

STATEMENT ON A NONPROPRIETARY NAME ADOPTED BY THE USAN COUNCIL

USAN (KL-107)	EXAGAMGLOGENE AUTOTEMCEL
PRONUNCIATION	ex gam" gloe jeen aw" toe tem' sel
THERAPEUTIC CLAIM	Treatment of hemoglobinopathies such as severe sickle cell disease (SCD) and transfusion dependent β -thalassemia (TDT)

PRODUCT DESCRIPTION

CTX001 consists of autologous CD34+ human hematopoietic stem and progenitor cells (hHSPCs) modified by CRISPR-Cas9-mediated gene editing. (CRISPR-Cas9 is "clustered regularly interspaced short palindromic repeats-associated 9 nuclease.") The goal of this genetic modification is to induce the expression of γ -globin mRNA in erythroid precursors, which in turn leads to an increase in HbF levels in adult erythroid cells. CD34+ cells are isolated from mobilized peripheral blood prior to genetic modification. The CRISPR-Cas9 editing components are transiently introduced into the target cell population by electroporation as a ribonucleoprotein complex consisting of Cas9 and a gRNA that targets the erythroid lineage-specific enhancer of the BCL11A gene. The site-specific cleavage by Cas9 forms a double strand break (DSB). The DSB is repaired by the cell's endogenous non-homologous end-joining (NHEJ) pathway and leads to the creation of Indels (Insertions and deletions) at the cleavage site.

Autologous CD34+ cells isolated from mobilised peripheral blood by positive selection, modified by CRISPR/Cas9 (clustered regularly interspaced short palindromic repeats/CRISPR-associated protein 9) mediated gene editing consisting of a guide RNA (gRNA) introduced transiently as ribonucleoprotein (RNP) complex, targeting the erythroid lineage-specific enhancer region of BCL11A (B-cell lymphoma/leukemia 11A). The site-specific cleavage by Cas9 forms a double strand break (DSB), which is subsequently repaired by nonhomologous end-joining (NHEJ), leading to the transcriptional repression of BCL11A, a repressor of γ -globin gene transcription. (Source INN Recommended List #86)

TRADEMARK	None
SPONSOR	Vertex Pharmaceuticals
CODE DESIGNATION	CTX001
UNII	S53L777GM8
WHO NUMBER	11560

SCS