

GLOSSARY

This glossary contains certain technical terms used in this Document in connection with us and our business. Such terms and their meaning may not correspond to standard industry definitions or usage.

“activated partial thromboplastin time” or “aPTT”	a laboratory test that measures the time it takes for blood to clot via the intrinsic and common coagulation pathways, used to assess bleeding disorders and monitor anticoagulant therapy
“activin receptor-like kinase 7” or “ALK7”	a receptor involved in TGF- β signaling, with roles in metabolism and inflammation
“acute limb ischemia” or “ALI”	a sudden decrease in limb perfusion causing a potential threat to limb viability, usually resulting from embolism or thrombosis
“adverse event” or “AE”	any untoward medical occurrence in a participant administered a pharmaceutical product, which does not necessarily have a causal relationship with the trial intervention
“alanine aminotransferase” or “ALT”	a liver enzyme primarily found in hepatocytes, and its elevated levels in blood serve as a biomarker for liver cell injury or inflammation
“angiotensinogen” or “AGT”	a precursor protein in the renin-angiotensin system that regulates blood pressure, fluid balance, and electrolyte homeostasis
“antisense oligonucleotide” or “ASO”	a short, single-stranded synthetic nucleic acid sequence designed to bind specifically to messenger RNA (mRNA) through Watson-Crick base pairing
“apolipoprotein(a)” or “Apo(a)”	a glycoprotein covalently linked to apoB100, forming lipoprotein(a); elevated levels are an independent causal risk factor for atherosclerotic cardiovascular disease
“apolipoprotein B” or “ApoB”	a primary structural protein of atherogenic lipoproteins, including low-density lipoprotein (LDL) and lipoprotein(a)
“apolipoproteinB100” or “apoB100”	the full-length form of ApoB found in VLDL, IDL, LDL, and Lp(a), essential for lipoprotein assembly and cholesterol transport
“atrial fibrillation” or “AF”	an irregular and often rapid heart rhythm that increases the risk of stroke, heart failure, and other cardiovascular complications
“asialoglycoprotein receptor” or “ASGPR”	a receptor on the surface of hepatocytes in the liver, recognizes and internalizes N-acetyl galactosamine (GalNAc), primarily used for delivery siRNA to the liver

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“atherosclerotic cardiovascular disease” or “ASCVD”	a group of cardiovascular diseases including coronary heart disease, stroke, and peripheral vascular disease, characterized by the formation of lipid plaques and thickening and hardening of the vessel walls, leading to narrowing and blockage
“autoimmune”	relating to a process in which the immune system mistakenly targets and attacks the body’s own cells and tissues
“biomarker”	a defined characteristic that is measured as an indicator of normal biological processes, pathogenic processes, or responses to an exposure or intervention, including therapeutic interventions
“CAGR”	compound annual growth rate
“cancer-associated thrombosis” or “CAT”	venous or arterial thromboembolic events that occur in association with malignancy and its treatment
“cardiovascular disease” or “CVD”	a broad therapeutic area encompassing a group of disorders affecting the heart and blood vessels
“causal risk factor”	a biological factor that is not only statistically associated with a disease, but has been demonstrated through genetic, mechanistic, or interventional evidence to directly contribute to the onset or progression of the disease
“central nervous system” or “CNS”	the system comprising the brain and spinal cord
“CDMO”	contract development and manufacturing organization
“cGMP”	current Good Manufacturing Practice regulations enforced by the FDA
“coronary heart disease” or “CHD”	a type of cardiovascular disease caused by narrowing or blockage of the coronary arteries
“chronic kidney disease” or “CKD”	a progressive loss of kidney function over months or years, leading to accumulation of waste products and increased risk of cardiovascular disease
“CMC”	activities related to chemistry, manufacturing, and quality control of drug development
“coagulation”	the physiological process by which blood forms clots to stop bleeding, involving platelets, coagulation factors, and fibrin formation
“cohort”	a group of patients as part of a clinical trial who share a common characteristic or experience within a defined period and who are monitored over time

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“combination therapy”	the use of two or more drugs or treatment modalities simultaneously to manage or treat a disease, often to enhance efficacy, reduce resistance, or minimize side effects
“coronary artery disease” or “CAD”	a condition characterized by narrowing or blockage of the coronary arteries due to atherosclerosis, leading to reduced blood supply to the heart muscle
“CRO”	contract research organization
“CTN”	clinical trial notification
“diabetes”	a chronic metabolic disease characterized by elevated blood glucose levels, leading to long-term complications affecting the cardiovascular system, kidneys, nerves, eyes, and other organs
“direct oral anticoagulant” or “DOAC”	a class of oral anticoagulant drugs that directly inhibit either thrombin or Factor Xa
“drug-drug interaction” or “DDI”	a modification in the effect of a drug when administered with another drug, which may increase toxicity or reduce efficacy
“dyslipidemia”	a metabolic disorder characterized by abnormal amounts of lipids or lipoproteins in the blood
“EMA”	the European Medicines Agency, responsible for the scientific evaluation, supervision, and safety monitoring of medicines within the EU and the European Economic Area
“extrahepatic” or “ex-hepatic”	occurring outside the liver
“Factor XI” or “FXI”	a clotting factor in the blood that, when activated (FXIa), plays a role in the intrinsic pathway of the coagulation cascade
“Factor Xa” or “FXa”	a clotting factor in the blood that plays a central role in the common pathway of the coagulation cascade
“FDA”	the U.S. Food and Drug Administration, responsible for ensuring the safety, efficacy, and quality of drugs, biologics, and medical devices
“glucagon-like peptide-1” or “GLP-1”	an incretin hormone that stimulates insulin secretion, inhibits glucagon release, slows gastric emptying, and reduces appetite
“GMP”	the aspects of quality assurance that ensure that medicinal products are consistently produced and controlled to the standards required for their intended use

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“good clinical practice” or “GCP”	a set of international ethical and scientific quality standards for designing, conducting, and reporting clinical trials to protect participants and ensure data integrity
“HbA1c”	glycated hemoglobin, formed when hemoglobin binds glucose in the blood, used as a marker of glucose levels in the blood over the last two to three months
“hepatic”	relating to the liver
“high-density lipoprotein cholesterol” or “HDL-C”	a type of cholesterol carried by high-density lipoprotein particles, often referred to as “good cholesterol,” as it helps remove excess cholesterol from the bloodstream and transport it to the liver for excretion or recycling, thereby reducing the risk of atherosclerotic cardiovascular disease
“hypercholesterolemia”	a condition of abnormally elevated cholesterol levels in the blood
“hyperlipidemia”	abnormally elevated levels of any or all lipids or lipoproteins in the blood
“IND”	a request for authorization to administer an investigational new drug or biological product to humans
“inhibin beta E subunit” or “INHBE”	a liver-expressed gene implicated in metabolic regulation and a potential biomarker for non-alcoholic fatty liver disease progression
“ <i>in vitro</i> ”	Latin for “within the glass”, referring to studies that are performed with microorganisms, cells, or biological molecules outside their normal biological context
“ <i>in vivo</i> ”	Latin for “within the living”, referring to studies in which the effects of various biological entities are tested on whole, living organisms or cells, usually animals, including humans, and plants, as opposed to a tissue extract or dead organism
“Key Product(s)”	for the purposes of this Document, our Key Products refer to SRSD216 and SRSD384
“lipoprotein(a)” or “Lp(a)”	a cholesterol-carrying particle in the blood that resembles LDL but contains an additional protein called apolipoprotein(a)
“lipoprotein(a) gene” or “LPA gene”	a gene that encodes apolipoprotein(a), the distinctive protein component of lipoprotein(a)
“low-density lipoprotein cholesterol” or “LDL-C”	a type of cholesterol that is often referred to as “bad” cholesterol as it may build up in the walls of blood vessels and cause atherosclerotic diseases

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“lipid metabolism”	the biochemical processes that involve the synthesis, degradation, and utilization of lipids in the body, including fatty acids, triglycerides, and cholesterol
“loss-of-function” or “LoF”	a genetic variant or mutation that results in reduced or abolished activity of the encoded protein
“lower limit of quantification” or “LLOQ”	the lowest concentration of an analyte that can be reliably measured with acceptable accuracy and precision
“messenger RNA” or “mRNA”	a type of single-stranded RNA molecule that carries genetic information transcribed from DNA and serves as a template for protein synthesis
“mixed dyslipidemia”	a condition characterized by abnormal levels of multiple blood lipids simultaneously — typically elevated LDL cholesterol and triglycerides. Mixed dyslipidemia is a subtype of HTG
“monoclonal antibody”	a type of antibody produced by identical immune cells that are clones of a unique parent cell, designed to target and bind to a specific antigen with high specificity, often used in diagnostics and therapies
“monotherapy”	a treatment regimen involving only one therapy, without combination with other drugs
“multiregional clinical trial” or “MRCT”	a clinical trial conducted simultaneously in multiple countries or regions
“N-acetyl galactosamine” or “GalNAc”	a molecule used for targeting RNA drugs to liver cells
“NDA”	new drug application, a formal proposal submitted to the FDA seeking approval to market a new pharmaceutical for sale and use in the United States, including data on the drug’s safety, efficacy, and manufacturing process
“NMPA”	the National Medical Products Administration of the PRC (中華人民共和國國家藥品監督管理局)
“non-human primates” or “NHP”	all primate species except humans, such as monkeys and apes
“off-target effects”	side effects caused by a drug acting on molecules other than its intended targets
“oligonucleotide drug”	a drug that targets the regulation of gene expression using short nucleic acid sequences
“oxidized phospholipids” or “OxPL”	phospholipids that have undergone oxidative modification, implicated in inflammation and atherosclerosis

GLOSSARY

“PCT”	Patent Cooperation Treaty, an international treaty administered by the World Intellectual Property Organization that allows inventors and companies to seek patent protection for their inventions simultaneously in multiple countries through a single international patent application, simplifying the process of securing patent rights across different jurisdictions and providing a standardized procedure for the initial phase of patent filing
“peripheral artery disease” or “PAD”	a cardiovascular disease characterized by narrowing of peripheral arteries, most commonly in the legs, leading to reduced blood flow
“peripheral vascular disease” or “PVD”	a condition characterized by narrowing, blockage, or dysfunction of blood vessels outside the heart and brain, most commonly affecting the arteries in the legs, which can lead to reduced blood flow, pain, and increased risk of cardiovascular events
“pharmacodynamics” or “PD”	the study of how a drug affects the body, including its mechanism of action, therapeutic effects, and potential side effects
“pharmacokinetics” or “PK”	the study of how a drug is absorbed, distributed, metabolized, and eliminated by the body, providing crucial information on the drug’s behavior and dosing regimen
“primary endpoint”	the main outcome measure used in a clinical trial to determine the effect of a treatment, reflecting the primary objective of the study, such as overall survival or disease progression
“proprotein convertase subtilisin/kexin type 9” or “PCSK9”	a protein synthesized by the liver, it binds to the LDL receptor on the surface of hepatocytes, leading to the degradation of the LDL-R and subsequently to higher plasma LDL-C levels, a therapeutic target for cholesterol-lowering drugs
“Q3M”	every three months
“Q6M”	every six months
“renin-angiotensin system” or “RAAS”	a hormone-based regulatory pathway that controls blood pressure, fluid balance, and vascular resistance through the sequential activation of renin, angiotensin I and II, and aldosterone
“RNA-induced silencing complex” or “RISC”	a protein complex involved in RNA interference, which binds to small RNAs and recognizes and degrades target mRNA, thereby suppressing mRNA expression

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“RNA interference” or “RNAi”	a biological process that regulates mRNA expression through small RNA molecules, which can specifically degrade homologous mRNA and further inhibit mRNA expression
“secondary endpoint”	an additional outcome measure in a clinical trial used to evaluate the effects of a treatment, providing supplementary information on efficacy and safety, such as quality of life or biomarker changes
“serious adverse event” or “SAE”	adverse events occurring during clinical drug use that pose a significant threat to the patient’s health or life, including those leading to death, life-threatening conditions, the need for hospitalization or prolonged hospitalization, permanent or severe disability/loss of function, or congenital abnormalities/birth defects
“single ascending dose” or “SAD”	a study design in which single doses of a drug are gradually increased to evaluate safety and tolerability
“siRNA”	a class of double-stranded RNA molecules, typically 20-25 base pairs in length, that mediates RNA interference by guiding the sequence-specific degradation of complementary mRNA
“subcutaneous”	applied under the skin
“TGA”	Therapeutic Goods Administration; Australia’s regulatory authority for therapeutic goods such as medicines, medical devices, and diagnostic tests
“tissue factor” or “TF”	a transmembrane protein that initiates the extrinsic pathway of coagulation by binding Factor VIIa
“therapeutic window”	the range of drug dosages that can treat disease effectively without having toxic effects, or the time interval during which a particular therapy can be given safely and effectively
“thrombosis”	the formation of a blood clot within a blood vessel that impedes normal blood flow
“thrombin”	a serine protease that converts fibrinogen to fibrin during blood coagulation
“total knee arthroplasty” or “TKA”	a surgical procedure to replace the weight-bearing surfaces of the knee joint with prosthetic components
“treatment-emergent adverse events” or “TEAEs”	adverse events that occur during treatment, regardless of whether they are drug-related or the severity

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“triglycerides” or “TG”	the most common type of fat in the human body. Triglycerides in the blood are associated with an increased risk of cardiovascular disease and pancreatitis
“venous thromboembolism” or “VTE”	an impairment of venous return due to the obstruction of blood vessels caused by venous thrombosis, which includes deep vein thrombosis and pulmonary embolism