

GLOSSARY OF TECHNICAL TERMS

Unless the context otherwise requires, this glossary contains explanations of certain technical terms used in this document in connection with us and our business. Such terminology and meanings may not correspond to standard industry meanings or usages of those terms.

“ACR”	American College of Rheumatology
“ACR20/ACR50/ACR70”	a clinical trial endpoint in rheumatoid arthritis indicating a 20%/50%/70% improvement in the American College of Rheumatology criteria
“acute gout”	an inflammatory arthritis triggered by monosodium urate crystal deposition in joints, leading to sudden pain, swelling, and erythema
“AD”	atopic dermatitis, a chronic inflammatory skin disease marked by pruritus, eczematous lesions, and skin barrier dysfunction
“AE”	adverse event, any untoward medical occurrence may be mild, moderate, or severe in a patient or subject receiving a drug or other pharmaceutical product in a clinical trial and which does not necessarily have a causal relationship with the treatment
“Alzheimer’s disease”	a neurodegenerative disorder marked by progressive cognitive decline, amyloid- β plaques, and tau pathology
“antibody”	a blood protein produced in response to and counteracting a specific antigen. Antibodies combine chemically with substances which the body recognizes as alien, such as bacteria, viruses, and foreign substances in the blood
“astrocyte”	star-shaped glial cell in the central nervous system that supports neuronal function, regulates neurotransmitter balance, and maintains the blood-brain barrier
“ATP”	adenosine triphosphate, a nucleotide that provides energy to drive and support many processes in living cells, such as muscle contraction, nerve impulse propagation, condensate dissolution, and chemical synthesis
“AUC”	area under the curve, a pharmacokinetic parameter that measures the body’s exposure to a drug, i.e., how much of the drug reaches a person’s bloodstream over a given period of time after a dose is administered
“autoimmune diseases”	a class of disorders in which the immune system mistakenly attacks the body’s own tissues, leading to chronic inflammation and organ or tissue damage
“BBB” or “blood-brain barrier”	a highly selective physiological barrier formed by endothelial cells, pericytes, and astrocytic end-feet, which regulates the passage of substances between the systemic circulation and the central nervous system
“BID”	twice daily

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“biomarker”	a naturally occurring molecule, gene, or characteristic by which a particular pathological or physiological process, disease, etc. can be identified
“brain-penetrant compound”	A drug molecule designed to cross the blood-brain barrier and achieve therapeutic concentrations in the CNS
“CAGR”	compound annual growth rate
“cardiovascular”	relating to the heart and blood vessels, encompassing the structure and function of the circulatory system
“CDMO”	contract development and manufacturing organization, a company that provides support to the pharmaceutical, biotechnology, and medical device industries that develops and manufactures drugs for other pharmaceutical companies on a contractual basis
“C _{max} ”	maximum plasma concentration, a pharmacokinetic parameter that measures the highest concentration of a drug in the blood, cerebrospinal fluid, or target organ after a dose is given
“CMC”	chemistry, manufacture and control, also commonly referred to as process development, which covers the various procedures used to assess the physical and chemical characteristics of drug products, and to ensure their quality and consistency during manufacturing
“CNS”	central nervous system, the part of the nervous system consisting primarily of the brain and spinal cord
“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
“corticosteroids”	hormonal agents produced by the adrenal cortex or synthesized as drugs, used to regulate inflammation, immune responses, and metabolic processes
“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
“CSF”	cerebrospinal fluid, clear, colorless body fluid surrounding the brain and spinal cord, providing mechanical protection, nutrient transport, and waste removal
“CSO”	contract sales organization, a company that provides a series of services and solutions related to marketing and sales activities under contracts with pharmaceutical, biotechnology, and medical device companies
“CSU”	chronic spontaneous urticaria, a skin disorder characterized by recurrent hives and/or angioedema without an identifiable trigger, persisting for six weeks or longer

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“cytokine”	a broad category of small proteins that are important in cell signaling, whose release has an effect on the behavior of cells expressing corresponding receptors
“DMARDs”	disease-modifying anti-rheumatic drugs, a group of agents that slow or alter the underlying pathophysiology of rheumatic diseases, aiming to reduce inflammation, prevent joint damage, and preserve function
“dose-escalation study”	a type of study where different doses of an agent (e.g. a drug) are tested against each other to establish which dose works best and/or is least harmful
“ER”	extended-release, a drug formulation designed to release the active ingredient gradually over an extended period, maintaining therapeutic levels and reducing dosing frequency
“first line”	with respect to any disease, the first line treatment, which is the treatment regimen or regimens that are generally accepted by the medical establishment for initial treatment. It is also called primary treatment or therapy
“FTE”	a unit representing the workload of one full-time employee, commonly applied in the biopharmaceutical industry to measure research effort and project resources
“GCP”	good clinical practice, an international ethical and scientific quality standard for the performance of a clinical trial on medicinal products involving humans
“GMP”	good manufacturing practice, the practices required in order to conform to the guidelines recommended by agencies that control the authorization and licensing of the manufacture and sale of products
“H-donor”	hydrogen bond donor, a functional group or atom within a molecule that provides a hydrogen atom capable of participating in hydrogen bonding interactions, typically through attachment to an electronegative atom such as oxygen or nitrogen
“hsCRP”	high-sensitivity C-reactive protein, a biomarker of systemic inflammation, measured with high-sensitivity assays to detect low concentrations associated with cardiovascular risk and chronic inflammatory conditions
“HSS7”	weekly hives severity score, a patient-reported outcome measure evaluating the frequency, intensity, and overall impact of hives over a seven-day period, commonly used in clinical trials of urticaria
“hydrogen-donor-free scaffold”	a chemical design strategy removing hydrogen bond donor groups to improve blood-brain barrier penetration and kinase selectivity

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“IC ₅₀ ”	concentration at half maximal inhibition, a measure of the potency of a substance in inhibiting a specific biological or biochemical function
“IFN-α/IFN-β/IFN-γ”	cytokines with antiviral, immunomodulatory, and pro-inflammatory functions; type i interferons (α, β) and type ii interferon (γ) signal through TYK2/JAK1 pathways
“IL-1β/IL-18”	potent pro-inflammatory cytokines activated via inflammasome signaling; key mediators in gout, neuroinflammation, and systemic inflammation
“IL-6/IL-17/IL-23”	pro-inflammatory interleukins involved in autoimmune pathogenesis; IL-17 and IL-23 are central to the TH17 immune axis
“ <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
“ <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>
“INAD”	investigational new animal drug or investigational new animal drug application
“IND”	investigational new drug or investigational new drug application, also known as clinical trial application in China or the United States
“IP-10”	interferon-γ-inducible protein 10, chemokine involved in immune responses, promoting recruitment of activated T cells and other leukocytes to sites of inflammation
“IR”	immediate-release, a dosage form designed to rapidly disintegrate and release the active drug substance into the body, resulting in prompt absorption and onset of action
“ISS7”	itch severity score, a patient-reported assessment tool measuring the intensity and impact of pruritus over a seven-day period, commonly used in clinical studies of dermatological conditions
“JAK1/JAK2/JAK3”	intracellular tyrosine kinases that mediate cytokine receptor signaling via the JAK-STAT pathway, regulating immune cell development, activation, and inflammatory responses
“JAK-STAT pathway”	a signal transduction cascade activated by cytokines and growth factors, leading to transcription of genes involved in immunity, inflammation, and cell growth
“kinase selectivity”	the degree to which a kinase inhibitor targets specific kinases over others, reducing off-target effects

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“LRRK2”	leucine-rich repeat kinase 2, a kinase implicated in familial and sporadic parkinson’s disease; mutations can increase kinase activity and contribute to neurodegeneration
“MAD”	multiple ascending dose, a clinical study design in which multiple doses of an investigational drug are administered to sequential cohorts of participants at escalating dose levels to evaluate safety, tolerability, and pharmacokinetics over repeated exposure
“microglia”	resident immune cell of the central nervous system responsible for maintaining homeostasis, mediating immune defense, and responding to injury or disease
“MNC”	multinational corporations
“monotherapy”	therapy that uses a single drug to treat a disease or condition
“NDA”	new drug application, a regulatory submission seeking marketing approval for a new pharmaceutical product
“neurodegenerative diseases”	a group of progressive disorders characterized by the gradual loss of structure or function of neurons, often leading to cognitive, motor, and functional impairments
“NLRP3 inflammasome”	multiprotein complex that detects cellular stress signals and activates caspase-1, leading to maturation of IL-1 β and IL-18 and induction of pyroptosis
“NSAIDs”	nonsteroidal anti-inflammatory drugs, a class of medications that reduce inflammation, pain, and fever by inhibiting cyclooxygenase enzymes, without possessing steroidal structure
“Parkinson’s disease”	a progressive neurodegenerative disorder characterized by motor and non-motor symptoms, linked to dopaminergic neuron loss
“PASI”	psoriasis area and severity index, a measure of psoriasis severity based on lesion characteristics and body surface area affected
“PD”	pharmacodynamics, the study of the biochemical and physiological effects of drugs and their mechanisms of action
“PGA”	physician global assessment, clinician-reported outcome measure used to evaluate the overall severity of a disease, typically based on observable signs and clinical judgment
“Phase I/II/III trials”	sequential stages of clinical testing: Phase I (safety, tolerability, pharmacokinetics), Phase II (efficacy, dose-finding), Phase III (confirmatory efficacy and safety)
“PK”	pharmacokinetics, the study of drug absorption, distribution, metabolism, and excretion in the body

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“placebo”	any dummy medical treatment administered to the control group in a controlled clinical trial in order that the specific and non-specific effects of the experimental treatment can be distinguished
“plaque psoriasis”	a chronic immune-mediated skin disorder characterized by erythematous, scaly plaques resulting from excessive keratinocyte proliferation and inflammation
“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
“QD”	once daily
“RA”	rheumatoid arthritis, a chronic autoimmune disease causing joint inflammation, pain, and progressive joint damage
“SAD”	single ascending dose, a clinical study design in which a single dose of an investigational drug is administered to sequential cohorts of participants at increasing dose levels to assess safety, tolerability, and pharmacokinetics
“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
“second line”	with respect to any disease, the therapy or therapies that are given when initial treatments (first-line therapy) do not work, or stop working
“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
“SLE”	systemic lupus erythematosus, a systemic autoimmune disease affecting multiple organs, characterized by autoantibody production and immune complex deposition
“SMO”	site management organization, an organization that contractually provides clinical trial related services to a study sponsor, CRO or clinical investigator
“TEAE”	treatment-emergent adverse event, either an adverse event with onset after the initiation of the study medication or an adverse event with onset before study medication that worsened in severity after the initiation of study medication
“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

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“T _{max} ”	the time after drug administration at which the maximum plasma concentration is reached, commonly used to characterize the absorption rate of a compound
“TNF-α”	a pro-inflammatory cytokine involved in systemic inflammation and targeted by several biologic therapies
“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
“TYK2”	tyrosine kinase 2, a member of the Janus kinase family involved in cytokine signaling (e.g., IL-12, IL-23, type I interferons) and implicated in autoimmune and inflammatory diseases
“UAS7”	urticaria activity score over 7 days, a composite score assessing urticaria severity over a week