bluebird bio Announces European Medicines Agency's Acceptance of Marketing Authorization Application (MAA) for elivaldogene autotemcel (eli-cel, Lenti-D™) Gene Therapy for Cerebral Adrenoleukodystrophy (CALD)

European Medicines Agency will evaluate the MAA for the experimental treatment under accelerated assessment

ZUG, Switzerland – 1 October 2020 – bluebird bio, Inc. today announced that the European Medicines Agency (EMA) accepted the company's marketing authorisation application (MAA) for its investigational elivaldogene autotemcel (eli-cel, Lenti-D™) gene therapy for the treatment of a subset of patients with cerebral adrenoleukodystrophy (CALD), an ultra-rare but often fatal neurodegenerative disease primarily affecting young boys.

"CALD is a devastating disease, often marked by rapid neurodegeneration, the development of major functional disabilities, and eventual death. The acceptance of the MAA is a critical milestone in our continued collaboration with EMA to potentially deliver gene therapy for boys with CALD," said Gary Fortin, Ph.D., SVP, severe genetic diseases, bluebird bio. "Data from clinical studies conducted in patients with early CALD suggest a stabilization of the progression of the disease. If approved, it would represent the first therapy for CALD that uses a patient's own haematopoietic stem cells, potentially mitigating the risk of life-threatening immune complications associated with transplant using cells from a donor."

Data from the Phase 2/3 Starbeam study (ALD-102) formed the basis of the MAA, which is also supported with data from the ongoing Phase 3 ALD-104 study and the long-term follow-up study (LTF-304). The most recent results from these studies were presented at the 46th Annual Meeting of the European Society for Blood and Marrow Transplantation (EBMT 2020) in August 2020.[1]

The one-time investigational gene therapy is designed to add functional copies of the *ABCD1* gene into a patient's own haematopoietic (blood) stem cells (HSCs). Clinical data suggest that the addition of a functional gene allows patients to produce the adrenoleukodystrophy protein (ALDP), which is thought to allow for the breakdown of very-long-chain fatty acids (VLCFAs) that accumulate to toxic levels in the brain. There is no need for donor HSCs from another person. The treatment regimen, comprising mobilisation/apheresis, conditioning, and eli-cel infusion, had a safety and tolerability profile primarily reflective of the known effects of mobilisation/apheresis and conditioning.

The EMA accepted the gene therapy for the treatment of CALD for a subset of patients into its Priorities Medicines scheme (PRIME) in July 2018, and previously granted Orphan Medicinal Product designation. In July 2020, the Committee for Medicinal Products for Human Use (CHMP) of the EMA reduced the MAA review time to 150 days, instead of the standard 210 days. Accelerated MAA is granted by EMA for products considered of major interest for public health and therapeutic innovations.

The U.S. Food and Drug Administration (FDA) granted the investigational therapy Orphan Drug status, Rare Pediatric Disease designation, and Breakthrough Therapy designation for a subset of CALD patients. bluebird bio is currently on track to submit the Biologics License Application (BLA) in the U.S. in mid-2021.

Eli-cel is not approved for any indication in any geography.

About Cerebral Adrenoleukodystrophy (CALD)
Adrenoleukodystrophy (ALD) is a rare, X-linked metabolic disorder that is estimated to affect one in 21,000 male newborns worldwide.[2,3] ALD is caused by mutations in the *ABCD1* gene that affect the production of adrenoleukodystrophy protein (ALDP) and subsequently cause toxic accumulation of very long-chain fatty acids (VLCFAs) primarily in the adrenal cortex and white matter of the brain and spinal cord.[2,3]

Approximately 40% of boys with adrenoleukodystrophy are estimated to develop CALD, the most severe form of ALD.[3,4] CALD usually occurs in early childhood and can rapidly compromise a patient's ability to function independently. It can lead to complete loss of communication, blindness, need for tube feeding, incontinence, wheelchair dependence, complete loss of voluntary movement, and eventually death if left untreated.[5,6,7,8,9,10]

Although allogeneic haematopoietic stem cell transplantation (allo-HSCT) has been shown to have a beneficial effect on the progression of the disease and long-term survival,[11] and can arrest disease progression if performed at the early stage of cerebral involvement, it has significant associated risks, such as transplant-related mortality (TRM), graft failure or rejection, graft-versus-host disease, and potential for opportunistic infections.[6,11] Safety outcomes are typically more favourable if allo-HSCT is performed using cells from a human leukocyte antigen (HLA)-matched sibling donor, however, this is not always available.[6,11]

Early diagnosis of CALD is important, as the outcome of available treatment varies with the clinical stage of the disease.[6,11,12,13,14] Newborn screening for ALD is a critical enabler of early diagnosis and thus of successful treatment of ALD. Once a patient has been diagnosed with ALD, regular MRI scans are critical to detect white matter changes indicative of progression to CALD.

About bluebird bio, Inc.
bluebird bio is pioneering gene therapy with purpose. From our Cambridge, Mass., headquarters, we're developing gene and cell therapies for severe genetic diseases and cancer, with the goal that people facing potentially fatal conditions with limited treatment options can live their lives fully. Beyond our labs, we're working to positively disrupt the healthcare system to create access, transparency and education so that gene therapy can become available to all those who can benefit.

bluebird bio is a human company powered by human stories. We're putting our care and expertise to work across a spectrum of disorders: cerebral adrenoleukodystrophy, sickle cell disease, β-thalassaemia and multiple myeloma, using gene and cell therapy technologies including gene addition and (megaTAL-enabled) gene editing.

bluebird bio has additional nests in Seattle, Wash.; Durham, N.C.; Zug, Switzerland Munich, Germany; Milan, Italy; Utrecht, the Netherlands; Hampshire, United Kingdom; Paris, France and Athens, Greece.

For more information about bluebird bio in the UK, visit **bluebirdbio.co.uk**.
For more information about bluebird bio in the EU, visit **bluebirdbio.eu**

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