

## AB Science (EURONEXT: AB)

### Executive Summary

#### Stock Summary (03/04/24)

Share Price	
EUR€	2.13
USD\$	2.31
52-Week Price Range	
EUR€	1.55 - 6.73
USD\$	1.68 - 7.30
Market Cap.	
EUR€	108.8 million
USD\$	118.0 million
Enterprise Value	
EUR€	125.0 million
USD\$	135.7 million

Source : Bloomberg

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**Figure 1 – AB Science stock chart from 03/04/23 to 03/04/24 (€)**



- We believe AB Science stands as a compelling investment opportunity in the biotech sector, with a strategic investment horizon of four years, aligning with the results of its three confirmatory Phase III studies with masitinib, the company's main drug candidate, in the field of neurology. These studies focus on therapeutical areas with critical medical needs in neurology: Amyotrophic Lateral Sclerosis (ALS), Multiple Sclerosis (MS) and Alzheimer's disease (AD). Given the substantial market potential within each, coupled with the pressing demand for effective treatments, the assumption of success in any one trial could substantially impact the company's stock valuation. The three confirmatory Phase III results are expected over the next four years.
  - In case a single study is positive, we estimate that the financial return for a long-term investor can be significant (in multiple of his initial investment). To minimize risks, we recommend the optimization of the entry point or an investment strategy through several instalments, as on the short-term some events can generate volatility.
- **Masitinib: A robust mechanism of action with strong intellectual property**
- Masitinib, originally developed as a tyrosine kinase inhibitor for cancer treatment, has shown neuroprotective effects in various neurological disorders by modulating key pathways implicated in neurodegeneration. Moreover, masitinib also modulates the activity of microglia, which are resident immune cells in the central nervous system. Their dysregulation has been proven to be actively involved in neurodegenerative disorders like ALS, MS, and AD.
  - AB Science's clinical Phase IIb/III and nonclinical data have been deemed sufficient and robust to receive authorization from key National Health Agencies (e.g., FDA, EMA) to initiate confirmatory Phase III studies in each indication.
  - Moreover, the duration of the patents covering the indications range from 2036 to 2041, indicating a highly robust intellectual property protection.
- **Three confirmatory Phase III studies in neurological indications with billion-dollar markets**
- AB Science currently conducts three confirmatory studies in major pathologies affecting the nervous system, specifically ALS, MS and AD. Each of these diseases is a multi-billion-dollar market, driven by rapid growth attributed to an aging population and improved disease diagnostics. We estimate potential peak sales for masitinib at \$1.3 billion for ALS, \$2.9 billion for MS and \$1.8 billion for AD. While the medical need is urgent, long-term efficacy and tolerance data for current drugs addressing these neurodegenerative conditions remain limited and cover only subsets of patients, opening an avenue for AB Science's new treatment.

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- The company has achieved its most advanced stage in the development of masitinib after two decades, accumulating strong safety and efficacy data and positioning itself well for the release of confirmatory and final Phase III results. Considering the various results of Phase IIb/III trials, we assign varying probabilities of success for each indication. We believe that a successful outcome from any of these trials would generate a strong financial return, given the significant size of the respective markets. Considering an investment today with a 4-year time horizon, we have estimated a potential financial return of 7x the initial investment. This estimation takes into account risk-adjusted valuation and the valuation of listed comparable companies.

#### ■ A well-documented and manageable safety profile

- Masitinib has a thoroughly studied safety profile with the commonly associated adverse effects of diarrhoea, maculopapular rash, nausea/vomiting, peripheral oedema, pruritus, asthenia, and neutropenia. But positive signs have been highlighted during the finished Phase IIb/III trials, as emerging evidence of a substantial improvement in tolerance of masitinib occurs after the initial treatment period. These toxicities could eventually be mitigated through the implementation of a dose-escalation scheme.
- In the broader perspective, it is also essential to note that the indications in confirmatory Phase III trials for masitinib are crippling and benefit from very few efficient treatment options. The three neurological indications are also life-threatening. For example, approximately 50% of people diagnosed with ALS die in the three years following their diagnosis. In this context, health authorities are likely to be more lenient related to masitinib's safety profile.

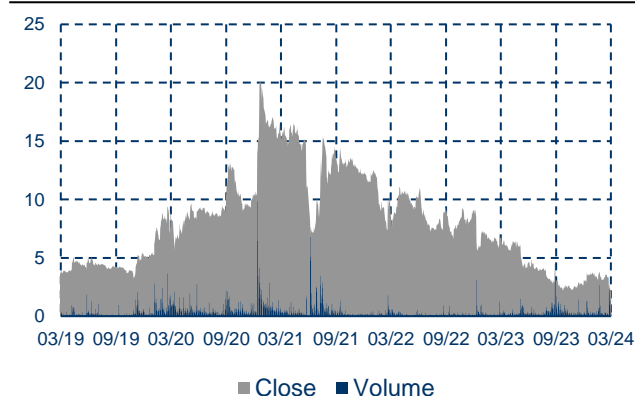
#### ■ A historically low stock price in a biotech depressed market

- During the last five years, AB Science's stock fluctuated between €1.55 and €21.75 and is currently at a price of €2.13 (03/04/24). The company's stock is now trading at historically low levels.
- This decline can be mainly attributed to the biotech market downturn. Indeed, between February 2021 and June 2022, the XBI, which is an equally weighted biotech ETF, lost 65% of its value. This crash represents the most significant downturn, both in terms of intensity and duration in the past twenty years. Various factors contributed to this decline, including escalating interest rates due to higher-than-expected inflation, reimbursement pressures in the US, and an economic downturn following the COVID-19 pandemic.

These factors collectively created a challenging environment for the global biotech industry, consequently impacting the French biotech sector as well. In this turmoil, most investors have directed their focus towards low-risk sectors, reducing their exposure to biotech positions.

- Upon closer inspection of AB Science's recent stock price movement, it significantly dropped following Health Canada's issuance of a Notice of Non-Compliance-Withdrawal regarding masitinib's conditional approval submission for ALS treatment in Canada on the evening of 02/26/24. The stock experienced a sharp decline of 51%, falling from €3.29 at the market close on 02/26/24 to €1.60 at the market close on 02/28/24.

Figure 2 – AB Science stock chart



Source : Bloomberg

## ■ Optimizing the entry point

- In an effort to mitigate potential volatility, investors may seek to optimize their entry point. We identified two key events that could cause volatility in 2024 for AB Science's stock:
  - The first upcoming pivotal event, expected in Q2 2024, is the feedback of the EMA regarding the conditional marketing authorization application of masitinib in ALS. It is important to note that AB Science submitted this application based on data from a single-Phase IIb/III clinical trial, whereas regulatory authorities typically require data from two Phase III trials for full approval. The ongoing confirmatory Phase III study in ALS serves as the second trial in question.

In January 2024, the EMA proposed to AB Science to address the remaining Major Objections in writing instead of the planned Oral Explanation and postponed their feedback from Q1 to Q2 2024. The recent negative feedback from Health Canada regarding similar concerns for the same indication certainly increases the risk of an aligned response from EMA, even if AB Science is asking for a second review from the Canadian agency. The final decision from Health Canada is anticipated in Q3 2024.

With the 50% drop of the stock price related to Health Canada feedback, we believe a negative decision from the EMA has already been integrated by the market into the company's stock price, at least partially.
  - Another factor contributing to potential volatility is the need for refinancing. The company has sufficient cash runway until the end of 2024 and is likely to seek additional financings in the coming months.
- In the context of biotech investments, we maintain a cautious stance toward binary events, recognizing their potential to introduce significant volatility. We advise investors to carefully consider their entry points based on their individual risk tolerance levels. One strategy to mitigate the impact of short-term fluctuations is dollar-cost averaging, where investors regularly allocate a fixed amount of funds at predetermined intervals, irrespective of the asset's current price. This approach helps smooth out the overall average cost of investment over time.
- For risk-averse investors, another prudent strategy could involve waiting until the conclusion of the volatile period, spanning the next four years, which aligns with the expected release of various confirmatory Phase III results. By adopting a patient approach, investors can assess the outcomes of these pivotal events before committing capital, potentially reducing exposure to short-term market fluctuations.

## ■ Upsides to the investment thesis

- We have identified potential upsides to our investment thesis that could positively impact AB Science's share price:
  - Establishment of a partnership with a pharmaceutical company
  - Favourable results across various indications within the pipeline based on the masitinib platform:
    - Confirmatory Phase III trials for Mastocytosis
    - Confirmatory Phase III trials in Metastatic Prostate Cancer
    - Phase II trials in Sickle Cell Disease (SCD)
    - Phase II trials in Mast Cell Activation Syndrome (MCAS)
  - Positive results from Phase I/II trials with the microtubule destabilizer agent platform (AB8939 platform)

## ■ Risks and downsides to the investment thesis

- We have also identified risks that could potentially have a negative impact on AB Science's share price:
  - Negative results across all three ongoing confirmatory Phase III trials in neurological indications
  - The risk associated with not securing a healthy refinancing option

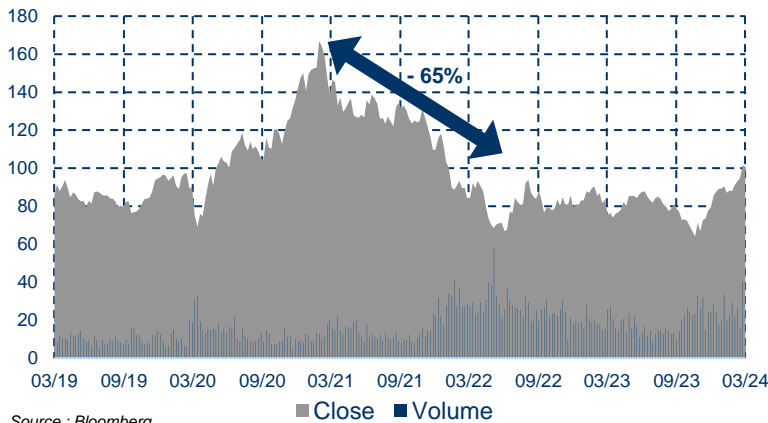
## Agenda

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## The biotech market is still undervalued

- Over the last twenty years, biotechnology stocks outperformed the broader S&P 500 Index, while presenting a higher volatility. During this period, the Nasdaq Biotechnology Index (NBI) surged by 495%, surpassing the S&P 500 Index's gain of 349%.

Figure 3 – XBI performance



Source : Bloomberg

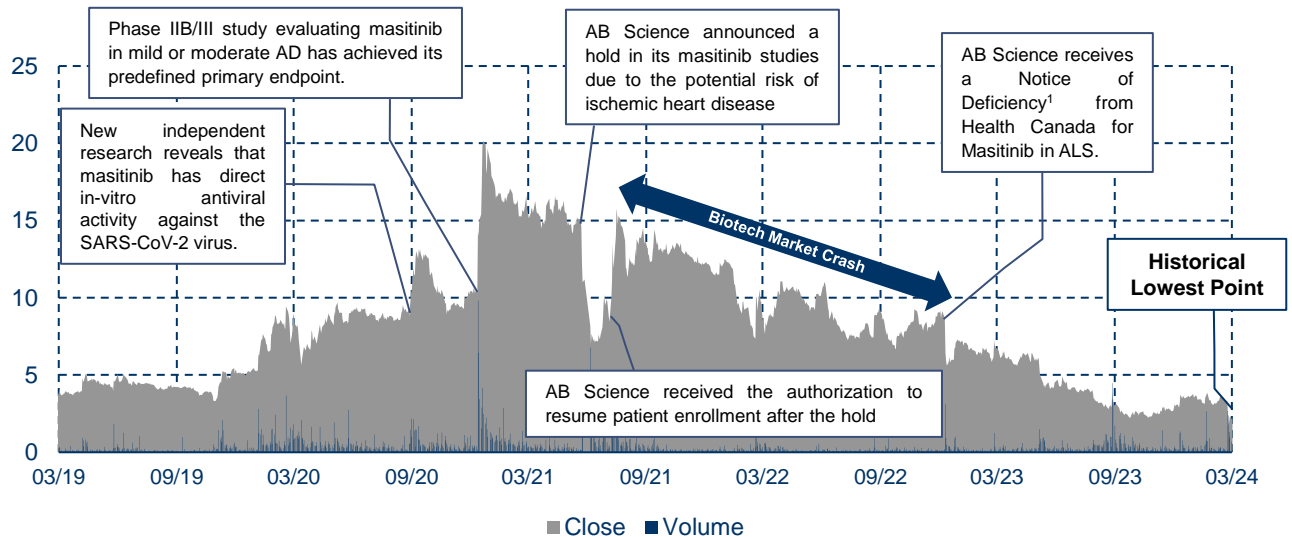
- However, from February 2021 to June 2022, the global biotech market experienced one of the most severe financial crashes of the last twenty years, lasting approximately eighteen months. The XBI, the most used ETF for tracking small-cap biotech companies, dropped by almost 65% over that period.

- The main cause of this unprecedented decline is a succession of events that unfolded right after the end of the pandemic. Post-COVID global inflation soared to 7.5% as of August 2022, from 3.4% in 2020 and an average of 2.1% during the period 2010-2020. The only biotech companies that managed to raise prices and keep up with the inflationary environment were those generating revenue and offering products and services considered essential. Biotech companies in their pre-revenue stage did not have the ability to raise prices, while R&D costs were escalating rapidly.
- In response to inflation, central banks, with the Federal Reserve at the helm, began tightening monetary policy and raising interest rates from 0.25% in March 2022 to 5.50% in July 2023, which has led to increased bond yields and decreased stock attractiveness. This shift, aimed at curbing inflation, triggered volatility and a sell-off in equity markets, notably impacting sectors perceived as risky, as biotechnology. These sectors had to navigate a recalibration of valuations in response to the changing economic conditions and higher interest rates.
- The initial excitement and investment in biotech solutions for COVID-19 gave way to a more cautious approach, as investors reassessed the risks and potential long-term returns in a more stable environment. Investors began to shift their focus to other sectors that are less interest-rate sensitive, including technology, commodities, real-estate, consumer staples, and renewable energy, which offered a hedge against inflation and potential growth opportunities.
- Many biotech firms struggled for survival during the crash, especially small and mid-caps as R&D is their main focus and finding refinancing options is more complicated in such an environment. Negative news generated sharp falls in the share prices, while good news did not trigger any sustainable strong upsides. Investors' interest in life sciences in general was low, as we counted 90 IPOs in 2020, while 2022 only witnessed 8 IPOs. As of today, most biotech companies remain strongly undervalued and we believe AB Science is one of them.

- Since June 2022, the market stabilized, and some signs lead to believe that the market has regained confidence. Despite the challenging environment, we believe that stocks in the biotech sector are now attractively valued and provide a good buying opportunity for investors. The sector is on a good trajectory, with many new products in clinical development, and more and more new technologies on the brink of making it to market. Growth continues to be strong, and innovation is looking robust, as interest rates are stabilizing. Positive results are being rewarded again with increases in stock prices and M&A activity rebounded. Aggregate deal value surged by 79% compared to 2022, reaching around \$152 billion for the full year 2023, the highest deal value since 2019.
- The U.S. Food and Drug Administration (FDA) approved nearly 50% more novel drugs in 2023 than in 2022, putting it back on pace with historical levels of approximately 50 approvals per year.

## AB Science is trading at historically low levels

Figure 4 – AB Science stock chart and major events



Sources : Bloomberg, www.ab-science.com

<sup>1</sup>Notice of Deficiency: A request for additional information sent if deficiencies and/or significant omissions are identified during the scientific review of the submission

- Over the past 5 years, AB Science's stock price has fluctuated between €1.55 and €21.75. From 07/20/2021 to 09/28/2023, it experienced a general downward trend, resulting in an 86% decrease in its share price before stabilizing between €3 and €4 per share. The recent negative decision of Health Canada that just came out, was a huge catalyst in the drop of the stock, which is today trading at its almost historically lowest level ever.

**AB Science has reached the culmination of two decades of intensive research and development**

- Since its inception, in 2001 by Alain Moussy, CEO, and Olivier Hermine, President of the Scientific Committee, AB Science has successfully raised a total of €257 million from private investors and public grants. These funds have been strategically allocated towards the development of its core molecule, masitinib, targeting various indications. Leveraging its accumulated financial resources, AB Science has conducted extensive preclinical and clinical safety and efficacy research, resulting in positive results in Phase IIb/III trials across the three neurological indications. With its most robust dataset to date, AB Science is now well positioned to advance or initiate the three confirmatory Phase III trials, with the most promising prospects it has ever had.

**AB Science’s pipeline is structured on an advanced multi-indication product, masitinib, and an earlier stage platform based on microtubule stabilizer agents**

- AB Science’s pipeline is structured around two platforms, the masitinib platform and its microtubule destabilizer agent platform:
  - Masitinib is in advanced development for six indications: three in neurology (ALS, progressive forms of MS, and mild-to-moderate AD), two in inflammatory diseases (Indolent Systemic Mastocytosis and Mast Cell Activation Syndrome), and one in oncology (Metastatic Prostate Cancer)
  - The microtubule destabilizer platform is at an earlier stage of development, targeting hematology and oncology, with a product currently in Phase I/II in AML

**Figure 5 – AB Science’s pipeline based on its masitinib late-stage platform and microtubule destabilizer agent earlier-stage platform**

Compound	Drug	Therapeutic Area	Indication	Preclinical	Phase I	Phase II	Phase IIb/III	Confirmatory Phase III
Tyrosine Kinase Inhibitor	Masitinib (Oral)	Neurodegenerative Diseases	Amyotrophic Lateral Sclerosis	█	█	█	█	█
			Progressive forms of Multiple 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	█	█			
	ABXXXX (Oral)	Oncology	Sarcoma, Solid Tumors	█				

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## Masitinib's mechanism of action is well documented

- Masitinib belongs to the tyrosine kinase inhibitor (TKI) family, which has witnessed the development and commercialization of several robust and well-tolerated drug candidates over the past two decades. What sets masitinib apart from other TKIs is its heightened affinity and selectivity for certain receptors, while avoiding inhibition of kinases linked to toxic effects, thus offering a superior safety profile, particularly concerning cardiotoxicity.
- The focus of TKI development has predominantly been cancer treatment, and masitinib followed this trend with its initial first developments in cancer.
- Masitinib's mechanism of action has demonstrated promising efficacy and safety throughout preclinical, Phase I, and Phase IIb/III trials across various indications. In neurodegenerative diseases such as ALS, MS, and AD, AB Science's trials have shown that masitinib disrupts cellular events triggered by its specific kinases receptor, exhibiting neuroprotective properties by targeting innate immune cells — mast cells, microglia, and macrophages — in the central and peripheral nervous system. This modulation potentially shifts the neuroimmune system from a neurotoxic state to a neuroprotective one, reshaping the neuronal microenvironment.
- The Phase IIb/III results garnered sufficient proofs from the FDA, leading to the authorization to launch confirmatory Phase III trials for masitinib in ALS, MS and AD.

## AB Science's key valuation milestones consist of the results of three ongoing confirmatory Phase III trials in neurological indications

### ■ AB Science's flagship indication: Amyotrophic Lateral Sclerosis (ALS)

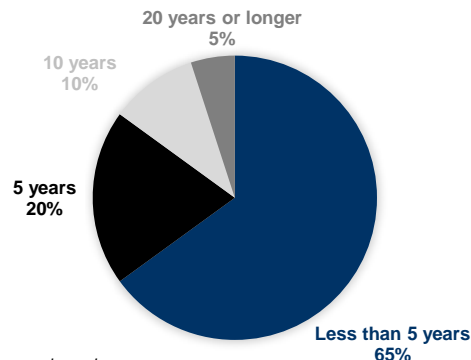
- We anticipate two pivotal milestones that could significantly impact AB Science's stock performance in the near to medium term, both centred around the development of masitinib for the treatment of ALS.
  - The first one is the imminent decision from the EMA regarding the conditional marketing approval of masitinib in ALS. AB Science submitted Marketing Authorization applications in the first half of 2022, supported by promising data from Phase IIb/III trials and favorable long-term patient survival rates. However, as of Day 195 of the EMA's procedure, certain Major Objections persisted, leading to the scheduling of an Oral Explanation initially set for January 24, 2024. Just prior to this date, the CHMP recommended that AB Science addresses these concerns in written format. The outcome of this EMA decision, expected in Q2 2024, remains uncertain and could potentially result in significant stock price volatility. The recent Notice of Non-Compliance-Withdrawal from Health Canada raised major concerns regarding the Canadian conditional approval based on Phase IIb/III trial data. Although AB Science intends to submit a Request for Reconsideration, the decision from Health Canada does not appear optimistic and does not bode well for a positive outcome from the EMA. History has shown that the chances for conditional approval success based on a single Phase IIb/III study are low, especially considering there have been amendments to the study.
  - The second milestone corresponds to the results of the confirmatory Phase III trial for ALS, which aims to validate the conclusions of the Phase IIb/III and post-hoc long-term analysis, meaning an absolute change from baseline in functional score after 48 weeks of treatment in non-severe ALS patients who progress normally. The long-term analysis revealed an excellent survival benefit of 25 months and 47% reduced risk of death on this specific population. A positive outcome would be game-changing for AB Science and its investors, as ALS is a rare and fatal neurological disorder, for which the field is desperate for more effective treatments.



## ALS is a fast-growing and life-threatening disease

- ALS is a rare and fatal neurological disorder that affects motor neurons, the nerve cells in the brain and spinal cord that control voluntary muscle movement and breathing. The illness is progressive, and the average life expectancy for ALS patients after diagnosis is three years.
- Globally, ALS prevalence is rapidly increasing, currently estimated at around 250,000 patients, with projections indicating it could reach 375,000 by 2040.

**Figure 6 – Life expectancy after diagnosis in ALS**



Source : [www.hss.edu](http://www.hss.edu)

## ALS treatment landscape requires more efficient options than those currently available on the market

- Today, three FDA-approved compounds affect ALS progression: the glutamate antagonist riluzole (available orally in various formulations such as tablets, films, or liquid), the antioxidant edaravone, and sodium phenylbutyrate / taurursodiol. However, these medications have demonstrated a modest ability to slow down disease progression, as measured by the revised ALS Functional Rating Scale (ALSFRS-R), showing a limited impact on increasing survival rates. Their poor efficacy leaves room for the development of more effective drugs.

**Table 1 – Overview of masitinib positioning compared to marketed drugs for ALS**

	Masitinib	Riluzole	Edaravone	Phenylbutyrate- taurursodiol
<b>Company</b>	AB Science	Sanofi / Italfarmaco / Martindale Pharmaceuticals	Mitsubishi Tanabe	Amylyx
<b>Regulatory Phase</b>	Under review for conditional approval (EMA and Health Canada) Ongoing confirmatory Phase III	FDA (1995), EMA (1996)	FDA (2017), Canada (2018) and Japan (2015) approval Not approved in the EU (Ferrer trial failed 2024)	FDA (2022), Conditional approval Health Canada (2022) Ongoing Phase III for EMA approval
<b>Mechanism of action</b>	Anti-inflammatory & immunomodulation	Reduction of excitotoxicity	Anti-oxidative stress	Anti apoptotic
<b>Drug formulation</b>	Oral	Oral (Pill, film, and liquid)	Oral suspension (2022) and intravenous infusion of 60 mg per cycle of 14 days per month (2017)	Oral
<b>Intellectual Property</b>	Patented until 2037	Generic drug	Patented until 2039	Patented until 2033
<b>Efficacy in <math>\Delta</math>ALSFRS-R between treated ALS patients and placebo</b>	$\Delta$ ALSFRS-R = +3.3 (week 48)	No data available	$\Delta$ ALSFRS-R = +2.5 (week 24)	$\Delta$ ALSFRS-R = +2.1 (week 24)
<b>Efficacy in Overall Survival</b>	Survival benefit of 25 months and 47% reduced risk of death on early-stage and "Normal Progressor" patients	Survival benefit of 2 or 3 months	Survival benefit of 6 months	Survival benefit of 6.5 months
<b>Safety</b>	<b>CAE<sup>1</sup></b> Diarrhoea, maculopapular rash, nausea/vomiting, peripheral oedema, pruritus, asthenia, neutropenia	Neck or arm or shoulder pain, arm paraesthesia, dysphagia, worsening of myelopathy	Reddening of the skin, chest pain or tightness, change in walking and balance, unsteadiness, cough, confusion, dry skin, difficult or troubled breathing, dizziness, fast heartbeat, rash, unusual bruising	Diarrhoea, abdominal pain, nausea, respiratory failure
	<b>SAE<sup>2</sup></b> One case of auto-immune-like hepatitis, three non-severe cases of increased transaminases	Increase in aminotransferase levels, in alanine aminotransferase, in aspartate aminotransferase	No serious adverse effect reported	No serious adverse effect reported
<b>Annual treatment price</b>	/	\$5,000	\$190,000	\$158,000

Sources : Phase III publications for masitinib, riluzole, edaravone, and phenylbutyrate-taurursodiol

<sup>1</sup>CAE: Common Adverse Effects, <sup>2</sup>SAE: Severe Adverse Effects

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- Both drugs from Amylyx (phenylbutyrate-taurursodiol) and Mitsubishi Tanabe (edaravone) are undergoing confirmatory evaluation, as the EMA did not approve the drugs based on the 24-week Phase III results. Amylyx's drug is currently undergoing a 48-week trial to seek EMA approval, whereas for edaravone, the last 48-week trial (Ferrer trial) did not provide sufficient evidence for EMA approval. In addition, Biogen's drug (tofersen), indicated for the treatment of adults with ALS who have a mutation in the superoxide dismutase 1 (SOD1) gene – which represents a minority (around 2%) of the entire ALS population – received approval from the FDA in April 2023 and positive recommendation from the EMA in February 2024 (final decision expected in Q2 2024).
- In terms of mechanism of action, oxidative stress and excitotoxicity are the only two pathways targeted by the current approved drugs among several others considered important contributors to ALS disease development. Therefore, the exploration of alternative disease mechanisms, such as neuroinflammation as targeted by masitinib, are crucial for identifying new therapeutic drugs that could offer additive or more effective treatment options. Thus, numerous Phase II/III and Phase III clinical trials are undergoing targeting various pathways.

Table 2 – Overview of advanced clinical trials in SLA

Therapeutic compound tested	Pathway	Number of patients	Clinical Phase	Estimated study completion
<b>CBD oil</b>	Excitotoxicity	17	Phase III	2024
<b>Memantine</b>	Excitotoxicity	800	Phase II/III	2026
<b>Trazodone</b>	Oxidative stress	800	Phase III	2026
<b>Deferiprone</b>	Oxidative stress	372	Phase II/III	2024
<b>Triumeq</b>	Neuroinflammation	390	Phase III	2026
<b>MN-166/Ibudilast</b>	Neuroinflammation	230	Phase II/III	2024
<b>Methylcobalamin</b>	Reduction of denervation and muscle weakness	128	Phase III	Unknown
<b>Trehalose</b>	Enhancing of autophagy, Decrease of SOD1 aggregates	161	Phase II/III	2024
<b>Tofersen/BIB067</b>	Gene specific–ASO, SOD1-mutations	150	Phase III	2027
<b>Jacifusen/ION363</b>	Gene specific–ASO, FUS-mutations	77	Phase III	2028
<b>NurOwn</b>	Stem cells	Unknown	Phase III	Unknown
<b>Lenzumestrocel</b>	Stem cells	115	Phase III	2026

Source : Current State and Future Directions in the Therapy of ALS - Cells

- Sanofi and Denali's Phase II targeting the neuroinflammation pathway in ALS failed, as announced on February 16, 2024, involving molecules targeting an important signaling protein known as "receptor serine/threonine-protein kinase 1" (or RIPK1) in the TNF receptor pathway, which regulates inflammation and cell death in human tissues.
- In the current ALS treatment landscape, we believe masitinib is well-positioned in terms of its progress in the clinical phases, its latest results in Phase IIb/III and ad-hoc analysis, and the number of patients involved in the confirmatory Phase III trial. If the confirmatory Phase III trial validates the promising results of the long-term Phase IIb/III trial regarding the two-year survival rate for "Normal Progressor" patients who are not severely advanced in the disease, masitinib could establish itself as a groundbreaking drug, offering substantial benefits compared to currently marketed drugs.

AB Science's confirmatory Phase III has been designed to replicate the positive results of Phase IIb/III

- The initial effectiveness results of masitinib in ALS were evidenced by AB Science's Phase IIb/III study, demonstrating a 27% decrease in the rate of functional decline. This was assessed using the change from baseline to week 48 in ALSFRS-R ( $\Delta$ ALSFRS-R), recommended by both the FDA and EMA as an instrument to evaluate functional status and disease progression in ALS patients. This score has been used as primary endpoint for the products already approved in ALS. The observed reduction was achieved with a posology of 4.5mg/kg/day in the "Normal Progressor" cohort, which constituted the primary efficacy population and around 84% of the total Phase IIb/III patients. The practice of distinguishing between "Normal Progressors" and "Fast Progressors" through this inclusion criterion is a common approach in ALS clinical studies.

The positive outcomes of this Phase IIb/III in ALS were well-received by the scientific community, getting published in the two peer-reviewed journals *Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration*, and *Therapeutic Advances in Neurological Disorders*.

- Subsequently, a long-term survival analysis, with an average follow-up of 75 months from diagnosis, was conducted on participants from the Phase IIb/III study. This analysis revealed a significant benefit for the "Normal Progressors" patients, as defined in the Phase IIb/III study, but specifically limited to those in the early stages of the disease. This subgroup, not pre-specified, demonstrated a greater magnitude of effect than the full study population. Specifically, this subgroup experienced a statistically significant 25-month extension in survival and a 47% reduction in the risk of death, results that are excellent when compared to the outcomes of other drugs on the market.
- Aiming to replicate the promising efficacy of the Phase IIb/III, based on the ALSFRS-R score, AB Science initiated the confirmatory Phase III trial for masitinib in ALS in 2021, setting the primary endpoint as the  $\Delta$ ALSFRS-R and targeting a large cohort of "Normal Progressor" patients at early stage of the disease.
- We maintain an optimistic stance regarding the anticipated results of the confirmatory Phase III trial, given its focus on the subgroup of early stage and "Normal Progressors" that has demonstrated excellent outcomes. If approved, which we estimate at a 50% likelihood, in line with the typical success rates at this stage of development, this would stand as a pivotal milestone for the company, with estimated peak sales projected to reach over \$1 billion worldwide.

■ **AB Science's promising efficacy results in severe and progressive forms of Multiple sclerosis (MS)**

- By capitalizing on masitinib's mechanism of action, which targets mastocytes and microglia, inhibiting the activation of the inflammatory process, AB Science has enriched its late-stage pipeline with a second indication in neurology, severe multiple sclerosis (MS) without relapses (i.e. Primary Progressive and Secondary Progressive non-active MS), for which there are currently no or poor treatments.
- These forms of MS are primarily driven by persistent innate immunity-related inflammation within the central nervous system. Microglia and mast cells play a significant role in the pathophysiology of MS. By targeting these cells, AB Science aims to intervene in the disease progression and potentially slow or prevent further disability in progressive MS patients.
- Phase IIb/III results have already been published, demonstrating that a masitinib dose of 4.5mg/kg/day slowed disease progression in patients, which was the study's primary objective. A confirmatory Phase III trial is currently underway, with ongoing patient recruitment and study completion anticipated by 2028.

*AB Science positions itself to treat a significant proportion of MS population*

**Table 3 – Distribution of the proportion of patients across different MS forms**

	Relapsing Remitting (RRMS)	Progressive MS (PMS)		
		Primary Progressive MS (PPMS)	Secondary Progressive MS (SPMS)	
Symptoms	Episode of acute exacerbations or relapses with recovery and stable course between relapse	Gradual deterioration with no relapse or remission	Stage following RRMS with gradual deterioration	
			Active SPMS With relapse	Non-Active SPMS No more relapse
Proportion of MS patients	40%	<u>15%</u>	10%	<u>35%</u>

Sources : Antel J, Antel Svand, and al. Primary progressive multiple sclerosis: part of the MS disease spectrum or separate disease entity? Acta Neuropathol. 2012 May, Paz Soldán MM, and al. Relapses and disability accumulation in progressive multiple sclerosis. Neurology. 2015 Jan.

- MS manifests in two main forms: relapsing-remitting MS (RRMS), marked by periodic disease relapses, and progressive MS (PMS), which includes Primary Progressive MS (PPMS) and Secondary Progressive MS (SPMS). PPMS entails a continuous deterioration of symptoms from onset, whereas SPMS typically follows RRMS, usually developing 15 to 20 years after initial symptoms. In SPMS, neurological function declines steadily over time, leading to increased disability. This last form can be categorized as active (with relapses and/or new MRI activity) or inactive, with no more relapse.
- Masitinib targets patients with PPMS and non-active SPMS, which are the more severe forms of MS without collapses, comprising roughly 50% of all MS cases, and constituting a challenging-to-treat population. Currently, only one drug is approved for PPMS: ocrelizumab, an anti-CD20 monoclonal antibody for PPMS, and there is currently no treatment for non-active SPMS.
- In completed Phase IIb/III clinical trials, masitinib demonstrated better reduction in confirmed disability progression compared to both authorized treatments. This improvement was measured on the Kurtzke's Expanded Disability Status Scale (EDSS), which is considered the gold standard to assess disability progression in both PPMS and SPMS, in alignment with the EMA's 2015 guidance on clinical investigation of medicinal products for MS treatment.

Table 4 – Overview of masitinib positioning compared to Roche's drug in PPMS

	Masitinib	Ocrelizumab
<b>Company</b>	AB Science	Roche
<b>Regulatory Phase</b>	Ongoing confirmatory phase III	FDA (2017), Conditional approval Health Canada (2017) EMA (2018)
<b>Mechanism of action</b>	Anti-inflammatory & immunomodulation (microglia, mast cells, macrophages)	Anti-inflammatory & immunomodulation (B cells)
<b>Target population</b>	PPMS & non-active SPMS EDSS between 2.0 and 6.0	PPMS EDSS between 3 and 6.5
<b>Drug formulation</b>	Oral	IV
<b>Intellectual Property</b>	Pending, if granted secured until 2041	Until 2029
<b>Efficacy</b>	37% of reduction of the risk in disability progression in 12 weeks	24% of reduction of the risk in disability progression in 12 weeks
<b>Safety</b>	<b>CAE<sup>1</sup></b>	Diarrhoea, maculopapular rash, nausea/vomiting, peripheral edema, pruritus
	<b>SAE<sup>2</sup></b>	Maculopapular rash, erythema multiforme, elevated gamma-glutamyl transferase, neutropenia, palmar-plantar erythrodysesthesia syndrome
<b>Annual treatment price</b>	/	\$32,600

Sources : Phase III publications for masitinib and ocrelizumab

<sup>1</sup>CAE: Common Adverse Effects, <sup>2</sup>SAE: Severe Adverse Effects

- The other emerging class of late-stage drug candidates targeting PPMS or SPMS is Bruton's Tyrosine Kinase inhibitors (BTKi). These inhibitors operate by modulating the peripheral adaptive immune system, specifically by targeting B-cell proliferation and differentiation. Notable candidates within this class include tolebrutinib from Sanofi and fenebrutinib from Roche, both in Phase III trials for various forms of MS. However, they are currently subject to a Clinical Hold by the FDA due to instances of drug-induced liver injury. Additionally, Merck's evobrutinib, another BTKi, failed to meet its primary endpoint in RRMS.
- Another notable late-stage drug in this segment is the statin simvastatin, which has demonstrated a significant reduction in the annualized rate of whole-brain atrophy in SPMS. This Phase III is scheduled for completion by the end of August 2024.

*Phase IIb/III results in PPMS and non-active SPMS are a good omen for the outcome of the confirmatory Phase III*

- AB Science's Phase IIb/III trial in PPMS and non-active SPMS successfully met its primary endpoint of overall EDSS change from baseline, showing positive results in the masitinib 4.5 mg/kg/day cohort. The trial revealed a significant 37% and 42% risk reduction with masitinib over 12 and 96 weeks, respectively, surpassing the efficacy of current drugs on the market. However, changes in the primary endpoint were made during the trial to be aligned with the new FDA guidance, and a lack of response to the 6.0 mg/kg/day dosage made direct clinical interpretation more challenging. The limited size of the patient cohort resulted in difficulties with statistical methods and underpowered secondary endpoints.
- Regarding the specific cohort treated with masitinib 6.0 mg/kg/day, it did not demonstrate any treatment effect. According to AB Science's management, the reason for this divergent result is the combination of a plateau effect and a better than anticipated EDSS improvement relative to baseline for the placebo arm. Acknowledging this observation, AB Science now considers masitinib 4.5 mg/kg/day as the sole recommended dose for future development.
- Aligned with the updated regulatory guidelines, the confirmatory Phase III trial will aim to validate the findings of the Phase IIb/III study, with a large cohort of approximately 800 patients undergoing evaluation over a 96-week period. The primary objective will be to confirm the progression of the EDSS score in patients with PPMS and non-active SPMS.
- Considering Phase IIb/III results and the well-optimized design of the confirmatory Phase III, we are confident about the next steps in this indication, which we estimate to have a 40% likelihood of success. The MS indication should be viewed as a long-term endeavour, as outcomes are anticipated for 2028, following ALS and AD's confirmatory Phase III results. It could generate significant peak sales that we estimate around \$3 billion worldwide.

**■ AB Science's promising path in mild-to-moderate Alzheimer's Disease (AD) treatment**

- After around twenty years of unsuccessful research in the field of Alzheimer's disease (AD), during which no drug had been approved, the past three years have witnessed an acceleration of positive Phase III trials and FDA approvals of new anti-amyloid treatments. Indeed, aducanumab by Biogen, approved in February 2021 - now withdrawn from the market due to controversy - and replaced by lecanemab by Eisai and Biogen, approved by the FDA in July 2023, along with the conclusive Phase III results of donanemab by Eli Lilly, pave the way for new therapeutic hopes in Alzheimer's drug development segment.
- However, these current symptomatic treatments are only approved for patients with mild cognitive impairment or mild dementia, which corresponds to the early stage of Alzheimer's disease and is characterized by a Mini-Mental State Examination (MMSE) score > 20, on a 30 point-scale which qualifies the severity of cognitive impairment (a lower score corresponding to a stronger cognitive impairment).
- For mild-to-moderate forms of AD, corresponding to more advanced stages (MMSE of 12 – 25), only cholinesterase inhibitors (galantamine, rivastigmine, and donepezil) and memantine, approved around the 2000s, demonstrated efficacy, albeit still limited, in managing symptoms of the disease. Masitinib, on the other hand, targets other AD pathways, specifically the cell-signaling pathways associated with neurodegeneration, aiming to decrease neuroinflammation as well as excitotoxicity, and to improve cognitive functions. If approved by regulatory authorities, following positive confirmatory Phase III results, masitinib could emerge as a new treatment for mild-to-moderate forms of AD, used in combination with the current standard-of-care.

### *AD is a fast-growing market with an urgent medical need*

AD stands as a relentless neurodegenerative condition, ranking as the leading cause of dementia among the elderly population. Globally, an estimated 47 million individuals grapple with dementia, with the majority afflicted by AD. Projections indicate a worrisome trend: the prevalence of dementia is set to double approximately every two decades, with an anticipated surge to 132 million cases by 2050. Consequently, there is a pressing need for the swift advancement of therapeutical approaches capable of effectively addressing all the progressive steps of the disease.

### *Masitinib's mechanism of action reduces neuroinflammation, a key pathology of AD*

- The defining pathological features of AD are the presence of extracellular amyloid plaques containing amyloid- $\beta$  [A $\beta$ ] peptide and neurofibrillary tangles composed of hyperphosphorylated tau protein. Consequently, over recent years, the prevailing strategy for treating AD has centered on therapies utilizing antibodies targeting amyloid- $\beta$  to reduce amyloid accumulations. Within this therapeutic landscape, the only FDA-approved drugs have been monoclonal antibodies: aducanumab and lecanemab, which have demonstrated efficacy in amyloid plaque clearance, leading to clinical benefits. However, recent data suggest that clearing amyloid is insufficient to stop dementia progression. In fact, a persistent immune response in the brain has emerged as a crucial third core pathology in AD. In many dementia patients, the inflammatory system becomes overactivated: there is a noticeable increase in inflammatory cells in the spinal fluid, evidence of increased microglia activity (the primary immune cells) on brain scans, and observable differences in immune cell functionality. This sustained activation of the brain's microglia and other immune cells has been shown to exacerbate both amyloid and tau pathology, potentially serving as a significant link in the disorder's pathogenesis.
- By focusing on this novel pathway and inhibiting the activity of microglia and mast cells, masitinib has demonstrated promising results in both preclinical and clinical studies. Its synapto-protective effects are directly linked to the inhibition of mast cells, further enhancing its potential efficacy.
- AB Science is not alone in its pursuit of an anti-inflammatory strategy against mild-to-moderate AD. BioVie, another advanced company in this field, has conducted a Phase III trials targeting mild-to-moderate Alzheimer's patients. Their approach involved, a blood-brain permeable anti-inflammatory insulin sensitizer that acts by binding extracellular signal-regulated kinase. However, challenges arose during the trial, primarily due to the exclusion of patients associated with sites suspected of improprieties, leading to a study failure.

### *The confirmatory Phase III will be crucial to validate the efficacy of masitinib in AD*

- The Phase IIb/III trial evaluating a 4.5 mg/kg/day dose of masitinib in mild-to-moderate AD has demonstrated promising outcomes over 24 weeks. The study revealed significant improvements on the Alzheimer's Disease Assessment Scale-Cognitive Subscale (ADAS-Cog), a neuropsychological assessment used to evaluate the severity of cognitive symptoms of dementia, and positive albeit non-significant (p-value = 0.038, slightly above the 0.025 threshold for significance) outcomes on the Alzheimer's Disease Cooperative Study – Activities of Daily Living Scale (ADSC-ADL), assessing patients' ability to perform activities of daily living. These findings were published in the prestigious *Alzheimer's Research & Therapy journal*.
- Both scales selected as primary endpoints in the design of this Phase IIb/III trial adhere to the regulatory guidance provided by the FDA. Notably, the ADAS-Cog emerges as the most employed primary endpoint in late-stage AD trials. However, in its guidance, the FDA has underlined the importance of evaluating both cognitive and daily functional outcomes in early Alzheimer's disease trials to comprehensively capture the disease's clinical impact. Furthermore, approved medications in the field have demonstrated efficacy in addressing both cognitive symptoms and daily life challenges, utilizing various scoring systems that encompass the two aspects. This suggests that both primary study criteria, ADAS-Cog and ADSC-ADL should be achieved significantly in the confirmatory Phase III trial, to bolster AB Science chances upon market submission to health authorities.

- Concerning the efficacy results, with a  $\Delta$ ADAS-Cog difference of -2.2 between the masitinib-treated group and the placebo, masitinib demonstrated an effect comparable to cholinesterase inhibitors (donepezil, galantamine, or rivastigmine) currently on the market, which have shown an average  $\Delta$ ADAS-Cog difference of -2.7 points. Therefore, utilizing masitinib as an adjunct to current therapies could potentially yield a >4-point improvement in the ADAS-Cog.
- During the Phase IIb/III trial, the 6.0 mg/kg/day dose of masitinib did not demonstrate efficacy, like the findings in the MS Phase IIb/III trial, which was attributed again to a plateau effect and an atypical improvement observed in the placebo group. AB Science intends to conduct the confirmatory Phase III trial with a large cohort, targeting approximately 600 patients, to validate significant results on both the ADAS-Cog and ADSC-ADL, which are the primary endpoints of the confirmatory Phase III study.
- Regarding safety concerns, the analysis of common severe adverse events revealed an increased incidence of neutropenia, a condition leading to weakened immunity against infection, and pneumonia. Additionally, treatment-related adverse events resulting in permanent discontinuation of treatment, excluding death, were observed in some patients. The confirmatory Phase III trial will need to provide reassurance regarding the long-term effects of masitinib concerning adverse events, as it may affect the daily medication intake of patients.
- We estimate masitinib in AD peak sales to be approximately \$2 billion, given that AD is a well-known complex condition with very few drugs successfully approved, leading us to assess a success probability of 15%.

### Masitinib is protected until 2036 and up to 2041 through use of patents strategy

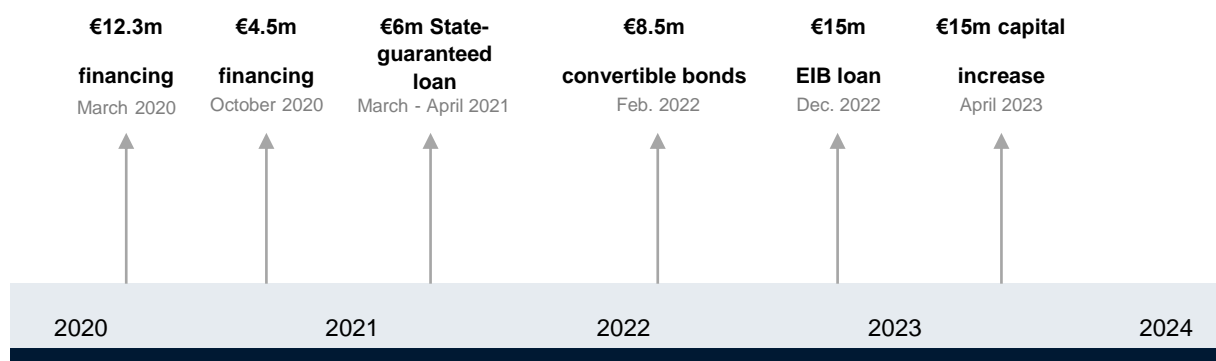
- AB Science's first patents were filed in 2002, covering the screening, identification, and selection of non-toxic c-kit inhibitors, as well as the use of TKIs for treating rheumatoid arthritis, inflammatory bowel diseases, and allergic diseases. These patents were active up until 2024.
- Nevertheless, the company has been consistently filing for medical use patents alongside the development of masitinib and its newer indications, granting the compound strong IP. The composition and synthesis process of masitinib is patented until 2028, making AB Science its sole legal producer until that year. Besides, masitinib and its related compounds have protection in ALS until 2037. The same medical use patent strategy is being pursued in the other confirmatory phase III indications, as AB Science filed patents for MS and AD in 2020. If granted, these patents would protect the use of masitinib until 2041 in these indications.

### AB Science has always managed to get financing, even in a tough environment

- In the challenging landscape of refinancing for public companies, AB Science has demonstrated a remarkable ability to secure funding, with a total of €257 million raised since its creation. Recently, the company obtained a €15 million loan structured in three tranches, from the European Investment Bank (EIB). The final tranche, amounting to €3 million will be disbursed upon the fulfilment of specific suspensive conditions. Moreover, in April 2023, AB Science successfully completed a €15 million capital increase, comprising €11.5 million in cash and €3.5 million in debt settlement.



Figure 7 – Overview of AB Science's financings since 2020



Source : AB Science's annual 2021 and 2022 reports

As AB Science has a cash runway until the end of 2024, we anticipate an imminent refinancing, which should proceed smoothly given the company's successful history of raising capital when needed. Additionally, Alpha Blue Ocean committed in April 2023, for a 2-year period, to subscribe to capital increases at AB Science's request, securing, at least partially, the potential upcoming financing needs through the issuance of shares at market price.

Table 5 – AB Science's current financial situation

<b>Cash</b> As of 06/2023	€14.8 million
<b>Debt</b> As of 06/2023	€30.8 million
<b>Cash Burn</b> 06/2022-06/2023	€12.0 million
<b>Market Cap.</b> As of 03/04/2024	€108.8 million

Sources : AB Science, Bloomberg

- As of June 2023, the cash balance stood at €14.8 million. The non-current portion of debt amounted to €29.0 million, with €12.2 million in conditional advances and €16.8 million in credit/bank loans. Additionally, the current portion of debt stood at €1.8 million, consisting of credit/bank loans.
- All historical convertible bonds have been converted.

### Current valuation is low, with regards to fundamentals

- AB Science has recently reached its historically lowest stock price following the negative response of Health Canada on masitinib conditional approval in ALS on February 26, 2024. Subsequently, we believe the market has already been pricing an anticipated negative decision from the EMA based on the feedback from Health Canada, at least partially.
- Nevertheless, the fundamentals of the company are strong as it has currently three confirmatory Phase III trials in neurology poised for significant markets that suffer from a severe lack of effective medications.
- Taking into account a 50% chance of success for the confirmatory Phase 3 trial in ALS, a 40% chance of success in MS, and a 15% chance for AD, with assets valued at 1x peak sales upon drug approval, investors can anticipate a total risk-adjusted valuation of \$1.83 billion. Considering the need to refinance the company on the four coming years, and the current debt, this corresponds to a potential financial return of 8x the initial investment, if they invest today, with a 4-year time horizon.

This report has been commissioned by AB Science and prepared and issued by DNA Finance, in consideration of a fee payable by AB Science.

**Table 6 – Risked-adjusted valuation of AB Science’s confirmatory Phase III trials in neurological indications**

Indication	Estimated peak sales		Estimated probability of successful approval	Risk-adjusted valuation of each asset	
	EUR	USD		EUR	USD
<b>ALS</b>	€1.3 billion	\$1.4 billion	50%	€650 million	\$700 million
<b>MS</b>	€2.9 billion	\$3.1 billion	40%	€1.45 billion	\$1.55 billion
<b>AD</b>	€1.8 billion	\$2.0 billion	15%	€450 million	\$500 million

- This valuation only considers the three Phase III therapeutic assets in the neurological domain and does not include the rest of AB Science's pipeline, which is mostly in earlier stages of development but nonetheless well advanced.
- Another valuation approach involves benchmarking to listed comparable companies within the sector, in advanced clinical phases within the field of neurological diseases. The average market capitalization of these comparable companies is \$728.0 million compared to €108.8 million for AB Science today. Therefore, AB Science is undervalued by approximately 6x compared to the average market capitalization of listed comparable companies within the sector.

**Table 7 – AB Science’s comparable market capitalization**

Company (Ticker)	Currency	Market Capitalization
<b>Alector</b> (NASDAQ : ALEC)	USD\$	667.9 million
<b>Annovis Bio</b> (NASDAQ : ANVS)	USD\$	96.3 million
<b>Athira Pharma</b> (NASDAQ : ATHA)	USD\$	156.8 million
<b>Capricor Therapeutics</b> (NASDAQ : CAPR)	USD\$	145.5 million
<b>Cassava Sciences</b> (NASDAQ : SAVA)	USD\$	951.2 million
<b>Denali</b> (NASDAQ : DNLI)	USD\$	2,883.0 million
<b>FibroGen</b> (NASDAQ : FGEN)	USD\$	195.6 million
<b>Mean</b>	<b>USD\$</b>	<b>728.0 million</b>

Source : Bloomberg

- By equally weighting the two distinct valuation methodologies, we estimate that over a 4-year period, the return on investment for an investor investing today would be around 7x.

The upsides to our investment thesis rely on AB Science’s capacity to establish out-licensing deals and to successfully pursue the clinical development of its other programs

- We have identified significant potential upsides that could positively impact AB Science's share price:
  - **A partnership with a pharmaceutical company:** A deal would be a major development for the company and the management is exerting considerable efforts to secure a partnership with a pharmaceutical company in 2024. While this option is not explicitly factored into our investment thesis, due to the absence of prior deals by AB Science, it merits consideration. Even if the diverse range of indications for masitinib presents challenges in securing a comprehensive global deal, we see potential in exploring geographical partnerships that could target specific markets with greater feasibility.

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➤ **Positive confirmatory Phase III in Mastocytosis:** Since 2020, a confirmatory Phase III trial has been underway for masitinib in indolent or smoldering systemic Mastocytosis, the most prevalent forms of Mastocytosis. Results of this confirmatory Phase III are anticipated in 2026. Masitinib's mechanism of action is interesting in this rare disease, as it induces a reduction in mast cell and microglia activity, both critical players in Mastocytosis, through its inhibitory action on wild-type tyrosine kinases. This action potentially reduces neuroinflammation and associated symptoms in Mastocytosis patients. The overall indolent systemic treatment market is estimated to around \$450 million. While not on the same scale as neurological indications, it remains attractive, considering there is currently only one drug on the market (avapritinib by Blueprint Medicines) to treat indolent systemic Mastocytosis, while there is no treatment available for smoldering systemic Mastocytosis.

Based on a single study for a conditional approval application, the EMA refused approval in 2017 due to specific shortcomings mainly associated with significant protocol changes in the Phase IIb/III trial. The results of the confirmatory Phase III trial will be crucial for AB Science. The ongoing study will need to show a significant response in at least one of three severe symptoms of Mastocytosis.

➤ **Positive confirmatory Phase III in metastatic castration-resistant prostate cancer (mCRPC) in combination with docetaxel:** There remains an unmet medical need in metastatic prostate cancer following failure of hormone therapy and eligibility for docetaxel, the only approved drug. Masitinib's Phase IIb/III trial successfully achieved its predefined primary endpoint, demonstrating a 21% reduction in the risk of progression, as measured by an improvement in progression-free survival compared to the control group. A new European patent secures intellectual property rights for Masitinib in mCRPC until 2042.

➤ **Initiation of Phase II in Sickle Cell Disease (SCD):** A new Phase II clinical trial for masitinib in SCD is expected to start in 2024, with Assistance Publique-Hôpitaux de Paris as its promoter. This study got a €9.2 million funding through a call for projects operated by the National Research Agency. Despite the emergence on the market of approved gene therapies to treat patients with SCD, considering the vast and fast-growing SCD market valued at €2.5 billion, and the high costs and safety issues associated with gene therapies, SCD remains an appealing indication for masitinib.

➤ **Positive Phase II results in Mast Cell Activation Syndrome:** Masitinib is currently in the enrolment stage for a Phase II clinical trial in severe Mast Cell Activation Syndrome. There are currently no approved therapies for this indication, and no drugs in clinical development, despite the estimated number of patients amounting to 500,000 in the USA and EU.

➤ **Positive Phase I/II results with the AB8939 platform:** AB8939 is the second main compound currently developed by AB Science. It is a synthetic tubulin inhibitor undergoing a Phase I/II study for patients with Acute Myeloid Leukemia (AML) in second or third-line treatment and who are unfit to receive intensive chemotherapy. The drug strongly differs from other microtubule targeting chemotherapies since it is not transported by efflux pumps, which are notorious for resistance development in patients. Moreover, AB8939 is not metabolized by the enzyme myeloperoxidase, which is produced by the disease itself, unlike other microtubules destabilizer agents. The drug has received an Orphan Drug Designation for AML from the FDA, and has showcased promising potential during preclinical tests, being active against chemotherapy naïve or chemotherapy refractory/relapse AML cancer cells *ex vivo*, as well as systematically killing cancer cells present in the blood, spleen, and bone marrow of all mouse models. Positive preliminary findings from Phase I/II were released, indicating an absence of drug-related adverse reactions, as well as no dose limiting toxicity. The complete study results are expected for 2025.

The potential downsides to our investment thesis include negative results from the three confirmatory Phase III trials in neurology, as well as the risk of refinancing

- We have also identified risks that could have a negative impact on AB Science's share price:
  - **Negative results across all three confirmatory phase III trials in neurological indications:** Our investment thesis assumes that only one success out of the three confirmatory Phase III is sufficient to make considerable financial gains. If the three studies were to fail, AB Science's share price might get heavily impacted, and focus should be turned towards the new AB8939 platform.
  - **Refinancing risk:** The risk of not finding a healthy refinancing option during this low point of interest in biotech exists for any biotech company, but it is mitigated by the fact that AB Science successfully managed to raise an average of €18 million every year since the start of the biotech market crash in February 2021. This accomplishment gives confidence in the company's ability to find refinancing options this year, in a more stabilized biotech market.

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