Eiger Receives Positive CHMP Opinion for Zokinvy as a Treatment for Hutchinson-Gilford Progeria Syndrome and Processing-Deficient Progeroid Laminopathies

- *If authorized, Zokinvy® (lonafarnib) will be the first and only treatment approved in Europe to treat Hutchinson-Gilford progeria syndrome and processing-deficient progeroid laminopathies - collectively known as progeria.*
- *CHMP based its opinion on the results of data demonstrating Zokinvy increased survival by 4.3 years in children and young adults with HGPS.*
- *Zokinvy was approved by the U.S. FDA as the first and only treatment for progeria in November 2020.*

PALO ALTO, Calif., May 20, 2022 /PRNewswire/ --Eiger BioPharmaceuticals Inc. (Nasdaq: EIGR), a commercial-stage biopharmaceutical company focused on the development of innovative therapies to treat and cure hepatitis delta virus and other serious diseases, announced today that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) issued a positive opinion recommending the European Commission approve Zokinvy, a first-in-class breakthrough therapy for Hutchinson-Gilford progeria syndrome (HGPS) and processing-deficient progeroid laminopathies (PL).

HGPS and PL are devastating, ultra-rare, and fatal pediatric diseases that cause dramatically accelerated aging and premature death. The main cause of death from these conditions is heart attack or stroke due to severe hardening of the arteries. Without Zokinvy treatment, children with HGPS die at an average age of 14.5 years.

The CHMP based its decision on the results of two clinical trials which showed that Zokinvy, a disease-modifying agent, lowered the risk of death in children with HGPS by 72%. Zokinvy extended life by an average of 4.3 years in children and young adults with HGPS. The science and innovation for Zokinvy spans 13 years of clinical research, including clinical trials involving almost 100 children diagnosed with progeria from 37 different countries across six continents. The U.S. approval and positive CHMP opinion are the result of a pioneering partnership between Eiger and the Progeria Research Foundation to bring Zokinvy to market and hope to patients.

“If authorised, Zokinvy will represent the only therapeutic option that has been proven to meaningfully extend the lives of children with HGPS – with the significant effect of extending their average life span by nearly one third,” said Prof. Thorsten Marquardt, Paediatric and Adolescent Medicine, University of Münster. “The development of therapies for ultra-rare diseases like progeria is often ignored leaving patients, families, and physicians to cope alone, so progress like this is extremely impactful to the entire rare disease community.”

“Today’s positive opinion from the CHMP brings us one step closer to making Zokinvy available to help HGPS patients in Europe live longer lives. With this news, our recently announced partnership agreement in Japan, and our ongoing commercialization in the U.S., we are executing our strategy to give hope to vulnerable patients around the world,” said David Cory, President and CEO, Eiger. “Additionally, Eiger continues to drive positive momentum by advancing our late-stage pipeline of

breakthrough therapies which include much needed potential treatments for devastating global diseases like hepatitis delta virus, congenital hyperinsulinism, and COVID-19."

Based on the CHMP recommendation, a decision by the European Commission is anticipated within approximately two months. If granted, the centralized marketing authorization would be valid in all 27 EU member states as well as the United Kingdom, Iceland, Liechtenstein, and Norway. Zokinvy is expected to be made available commercially following successful completion of reimbursement discussions country-by-country.

"On behalf of the progeria community of children, families, and healthcare providers across Europe, I am extremely pleased with the CHMP's decision today. This important milestone brings us closer to the first approved treatment for progeria in Europe," added Maryet Stamsnijder, President, Progeria Family Circle. "Importantly, it also helps us build much-needed awareness of progeria to better support families impacted by this devastating disease as well as encourage additional research."

Zokinvy was approved in the U.S. in November 2020 to reduce the risk of death in Hutchinson-Gilford progeria syndrome, and to treat processing-deficient progeroid laminopathies. It is indicated for adults and children over 12 months of age. This month, Eiger announced a strategic partnership with AnGes, a biopharmaceutical company focused on development of gene-based medicines, to seek regulatory approval and commercialization of Zokinvy in Japan.

ENDS

ABOUT PROGERIA AND PROGEROID LAMINOPATHIES
Hutchinson-Gilford progeria syndrome, and progeroid laminopathies are separate and distinct ultra-rare, fatal, genetic premature aging diseases that accelerate mortality in young patients. It is estimated that there are 400 children and young adults worldwide with HGPS and 200 with PL, with approximately 20 children and young adults identified across Europe.

HGPS is caused by a point mutation in the LMNA gene, yielding the farnesylated aberrant protein, progerin. Progeroid laminopathies are genetic conditions of accelerated aging caused by a constellation of mutations in the LMNA and/or ZMPSTE24 genes yielding farnesylated proteins that are distinct from progerin.

Without Zokinvy therapy, children with HGPS commonly die of the same heart disease that affects millions of normally aging adults (arteriosclerosis), by an average age of 14.5 years. Disease manifestations include severe failure to thrive, scleroderma–like skin, global lipodystrophy, alopecia, joint contractures, skeletal dysplasia, global accelerated atherosclerosis with cardiovascular decline, and debilitating strokes.

ABOUT ZOKINVY® (LONAFARNIB)
Zokinvy blocks the accumulation of defective, permanently farnesylated proteins which form tight associations with the nuclear envelope, leading to cellular instability and premature aging in children and young adults with progeria and processing-deficient progeroid laminopathies.

Zokinvy is a first-in-class disease-modifying agent that has demonstrated a statistically significant survival benefit in children and young adults with HGPS. In clinical trials, Zokinvy reduced the incidence of mortality by 72% and increased average survival time by at least 4.3 years in patients with HGPS. The most commonly reported adverse reactions were gastrointestinal (vomiting, diarrhea, nausea), and most were mild or moderate (Grade 1 or 2) in severity. Many progeria patients have received continuous Zokinvy therapy for more than 10 years.

Eiger licensed exclusive worldwide rights to lonafarnib from Merck, known as MSD outside of the United States and Canada. Merck will not receive any milestone payments for the development of lonafarnib for the treatment of progeria and has waived royalty obligations from Eiger for a specified quantity of lonafarnib.

For more information including prescribing information for Zokinvy in the U.S. please go to www.zokinvy.com. Zokinvy is not currently approved for any indication in Europe or Japan.

U.S INDICATION

In the U.S., ZOKINVY is indicated in adult and pediatric patients 12 months of age and older with a body surface area (BSA) of 0.39 m^2 and above:

- To reduce the risk of mortality in Hutchinson-Gilford Progeria Syndrome (HGPS)
- For the treatment of processing-deficient Progeroid Laminopathies with either:
    - Heterozygous LMNA mutation with progerin-like protein accumulation
    - Homozygous or compound heterozygous ZMPSTE24 mutations

LIMITATIONS OF USE

ZOKINVY is not indicated for use in patients with non-HGPS Progeroid Syndromes or with Progeroid Laminopathies known to be processing-proficient. Based upon its mechanism of action, ZOKINVY would not be expected to be effective in these populations.

CONTRAINDICATIONS

- Strong or moderate CYP3A inhibitors or inducers
- Midazolam
- Lovastatin, simvastatin, and atorvastatin

U.S. IMPORTANT SAFETY INFORMATION

- The most common adverse reactions are vomiting (90%), diarrhea (81%), infection (78%), nausea (56%), decreased appetite (53%), fatigue (51%), upper respiratory tract infection (51%), abdominal pain (48%), musculoskeletal pain (48%), electrolyte abnormalities (43%), headache (37%), decreased weight (37%), increased aspartate aminotransferase (35%), myelosuppression (35%), cough (33%), decreased blood bicarbonate (33%), hypertension (29%), and increased alanine aminotransferase (27%).

GASTROINTESTINAL ADVERSE REACTIONS

- Gastrointestinal adverse reactions were the most frequently reported adverse reactions. Of the 57 patients (90%) that experienced vomiting, 30 (53%) patients had mild vomiting, 26 (46%) patients had moderate vomiting, and 1 (2%) patient had severe vomiting.
- Of the 35 patients (56%) that experienced nausea, 34 (97%) patients had mild nausea and 1 (3%) patient had moderate nausea.
- Of the 51 patients (81%) that experienced diarrhea, the majority of patients (92%) experienced mild or moderate diarrhea; 38 (75%) patients reported mild diarrhea and 9 (18%) patients reported moderate diarrhea. Four (8%) patients reported severe diarrhea.
- Loss of fluids and dehydration can be severe, leading to hospitalization. As a result, patients should receive therapy for diarrhea at the earliest signs in order to avoid possible severe complications.

ALANINE AMINOTRANSFERASE AND ASPARTATE AMINOTRANSFERASE ELEVATIONS

- Increased alanine aminotransferase was commonly reported (17 [27%] patients). Of the 17 patients with increased alanine aminotransferase, 14 (82%) patients had mild increases, 1 (6%) patient had moderate increases, and 2 (12%) patients had severe increases.
- Increased aspartate aminotransferase was also commonly reported (22 [35%] patients). Of the 22 patients with increased aspartate aminotransferase, 21 (95%) patients had mild increases and 1 (5%) patient had a severe increase.

HYPERTENSION

- Increases in blood pressure have been documented in patients treated with ZOKINVY. At baseline 22 (35%) patients had either a systolic blood pressure or a diastolic blood pressure or both above the 95th percentile. Over the course of the trials, 18 (29%) patients had hypertension based on systolic blood pressure or diastolic blood pressure measurements above the 95th percentile on 3 or more occasions. Five (8%) patients who were normotensive at baseline had either systolic blood pressure or diastolic blood pressure above the 95th percentile at the end of treatment.

OPHTHALMIC ADVERSE REACTIONS

- Lonafarnib caused retinal toxicity in monkeys at 3.7 times the human dose based on plasma drug exposure, but not at 2.1 times the human dose.

LABORATORY ABNORMALITIES

Some patients treated with ZOKINVY developed laboratory abnormalities. These included:

- Electrolyte abnormalities (43%), such as hyperkalemia, hypokalemia, hyponatremia, or hypercalcemia
- Myelosuppression (35%), such as reductions in absolute neutrophil count, white blood cell counts, lymphopenia, hemoglobin, or hematocrit
- Increased liver enzymes, such as aspartate aminotransferase (35%), or alanine aminotransferase (27%)

These laboratory abnormalities often improved while continuing ZOKINVY, but it is not possible to exclude ZOKINVY as a cause of the abnormalities. Periodically monitor electrolytes, complete blood counts, and liver enzymes, and manage abnormalities accordingly.

NEPHROTOXICITY

- Lonafarnib caused nephrotoxicity in rats at plasma drug exposures approximately equal to that achieved with the human dose. Monitor renal function at regular intervals during ZOKINVY therapy.

RETINAL TOXICITY

- Lonafarnib caused rod-dependent, low-light vision decline in monkeys at plasma drug exposures similar to that achieved with the human dose. Perform ophthalmological evaluation at regular intervals and at the onset of any new visual changes during ZOKINVY therapy.

IMPAIRED FERTILITY

- Lonafarnib caused impaired fertility in female rats at 1.2 times the human dose based on plasma drug exposure.
- Lonafarnib caused impaired fertility and testicular toxicity in male rats at 1.5 times the human dose based on plasma drug exposure, and toxicity in the male reproductive tract in monkeys at doses lower than the human dose based on plasma drug exposure.

ABOUT EIGER

Eiger is a commercial-stage biopharmaceutical company focused on the development of innovative therapies to treat and cure hepatitis delta virus (HDV) and other serious diseases. The Eiger HDV platform includes two first-in-class therapies in Phase 3 that target critical host processes involved in viral replication. Eiger is also developing peginterferon lambda as a therapeutic for COVID-19 and is planning to submit an emergency use authorization application to FDA based on positive results from the investigator sponsored Phase 3 *TOGETHER* study.

All five Eiger rare disease programs have been granted FDA Breakthrough Therapy designation: lonafarnib and peginterferon lambda for HDV, Zokinvy for progeria, and avexitide for both congenital hyperinsulinism and post-bariatric hypoglycemia.

For additional information about Eiger and its clinical programs, please visit www.eigerbio.com.

ABOUT PROGERIA FAMILY CIRCLE

The Progeria Family Circle (PFC) is a European patient network, founded in 1997, supporting children and young adults with progeria and their families on a European level. The PFC consists of a network of parents and experts in Europe, visiting medical congresses to keep informed about research developments in progeria. The PFC goal is to support better and faster recognition of symptoms of progeria, raise awareness for a better acceptance of progeria children and young adults in public communities, provide opportunities for families to meet each other through many annual reunions throughout Europe, and offer other necessary and permanent support for families with children with progeria.

For more information, please visit www.progeriafamilycircle.blogspot.com.

Note Regarding Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the safe harbor provisions of the U.S. Private Securities Litigation Reform Act of 1995. All statements other than statements of historical facts, including statements regarding our future financial condition, timing for and outcomes of clinical results, prospective products, preclinical and clinical pipelines, regulatory objectives, business strategy and plans and objectives for future operations, are forward looking statements. Forward-looking statements are our current statements regarding our intentions, beliefs, projections, outlook, analyses or current expectations concerning, among other things, our anticipated significant milestones in 2022; the timing of our ongoing and planned clinical development across our pipeline; the approval of Zokinvy in jurisdictions outside of the U.S.; our ability to finance the continued advancement of our development pipeline products; and the potential for success of any of our product candidates. Various important factors could cause actual results or events to differ materially from the forward-looking statements that Eiger makes, including additional applicable risks and uncertainties described in the "Risk Factors" sections in the Annual Report on Form 10-Q for the quarter ended March 31, 2022 and Eiger's subsequent filings with the SEC. The forward-looking statements contained in this press release are based on information currently available to Eiger and speak only as of the date on which they are made. Eiger does not undertake and specifically disclaims any obligation to update any forward-looking statements, whether as a result of any new information, future events, changed circumstances or otherwise.

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