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 similarly terms adopted by other companies.

"3 + 3 design"	starts off by treating three patients at a conservative low dose. If no dose-limiting toxicities (DLTs) occur, escalation proceeds; if one DLT occurs, three additional patients are treated at the same dose. Escalation continues if ≤1 of 6 patients experiences a DLT; if ≥2 patients experience DLTs (among 3 or 6), the maximum tolerated dose (MTD) is defined as the previous dose. This continues until an MTD is defined
"5-FU"	5-Fluorouracil, a widely used chemotherapeutic agent that inhibits DNA synthesis and is commonly used in the treatment of various solid tumors
"adenovirus"	a type of virus used as a viral vector in oncolytic virotherapy
"ATP"	extracellular adenosine triphosphate, a danger signal that alerts the immune system to tissue injury
"BRAF/MEK-targeted therapy"	a type of targeted cancer treatment that blocks two key proteins — BRAF and MEK — in the MAPK (mitogen-activated protein kinase) signaling pathway, which controls cell growth and survival
"BRAFV600"	a common mutation in the BRAF that leads to a hyperactive protein, promoting uncontrolled cell growth and cancer
"BsAb"	bispecific antibody
"BTC"	biliary tract cancer, a class of malignant tumors arising from the biliary system, including cancers of the bile ducts and gallbladder
"$CCID_{50}$"	Median Cell Culture Infectious Dose, a measure used in virology to quantify the amount of virus required to produce cytopathic effects in 50% of inoculated cell cultures
"CD3"	a protein complex found on the surface of T cells that plays a critical role in T-cell receptor signaling and activation
"CD40L"	also known as CD154, a protein that plays a key role in the immune system by helping to regulate both cellular and humoral immune responses
"CD8 + T cells/cytotoxic T lymphocytes"	a subset of T cells that play a crucial role in the immune response by directly killing infected or cancerous cells
"central nervous system tumor"	refers to a neoplasm arising in the brain or spinal cord, including primary tumors of the central nervous system such as malignant glioma and its subtypes, including GBM
"CMC"	chemistry, manufacturing and controls

GLOSSARY OF TECHNICAL TERMS

"CMV"	cytomegalovirus immediate-early promoter, a strong viral promoter widely used in genetic engineering to drive high-level transgene expression in mammalian cells
"cocktail therapy"	a treatment approach involving the concurrent use of multiple therapeutic agents with complementary mechanisms of action to achieve synergistic anti-tumor effects
"cold tumor"	a tumor type with low immune cell infiltration, making it less responsive to immunotherapy, as the immune system fails to recognize and attack the tumor effectively
"CR"	complete response, patients in a clinical trial whose cancer entirely disappears after treatment
"CRC"	colorectal cancer, a malignant disease arising in the colon or rectum
"CSF"	cerebrospinal fluid
"cynomolgus"	refers to the cynomolgus monkey (Macaca fascicularis), a non-human primate species widely used in preclinical toxicology and pharmacokinetic studies due to its similarity to humans
"cytotoxic T lymphocytes (CTLs)"	subsets of T cells (CD8+) that can directly kill infected or malignant cells by recognizing antigens on their surface
"cytotoxicity"	the quality of being toxic to cells, particularly referring to the ability of immune cells (such as T cells or NK cells) or therapeutic agents to kill target cells, including cancer cells
"dendritic cell"	a type of antigen-presenting cell (APC) that plays a central role in initiating adaptive immune responses by capturing, processing, and presenting tumor antigens to T cells
"DLTs"	dose-limiting toxicity, toxicities of a drug or other treatment that are serious enough to prevent an increase in dose or level of that treatment
"E1"	an early adenoviral transcription unit that is expressed early in infection and comprises the E1A and E1B regions
"E3"	encodes proteins involved in immune evasion
"G47Δ"	DELYTACT®, an oncolytic virus developed by Daiichi Sankyo Company, Limited
"GAG"	glycosaminoglycan
"GBM"	glioblastoma, an aggressive and the most prevalent primary brain tumor in adults

GLOSSARY OF TECHNICAL TERMS

"GFP"	green fluorescent protein, a reporter protein that emits green fluorescence and is commonly used to monitor gene expression and viral infection in recombinant systems
"Glioma"	a type of tumor originating from glial cells in the central nervous system, including glioblastoma (GBM)
"GLP"	Good Laboratory Practice
"HER2"	a protein involved in normal cell growth
"HFF"	human foreskin fibroblast
"HG52"	a laboratory strain of herpes simplex virus type 2 (HSV-2) used as a reference in virology research
"hGM-CSF"	human granulocyte-macrophage colony-stimulating factor, a cytokine that promotes the activation and recruitment of immune cells, including dendritic cells and T cells, thereby enhancing anti-tumor immune responses
"HLA-E"	HLA class I histocompatibility antigen, alpha chain E. The human HLA-E is characterized by a limited polymorphism and a lower cell surface expression than its classical paralogues
"HMGB1"	high-mobility group box 1, a protein that plays a dual role as an alarmin (a danger signal) when released outside the cell
"hot tumor"	a tumor type rich in infiltrating immune cells—especially T-cells—with high PD-L1 expression and mutation burden, making it more likely to respond to immunotherapy
"HSV-1"	herpes simplex virus type 1, a common double-stranded virus causing oral herpes; used experimentally as a vector or naturally studied in oncology and virology contexts
"HSV-2/HSV-II"	herpes simplex virus type 2, closely related to HSV-1 but primarily associated with genital infections
"ICP34.5"	infected cell protein 34.5, a neurovirulence-associated nucleic acid sequence in wild-type herpes simplex virus that enables viral replication in normal cells (particularly neurons) and counteracts host antiviral responses; its deletion restricts replication to tumor cells and enhances safety
"ICP47"	infected cell protein 47, an immunosuppressive nucleic acid sequence in wild-type HSV that inhibits antigen presentation by blocking the transporter associated with antigen processing (TAP) and downregulating MHC class I expression; its deletion enhances immune recognition of infected tumor cells
"IFN"	interferons, a group of signaling proteins made and released by host cells in response to the presence of several viruses

GLOSSARY OF TECHNICAL TERMS

"IL-2"	Interleukin-2
"IL-2 analog"	a modified form of IL-2 engineered to preferentially stimulate anti-tumor effector T cells over regulatory T cells, thereby improving the therapeutic index
"IL-2R α"	CD25, the alpha chain of the interleukin-2 receptor (IL-2R α), a protein found on the surface of immune cells
"IL-2R β γ"	a dimeric complex of two receptor subunits, IL-2R β (CD122) and IL-2R γ (CD132), that binds to Interleukin-2 (IL-2) to form an intermediate-affinity receptor
"immunotherapy"	the ability to induce humoral and/or cell-mediated immune responses
"IRL"	internal repeat long, internal repeat sequences adjacent to the UL region that facilitate genome isomerization and recombination
"IRS"	internal repeat short, internal repeat sequences adjacent to the US region that enable genome isomerization and structural flexibility
"JAK-STAT"	a chain of interactions between proteins in a cell involved in processes such as immunity, cell division, cell death, and tumor formation
"KIT"	also known as CD117, a cytokine receptor expressed on the surface of hematopoietic stem cells as well as other cell types
"LNP"	lipid nanoparticle, it is designed to encase and deliver therapeutic nucleic acids into target cells, improving stability and facilitating cellular uptake
"MAPK"	a type of serine/threonine-specific protein kinases involved in directing cellular responses to a diverse array of stimuli
"MDSCs"	myeloid-derived suppressor cells
"Melanoma"	a malignant tumor arising from melanocytes
"mOS"	median overall survival
"MTD"	maximum tolerated dose
"NDV"	newcastle disease virus, an avian paramyxovirus with natural oncolytic properties against certain human cancers
"NK cell"	natural killer cell, a component of the innate immune system capable of directly lysing tumor cells
"NKG2A"	CD159a (Cluster of Differentiation 159a), an inhibitory NK cell receptor that is part of the NKG2 family and encoded by the KLRC1

GLOSSARY OF TECHNICAL TERMS

"NTRK"	a family of neurotrophic tropomyosin kinase receptors that is a part of the transmembrane tyrosine kinases responsible for neuronal development
"oHSV2 backbone"	oncolytic herpes simplex virus type 2 backbone, a genetically modified HSV-2 (typically derived from strain HG52) with deletions of virulence-associated genes such as ICP34.5 and ICP47, used as a viral vector for tumor-selective oncolytic therapy
"oHSV2 GFP"	oncolytic HSV-2 expressing green fluorescent protein, an intermediate recombinant virus used to verify successful gene insertion and expression prior to replacement with a therapeutic transgene
"Ommaya"	a subcutaneous reservoir connected to a catheter implanted into the brain's ventricular system, allowing direct administration of therapeutics into the cerebrospinal fluid (CSF) to deliver drugs to the central nervous system, bypassing the blood-brain barrier
"ORR"	overall objective response rate
"OS"	overall survival
"OVT"	Oncolytic virus therapy, a form of cancer immunotherapy that uses modified or naturally occurring viruses to selectively infect and lyse tumor cells while stimulating systemic anti-tumor immunity, which can be engineered to express immunostimulatory payload to enhance immune activation within the tumor microenvironment
"PA"	polyadenylation signal, a regulatory nucleotide sequence that directs the addition of a poly(A) tail to mRNA, ensuring proper transcription termination and stability
"PD-1"	programmed cell death protein 1
"PD-1 inhibitor"	monoclonal antibodies that inhibit the PD-1 immune checkpoint pathway, enhancing T-cell activation and anti-tumor immunity
"PD-L1"	programmed death-ligand 1
"PFS"	progression free survival
"PI3K/AKT"	a crucial intracellular signaling pathway that regulates fundamental cellular processes like growth, proliferation, survival, and metabolism
"pMMR/MSS CRCLM"	proficient mismatch repair/microsatellite stability colorectal cancer patients with liver metastases
"poly-epitope TCR activation"	involves T cells recognizing multiple epitopes presented together by an antigen-presenting cell (APC) to trigger an immune response

GLOSSARY OF TECHNICAL TERMS

"PR"	partial response typically defined as at least a 30% reduction in the sum of target lesion diameters
"rHSV2$^{hGM\text{-}CSF}$"	recombinant herpes simplex virus type 2 expressing human granulocyte-macrophage colony-stimulating factor (hGM-CSF), an engineered oncolytic virus designed to selectively replicate in tumor cells, induce oncolysis, and release hGM-CSF to stimulate dendritic cell activation and systemic anti-tumor immunity
"RP2D"	recommended Phase II dose
"SD"	stable disease
"SOC"	standard-of-care
"STS"	soft tissue sarcoma
"T cell"	a lymphocyte produced or processed by the thymus gland, distinguished from other lymphocytes by the presence of a T cell receptor on their surface
"T-cell engager"	a bifunctional molecule, typically a bispecific antibody, that simultaneously binds a tumor-associated antigen and CD3 on T cells, thereby redirecting T cells to recognize and kill cancer cells independent of MHC restriction
"T-VEC"	talimogene laherparepvec, an engineered oncolytic HSV-1 virus (brand name Imlygic®)
"TCE"	T-cell engager, a molecule designed to simultaneously bind tumor cells and T cells, thereby redirecting and activating T cells to kill tumor cells
"TCR"	T-cell receptor, a complex receptor that plays a central role in T cell biology, facilitating the recognition of antigens and influencing the immune response in various diseases, including cancer and autoimmune conditions
"TRAEs"	treatment-related adverse event
"TRL"	terminal repeat long, repeated nucleotide sequences flanking the unique long (UL) region of the HSV genome, involved in viral DNA replication, recombination and genome isomerization
"TRS"	terminal repeat short, repeated nucleotide sequences flanking the unique short (US) region of the HSV genome, contributing to viral genome replication and structural rearrangement
"UL"	unique long region, the larger unique region of the HSV genome encoding essential viral genes for replication and structural proteins

GLOSSARY OF TECHNICAL TERMS

"US"	unique short region, the smaller unique region of the HSV genome encoding genes including those associated with immune evasion and host interaction
"UTP"	uridine triphosphate, a nucleotide that serves as a building block for RNA and plays several other essential roles in cell metabolism
"Vero Cell"	a lineage of kidney epithelial cells isolated from the African green monkey (Chlorocebus aethiops)
"VP5"	viral protein 5 (major capsid protein), one of the two proteins (with VP2) which constitute the virus particle outer capsid