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## GLOSSARY OF TECHNICAL TERMS

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*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.*

“Adenovirus”	non-enveloped, double-stranded DNA virus that commonly causes respiratory, gastrointestinal, and eye infections, and is widely used as a vector in gene therapy and vaccine development
“Ad5”	adenovirus serotype 5, a non-enveloped double-stranded DNA virus commonly used as a gene therapy vector
“AE”	adverse event, a harmful and negative outcome that happens when a patient has been provided with medical care
“AGA”	androgenetic alopecia, male or female pattern baldness — a hormonally influenced, progressive thinning of scalp hair
“anagen”	the active growth phase of hair follicles
“BAT”	brown adipose tissue, a fat tissue type specialized in heat generation through burning calories
“Bacillus Calmette-Guérin” or “BCG”	a weakened strain of Mycobacterium bovis vaccine used intravesically (directly into the bladder) to treat early-stage bladder cancer by triggering a local immune response against tumors
“BLA”	biologics license application
“BMI”	body mass index, a simple measure of body fat based on height and weight that applies to adult men and women: weight in kilograms divided by height in meters squared
“BSL-2”	Biological Safety Level 2
“CAR-T”	chimeric antigen receptor T cell

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“CCK8”	cell counting kit-8, a colorimetric cell viability assay using WST-8, where living cells convert it into a soluble dye whose intensity at 450 nm directly correlates with cell number
“CD4”	cluster of differentiation 4, a transmembrane glycoprotein found on the surface of immune cells such as T helper cells
“CD8”	cluster of differentiation 8, a transmembrane glycoprotein that serves as a co-receptor for the T-cell receptor, primarily found on cytotoxic T cell
“CDMO”	contract development and manufacturing organization
“CED”	convection-enhanced delivery, a localized infusion technique creating pressure-driven flow via a catheter to deliver high concentrations of drugs — commonly into the brain — bypassing the blood-brain barrier
“cGMP”	current good manufacturing practice, regulations enforced by the U.S. FDA, which provide for systems that assure proper design, monitoring and control of manufacturing process and facilities
“chemotherapy”	a category of cancer treatment that uses one or more small molecular chemical anti-cancer agents as part of its standardized regime
“CIS”	carcinoma <i>in situ</i> , a form of early-stage cancer in which malignant cells are present but have not yet invaded deeper tissues
“CMC”	chemistry, manufacturing and controls
“CNS”	central nervous system, consisting of the brain and spinal cord, forming the central processing center for the nervous system
“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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“collagen”	the most abundant structural protein in the extracellular matrix, providing tensile strength and scaffolding for tissues
“‘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
“CRO”	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
“CRR”	complete response rate, the proportion of patients in a clinical trial whose cancer entirely disappears after treatment
“cSCC”	cutaneous squamous cell carcinoma, a type of non-melanoma skin cancer that originates from the squamous cells of the epidermis
“CSF”	cerebrospinal fluid, the clear fluid that surrounds the brain and spinal cord, providing protection and nutrient transport
“CTL”	cytotoxic T-lymphocyte, a subset of T cells (CD8+) that can directly kill infected or malignant cells by recognizing antigens on their surface
“DC”	dendritic cell
“DCR”	disease control rate, the total proportion of patients who demonstrate a response to treatment, equal to the sum of complete responses (CR), partial responses (PR) and stable disease (SD)
“DDM”	dodecyl $\beta$ -D-maltoside, a non-ionic detergent used to solubilize and stabilize membrane proteins or enhance viral vector delivery, such as by surfactant action on urothelium
“DFU”	diabetic foot ulcer

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“DLT”	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
“DOR”	duration of response, the length of time that a tumor continues to respond to treatment without the cancer growing or spreading
“EMT”	epithelial–mesenchymal transition, a biological program where epithelial cells lose adhesion and gain migratory mesenchymal properties, playing key roles in cancer invasion and metastasis
“extracellular matrix”	a dynamic, three-dimensional network of proteins (e.g., collagen, glycoproteins) and polysaccharides that supports tissue structure, cell adhesion, and signaling
“Fast Track Designation”	a designation granted by the FDA to facilitate the development, and expedite the review of drugs that to treat serious conditions and fill an unmet medical need
“Fc”	fragment crystallisable region, which is the tail region of an antibody that interacts with cell surface receptors called Fc receptors and some proteins of the complement system
“GAG”	glycosaminoglycan, long-chain polysaccharides in the extracellular matrix (such as hyaluronan, chondroitin), involved in tissue hydration, structural integrity, and cell signaling
“GMP”	Good Manufacturing Practices
“HNC”	head and neck cancer
“HNSCC”	head and neck squamous cell carcinoma
“‘hot’ tumor”	a tumor type with high immune cell infiltration and active immune responses, which is more likely to respond effectively to immunotherapy, especially immune checkpoint inhibitors like anti-PD-(L)1 and anti-CTLA-4

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“herpes simplex virus type 1” or “HSV-1”	a common double-stranded DNA virus causing oral herpes; used experimentally as a vector or naturally studied in oncology and virology contexts
“herpes simplex virus type 2” or “HSV-2”	a virus closely related to HSV-1 but primarily causes genital infections; similarly used or considered in viral therapy research
“ICP0”	infected cell polypeptide 0, an immediate-early regulatory protein of herpes simplex virus that promotes viral gene expression and counteracts host antiviral defenses
“ICP4”	infected cell polypeptide 4, the major transcriptional activator of herpes simplex virus, essential for initiating and regulating the expression of early and late viral genes
“IFN- $\gamma$ ”	interferon gamma, a cytokine for activation and regulation of the immune system
“IIT”	investigator-initiated trial, a clinical trial sponsored and conducted by independent investigators
“IL”	interleukin, a type of cytokine that secreted by lymphocytes that promote the development and maturation of T cell and B cell population
“immunotherapy”	the ability of a particular substance, such as an antigen or epitope, to provoke an immune response in the body of a human and other animal. In other words, immunogenicity is the ability to induce humoral and/or cell-mediated immune responses
“ <i>in situ</i> ”	Latin for “in the original place”, in oncology, refers to early-stage cancer contained within its tissue of origin, without invasion or spread

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“ <i>in vitro</i> ”	Latin for “within the glass”, studies using components of an organism that have been isolated from their usual biological surroundings, such as microorganisms, cells or biological molecules in an artificially controlled environment outside a living organism, such as a petri dish, test tube, or multi-well plate
“ <i>in vivo</i> ”	Latin for “within the living”, studies <i>in vivo</i> are those in which the effects of various biological or chemical substances are tested on whole, living organisms including animals, humans and plants, as opposed to a partial or dead organism, or those done <i>in vitro</i>
“INCI”	International Nomenclature Cosmetic Ingredient, an internationally recognized system for naming ingredients in cosmetics and topical formulations, ensuring consistent disclosure in labeling
“IND”	investigational new drug
“internal repeat region”	a segment within a DNA or RNA molecule that contains sequences repeated in tandem or dispersed
“IPF”	idiopathic pulmonary fibrosis
“IR”	inverted repeat, a DNA sequence motif in HSV viral genomes consisting of two identical or nearly identical sequences arranged in reverse orientation, which can play roles in recombination, genome stability, or regulation of viral gene expression
“Kaplan-Meier curve”	a statistical method used to visualize time-to-event data
“LAT”	latency-associated transcript, a type of RNA molecule involved in the latency phase of viral infections
“LNP”	lipid nanoparticle, a tiny, lipid-based carrier system designed to encase and deliver therapeutic nucleic acids into target cells, improving stability and facilitating cellular uptake

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"MAD"	multiple ascending dose, a type of clinical trial that is used to evaluate the safety and efficacy of a drug over an extended period of time, typically involving multiple doses
"MIBC"	muscle-invasive bladder cancer
"miRNA"	microRNA, small molecule in cells, typically about 21–25 nucleotides in length, that plays a crucial role in the regulation of gene expression
"MRCT"	multi-regional clinical trial
"mRNA"	messenger RNA, a single-stranded RNA molecule that carries encoded instructions from DNA to the protein-synthesis machinery; it is the basis for mRNA-based therapies such as vaccines and therapeutic protein delivery
"MSC"	mesenchymal stem cell, derived from bone marrow, fat, or other tissues, capable of differentiating into bone, cartilage, and fat cells; often explored as delivery vehicles for therapeutic agents
"MTD"	maximum tolerated dose, the highest dose of a drug or treatment that does not cause unacceptable side effects
"Nab"	neutralizing antibody, a class of specific antibodies produced by the immune system, whose core function is to block pathogens (such as viruses or bacterial toxins) from entering host cells by directly binding to key surface proteins involved in infection
"NDA"	new drug application
"NMIBC"	non-muscle-invasive bladder cancer
"oHSV"	oncolytic herpes simplex virus, a genetically modified HSV engineered to selectively infect and kill cancer cells while sparing normal tissues

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“OriS”	a specific origin of DNA replication (located in inverted repeat short regions) found in herpesviruses like HSV-1, essential for copying viral DNA during replication
“Orphan Drug Designation”	a facilitated regulatory pathway granted by the U.S. FDA to a drug or biological product intended to prevent, diagnose or treat a rare disease or condition, with certain incentives for qualified sponsors
“ORR”	overall objective response rate, the proportion of patients with a complete response or partial response to treatment
“OS”	overall survival, the length of time from either the date of diagnosis or the start of treatment for a disease which patients diagnosed with the disease are still alive. It is used in clinical trials to measure a drug’s effectiveness
“PBS”	phosphate-buffered saline, a buffer solution commonly used in biological research to maintain a constant pH and osmotic balance. It is widely applied in cell culture, washing, and dilution procedures
“PD”	pharmacodynamic, the study of the biochemical and physiological effects of drugs on the body, including the mechanisms of action and the relationship between drug concentration and effect
“PD-1”	programmed cell death protein 1, an immune checkpoint receptor expressed on T cells, B cells and macrophages
“PD-L1”	programmed death-ligand 1, a protein on the surface of a normal cell or a cancer cell that attaches PD-1, on the surface of the T cell that causes the T cell to turn off its ability to kill the cancer cell
“PD-(L)1”	refers to PD-1 or PD-L1
“PFS”	progression free survival

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“PFU”	plaque-forming unit, a virology measure of infectious virus concentration, defined by the number of virus particles capable of forming visible plaques (areas of infected cell lysis) in cell cultures
“Phase I clinical trial”	a trial that tests the safety of a new drug candidate
“Phase I/IIa clinical trial”	a trial that begins by testing a new drug candidate in a small group of patients to evaluate its safety, dosage range, and pharmacokinetics (Phase I), and then transitions into a slightly larger group of patients to gather preliminary data on how well the drug works and to further assess its safety and biological activity (Phase IIa)
“Phase II clinical trial”	a trial that tests a new drug candidate on a larger group of patients to gather information about whether and how well it works
“Phase III clinical trial”	a trial for a new drug candidate that has already passed Phase I and II, which tests the new drug candidate in larger groups of patients, 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
“PI”	principal investigator
“PK”	pharmacokinetic, a measurement of how fast and how completely a drug is absorbed into animal or human body, including the distribution, metabolism, and excretion of drugs in animal or human body
“pulmonary fibrosis”	a chronic lung condition characterized by thickening or scarring of lung tissues, impairing oxygen transfer, labeled “idiopathic” (IPF) when the cause is unknown
“RFS”	recurrence free survival, a clinical trial endpoint measuring the length of time after treatment during which a patient remains free of cancer recurrence; used to evaluate efficacy in oncology studies

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“RNA”	ribonucleic acid, a crucial molecule involved in various biological roles, including coding, decoding, regulation, and expression of genes
“RP2D”	recommended Phase II dose, typically the highest dose with acceptable toxicity, usually defined as the dose level that produces around 20% of dose-limiting toxicity
“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 prolongs existing hospitalization; results in persistent or significant disability/incapacity; may cause a congenital anomaly/birth defect; or requires intervention to prevent permanent impairment or damage
“SOC”	standard-of-care, treatment accepted by medical experts as proper for a certain type of disease and widely used by healthcare professionals
“T cell”	a lymphocyte produced or processed by the thymus gland, actively participating in the immune response and playing a central role in cell-mediated immunity. T cells are distinguished from other lymphocytes, such as B cells and NK cells, by the presence of a T cell receptor on their surface
“Tis”, “Ta”, “T1”, “T2”, “T3”, and “T4”	standard staging categories for cancer, in the context of bladder cancer means: <ul style="list-style-type: none"><li>• Tis: carcinoma <i>in situ</i> (flat, non-invasive)</li><li>• Ta: non-invasive papillary tumor</li><li>• T1: invades connective tissue below lining</li><li>• T2: invades muscle</li><li>• T3: extends beyond bladder into perivesical tissue</li><li>• T4: invades adjacent organs (e.g. prostate, uterus, pelvic wall)</li></ul>
“TAA”	tumor-associated antigen, a class of antigenic molecules that are abnormally overexpressed in tumor cells but show low expression in normal tissues or are only present during specific developmental stages

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"telogen"	the resting phase of the hair growth cycle
"TEAE"	treatment-emergent adverse event, either an adverse event that starts after the initiation of the study medication or one that existed before study medication but worsened in severity after the initiation of study medication
"TG"	trigeminal ganglion, a cluster of sensory nerve cell bodies of the trigeminal nerve, which transmits sensations of the face to the brain
"Th1"	T helper 1, a subtype of immune T cells that produce inflammatory cytokines like IFN- $\gamma$ to enhance cell-mediated immunity, crucial for anti-tumor and anti-viral responses
"tumor microenvironment"	the complex ecosystem surrounding a tumor that includes various cell types, signaling molecules, and extracellular matrix components
"TNF- $\alpha$ "	tumor necrosis factor alpha, a pro-inflammatory cytokine released by immune cells that can induce tumor cell death, regulate immune responses, and stimulate inflammation
"TRAE"	treatment-related adverse event, an adverse event that, in the investigator's opinion, may have been caused by the study medication with reasonable possibility
"TTF"	time to failure, an endpoint in clinical research defined as the time from treatment start until treatment stops due to disease progression, toxicity, or death
"TURBT"	transurethral resection of bladder tumor, a minimally invasive surgical procedure performed via the urethra to remove bladder tumors, usually used to diagnose and treat early-stage bladder cancer
"T-VEC"	talimogene laherparepvec, a genetically engineered oncolytic HSV-1 virus (brand name Imlygic <sup>®</sup> )
"Type C meeting"	A type of formal meeting with the FDA regarding the development and review of a product

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“VEGF”

vascular endothelial growth factor

“WAT”

white adipose tissue, the body’s primary site for storing fat as energy, composed mostly of lipid-storing cells