Lexicon

Black font represents terminology for healthcare professionals; blue font is patient/caregiver/advocate specific

Hemophilia B: General terminology		
Preferred terms/phrases	**Non-preferred terms/phrases**	**Description and guidance for use**
Burden of disease or condition (HCPs, payers) Impact of condition (patients, caregivers, advocates)	Impact of disease (patients, caregivers, advocates)	Use when referring to the consequences of hemophilia for people with the disorder, however, terminology should differ according to stakeholder audience
Burden of treatment (HCPs, payers) Impact of treatment (patients, caregivers, advocates)		Use when referring to the impact of treatment on patients' functioning and well-being
Coagulation factor IX, factor IX, or FIX	Factor 9, *F9* (this refers to the gene that encodes factor IX)	Use when discussing the factor IX protein. Use of 'coagulation' is not essential but may be helpful when describing the function of factor IX as a blood clotting factor At first use, factor IX should be spelled out in full; FIX can be used thereafter. It should always be lower case (i.e. factor IX should be used rather than Factor IX), except when starting a sentence
Disease, condition, or disorder (HCPs, payers) Condition (patients, caregivers, advocates)	Disease, disorder (patients, caregivers, advocates)	Use when describing hemophilia in broad terms; once the term is chosen, use consistently within a document or asset For lay audiences, the rationale for using 'condition/disorder' rather than 'disease' is to avoid defining people with hemophilia by their disease *Example: Hemophilia B is a rare, hereditary, X-linked recessive bleeding disorder*
Endogenous FIX activity/expression Body produces FIX on its own (patients, caregivers, advocates)	Naturally produced FIX activity/expression	Use when describing FIX produced in the body (vs exogenous FIX activity provided by factor replacement products)

F9 or the gene encoding factor IX	Factor IX gene, FIX gene (in publications)	Use when discussion to the *F9* gene that encodes factor IX. The protein is referred to as factor IX (FIX)
Factor replacement products		Use when referring to current standard of care factor replacement therapy
Genetic mutation or genetic variant	Defect, mistake, hiccup, disease, abnormality, variation, change	Use when describing the root cause of genetic conditions. Since genetic mutation is a broad term, for HCPs it may be helpful to provide additional information on the mutation type – e.g., missense mutation, frame-shift mutation, etc.
People with hemophilia/people with hemophilia B (PWH/PWHB) Participants/subjects with hemophilia (when referring to clinical trial data)	Hemophilia patients, hemophiliacs	Use when describing those with hemophilia/hemophilia B to avoid defining individuals by their disease At first use, these should be spelled out in full; the abbreviated version (PWH/PWHB) can be used thereafter Please ensure consistent use of a single term (e.g., 'people' or 'participants') within a document
Phase 1, Phase 2, Phase 3	Phase I, Phase II, Phase III	Use uppercase **P**hase and numbers rather than Roman numerals when describing phases of a clinical study
Gene therapy: General terminology		
Preferred terms/phrases	**Non-preferred terms/phrases**	**Description and guidance for use**
Adeno-associated virus (AAV)-based gene therapy (HCPs, payers) AAV gene transfer (patients, caregivers, advocates)	Gene supplementation, gene replacement, gene augmentation, AAV gene therapy, AAV gene transfer	Use when discussing gene therapy with AAV vectors (vs other gene therapy approaches) In gene therapy for hemophilia B, AAV gene transfer is used to describe the addition of a functional version of the dysfunctional/mutated gene back into the cell. More accurately describes the gene therapy process where a gene is added, while the host gene is unaffected. AAV gene transfer can be included in the hierarchical terms' gene transfer and gene therapy

AAV neutralizing antibodies (NAbs) Antibodies to the vector shell (patients, caregivers, advocates)	AAV inhibitors, neutralizing antibodies	Use when describing neutralizing antibodies against wild-type AAV or AAV vectors in narratives that do not refer to specific serotypes. If specific to serotype, use the specific AAV vector e.g., AAV5 neutralizing antibodies *Note: AAV NAbs are distinct from FIX inhibitors. AAV NAbs are antibodies produced against the AAV capsid, whereas FIX inhibitors are produced against the exogenous FIX replacement products*
Capsid (HCPs, payers) Viral shell or vehicle (patients, caregivers, advocates)	Capsule, polyhedron, carrier, envelope	Use when describing the outer protein component of an AAV vector that surrounds the therapeutic genetic material
Expression cassette or gene expression cassette (HCPs, payers) Functional gene cassette (patients, caregivers, advocates)	Vector or DNA components	Use to describe the genetic material, or the functional copy of the gene, contained in a gene therapy vector. The expression cassette typically contains the functional gene and other regulatory elements
Ex vivo gene therapy		Use to describe gene therapy that is delivered to cells extracted from the patient which are then transferred back into the patient
Gene inactivation or gene silencing	Gene knockdown, gene negative regulation or gene expression lowering	Use to describe the process of turning off or suppressing transcription of a gene so that no protein or a reduced amount of protein is expressed *Note: This is the underlying mechanism behind approaches such as siRNA and miRNA, where gene transcription is reduced/precluded*
Gene therapy	Gene supplementation, gene replacement, gene modification, gene/genome editing, genetic engineering	Gene therapy is the hierarchical term that encompasses AAV gene transfer and other techniques that use genetic materials to treat or cure disease. The term should be used when speaking generally about using genetic materials to treat or cure disease

Gene transfer	Gene replacement, gene augmentation, gene correction, gene addition	Gene transfer is a hierarchical term under which AAV gene transfer, gene addition and gene editing would be examples
Inactivated viral vector (HCPs, payers) Inactivated and/or non-disease-causing viral shell (patients, caregivers, advocates)	Neutralized virus; harmless virus	Use to highlight that vectors are derived from viruses but modified to ensure safe use. Use of 'inactivated' is not essential but may be helpful when introducing the basics of gene therapy *Example: A functional gene is inserted into the shell of an inactivated, non-disease-causing viral shell, which delivers the new gene into the liver*
Innovative and/or transformative treatment	Revolutionary treatment	Use to consistently describe gene therapy *Example: Gene therapy is a transformative treatment that addresses underlying genetic mutations to treat or cure a disease, with several agents already approved for use*
Integrating viral vector (HCPs, payers) Viral vector that can insert into the recipient's own genes (patients, caregivers, advocates)		Use when describing integrating vectors such as lentivirus vectors in which the vector genome predominantly integrates into the host genome
In vivo gene therapy	Directed gene therapy	Use to describe gene therapy that is delivered directly to the patient to modify cells
Method of treatment	Treatment approach, mode of treatment, scientific technique, form of treatment, medical approach	Use to describe gene therapy approaches
Non-integrating viral vector		Use when comparisons are made with integrating vectors, such as lentiviral vectors. With non-integrating vectors (i.e. AAV, adenovirus), the vector genome is predominantly maintained episomally (outside of the host genome) with low rates of integration

Packaging capacity	Packaging limitation	Use when referring to the maximum size of the expression cassette that can be packaged within the vector
Promoter	Start codon	Use when describing the sequence of DNA that initiates transcription of a gene (or transgene)
Transgene *Also known as therapeutic gene* Functional gene (patients, caregivers, advocates)	Healthy gene	Use when describing the gene product following gene transfer. Describes the working gene/genetic material that has been inserted in the gene therapy vector
Tissue-specific promoter	Promoter	Use when describing gene therapy vectors that have been designed with a promoter that is only active in certain cell types. 'Tissue' can be replaced with the specific organ/tissue of interest, for example 'liver-specific promoter'
Vector particle shedding	Vector excretion/expulsion Viral shedding	Vector particle shedding should be used when referring to the dissemination of gene therapy vector components (vector DNA or viral particles) into the environment via excreta (i.e. bodily fluids) from the treated patient *Example: **Vector particle shedding** was detected two weeks after AMT-060 infusion*
Vector clearance		Use when describing the point at which vector shedding is no longer detectable in any given body fluid *Example: **Vector clearance** from the urine was demonstrated in all subjects following AMT-060 infusion*
Etranacogene dezaparvovec: Background		
Preferred terms/phrases	**Non-preferred terms/phrases**	**Description and guidance for use**
AAV5-hFIXco-WT (formerly AMT-060)	Precursor to AMT-061, first-generation gene therapy	Use to describe the uniQure AAV5 vector with a liver-specific promoter driving expression of a codon-optimized wild-type human FIX gene

AMT-060 comprises a recombinant AAV5 vector incorporating an expression cassette containing codon-optimized human wild-type FIX under the control of a liver-specific promoter		Short descriptor to be used at first mention of AMT-060
External communications: Etranacogene dezaparvovec or EtranaDez (formerly AMT-061) **Internal communications:** Etranacogene dezaparvovec or EtranaDez (CSL222)	CSL222, AMT-061, second-generation gene therapy, Hemgenix (until confirmed and approved)	For **external communications:** • Use etranacogene dezaparvovec/ EtranaDez (formerly AMT-061); include 'formerly AMT-061' only on first mention in a document/material and then refer to it as etranacogene dezaparvovec or EtranaDez • AMT-061 may continue to be used in agency and regulatory interactions and in publications • For publications the full name (etranacogene dezaparvovec) should be used; EtranaDez can be used in slide decks and where character count is limited **For internal communications:** • Use EtranaDez (CSL222)
Etranacogene dezaparvovec (formerly AMT-061) is a transformative recombinant AAV5 vector that includes an expression cassette containing a codon-optimized Padua variant of FIX under the control of a liver-specific promoter (LP-1)		Short descriptor to be used at first mention of etranacogene dezaparvovec. Liver-specific promoter 1 (LP-1) is the liver-specific promoter used in AMT-060 and etranacogene dezaparvovec
Etranacogene dezaparvovec is similar to AMT-060, differing only in a single amino acid substitution in the *F9* gene encoding the highly active, naturally occurring Padua variant		Short descriptor to be used to describe the difference between AMT-060 and etranacogene dezaparvovec
Naturally occurring AAV5-capsid (HCPs, payers) AAV5-vector shell or AAV5-delivery vehicle (patients, caregivers, advocates)	AAV5 capsule, AAV5 polyhedron, AAV5 carrier, AAV5 shell (for HCPs)	Use when describing the outer protein component of an AAV vector that surrounds the therapeutic genetic material

Highly active Padua variant, gain-of-function variant, or Padua variant of factor IX (FIX-Padua)	Hyperactive Padua variant, hyper-functional Padua variant	Use to describe the Padua variant of the *F9* gene that encodes a FIX protein with increased activity compared with wild type
Liver-specific promoter	Promoter	Use when describing the design of etranacogene dezaparvovec *Example: Etranacogene dezaparvovec comprises codon-optimized human FIX-Padua under the control of **a liver-specific promoter**, LP-1*
Etranacogene dezaparvovec: Clinical development		
Preferred terms/phrases	**Non-preferred terms/phrases**	**Description and guidance for use**
Phase 1/2 study of AMT-060 (NCT02396342) (at first mention)	AMT-060 clinical study NCT02396342 Phase 1/2 study of etranacogene dezaparvovec	Use when first describing the Phase 1/2 study of AMT-060 in patients with severe or moderately severe hemophilia B; the term 'Phase 1/2 study' can be used thereafter
The Phase 1/2 study of AMT-060 (NCT02396342) is a multinational, open-label, Phase 1/2 dose-escalation study investigating AMT-060 in adults with severe or moderately severe hemophilia B (HCPs, payers) The Phase 1/2 study of AMT-060 was designed to determine the safety and optimal dose of AMT-060 in adults with severe or moderately severe hemophilia (patients, caregivers, advocates)		Short descriptor to be used at first mention of the Phase 1/2 study
Phase 2b study of etranacogene dezaparvovec (NCT03489291) (at first mention)	Phase 2 clinical study, NCT03489291	Use at first mention of the Phase 2b study of etranacogene dezaparvovec in patients with severe or moderately severe hemophilia B; the term 'Phase 2b study' can be used thereafter

The Phase 2b study of etranacogene dezaparvovec (NCT03489291) is an open-label, single-dose, single-arm, multicenter study in adults with severe or moderately severe hemophilia B (HCPs, payers) The Phase 2b study of etranacogene dezaparvovec (NCT03489291) examines the safety and efficacy of a single dose of etranacogene dezaparvovec in adults with severe or moderately severe hemophilia B (patients, caregivers, advocates)		Short descriptor to be used at first mention of the Phase 2b study
HOPE-B (Health Outcomes with Padua gene: Evaluation in Hemophilia B; NCT03569891) (at first mention) HOPE-B	HOPEB, Hope-B, NCT03569891 Phase 3 clinical study	Use when first describing the Phase 3 study of etranacogene dezaparvovec gene therapy for hemophilia B; the term 'HOPE-B' can be used thereafter
HOPE-B (Health Outcomes with Padua gene: Evaluation in Hemophilia B; NCT03569891) is a Phase 3, open-label, single-dose, single-arm, multinational trial in adults with severe or moderately severe hemophilia (HCPs, payers) HOPE-B (Health Outcomes with Padua gene: Evaluation in Hemophilia B; NCT03569891) is a Phase 3 clinical study investigating the safety and efficacy of a single dose of etranacogene dezaparvovec in adults with severe or moderately severe hemophilia (patients, caregivers, advocates)		Short descriptor to be used at first mention of the Phase 3 HOPE-B clinical trial
The primary endpoint of the HOPE-B study is the annualized bleeding rate (ABR) at 52 weeks, compared to lead-in. ABR will be measured between 26 and 78 weeks after administration		Short descriptor of the primary endpoint of the Phase 3 HOPE-B clinical trial

The secondary endpoints of the HOPE-B study include FIX activity at 6, 12 and 18 months after dosing, rates of total, spontaneous, traumatic, and treated/untreated bleeds, FIX replacement product consumption, correlation of FIX activity levels and safety with pre-treatment, AAV5 NAb titers over 26 weeks' follow-up, and safety		Short descriptor of the secondary endpoints of the Phase 3 HOPE-B clinical trial
Etranacogene dezaparvovec: Efficacy and safety		
Preferred terms/phrases	**Non-preferred terms/phrases**	**Description and guidance for use**
AAV5 neutralizing antibodies (NAbs) Antibodies to AAV5-vector shell (patients, caregivers, advocates)	AAV Nabs, NAbs, neutralizing antibodies	Use specific terminology when referring to NAbs to the AAV5 capsid and to distinguish from NAbs for other AAV serotypes/capsids
No relationship between safety and titers of pre-existing AAV5 NAbs has been observed with etranacogene dezaparvovec; the most common treatment-related AEs were similar between participants with and without pre-existing AAV5 NAbs		Short descriptor to cover safety associated with pre-existing AAV5 NAbs in the HOPE-B study
Endogenous FIX activity levels (HCPs, payers) FIX is produced from cells in the liver (patients, caregivers, advocates)	FIX expression	Use when describing FIX activity levels following gene therapy *Example: The primary objective was to assess whether **endogenous FIX activity levels** of ≥5% were achieved at 6 weeks*
Exogenous FIX product	Exogenous FIX concentrate	Use when describing the change in exogenous FIX product requirements (vs endogenous FIX activity levels) following treatment with etranacogene dezaparvovec *Example: Etranacogene dezaparvovec resulted in a decrease in **exogenous FIX product** use*

Based on the results of a comprehensive investigation conducted by an independent laboratory and reviewed by leading external experts in the field, etranacogene dezaparvovec was determined to be highly unlikely to be the cause of a single case of hepatocellular carcinoma (HCC) in the HOPE-B study		Short descriptor to cover the case of HCC diagnosed in a HOPE-B study participant post-treatment
Mean endogenous FIX activity increased to near-normal levels	Functional cure, curative/cure, near cure	Use when describing the potential benefit of etranacogene dezaparvovec gene therapy for hemophilia B (based on 26-week HOPE-B data) *Example: Mean endogenous FIX activity levels increased into the **near-normal** range* Claims about the benefits of gene therapy should be in line with the current data
Sustained and durable (HCPs, payers) Long-lasting (patients, caregivers, advocates)	Long-term Permanent/lifetime/ enduring/one-time treatment (non-preferred patient terms)	Use when describing endogenous FIX activity levels at 5 years/2 years of follow-up for AMT-060/etranacogene dezaparvovec *Example: Endogenous FIX activity levels are **sustained and durable** at 2 years of follow-up for etranacogene dezaparvovec*
Etranacogene dezaparvovec: Administration and monitoring		
Preferred terms/phrases	**Non-preferred terms/phrases**	**Description and guidance for use**
Administered via a single, one-time intravenous (IV) infusion	Unlike traditional factor replacement therapy	Use when discussing the administration of etranacogene dezaparvovec to highlight the one-time treatment. Intravenous should be spelled out in full at first use; IV can be used thereafter *Example: Etranacogene dezaparvovec is administered via a single, one-time intravenous (IV) infusion in an outpatient setting*

Companion diagnostic (CDx) for AAV5 NAbs	Biomarker test	A companion diagnostic (CDx) is a diagnostic test used as a companion to a therapeutic drug to determine its applicability to a specific person The FDA has requested a CDx test to assess the pre-existing AAV5 NAb levels in PWHB prior to treatment with etranacogene dezaparvovec
Genome copies (gc), vector genomes (vg), or vector genome copies (VGC)	Vector copies	Use to describe the dose of etranacogene dezaparvovec given to a PWH (in gc/kg) Note: uniQure has been describing the dose in terms of genome copies vs Freeline, Pfizer/Spark, who use the terminology vector genomes