

GLOSSARY OF TECHNICAL TERMS

The following is a glossary of certain terms used in this document in connection with us and/or our business. As such, these terms and their meanings may not correspond to standard industry meanings or usage of these terms.

“ADC”	Antibody-Drug Conjugate, a promising cancer treatment modality that enables the selective delivery of highly cytotoxic payloads to tumours
“ADCs”	Antibody-drug Conjugates, class of targeted therapeutic agents comprising a monoclonal antibody chemically linked to a potent cytotoxic drug (payload). The antibody component selectively binds to antigens overexpressed on the surface of cancer cells, enabling specific delivery of the cytotoxic payload directly to tumour cells
“adverse drug reaction”	an unintended, harmful response caused by the investigational drug in humans that occurs at normal therapeutic doses
“adverse event”	undesirable medical occurrences that arise during medicinal use or clinical studies, whether or not causally related to the medicinal product, and are assessed for severity, seriousness, causality, grading and outcome as part of safety and tolerability evaluation
“AGA positive”	a diagnostic or biomarker status indicating the presence of Anti-gliadin Antibodies in a patient’s blood. AGA are autoantibodies directed against gliadin, a component of gluten
“AIDD”	AI-Driven Drug Design, the application of artificial intelligence to the process of discovering and designing novel therapeutic compounds, particularly machine learning, deep learning, and related computational techniques
“AKT activation”	the process by which the serine/threonine kinase AKT is phosphorylated and functionally activated, typically through the PI3K-dependent signalling pathway
“allosteric inhibitor”	a type of enzyme or protein inhibitor that binds to a site other than the active site (the allosteric site), causing a conformational change in the target protein that reduces or prevents its biological activity
“AML”	Acute Myeloid Leukaemia, a rapidly progressing cancer of the blood and bone marrow, characterised by the overproduction of abnormal myeloid precursor cells (blast cells) that interfere with normal haematopoiesis”
“angiogenesis”	the physiological process of forming new blood vessels from pre-existing vasculature, essential for tissue growth, wound healing, and embryonic development
“AUC”	Area Under the Concentration-Time Curve, the area under the plasma concentration-time curve
“BID”	twice daily, an occurrence or action that takes place two times throughout a 24-hour period
“bioavailability”	the rate and extent to which the active moiety is absorbed and becomes available at the site of action

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“biomarker”	a measurable biological indicator that can be used to assess normal physiological processes, pathological conditions, or responses to therapeutic interventions
“BIW”	twice-weekly, an occurrence or action that takes place two times throughout a 7-day period
“BRAF inhibitor”	a class of targeted therapeutic agents that selectively inhibit the activity of the BRAF protein kinase, a key component of the MAPK/ERK signalling pathway
“BRCA1/2-mutant tumour”	a cancer that harbours pathogenic mutations in either the BRCA1 or BRCA2 genes, which are critical for homologous recombination repair (HRR) of DNA double-strand breaks
“Breakthrough Therapy Designation”	a prestigious and significant regulatory status granted by a medicines regulator to an investigational medicinal product during its clinical development
“C _{max} ”	Maximum Plasma Concentration, the maximum concentration of a drug in the plasma after administration, typically observed during clinical pharmacokinetic studies
“CIN”	Chromosomal Instability, a state in which cells exhibit an increased rate of whole-chromosome or large-scale structural alterations during cell division
“clinical trial”	research studies performed on humans to evaluate the effectiveness and safety of new treatments
“CL/F”	Clearance, a fundamental pharmacokinetic parameter that quantifies the intrinsic capacity of the body, or of a specific organ, to irreversibly remove a drug from the systemic circulation
“CNS”	Central Nervous System, the primary command and processing centre of the body’s entire nervous system, comprised of the brain and the spinal cord
“combination therapy”	the therapeutic strategy of using two or more distinct medicinal agents concurrently in the treatment of a single medical condition
“CSCO”	Chinese Society of Clinical Oncology, China’s the leading nationwide professional academic society dedicated to clinical oncology
“CTCAE”	Common Terminology Criteria for Adverse Events, a comprehensive, standardised classification system used to grade the severity of adverse events experienced by patients participating in clinical trials of cancer therapies and other interventions
“DCR”	Disease Control Rate, the proportion of patients who, according to internationally recognised criteria for alleviating evaluation, achieve complete response, partial response, or stable disease after treatment and can maintain for the minimum duration requirement

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“DLTs”	Dose-Limiting Toxicities, severe adverse effects that define the maximum tolerated dose of a cancer drug. In addition to the specific mechanisms of each drug, common contributing factors include inflammation, apoptosis, ion imbalances, and tissue-specific enzyme deficiencies
“DoR”	Duration of Response, the time from the first documented objective response (e.g., complete response or partial response) to disease progression or death, whichever occurs first
“EGFR”	Epidermal Growth-Factor Receptor, a protein embedded in the outer membrane of epithelial and mesenchymal cells, bone cells, blood and immune cells, heart cells, glia and stem neural cells
“EGFR-TKIs”	Epidermal Growth Factor Receptor Tyrosine Kinase Inhibitors. First-generation EGFR-TKIs refer to reversible EGFR tyrosine kinase inhibitors targeting sensitising EGFR mutations, with approved examples including gefitinib and erlotinib. Second-generation EGFR-TKIs refer to irreversible ErbB family inhibitors, with approved examples including afatinib and dacomitinib. Third-generation EGFR-TKIs refer to mutant-selective, irreversible EGFR tyrosine kinase inhibitors designed to target sensitising EGFR mutations and resistance mutations such as T790M, with osimertinib being a representative approved example
“EOT”	End of Treatment, the formal point at which a specific, planned course of medical intervention is concluded, as determined by the responsible clinician or multidisciplinary team
“ERKi”	ERK inhibitors, a class of targeted therapeutic agents that specifically modulate the extracellular signal-regulated kinase (ERK), a core component of the mitogen-activated protein kinase (MAPK) signalling cascade
“FAS”	Full Analysis Set, an intention-to-treat analysis set that is as complete and as close as possible to the ideal of including all randomised clinical trial subjects
“FBDD”	Fragment-Based Drug Design, a rational drug discovery methodology that identifies low molecular weight chemical fragments which bind weakly but measurably to a defined biological target
“FDA”	U.S. Food and Drug Administration, the federal agency of the United States department of health and human services responsible for protecting and promoting public health through the regulation and supervision of food safety, pharmaceuticals, medical devices, biologics, cosmetics, tobacco products, and radiation-emitting products
“FOLFIRINOX”	the chemotherapy combination contains the drugs leucovorin calcium (folinic acid), fluorouracil, irinotecan hydrochloride, and oxaliplatin
“GDP-bound”	the inactive conformation of a GTPase when it is bound to guanosine diphosphate

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“genomic scar”	a quantifiable pattern of genomic alterations resulting from the use of error-prone DNA repair pathways, particularly in the context of homologous recombination deficiency (HRD). It serves as a core biomarker for assessing HRD status and guiding treatments such as PARP inhibitors
“GMP”	Good Manufacturing Practice, being standards and guidelines that ensure products are consistently produced and controlled according to quality standards, covering aspects such as manufacturing processes, facilities, documentation, and quality control
“HGSOC”	High-Grade Serous Carcinoma, the type of ovarian cancer, developing when cells in the ovaries, fallopian tubes, or peritoneum grow uncontrollably
“HRAS”	HRas Proto-Oncogene, GTPase is a protein coding gene. Diseases associated with HRAS include costello syndrome and schimmelpenning-feuerstein-mims syndrome
“HRD”	Homologous Recombination Deficiency, pivotal biomarker in precision oncology, driving therapeutic strategies for ovarian and breast cancers through impaired DNA double-strand break repair
“HRR/HR-DDR”	Homologous Recombination Repair/DNA Damage Repair, a high-fidelity, template-dependent DNA repair pathway that accurately repairs DNA double-strand breaks and interstrand crosslinks during the S and G2 phases of the cell cycle
“ICF”	Informed Consent Form, a legal and ethical document that serves as a written record of the process by which a patient or participant voluntarily agrees to undergo a specific medical procedure, treatment, or to take part in a research study, after having been provided with, and understood, all relevant information
“IGF”	Insulin-like growth factor, a hormone with a molecular structure similar to insulin. It plays a central role in childhood growth and continues to have anabolic effects (promoting tissue building) in adults
“IRC”	Independent Review Committee, an autonomous, multidisciplinary panel of experts convened to provide external, impartial oversight of a clinical trial or other significant research undertaking
“JAK/STAT”	one of a handful of pleiotropic cascades used to transduce a multitude of signals for development and homeostasis in animals
“JDC”	Joint Development Committee, the committee is responsible for overseeing the planning, implementation, and management of the project, ensuring that the goals and objectives of the collaboration are met
“JSC”	Joint Steering Committee, a collaborative group formed by representatives from two or more organisations, businesses, or parties, tasked with overseeing, guiding, and making decisions related to a particular project, initiative, or programme

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“KOL”	Key Opinion Leader, an individual or entity recognised as an expert and a trusted source of insight within a specific field, industry, or community. Their opinions and endorsements hold significant weight and can influence the attitudes, behaviours, and purchasing decisions of a target audience
“KRAS ^{G12C} ”	a specific oncogenic mutation in the KRAS gene, in which the glycine (G) at codon 12 is substituted by a cysteine (C) in the encoded KRAS protein
“LOH”	Loss of Heterozygosity, a genomic aberration in diploid cells where the heterozygous state at a specific locus is lost, resulting in a hemizygous state at that site
“LST”	Large-scale State Transitions, Chromosomal breakage that generates 10 Mb or larger fragments. The quantification of these breaks can be used as a surrogate measure for genomic instability, which may be caused by mutation of DNA repair genes, including BRCA1 or BRCA2
“MAPK”	mitogen activated protein kinase, a family of serine/threonine-specific protein kinases that are highly conserved in eukaryotes and play a central role in transducing extracellular signals into intracellular responses
“MAT2A”	Methionine adenosyltransferase 2A, a rate-limiting enzyme in the methionine cycle that primarily catalyses the synthesis of S-adenosylmethionine from methionine and adenosine triphosphate
“MET amplification”	a genetic alteration characterised by an increased copy number of the MET proto-oncogene, which encodes the hepatocyte growth factor receptor
“mPFS”	median Progression-Free Survival, a survival endpoint used in clinical trials to assess treatment efficacy, defined as the time from randomisation until disease progression or death from any cause
“MSI”	Microsatellite Instability, a condition characterised by the accumulation of mutations in microsatellites, which are short, repetitive DNA sequences, and is significant in cancer diagnosis and treatment
“MTA”	Methylthioadenosine, a naturally occurring sulphur-containing nucleoside present in all mammalian tissues
“MTAP”	Methylthioadenosine Phosphorylase, catalyses the reversible phosphorolysis of 5'-methylthioadenosine, a by-product produced from polyamine biosynthesis
“MTD”	Maximum Tolerated Dose, highest dose that an animal can tolerate without experiencing lethal effects
“NALIRIFOX”	the chemotherapy combination contains Irinotecan liposomal (Onivyde), Oxaliplatin, Fluorouracil and Leucovorin
“NCCN”	National Comprehensive Cancer Network, the guidelines were developed to help guide quality patient care

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“NDA”	New Drug Application, a comprehensive regulatory submission filed by a pharmaceutical sponsor with a regulatory authority, such as the U.S. FDA or China NMPA, to seek approval for the marketing and commercialisation of a new drug product
“NRAS”	NRAS is a proto-oncogene that encodes a GTPase protein involved in signal transduction
“NSCLC”	Non-Small-Cell Lung Cancer, a subtype of lung cancer
“ORR”	Objective Response Rate, the proportion of patients in a clinical trial who experience a predefined reduction in tumour size or the complete disappearance of the tumour after receiving a specific treatment
“OS”	Overall Survival, the length of time from either the date of diagnosis or the start of treatment until death from any cause
“pan-TEAD”	A pan-TEAD inhibitor, which can inhibit the activity of all four TEAD subtypes: TEAD1, TEAD2, TEAD3, and TEAD4
“PARP”	Poly-(ADP-ribose) Polymerase, a crucial enzyme involved in DNA repair, cellular stress responses, and apoptosis, playing a significant role in maintaining genomic stability
“PBMCS”	Peripheral Blood Mononuclear Cells, a diverse population of immune cells circulating in the bloodstream, including lymphocytes (T cells, B cells, and NK cells) and monocytes
“PD”	Pharmacodynamic, the study of the biochemical and physiological effects of drugs and their mechanisms of action in the body
“PD-1”	programmed cell death protein 1, an immune checkpoint receptor protein primarily expressed on the surface of activated T cells, B cells, and myeloid cell
“PDAC”	Pancreatic Ductal Adenocarcinoma, the form of pancreatic cancer, arises from the epithelial cells lining the pancreatic ducts and is characterised by early local invasion, rapid metastasis, and profound resistance to conventional therapies
“PDGF”	platelet-derived growth factor, a potent signalling protein (cytokine) that stimulates cell growth, proliferation, and survival. It is particularly important for the growth and development of blood vessels (angiogenesis) and connective tissue cells
“PDX model”	Patient-Derived Xenograft model, an advanced tool in cancer research. They are developed by implanting human tumour tissue into specially bred mice with compromised immune systems
“PFS”	Progression-Free Survival, the length of time from randomisation or treatment initiation until disease progression or death from any cause, whichever occurs first
“phase 1”	a study in which a drug is introduced into healthy human subjects or patients with the target disease or condition and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion, and if possible, to gain an early indication of its effectiveness

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“phase 2”	a study in which a drug is administered to a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the drug for specific targeted diseases, and to determine dosage tolerance and optimal dosage
“PI3K/AKT”	the signalling pathway activated by many types of cellular stimuli or toxic insults and regulates fundamental cellular functions such as transcription, translation, proliferation, growth, and survival
“PK”	Pharmacokinetic, the study of the bodily absorption, distribution, metabolism, and excretion of drugs, which, together with pharmacodynamics, influences dosing, benefit, and adverse effects of the drug
“PR”	Partial Responses, a category of tumour response to therapy, defined according to internationally recognised solid-tumour response criteria, where the sum of the longest diameters of target lesions decreases by $\geq 30\%$ from baseline, with no new lesions or unequivocal progression of non-target lesions
“PRMT5”	Protein arginine methyltransferase 5, an enzyme involved in gene expression regulation, RNA processing, DNA damage repair and immune responses
“PTP”	Protein Tyrosine Phosphatase, key regulators in multiple signal transduction pathways and therefore they play important roles in many cellular processes, including immune response
“QD”	Once-Daily, a standard posology term denoting a dosing frequency of one time per 24-hour period
“RAS signalling pathway”	one of the crucial intracellular signal transduction mechanisms, playing a key role in regulating various physiological processes such as cell growth, differentiation, and proliferation
“RAS/ERK”	a critical regulator of cellular processes such as proliferation, differentiation, and survival, core mechanisms that drive development
“ R_{Auc} ”	accumulation ratio, quantifies how much higher drug concentrations are at steady-state compared to after a single dose
“RDEs”	Recommended Dose(s) for Expansion, the one or more dose levels selected for further investigation in a subsequent patient cohort, known as the expansion cohort. This selection is based on integrated data concerning safety, tolerability, pharmacokinetics, and preliminary efficacy gathered during the initial dose-finding phase of an early-stage clinical trial
“RP2D”	recommended phase 2 dose, the dose and schedule selected for further evaluation in subsequent Phase 2 trials, based on a comprehensive integration of all available data from the dose-finding (escalation) and often the dose-expansion phases
“RTKs”	Receptor Tyrosine Kinases, a class of protein kinases that play crucial roles in various cellular processes, including cell migration, morphological differentiation, cell growth, and angiogenesis

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“SAM”	S-adenosyl-L-methionine, a naturally occurring trialkyl sulfonium molecule that is typically associated with biological methyltransfer reactions
“SAR”	Structure-Activity Relationship, the correlation between the chemical structure of compounds and their biological activity, which can be analysed through an iterative cycle of design, synthesis, screening, and analysis
“SBDD”	Structure-Based Drug Design, a rational, iterative drug discovery methodology that exploits the three-dimensional atomic structure of a biological target, typically a protein or nucleic acid, to guide the creation, optimisation, and development of novel, potent, and selective therapeutic compounds
“SD”	Stable Disease, a tumour has not grown or shrunk significantly and no new tumours have developed
“SDMA modification”	a post-translational modification in which a methyl group is added to each of the two nitrogen atoms on an arginine residue, with key residues including H3R2 and H4R3, conferring unique regulatory functions
“SHP2 inhibitor”	a class of therapeutic agents designed to selectively inhibit the activity of SHP2. SHP2 regulates cell proliferation, differentiation, apoptosis, and survival by dephosphorylating tyrosine residues and modulating multiple signalling pathways, including RAS/MAPK, PI3K/AKT, JAK/STAT, and PD-1/PD-L1
“SPR”	Structure-Property Relationships, the fundamental scientific principle that the properties (chemical, physical, mechanical, biological, or electronic) of a material or molecule are intrinsically determined by its structure at the atomic, molecular, or supramolecular level
“TAI”	Telomeric Allelic Imbalance, a genomic alteration characterised by asymmetric allelic dosage at the telomeric region of a chromosomal arm due to aberrant DNA replication or repair during mitosis
“TEAEs”	Treatment-Emergent Adverse Events, any adverse event that occurs during or shortly after drug administration and is not present at baseline, regardless of whether a definite causal relationship has been established
“TKIs”	Tyrosine Kinase Inhibitors, small molecules that compete with the adenosine triphosphate-binding site of the catalytic domain of a tyrosine kinase
“TNBC”	Triple-Negative Breast Cancer, a subtype of breast cancer
“TOP1”	DNA Topoisomerase I, which encodes DNA topoisomerase I
“TRAEs”	Treatment-Related Adverse Events, adverse events definitely or possibly related to the study drug
“TRSAEs”	Treatment-Related Serious Adverse Events, a critical subset of adverse events recorded during clinical trials or post-marketing surveillance

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“TTR”	Time to Response, the measured duration from the initiation of a specific treatment, or from a defined baseline point, until the first observation of a pre-specified, clinically meaningful response to that intervention
“type II diabetes”	a chronic metabolic disorder characterised by insulin resistance and relative insulin deficiency, leading to persistent hyperglycaemia
“UC”	Urothelial Cancer, an epithelial malignancy arising from the urothelial lining, which includes the renal pelvis, ureters, urinary bladder, and parts of the posterior urethra and major ducts of the prostate
“Vd/F”	Volume of distribution, a theoretical pharmacokinetic parameter that quantifies the apparent volume into which a drug dose would need to be uniformly distributed to achieve the observed concentration in the blood plasma
“WGD”	Whole-Genome Doubling, a genetic event in which a cell undergoes duplication of its entire set of chromosomes during a single mitotic cycle, resulting in a transition from a diploid (2n) to a tetraploid (4n) genome
“WRN”	Werner Syndrome RecQ Helicase, a prototypical segmental progeroid syndrome characterised by multiple features consistent with accelerated ageing