About Basal Cell Carcinoma

BCC consists of abnormal, uncontrolled growths or lesions that arise in the skin's basal cells, which line the deepest layer of the epidermis (the outermost layer of the skin)[6] and accounts for more than 80% of non-melanoma skin cancers.[7] It occurs most frequently on the head and neck, with the nose being the most common site.[7] BCC that spreads from where it started to nearby tissue is called locally advanced[8] and can be highly disfiguring.[2] Advanced BCC is thought to represent roughly 1–10% of all cases of BCC. [9-11] While BCC is generally diagnosed and treated early, it may recur in an estimated 3% of patients after five years. [12] Although BCC rarely becomes advanced, there have been few treatment options at this stage of the disease. Worldwide incidence of BCC is rising by 10% each year due to factors such as an aging population and increased ultraviolet exposure. Incidence rates are estimated to be between 0.003% and 0.55% worldwide.[13]

About Odomzo

Odomzo (sonidegib, formerly LDE225) is an oral, selective smoothened (SMO) inhibitor approved by the FDA for the treatment of adult patients with locally advanced basal cell carcinoma (laBCC) that has recurred following surgery or radiation therapy, or those who are not candidates for surgery or radiation therapy. [1] SMO is a molecule that regulates the hedgehog (Hh) signaling pathway, which plays a critical role in stem cell maintenance and tissue repair, as well as in advanced basal cell carcinoma[3-5]. Odomzo is currently in clinical development in other diseases.

Odomzo was approved in Switzerland for the treatment of advanced BCC that is not amenable to curative surgery or radiotherapy on June 30, 2015. The CHMP granted a positive opinion on June 25, 2015. Additional regulatory submissions are being reviewed by health authorities worldwide.

IMPORTANT SAFETY INFORMATION

Odomzo can cause a patient's baby to die before it is born (be stillborn) or cause a patient's baby to have severe birth defects.

Females who can become pregnant should talk to their doctor about the risks of Odomzo to their unborn child. Before starting Odomzo females who can become pregnant should have a pregnancy test. Birth control should be used during Odomzo treatment and for at least 20 months after the final dose of Odomzo. Patients should

talk to their doctor right away if they have unprotected sex or think they may be pregnant.

Males taking Odomzo should not donate semen while taking Odomzo and for at least 8 months after their final dose. Also, males taking Odomzo should always use a condom, even if they have had a vasectomy, during sex with a female partner who is pregnant or can become pregnant during treatment with Odomzo and for at least 8 months after their final dose. Patients should talk to their doctor right away if they are taking Odomzo and their partner becomes pregnant or thinks she is pregnant.

Patients should not donate blood or blood products while taking Odomzo or for 20 months after their final dose of Odomzo.

Muscle spasms and muscle pain are common with Odomzo, but can also sometimes be symptoms of serious muscle problems. Odomzo can increase the risk of muscle pain and, rarely a serious condition caused by injury to the muscles (rhabdomyolysis) that can lead to kidney damage. Patients should tell their healthcare provider right away if they develop any new or worsening muscle spasms, pain or tenderness, dark urine, or decreased amount of urine during treatment with Odomzo. Their doctor should do a blood test to check for muscle problems and to check kidney function before starting Odomzo, during treatment, and if muscle problems develop.

Other common side effects of Odomzo include hair loss, change in taste, tiredness, nausea, diarrhea, weight loss, decreased appetite, stomach area (abdominal) pain, headache, vomiting, and itching.

Odomzo can cause absence of menstrual periods (amenorrhea) in females who are able to become pregnant. It is not known if amenorrhea is permanent. Patients should talk to their doctor for concerns about fertility.

Please see full Prescribing Information for Odomzo at:
http://www.pharma.us.novartis.com/product/pi/pdf/odomzo.pdf

Disclaimer

The foregoing release contains forward-looking statements that can be identified by words such as "can," "expanding," "offers," "potentially," "growing," "commitment," "developing," "bringing to market," "in clinical development," "positive opinion," "are being reviewed," or similar terms, or by express or implied discussions regarding potential additional marketing approvals or new indications or labeling for Odomzo, or regarding potential future revenues from Odomzo. 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 Odomzo will be submitted or approved for any additional indications or labeling in any market, or at any particular time. Neither can there be any guarantee that Odomzo will be submitted or approved for sale in any additional markets or at any particular time. Nor can there be any guarantee that Odomzo will be commercially successful in the future, or will achieve any particular level of revenue. In particular, management's expectations regarding Odomzo 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 and reimbursement issues; unexpected safety issues; 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 medicines aimed at improving patients' lives. We offer a broad range of medicines for cancer, cardiovascular disease, endocrine disease, inflammatory disease, infectious disease, neurological disease, organ transplantation, psychiatric disease, respiratory disease and skin conditions. 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 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 150 countries around the world. For more information, please visit http://www.novartis.com.

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