Press Release

FDA Grants Ofev® Breakthrough Therapy Designation for Chronic Fibrosing ILDs with a Progressive Phenotype

- The designation was supported by results from the Phase III INBUILD® study that met its primary endpoint and was recently published in the *New England Journal of Medicine*

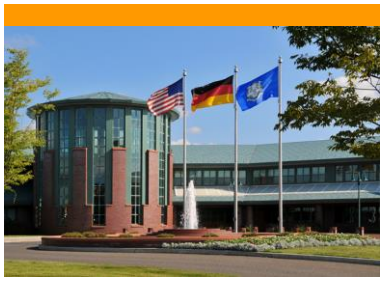
Ridgefield, Conn., October 10, 2019 – Boehringer Ingelheim announced today that the U.S. Food and Drug Administration (FDA) granted Breakthrough Therapy Designation to Ofev® (nintedanib), which is currently under FDA review for the treatment of people with chronic fibrosing interstitial lung diseases (ILDs) with a progressive phenotype. Regulatory applications have been submitted to other regulatory bodies, including the European Medicines Agency.

The Breakthrough Therapy Designation was supported by results from the Phase III INBUILD® study – the first clinical trial of these ILDs that met its primary endpoint and showed nintedanib slowed the rate of ILD progression in patients with a broad range of progressive fibrosing interstitial lung diseases other than idiopathic pulmonary fibrosis (IPF). The results were recently presented at the European Respiratory Society (ERS) International Congress in Madrid and published in the *New England Journal of Medicine*.

Interstitial lung diseases encompass a large group of more than 200 disorders that may lead to pulmonary fibrosis – an irreversible scarring of lung tissue that negatively impacts lung function. When a progressive phenotype is present, a life threatening condition can result that causes difficulty breathing and a decrease in the amount of oxygen the lungs can supply to the body, measured through lung function decline.

"We believe Ofev may help address an unmet medical need by providing a therapy for patients across a spectrum of ILDs with a progressive phenotype," said Thomas Seck, M.D., senior vice president, Medicine and Regulatory Affairs, Boehringer Ingelheim Pharmaceuticals, Inc. "We are encouraged by this Breakthrough Therapy Designation and look forward to working closely with the agency to offer this therapy to patients for which there are no FDA-approved treatment options."

The Breakthrough Therapy Designation process was established by the FDA to expedite the development and review of drugs for serious or life-threatening conditions where preliminary clinical evidence indicate that the therapy may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints. In July 2014, the FDA granted nintedanib Breakthrough Therapy Designation for the



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treatment of people with idiopathic pulmonary fibrosis (IPF) and approved the drug for that use in October 2014.

The efficacy and safety of nintedanib in the treatment of these ILDs has not been established. However, one of the expectations of investigational therapies that have Breakthrough Therapy Designation is that sponsors initiate a program to make the investigational therapy available to appropriate patients through a compassionate use program. BI has a compassionate use protocol that makes nintedanib available to appropriate patients who do not otherwise qualify or are unable to participate in clinical studies.

About INBUILD

INBUILD is the first clinical trial in the field of ILDs to group patients based on the clinical behavior of their disease, rather than the primary clinical diagnosis. The trial was a randomized, double-blind, placebo-controlled, parallel group trial conducted at 153 sites in 15 countries that evaluated the efficacy and safety tolerability of nintedanib (150 mg, 2 x daily) over 52 weeks in patients with progressive fibrosing ILD.

Results showed nintedanib slowed lung function decline by 57% across the overall study population, as assessed by the annual rate of decline in forced vital capacity (FVC) over 52 weeks in patients with fibrosing ILDs with a progressive phenotype. The most common adverse event was diarrhea, reported in 66.9% and 23.9% of patients treated with nintedanib and placebo, respectively, with a safety profile consistent to what has previously been seen in nintedanib.

About the disease

Patients with ILDs can develop a progressive phenotype that causes pulmonary fibrosis, leading to lung function decline, deterioration in quality of life and early mortality similar to IPF, the most frequent form of idiopathic interstitial pneumonias. The course of the disease and the symptoms are similar in progressive fibrosis ILDs regardless of the underlying disease. Chronic hypersensitivity pneumonitis, autoimmune ILDs such as rheumatoid arthritis-associated ILD, systemic sclerosis-associated ILD (SSc-ILD), mixed connective tissue disease-associated ILD, sarcoidosis and idiopathic forms of interstitial pneumonias, i.e. non-specific interstitial pneumonia, and unclassified idiopathic interstitial pneumonia are among these diseases.

About Ofev

Ofev is already approved in the U.S. and more than 70 countries for the treatment of patients living with idiopathic pulmonary fibrosis (IPF) – a chronic and ultimately fatal disease characterised by a decline in lung function. In September 2019, Ofev was approved in the U.S. as the first and only therapy to slow the rate of decline in pulmonary function in patients with systemic sclerosis-associated ILD. Submissions have been made to other major regulatory bodies across the globe.

What is Ofev?

- Ofev is a prescription medicine used:
  - to treat people with a lung disease called idiopathic pulmonary fibrosis (IPF).

  or
  - to slow the rate of decline in lung function in people with systemic sclerosis-associated interstitial lung disease (SSc-ILD) (also known as scleroderma-associated ILD).

- It is not known if Ofev is safe and effective in children.

Important Safety Information

What is the most important information I should know about Ofev (nintedanib)?

Ofev can cause harm, birth defects, or death to an unborn baby. Women should not become pregnant while taking Ofev. Women who are able to become pregnant should have a pregnancy test before starting treatment and should use highly effective birth control during and for at least 3 months after your last dose. Talk with your doctor about what birth control method is right for you during this time. Women using hormonal birth control should add a barrier method of birth control (such as male condoms or spermicide). If you become pregnant or think you are pregnant while taking Ofev, tell your doctor right away.

What should I tell my doctor before using Ofev?

Before you take Ofev, tell your doctor about all of your medical conditions, including if you have:

- liver problems.
- heart problems.
- a history of blood clots.
- a bleeding problem or a family history of a bleeding problem.
- had recent surgery in your stomach (abdominal) area.

Tell your doctor if you:

- are pregnant or plan to become pregnant.
- are breastfeeding or plan to breastfeed. It is not known if Ofev passes into your breast milk.

  You **should not** breastfeed while taking Ofev.
- are a smoker. You should stop smoking prior to taking Ofev and avoid smoking during treatment.

Tell your doctor about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements such as St. John's wort.

What are the possible side effects of Ofev?

Ofev may cause serious side effects.

TELL YOUR DOCTOR RIGHT AWAY if you are experiencing any side effects, including:

Liver problems. Unexplained symptoms may include yellowing of your skin or the white part of your eyes (jaundice), dark or brown (tea-colored) urine, pain on the upper right side of your stomach area (abdomen), bleeding or bruising more easily than normal, feeling tired, or loss of appetite. Your doctor will do blood tests to check how well your liver is working before starting and during your treatment with Ofev.

Diarrhea, nausea, and vomiting. Your doctor may recommend that you drink fluids or take medicine to treat these side effects. Tell your doctor if you have these symptoms, if they do not go away, or get worse, and if you are taking over-the-counter laxatives, stool softeners, and other medicines or dietary supplements.

Heart attack. Symptoms of a heart problem may include chest pain or pressure, pain in your arms, back, neck, or jaw, or shortness of breath.

Stroke. Symptoms of a stroke may include numbness or weakness on one side of your body, trouble talking, headache, or dizziness.

Bleeding problems. Ofev may increase your chances of having bleeding problems. Tell your doctor if you have unusual bleeding, bruising, wounds that do not heal, and/or if you are taking a blood thinner, including prescription blood thinners and over-the-counter aspirin.

- **Tear in your stomach or intestinal wall (perforation).** Ofev may increase your chances of having a tear in your stomach or intestinal wall. Tell your doctor if you have pain or swelling in your stomach area.

The most common side effects of Ofev are diarrhea, nausea, stomach pain, vomiting, liver problems, decreased appetite, headache, weight loss, and high blood pressure.

These are not all the possible side effects of Ofev. For more information, ask your doctor or pharmacist. You are encouraged to report negative side effects of prescription drugs to the FDA. Visit: http://www.fda.gov/medwatch or call 1-800-FDA-1088.

Please see full Prescribing Information, including Patient Information.

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About Boehringer Ingelheim Pharmaceuticals, Inc.

Boehringer Ingelheim Pharmaceuticals, Inc., based in Ridgefield, Conn., is the largest U.S. subsidiary of Boehringer Ingelheim Corporation.

Boehringer Ingelheim is one of the world's top 20 pharmaceutical companies. Headquartered in Ingelheim, Germany, the company operates globally with approximately 50,000 employees. Since its founding in 1885, the company has remained family-owned, and today our goal is to improve the lives of humans and animals through its three business areas: human pharmaceuticals, animal health and biopharmaceutical contract manufacturing.

Boehringer Ingelheim concentrates on developing innovative therapies that can improve and extend patients' lives. As a research-driven pharmaceutical company, it plans in generations for long-term success. Its research efforts are focused on diseases with high, unmet medical need. In animal health, the company stands for advanced prevention.

In 2018, Boehringer Ingelheim achieved net sales of around $20.7 billion (17.5 billion euros). R&D expenditure of almost $3.7 billion (3.2 billion euros) corresponded to 18.1 per cent of net sales.

Boehringer Ingelheim is committed to improving lives and strengthening our communities. Please visit www.boehringer-ingelheim.us/csr to learn more about Corporate Social Responsibility initiatives.

For more information, please visit www.boehringer-ingelheim.us, or follow us on Twitter @BoehringerUS.