FDA Approves Revcovi™, a New Enzyme Replacement Therapy Developed by Leadiant Biosciences, for the Treatment of ADA-SCID in Pediatric and Adult Patients

Gaithersburg, MD – October 5, 2018 – Leadiant Biosciences, Inc. today announced that the Food and Drug Administration (FDA) has granted approval to Revcovi™ (elapegademase-lvlr) injection in the U.S. Revcovi is a new enzyme replacement therapy (ERT) for the treatment of adenosine deaminase severe combined immune deficiency (ADA-SCID) in pediatric and adult patients.

"We are gratified by the FDA's timely recognition of Revcovi as an effective and safe treatment for ADA-SCID, which, in addition to being ultra-rare, is one of the most devastating genetic disorders," said Michael Minarich, Chief Executive Officer, Leadiant Biosciences, Inc. "We extend our deepest gratitude to the patients who participated in the clinical trials and their families and caregivers who supported them. We also appreciate the hard work of the investigators, clinicians, and study staff to bring this therapy to patients in need. We look forward to continuing to work together to serve the ADA-SCID community."

Revcovi is a PEGylated recombinant adenosine deaminase (rADA) enzyme developed by Leadiant Biosciences to treat ADA-SCID. The product of recombinant technology, Revcovi eliminates the need to source the enzyme from animals and works by supplementing levels of an essential enzyme called adenosine deaminase (ADA).

ADA-SCID is an ultra-rare, inherited genetic disorder, caused by a deficiency in the ADA enzyme that is fatal if left untreated. Patients affected by ADA-SCID have compromised immune systems that leave them unprotected from infection-producing bacteria, viruses, and fungi. ADA-SCID primarily affects infants and young children. The disease is typically diagnosed within the first few months of life. Undiagnosed babies with ADA-SCID usually die before they reach age two due to infections. SCID newborn screening in most states has allowed detection of ADA-SCID in newborns and has led to early initiation of ADA enzyme therapy and improved outcomes.

"For decades, physicians, patients, and their families have relied upon enzyme replacement therapy as a life-saving treatment for adenosine deaminase severe combined immunodeficiency, a disease in which the buildup of toxic metabolites can cripple children's immune systems," said Morna Dorsey, M.D., MMSc, Professor of Pediatrics at the University of California, San Francisco. "Individuals with ADA-SCID are at an increased risk of severe and recurrent infections and often fail to thrive. By providing specific and direct replacement of the adenosine deaminase enzyme, Revcovi can reduce patients' risk of potentially serious, life-threatening infections and their debilitating complications."

The approval is based on results from two multicenter, open-label clinical trials which demonstrate that Revcovi increases ADA activity, reduces concentrations of toxic metabolites that are the hallmark of ADA-SCID and improves total lymphocyte counts.[1]

"This is a great day for people living with ADA-SCID and their families as the approval of Revcovi gives them a path forward," commented John Boyle, President and Chief Executive

Officer of the Immune Deficiency Foundation. “We commend Leadiant Biosciences for bringing this innovative enzyme replacement therapy to market, and for helping to advance scientific understanding of ADA-SCID.”

“The competence and dedication of our staff was instrumental to obtain this important achievement for the ADA-SCID community," said Dr. Marco Brughera, Chief Executive Officer, Leadiant Biosciences Corporate. “With the FDA's approval of Revcovi, we reaffirm our commitment and rare dedication to providing a reliable supply of quality, innovative therapies that serve the needs of rare disease communities.”

Leadiant is working with physicians, payers, and policymakers to bring Revcovi to patients who need it. The Company offers comprehensive treatment support, from educating about the disease, to navigating reimbursement, to offering patient assistance programs. The Company’s post-marketing commitment includes a clinical study, which will record information about the health status of patients using Revcovi. This initiative will help Leadiant better understand and track information about Revcovi following approval as well as provide critical information about Revcovi’s efficacy and safety, especially in newly diagnosed patients.

Leadiant is a research-based pharmaceutical company that dedicates considerable scientific and financial resources to the research, development, and distribution of novel and effective therapies to address the needs of people living with rare diseases. The Company markets five rare disease products in North America and has been working in the enzyme replacement therapy space for more than 30 years. The Company is committed to serving the needs of patients, caregivers, and families affected by ADA-SCID.

The FDA granted this application Fast Track and Priority Review. Revcovi also received Orphan Drug designation.

About Revcovi

Revcovi (elapegademase-lvlr) is a recombinant adenosine deaminase indicated for the treatment of adenosine deaminase severe combined immune deficiency (ADA-SCID) in pediatric and adult patients. In the two multicenter trials, Revcovi supplemented ADA levels, reduced concentrations of toxic metabolites that are the hallmark of ADA-SCID and improved total lymphocyte counts.[1] Revcovi is the product of recombinant technology, thus eliminating the need to source the adenosine deaminase (ADA) enzyme from animals.

Important Safety Information for Revcovi

Indication

Revcovi (elapegademase-lvlr) is indicated for the treatment of adenosine deaminase severe combined immune deficiency (ADA-SCID) in pediatric and adult patients.

WARNINGS AND PRECAUTIONS:

- Injection site bleeding in patients with thrombocytopenia: Increased risk of local bleeding in patients with thrombocytopenia; should not be used if thrombocytopenia is severe.
- Delay in improvement of immune function: Protect immune deficient patients from infections until improvement in immune function.

ADVERSE REACTIONS:
The most commonly reported adverse reactions were cough and vomiting.

In addition, the following post-marketing reports for the same class of enzyme replacement therapy used in the treatment of ADA-SCID, may also be seen with Revcovi treatment:

- Hematologic events: hemolytic anemia, autoimmune hemolytic anemia, thrombocythemia, thrombocytopenia and autoimmune thrombocytopenia
- Dermatological events: injection site erythema, urticaria
- Lymphomas

IMPORTANT MONITORING INFORMATION:
Treatment with Revcovi should be monitored by measuring trough plasma ADA activity and trough dAXP levels for maintenance of therapeutic targets. If a persistent decline in plasma ADA activity occurs, immune function and clinical status should be monitored closely, and precautions should be taken to minimize the risk of infection.

Please refer to Revcovi's Full Prescribing Information.

About ADA-SCID
Adenosine deaminase severe combined immune deficiency (ADA-SCID) is an ultra-rare, inherited genetic disorder, caused by a deficiency in the adenosine deaminase (ADA) enzyme that is fatal when left untreated. ADA-SCID primarily affects infants and young children whose compromised immune system leaves them unprotected from infection-producing bacteria, viruses, and fungi. ADA-SCID is characterized by severe and recurrent opportunistic infections, failure to thrive, profound lymphopenia (reduced number of lymphocytes in the blood) with absent or severely impaired immune function, and metabolic abnormalities (abnormally high intracellular accumulation of purine nucleotides). Patients with ADA-SCID are also predisposed to recurrent illnesses caused by pathogens that often begin within the first few weeks of life.[2,3] ADA-SCID is typically diagnosed within the first few months of life.[4] Left untreated, babies with ADA-SCID usually die before they reach the age of 2 due to recurrent infections unless they are diagnosed early and effective treatment is started.[5]

ADA-SCID results from mutations in the ADA gene, which provides instructions for producing the ADA enzyme.[6] When functioning properly, ADA eliminates molecules called adenosine and deoxyadenosine, which are toxic to lymphocytes, a type of white blood cell. ADA converts adenosine to inosine and deoxyadenosine to deoxyinosine, molecules that do not harm lymphocytes. However, mutations in the ADA gene reduce or eliminate the protective activity of adenosine deaminase, allowing the buildup of adenosine and deoxyadenosine to toxic levels. These toxic levels cause specialized lymphocytes called T-cells and B-cells to accumulate biologic chemicals that would normally be processed by ADA. The buildup of these biologic products in excess of normal causes the T-cells and B-cells to die, leaving affected individuals with no significant immune defense and increasing their risk of infection.[6]

ADA-SCID is estimated to occur in approximately one in 200,000 to one in 1,000,000 newborns around the world.[3] The disorder is responsible for approximately 15% of SCID cases.[7]

About Leadiant Biosciences, Inc.
Leadiant Biosciences, Inc., a wholly-owned subsidiary of Leadiant Biosciences S.p.A., is a research-based pharmaceutical company that dedicates considerable scientific and financial resources to the research, development, and distribution of novel and effective therapies to

address the needs of people living with rare diseases and improve their quality of life. For additional information, please visit Leadiant.com.

About Leadiant Biosciences, S.p.A. (Corporate)
Leadiant Biosciences, S.p.A. is a Rome-based global holding company with subsidiaries in the US (Leadiant Biosciences, Inc.) and Europe (Leadiant Biosciences, Ltd.) For additional information, please visit leadiantbiosciences.com.

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