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MEDIA RELEASE • COMMUNIQUE AUX MEDIAS • MEDIENMITTEILUNG

Novartis receives positive CHMP opinion for first-line use of Zykadia® in ALK-positive advanced non-small cell lung cancer (NSCLC)

- *Phase III trial, first-line treatment with Zykadia resulted in improved progression-free survival (PFS) over SOC chemotherapy with maintenance, including in patients with brain metastases*[1]

- *Zykadia is currently approved in the European Union (EU) for the treatment of adult patients with ALK-positive advanced NSCLC previously treated with crizotinib*

Basel, May 19, 2017 – Novartis today announced the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) has recommended approval of expanding the use of Zykadia® (ceritinib) to include the first-line treatment of patients with advanced non-small cell lung cancer (NSCLC) whose tumors are anaplastic lymphoma kinase (ALK)-positive. If approved, Zykadia will provide a new treatment option for previously untreated and newly diagnosed patients with ALK-positive advanced NSCLC.

“Novartis is committed to bringing targeted treatment options to more patients living with lung cancer who may benefit from them,” said Bruno Strigini, CEO, Novartis Oncology. “Today, we’ve taken an important step towards fulfilling that commitment with the potential approval of Zykadia as a first-line treatment option for those in the EU diagnosed with ALK-positive advanced NSCLC.”

The positive CHMP opinion was based on results from the ASCEND-4 study, a randomized, open-label, global Phase III trial. The study showed that patients treated with first-line Zykadia experienced a 45% reduction in the risk of disease progression compared to patients treated with standard first-line pemetrexed-platinum chemotherapy with pemetrexed maintenance (hazard ratio [HR] = 0.55 [95% CI: 0.42, 0.73])[1]. The median progression-free survival (PFS) was 16.6 months (95% confidence interval [CI]: 12.6, 27.2) for patients receiving Zykadia compared to 8.1 months (95% CI: 5.8, 11.1) for patients in the chemotherapy arm of the study[1].

Additionally, patients receiving Zykadia without brain metastases at baseline experienced a median PFS of 26.3 months (95% CI: 15.4, 27.7), compared with 8.3 months (95% CI: 6.0, 13.7) among patients treated in the chemotherapy arm (HR = 0.48 [95% CI: 0.33, 0.69])[1]. Among patients with brain metastases at baseline, the median PFS was 10.7 months (95% CI: 8.1, 16.4) in the Zykadia group versus 6.7 months (95% CI: 4.1, 10.6) in the chemotherapy group (HR = 0.70 [95% CI: 0.44, 1.12])[1]. Of these patients, 59% did not receive prior brain radiotherapy[1]. The high intracranial overall response rate (ORR) (72.7% [95% CI: 49.8, 89.3]) was consistent with whole body ORR (72.5% [95% CI: 65.5, 78.7])[1].

The CHMP recommendation will now be reviewed by the European Commission (EC), which holds the authority to approve medicines for the European Union (EU). The EC typically follows the CHMP recommendation and typically issues an approval decision within two

months, applicable to all 28 European Union member states plus Iceland, Lichtenstein, and Norway. Earlier this year, the US Food and Drug Administration (FDA) granted Zykadia Breakthrough Therapy designation for first-line treatment of patients with ALK-positive NSCLC with metastases to the brain. The application for first-line use of Zykadia is under Priority Review by the FDA.

Novartis Commitment to Lung Cancer
Worldwide, lung cancer causes more deaths than colon, breast and prostate cancer combined, and an estimated 1.8 million new cases of lung cancer are diagnosed each year[3,4]. Among patients with NSCLC, roughly 25% have an actionable mutation that may be targeted with available therapies[5-8]. To determine that treatment, medical organizations recommend biomarker testing for patients with lung cancer[9].

Over the past decade, Novartis Oncology's research has supported the evolution of treatment approaches for patients living with mutation-driven types of lung cancer. The company continues its commitment to the global lung cancer community through ongoing studies, as well as the exploration of investigational compounds that target genomic biomarkers in NSCLC.

About ASCEND-4
ASCEND-4 was a Phase III randomized, open-label, multicenter, global clinical trial to evaluate the safety and efficacy of Zykadia compared to standard chemotherapy, including maintenance, in adult patients with Stage IIIB or IV ALK-positive advanced NSCLC who received no prior therapy for their advanced disease. Patients received Zykadia orally at 750 mg/daily or standard pemetrexed-based platinum doublet chemotherapy (pemetrexed 500 mg/m2 plus cisplatin 75 mg/m2 or carboplatin AUC 5-6) for four cycles followed by pemetrexed maintenance.

Of 376 patients, 189 (59 with brain metastases) were randomized to Zykadia and 187 (62 with brain metastases) to chemotherapy. Approximately 60% of patients with baseline brain metastases treated with Zykadia did not have prior radiation therapy, the current standard of treatment for baseline brain metastases.

The most common adverse events (AEs) occurring in more than 25% of Zykadia patients were diarrhea (85% vs. 11% with chemotherapy), nausea (69% vs. 55% with chemotherapy), vomiting (66% vs. 36% with chemotherapy), ALT increase (60% vs. 22% with chemotherapy), AST increase (53% vs. 19% with chemotherapy), GGT increase (37% vs. 10% in chemotherapy), decreased appetite (34% vs. 31% with chemotherapy), blood alkaline phosphate increase (29% vs. 5% with chemotherapy) and fatigue (29% vs. 30% with chemotherapy)[1].

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 over 69 countries worldwide. Please visit www.NovartisOncology.com/news/product-portfolio/zykadia for additional information.

Zykadia Important Safety Information
Zykadia may cause serious side effects.

Zykadia may cause stomach upset and intestinal problems in most patients, 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 three months 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, or 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 levels 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.

Zykadia may cause high levels of pancreatic enzymes in the blood and may cause pancreatitis. Patients should have blood tests prior to the start of treatment with Zykadia and as needed during their treatment with Zykadia. Patients should talk to their doctor if they experience signs and symptoms of pancreatitis which including upper abdominal pain that may spread to the back and get worse with eating.

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 while using oral contraceptives, the oral contraceptives may become ineffective.

The most common adverse reactions with an incidence of ≥10% were diarrhea, nausea, vomiting, liver laboratory test abnormalities (requires blood test monitoring), tiredness (fatigue), abdominal pain, decreased appetite, weight decreased, constipation, kidney laboratory test abnormalities (requires blood test monitoring), rash, anemia and heartburn. Grade 3-4 adverse reactions with an incidence of ≥5% were liver laboratory test abnormalities, tiredness (fatigue), vomiting, hyperglycemia (requires blood test monitoring), nausea and diarrhea.

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 at least 2 hours before and 1 hour 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.

Disclaimer
The foregoing release contains forward-looking statements that can be identified by words such as “positive CHMP opinion,” “recommended,” “will,” “committed,” “may,” “step towards,” “commitment,” “potential,” “recommendation,” “Breakthrough Therapy designation,” “Priority Review,” “ongoing,” “investigational,” or similar terms, or by express or implied discussions regarding potential new indications or labeling 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 submitted or approved for any additional indications or labeling in any market, or at any particular time. Nor 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, the uncertainties inherent in research and development, including clinical trial results and additional analysis of existing clinical data; 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 and reimbursement pressures; safety, quality or 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, cost-saving generic and biosimilar pharmaceuticals and eye care. Novartis has leading positions globally in each of these areas. In 2016, the Group achieved net sales of USD 48.5 billion, while R&D throughout the Group amounted to approximately USD 9.0 billion. Novartis Group companies employ approximately 118,000 full-time-equivalent associates. Novartis products are sold in approximately 155 countries around the world. For more information, please visit http://www.novartis.com.

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