NICE Draft Guidance Recommends that Patients be Denied Access to bluebird bio's Gene Therapy for Life-Limiting Rare Blood Disease

This guidance fails to recognise the severe burden for patients with transfusion-dependent β-thalassaemia (TDT), who depend on lifelong blood transfusions every two to five weeks to survive[1] and have an average age of death of around 45[2]

NICE's decision threatens the future of gene therapies in the UK, despite the government's clear commitment to bring these transformative treatments to patients

bluebird bio's ZYNTEGLO® ▼ (betibeglogene autotemcel gene therapy; beti-cel) is a one-time gene therapy that addresses the underlying cause of TDT and offers eligible people living with the disease the potential to live life free from transfusions[3,4,5]

BASINGSTOKE, UK – **11 February 2021**—bluebird bio, Inc. today expressed significant concern that eligible people in England and Wales with transfusion-dependent β-thalassaemia (TDT) could be denied access to its gene therapy, beti-cel, under draft guidance issued by the National Institute for Health and Care Excellence (NICE). NICE is recommending against routine NHS funding for this innovative, one-time therapy, despite recognising it as a potentially curative treatment. The draft guidance disregards the significant burden TDT has on people's quality of life and life expectancy, and outlines their intention to use a health economic model to assess the value of beti-cel, which NICE itself has acknowledged needs to be updated in order to appropriately evaluate gene therapies.

"We are shocked and disappointed by this recommendation and strongly believe that NICE has failed to act in the best interests of people with TDT and their families in England and Wales," comments Nicola Redfern, UK General Manager at bluebird bio. "It is baffling that NICE disregarded the testimonies of patients, advocacy groups and clinicians and, despite recognising beti-cel as a potential cure for patients with TDT, has chosen to deny access and has dismissed the obvious unmet need. This decision is deeply concerning and will not only come as a huge blow to the TDT community, but also sets a dangerous precedent which could limit access to other gene therapies in the UK in the future."

"Living with thalassaemia is a difficult and challenging experience not just for patients but for their entire families," said Romaine Maharaj, Executive Director, UK Thalassaemia Society. "Our main aim at the UKTS is to improve the quality of life and experience of people living with thalassaemia through education, one to one support, research, service improvements and policy changes. We aspire to provide our members with empathy and the necessary hope to be optimistic about their futures. We are extremely disappointed with NICE'S decision not to recommend betibeglogene autotemcel as a treatment option in the UK. We also feel disheartened that our patient experts were misquoted and used out of context and feel that NICE needs to rectify this. Having an option and the access to a potentially curable treatment is vital and should be offered to patients."

People with thalassaemia inherit a faulty gene that means they are unable to produce normally functioning haemoglobin – the protein responsible for carrying oxygen around the body.[6,7] TDT is the

most severe form of the disease[8,9] and requires life-long blood transfusions every two to five weeks.[1] However, these transfusions carry significant risks of iron overload, and even when treated optimally, excess iron will build up in tissues, leading to unavoidable and progressive multi organ damage.[6] Having to rely on regular blood transfusions has a significant impact on day-to-day life, including education, work, and mental and physical wellbeing.[10,11]

"TDT impacts life expectancy and quality of life for sufferers, and involves gruelling, life-long treatment," said Professor John B. Porter, MA, M.D., FRCP, FRCPath, University College London Hospitals, London, UK. "Gene therapy could offer a potentially transformative option for eligible patients with TDT, by freeing them from the burden of regular blood transfusions and enabling them to live a more normal life. As a clinician who has worked to advance therapies for patients with TDT over the last three decades and understands the demands and limitations of current therapies, as well as the potential of gene therapy from first-hand experience, I very much hope that people with TDT in England and Wales will soon have the opportunity to benefit from this significant advancement."

The position outlined by NICE in its Appraisal Consultation Document (ACD) recommends against the routine funding of beti-cel for people with TDT in England and Wales, aged 12 years and over, who do not have a β0/β0 genotype and for whom haematopoietic stem cell (HSC) transplantation is appropriate but a human leukocyte antigen (HLA)-matched related HSC donor is not available. In its ACD, NICE has recommended against applying the 1.5% discount rate to beti-cel, an economic principle NICE developed to ensure that the value of treatments with long-term health benefits could be accurately assessed. By failing to apply this discount rate, NICE has chosen to use a reimbursement framework that is not fit to evaluate transformative treatments such as gene therapies and places the UK at risk of falling behind other nations in advancing the best possible care for patients.

Under the NICE review process beti-cel was assessed in comparison to the current standard of care for all TDT patients, which is regular blood transfusions and therapy to reduce iron overload. Clinical data submitted to NICE showed that, of 24 people living with TDT, 83.3% achieved blood transfusion independence (living transfusion-free for at least 12 months) after being treated with beti-cel.[5] In preparation for the next NICE appraisal committee meeting, bluebird bio will be submitting updated data from the ongoing Phase 3 Northstar-2 study, which showed that 89% of people (n=17) treated achieved transfusion independence (defined as living transfusion-free for at least 12 months).[12]

This guidance is draft and open for consultation until 4 March 2021, during which time anyone wishing to comment can do so on the NICE website.

About beti-cel

The European Commission granted conditional marketing authorisation (CMA) for betibeglogene autotemcel (beti-cel; formerly LentiGlobin™ gene therapy for β-thalassemia), to be marketed as ZYNTEGLO® ▼gene therapy, for people 12 years and older with transfusion-dependent β-thalassaemia (TDT) who do not have a β^0/β^0 genotype, for whom HSC transplantation is appropriate, but a human leukocyte antigen (HLA)-matched related HSC donor is not available. On April 28, 2020, the European Medicines Agency (EMA) renewed the CMA for beti-cel, supported by data from 32 patients treated with beti-cel, including three patients with up to five years of follow-up.[5]

The CMA for beti-cel is valid in the 27 member states of the EU as well as the UK, Iceland, Liechtenstein and Norway. For details, please see the Summary of Product Characteristics (SmPC).[5] The U.S. Food and Drug Administration (FDA) granted beti-cel Orphan Drug status and Breakthrough Therapy designation for the treatment of TDT.

Beti-cel continues to be evaluated in the ongoing Phase 3 Northstar-2 and Northstar-3 studies. For more information about the ongoing clinical studies, visit clinicaltrials.gov and use identifier NCT02906202 for Northstar-2 (HGB-207) and NCT03207009 for Northstar-3 (HGB-212).

▼ This medicinal product is subject to additional monitoring.

About bluebird bio
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-thalassemia 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 further information, visit **bluebirdbio.co.uk**

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