

MEDIA RELEASE • COMMUNIQUE AUX MEDIAS • MEDIENMITTEILUNG**Novartis lung cancer drug Zykadia[®] recommended for EU approval in patients with ALK+ NSCLC previously treated with crizotinib**

- *If approved, Zykadia (ceritinib) would be the first treatment option for patients in Europe with ALK+ NSCLC previously treated with crizotinib*
- *ALK+ NSCLC is driven by a rearrangement of the ALK gene, which is responsible for cancer cell growth in 2-7% of patients with NSCLC¹*
- *Positive CHMP opinion represents a critical milestone for Zykadia; now approved in several countries worldwide, with additional regulatory filings underway*

Basel, February 27, 2015– Novartis announced today that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency adopted a positive opinion for Zykadia[®] (ceritinib) to treat adult patients with anaplastic lymphoma kinase (ALK)-positive advanced non-small cell lung cancer (NSCLC) previously treated with crizotinib². If approved in the European Union (EU), Zykadia will be the first treatment option to address an unmet medical need for patients with ALK+ NSCLC previously treated with crizotinib.

“Patients with advanced ALK+ NSCLC have few options when their cancer does not respond to currently approved therapy,” said Alessandro Riva, MD, Global Head, Novartis Oncology Development and Medical Affairs. “As a leader in the development of precision oncology medicines, Novartis is committed to developing and bringing to market new treatments for patients with ALK+ NSCLC. This positive CHMP opinion for Zykadia brings us one step closer to providing the lung cancer community with new hope in the fight against this terrible disease.”

Each year, there are 1.6 million people diagnosed with lung cancer, the leading cause of cancer death worldwide³. The most common type of lung cancer is NSCLC, accounting for 85-90% of all cases⁴. Of those, 2-7% are driven by a rearrangement of the ALK gene, which increases the growth of cancer cells and can be identified by a molecular test of the cancer tumor¹. Despite significant treatment advances for patients with ALK+ NSCLC, disease progression is often inevitable and more treatment options are needed⁵.

In the EU, the European Commission generally follows the recommendations of the CHMP and delivers its final decision within three months of the CHMP recommendation. The decision will be applicable to all 28 EU member states plus Iceland, Norway and Liechtenstein. Zykadia is currently approved in the United States, Mexico, Chile, South Korea, Guatemala and Ecuador. Additional regulatory reviews are underway in North America, South America, Central America and Asia.

The CHMP recommendation for Zykadia was based on results from two global, multicenter, open-label, single-arm studies (Study A and Study B). Comparative efficacy data from randomized clinical studies are not yet available. The primary efficacy endpoint for these studies was overall response rate (ORR), including complete response and partial response, for patients who were treated with a 750 mg dose of Zykadia, confirmed

by repeat assessments performed not less than four weeks after the criteria for response was first met. Additional evaluations included duration of response (DOR) and progression-free survival (PFS) by investigator and blinded independent review committee (BIRC) assessment, and overall survival (OS). Tumor evaluations were performed according to Response Evaluation Criteria in Solid Tumors (RECIST) 1.0 in Study A and RECIST 1.1 in Study B².

About the Zykadia Clinical Trials

Study A was a Phase I study that included a dose-escalation phase and an expansion phase, at the recommended dose of 750 mg. The study evaluated a total of 246 ALK+ NSCLC patients who were treated with 750 mg of Zykadia: 163 had received prior treatment with an ALK inhibitor and 83 were ALK inhibitor-naïve. In patients who had previously received treatment with an ALK inhibitor, the ORR was 56.4% [95% CI, 48.5-64.2%], the median DOR was 8.3 months [95% CI, 6.8-9.7 months] and the median PFS was 6.9 months [95% CI, 5.6-8.7 months] based on investigator assessment².

Study B was a Phase II study designed to evaluate the efficacy and safety of 750 mg Zykadia in patients with locally advanced or metastatic ALK+ NSCLC. Study B involved 140 patients who had been previously treated with one to three lines of chemotherapy followed by treatment with crizotinib, and who had then progressed on crizotinib².

In Studies A and B, brain metastases at baseline were seen in 60.1% and 71.4% of patients who had received prior treatment with an ALK inhibitor, respectively. The ORR, DOR and PFS (by BIRC assessment) for patients with brain metastases at baseline were similar with those reported for the overall population of these studies².

The most common adverse reactions with an incidence of $\geq 10\%$ were diarrhea, nausea, vomiting, tiredness (fatigue), liver function test abnormalities (require blood test monitoring), abdominal pain, decreased appetite, constipation, rash, kidney function test abnormalities (require blood test monitoring), heartburn and anaemia. Grade 3-4 adverse reactions with an incidence of $\geq 5\%$ were liver function test abnormalities, tiredness (fatigue), diarrhea, nausea and hyperglycemia².

About Zykadia

Zykadia is an oral, selective inhibitor of anaplastic lymphoma kinase (ALK), a gene that can fuse with others to form an abnormal “fusion protein” that promotes the development and growth of certain tumors in cancers including non-small cell lung cancer (NSCLC). Zykadia is currently approved in the United States, Mexico, Chile, South Korea, Guatemala and Ecuador to treat adult patients with ALK+ NSCLC. Additional regulatory reviews are underway in North America, South America, Central America and Asia.

In the European Union, Zykadia (ceritinib) is an investigational agent and has not been approved by regulatory authorities.

Zykadia Important Safety Information

Zykadia may cause serious side effects.

Zykadia causes stomach and intestinal problems in most people, including diarrhea, nausea, vomiting, and stomach-area pain. These problems can be severe. Patients should follow their doctor's instructions about taking medicines to help these symptoms, and should call their doctor for advice if symptoms are severe or do not go away.

Zykadia may cause severe liver injury. Patients should have blood tests prior to the start of treatment with Zykadia, every two weeks for the first month of treatment and monthly thereafter, and should talk to their doctor right away if they experience any of the following symptoms: tiredness (fatigue), itchy skin, yellowing of the skin or the whites of the eyes, nausea or vomiting, decreased appetite, pain on the right side of the abdomen, urine turns dark or brown, bleeding or bruising more easily than normal.

Zykadia may cause severe or life-threatening swelling (inflammation) of the lungs during treatment that can lead to death. Symptoms may be similar to those symptoms from lung cancer. Patients should tell their doctor right away about any new or worsening symptoms, including trouble breathing or shortness of breath, fever, cough, with or without mucous, or chest pain.

Zykadia may cause very slow, very fast, or abnormal heartbeats. Doctors should check their patient's heart during treatment with Zykadia. Patients should tell their doctor right away if they feel new chest pain or discomfort, dizziness or lightheadedness, faint, or have abnormal heartbeats, blue discoloration of lips, shortness of breath, swelling of lower limbs or skin, or if they start to take or have any changes in heart or blood pressure medicines.

Zykadia may cause high level of glucose in the blood. People who have diabetes or glucose intolerance, or who take a corticosteroid medicine have an increased risk of high blood sugar with Zykadia. Patients should have glucose blood tests prior to the start of treatment with Zykadia and during treatment. Patients should follow their doctor's instructions about blood sugar monitoring and call their doctor right away with any symptoms of high blood sugar, including increased thirst and/or urinating often.

Before patients take Zykadia, they should tell their doctor about all medical conditions, including liver problems; diabetes or high blood sugar; heart problems, including a condition called long QT syndrome; if they are pregnant, if they think they may be pregnant, or if they plan to become pregnant; are breastfeeding or plan to breastfeed.

Zykadia may harm unborn babies. Women who are able to become pregnant must use a highly effective method of birth control (contraception) during treatment with Zykadia and up to 3 months after stopping Zykadia. It is not known if Zykadia passes into breast milk. Patients and their doctor should decide whether to take Zykadia or breastfeed, but should not do both.

Patients should tell their doctor about medicines they take, including prescription medicines, over-the-counter medicines, vitamins and herbal supplements. If they take Zykadia whilst using oral contraceptives, the oral contraceptives may become ineffective.

The most common adverse reactions with an incidence of $\geq 10\%$ were diarrhea, nausea, vomiting, tiredness (fatigue), liver function test abnormalities (require blood test monitoring), abdominal pain, decreased appetite, constipation, rash, kidney function test abnormalities (require blood test monitoring), heartburn and anaemia. Grade 3-4 adverse reactions with an incidence of $\geq 5\%$ were liver function test abnormalities, tiredness (fatigue), diarrhea, nausea and hyperglycemia.

Patients should stop taking Zykadia and seek medical help immediately if they experience any of the following, which may be signs of an allergic reaction:

- Difficulty in breathing or swallowing
- Swelling of the face, lips, tongue or throat
- Severe itching of the skin, with a red rash or raised bumps

Patients should tell their doctor of any side effect that bothers them or does not go away. These are not all of the possible side effects of Zykadia. For more information, patients should ask their doctor or pharmacist.

Patients should take Zykadia exactly as their health care provider tells them. Patients should not change their dose or stop taking Zykadia unless their health care provider advises them to. Zykadia should be taken once a day on an empty stomach. Patients should not eat for 2 hours before and 2 hours after taking Zykadia. If a dose of Zykadia is

missed, they should take it as soon as they remember. If their next dose is due within the next 12 hours, they should skip the missed dose and take the next dose at their regular time. They should not take a double dose to make up for a forgotten dose. Patients should not drink grapefruit juice or eat grapefruit during treatment with Zykadia, as it may make the amount of Zykadia in their blood increase to a harmful level. If patients have to vomit after swallowing Zykadia capsules, they should not take more capsules until their next scheduled dose.

Please see full Prescribing Information for Zykadia.

Disclaimer

The foregoing release contains forward-looking statements that can be identified by words such as “recommended,” “would,” “positive CHMP opinion,” “milestone,” “underway,” “positive opinion,” “will,” “can,” “committed,” “one step closer,” “hope,” “generally follows,” “recommendations,” “ongoing,” “investigational,” or similar terms, or by express or implied discussions regarding potential marketing approvals for Zykadia, or regarding potential future revenues from Zykadia. 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 Zykadia will be approved for sale in any market, or submitted for approval in any additional markets, or at any particular time. Neither can there be any guarantee that Zykadia will be commercially successful in the future. In particular, management’s expectations regarding Zykadia 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 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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