GLOSSARY OF TECHNICAL TERMS

This glossary contains definitions of certain technical terms used in this document in connection with us and our business. These may not correspond to standard industry definitions, and may not be comparable to similar terms adopted by other companies.

"AAV"	adeno-associated virus, which has emerged as an attractive vector for gene therapy to promote sustained gene expression in a variety of tissues such as muscle, eye, brain, liver, and lung
"AAV2"	adeno-associated virus serotype 2
"AAVANCE™"	AAV Advanced Next-gen CGMP Excellence, our manufacturing platform which we created to deliver scalable, high-quality and low-cost production of rAAV gene therapy products
"ACE inhibitors"	angiotensin converting enzyme inhibitors, a class of drugs treating hypertension by blocking the ACE enzyme
"adRP"	autosomal dominant RP
"AE"	adverse event, a harmful and negative outcome that happens when a patient has been provided with medical care
"Aflibercept"	a humanized recombinant fusion protein which is a soluble decoy receptor that binds vascular endothelial growth factor A and B, and placental growth factor with a greater affinity than the body's native receptors. It is called a decoy receptor since VEGF does not bind to its original receptors and mistakenly binds with aflibercept, thereby reducing VEGF activity
"AMD"	age-related macular degeneration, a degenerative retinal disease that causes progressive loss of central vision, and the leading cause of irreversible blindness in aged people
"ANGPT2"	an angiogenic factor primarily secreted by endothelial cells which exacerbates inflammatory responses and serves as an early biomarker of endothelial injury during sepsis
"anti-VEGF"	a medicine that slows or stops the damage caused by the abnormal growth of blood vessels

"annualized anti-VEGF injection rate"	calculated as the percentage difference between the number of pre- and post-treatment annualized anti-VEGF injections, where (i) the number of pre-treatment annualized anti-VEGF injections is calculated as total anti-VEGF injections in the one year preceding treatment divided by the smaller of 366 days or the time between when a study eye first received anti-VEGF treatment and the injection time of the studied product candidate, and (ii) the number of post-treatment annualized anti-VEGF injections is calculated as total anti-VEGF injections after treatment divided by the quotient of (x) the time between the last visit and the injection time of the studied product candidate, divided by (y) 365.25 days
"ARVC"	arrhythmogenic right ventricular cardiomyopathy, a genetically determined heart muscle disease characterized by progressively fibrofatty replacement of the right ventricular myocardium
"Bac/Sf9"	Baculovirus/Spodoptera frugiperda 9
"BCVA"	best corrected visual acuity, the highest level of vision a person can achieve using the best possible corrective lenses (like glasses or contacts) to treat refractive errors
"BLA"	the Biologics License Application, a request to the FDA for permission to introduce, or deliver for introduction, a biologic product into interstate commerce
"CDE"	the Center for Drug Evaluation (國家藥品監督管理局藥品審評中心), a department of the NMPA responsible for evaluating drug clinical trial applications, drug marketing authorization applications, supplementary applications, and overseas production drug re-registration applications
"CDMO"	contract development and manufacturing organization, a company that serves other companies in the pharmaceutical industry on a contract basis, providing drug development and drug manufacturing services
"CEP290"	centrosomal protein 290, a vital gene and protein crucial for building and maintaining primary cilia and centrosomes, cellular structures involved in cell division, shape, and sensory functions like vision and hearing
"cGMP"	current good manufacturing practices, regulations enforced by regulatory authorities such as the U.S. Food and Drug Administration, the World Health Organization, and the European Medicines Agency to ensure that pharmaceutical products, medical devices, and food products are consistently produced and controlled according to strict quality standards

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"cKO"	conditional knockout, a genetic technique where a specific gene is turned off or deleted in targeted cells, tissues, or at specific times, rather than globally, allowing researchers to study gene function and model diseases without causing early lethality or widespread effects seen in traditional gene knockouts
"CMC"	chemistry, manufacturing, and controls processes in the development, licensure, manufacturing, and ongoing marketing of pharmaceutical products
"codon optimization"	a process used to improve gene expression and increase the translational efficiency of a gene of interest by accommodating codon bias of the host organism
"connecting cilium"	a specialized, narrow stalk in photoreceptor cells (rods & cones) linking the inner segment (protein factory) to the light-sensing outer segment, acting as a bridge between the inner and outer segments of photoreceptors, facilitating the movement of essential proteins and materials required for photoreceptor survival and function
"COR"	class of recommendation, a system rating the strength of advice for a treatment or test, indicating how likely its benefits outweigh risks
"CpG motif"	Cytosine-Guanine motif, a DNA sequence where a Cytosine (C) nucleotide is directly followed by a Guanine (G) nucleotide, linked by a phosphate group (p)
"CRO(s)"	contract research organization, a company that provides support to the pharmaceutical, biotechnology, and medical device industries in the form of research services outsourced on a contract basis
"CSME"	clinically significant macular edema
"CSO(s)"	contract sales organization, a company that provides services and solutions related to pharmaceutical marketing and sales activities on a contract basis
"CST"	central subfield thickness, an objective, quantifiable measure of retinal thickness in the central part of the macula (1mm diameter), often used in conditions like diabetic macular edema or age-related macular degeneration
"dB"	a logarithmic unit for sound, used in audiometry (hearing tests) to measure hearing thresholds and in ultrasound imaging

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"DLT"	dose limiting toxicities, a clinically significant adverse event or abnormal laboratory value assessed as unrelated to disease progression, intercurrent illness, or concomitant medications and meeting the US National Cancer Institute common terminology criteria that are Common Terminology Criteria for Adverse Events Grade 3 (severe) or 4 (life-threatening)
"DME"	diabetic macular edema
"dose-escalation"	a process used in early-phase clinical trials, particularly Phase I studies, to identify the maximum tolerated dose of an investigational treatment
"dose-limiting toxicity"	side effects of a drug or other treatment that are serious enough to prevent an increase in dose or level of that treatment
"DR"	diabetic retinopathy, a microvascular and neurodegenerative complication of diabetes mellitus, characterized by pericyte loss, basement membrane thickening, microaneurysm formation, neovascularization, and blood-retinal barrier disruption
"empty capsid"	viral capsids that do not contain vector genome, formed when adeno-associated viruses are packaged for use as viral vectors in gene therapy
"EOSRD"	early-onset severe retinal dystrophy, a group of rare, inherited genetic eye conditions causing profound vision loss starting in infancy or early childhood (before age 5), characterized by poor night/central vision, nystagmus (involuntary eye movements), light sensitivity, and slow pupil response, often overlapping with Leber congenital amaurosis, with vision worsening progressively over time
"ETDRS letters"	letters used in the Early Treatment Diabetic Retinopathy Study chart, which is a standardized tool for measuring visual acuity in eye exams, particularly for diabetic eye disease
"EXACTE™"	Excellence in AAV Capsid and Transgene Engineering, our rAAV gene therapy R&D platform which we created to drive innovation, efficiency, and safety in the creation of gene therapies
"EZ width"	the transverse distance of the continuously visible portion of the ellipsoid zone (EZ) measured along the horizontal direction of the retina on optical coherence tomography (OCT) images
"Fast Track Designation"	status assigned by the FDA to a drug or product in clinical trials signifying that the FDA will facilitate and expedite the development and review of the application for the approval of the new drug

"Fc"	Fragment crystallizable, the tail region of an antibody, responsible for effector functions, distinct from the antigen-binding Fab arms
"FDA" or "US FDA"	The United States Food and Drug Administration, a federal agency of the Department of Health and Human Services
"first-line"	the initial, preferred, or standard therapy given for a specific disease or condition, chosen for its high effectiveness and generally lower risk
"FPI"	first patient in, the official date and/or date and time the first participant meets all criteria and is officially accepted into or receives treatment in a clinical trial
"FST"	full-field stimulus threshold, a psychophysical measure of whole-field retinal light sensitivity
"GCP"	good clinical practice, an international ethical and scientific quality standard for designing, conducting, recording and reporting trials that involve the engagement of human participants
"gene therapy"	the use of various genetic altering techniques to treat diseases at their sources
"GMP"	good manufacturing practice, the systems and procedures required to ensure that pharmaceutical products are consistently produced and controlled according to quality standards. In the context of clinical trials, GMP ensures that investigational medicinal products are manufactured in a way that upholds participant safety, product integrity, and regulatory compliance
"GUCY2D"	Guanylate Cyclase 2D, a gene crucial for vision, producing an enzyme in the retina that helps convert light into electrical signals, and mutations in it cause inherited retinal diseases
"HCM"	hypertrophic cardiomyopathy, a genetic condition characterized by the abnormal thickening of the heart muscle, particularly the ventricular walls. This thickening can obstruct blood flow and impair the heart's ability to pump blood effectively, potentially leading to arrhythmias, heart failure, or sudden cardiac death
"HEK293"	human embryonic kidney 293
"IgG1"	Immunoglobulin G1, the most abundant human IgG subclass, known for potent immune activation and therapeutic utility
"IND"	investigational new drug or investigational new drug application, also known as clinical trial application in China

"intravitreal injection"	a medical procedure in which medication is delivered directly into the vitreous humor, the clear gel-like substance that fills the space between the lens and the retina of the eye. This method of administration allows for targeted treatment of various eye conditions, such as age-related macular degeneration, diabetic retinopathy, and retinal vein occlusion
"investigator-initiated trial" or "IIT"	investigator-initiated trial, a clinical trial in which the investigator conceives the research, develops the protocol
"*in vitro*"	latin for "within the glass", referring to studies that are performed with entities outside their normal biological context
"*in vivo*"	latin for "within the living", referring to studies in which the effects of various entities are tested on whole, living organisms or cells, usually animals, including humans, and plants
"IRD"	inherited retinal disease
"LCA"	Leber congenital amaurosis, a severe form of retinal dystrophy that results in partial or total loss of both cone and rod photoreceptors, leading to congenital blindness, typically inherited in an autosomal recessive manner
"LCA2"	Leber congenital amaurosis type 2, a severe inherited retinal degeneration, which results in severe hypovision early in life
"MLMT"	the Multi-Luminance Mobility Test, a relatively novel method that provides a measure of vision-related activities of daily living, namely ambulatory vision
"MYBPC3"	myosin-binding protein C3, a protein coding gene
"nAMD"	neovascular AMD, a severe form of macular degeneration where abnormal, leaky blood vessels grow under the retina, causing swelling, bleeding, scarring, and rapid central vision loss, making it a major cause of blindness
"NDA"	new drug application
"NEI VFQ-25 Score"	the National Eye Institute Visual Function Questionnaire-25, a standard participant-reported questionnaire assessing vision-related quality of life across 12 domains like near/distance vision, ocular pain, social functioning, and driving, with scores from 0 (worst) to 100 (best), used in clinical trials for eye diseases (cataracts, AMD, glaucoma) to measure how vision problems impact daily life and treatment effectiveness

"NMPA"	the National Medical Products Administration (國家藥品監督管理局), which is in charge of comprehensive supervision on the safety management of food, health and cosmetics and is the competent authority of drug regulation in China, formerly known as China Food and Drug Administration ("**CFDA**") (國家食品藥品監督管理局)
"NPDR"	non-proliferative DR
"OCT"	optical coherence tomography, a non-invasive diagnostic technique that renders an *in vivo* cross-sectional view of the retina
"open-label"	a trial where both the study participants and the healthcare providers know which treatment (experimental drug, existing treatment, or placebo) is being given, which is also called nonblinded
"Orphan Drug Designation"	a status given to certain drugs called orphan drugs, which show promise in the treatment, prevention, or diagnosis of orphan diseases
"PCT"	the Patent Cooperation Treaty, an international patent law treaty, concluded in 1970. It provides a unified procedure for filing patent applications
"PD"	Parkinson's disease
"PDR"	proliferative diabetic retinopathy, the advanced, sight-threatening stage defined by the growth of abnormal, fragile new blood vessels on the retinal, which can lead to severe bleeding and retinal detachment
"PDT"	photodynamic therapy, or ophthalmic photodynamic therapy, which is a minimally invasive treatment method that utilizes specific light to activate a photosensitizer, thereby selectively destroying pathological ocular tissues
"Phase I clinical trial"	a study that tests the safety of a new drug candidate
"Phase II clinical trial"	a study that tests the new drug candidate on a larger group of participants, to gather information about whether and how well it works
"Phase III clinical trial"	a study for a new drug candidate that has already passed Phases I and II, which tests the new drug candidate in larger groups of participants and compares the new drug candidate against an existing treatment or a placebo to see if it works better in practice and if it has important side effects
"PKP2"	the gene encoding Plakophilin-2, a protein crucial for heart muscle cell structure (desmosomes)

"PlGF"	placental growth factor, a key protein and biomarker, primarily used in pregnancy to help diagnose early-onset pre-eclampsia by assessing placental health
"PPV"	pars plana vitrectomy
"protein engineering"	the deliberate modification of amino acids in a protein, typically utilizing the known three-dimensional structure and biochemical mechanisms of the protein, often through techniques such as site-directed mutagenesis to enhance properties like stability and activity
"QA"	quality assurance, the systematic efforts taken to assure that a drug meets with all the quality expectations
"QC"	a process by which a company reviews the quality of all factors involved in the production of a drug
"rAAV"	recombinant adeno-associated virus, a small, non-pathogenic viral vector that has become the leading platform for *in vivo* gene therapy and a modified, gene-carrying version of the AAV
"RP"	retinitis pigmentosa, an inherited retinal disease causing retinal degeneration and a decline in vision
"RPE"	retinal pigment epithelium
"RPE65"	retinal pigment epithelium-specific protein 65 kDa, a crucial enzyme in the visual cycle, essential for regenerating light-sensitive visual pigments in the retina
"Rpgr-KO mice"	Rpgrip1 knockout mice
"RPGR-ORF15"	the Open Reading Frame 15 region of the Retinitis Pigmentosa GTPase Regulator gene
"RP2D"	recommended Phase II dose
"RVO"	retinal vein occlusion
"SAE"	serious adverse event, any medical occurrence in human drug trials that at any dose: results in death; is life-threatening; requires inpatient hospitalization or causes prolongation of existing hospitalization; results in persistent or significant disability/incapacity; may have caused a congenital anomaly/birth defect, or requires intervention to prevent permanent impairment or damage
"SMO(s)"	site management organization
"SUSAR"	suspected unexpected serious adverse reactions
"TEAE"	an adverse medical event occurring during the treatment period

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"vascular permeability"	the ability of blood vessels to allow the passage of plasma proteins and other macromolecules into surrounding tissues. It is a process significantly influenced by factors such as vascular endothelial growth factor
"Vector"	a DNA molecule (often plasmid or virus) that is used as a vehicle to carry a particular DNA segment into a host cell as part of a cloning or recombinant DNA technique
"VEGF"	vascular endothelial growth factor, a gene critical for the growth and development of cancer cells. There are three main subtypes of VEGF receptors, including VEGFR-1, VEGFR-2 and VEGFR-3
"VEGF-A"	a biochemical signal protein that promotes angiogenesis throughout the body and in the eye. By decreasing VEGF-A activation of its native receptors, aflibercept reduces subsequent growth of new blood vessels
"VEGF-B"	a growth factor involved in blood vessel support, tissue protection, and neuronal survival, with roles beyond simple blood vessel formation (angiogenesis), acting as a crucial antioxidant to combat oxidative stress in diseases like heart disease, glaucoma, and Parkinson's
"VEGFR"	vascular endothelial growth factor receptor, a family of receptor tyrosine kinases (VEGFR-1, -2, -3) on cell surfaces that bind VEGF, initiating signals for blood vessel growth
"XLRP"	X-linked retinitis pigmentosa