Certain information and statistics set out in this section have been extracted from various official government publications, market data providers and a report commissioned by us and prepared by an independent third party, Frost & Sullivan. The information from official government sources has not been independently verified by us, the [**REDACTED**]*, Joint Sponsors,* [**REDACTED**]*, any of the* [**REDACTED**]*, any of their respective directors and advisers, or any other persons or parties involved in the* [**REDACTED**]*, and no representation is given as to its accuracy.*

THE AUTOIMMUNE/INFLAMMATORY DISEASES MARKET

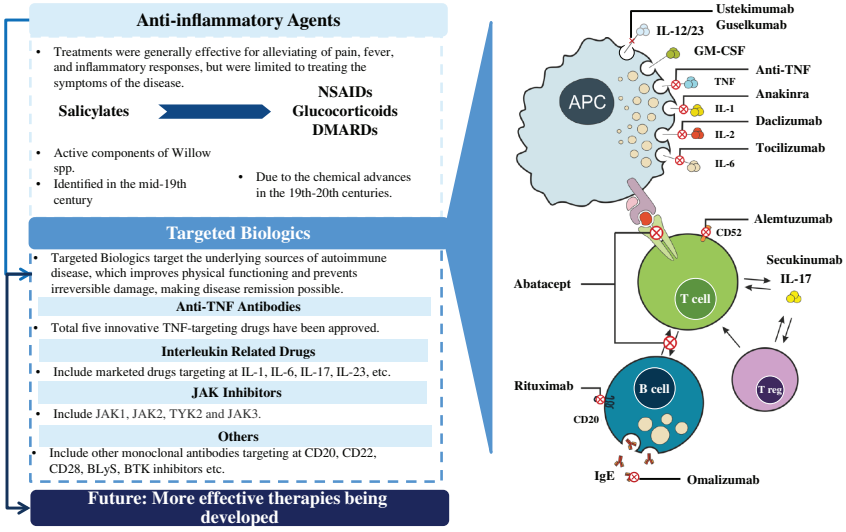
Overview

Autoimmune diseases arise from dysregulation of the immune system, in which immune cells mistakenly recognize the body's own healthy cells and tissues as foreign. This misdirected immune response triggers a cascade of inflammatory processes — including the release of pro-inflammatory cytokines, recruitment of immune cells, and activation of tissue-damaging pathways — ultimately leading to chronic or recurrent inflammation. In many autoimmune conditions, it is this persistent inflammation that drives tissue injury, functional impairment, and disease progression.

There are over 100 existing types of autoimmune disorders, which can affect almost any part of the body. Autoimmune diseases can be divided into organ specific autoimmune diseases such as systemic lupus erythematosus ("**SLE**") and rheumatoid arthritis ("**RA**") and systemic autoimmune diseases such as psoriasis, chronic spontaneous urticaria ("**CSU**") and atopic dermatitis ("**AD**") based on self-antigens targeted by immune cells and the extent of organ involvement. Both genetic and environmental factors may contribute to the development of autoimmune diseases, which can lead to symptoms of inflammation that affect patients' quality of life or even pose life-threatening risks.

Evolution of Autoimmune Disease Treatments

In managing autoimmune diseases, therapeutic options span from traditional anti-inflammatory agents to disease-modifying antirheumatic drugs ("**DMARDs**"), including conventional synthetic DMARDs ("**csDMARDs**") and biologic DMARDs ("**bDMARDs**") that target specific immune pathways. More recently, cell-based approaches have emerged, offering the potential to reset immune tolerance, while small-molecule inhibitors of intracellular signaling, notably JAK inhibitors, provide oral, targeted blockade of cytokine-driven inflammation. The following diagram illustrates the evolution of major autoimmune diseases treatments.



Abbreviations: NSAIDs = Non-steroidal anti-inflammatory drugs; DMARDs = Disease-modifying anti-rheumatic drugs

Source: Frontiers in Pharmacology, BMC Medicine, Frontiers in Immunology, Nature Reviews Drug Discovery, Rheumatology, Annals of the New York Academy of Sciences, FDA, Frost & Sullivan

The following chart illustrates the mechanism of action, representative drug, benefits and drawbacks of major treatment of autoimmune diseases.

Type	Mechanism of Action	Representative Drugs	Benefits	Drawbacks
Glucocorticoids	Prevent the formation of both PGs and LTs by causing the release of lipocortin, which by inhibition of phospholipase A2 reduces arachidonic acid release.	Prednisone, Cortisone	• GCs have **a wide range of anti-inflammatory actions**, affecting multiple components of the immune system. Hence, GCs are effective in treating a wide range of autoimmune conditions.	• Can cause a range of **adverse effects** such as osteoporosis, weight gain, high blood pressure, diabetes, increased susceptibility to infections, and adrenal suppression with long-term use. • **Cannot block RA progression and joint damage.**
NSAIDs	Exert an anti-inflammatory effect by inhibiting the activity of cyclooxygenase (COX)	Aspirin, Ibuprofen	• **Fast-acting**, with generally fewer side effects than glucocorticoids.	• Traditional non-selective NSAIDs inhibit platelet aggregation and cause significant **gastrointestinal disorders** such as bleeding, ulcers, and perforation. • Primarily exert anti-inflammatory and analgesic effects, and are **ineffective** in improving the disease condition or slowing joint damage.
csDMARDs	Suppress immune cell activity, inhibit specific inflammatory pathways, or interfere with cellular processes involved in immune responses.	Methotrexate, Sulfasalazine	• **Early intervention** with these drugs is emphasized to prevent joint damage, improve clinical symptoms, and enhance patient outcomes. • Reduce inflammation, relieve symptoms, and to some extent, **slow down** the progression of joint damage.	• csDMARDs generally have a **slow onset** of action. It may take several weeks or even months to achieve the desired therapeutic effect. • Associated with a variety of **adverse effects**.
bDMARDs	Work by inhibiting cytokines like TNF-α and IL-6, suppressing T cell activation, and depleting B cells, all of which contribute to the inflammation in autoimmune conditions.	TNF inhibitors, Interleukin inhibitors	• Due to their selective targeting of specific immune components, bDMARD scan effectively reduce inflammation, alleviate symptoms, and **slow disease progression**. • **Fewer** systemic side effects compared to csDMARDs.	• **Expensive** and require regular injections or infusions, which can be a barrier for some patients. • Increase the risk of **infection and malignancy**.
tsDMARDs	Involved in blocking several pro-inflammatory pathways including JAK/MAPK/SYK-BTK/NF-κB signaling.	JAK inhibitors	• Usually taken **orally**, which is more convenient for patients and improves treatment adherence. This is especially advantageous for patients who find it difficult to tolerate injections or infusions. • Can effectively reduce inflammation, alleviate symptoms, and **slow disease progression**. • tsDMARDs generally have a relatively lower risk of infections. This makes them a **safer** choice for patients with a higher susceptibility to infections.	• **Expensive** and may pose economic burdens on patients and healthcare systems. • May cause various **adverse effects**, such as hepatotoxicity, bone marrow suppression, gastrointestinal discomfort, and elevated liver enzymes.
Cell Therapy	Target and eliminate the pathogenic immune cells driving the condition.	Under development	• By addressing the underlying cause of autoimmunity, cell therapy can offer the potential for **long-term remission**.	• **Expensive** due to its complex procedures, high-cost reagents and equipment. • Long-term studies are needed to assess the durability and long-term **safety** of cell therapies.

Source: Cells, Expert Opinion on Pharmacotherapy, International Journal of Clinical Rheumatology, The Rheumatologist, Frontiers in Medicine, Frost & Sullivan

Unmet Clinical Needs of Autoimmune Disease Treatment

- *Current treatments for autoimmune diseases frequently fall short of delivering sustained efficacy or acceptable tolerability.* Studies in RA patients demonstrate that approximately 58 percent fail biologic DMARD therapy, with 77 percent being primary failures, defined as an inadequate initial response, and 23 percent being secondary failures, characterized by a loss of benefit over time. In addition, intolerance leads about 10 percent of patients to discontinue biologic agents and 21.8 percent to stop conventional synthetic DMARDs, while acute adverse reactions account for a 6.3 percent withdrawal rate among those receiving biologics. Although targeted therapies against key pathogenic pathways have enhanced clinical outcomes and reduced disease activity, these rates of nonresponse and treatment limiting toxicity reveal critical gaps in current approaches. Addressing the full spectrum of patient needs will require novel mechanisms of action, improved safety profiles and optimized combination regimens that can deliver both durable disease control and broader tolerability.

- *Insufficient enzyme selectivity remains a key limitation of current targeted biologics.* Broad-spectrum JAK inhibitors inhibit multiple JAK enzymes, leading to unintended suppression of diverse cytokine pathways and depletion of T cells and natural killer cells while sparing B cells. This imbalance heightens susceptibility to upper respiratory and urinary tract infections, particularly in patients already immunocompromised by autoimmune disease. Moreover, tofacitinib, baricitinib and upadacitinib carry FDA boxed warnings for serious cardiovascular events, malignancies, thromboembolic complications and death, highlighting the urgent need for therapies with precise target engagement and improved safety profiles.

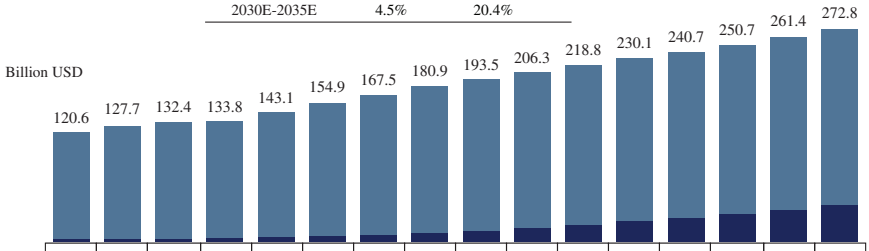
- *The complexity of autoimmune diseases is amplified by the limited understanding of their underlying pathogenesis.* Despite advancements, the precise pathogenesis of many autoimmune diseases remains unclear, which hinders the development of targeted therapies and personalized treatment approaches. Furthermore, certain populations are disproportionately affected by autoimmune diseases like lupus, experiencing higher hospitalization rates due to factors such as delayed diagnoses and limited access to care, underscoring the urgent need for more equitable healthcare strategies and earlier intervention measures.

Market Size of Autoimmune Disease Drugs

The global autoimmune disease drug market has demonstrated consistent growth in recent years. The following charts set for the global and China's autoimmune disease pharmaceutical market for the periods indicated.

Global and China's Autoimmune Diseases Pharmaceutical Market, 2020-2035E

Period	CAGR	
	Global	China
2020-2025	5.1%	15.9%
2025-2030E	7.2%	26.6%
2030E-2035E	4.5%	20.4%

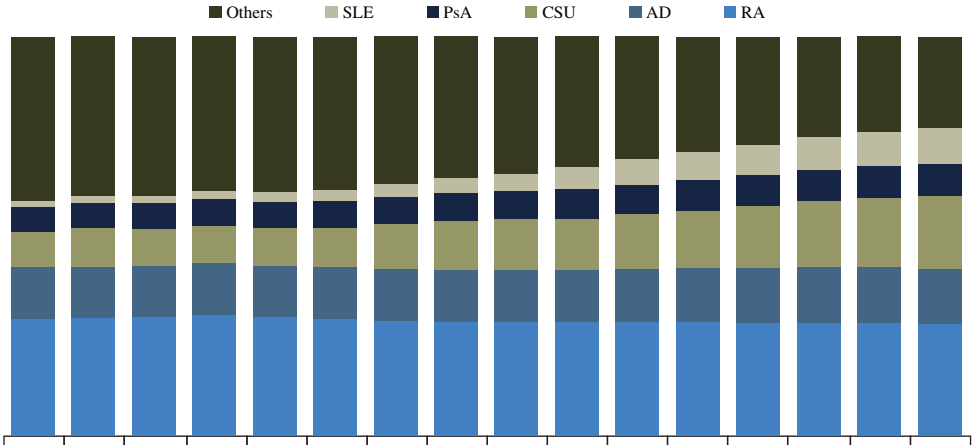


	2020	2021	2022	2023	2024	2025	2026E	2027E	2028E	2029E	2030E	2031E	2032E	2033E	2034E	2035E
Global	120.6	127.7	132.4	133.8	143.1	154.9	167.5	180.9	193.5	206.3	218.8	230.1	240.7	250.7	261.4	272.8
RoW	118.0	124.7	129.4	130.0	138.5	149.6	161.1	172.8	183.1	192.8	201.6	208.5	214.3	218.8	223.8	229.2
China	2.5	3.0	2.9	3.8	4.6	5.3	6.5	8.1	10.4	13.5	17.2	21.5	26.5	31.8	37.6	43.6

Source: Public Information, Expert Interview, Frost & Sullivan

Drugs for rheumatoid arthritis ("**RA**"), atopic dermatitis ("**AD**"), and chronic spontaneous urticaria ("**CSU**") constitute the majority of the autoimmune disease pharmaceutical market. The global pharmaceutical markets for CSU, RA and AD are expected to record overall CAGRs of approximately 9.8%, 4.2% and 5.1%, respectively, from 2020 to 2035. Over the same period, China's pharmaceutical markets for CSU, RA and AD are expected to record overall CAGRs of approximately 14.4%, 15.1% and 18.7%, respectively. The following charts set for the breakdown of global and China's autoimmune disease pharmaceutical market by indications, respectively.

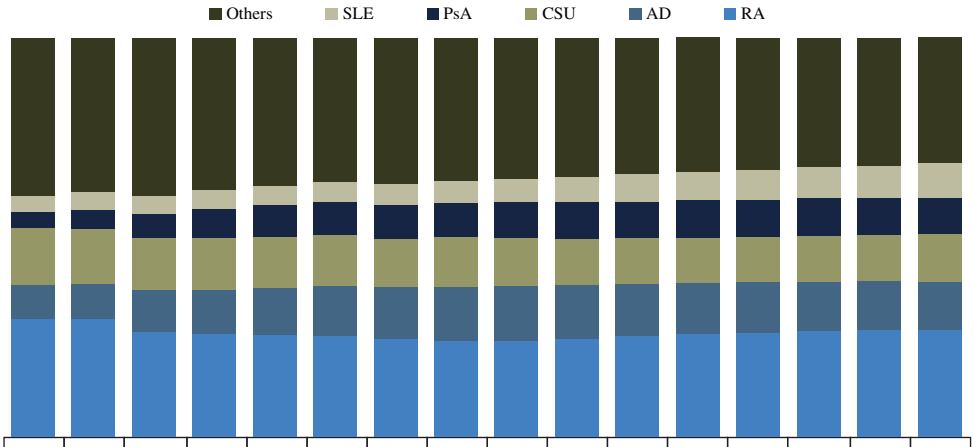
Breakdown of Global Autoimmune Diseases Pharmaceutical Market by Indications, 2020-2035E



	2020	2021	2022	2023	2024	2025	2026E	2027E	2028E	2029E	2030E	2031E	2032E	2033E	2034E	2035E
Others	41.3%	39.9%	39.9%	38.8%	39.0%	38.5%	37.1%	35.4%	34.2%	32.9%	30.7%	29.0%	27.0%	25.3%	24.0%	22.8%
SLE	1.4%	1.7%	1.8%	2.1%	2.4%	2.7%	3.2%	3.8%	4.5%	5.6%	6.5%	7.1%	7.6%	8.1%	8.6%	9.2%
PsA	6.4%	6.5%	6.5%	6.6%	6.7%	6.8%	6.9%	7.0%	7.1%	7.3%	7.4%	7.6%	7.7%	7.9%	8.0%	8.0%
CSU	8.8%	9.6%	9.2%	9.4%	9.3%	9.8%	11.2%	12.4%	12.6%	12.7%	13.7%	14.4%	15.7%	16.6%	17.4%	18.2%
AD	12.8%	12.9%	12.9%	13.1%	13.0%	13.0%	12.9%	12.9%	13.0%	13.2%	13.3%	13.5%	13.6%	13.8%	13.9%	13.9%
RA	29.3%	29.4%	29.6%	30.1%	29.6%	29.2%	28.8%	28.5%	28.5%	28.4%	28.4%	28.4%	28.3%	28.3%	28.2%	27.9%

Source: Public Information, Expert Interview, Frost & Sullivan

Breakdown of China Autoimmune Diseases Pharmaceutical Market by Indications, 2020-2035E



	2020	2021	2022	2023	2024	2025	2026E	2027E	2028E	2029E	2030E	2031E	2032E	2033E	2034E	2035E
Others	39.5%	38.8%	39.5%	38.1%	37.1%	36.2%	36.7%	35.9%	35.4%	34.7%	34.0%	33.6%	33.1%	32.4%	31.9%	31.5%
SLE	4.0%	4.3%	4.6%	4.8%	4.9%	5.0%	5.1%	5.3%	5.7%	6.4%	7.0%	7.2%	7.4%	7.8%	8.2%	8.8%
PsA	4.1%	4.9%	6.1%	7.3%	7.9%	8.3%	8.5%	8.7%	9.0%	9.1%	9.2%	9.4%	9.5%	9.4%	9.2%	9.1%
CSU	14.3%	13.7%	13.1%	13.1%	12.8%	12.6%	12.2%	12.5%	12.1%	11.7%	11.4%	11.2%	11.3%	11.5%	11.6%	11.9%
AD	8.5%	8.9%	10.3%	11.1%	11.9%	12.7%	13.1%	13.5%	13.8%	13.6%	13.2%	13.0%	12.7%	12.5%	12.4%	12.2%
RA	29.5%	29.4%	26.3%	25.6%	25.4%	25.2%	24.4%	24.0%	24.0%	24.4%	25.1%	25.7%	26.0%	26.4%	26.6%	26.6%

Source: Public Information, Expert Interview, Frost & Sullivan

While the prevalence growth of major indications such as RA, CSU and AD remains relatively stable, the autoimmune disease pharmaceutical market globally and in China continues to deliver steady CAGR growth, driven not only by the underlying patient base, but more importantly by higher diagnosis and treatment coverage, longer treatment duration, greater penetration of innovative and higher-value therapies, expansion of eligible treated populations and improving reimbursement access.

- The number of patients entering treatment and the aggregate treated patient-years may grow faster than the overall prevalent population. In autoimmune and related immune-mediated diseases, a meaningful proportion of patients remain subject to delayed diagnosis, undertreatment or limited use of advanced therapies. For example, published Chinese literature indicates that the average time from symptom onset to diagnosis of RA in China is approximately 2.5 years, while Chinese guidelines state that only approximately 8.3% of RA patients in China were treated with biologic DMARDs. These data indicate substantial room for earlier diagnosis, earlier intervention and broader adoption of advanced therapies, which may expand the actively treated population and support continued market growth even without significant prevalence expansion.

- Market value growth is materially supported by treatment upgrading. The autoimmune pharmaceutical market has been shifting from conventional, relatively low-cost therapies toward biologics and innovative targeted therapies, thereby significantly increasing the value generated per treated patient. By way of illustration, AbbVie discloses that the current U.S. list price for a 30-day supply of RINVOQ is US$7,090.41, while Sanofi reported that Dupixent generated global sales of €15.7 billion in 2025. These data demonstrate that continued launch and penetration of premium-priced innovative therapies may drive market value growth materially faster than prevalence growth, even where patient number growth remains modest.

- Expansion of labels, age groups and treatment settings may cause the treated population to grow faster than the underlying prevalence base. For example, in AD, DUPIXENT expanded in the U.S. from adults in 2017 to adolescents in 2019, children aged 6-11 in 2020 and children aged 6 months to 5 years in 2022. In CSU, expert consensus indicates that approximately 50% of patients remain inadequately controlled on or resistant to antihistamine therapy. DUPIXENT was subsequently approved in the U.S. in 2025 for CSU patients who remain symptomatic despite H1 antihistamine treatment and was described as the first new targeted treatment in over a decade for CSU. These developments demonstrate that market expansion is driven not only by prevalence growth, but also by broader treatment eligibility and continued treatment upgrading.

- Improving reimbursement coverage and patient access may also enable market growth to outpace prevalence growth. In China, innovative targeted therapies have gradually been included in the NRDL. For RA, public NHSA materials show that the reimbursement scope for upadacitinib includes "second-line treatment for adults with moderate-to-severe active rheumatoid arthritis," while the reimbursement scope for baricitinib includes "patients with confirmed rheumatoid arthritis whose disease activity has declined by less than 50% after 3-6 months of traditional DMARD treatment, subject to prescription by a rheumatology specialist." This demonstrates that improving reimbursement access may enable a larger proportion of patients to receive advanced therapies, thereby supporting pharmaceutical market growth at a rate exceeding prevalence growth.

Specifically, in 2025, small-molecule drugs accounted for approximately 25% of the global autoimmune disease drug market, while biologics accounted for approximately 75%. In the China market of autoimmune disease drug during the same year, small-molecule drugs represented approximately 46% of the market, with biologics accounting for approximately 54%. The following chart sets forth the details of top five global autoimmune disease drugs in 2025.

Brand Name	Generic Name	Companies	Sales Revenue (2025, Million USD)	Indications	Market Share (2025, %)
DUPIXENT	Dupilumab	Regeneron+Sanofi	17,740.5	Atopic dermatitis; asthma; chronic rhinosinusitis with nasal polyps; eosinophilic esophagitis; prurigo nodularis	11.5%
Skyrizi	Risankuzumab-rzaa	Abbvie	17,562.0	Plaque psoriasis; psoriatic arthritis; Crohn's disease; ulcerative colitis	11.3%
Rinvoq	Upadacitinib	Abbvie	8,304.0	Rheumatoid arthritis; Psoriatic arthritis; Atopic dermatitis; Ulcerative colitis; Crohn's disease; Ankylosing spondylitis; Non-radiographic axial Spondyloarthritis; Polyarticular Juvenile Idiopathic Arthritis; Giant Cell Arteritis	5.4%
Cosentyx	Secukinumab	Novartis	6,668.0	Plaque psoriasis; psoriatic arthritis; ankylosing spondylitis; non-radiographic axial spondyloarthritis; enthesitis-related arthritis; hidradenitis suppurativa	4.3%
ENTYVIO	Vedolizumab	Takeda	6,413.1	Moderately to severely active ulcerative colitis; Moderately to severely active Crohn's disease	4.1%

Source: Public Information, Frost & Sullivan

Market Drivers and Future Trends for Autoimmune Disease Drug Market

The growth of the autoimmune disease drug is expected to be driven by the following factors:

- *Expanding patient base with unmet need.* The growing proportion of older adults, who are more prone to autoimmune conditions due to immunosenescence and cumulative environmental exposures, is a key market driver. In China the population aged over 65 reached 223.7 million and accounted for 15.9% of the total in 2025 and such proportion is expected to keep growing in the following years, fueling the prevalence of chronic

autoimmune disorders. Combined with urbanization and lifestyle changes, this expanding patient pool underpins sustained demand for effective therapies and positions autoimmune disease treatments as a vital growth segment in the pharmaceutical industry.

- *Innovative therapies expanding market capacity.* Breakthroughs in targeted treatments have transformed autoimmune disease management, with JAK inhibitors delivering superior efficacy and safety compared to conventional immunosuppressants. By broadly disrupting cytokine signaling via the JAK-STAT pathway, these oral small molecules achieve rapid onset and flexible dosing while eliminating the need for infusions or injections, thereby enhancing adherence and quality of life in chronic conditions such as rheumatoid arthritis and psoriasis. Their combined clinical benefits and patient convenience are poised to enlarge the addressable patient population and strengthen the therapeutic landscape for autoimmune disorders. For example, as of the Latest Practicable Date, no therapy has been approved for patients who have failed both biological disease-modifying anti-rheumatic drugs and JAK inhibitors — representing a difficult-to-treat population with significant unmet medical need. Innovative therapies that address this gap could not only transform patient outcomes but also expand the overall market by reaching populations currently underserved by existing treatments.

- *Policy support for treatment innovation.* Accelerated regulatory pathways are catalyzing breakthroughs in small-molecule autoimmune disease therapies. The NMPA has introduced incentive policies under the "Healthy China 2030" plan to deepen review and approval reforms oriented toward clinical efficacy, strengthen approval standards, and expedite evaluation of innovative and clinically urgent drugs. These reforms have strengthened registration, communication and review mechanisms for innovative therapies with clear differentiated clinical value, thereby supporting the development of our Core Product and other drug candidates. Our Core Product and other drug candidates may be eligible for priority communication, breakthrough designation-related pathways and expedited review procedures where they demonstrate significant clinical value or address urgent unmet medical needs, which may facilitate more efficient clinical advancement and regulatory approval. Reforms explicitly encourage novel mechanisms such as dual-target small molecules such as TYK2/JAK1 inhibitors that address more complex immune pathways with enhanced precision, which is aligned with our development strategy and may further support the regulatory progression of our pipeline candidates under applicable accelerated pathways.

- *Dynamic collaboration among market players.* Growing investments and strategic partnerships among pharmaceutical companies, research institutions and government agencies are fueling R&D in autoimmune disease therapies. Capital inflows support the discovery and optimization of novel agents, while resource- and expertise-sharing through collaborations expedites development timelines and streamlines commercialization. These cooperative efforts are yielding more effective and safer treatments, meeting rising patient demand and sustaining market expansion.

The future development of autoimmune disease drug is likely to witness the following trends:

- *Advances in dual-target and multi-target inhibitors.* Innovative therapies such as dual-target small molecules, including TYK2/JAK1 inhibitors, are enhancing treatment precision by simultaneously modulating multiple immune pathways. Compared with traditional approaches, these agents address key limitations such as incomplete efficacy and relapse risk by targeting interconnected inflammatory cascades with greater specificity. Their high potency and reduced off-target effects enable superior disease control while meeting the clinical need for safer and more effective options. As research progresses, multi-target inhibitors are poised to play an increasingly important role in the treatment of autoimmune diseases.

- *Improved patient compliance through oral administration and sustained-release technologies.* Oral administration and sustained-release technologies are becoming increasingly important in the treatment of autoimmune diseases. Oral drugs provide greater convenience than injections, significantly improving patient adherence. For example, orally administered JAK inhibitors rapidly achieve effective concentrations, enabling early disease control. Sustained-release formulations further enhance outcomes by reducing dosing frequency, minimizing fluctuations in drug exposure, and improving overall treatment effectiveness. Continued advancements in these technologies are expected to strengthen drug-delivery efficiency, enhance patient compliance, and support growing demand in the autoimmune disease market.

- *Expanded indications and unmet need exploration.* Drug developers are actively broadening the indications of existing autoimmune disease therapies while addressing unmet needs to enhance clinical benefits. Many agents initially approved for a single condition, such as JAK inhibitors for rheumatoid arthritis, are now demonstrating efficacy in ulcerative colitis, alopecia areata and vitiligo, thereby expanding the treatable patient population. At the same time, companies are targeting niche and rare autoimmune diseases to provide additional therapeutic options. Continued R&D and clinical-trial efforts are expected to yield further indication expansions and new therapy launches, strengthening treatment choices and improving patient outcomes in autoimmune disorders.

Entry Barriers for Autoimmune Disease Drug Market

The major entry barriers for new entrants to the autoimmune disease drug market are set forth as follows:

- *High technical barriers to achieving high selectivity, efficacy, and safety in chronic autoimmune disease management.* The development of therapies for autoimmune diseases demands the integration of pharmacology, immunology, and medicinal chemistry to precisely target pathogenic pathways while maintaining optimal drug-like properties and bioavailability. Achieving high selectivity is critical to maximizing therapeutic efficacy and minimizing off-target effects, particularly for chronic conditions requiring long-term treatment. Our TLL-018 exemplifies this approach, combining exceptional selectivity with a dual-target mechanism — a design rarely achieved in the industry. Equally important are advanced drug-delivery technologies that enable controlled release and efficient systemic absorption. Oral formulations, in particular, require sophisticated engineering to enhance stability in the gastrointestinal tract and improve bioavailability, representing a significant technical hurdle for new market entrants.

- *Talent gap in expertise.* Developing autoimmune disease therapies demands professionals with deep expertise across drug design, synthetic chemistry, pharmacology, toxicology and clinical research, each discipline informing compound optimization and safe delivery. Assembling and managing such multidisciplinary teams is challenging and often requires strategic partnerships and effective project management.

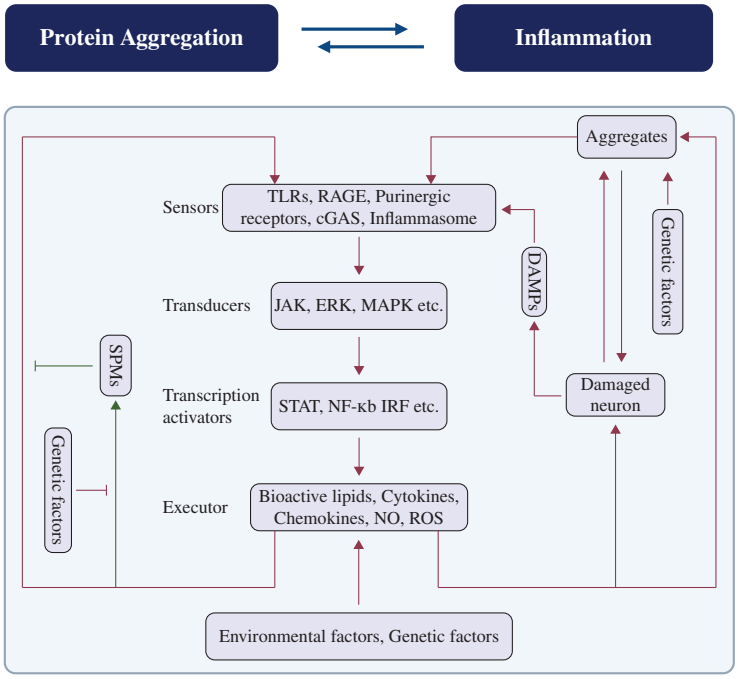
- *High upfront capital demands.* Significant financial resources are required to establish manufacturing facilities, conduct research and development, and navigate the complex regulatory landscape in the autoimmune disease therapeutics market. The need for specialized equipment and technology further elevates these requirements, while stringent quality-control standards and extensive clinical trials add to the cost of market entry.

THE NEURODEGENERATIVE DISEASES MARKET

Overview

Neurodegenerative diseases are a heterogeneous group of neurological disorders characterized by the progressive loss of neurons in the central or peripheral nervous system, profoundly impairing memory, cognition, behavior, sensory function, and motor control. Because neurons are terminally differentiated and unable to efficiently renew themselves, their degeneration results in the collapse of neural networks and disruption of essential communicative circuitry, thereby causing long-term functional decline.

A common hallmark across neurodegenerative diseases is neuroinflammation. Prolonged inflammatory responses in the brain, primarily driven by microglia and astrocytes, release cytotoxic mediators that exacerbate neuronal damage. Inflammation not only results from neurodegeneration but also actively contributes to its progression: protein aggregates, a frequent pathological feature in these disorders, can trigger neuroinflammation, which in turn accelerates protein aggregation and neuronal loss. In certain susceptible populations, neuroinflammation may even precede protein deposition, being induced by genetic variations in central nervous system cells or by peripheral immune cell infiltration. The following diagram illustrates the role of inflammation in neurodegeneration.

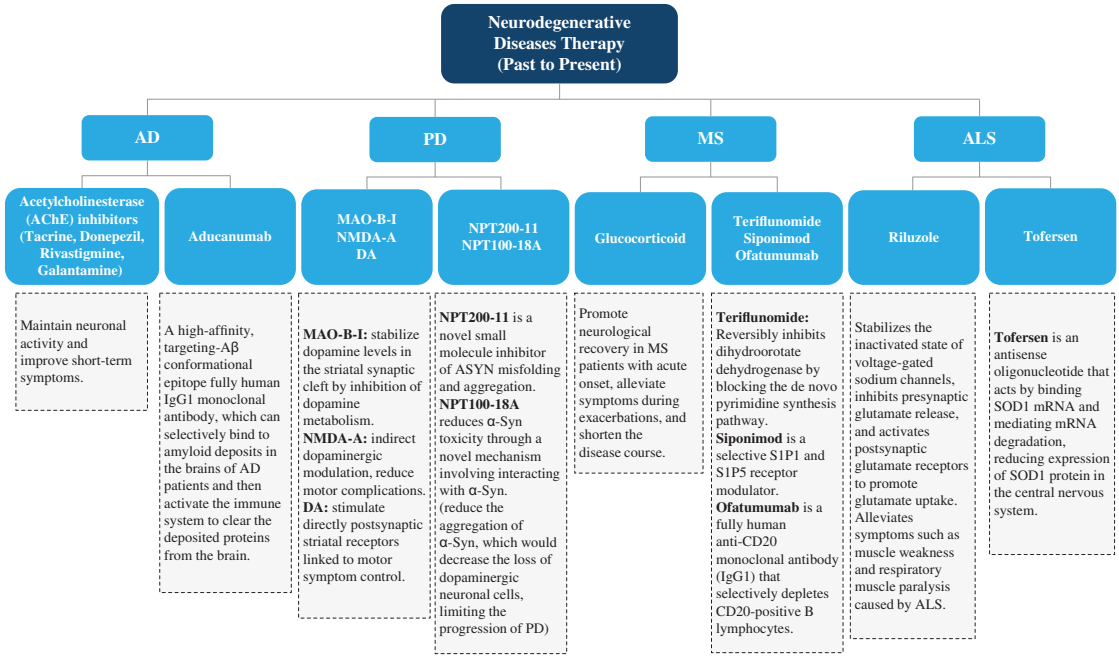


Source: Signal Transduction and Targeted Therapy, Frost & Sullivan

Clinically, neurodegenerative diseases encompass both acute conditions, such as cerebral ischemia, brain injury and epilepsy, and chronic disorders, including Alzheimer's disease, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis, multiple sclerosis, frontotemporal dementia and neuromyelitis optica spectrum disorders. Together, these conditions represent a major global health challenge, creating significant demand for novel treatment modalities and offering substantial opportunities to address the growing burden of neurodegenerative diseases.

Treatment Paradigm and Unmet Clinical Need of Neurodegenerative Diseases

Researchers have identified several shared mechanistic targets that may enable pan-neurodegenerative therapeutic strategies including environmental factors, neuroinflammation, metabolic stress, neurovascular coupling and genetic contributors. Traditional treatments for neurodegenerative diseases could only alleviate symptoms without slowing progression. For Alzheimer's disease, early drugs were acetylcholinesterase inhibitors that sustained neuronal activity to improve memory and learning; in recent years, aducanumab, which targets β-amyloid deposits, has begun to address disease progression at its root. For Parkinson's disease, initial therapies centered on levodopa-based regimens to restore dopaminergic signaling and control motor symptoms, whereas emerging approaches now focus on targeting α-synuclein aggregation and neuroinflammatory pathways to modify disease course. The following diagram demonstrates the evolution of neurodegenerative diseases therapy.



Abbreviations: *AD = Alzheimer's disease; PD = Parkinson's disease; MS = multiple sclerosis; ALS = amyotrophic lateral sclerosis*

Source: International Journal of Neurology and Neurosurgery, Translational Neurodegeneration, Scientific Reports, Brain Disorders, Neurodegenerative Disease Management, Chinese Guidelines for the Diagnosis and Treatment of Multiple Sclerosis (2023 Edition), Chinese Expert Consensus on Diagnosis and Treatment of Amyotrophic Lateral Sclerosis (ALS) 2022, Public Information, Frost & Sullivan

However, there remain unmet needs in current neurodegenerative disease treatment:

- *Absence of disease-modifying therapies.* Current treatments for neurodegenerative diseases deliver only symptomatic relief and fail to alter the underlying course, creating an urgent need for mechanism-based interventions. For instance, donanemab, a monoclonal antibody targeting amyloid-β plaques, has shown promise in slowing Alzheimer's disease progression in clinical trials, illustrating the potential of pathogenically directed agents to fill this critical therapeutic gap.

- *Blood-brain barrier delivery challenges.* The blood-brain barrier is a vital defense for the central nervous system, and it restricts more than 99% of therapeutic agents and limits clinical efficacy. Nanoparticle-based platforms. such as liposomes, polymeric nanoparticles and dendrimers, offer promise by leveraging receptor-mediated

transcytosis to ferry drugs into targeted brain regions. However, optimizing these systems for safe, efficient and reproducible delivery remains a significant challenge, necessitating further refinement to overcome this critical obstacle in neurotherapeutic development. There are currently no approved targeted therapies for neuroinflammation; biologics and immunotherapies face substantial limitations in crossing the blood-brain barrier, and existing JAK inhibitors lack clinically meaningful blood-brain barrier penetration.

- *Early and accurate diagnosis gap.* Neurodegenerative disorders unfold silently for years before clinical signs emerge, yet conventional diagnostic methods detect disease only after irreversible neuronal loss. Emerging technologies, most notably AI-enhanced blood assays, offer the potential to identify pathologic changes in conditions such as Parkinson's disease long before symptom onset, enabling timely therapeutic intervention and improving the prospects for disease modification.

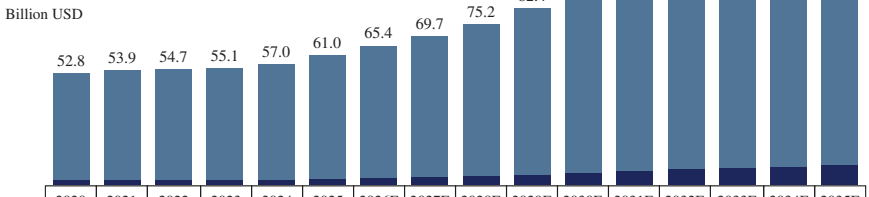
- *Inadequate multidisciplinary care systems.* Current healthcare systems lack integrated medical, social and caregiver support, leaving rising neurodegenerative burdens, particularly in aging populations poorly managed. The COVID-19 pandemic exacerbated these gaps in dementia care by disrupting services and increasing isolation. There is an urgent need to establish person-centered care models that formally include caregivers and leverage digital platforms for seamless coordination across clinical, social and support networks.

Market Size of Neurodegenerative Disease Drugs

Neurodegenerative disorders, which include Alzheimer's disease, Parkinson's disease and other progressive conditions of the central nervous system, represent a substantial and growing healthcare burden worldwide. The following chart sets for the global and China's neurodegenerative disease pharmaceutical market for the periods indicated.

Global and China's Neurodegenerative Disease Pharmaceutical Market, 2020-2035E

Period	CAGR	
	Global	China
2020-2025	2.9%	5.1%
2025-2030E	8.1%	16.0%
2030E-2035E	4.9%	10.1%



	2020	2021	2022	2023	2024	2025	2026E	2027E	2028E	2029E	2030E	2031E	2032E	2033E	2034E	2035E
Global	52.8	53.9	54.7	55.1	57.0	61.0	65.4	69.7	75.2	82.4	89.9	96.2	102.8	106.7	110.7	114.1
RoW	50.8	51.6	52.8	53.0	54.7	58.4	62.3	66.1	71.0	77.7	84.4	89.8	95.5	98.8	102.3	105.2
China	2.0	2.3	1.9	2.1	2.3	2.6	3.1	3.7	4.2	4.7	5.5	6.4	7.3	7.9	8.4	8.9

Source: Public Information, Expert Interview, Frost & Sullivan

The following chart sets forth the details of top five global neurodegenerative disease drugs in 2025.

Brand Name	Generic Name	Companies	Sales Revenue (2025, Million USD)	Indications	Market Share (2025, %)
Ocrevus	ocrelizumab	Roche	8,438.2	Relapsing multiple sclerosis; primary progressive multiple sclerosis	13.8%
Vyndaqel family	Tafamidis	Pfizer	6,380.0	Wild-type or hereditary transthyretin amyloid cardiomyopathy (ATTR-CM)	10.5%
Kesimpta	ofatumumab	Novartis	4,426.0	Relapsing forms of multiple sclerosis (RMS)	7.3%
REXULTI/RXULT	Brexpiprazole	Otsuka Holdings/Lundbeck	3,152.0	Schizophrenia; major depressive disorder (adjunctive); agitation associated with Alzheimer's dementia	5.2%
AUSTEDO	deutetrabenazine	Teva	2,260.0	Chorea associated with Huntington's disease;Tardive dyskinesia	3.7%

Source: Public Information, Frost & Sullivan

Notable BD Deals in Neurodegenerative Disease

Given the high barriers to entry in neurodegenerative drug development, only a handful of business development deals have materialized in this space. Our collaboration with Biohaven — an accomplished multinational pharmaceutical company — stands out as one of the largest transactions among them in terms of disclosed total deal value since 2019, underscoring both the strategic significance and commercial strength of the partnership. The following chart demonstrates China's license-out deals in neurogenerative diseases since 2019 as of the Latest Practicable Date.

China's License-out Deals in Neurogenerative Diseases since 2019, as of the Latest Practicable Date

Licensor	Licensee	Target	Indications	Type of Drugs	Phase	Total Deal Value (USD Million)
索元生物医药	Chuang Yi Global Asset Management	SLC6A4, SLC6A3, SLC6A2	Treatment-Resistant Depression	Chemical Drug	Phase II	–
Ractigen	University Medical Center Utrecht	–	Neurodegenerative Disease	Chemical Drug	Preclinical	–
Neurophth	Apellis Pharmaceuticals	–	Neurodegenerative Disease	Biologic Drug	Preclinical	–
高光制药 HIGHLIGHTLL PHARMA	Biohaven	TYK2, JAK1	AD, PD	Chemical Drug	Preclinical	960
Luye Pharma 绿叶制药	Exeltis	AChE, BCHE	AD, PD	Chemical Drug	Approved	–
Luye Pharma 绿叶制药	Towa Pharmaceutical	AChE, BCHE	Neurodegenerative Disease	Chemical Drug	Clinical Application	–
SCINEURO	Novartis	Amyloid beta	Alzheimer's disease	Biologic Drug	Preclinical	Up to ~1,665

* Referred to the clinical stage at which the licensing deal was disclosed.

Abbreviations: AD = Alzheimer's disease, PD = Parkinson's disease

Source: Insights Database, Public Information, Frost & Sullivan

Market Drivers and Future Trends for Neurodegenerative Disease Drug Market

The growth of the neurodegenerative disease drug is expected to be driven by the following factors:

- *Expanding patient base with unmet need.* Expanding patient base with unmet needs. The global neurodegenerative drug market is propelled by accelerated demographic aging, particularly in regions like China where the population aged above 65 reached 216.8 million in 2023 and grows to 223.7 million in 2025, driving higher incidence of Alzheimer's, Parkinson's and ALS. Urbanization and sedentary lifestyles further amplify these trends, expanding the patient pool and sustaining demand for effective therapeutic interventions.

- *Market expansion through innovative therapies.* Disease modifying therapies such as monoclonal antibodies against amyloid β and tau pathologies and gene therapies for rare disorders like spinal muscular atrophy are transforming treatment beyond symptomatic relief by targeting core disease mechanisms. Advances in blood-brain barrier penetration using nanoparticle carriers and receptor mediated transport overcome historic delivery obstacles to the central nervous system, while small molecule JAK inhibitors provide anti-inflammatory activity. These high value innovations command premium pricing and attract substantial research and development investment, thus broadening market capacity for neurodegenerative disease therapies.

- *Accelerated approval through regulatory reform.* The growth of the neurodegenerative disease drug industry has been supported in large part by a series of favorable government policies in China spanning regulatory approval, innovation incentives, medical insurance coverage and public health strategy. In particular, the NMPA has established and refined accelerated regulatory pathways, including breakthrough therapy designation, conditional approval and priority review and approval procedures, which are applicable to innovative therapies addressing serious or life-threatening diseases or conditions that severely affect quality of life, such as Alzheimer's disease and Parkinson's disease. In addition, regulatory policies addressing clinically urgent and overseas-approved innovative drugs provide further support for the introduction of novel neurodegenerative disease therapies into the China market. On the reimbursement side, the Chinese government has continued to advance healthcare security reform through the dynamic adjustment of the NRDL, with an emphasis on supporting drugs with high clinical value and a high degree of innovation through price negotiations and broader insurance coverage. Such measures have improved affordability and are expected to enhance post-approval market penetration of innovative therapies.

  At the strategic level, national public health initiatives, including the "Healthy China 2030" Plan, the Healthy China Action (2019–2030) and elderly-health management policies have continuously promoted early screening, disease awareness, health guidance and standardized long-term management for neurodegenerative disorders including Alzheimer's disease and Parkinson's disease. These measures directly improve patient identification, diagnosis and treatment pathways and create a more favorable clinical development and future commercialization environment for our Core Product and other drug candidates. Specifically, our Core Product and other drug candidates may qualify for expedited regulatory communication, review and approval where they demonstrate significant clinical value or address urgent unmet medical needs, which may accelerate their clinical development and registration.

- *Enhanced investments and R&D collaborations.* Increased investments and extensive R&D partnerships are powering expansion in the neurodegenerative disease drug market. A substantial influx of capital fuels the pursuit of innovative therapies, while collaborations among companies, research institutions and government bodies enable

resource and expertise sharing. These alliances accelerate development and commercialization timelines, yielding more effective and safer treatments that address rising patient demand and further propel market growth.

The future development of neurodegenerative disease drug is likely to witness the following trends:

- *Early detection and preventive intervention.* Advances in biomarkers and neuroimaging now enable diagnosis of neurodegenerative diseases at pre-symptomatic or prodromal stages, long before irreversible neuronal loss. This expanding early-stage patient population is driving a shift toward disease-modifying therapies aimed at halting or significantly slowing pathology and prompting the development of prophylactic treatments for high-risk individuals.

- *Enhanced CNS delivery strategies.* Novel therapies capable of penetrating the blood-brain barrier are addressing the historic limitation of inadequate central nervous system access. Engineered modalities — including sophisticated antibody formats, optimized small molecules leveraging novel transporters, and advanced platforms such as nanoparticle carriers, exosomes and focused ultrasound-mediated BBB disruption — enable direct delivery of monoclonal antibodies, gene therapies and neuroprotective agents to CNS targets. By overcoming this critical obstacle, these innovations promise to improve efficacy and redefine treatment paradigms for neurodegenerative diseases.

- *Expansion of combination and multi-target strategies.* The multifactorial nature of neurodegenerative diseases limits the efficacy of single-target agents, driving interest in combination regimens and multi-target molecules. Combination therapies harness drugs with complementary mechanisms — such as pairing disease-modifying agents with symptomatic treatments — to address multiple pathological processes simultaneously. For example, in Alzheimer's disease, future therapeutic strategies may increasingly involve the combination of approved anti-amyloid-β agents with interventions targeting neuroinflammation, with the potential to achieve greater efficacy than monotherapy. Multi-target compounds are engineered to engage several critical nodes within a disease pathway, potentially enhancing efficacy and reducing resistance. Although these approaches demand sophisticated research frameworks and complex clinical-trial designs, they promise more comprehensive disease control and improved patient outcomes, and are poised to reshape the therapeutic landscape for neurodegenerative disorders.

Entry Barriers for Neurodegenerative Disease Drug Market

The major entry barriers for new entrants to the neurodegenerative disease drug market are set forth as follows:

- *Complex technical barriers to modulating neuroinflammation and achieving effective blood brain barrier penetration.* The development of therapies for neurodegenerative diseases is constrained by profound technical hurdles, particularly in modulating neuroinflammation and achieving effective blood-brain barrier penetration. Controlling neuroinflammation requires highly selective targeting of glial cells such as microglia and astrocytes to suppress harmful cytokines like TNF-α and IL-1β while preserving protective functions, a task complicated by the dynamic nature of inflammatory responses across disease stages. At the same time, the blood-brain barrier prevents most conventional drugs from reaching the central nervous system, necessitating advanced delivery technologies and deep insight into its physiological and pathological features. These challenges make therapeutic innovation resource-intensive and raise the threshold for new entrants, underscoring the need for sustained research investment and specialized expertise.

- *Shortage of specialized talent.* The neurodegenerative disease drug market faces significant challenges related to talent availability. Developing effective therapies requires professionals with deep expertise across neurology, pharmacology, medicinal chemistry, and clinical research. However, there is a pronounced shortage of specialists with the requisite knowledge and hands-on experience in neurodegenerative disease drug development. Recruiting and retaining such talent is both highly competitive and costly, creating a substantial barrier for new entrants. This shortage of expertise remains a critical constraint on advancing innovation and expanding capacity within the field.

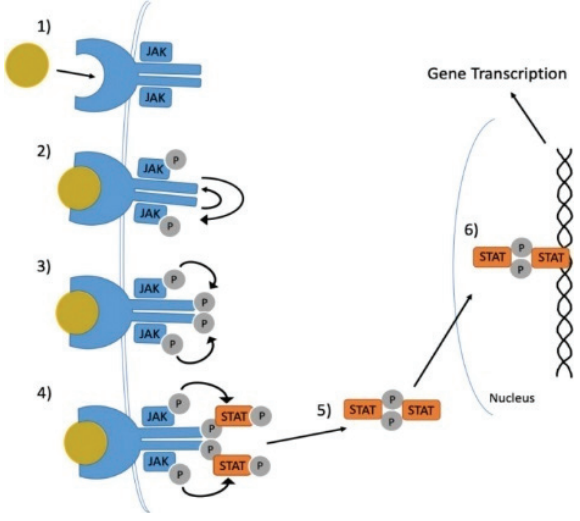
- *High and sustained financial demands.* The development of novel neurodegenerative disease therapies requires substantial financial resources across all stages, from basic research to clinical trials and eventual regulatory approval. Early research demands significant investment in target discovery, drug design, and preclinical studies, while clinical trials are particularly costly due to large patient cohorts, extended observation periods, and rigorous regulatory standards. The long development timelines necessitate continuous funding, and the high risk of failure further compounds the financial burden. These factors make the cost of entry especially prohibitive for new entrants, posing a critical barrier to broader innovation in the field.

GLOBAL JAK INHIBITOR MARKET

Overview

Janus kinases ("**JAKs**") are a family of cytoplasmic, non-receptor tyrosine kinases — including JAK1, JAK2, JAK3, and TYK2 — that associate with type I/II cytokine receptors and mediate signal transduction via the JAK-STAT pathway. Upon cytokine engagement, receptor-bound JAKs trans-phosphorylate one another and create docking sites for STAT transcription factors, whose subsequent phosphorylation, dimerization, and nuclear translocation drive expression of genes governing immune cell activation, proliferation, and inflammatory mediator production. Aberrant JAK-STAT signaling underlies the pathogenesis of autoimmune disorders such as rheumatoid arthritis, urticaria, and atopic dermatitis by perpetuating pro-inflammatory cytokine networks. Consequently, selective small-molecule inhibitors targeting the ATP-binding sites of specific JAK isoforms have emerged as effective oral therapies to restore immune homeostasis and control disease activity.

Mechanistically, the JAK/STAT pathway consists of the following steps: Step 1) The ligand (usually a cytokine) binds and cross-links its receptor. Step 2) The associated JAKs transphosphorylate and activate each other. Step 3) The activated JAKs phosphorylate the receptor tail. Step 4) The receptor tail becomes a docking site for recruited STAT proteins, which themselves are phosphorylated by the activated JAKs. Step 5) The phosphorylated STATs dissociate from the receptor and dimerise. Step 6) STAT dimers translocate to the nucleus where they regulate gene transcription. The following diagram shows the JAK/STAT pathway steps.



Source: Mediterranean Journal of Rheumatology, Frost & Sullivan

The JAK family is central to the JAK/STAT pathway and is involved in many inflammatory and immune diseases. Single-target JAK inhibitors, with good selectivity and safety, are widely used, but for complex, multi-pathway diseases, dual-target JAK inhibitors offer stronger efficacy, broader indications, and the potential to overcome drug resistance.

TLL-018 exhibits outstanding kinase selectivity, showing highly targeted inhibition of JAK1 and TYK2, with minimal inhibitory effect on non-target kinases such as JAK2. The following diagram illustrates a comparison of selectivity of JAK inhibitors.

Target	Genetic Name	Selectivity for TYK2/JAK1 vs. JAK2 *in vitro*, IC50(nM)			Conclusion
		Target kinases		Non-target kinases	
		JAK1	TYK2	JAK2	
JAK1, TYK2	TLL-018	4	5	>1000	• Confers **>200-fold** selectivity for JAK1 and TYK2 over JAK2. • Profiling against a panel of over 350 human kinase showed that TLL-018 is exclusively selective for JAK1 and TYK2, with **≥90-fold** selectivity against all other kinases tested. • TLL-018 exhibited potent cellular activity for JAK1-mediated IL-6 signaling (IC50 = 0.6 μM) with **greater than 100-fold** selectivity against JAK2-mediated cytokine (e.g., TPO) signaling in human whole blood-based assays.
	Brepocitinib	23	17	77	• Confers **<5-fold** selectivity for JAK1 and TYK2 over JAK2. • efficacy observed in other indications but with potential limitations from lower selectivity
	Soficitinib	19	0.5	191	• Confers **<15-fold** selectivity for JAK1 over JAK2.
JAK	Tofacitinib	1	42	2	• In head-to-head Phase 2 mid-term analysis, **TLL-018 vs. tofacitinib**, ACR50 response rates were 48.0% (10mg), 65.4% (20mg), and 72.0% (30mg), exceeding tofacitinib's 41.7%.
JAK1	abrocitinib	29	1247	803	• Confers **<30-fold** selectivity for JAK1 over JAK2.

Source: Annals of the Rheumatic Diseases, Arthritis & Rheumatology, Journal of the American Academy of Dermatology, Anais Brasileiros De Dermatologia, Public Information, Frost & Sullivan

Competitive Landscape of JAK Inhibitors Indicated for Autoimmune Disease

As of the Latest Practicable Date, there are over ten approved JAK inhibitors globally, in which five of them are mono-selective and six are dual-target or multi target. The following table sets forth the global marketed JAK inhibitors as of the Latest Practicable Date.

Global Marketed JAK Inhibitors Indicated for Autoimmune Diseases as of the Latest Practicable Date

Target	Genetic Name	Manufacturer	Approved Indications	Market Authority	First Approval Date	Sales Revenue (2024, Million USD)	Sales Revenue (2025, Million USD)
JAK1, JAK2, JAK3	Tofacitinib	Pfizer	Rheumatoid Arthritis, Juvenile Idiopathic Arthritis, Psoriatic Arthritis, Ulcerative Colitis, Polyarticular Juvenile Idiopathic Arthritis, Juvenile Psoriatic Arthritis, Ankylosing Spondylitis	FDA, EMA, NMPA	2012-11-06 (FDA) 2017-03-22 (EMA) 2017-03-10 (NMPA)	1,168	1,087
JAK1, JAK2	Baricitinib	Incyte Corporation, Lilly	Rheumatoid Arthritis, Atopic Dermatitis, COVID-19, Alopecia Areata, Juvenile Idiopathic Arthritis, Enthesitis-Related Arthritis, Juvenile Psoriatic Arthritis, Polyarticular Juvenile Idiopathic Arthritis	FDA, EMA, NMPA	2018-05-31 (FDA) 2017-02-13 (EMA) 2019-06-24 (NMPA)	957	NA
	Ruxolitinib	Lilly	Myelofibrosis, Polycythemia vera, Graft versus host disease	FDA, EMA, NMPA	2011/11/16 (FDA) 2012/8/23 (EMA) 2017/3/10 (NMPA)	4,728	5,203
	Ruxolitinib Cream	Incyte Corporation	Atopic Dermatitis, Non-Segmental Vitiligo	FDA, EMA	2021-09-21 (FDA) 2023-04-19 (EMA)	508	679
	Deuterated ruxolitinib	Sun Pharmaceutical Industries	Alopecia Areata	FDA	2024-07-25 (FDA)	NA	NA
JAK1, JAK2, ROCK1, ROCK2	Rovadicitinib	Chia Tai Tianqing	Myelofibrosis	NMPA	2026-02-25 (NMPA)	NA	NA
JAK1, JAK, JAK3, TYK2, ALK2	Gecacitinib	Zelgen Biopharmaceuticals	Myelofibrosis	NMPA	2025-05-27 (NMPA)	NA	NA
JAK1, JAK2, ALK2	Momelotinib	Gilead	Myelofibrosis	FDA, EMA	2023-09-15 (FDA) 2024-01-25 (EMA)	477	748
JAK3, TEC	Ritlecitinib	Pfizer	Alopecia Areata	FDA, EMA, NMPA	2023-06-23 (FDA) 2023-09-15 (EMA) 2023-10-18 (NMPA)	NA	NA
JAK1	Upadacitinib	AbbVie	Rheumatoid Arthritis, Psoriatic Arthritis, Ankylosing Spondylitis, Atopic Dermatitis, Ulcerative Colitis, Non-Radiographic Axial Spondyloarthritis, Crohn's Disease, Polyarticular Juvenile Idiopathic Arthritis, Juvenile Psoriatic Arthritis, Giant Cell Arteritis	FDA, EMA, NMPA	2019-08-16 (FDA) 2019-12-16 (EMA) 2022-02-18 (NMPA)	5,971	8,304
	Filgotinib	Galapagos	Rheumatoid Arthritis, Ulcerative Colitis	EMA	2020-09-24 (EMA)	NA	NA
	Abrocitinib	Pfizer	Atopic Dermatitis	FDA, EMA, NMPA	2022-01-14 (FDA) 2021-12-09 (EMA) 2022-04-08 (NMPA)	215	271
	Golidocitinib	Dizal Pharmaceutical	Peripheral T-cell lymphoma	NMPA	2024-06-18 (NMPA)	NA	NA
	Ivarmacitinib	Hengrui	Ankylosing Spondylitis, Rheumatoid Arthritis, Atopic Dermatitis, Alopecia Areata	NMPA	2025-3-18 (NMPA)	NA	NA
TYK2	Deucravacitinib	Bristol Myers Squibb	Plaque Psoriasis, Pustular Psoriasis, Erythrodermic Psoriasis	FDA, EMA, NMPA	2022-09-09 (FDA) 2023-03-24 (EMA) 2023-10-18 (NMPA)	246	291
JAK	Delgocitinib	Japan Tobacco, Torii Pharmaceutical, Akros Pharma	Atopic Dermatitis, Eczema	EMA	2024-09-19 (EMA)	NA	NA
	Peficitinib	Astellas	Rheumatoid Arthritis	NMPA	2024-07-30 (NMPA)	NA	NA
JAK2	Bezacitinib	Bangshun Pharmaceutical	Myelofibrosis	NMPA	2026-04-29 (NMPA)	NA	NA
JAK2, FLT3	Fedratinib	Sanofi	Myelofibrosis	FDA, EMA	2019-08-16 (FDA) 2021-02-08 (EMA)	NA	NA
	Pacritinib	S-BIO	Myelofibrosis	FDA	2022-02-28 (FDA)	146	120

Note: The JAK target in the table is a broad-spectrum target, and specific targets have not been publicly disclosed.

Source: FDA, EMA, Frost & Sullivan

The rapid sales growth of leading JAK inhibitors underscores the segment's strong commercial momentum and substantial market potential. For example, global sales of Rinvoq® (upadacitinib) reached US$5,971.0 million in 2024 and surged to US$8,304.0 million in 2025, reflecting year-over-year growth of approximately 40%. This growth trajectory highlights the expanding adoption of JAK inhibitors across multiple indications and position the class as one of the most promising therapeutic categories in the autoimmune and inflammatory disease market.

Market Opportunities of JAK Inhibitors in Autoimmune Diseases

Rheumatoid Arthritis

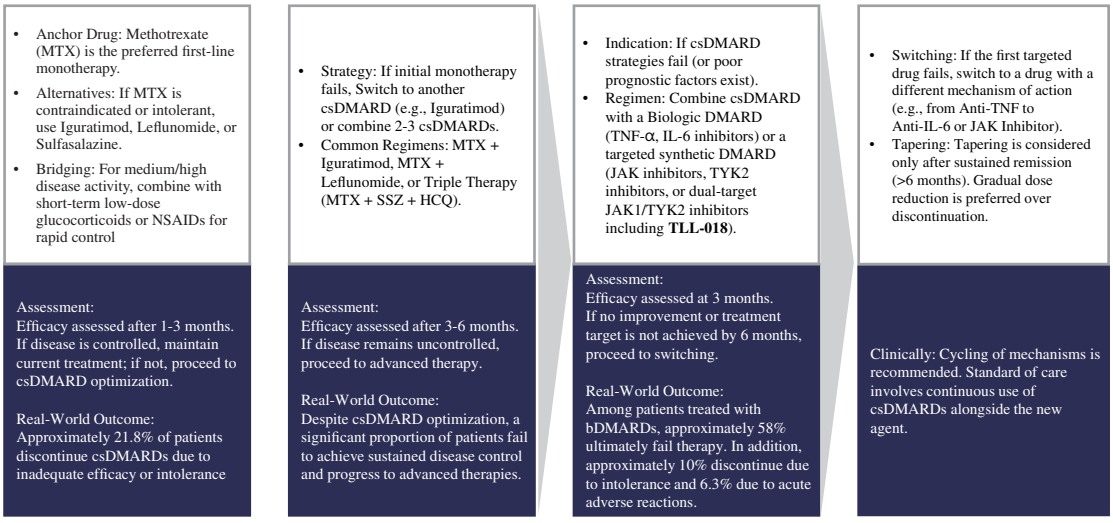
Rheumatoid arthritis ("**RA**") is a chronic, systemic autoimmune disorder characterized by persistent synovial inflammation, which manifests clinically as joint stiffness, pain, and swelling, ultimately leading to cartilage destruction, joint deformity, functional impairment and increased mortality. The pathological hallmark of RA is hyperplasia of the synovial lining, driven by pro-inflammatory cytokines and immune cell infiltration, which not only compromises joint integrity but also produces systemic symptoms such as fever, fatigue, myalgia and anorexia. The primary objectives of RA management are to suppress inflammation, prevent structural joint damage, preserve physical function, alleviate pain and enhance patient quality of life.

RA is a mature disease area with a well-established epidemiological profile, and its prevalence would generally not be expected to rise materially over a short period. Accordingly, the projected increase in patient numbers remains limited. Published guidelines and epidemiological studies generally indicate that RA has a prevalence of approximately 0.42% in China and approximately 0.5%-1.0% globally. In China, the prevalence of RA remained relatively stable as the prevalence increased from 6.0 million cases in 2020 to 6.2 million cases in 2025 at a CAGR of 0.7%, and is projected to reach 6.4 million cases by 2030 and further reach 6.7 million cases by 2035, representing a CAGR of 0.8% from 2025 to 2030 and 0.9% from 2030 to 2035, respectively. The global prevalence of RA increased from 39.8 million cases in 2020 to 41.8 million cases in 2025 at a CAGR of 1.0%, and is projected to reach 43.7 million cases by 2030 and further reach 45.4 million by 2035, representing a CAGR of 0.9% from 2025 to 2030 and 0.8% from 2030 to 2035, respectively. Such increase is driven primarily by demographic factors, in particular population aging, rather than any marked uplift in the underlying prevalence rate.

First-line therapy of RA consists of conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) — notably methotrexate, sulfasalazine, leflunomide and hydroxychloroquine — often used in combination with non-steroidal anti-inflammatory drugs, low-dose corticosteroids, analgesics, physiotherapy and occupational therapy to optimize symptom control and functional capacity. In cases of inadequate response or intolerance to csDMARDs, biologic DMARDs targeting key pathogenic mediators are introduced. These include monoclonal antibodies and fusion proteins directed against tumor necrosis factor-alpha (TNF-α), CD20, interleukins (IL-1, IL-6) or the IL-6 receptor, as well as agents modulating T-cell co-stimulation.

Despite the proven efficacy of anti-TNF agents and other biologics in achieving disease remission and inhibiting radiographic progression, several unmet needs persist. Loss of therapeutic response may arise from high inflammatory burden, subtherapeutic serum drug levels, accelerated clearance or immunogenicity. Moreover, biologic therapies can be constrained by safety concerns, complex dosing regimens and high cost. Consequently, there remains an urgent demand for novel therapeutic modalities that combine enhanced efficacy, sustained response, favorable safety profiles and improved accessibility to optimize long-term outcomes for patients living with RA. While the overall treatment principles are broadly aligned with international standards, the treatment pathway for RA in China, as referenced from the Chinese Guidelines for the Diagnosis and Treatment of Rheumatoid Arthritis, differs in certain aspects, including greater retention of conventional synthetic DMARD combinations prior to escalation, broader positioning of JAK inhibitors alongside biologics, and the inclusion of certain locally approved small-molecule therapies as part of the standard of care.

Within this treatment paradigm, TLL-018 is developed for patients with active, moderate-to-severe rheumatoid arthritis who have demonstrated an inadequate response to, or intolerance of, prior therapies. Its primary target population comprises patients who are inadequate responders to, or intolerant of, biologic DMARDs, consistent with the inclusion criteria of our pivotal Phase III clinical trial. In addition, TLL-018 has been evaluated in Phase II studies in patients with inadequate response to, or intolerance of, methotrexate, supporting its potential use in conventional synthetic DMARD-inadequate responder populations. The diagram below illustrates the recommended treatment paradigm for RA in China.



Note: DMARDs (disease-modifying anti-rheumatic drugs) include methotrexate, leflunomide, sulfasalazine (SSZ), hydroxychloroquine (HCQ), azathioprine, cyclophosphamide and so on. NSAIDs (Nonsteroidal Anti-inflammatory Drugs) include aspirin, acetaminophen, indomethacin, naproxen, etc.

Source: 2024 Chinese Guidelines for the Diagnosis and Treatment of Rheumatoid Arthritis, Frost & Sullivan

In 2025, the RA indication market accounts for approximately 21% and 25% of global and Chinese JAK inhibitors market, respectively. As of the Latest Practicable Date, there are six JAK inhibitors approved for RA globally, including five available in China. As of the same date, there are nine JAK inhibitors targeting RA in clinical development globally (excluding China) and 14 JAK inhibitors targeting RA in clinical development in China, among which three drug candidates are in Phase III clinical-stage.

Global Marketed JAK Inhibitors Indicated for RA as of the Latest Practicable Date

Manufacture	Genetic Name	Target	Approved Indications	Market Authority	First Approval Date
Hengrui	Ivarmacitinib	JAK1	RA	NMPA	2025-03-18 (NMPA)
Astellas	Peficitinib	JAK3		NMPA	2024-07-30 (NMPA)
Galapagos	Filgotinib	JAK1		EMA	2020-09-24 (EMA)
AbbVie	Upadacitinib	JAK1		FDA, EMA, NMPA	2019-08-16 (FDA) 2019-12-16 (EMA) 2022-03-18 (NMPA)
Incyte	Baricitinib	JAK1, JAK2		FDA, EMA, NMPA	2018-05-31 (FDA) 2017-02-13 (EMA) 2019-06-24 (NMPA)
Pfizer	Tofacitinib	JAK1, JAK2, JAK3		FDA, EMA, NMPA	2012-11-06 (FDA) 2017-03-22 (EMA) 2017-03-10 (NMPA)

JAK Inhibitors at Clinical-Stage Globally (Excluding China) Indicated for RA as of the Latest Practicable Date

Manufacturer	Phase	Genetic Name/Code	Target	First Posted Date	Indications
Celon Pharma	II	CPL'116	JAK, ROCK	2022-05-10	RA
Pfizer	II	Tofacitinib Zimlovisertib Ritlecitinib	JAK1, JAK2, JAK3 IRAK4 JAK3, TEC	2020-04-14	
AbbVie	II	Elsubrutinib+Upadacitinib-ABBV-599 Elsubrutinib	BTK, JAK1 BTK	2018-09-25	
Gilead	II	Filgotinib Lanraplenib	JAK1, SYK	2016-08-26	
Vertex Pharmaceuticals	II	Decernotinib	JAK3	2012-12-18	
Incyte	II	Itacitinib	JAK1	2012-06-20	
EQRx	I	LNK01001	JAK1	2022-02-18	
HK inno.N	I	CJ-15314	JAK1	2020-03-06	
Highlightll Pharma	I	TLL-018	JAK1, TYK2	2020-01-28	

JAK Inhibitors at Clinical-Stage Indicated for RA in China as of the Latest Practicable Date

Manufacturer	Phase	Genetic Name/Code	Target	First Posted Date	Indications
Lynk	III	LNK01001	JAK1	2023-09-22	RA
Highlightll Pharma	III	TLL-018	JAK1, TYK2	2023-08-31	
Wuxi Fuxin Pharmaceutical	III	WXFL10203614	JAK1	2023-06-27	
Longwood Biopharmaceuticals	II	LW402	JAK1	2022-11-18	
Kelun-Biotech	II	KL130008	JAK1, JAK2	2020-12-30	
Synergy Pharmaceutical	I	HHT-109	JAK1	2026-04-02	
Jiangsu Vcare	I	VC005	JAK1	2023-05-04	
Chengdu Zeiling Biomedical	I	ZL-82	JAK3	2023-03-21	
Jiangsu Carephar, Nanjing Shenzhou Jiamei Pharmaceutical	I	H018	JAK1	2022-12-23	
Guangzhou Jiayue Pharmaceutical	I	JYP0061	JAK1	2021-09-16	
CSPC	I	SYHX1901	JAK1, TYK2, JAK3, SYK	2021-05-13	
Zhuhai United Laboratories	I	TUL01101	JAK1	2020-11-04	
Shanghai Fudan-Zhangjiang Bio-Pharmaceutical	I	FZJ-003	JAK1	2020-11-03	
Hangzhou Guangliang Biopharmaceutical	I	Bewintinib	JAK2	2019-06-04	

Source: FDA, EMA, Clinical Trial, NMPA, CDE, Frost & Sullivan

The following diagram sets forth details of end user price, market share, and reimbursement coverage for marketed JAK inhibitors indicated for RA globally and in China as of as of the Latest Practicable Date.

End User Price and Reimbursement Coverage for Global (Excluding China) Marketed JAK Inhibitors Indicated for RA

Manufacturer	Drug	End User Price	Medical Insurance Coverage
Galapagos	Filgotinib	**£28.77/tablet** (based on UK NHS indicative price of £863.10 per 30-tablet pack)	**US:** not approved; **UK:** NHS/NICE covered; **Japan:** NHI covered
AbbVie	Upadacitinib	**US$236.35/tablet** (based on U.S. official list price of US$7,090.41 for a 30-day supply; calculated on a once-daily basis)	**US:** commercial + Medicare Part D coverage; **UK:** NHS/NICE covered; **Japan:** NHI covered
Incyte	Baricitinib	**US$95.01/tablet** (based on U.S. official list price of US$2,850.41 for a 30-day supply of 2 mg tablets; calculated on a once-daily basis)	**US:** commercial + Medicare (plan-dependent); **UK:** NHS/NICE covered; **Japan:** NHI covered
Pfizer	Tofacitinib	**US$75.91/tablet** (based on U.S. WAC of US$4,554.86 per 60-tablet pack of 5 mg tablets)	**US:** commercial + Medicare (plan-dependent); **UK:** NHS/NICE covered; **Japan:** NHI covered

Abbreviations: NHS = National Health Service in UK; NICE = National Institute for Health and Care Excellence in UK; NHI = National Health Insurance in Japan; NRDL = National Reimbursement Drug List in China

Note: End-user prices are based on publicly available benchmark prices in the relevant markets and are presented on a per smallest dosage unit basis. For the U.S., prices are based on official list price or WAC disclosures; and for the UK, prices are based on publicly available reimbursement/listed prices. The smallest dosage unit price refers to the price of one minimum dosage unit, such as one tablet, capsule or vial. Such prices are shown for reference to illustrate the pricing and reimbursement environment of the relevant products in each market and may not be directly comparable across jurisdictions due to differences in pricing, procurement and reimbursement systems.

Source: Public Information, Frost & Sullivan

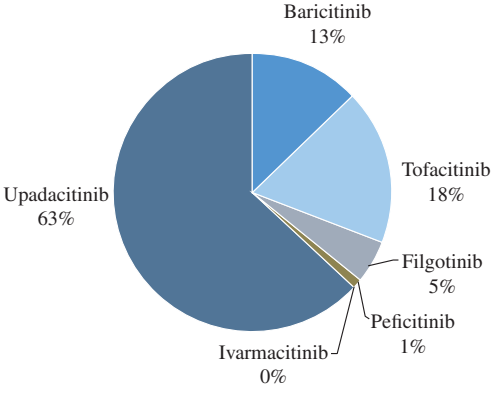
End User Price and Reimbursement Coverage for Marketed JAK Inhibitors Indicated for RA in China

Manufacturer	Drug	End User Price	Medical Insurance Coverage	Any Generic Drugs?	Generic Drugs Price
Hengrui	Ivarmacitinib	NA	Covered	No	NA
Astellas	Peficitinib	NA	Not Covered	No	NA
AbbVie	Upadacitinib	RMB65.48/tablet	Covered	No	NA
Incyte	Baricitinib	RMB38.00/tablet	Covered	Yes	RMB25.94/tablet
Pfizer	Tofacitinib	RMB1.27/tablet	Covered	Yes	RMB0.37/tablet

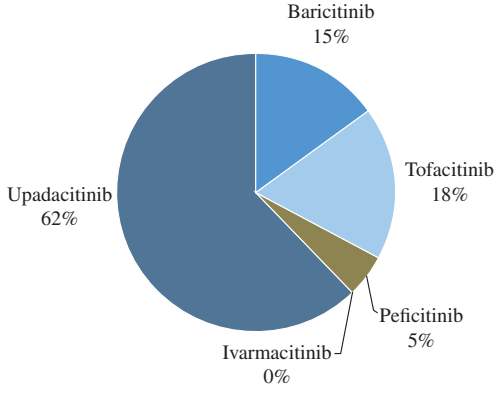
Note: End-user prices are primarily based on the lowest publicly available centralized procurement winning price or listed online price, and are presented on a per smallest dosage unit basis; the smallest dosage unit price refers to the price of one minimum dosage unit, such as one tablet, capsule or vial.

Source: Public Information, Frost & Sullivan

Market Share for Global Marketed JAK inhibitors indicated for RA in 2025



Market Share for Marketed JAK inhibitors indicated for RA in China in 2025



Note: Peficitinib is approved only in selected Asian markets, including China and Japan, and has not been approved by the FDA or EMA.

Source: Frost & Sullivan Analysis

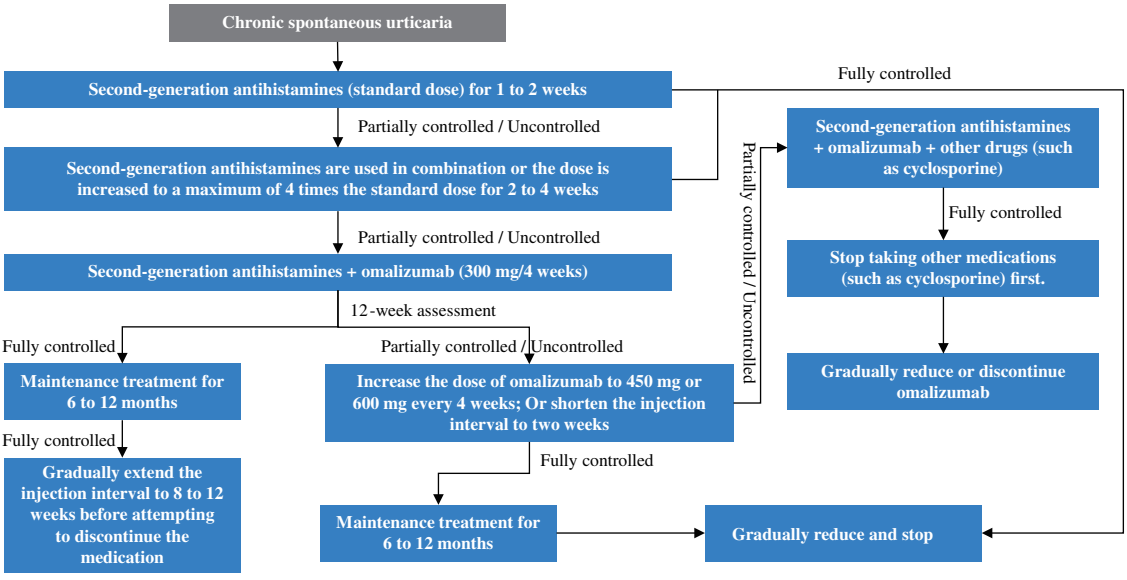
Chronic Spontaneous Urticaria

Urticaria is an allergic disorder mediated by a classic type I hypersensitivity reaction, characterized by intensely pruritic, transient wheals of variable size (1 mm to 10 cm) that appear and resolve within hours of cutaneous stimulation. While most episodes are acute which typically lasts from several days up to six weeks, some cases progress to chronic urticaria, defined by symptom persistence beyond six weeks. Chronic urticaria is divided into chronic spontaneous urticaria ("**CSU**") and chronic inducible urticaria ("**CIndU**"). CSU, the more common form, occurs in the absence of identifiable external triggers and is characterized by the spontaneous appearance of wheals, angioedema, or both for six weeks or longer. In contrast, CIndU encompasses physical triggers such as symptomatic dermographism, cold- or heat-induced urticaria, and non-physical triggers, including cholinergic urticaria, contact urticaria and aquagenic urticaria.

CSU is characterized by a persistent underlying patient population, but its epidemiological burden would not typically be expected to expand rapidly. As such, the projected growth in patient numbers is moderate and reflects gradual changes in the size of the affected population rather than any sudden increase in disease burden. Published guidelines and literature generally report that CSU has a prevalence of approximately 1.3% in China and approximately 0.7% globally. In China, the prevalence of CSU increased from 23.9 million cases in 2020 to 26.6 million cases in 2025 at a CAGR of 2.1%, and is projected to reach 29.6 million cases by 2030 and further reach 32.2 million cases by 2035, representing a CAGR of 2.2% from 2025 to 2030 and 1.7% from 2030 to 2035, respectively. The global prevalence of CSU increased from 60.6 million cases in 2020 to 69.9 million cases in 2025 at a CAGR of 2.9%, and is projected to reach 77.2 million cases by 2030 and further reach 84.8 million by 2035, representing a CAGR of 2.0% from 2025 to 2030 and 1.9% from 2030 to 2035, respectively.

First-line therapy for CSU in China consists of second-generation H1 antihistamines administered at standard doses for an initial treatment period, with the objective of achieving symptom control. In patients with partial or inadequate response, treatment escalation is recommended, including dose up-titration of second-generation antihistamines to up to four times the standard dose or the use of combination antihistamine therapy. For patients who remain symptomatic despite optimized antihistamine treatment, add-on therapy with omalizumab is introduced, with clinical response typically assessed after an appropriate treatment interval. In cases of insufficient response to standard-dose omalizumab, further dose escalation or shortened dosing intervals may be considered to enhance disease control. Once complete symptom control is achieved, maintenance therapy is generally continued for a defined period, followed by gradual tapering through extension of dosing intervals or dose reduction. Where additional immunosuppressive therapy is required, agents such as cyclosporine may be used as adjunctive treatment, with priority given to discontinuation of concomitant medications upon achieving disease control.

While the overall treatment paradigm is broadly aligned with international guidelines, the CSU treatment pathway in China, as referenced from Diagnosis and treatment of urticaria in China, differs in certain aspects, including greater flexibility in early treatment through combination antihistamine use, a standardized approach to biologic dose escalation prior to immunosuppressant initiation, and the allowance for combination therapy involving antihistamines, biologics and immunosuppressive agents in refractory cases. The diagram below illustrates the recommended treatment paradigm for CSU in China.



Note: The gradual tapering of second-generation antihistamines involves first reducing the dosage to half the standard dose daily or the standard dose every other day. If there is no recurrence of symptoms, after 3 to 4 weeks, the dosage can be further reduced to a quarter of the standard dose daily or half the standard dose every other day. If there is still no recurrence of symptoms, continue for another 3 to 4 weeks and reduce the dosage to a quarter of the standard dose twice a week. If there is still no recurrence of symptoms, the medication can be discontinued after 3 to 4 weeks. If symptoms recur during the tapering process, return to the previous dosage that completely controlled the symptoms.

Source: Diagnosis and treatment of urticaria in China (2022 ver.), Frost & Sullivan

As of the Latest Practicable Date, there is no JAK inhibitor or relevant generics approved for CSU globally. As of the same date, there are only two JAK inhibitors for CSU in clinical development globally (excluding China), and three in clinical development in China.

Global (excluding China) Clinical-stage JAK Inhibitors Indicated for CSU as of the Latest Practicable Date

Manufacturer	Phase	Genetic Name/Code	Target	First Posted Date	Indications
Incyte Corporation	II	Povorcitinib	JAK1	2023-07-07	CSU
Pfizer	II	Ritlecitinib	JAK3, TEC	2025-10-22	

JAK Inhibitors at Clinical Stage Indicated for CSU in China as of the Latest Practicable Date

Manufacturer	Phase	Genetic Name/Code	Target	First Posted Date	Indications
Highlightll Pharma	III	TLL-018	JAK1, TYK2	2024-03-19	CSU
InnoCare Pharma	II/III	ICP-332	JAK1, TYK2	2026-01-04	
Pfizer	II	Ritlecitinib	JAK3, TEC	2025-12-17	

Source: FDA, EMA, Clinical Trial, Frost & Sullivan

Atopic Dermatitis

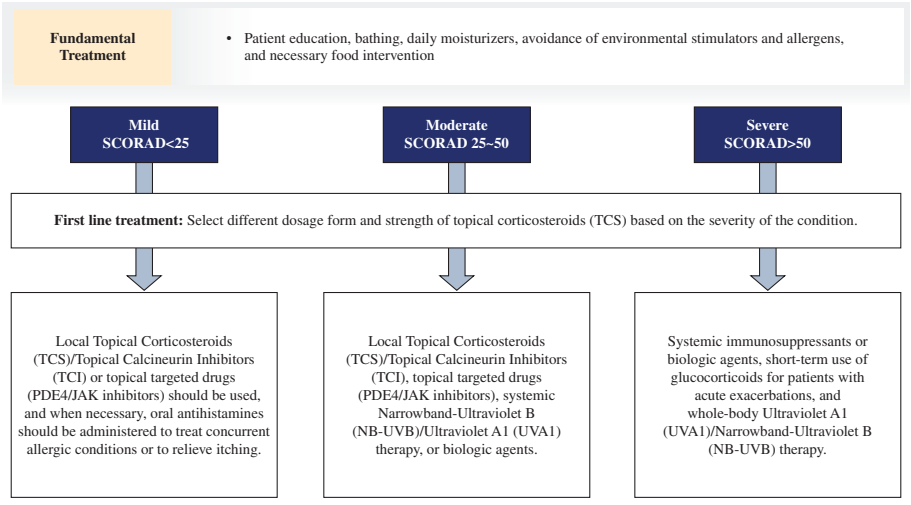
Atopic dermatitis ("**AD**") is a chronic, recurrent, immune-mediated dermatologic disorder defined by skin xerosis, severe pruritus, eczematous lesions and variable rash severity. Its multifactorial etiology involves genetic predisposition, environmental triggers, epidermal barrier impairment, a Th2-dominant adaptive immune response; and alterations in the cutaneous microbiome. Sustained inflammation and barrier dysfunction underlie the characteristic intense itching and recurring eczematous eruptions, which may present on a continuum from mild manifestations such as pityriasis alba or localized hand eczema to widespread erythroderma. Diagnostic criteria require the presence of pruritic lesions of typical morphology and distribution persisting beyond the acute phase.

Although AD is not life-threatening, it generates considerable physical, psychological and socioeconomic impact. Onset typically occurs in early childhood and frequently extends into adulthood. Patients with moderate to severe disease experience substantial skin morbidity, sleep disturbance, and elevated rates of anxiety and depression, all of which contribute to impaired quality of life, diminished self-esteem and reduced academic or occupational performance. These factors highlight the critical need for therapeutic interventions that deliver durable control of both immunologic activity and barrier restoration.

AD may arise across the lifespan and is not confined to a narrow age segment. This gives rise to a large and persistent patient base, while also meaning that prevalence growth is more likely to be gradual than driven by abrupt shifts in any single demographic cohort. Published guidelines and epidemiological studies indicate that AD has a substantial existing patient population, with a prevalence of approximately 4.6% in adults and 13% in children in China, and approximately 2.0% in adults and 4.0% in children globally. In China, the prevalence of AD increased from 67.4 million cases in 2020 to 74.1 million cases in 2025 at a CAGR of 1.9%, and is projected to reach 79.1 million cases by 2030 and further reach 81.2 million cases by 2035, representing a CAGR of 1.3% from 2025 to 2030 and 0.5% from 2030 to 2035, respectively. The global prevalence of AD increased from 659.0 million cases in 2020 to 711.4 million cases in 2025 at a CAGR of 1.5%, and is projected to reach 763.1 million cases by 2030 and further reach 814.4 million by 2035, representing a CAGR of 1.4% from 2025 to 2030 and 1.3% from 2030 to 2035, respectively. The moderate CAGR reflects the established epidemiological pattern of AD, rather than any assumption of accelerated disease expansion.

In China, management of atopic dermatitis is determined by disease severity as measured by the SCORAD index and begins with foundational measures such as patient education, trigger avoidance, regular bathing, liberal emollient use and, when appropriate, dietary adjustment. First-line pharmacotherapy emphasizes topical anti-inflammatory agents — including corticosteroids and calcineurin inhibitors — augmented by novel targeted options such as topical PDE4 and JAK inhibitors. Patients with moderate to severe disease may also receive phototherapy with narrowband UVB or UVA1 in addition to topical treatment. In refractory or high-burden cases, systemic immunosuppressants, biologic agents and short course systemic corticosteroids for acute flares are employed to achieve rapid inflammation control and restore epidermal barrier integrity.

The following sets forth the treatment diagram of AD as recommended by China's national guidelines:



Note: SCORAD = SCORing of Atopic Dermatitis

Source: Chinese guideline for diagnosis and treatment of atopic dermatitis (2020), Frost & Sullivan

In 2025, the AD indication market accounts for approximately 23% and 26% of global and Chinese JAK inhibitors market, respectively. As of the Latest Practicable Date, there are five JAK inhibitors approved for AD globally, including three available in China. As of the same date, there is one JAK inhibitor for AD in Phase III clinical development globally (excluding China), and seven in China.

Global Marketed JAK Inhibitors Indicated for AD as of the Latest Practicable Date

Manufacturer	Genetic Name	Target	Approved Indications	Market Authority	First Approval Date
OTCPK: TRXPF, Japan Tobacco, Akarx	Delgocitinib	JAK	AD	FDA, EMA	2025-07-23 (FDA) 2024-09-19 (EMA)
Pfizer	Abrocitinib	JAK1		FDA, EMA, NMPA	2022-01-14 (FDA) 2021-12-09 (EMA) 2022-04-08 (NMPA)
AbbVie	Upadacitinib	JAK1		FDA, EMA, NMPA	2019-08-16 (FDA) 2019-12-16 (EMA) 2022-02-18 (NMPA)
Incyte	Baricitinib	JAK1, JAK2		FDA, EMA	2018-05-31 (FDA) 2017-02-13 (EMA)
Hengrui	Ivarmacitinib	JAK1		NMPA	2025-03-18 (NMPA)

Global (excluding China) Clinical-stage JAK Inhibitors Indicated for AD as of the Latest Practicable Date

Manufacturer	Phase	Genetic Name/Code	Target	First Posted Date
Reistone Biopharma	III	Ivarmacitinib	JAK1	2021-05-06
Aclaris	II	ATI-2138	JAK3, ITK	2024-09-05
Tekoro	II	TDM-180935	JAK1, TYK2	2024-04-09
Aclaris	II	Lepzacitinib	JAK1, JAK3	2022-06-20
Pfizer	II	Brepocitinib	JAK1, TYK2	2019-04-02
Asana	II	Gusacitinib	SYK, JAK1, JAK2, JAK3, TYK2	2018-05-09
Novartis	I	CEE321	JAK	2020-10-27

JAK Inhibitors at Clinical Stage Indicated for AD in China as of the Latest Practicable Date

Manufacturer	Phase	Genetic Name/Code	Target	First Posted Date
Jiangsu Vcare Pharmatech	III	VC005	JAK1	2026-04-23
Longwood Biopharmaceuticals	III	LW402	JAK1	2026-01-27
Minghui Pharmaceutical	III	Tofacitinib etocomil	JAK	2025-04-02
E-nitiate Biopharmaceuticals	III	QY201	JAK1, TYK2	2025-02-07
Guangzhou InnoCare Pharma	III	Soficitinib	JAK1, TYK2	2024-08-26
Lynk Pharmaceuticals	III	LNK01001	JAK1	2024-01-03
Beijing Primegene Pharmaceutical	III	Pumecitinib	JAK1, JAK2	2023-02-27
China Medical System	II	CMS-D001	TYK2	2026-01-19
Jiangsu Carephar Pharmaceutical	II	H018	JAK1	2025-08-04
Chengdu Zeling Biomedical	II	ZL-82	JAK3	2025-04-30
Wuxi Fortune Pharmaceutical	II	WXFL10203614	JAK1	2024-08-14
Zhuhai United Laboratories	II	TUL01101	JAK1	2023-11-13
Guangzhou Jiayue Pharmaceutical	II	JYP0061	JAK1	2023-11-09
Medinno Pharmaceutical	II	MDI-1228	JAK	2023-09-27
Suzhou Zelgen Biopharmaceuticals	I/II	Gecacitinib cream	ALK2, JAK1, TYK2, JAK2, JAK3	2020-06-11
Highlightll Pharma	I	TLL-018	JAK1, TYK2	2023-07-07
E-nitiate Biopharmaceuticals	I	QY211	JAK1, TYK2	2023-02-15
Suzhou Longbotai Pharmaceutical	I	LBG-1600M	JAK1	2021-06-18

Source: FDA, EMA, Clinical Trial, Frost & Sullivan

Systemic Lupus Erythematosus

Systemic lupus erythematosus ("**SLE**") is an autoimmune disease associated with substantial morbidity and mortality. It is the most common type of lupus, causing widespread inflammation and tissue damage in the affected organs. Its precise cause remains unclear, but it is believed to result from a combination of genetic predisposition, hormonal influences and environmental triggers such as infections and ultraviolet light exposure. Globally, SLE represents a significant unmet medical need, with increasing disease awareness, improved diagnostic capabilities and ongoing investment in research driving demand for more effective and targeted therapies. Current treatment options — such as corticosteroids, immunosuppressants, antimalarials and biologics — are aimed at controlling symptoms and preventing flares, but there remains substantial opportunity for innovation to improve long-term outcomes and quality of life for patients.

In China, the prevalence of SLE presents an increasing trend with the prevalence increasing from 1.0 million cases in 2020 to 1.1 million cases in 2025 at a CAGR of 0.8%, and is projected to reach 1.1 million cases by 2030 and further reach 1.2 million cases by 2035, representing a CAGR of 1.1% from 2025 to 2030 and 1.0% from 2030 to 2035, respectively. The global prevalence

of SLE reached 8.2 million in 2025 with a CAGR of 1.1% from 2020 to 2025. It is expected to increase to 8.8 million in 2030 and 9.2 million in 2035, with a CAGR of 1.1% and 1.0% from 2025 to 2030 and 2030 to 2035, respectively.

As of the Latest Practicable Date, there were no JAK inhibitors approved for SLE globally. As of the same date, there are only two JAK inhibitors for SLE in Phase III clinical development globally (excluding China), and two in China.

Global (Excluding China) Clinical-stage JAK Inhibitors Indicated for SLE as of the Latest Practicable Date

Manufacturer	Phase	Genetic Name/Code	Target	First Posted Date	Indications
AbbVie	III	Upadacitinib	JAK1	2023-05-06	SLE
Bristol Myers Squibb	III	Deucravacitinib	TYK2	2022-11-17	
Alumis	II	Envudeucitinib	TYK2	2023-07-28	
Galapagos	II	GLPG3667	TYK2	2023-05-04	
Gilead	II	Filgotinib	JAK1	2017-09-18	

JAK Inhibitors at Clinical Stage Indicated for SLE in China as of the Latest Practicable Date

Manufacturer	Phase	Genetic Name/Code	Target	First Posted Date	Indications
AbbVie	III	Upadacitinib	JAK1	2024-01-19	SLE
Bristol Myers Squibb	III	Deucravacitinib	TYK2	2023-03-01	
CHIA TAI Tianqing	II	TQH3906	JAK1, TYK2	2026-04-10	
Inventisbio	II	Nomelcitinib	TYK2	2025-12-29	
Pfizer	II	Brepocitinib-PF-06700841	JAK1, TYK2	2020-03-19	
Hengrui	I	Ivarmacitinib	JAK1	2023-12-26	
Shiyao Group Ouyi Pharmaceutical	I	SYHX1901	JAK1, TYK2, JAK3, SYK	2021-05-13	

Source: FDA, EMA, Clinical Trial, Frost & Sullivan

Indications for Topical JAK Inhibitors

Topical Janus kinase (JAK) inhibitors represent an emerging class of targeted immunomodulatory therapies designed to locally inhibit the JAK-STAT signaling pathway, a key mediator of inflammatory and autoimmune processes in the skin. By selectively blocking intracellular signaling triggered by pro-inflammatory cytokines, topical JAK inhibitors reduce inflammation, alleviate pruritus, and, in certain conditions, promote repigmentation — while minimizing systemic exposure and associated safety risks.

Since 2021, regulatory approvals have expanded the clinical use of topical JAK inhibitors across multiple dermatologic indications:

- *Atopic dermatitis (AD).* Opzelura® (ruxolitinib cream) has been approved in the United States and other markets for the treatment of mild to moderate AD in adults and adolescents aged 12 years and older. Clinical studies have demonstrated rapid improvement in pruritus and lesion clearance, with a favorable safety profile due to minimal systemic absorption.

- *Non-segmental vitiligo.* Ruxolitinib cream is also approved for the treatment of non-segmental vitiligo, where it has been shown to facilitate repigmentation by modulating autoimmune destruction of melanocytes.

- *Chronic hand dermatitis.* Corectim® (delgocitinib ointment) has been approved in Japan for chronic hand dermatitis, including cases refractory to topical corticosteroids. Its efficacy in reducing erythema, scaling, and fissuring highlights the potential of JAK inhibition in persistent inflammatory dermatoses.

The expanding label indications for topical JAK inhibitors reflect their versatility in addressing immune-mediated skin diseases with high unmet medical need. Their targeted mechanism, rapid onset of action, and localized delivery position them as a differentiated therapeutic class within the dermatology market, with potential for further indication expansion in conditions such as alopecia areata, psoriasis, and other localized inflammatory disorders currently under clinical investigation.

As of the Latest Practicable Date, there are two approved topical JAK inhibitors for dermatological diseases globally, and no topical JAK inhibitors have been approved in mainland China. As of the same date, there are more than 20 topical JAK inhibitors for dermatological diseases globally in clinical development, including more than 15 in China.

Global Marketed Topical JAK Inhibitors as of the Latest Practicable Date

Target	Genetic Name	Manufacturer	Approved Indications	Market Authority	First Approval Date
JAK	Delgocitinib	Japan Tobacco, Torii Pharmaceutical, Akros Pharma	Atopic Dermatitis, Eczema	EMA	2024-09-19 (EMA)
JAK1, JAK2	Ruxolitinib Cream	Incyte Corporation, Tiofarma	Atopic Dermatitis, Nonsegmental Vitiligo	FDA, EMA	2021-09-21 (FDA) 2023-04-19 (EMA)

Source: FDA, EMA, Frost & Sullivan

Market Opportunities of JAK Inhibitors in Neurodegenerative Diseases

The absence of approved JAK inhibitors for neurodegenerative diseases (NDDs) stems from interconnected scientific and clinical challenges, with blood-brain barrier (BBB) penetration as the primary impediment, alongside selectivity, safety, and disease complexity.

- ***Structural limitations***. The BBB's tight endothelial junctions and efflux pumps (e.g., P-glycoprotein) exclude most of systemic drugs. Most JAK inhibitors (e.g., tofacitinib) are large (>400 Da) or polar, failing passive diffusion.

- ***Selectivity***. TYK2/JAK1 drive neuroinflammation, while JAK2/JAK3 inhibition causes anemia, thrombocytopenia, and infections. Non-selective JAK inhibitors (e.g., ruxolitinib) carry FDA black box warnings.

- ***Safety trade-offs***. Early candidates (e.g., pan-JAK inhibitors) showed efficacy *in vitro* but caused peripheral toxicity *in vivo*, halting CNS development.

- ***Complex neuroinflammation***. JAK-STAT pathways interact with NLRP3, α-synuclein, and Aβ, but their roles vary across NDDs (e.g., PD vs. AD). Single-target approaches often fail in clinical trials.

Alzheimer's disease

Alzheimer's disease is a progressive neurodegenerative disorder characterized by the cerebral accumulation of misfolded protein aggregates which precipitate neuronal loss, brain atrophy and consequent deficits in memory and executive function. Accounting for 60-70 percent of all dementia cases, AD follows an insidious course with gradual clinical deterioration over time. Its etiology is multifactorial, with advanced age as the most significant risk factor, alongside genetic predisposition, vascular comorbidities and lifestyle influences.

In China, the prevalence of Alzheimer's disease increased from 12.5 million cases in 2020 to 15.1 million cases in 2025 at a CAGR of 3.8%, and is projected to reach 18.0 million cases by 2030 and further reach 21.5 million cases by 2035, representing a CAGR of 3.7% from 2025 to 2030 and 3.6% from 2030 to 2035, respectively. The global prevalence of Alzheimer's disease increased from 36.3 million cases in 2020 to 39.0 million cases in 2025 at a CAGR of 1.5%, and is projected to reach 41.8 million cases by 2030 and further reach 44.6 million by 2035, representing a CAGR of 1.4% from 2025 to 2030 and 1.3% from 2030 to 2035, respectively.

Management of Alzheimer's disease requires early diagnosis, prompt initiation of therapy and lifelong, multidisciplinary care. Although current pharmacological agents can ameliorate symptoms and decelerate disease progression, none can reverse established pathology, creating a substantial unmet clinical need. In parallel, stage-appropriate supportive measures including speech and motor rehabilitation, dysphagia physical therapy, nutritional optimization and bowel training are integral to preserving patient function. Non-pharmacological strategies, emphasizing person-centered care, encompass environmental modifications, sensory stimulation, structured behavioral interventions and music therapy, all of which contribute to quality-of-life outcomes in Alzheimer's disease patients.

Cognitive enhancement agents remain the cornerstone of pharmacotherapy for Alzheimer's-related cognitive impairment. Cholinesterase inhibitors act by preventing the hydrolysis of acetylcholine at synaptic clefts, thereby augmenting cholinergic neurotransmission and improving attention and memory performance. Glutamate receptor antagonists mitigate excitotoxic neuronal injury by limiting excessive glutamatergic signaling, which can otherwise impair synaptic plasticity and cognitive function. Simultaneously, a substantial research effort is focused on disease-modifying treatments directed against the pathological hallmarks of Alzheimer's disease — namely β-amyloid (Aβ) aggregates and hyperphosphorylated tau. These novel approaches encompass passive and active immunotherapies designed to facilitate clearance of Aβ plaques, small molecules or biologics that inhibit tau aggregation, and emerging modalities such as antisense oligonucleotides and vaccine platforms, all aimed at intervening upstream in the neurodegenerative cascade.

As of the Latest Practicable Date, no JAK inhibitor have been approved for the treatment of Alzheimer's disease globally. Only one JAK inhibitor is in clinical development for this indication globally (excluding China), and TLL-041 is the only JAK inhibitor in clinical development for Alzheimer's disease in China.

Global (Excluding China) Clinical-stage JAK Inhibitors Indicated for Alzheimer's Disease as of the Latest Practicable Date

Manufacturer	Phase	Genetic Name/Code	Target	First Posted Date	Indications
Zhejiang Wenda PHARMA	I	WD-910	TYK2	2025-03-20	Alzheimer's Disease

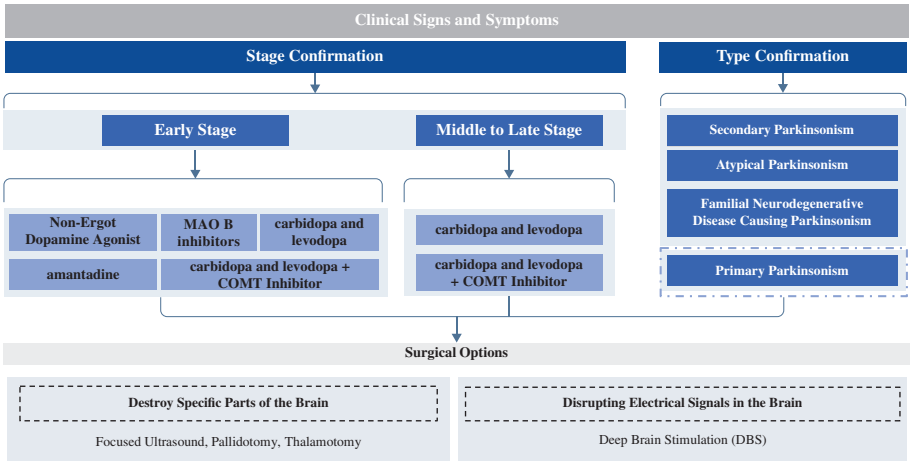
Source: FDA, EMA, Clinical Trial, Frost & Sullivan

Parkinson's Disease

Parkinson's disease is a progressive neurodegenerative disorder characterized by resting tremor, muscular rigidity and impairments in gait, balance and coordination. First published by Hoehn and Yahr in 1967, the Hoehn and Yahr scale was the inaugural system for staging disease progression in Parkinson's disease. Although no curative therapy exists, pharmacologic and supportive interventions can mitigate motor symptoms. Pathologically, Parkinson's disease is defined by the selective loss of dopaminergic neurons in the substantia nigra pars compacta, resulting in reduced striatal dopamine levels and consequent disruption of nigrostriatal signaling, which underlies the cardinal motor manifestations.

In China, the prevalence of Parkinson's disease increased from 2.8 million cases in 2020 to 3.5 million cases in 2025 at a CAGR of 4.8%, and is projected to reach 4.9 million cases by 2030 and further reach 7.4 million cases by 2035, representing a CAGR of 6.6% from 2025 to 2030 and 8.6% from 2030 to 2035, respectively. The global prevalence of Parkinson's disease increased from 8.7 million cases in 2020 to 10.3 million cases in 2025 at a CAGR of 3.3%, and is projected to reach 12.8 million cases by 2030 and further reach 15.9 million by 2035, representing a CAGR of 4.4% from 2025 to 2030 and 4.5% from 2030 to 2035, respectively.

Parkinson's disease is diagnosed through comprehensive assessment of medical history, clinical signs and symptoms, and detailed neurological and physical examinations. In the absence of a definitive laboratory or imaging test, diagnosis rests on the convergence of these evaluative components. Confirmation of disease stage and subtype constitutes an essential element of the diagnostic process. In early-stage PD, management may employ non-ergot dopamine agonists, MAO-B inhibitors or amantadine to ameliorate motor symptoms. As patients progress to mid and late stages, carbidopa/levodopa becomes the cornerstone of pharmacotherapy and may be combined with a COMT inhibitor to optimize dopaminergic function. Subtype determination distinguishes primary Parkinsonism from secondary, atypical or familial forms. For advanced disease refractory to medical management, neurosurgical interventions may be indicated. Lesioning procedures such as focused ultrasound, pallidotomy or thalamotomy target discrete brain regions to reduce symptom burden. Alternatively, DBS offers an adjustable and reversible approach to disrupt pathological circuitry and further improve motor control. The following sets forth the treatment diagram of Parkinson's disease.



Source: Guidelines for the Diagnosis and Treatment of Parkinson's Disease in China (4th Edition), Frost & Sullivan

As of the Latest Practicable Date, no JAK inhibitor have been approved for the treatment of Parkinson's disease globally, and TLL-041/BHV-8000 is the only JAK inhibitor in clinical development for Parkinson's disease globally.

Global Clinical-stage JAK Inhibitors Indicated for Parkinson's Disease as of the Latest Practicable Date

Manufacturer	Phase	Genetic Name/Code	Target	First Posted Date	Indications
Biohaven	II/III	TLL-041/BHV-8000	TYK2, JAK1	2025-05-16	Parkinson's Disease

Source: FDA, EMA, Clinical Trial, Frost & Sullivan

SOURCE OF INFORMATION

We commissioned Frost & Sullivan to conduct an analysis of and to prepare a report on the major markets for which our drug candidates are positioned. We agreed to pay Frost & Sullivan a total fee of approximately RMB0.55 million. Except as otherwise noted, all of the data and forecasts contained in this section are derived from the Frost & Sullivan Report. Frost & Sullivan is an independent global market research and consulting company which was founded in 1961 and is based in the United States. Services provided by Frost & Sullivan include market assessments, competitive benchmarking, and strategic and market planning for a variety of industries.

The Frost & Sullivan Report was compiled based on the following assumptions: (i) the overall social, economic and political environment globally and in China is expected to remain stable during the forecast period; (ii) the economic and industrial development globally and in China is likely to maintain a steady growth trend over the next decade; (iii) related key industry drivers are likely to continue driving the growth of the market during the forecast period; and (iv) there is no extreme force majeure or industry regulation in which the market may be affected dramatically or fundamentally.

In compiling and preparing the Frost & Sullivan Report, Frost & Sullivan used the following key methodologies to collect multiple sources, validate the data and information collected, and cross-check each respondent's information and views against those of others: (i) secondary research, which involved reviewing published sources including national statistics, annual reports of listed companies, industry reports and data based on Frost & Sullivan's own research database; and (ii) primary research, which involved in-depth interviews with the industry participants.

Frost & Sullivan's projections are made based on various market determinants and their coefficients assigned to a market which indicate their relative importance. The market determinants represent both subjective assumptions and objective factors, therefore, the projected data may not be consistent with the real data.

The Directors and Joint Sponsors have exercised reasonable care in selecting and identifying the named information sources, compiling, extracting and reproducing the information, and in ensuring that there is no material omission of the information.