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Rating	Buy
Price (05/19/2026)	$1.35
Price Target	↑ $9.00 ($8.00)

Market Data

% to Target	566.7%
52-Week High	2.60
52-Week Low	1.14
Market Cap (mil)	157.7
Cash & Equivalents	$12.0
Total Debt	$0.0
Enterprise Value	$145.7
Cash per Share	$0.10
Shares Outstanding (mil)	116.9
3-Month ADTV	147,983
Short Interest (% of Float)	1.9%
Short interest (mil)	1.4
Float	69.8
Fiscal Year-End	Dec

Estimates

FY	**2024A**	**2025A**	**2026E**
EPS Diluted	(0.11)	(0.16)	(0.16)
Prior	-	*(0.18)*	*(0.20)*
Revenue ($M)	0.0	0.0	0.0

Performance Chart

Tiziana Life Sciences Ltd (TLSA)

Foralumab Treatment Leads to Reduced Brain Inflammation and Functional Improvement - Increasing PT from $8 to $9

Tiziana Life Sciences (TLSA; Buy) reported long-term data from its multiple sclerosis expanded access program, indicating disease stabilization and reduction in fatigue, along with initial PET imaging data from a novel indication: Multiple System Atrophy (MSA). We are increasingly confident on the potential success of foralumab in multiple neuroinflammatory conditions. Therefore, we reiterate our Buy rating, but increase our 12-month price target from $8 to $9/share.

Updated Results from Foralumab for MS

Foralumab is a fully human anti-CD3 monoclonal antibody administered intranasally to induce regulatory T cells and modulate inflammatory immune responses through mucosal immune pathways. The reported updated clinical data from its Expanded Access (EA) program evaluating intranasal foralumab in 14 patients with non-active secondary progressive multiple sclerosis (na-SPMS). The updated dataset showed that intranasal foralumab remained well tolerated over extended treatment durations with no new safety signals identified. Investigators also observed encouraging trends toward stabilization of disability progression as well as clinically meaningful improvements in fatigue.

It was highlighted that the foralumab-treated cohort demonstrated a favorable trend toward reduced confirmed disability progression (CDP) relative to reference arms from the Phase 3 HERCULES trial evaluating tolebrutinib in non-relapsing SPMS. According to the analysis, the cumulative incidence graph showed only a single disability progression event in the foralumab EA cohort, suggesting potential stabilization in the majority of treated patients. The FDA recently rejected tolebrutinib, not based on lack of efficacy, but because of liver toxicity. With intranasal administration, it is very unlikely, that foralumab would lead to systemic adverse events.

Fatigue remains a major unmet need in progressive multiple sclerosis. Nine out of fourteen patients (64%) achieved a clinically meaningful improvement of at least four points on the Modified Fatigue Impact Scale, meeting established thresholds for clinically relevant benefit.

Clinical Development of Foralumab in MSA

MSA represents the third neurodegenerative indication in which treatment with foralumab has demonstrated a notable reduction in inflammatory PET imaging signals. The ongoing Phase 2a MSA study (NCT06868628) represents the first clinical efforts directly targeting adaptive immune dysfunction and neuroinflammation in MSA using an anti-CD3 immunotherapy approach. The open-label study enrolls patients with clinically established or probable MSA and incorporates both clinical and biomarker-based endpoints.

As reported last week, initial PET imaging data from the first two treated patients demonstrated substantial reductions in neuroinflammatory activity following intranasal foralumab. Quantitative PET analysis showed up to approximately 35% reduction in standardized uptake value (SUV) and approximately 24% reduction in standardized uptake value ratio (SUVR) within affected brain regions following treatment. Investigators noted that the magnitude of PET signal reduction appeared robust and comparable to anti-

inflammatory imaging changes previously observed in patients with multiple sclerosis treated with intranasal foralumab.

Foralumab: Non-invasive Immunomodulatory Therapy

Intranasal foralumab is an investigational formulation of foralumab, a fully human anti-CD3 monoclonal antibody, delivered via the intranasal route. It is being developed as a non-invasive immunomodulatory therapy for a range of conditions involving immune dysregulation, including MS, AD, ALS and MSA. Unlike traditional anti-CD3 therapies administered intravenously, intranasal delivery of foralumab is designed to modulate the immune system without inducing systemic immune suppression or cytokine release syndrome. The intranasal route targets the mucosal immune system, especially the nasal-associated lymphoid tissue (NALT), aiming to induce regulatory T cell (Treg) responses and dampen pro-inflammatory pathways.

Foralumab Mechanism of Action

Foralumab binds to the CD3ε subunit of the TCR complex on T lymphocytes. However, when administered via the nasal mucosa, the immune response is fundamentally different from systemic anti-CD3 antibodies (Figure 1).

Induction of Tregs. Intranasal foralumab promotes the generation and expansion of Tregs, which help suppress autoreactive effector T cells that drive inflammation in autoimmune diseases.

Immune Tolerization without T-cell Depletion. Unlike systemic CD3 antibodies, which result in T-cell activation, depletion, or redistribution, mucosal foralumab induces immune tolerance. It modulates T cell function rather than depleting T cells, preserving broader immune integrity.

Reduced Inflammatory Cytokine Signaling. Foralumab downregulates pro-inflammatory pathways, including interferon signaling, and reduces expression of genes linked to T cell activation (e.g. NKG7, CCL5), shifting the immune balance toward a regulatory phenotype.

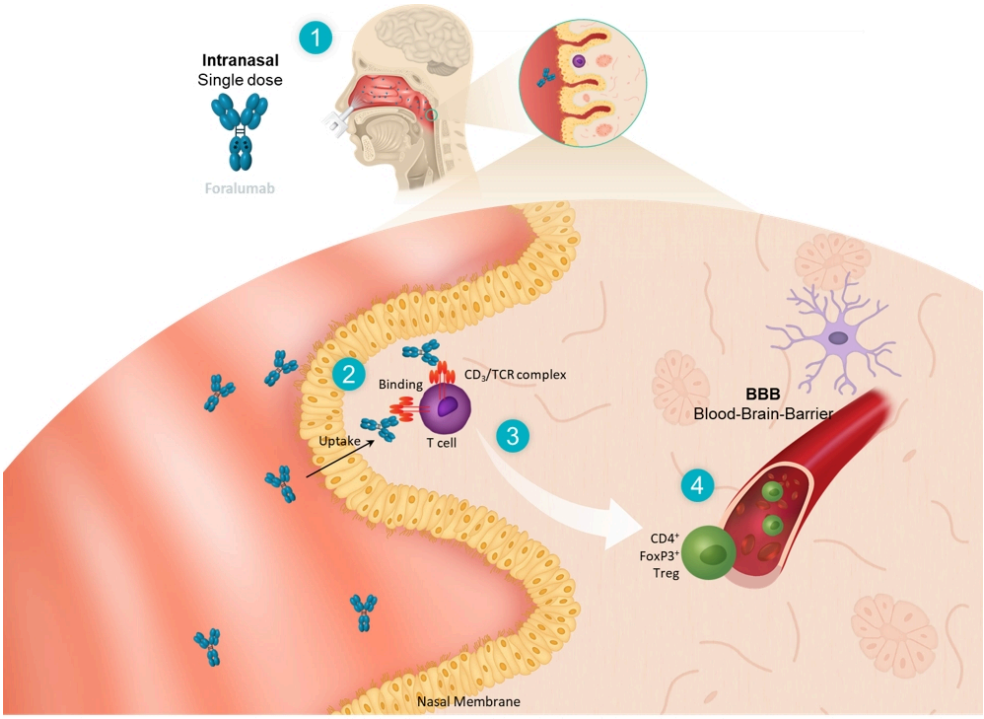
Non-invasive and patient friendly. Intranasal foralumab avoids the need for injections or infusions, making it more suitable for long-term or outpatient use, especially in chronic diseases like MS.

Targeting mucosal immune pathways. Foralumab stimulates mucosal-associated lymphoid tissue (MALT), particularly in the nasal cavity, a key site for immune tolerization and regulatory T cell induction.

Avoids Systemic Toxicity and CRS. Intranasal delivery of foralumab bypasses systemic circulation, significantly reducing the risk of cytokine release syndrome, which is a major concern with IV anti-CD3 therapies.

Potential CNS Effects via Nasal–Brain Pathway. There is emerging evidence that intranasal delivery may provide limited direct access to the CNS via the olfactory and trigeminal pathways, potentially modulating CNS inflammation locally in diseases like MSA.

Figure 1: Foralumab - Mechanism of Action



Source: Tiziana Life Science Corporate Presentation, June 2025

Safety and Delivery Challenges in Systemic Neuroimmune Modulation Highlight Opportunity for Intranasal Therapies

Limitation of Current Anti-CD3 Therapies for Treating MS

Current anti-CD3 therapies for treating MS face several important limitations, which have thus far restricted their clinical adoption and success compared to more established options like anti-CD20 agents .

Safety and Cytokine Release Syndrome (CRS). Anti-CD3 monoclonal antibodies (e.g., OKT3, teplizumab, otelixizumab) can trigger cytokine release syndrome, especially when given in higher doses. Anti-CD3 monoclonal antibodies (mAbs) can paradoxically induce CRS despite their long-term goal of immunosuppression. This occurs because CD3 is a central component of the TCR complex, and anti-CD3 mAbs—especially when first administered—can strongly activate T cells, leading to rapid release of proinflammatory cytokines such as IL-2, IFN-γ, and TNF-α. This "first-dose effect" results in systemic inflammation, presenting as fever, hypotension, and flu-like symptoms characteristic of CRS.

Broad Immunosuppression. CD3 is expressed on all mature T cells, not just the pathogenic autoreactive subsets. Thus, anti-CD3 therapy may non-selectively suppress the entire T cell population, risking opportunistic infections or reactivation of latent viruses (e.g., EBV, JC virus), particularly concerning in MS where patients may already be on other immunomodulatory agents.

BBB Permeability. Most conventional anti-CD3 monoclonal antibodies do not effectively cross the blood-brain barrier (BBB) under normal physiological conditions. Their limited BBB permeability remains a barrier for direct CNS effects for treating neurodegenerative diseases.

Systemic CNS Immunomodulation Faces Growing Safety Challenges, Supporting Interest in Non-Systemic Approaches

A key challenge in developing systemic immunomodulatory therapies for chronic neuroinflammatory diseases is balancing efficacy against long-term safety and tolerability. This issue has become increasingly relevant in progressive neurological disorders such as non-relapsing secondary progressive multiple sclerosis (nrSPMS), where durable suppression of chronic CNS inflammation often requires prolonged exposure to immune-targeting therapies. While systemic agents capable of penetrating the CNS may provide meaningful efficacy, they may also introduce significant off-target toxicities that complicate regulatory approval and long-term commercial adoption.

A recent example is tolebrutinib (Cenrifki), an oral, CNS-penetrant, irreversible Bruton's tyrosine kinase (BTK) inhibitor developed to target "smoldering" neuroinflammation within the brain and spinal cord. Unlike many conventional multiple sclerosis therapies that primarily act on peripheral immune cells, tolebrutinib was specifically designed to cross the blood-brain barrier and directly modulate inflammatory signaling within the CNS compartment. Clinical interest in the drug was driven by the hypothesis that compartmentalized microglial and B-cell-driven inflammation contributes to long-term disability progression in progressive MS.

The Phase 3 HERCULES trial demonstrated that tolebrutinib significantly delayed disability progression in patients with non-relapsing SPMS, providing important clinical validation for CNS-directed immunomodulation. In April 2026, the European Medicines Agency's Committee for Medicinal Products for Human Use (CHMP) adopted a positive opinion recommending approval of the drug, marketed as Cenrifki, for non-relapsing SPMS. However, despite the efficacy signal, the FDA issued a Complete Response Letter (CRL) in December 2025 declining approval, citing concerns regarding potentially severe drug-induced liver injury that regulators believed could not be sufficiently mitigated through the proposed monitoring strategies.

The divergence between the EMA and FDA decisions highlights the increasingly important risk-benefit debate surrounding systemic immunomodulatory therapies in chronic neurodegenerative disease. Although CNS penetration may improve efficacy against compartmentalized neuroinflammation, chronic systemic exposure can also increase the likelihood of hepatic toxicity, immune-related adverse events, and long-term safety liabilities. This challenge is particularly important in slowly progressive diseases where patients may require years of continuous treatment.

Against this backdrop, there is growing interest in alternative immunomodulatory approaches designed to modulate CNS inflammation while minimizing systemic immune exposure. Intranasal foralumab represents one such strategy. Rather than relying on continuous systemic BTK inhibition, foralumab is administered through the nasal mucosa to induce Tregs and promote immune tolerance via mucosal immune pathways. The approach is intended to modulate inflammatory signaling without inducing broad systemic immunosuppression or the cytokine release and organ toxicities historically associated with systemic immune therapies.

Importantly, the early clinical and PET imaging findings observed with intranasal foralumab in neuroinflammatory diseases including non-active SPMS and Multiple System Atrophy (MSA) may support the broader concept that localized or non-systemic immunomodulation could potentially achieve meaningful CNS anti-inflammatory activity while improving long-term tolerability. As the field increasingly recognizes chronic neuroinflammation as a driver of progressive neurodegeneration, the therapeutic landscape may gradually shift toward approaches capable of balancing CNS efficacy with safer long-term immune modulation.

New Positive Clinical Data for Foralumab in na-SPMS

Study Design

The study (NCT06802328) is an open-label, intermediate-size expanded access protocol evaluating intranasal foralumab in patients with na-SPMS who have failed currently available therapies. The program is designed to provide treatment access for patients with limited therapeutic options while also generating additional safety and translational data in progressive MS.

The study enrolls adults between 25 and 75 years old with non-active SPMS. Unlike a traditional randomized controlled trial, the protocol uses an expanded access design without placebo or blinding. Patients receive intranasal foralumab at a starting dose of 50µg per dosing day, with the possibility of escalation to 100µg depending on tolerability and investigator assessment.

Treatment is administered in repeating three-week cycles. Patients receive dosing on Days One, Three, and Five during the first two weeks, followed by one week off treatment. Initial administrations are supervised in clinic, while subsequent doses may be administered at home. The primary objective is to assess safety and tolerability, while secondary exploratory goals include evaluating immune-modulatory effects and potential impacts on neuroinflammation. Strategically, the expanded access program may serve both as a compassionate-use treatment pathway and as a real-world signal-generation platform supporting the broader development of intranasal foralumab in progressive neuroinflammatory diseases, including the company's randomized Phase 2a development program.

Updated Safety Results

Updated results from the ongoing expanded access program showed encouraging trends in safety, disability stabilization, and fatigue improvement in 14 treated patients. The updated dataset, covering follow-up through March 2026, suggested that intranasal foralumab remained well tolerated over extended treatment durations, with no new safety signals identified.

Figure 2 summarizes previously disclosed treatment-emergent adverse events (TEAEs) observed in 27 healthy volunteers[1] (nine per group) who received intranasal foralumab or placebo at doses of 10µg, 50µg, or 250µg daily for 5 days. Safety was assessed, and immune parameters were measured on Days 1 (pre-treatment), 7, 14, and 30.

Importantly, no liver-related adverse events or hepatotoxicity signals were reported across any dose cohort in the healthy volunteer study, including the highest 250µg dose. All reported treatment-emergent adverse events (TEAEs) were non-serious, with no serious adverse events observed in either the placebo or foralumab-treated groups. The adverse events were primarily limited to mild infections, nervous system disorders, skin disorders, and other low-grade events, with no evidence of clinically significant hepatic safety concerns.

This favorable safety profile may be strategically important in the current neuroimmunology landscape, particularly given the liver toxicity concerns associated with systemic CNS-penetrant immunomodulators such as tolebrutinib. While tolebrutinib demonstrated efficacy in slowing disability progression in non-relapsing SPMS, its regulatory review in the US was negatively impacted by cases of drug-induced liver injury. In contrast, intranasal foralumab's mucosal delivery approach may potentially reduce systemic exposure and avoid some of the hepatic liabilities commonly associated with orally administered systemic immunomodulatory therapies.

Updated Efficacy Results

The most notable finding was a favorable trend toward stabilization of disability progression, measured using the Expanded Disability Status Scale (EDSS). According to the analysis, the foralumab expanded access cohort experienced only a single confirmed disability progression event over the observed period (Figure 3A). The company compared the results against placebo and tolebrutinib reference arms from the Phase 3 HERCULES trial in non-relapsing SPMS. In the comparison graph, cumulative disability progression appeared substantially lower in the foralumab-treated patients relative to both comparator arms. The study defined a progression event using the same criteria applied in the HERCULES study: a sustained EDSS increase of at least 1.0 point for patients with baseline EDSS below 5.0, or at least 0.5 points for those with baseline EDSS of 5.0 or higher. The company emphasized that the foralumab curve showed only one progression event across the cohort, suggesting a potential signal of disease stabilization.

Fatigue outcomes were also encouraging (Figure 3B). Using the Modified Fatigue Impact Scale (MFIS), 9 of 14 patients (64%) achieved a clinically meaningful improvement of at least 4 points from baseline. Several patients demonstrated substantially larger reductions in fatigue burden, with some showing improvements exceeding 20–40 points based on the waterfall plot presented in the release. The ≥4-point threshold was based on previously established clinically meaningful change criteria from Rooney et al.

Importantly, the company acknowledged that the dataset remains exploratory and not statistically significant due to the small sample size and uncontrolled design of the expanded access program. The results were therefore presented as trend analyses rather than definitive efficacy conclusions. The data are supportive for intranasal foralumab's proposed mechanism as a non-systemic immunomodulatory therapy targeting neuroinflammation.

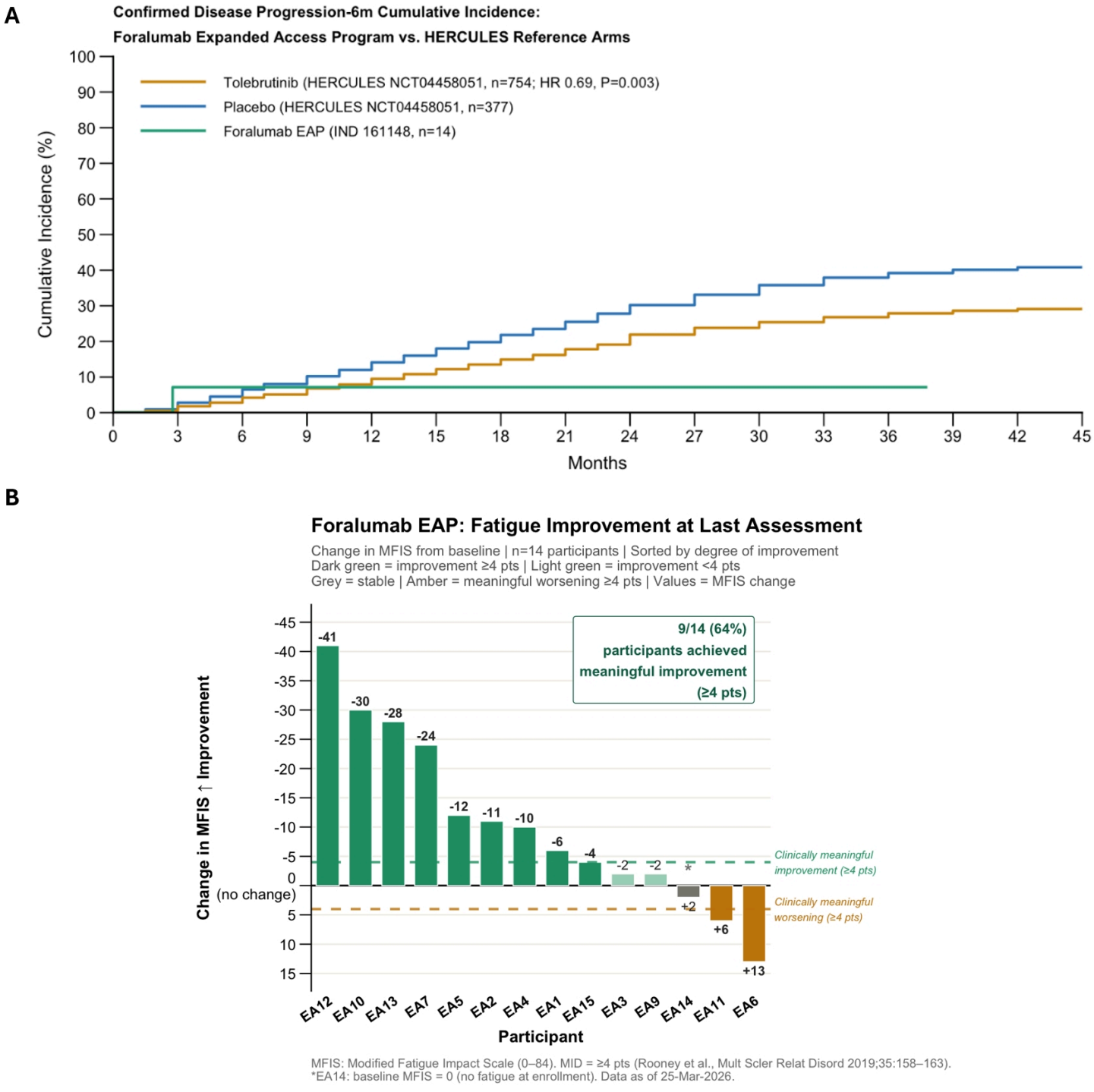
Figure 2: Published Safety Data for Intranasal Foralumab

System organ class	Placebo N=9	Foralumab (10ug) N=6	Foralumab (50ug) N=6	Foralumab (250ug) N=6	Foralumab-all doses N=18
Subjects with at least one TEAE	2	5	5	2	12
Number of TEAEs by severity	3	15	9	3	27
Severity					**27**
Non-serious	3	15	9	3	27
Serious	0	0	0	0	0
Ear and labyrinth disorders					**3**
Non-serious	0	2	1	0	3
Serious	0	0	0	0	0
Gastrointestinal disorders					**2**
Non-serious	0	0	2	0	2
Serious	0	0	0	0	0
Immune system disorder					**1**
Non-serious	0	0	1	0	1
Serious	0	0	0	0	0
Infections and infestations					**9**
Non-serious	0	8	0	1	9
Serious	0	0	0	0	0
Injury, poisoning and procedural complications					**1**
Non-serious	0	1	0	0	1
Serious	0	0	0	0	0
Nervous system disorders					**6**
Non-serious	0	3	2	1	6
Serious	0	0	0	0	0
Skin and subcutaneous tissue disorder					**5**
Non-serious	3	1	3	1	5
Serious	0	0	0	0	0

Bold values are $p<0.05$.

Source: Chitnis et al., 2025

Figure 3: New Positive Clinical Data for Intranasal Foralumab in na-SPMS



MFIS: Modified Fatigue Impact Scale (0–84). MID = ≥4 pts (Rooney et al., Mult Scler Relat Disord 2019;35:158–163).
*EA14: baseline MFIS = 0 (no fatigue at enrollment). Data as of 25-Mar-2026.

Source: Tiziana Corporate Press Release, May 2026

Foralumab Expands Into MSA With Early Proof-of-Concept Data

Multiple System Atrophy: Overview

Multiple system atrophy (MSA) is a progressive neurodegenerative disease that affects both the central nervous system (CNS), which controls movement, and the autonomic nervous system (ANS), which regulates involuntary functions such as blood pressure and digestion[2]. It is a rare disorder, affecting an estimated 15,000 to 50,000 people in the US across all racial groups. The condition results from the gradual loss and dysfunction of nerve cells in the brain and spinal cord. MSA is classified as an atypical parkinsonian disorder, as its early symptoms often resemble those of Parkinson's disease. These may include slowed movement, tremors, muscle stiffness, impaired coordination, a weak or quivering voice, dizziness or fainting, and bladder control issues. Symptoms typically appear in a person's 50s and worsen rapidly over five to ten years, eventually leading to severe mobility impairment and the need for full-time care.

Although some genetic variants have been linked to an increased risk of MSA, particularly those related to oxidative stress, inflammation, and genes associated with Parkinson's disease, a definitive genetic cause has not yet been identified. The genetic basis of MSA remains poorly understood, and there is currently no strong evidence linking environmental factors such as pollutants or chemicals to the disease. It is likely that a combination of genetic predisposition and environmental influences contributes to its onset and progression.

The underlying cause of MSA remains unclear, but it is linked to the abnormal accumulation of α-synuclein protein in oligodendrocytes, a type of glial cell in the brain. This leads to widespread neurodegeneration in areas responsible for movement and autonomic functions, including the basal ganglia, cerebellum, and brainstem. Unlike Parkinson's disease, MSA does not typically respond well to dopaminergic medications, which can make symptom management more challenging.

There is no cure for MSA, and treatment is focused on managing symptoms to improve quality of life. Medications, such as midodrine or fludrocortisone can help with orthostatic hypotension, while physical therapy and assistive devices can aid with mobility. Speech therapy is often necessary as the disease progresses to address communication difficulties and swallowing problems. Despite these interventions, MSA has a poor prognosis, with an average survival of six to ten years after symptom onset. Most patients eventually require full-time caregiving as they lose mobility and the ability to perform daily tasks independently.

Clinical Manifestation of MSA

Clinical Progression

MSA tends to progress more rapidly than Parkinson's disease, with most individuals requiring mobility aids like a cane or walker within a few years of symptom onset[3] (Figure 4A).

In the early stage (within the first two years after symptom onset), individuals may experience mild symptoms that are often mistaken for other neurological disorders. Early signs include movement difficulties such as muscle stiffness, tremors, and slowed motion, particularly in MSA Parkinsonian type (MSA-P). Those with MSA Cerebellar type (MSA-C) may develop balance and coordination issues, leading to frequent falls. Autonomic dysfunction can also emerge, causing symptoms including orthostatic hypotension, bladder control problems, and erectile dysfunction. Many individuals experience sleep disturbances, including REM sleep behavior disorder. Symptoms may respond slightly to medications such as dopamine therapy, but the response is typically poor compared to Parkinson's disease.

As the disease enters the middle stage (around two to five years after onset), symptoms become more severe and disabling. Movement difficulties worsen, often requiring the use of a cane or walker. Autonomic dysfunction progresses, leading to persistent low blood pressure, significant bladder incontinence, and gastrointestinal problems such as constipation or delayed stomach emptying. Speech and swallowing difficulties become more pronounced, increasing the risk of choking and malnutrition. Some individuals may experience cognitive and emotional changes, such as difficulty concentrating, depression, and anxiety. Most patients require assistance with daily activities, and falls become more frequent due to worsening motor impairment.

In the late stage (typically five to ten years after symptom onset), MSA leads to profound disability and complete dependence on caregivers. Most individuals become wheelchair-bound or bedridden as motor function declines. Speech and swallowing abilities deteriorate significantly, often necessitating a feeding tube to prevent choking and aspiration pneumonia. Autonomic dysfunction becomes more extreme, with severe blood pressure fluctuations that cause frequent fainting episodes. Many individuals develop breathing difficulties, which can contribute to respiratory failure.

In the end stage, complications from MSA become life-threatening. The average survival time from symptom onset is about six to ten years, though some patients may live longer with supportive care. The most common causes of death are respiratory complications, such as pneumonia and aspiration, or infections due to prolonged immobility.

Categories of MSA

MSA is classified into two main subtypes based on its predominant symptoms (Figure 4B). MSA-P (Parkinsonian type) presents with movement difficulties like Parkinson's disease, including muscle rigidity, bradykinesia (slowness of movement), and postural instability. MSA-C (Cerebellar type), on the other hand, is marked by cerebellar ataxia, which causes unsteady gait, poor coordination, and slurred speech. Regardless of the subtype, most patients eventually develop a combination of both motor and autonomic symptoms as the disease advances.

MSA-P exhibits a striatonigral pattern of degeneration (Figure 4C), while MSA-C is characterized by an olivopontocerebellar pattern (Figure 4D). Each pattern progresses through three severity grades, with increasing neuronal loss over time. In MSA-P, degeneration initially affects the substantia nigra, a stage known as minimal change MSA. As the disease advances, neurodegeneration spreads to the putamen, followed by the caudate nucleus and globus pallidus, leading to more severe motor impairment. In MSA-C, early pathology includes mild Purkinje cell loss and myelin pallor in the cerebellum, alongside degeneration in the substantia nigra. As the disease progresses, neuronal loss extends to the pons and inferior olives, eventually affecting the cerebellar vermis and cerebellar hemispheres. The overall severity of MSA symptoms is directly correlated with the extent of neuronal degeneration, with greater cell loss leading to more severe clinical impairment.

Neuroinflammation and Immune Dysregulation in MSA

MSA is increasingly understood not only as an α-synuclein aggregation disorder, but also as a neuroinflammatory disease characterized by substantial innate immune activation, oligodendrocyte dysfunction, and chronic glial-mediated neurodegeneration[4]. Historically, MSA pathology was defined primarily by the presence of α-synuclein-containing glial cytoplasmic inclusions (GCIs) within oligodendrocytes. However, accumulating evidence suggests that inflammatory signaling and immune dysregulation may actively contribute to disease progression rather than merely representing a secondary response to neuronal injury. Unlike Parkinson's disease, where α-synuclein pathology is largely neuronal, the prominent glial involvement in MSA creates a distinct inflammatory environment associated with myelin dysfunction, white matter injury, and rapid neurodegeneration.

A major proposed mechanism underlying inflammation in MSA involves activation of the innate immune system by misfolded α-synuclein aggregates. Pathological α-synuclein is believed to function as a danger-associated molecular pattern (DAMP), triggering microglial activation through receptors including Toll-like receptors (TLR2 and TLR4), CD36, and antigen presentation pathways[5]. Activated microglia subsequently release pro-inflammatory cytokines such as TNF-α, IL-1β, and IL-6, alongside reactive oxygen species and nitric oxide, thereby establishing a toxic inflammatory microenvironment. This process may create a self-amplifying cycle in which α-synuclein aggregation promotes inflammation, inflammatory signaling induces oxidative and cellular stress, and damaged cells release additional pathological α-synuclein that further propagates immune activation.

The inflammatory biology of MSA also shares certain mechanistic features with demyelinating disorders[6]. Activated microglia may impair oligodendrocyte precursor maturation and reduce remyelination capacity, thereby exacerbating myelin injury and neuronal vulnerability. Although MSA is not considered a classical autoimmune disease such as Multiple Sclerosis, increasing evidence suggests that adaptive immune responses may also contribute to disease progression. Studies have reported T-cell infiltration, altered peripheral cytokine profiles, and blood-brain barrier dysfunction in patients with MSA, raising the possibility that both central and systemic immune dysregulation participate in disease propagation.

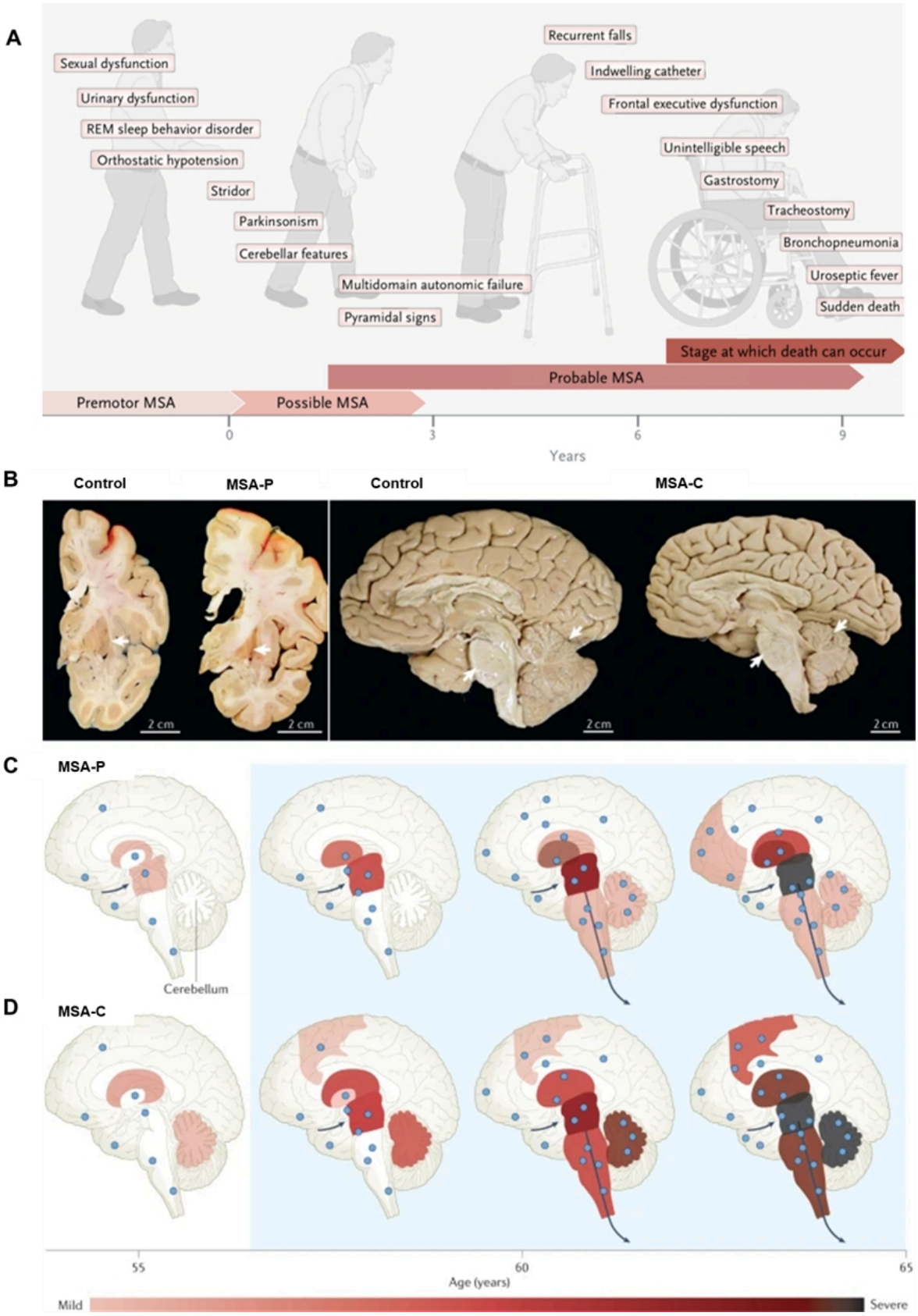
CD3+ T-Cell Involvement in MSA

CD3 is a core component of the T cell receptor (TCR) complex, playing a critical role in T cell activation and immune regulation. In autoimmune diseases, dysregulation of CD3-mediated signaling contributes to the breakdown of immune tolerance. Emerging evidence suggests that adaptive immune responses, particularly involving CD3+ T-cells, may contribute to the inflammatory pathology of MSA[7]. While MSA has traditionally been viewed primarily as an innate immune-driven synucleinopathy characterized by microglial activation and oligodendrocyte dysfunction, several recent studies have identified significant infiltration of CD3+ T-cells within affected brain regions. Postmortem analyses and preclinical MSA models have demonstrated increased CD3+ T-cell accumulation in areas with prominent α-synuclein pathology, including both perivascular and parenchymal regions of the central nervous system. These findings suggest that peripheral adaptive immune cells may actively participate in disease progression rather than representing a secondary bystander response.

In addition to CNS infiltration, peripheral immune profiling studies have identified alterations in circulating T-cell populations in patients with MSA[8]. Elevated CD3+ T-cell levels and altered CD4+/CD8+ ratios have been reported relative to healthy controls, supporting the concept of broader systemic immune dysregulation in the disease. These findings further strengthen the hypothesis that MSA involves both central and peripheral immune activation rather than a purely localized neurodegenerative process.

Overall, although innate immune activation remains the dominant inflammatory framework in MSA, increasing evidence supports a meaningful role for CD3+ T-cells and adaptive immunity in disease pathogenesis.

Figure 4: Stages and Categories of MSA



Source: Poewe et al., 2022

Clinical Development of Foralumab in MSA

Study Design

The ongoing Phase 2a study (NCT06868628) represents one of the first clinical efforts to directly target adaptive immune dysfunction and neuroinflammation in MSA using an anti-CD3 immunotherapy approach. The study is an open-label Phase 2a trial enrolling patients aged 30 to 85 years with clinically established or clinically probable MSA according to the 2022 Movement Disorder Society diagnostic criteria. The protocol includes a six-month observational lead-in period followed by a six-month treatment phase using intranasal foralumab. Patients receive eight dosing cycles, with nasal administration three times weekly during the first two weeks of each three-week cycle.

A particularly notable aspect of the study is its focus on neuroinflammation biomarkers rather than solely symptomatic outcomes. Primary endpoints include changes in microglial activation measured using TSPO PET imaging with [18F]PBR06, alongside changes in MDS-UMSARS clinical scores. Secondary endpoints include volumetric MRI assessments of brain atrophy, autonomic function measures, quality-of-life assessments, and immune biomarker analysis in blood and cerebrospinal fluid. This design reflects the growing view that microglial activation and immune dysregulation may be central drivers of MSA progression rather than secondary phenomena. The study is being conducted in collaboration with the Mass General Brigham MyTrial-MSA and Harvard Biomarkers programs, with leadership from Vikram Khurana at Brigham and Women's Hospital.

Reduced Brain Inflammation in MSA Patients Treated with Intranasal Foralumab

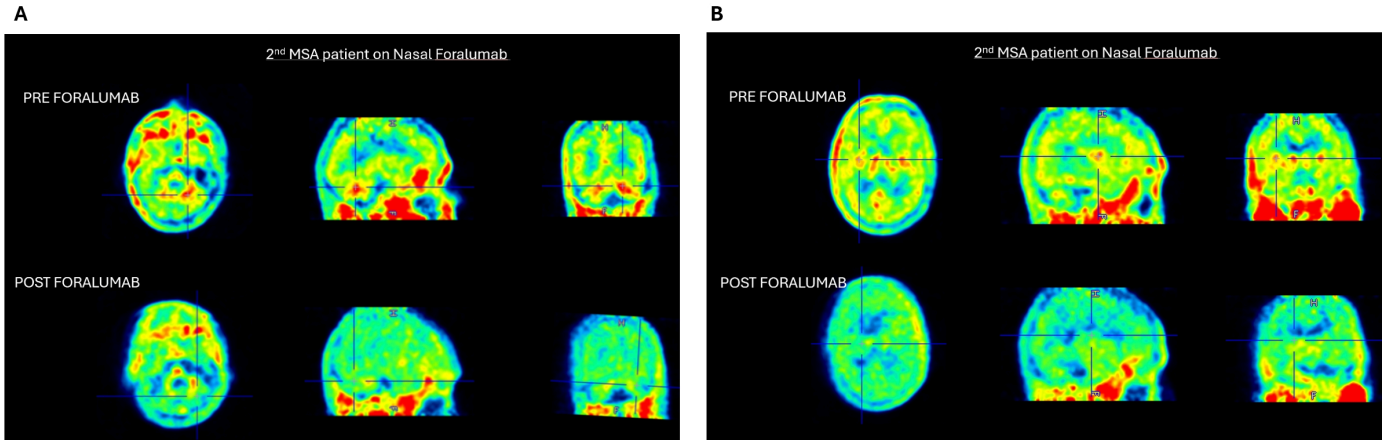
Quantitative PET imaging analysis demonstrated substantial reductions in neuroinflammatory activity in clinically relevant brain regions affected by MSA following treatment with intranasal foralumab. In the first two treated patients enrolled in the Phase 2 MSA study, investigators observed up to approximately 35% reduction in standardized uptake value (SUV) and approximately 24% reduction in standardized uptake value ratio (SUVR) within affected brain regions following treatment. These imaging findings provide early quantitative evidence suggesting that intranasal foralumab may reduce microglial activation and inflammatory signaling in MSA-associated neurodegenerative regions.

The reductions in PET tracer uptake were observed in anatomically and clinically relevant regions known to be heavily involved in MSA pathology, including the cerebellar white matter, basal ganglia, and thalamus. Figure 5A demonstrated a marked reduction in cerebellar white matter uptake following nasal foralumab administration, while Figure 5B showed significant reductions in uptake within the basal ganglia and thalamic regions. These regions are critically involved in the motor, autonomic, and cerebellar dysfunction characteristic of MSA, and are known to exhibit substantial neuroinflammatory and neurodegenerative changes during disease progression.

According to the investigators, the imaging analysis specifically focused on the most severely affected and clinically relevant brain regions in MSA. The observed reductions appeared quantitatively robust and were comparable to anti-inflammatory PET imaging changes previously observed in patients with multiple sclerosis treated with intranasal foralumab. The PET imaging comparisons performed before and after treatment demonstrated consistent reductions in radiotracer uptake across multiple disease-relevant regions, supporting the biological activity of intranasal foralumab in modulating neuroinflammation in MSA patients.

The reductions in PET signal are believed to reflect suppression of inflammatory immune activity, potentially involving modulation of CD3+ T-cell signaling, microglial activation, and downstream cytokine-mediated neurotoxicity within affected MSA brain regions.

Figure 5: Reduction in Cerebellar White Matter, Basal Ganglia and Thalamic Uptake Following Nasal Foralumab



Source: Tiziana Life Science Corporate Presentation, June 2025

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Income Statements

Tiziana Life Sciences											Elemer Piros, Ph.D. 646-350-1528 epiros@lucidcm.com
			2024A			2025A			2026E		
($ In thousands, except per share data)	**2022A**	**2023A**	**1HA**	**2HA**	**2024A**	**1HA**	**2HA**	**2025A**	**1HE**	**2HE**	**2026E**
Operating Expenses											
Research and development	**($12,955)**	**($8,113)**	($2,575)	($2,654)	**($5,229)**	($2,600)	($7,679)	**($10,279)**	($7,679)	($7,679)	**($15,358)**
Operating expenses	**($1,631)**	**($9,871)**	($3,931)	($6,634)	**($10,565)**	($6,000)	($4,853)	**($10,853)**	($4,853)	($4,853)	**($9,706)**
Loss from operations	**($14,586)**	**($17,984)**	($6,506)	($9,288)	**($15,794)**	($8,600)	($12,532)	**($21,132)**	($12,532)	($12,532)	**($25,064)**
Finance Income	($7)	$1,144	$112	$702	**$814**	$407	($406)	**$1**	($406)	($406)	**($812)**
FV Loss on Investment	($869)	($402)	($1,585)	($181)	**($1,766)**	-	$2,333	**$2,333**	2,333.00	2,333.00	4,666.00
Other Income	$65	-	-	-	-	-	$367	**$367**	367.00	367.00	734.00
Total Other Income	**($811)**	**$742**	($1,473)	$521	**($952)**	$407	$2,294	**$2,701**	$2,294	$2,294	**$4,588**
Income Tax / Credit	**-**	**($449)**	$3,326	$1,557	**$4,883**	-	($88)	**($88)**	-	-	-
Net (loss) income	**($15,397)**	**($17,691)**	($4,653)	($7,210)	**($11,863)**	($8,193)	($10,326)	**($18,519)**	($10,238)	($10,238)	**($20,476)**
Weighted average number of shares outstanding	**101,526**	**102,471**	103,098	106,672	**106,672**	113,135	116,529	**116,529**	127,259	131,077	**131,077**
Net loss attributable to common stockholders per share	**($0.15)**	**($0.17)**	($0.05)	($0.07)	**($0.11)**	($0.07)	($0.09)	**($0.16)**	($0.08)	($0.08)	($0.16)

Source: Tiziana Life Sciences SEC filings, Lucid Capital Markets estimates

Risks for: Tiziana Life Sciences Ltd (TLSA)

Tiziana Life Sciences is a development-stage company, and investment is subject to risk.

Clinical Trial Risk

The company is progressing on multiple clinical studies for intranasal foralumab. Early data are encouraging and warrant further clinical development. Intranasal foralumab was found to be safe and effective, without any serious adverse events. However, in the ongoing clinical trials, intranasal foralumab may not be deemed safe and effective. So far, interim safety analyses of all clinical trials conducted have not identified any significant safety concerns.

Regulatory Risk

The FDA and European regulators may require additional clinical trials for Intranasal foralumab beyond the ones Tiziana currently anticipates.

Competition Risk

Intranasal foralumab is facing competition from existing approved drugs and other drug candidates for treating MS, AD and ALS.

Financing Risk

The cash position was around $12M (January 2026). We estimate the company to burn approximately $21M over the next 12 months. The company needs to raise additional equity capital to support its clinical development, unless licensing deals are forged for its development-stage assets. Financing may not be available under favorable terms, or at all.

Valuation for: Tiziana Life Sciences Ltd (TLSA)

We arrive at our 12-month price target of $9 per share by assessing the after-tax, risk-adjusted NPV of potential future cash flows from foralumab in non-active SPMS. The probability-adjusted (45%), fully taxed (21%) NPV at a 15% discount rate of potential cash flows until 2043 is approximately $1.2B, equivalent to $9 per share, corresponding to our 12-month price target. Potential factors that could prevent shares from reaching our price target include the failure of foralumab to demonstrate significant efficacy benefits or being deemed unsafe, leading to the discontinuation of clinical programs and commercial launch. In addition, the company may not be able to raise additional funds to complete development.

Company Description for: Tiziana Life Sciences Ltd (TLSA)

Tiziana Life Sciences is a clinical-stage biopharmaceutical company developing breakthrough therapies using transformational drug delivery technologies to enable alternative routes of immunotherapy. Tiziana's innovative nasal approach has the potential to provide an improvement in efficacy as well as safety and tolerability compared to intravenous (IV) delivery. Tiziana's lead candidate, intranasal foralumab, which is the only fully human anti-CD3 mAb currently in clinical development, has demonstrated a favorable safety profile and clinical response in patients in studies to date. Tiziana's technology for alternative routes of immunotherapy has been patented with several applications pending and is expected to allow for broad pipeline applications.

Appendix

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Buy: We generally expect "Buy" rated stocks to have an above-average risk-adjusted total return over the next 12 months. We recommend that investors buy the securities at the current valuation.

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Sell: 0.8%	Sell: 0.0%
Not Rated: 3.8%	Not Rated: 0.0%

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Tiziana Life Sciences Ltd Rating History as of 05/18/2026