DNA Finance

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AB Science (EURONEXT: AB)

Introduction

In early February 2025, AB Science provided a long-awaited update on its masitinib platform, a cornerstone of the company's value given its late-stage clinical programs. To fully grasp the analysis presented in this note, we recommend referring to our primary research report of March 2024, updated in June 2024, which offers a detailed analysis of the platform and its financial valuation.

Executive Summary

STOCK SUMMARY
13.03.2025
Source: Boursorama

Share price
€1.36

52-weeks Price Range
€0.77– 2.68

Market cap.
€79M

Enterprise value
€98M

AB Science's current value is primarily driven by its advanced masitinib platform, which targets six indications, including three Phase III programs addressing high-value neurodegenerative markets: amyotrophic lateral sclerosis (ALS), multiple sclerosis (MS), and Alzheimer's disease (AD).

The Phase III ALS trial, launched in 2023, was recently halted due to recruitment challenges related to design features requested by health agencies. However, AB Science has announced that a new Phase III with a revised design has been approved by the FDA and the EMA. We believe the company is now well-positioned to resume development in this indication through partnership. Indeed, masitinib benefits from a strong preclinical and clinical data package, long-term efficacy follow-up results, and recent external publications reinforcing its mechanism of action (MoA). Coupled with robust intellectual property protection and with a revised and validated Phase III regulatory plan, the program is now in its strongest position to attract potential partners in an indication with blockbuster potential.

Furthermore, we do not rule out the possibility of a partnership on the company's second platform, AB8939, given the growing demand of pharmaceutical companies for early-stage oncology deals.

From an investment perspective, with a 10-month horizon through December 2025, the company's financial visibility appears secure, with cash runway extending through year-end 2025 and no major catalysts expected to negatively impact the newsflow. In case a deal occurs, depending on its terms, we estimate a minimum twofold increase in the share price. However, if no deal is secured during this period, we see little downside and the stock is likely to remain stable, justifying a reassessment of the investment at the end of the year.

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A late-stage pipeline set to advance into confirmatory Phase III trials for ALS, MS and AD

The company's most advanced programs target neurodegenerative diseases, with promising Phase IIb/III results already achieved in ALS, MS and AD. The designs of the Phase III confirmatory trials have been validated by regulatory agencies, positioning the company for the next stage of development in these three indications. To advance these trials, management is actively seeking financing through partnership. We believe recent developments have strengthened the data package, reducing risk for potential partners, a point we explore in further detail in the following analysis.

TABLE 1

AB Science's pipeline based on its masitinib late-stage platform and microtubule destabilizer agent earlier-stage platform

Compound	Drug	Therap. Area	Indication	Preclinical	Phase I	Phase II	Phase IIb/III	Confirm. Phase III
Tyrosine Kinase Inhibitor	**Masitinib (oral)**	Neurodegenerative Diseases	Amyotrophic Lateral Sclerosis					
			Progressive forms of Multilpie Sclerosis					
			Mild-to-moderate Alzheimer's Disease					
		Inflammatory Diseases	Indolent Systemic Mastocytosis					
			Mast Cell Activation Syndrome					
		Oncology	Metastatic Prostate Cancer					
Microtubule Destabilizer Agent	**AB8939 (IV)**	Hematology	Acute Myeloid Leukemia					
	AB12319 (oral)	Oncology	Sarcoma, Solid Tumors					

New elements supporting the rationale behind Masitinib's MoA, a product with reinforced efficacy data and a strong safety profile

Recent publications in leading scientific journals reinforce the therapeutic rationale behind masitinib's mechanism of action in targeting neuroinflammation. A study published in Nature (April 2024) highlights the central role of innate immune dysfunction in neurodegeneration, underscoring its significance as a key therapeutic target. Additionally, research in Frontiers in Molecular Neuroscience (April 2024) explores the critical role of neuroinflammation and the interaction between the central and peripheral immune systems in disease progression.

Regarding safety, the EMA has validated masitinib's favourable safety profile based on Phase IIb/III data in ALS. This significantly reduces potential safety concerns for future confirmatory Phase III trials and mitigates risks for any partner.

Masitinib in ALS: new confirmatory study set to launch, overcoming previous recruitment challenges

Masitinib's positioning in the ALS treatment landscape

ALS is a rare neurodegenerative disease that affects motor neurons, leading to progressive muscle control loss, with most patients surviving only three to five years post-diagnosis. Approximately 150,000 individuals are currently affected in the US and Europe.

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We maintain our conviction in AB Science's ALS program, as masitinib has demonstrated promising Phase IIb/III efficacy results in the population of 'Normal Progressors', along with a significant survival benefit in a subgroup of patients before complete loss of function, while bringing favorable safety data.

Our estimated peak annual sales of $2 billion and risk-adjusted valuation of $700 million remain unchanged since our last analysis, as the landscape of approved drugs has not evolved since March 2024. Treatment options remain limited, with only marginal efficacy in slowing disease progression.

TABLE 2

Masitinib efficacy clinical results regarding marketed drug efficacies in ALS

Drug	Sponsor	Approbation	Efficacy
Riluzole	Generic	FDA (1995), EMA (1997)	• No data on ΔALSFRS-R • 2-3 months of survival benefit
Edaravone	Mitsubishi Tanabe	FDA (2017), not approved by EMA	• ΔALSFRS-R= +2.5 (week 24) • 6 months of survival benefit
Tofersen	Biogen	FDA (2023), EMA (2024)	• Target only 2% of ALS patients • No significative results on ΔALSFRS-R • Demonstrated results on NfL biomarkers
Mastinib	AB Science	Not approved	• ΔALSFRS-R = +3.3 (week 48) • 12 months of survival benefit on the Phase IIb/III subpopulation corresponding to the Phase III target

Despite extensive research in ALS, no recent trials have yielded positive results, and, since our last update, several notable failures have occurred. Memantine and trazodone failed in Phase III to demonstrate efficacy. Additionally, after an initial failure with its drug developed in partnership with Sanofi, Denali experienced another failure with its second Phase II/III program in January 2025. On the same day, Calico Life Sciences, partnered with AbbVie, also failed. While these setbacks highlight the challenges in this field, they also underscore the opportunity for a new therapeutic approach like masitinib. By targeting neuroinflammation, an aspect largely overlooked by most ALS treatments, masitinib may provide a new avenue in the fight against this disease.

Importantly, follow-up data from the Phase IIb/III study revealed promising long-term survival benefits. In a compassionate use follow-up, 43% of patients treated with masitinib (55 out of 128) survived for at least five years.

Status update on the confirmatory ALS Phase III

As a reminder, AB Science's Phase IIb/III study demonstrated statistically significant results, particularly in a 'Normal Progressors' subgroup of patients without complete loss of function, who showed the most favourable response. This subgroup, representing 86% of the trial population, experienced a +3.3 improvement in ALSFRS-R and a survival benefit of 12 months.

Based on these results, AB Science submitted a Conditional Marketing Authorization request to the EMA. However, regulatory authorities raised concerns, inducing that while the data was promising, they required confirmation through a new Phase III study.

The initial confirmatory study, launched in 2023, faced significant recruitment challenges. Indeed, by excluding 'Fast Progressors' and focusing on 'Normal Progressors,' the study required patients to undergo a three-month 'run-in' period without standard of care. As patients were reluctant to discontinue their current therapies, recruitment was slow, freezing the clinical trial.

To address these challenges, AB Science, in collaboration with the EMA and FDA, agreed to end the first confirmatory trial and start a new one with a revised design that suppresses this three-month run-in period.

On January 31, 2025, AB Science announced that the new Phase III design had been approved by the two regulatory agencies. The study will be conducted on a larger cohort of 400 patients, over two years, with 12 months allocated for enrolment and another 12 months for data collection. The study design has been revised to address the major claims raised by the EMA regarding Phase IIb/III, with a specific focus on the patient population most likely to respond to the treatment. It integrates statistical methods that align with the requirements of both the EMA and the FDA. This revised approach is expected to generate robust results that are more likely to meet regulatory agencies standards.

If the confirmatory Phase III study replicates the Phase IIb/III results and meets statistically both primary and secondary endpoints with the same robust safety profile as demonstrated before, we anticipate a smooth pathway to the registration of masitinib for ALS treatment.

Potential for partnership in ALS

AB Science is now poised to launch its study, pending the securing of a partnership. The revised study design offers potential partners a lower-risk opportunity by focusing on the 'Normal Progressors' population before complete loss of function, who are most likely to benefit from the treatment. This design also aligns with the regulatory expectations of both the EMA and the FDA, paving the way for registration. Given the significant unmet treatment needs in ALS and the lack of effective competition, partnering on this confirmatory Phase III study is an attractive opportunity for pharmaceutical companies.

A deal in ALS announced in December 2024 between the biotech Dewpoint and the pharmaceutical company Mitsubishi Tanabe, valued at $480 million for a preclinical small molecule, underscores the potential value of partnership deals in this market.

Masitinib in Multiple Sclerosis (MS): a differentiated approach with a strong rationale poised for confirmatory Phase III upon partnership

Masitinib's positioning in the MS treatment landscape

Based on its Phase IIb/III study in MS, AB Science focuses on the progressive forms of MS, specifically Primary Progressive MS (PPMS), which affects 150,000 patients, and non-active Secondary Progressive MS (SPMS), affecting 350,000 patients, in Europe and the US. The competitive landscape for these forms is limited, with ocrelizumab (Ocrevus) being the only approved treatment for PPMS, and no treatment available for non-active SPMS. Together, we estimate the value of these two markets at $1.8 billion.

While Ocrevus is effective in reducing inflammation by targeting B cells, it primarily modulates the immune system without addressing the underlying neurodegeneration. In contrast, masitinib acts on the innate immune system, specifically targeting microglial cells and macrophages, which play a key role in neuroinflammation and neurodegeneration, offering a complementary approach to Ocrevus.

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Rationale to target MS with masitinib

Masitinib targets the innate immune system, a mechanism backed by scientific literature, AB Science's preclinical data from an induced mouse MS model, and studies on disease biomarkers. The recent success, in December 2024, of tolebrutinib, a BTK inhibitor targeting microglia in secondary progressive MS, further supports the potential of targeting microglia to address MS-related neurodegeneration. While direct head-to-head comparisons are not possible, the growing clinical evidence for microglia-targeting strategies strengthens the rationale behind AB Science's approach in this indication.

Future development plan in MS

AB Science's Phase IIb/III trial in PPMS and non-active SPMS has demonstrated strong potential, with positive results for the primary endpoint of "overall EDSS change". The trial showed a 37% and 42% risk reduction in the secondary endpoints "time to disease progression" and "time to confirmed (at 12 weeks) disease progression" respectively, surpassing the efficacy of current treatments.

A confirmatory study, which has already received regulatory approval by FDA and EMA, is set to proceed with 800 patients to confirm the efficacy of masitinib, with "time to confirmed disease progression" as the study's primary endpoint. To advance, AB Science will require a partnership to support further development; the recent approval of tolebrutinib could be a reassuring factor for a potential partner, as it validates the relevance of targeting microglia in the treatment of neurodegeneration associated with MS.

Masitinib in Alzheimer's disease: a potential combination therapy for early-stage Alzheimer's with a possibility for standalone treatment

A complementary mechanism of action to drugs currently approved in treating Alzheimer's

Alzheimer's pathophysiology is driven by three primary mechanisms: (i) β-amyloid plaques, (ii) tau protein aggregates, and (iii) neuroinflammation. While therapies like Lecanemab (Eisai/Biogen) and Donanemab (Eli Lilly) focus on β-amyloid, masitinib targets neuroinflammation by modulating microglia and mast cells. It may also offer synaptic protection, which is critical given the connection between synaptic loss and cognitive decline and could indirectly impact tau aggregation.

Phase IIb/III results and future development plan

Phase IIb/III results for masitinib showed significant improvements in cognitive scores for mild-to-moderate Alzheimer's patients, along with a positive trend in daily functional scores. The FDA requires both cognitive and functional outcomes to be significantly achieved in early Alzheimer's trials, as these measures reflect the disease's full clinical impact. To maximize AB Science's chances of regulatory approval, the confirmatory Phase III trial will have to demonstrate significant improvements in both scores.

If the confirmatory Phase III meets these endpoints, masitinib, with its distinct MoA, could emerge as a promising option for combination or adjuvant therapy alongside existing treatments (Lecanemab and Donanemab), which are approved for mild Alzheimer's patients.

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Additionally, if a significant effect is confirmed in the mild-to-moderate population of patients, masitinib could be used at a later stage of the disease, alongside the current standard of care for moderate Alzheimer's, where only generic cholinesterase inhibitors, offering limited efficacy, are approved.

TABLE 3

Intellectual property of AB Science for masitinib in neurodegenerative indications

Scope	Protection	Title	Duration of protection	Status
Amyotropic Lateral Sclerosis	Use patent	Use of masitinib for treatment of ALS patient subpopulation	2037	Granted
	Orphan Drug Status	Treatment of ALS	FDA – 7 years as of approval EMA – 10 years as of approval	Granted
Multiple sclerosis	Use patent	Treatment of MS	2031	Granted USA
		Masitinib for the treatment of MS patient subpopulation	2041	Pending
Alzheimer's disease	Use patent	Masitinib for the treatment of Alzheimer's disease (subpopulations)	2041	PCT application

Masitinib's use patents extend protection in key subpopulations, securing exclusivity until 2037 in ALS and potentially 2041 in MS and AD, reinforcing masitinib long-term market positioning.

In addition, the Orphan Drug designation in ALS grants 7 years of market exclusivity in the USA and 10 years in the EU upon approval, preventing competitors from launching a similar product for this indication.

Beyond patents, regulatory data exclusivity provides an additional layer of protection for AB Science by delaying generic competition. This exclusivity prevents competitors from relying on AB Science's clinical trial data to obtain regulatory approval for a generic version. In the USA, the Hatch-Waxman Act grants 5 years of data exclusivity, which typically extends to 7.5 years in practice and up to 8 years if masitinib is approved for a new indication, formulation, or administration route. In the EU, data exclusivity lasts for 8 years, followed by a 10-year market protection period, extendable to 11 years for new indications.

Our investment thesis: an undervalued company presenting a strategic opportunity for partnership

AB Science appears to be at its best position to date to secure a partnership on its masitinib programs, driven by a compelling combination of factors: a therapeutic target increasingly recognized by external scientific literature, promising Phase IIb/III efficacy results, a proven safety profile, a clear regulatory plan for the confirmatory Phases III validated by agencies and a strong intellectual property providing exclusivity until 2037. The ALS indication seems particularly attractive for a partner with the new follow-up survival data. Additionally, the AB8939 platform could also attract interest from potential partners, as oncology deals are increasingly made at earlier stages.

Should a partnership materialize for AB Science in the next ten months, based on the recent terms disclosed in the Dewpoint deal or other deal benchmarks, we anticipate at least a twofold increase in share price. Even if not, looking ahead, the company's financial runway extends for the next 10 months, with no major clinical or regulatory updates expected that, we believe, could negatively impact the newsflow by the end of 2025. Thus, in that case, we would anticipate AB Science's stock to remain relatively stable. In summary, at the current stock price, we see a strong upside with a limited downside for an investment, and a strong probability for this upside to materialize.

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