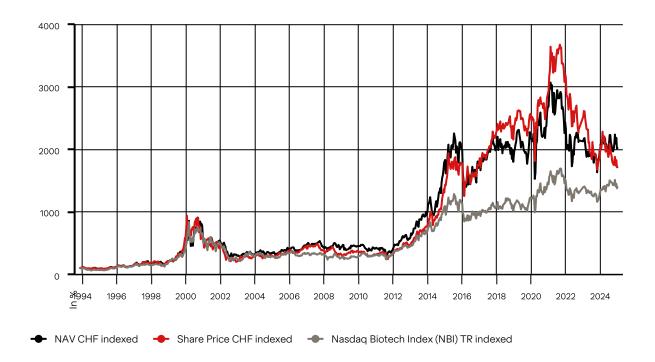
# Business report

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# Performance/Multi-year comparison

## Indexed performance since launch

#### BB Biotech AG (SIX)-CHF



#### Annual performance

31.12.2024

	SHARE	NAV	NBI TR
2024	(13.5%)	3.0%	7.6%
2023	(18.1%)	(7.4%)	(4.8%)
2022	(24.3%)	(11.0%)	(9.1%)
2021	8.3%	(11.5%)	3.0%
2020	19.3%	24.3%	15.8%

### Cumulated performance

31.12.2024

	SHARE	NAV	NBI TR
1 year	(13.5%)	3.0%	7.6%
3 years	(46.4%)	(15.1%)	(6.9%)
5 years	(30.7%)	(6.6%)	11.0%
10 years	22.8%	16.9%	31.6%
since inception 1)	1 612%	1 918%	1 293%

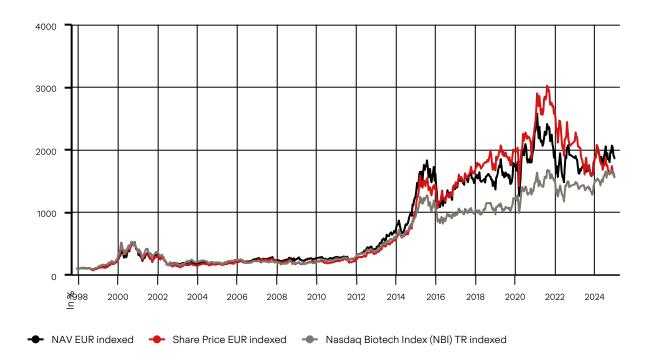
<sup>1 09.11.1993</sup> 

# Annualized performance 31.12.2024

	SHARE	NAV	NBI TR
1 year	(13.5%)	3.0%	7.6%
3 years	(18.8%)	(5.3%)	(2.4%)
5 years	(7.1%)	(1.4%)	2.1%
10 years	2.1%	1.6%	2.8%
since inception 1)	9.5%	10.1%	8.8%

<sup>1 09.11.1993</sup> 

#### **BB BIOTECH AG (XETRA)-EUR**



#### Annual performance

31.12.2024

SHARE	NAV	NBI TR
(14.1%)	1.7%	6.3%
(15.2%)	(1.3%)	1.3%
(19.0%)	(6.7%)	(4.5%)
13.3%	(7.8%)	7.4%
18.1%	24.8%	16.1%
	(14.1%) (15.2%) (19.0%) 13.3%	(14.1%) 1.7% (15.2%) (1.3%) (19.0%) (6.7%) 13.3% (7.8%)

# Cumulated performance 31.12.2024

	SHARE	NAV	NBI TR	
1 year	(14.1%)	1.7%	6.3%	
3 years	(41.0%)	(6.3%)	2.8%	
5 years	(21.0%)	7.7%	28.2%	
10 years	54.6%	49.4%	68.5%	
since inception 1)	1 467%	1763%	1 459%	

<sup>1 10.12.1997</sup> 

## Annualized performance 31.12.2024

	SHARE	NAV	NBI TR
1 year	(14.1%)	1.7%	6.3%
3 years	(16.1%)	(2.2%)	0.9%
5 years	(4.6%)	1.5%	5.1%
10 years	4.5%	4.1%	5.4%
since inception 1)	10.7%	11.4%	10.7%
since inception 1)	10.7%	11.49	6

<sup>1 10.12.1997</sup> 

## Multi-year comparison

	2024	2023	2022	2021	2020
Market capitalization at the end of the period (in CHF mn)	1 961.2	2 368.4	3 058.1	4 274.1	4 107.9
Net Asset Value at the end of the period (in CHF mn)	2 286.3	2 323.2	2 686.1	3 283.5	3 887.5
Number of shares (in mn)	55.4	55.4	55.4	55.4	55.4
Trading volume (in CHF mn)	974.0	906.3	1 482.0	2 101.0	2 315.6
Profit/(loss) (in CHF mn)	75.9	(206.6)	(357.8)	(404.8)	691.2
Closing price at the end of the period in CHF	35.40	42.75	55.20	77.15	74.15
Closing price at the end of the period in EUR	37.45	45.50	56.70	74.05	68.00
Stock performance (incl. distributions) 1)	(13.5%)	(18.1%)	(24.3%)	8.3%	19.3%
High/low share price in CHF	49.35/35.30	60.70/35.60	78.15/51.00	92.20/73.40	74.70/45.44
High/low share price in EUR	52.00/37.45	60.50/37.10	75.40/49.60	86.20/67.80	69.00/43.04
Premium/(discount) (annual average)	(6.6%)	7.5%	20.5%	19.5%	9.2%
Dividend in CHF (*proposal)	1.80*	2.00	2.85	3.85	3.60
Degree of investment (quarterly figures)	111.3%	113.7%	112.8%	108.6%	106.8%
Total Expense Ratio (TER) p.a. 2)	1.33%	1.34%	1.27%	1.22%	1.25%

All figures in CHF %, total return-methodology
 Based on market capitalization

# 2024: navigating challenges and seizing opportunities

#### Dear Shareholders

2024 marked a transformative year for BB Biotech and the broader biotech sector. Over the past four years, we have navigated NAV underperformance and a shift from our share price trading at a premium to a discount, driven by sector-wide volatility and our strategic focus on high-growth small and mid-cap companies. This emphasis, which became more pronounced following our 2018 pivot away from large-cap holdings, initially aligned well with biotech's momentum leading up to its 2021 peak. However, as market conditions reversed, our positioning magnified underperformance over the past three years.

While this period was challenging, it has also created a compelling investment opportunity. Many of our holdings now trade at historically low valuations despite delivering fundamental progress. Innovation remains the cornerstone of biotech investing, but disciplined valuation is equally critical for sustainable long-term returns.

Many of our holdings now trade at historically low valuations despite delivering fundamental progress.

At the outset of the pandemic, biotech companies were at the forefront of vaccine and therapeutic development, driving an unprecedented rally in the sector. However, beginning in mid-2021, investor sentiment shifted as macroeconomic pressures – including rising interest rates, inflationary concerns, and capital market constraints – intensified. The Federal Reserve's tightening cycle drove discount rates sharply higher, disproportionately affecting high-growth, long-duration sectors like biotech. The expectation of prolonged higher rates led to capital flowing into near-term cash-generating industries such as big tech and Al, leaving biotech at a relative disadvantage despite continued scientific progress.

Early in 2024, optimism around stabilizing inflation and potential rate cuts initially boosted risk assets, including biotech. However, by mid-year, prolonged inflationary pressures and rising long-term yields tempered those expectations. In September, a combination of moderating inflation figures and softening labor market data allowed the Fed to cut its key interest rate in three steps from 5.5% to 4.5%. Despite this, with US inflation still well above the Fed's 2% target, the room for further rate cuts remains limited. At its January 2025 policy meeting, the Fed signaled caution, holding rates steady as it assesses inflation risks, labor market dynamics, and potential policy shifts under the new US administration.

While these macroeconomic shifts shaped investor sentiment in 2024, longer-term demographic forces are also reshaping capital flows into biotech. Declining fertility rates and aging populations are creating structural pressures on healthcare systems, increasing demand for innovative therapies while reshaping capital allocation dynamics. Many retirees and income-focused investors are prioritizing capital return strategies, while generalist investors have shown a growing preference for dividend-paying stocks and fixed-income assets amid a higher-rate environment. Against this backdrop, BB Biotech's stable dividend policy remains an attractive differentiator in a sector traditionally focused on growth. This balance between long-term innovation and stable returns is further reflected in our dividend policy.

Today, this reset presents a rare opportunity. Many companies in the sector have significantly derisked their pipelines with mid to late-stage clinical data, yet valuations remain at early-stage levels. We are actively deploying capital to capture these opportunities, focusing on differentiated, high-conviction investments.

M&A activity, historically a key driver of biotech alpha, was relatively subdued across the sector in recent years. However, the landscape is evolving. While M&A is not the dominant driver of our investment thesis, our stock selection is adapting to this shift, placing greater emphasis on assets with strong clinical differentiation, clear commercial paths, and strategic relevance to large pharma buyers – factors that naturally improve M&A potential. At the same time, several of our core holdings have now matured, secured product approvals, or built growing revenue lines, making them more attractive strategic targets. As capital constraints ease and valuations stabilize, M&A could regain momentum – especially for companies with strong commercial assets and strategic relevance.

Encouragingly, 2024 marked more than a rebound – it signaled the early stages of a structural recovery in biotech.

Encouragingly, 2024 marked more than a rebound – it signaled the early stages of a structural recovery in biotech. While macroeconomic volatility remains a factor, investor focus is returning to fundamentals, with clinical data readouts, regulatory approvals, and commercial execution driving renewed momentum. For the first time in many quarters, multiple tail-end portfolio stories have begun to validate our investment thesis. In Q4, companies such as Scholar Rock, Wave Life Sciences, and Edgewise Therapeutics saw strong share price appreciation, reflecting renewed investor confidence. These developments, alongside broader sector tailwinds, contributed to significant benchmark outperformance and an absolute NAV gain in the final quarter of the year.

While the macroeconomic backdrop remains uncertain, biotech remains one of the most structurally attractive long-term investment themes. The combination of scientific breakthroughs, growing unmet medical need, and favorable valuation entry points provides a strong foundation for long-term returns.

At BB Biotech, we continue to balance high-growth innovation with stable capital returns. Since 2013, BB Biotech has consistently paid an annual dividend of 5% based on the average share price in December. For 2024, the Board of Directors will propose a dividend of CHF 1.80 per share at the next Annual General Meeting, ensuring continued alignment with shareholder interests while maintaining flexibility for reinvestment.

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This positive momentum has carried into 2025, underscored by Johnson & Johnson's USD 14.6 bn acquisition of one of our core holdings, Intra-Cellular Therapies. The transaction not only delivers a strong absolute and relative return but also enhances our ability to reinvest in new opportunities while sustaining shareholder returns through our dividend.

With these developments, BB Biotech enters 2025 well positioned and ready to seize opportunities in an evolving biotech landscape. As fundamentals reassert their importance and valuation dislocations create compelling entry points, we remain confident in the long-term value creation potential of our investment strategy, process, and evolving portfolio.

#### Share price performance and financial results

In 2024, BB Biotech shares delivered a total return of -13.5% in CHF and -14.1% in EUR, including the CHF 2.00 dividend paid in March 2024. Our Net Asset Value (NAV) performance showed greater resilience, increasing by 3.0% in CHF and 1.7% in EUR for the year, while declining by 4.6% in USD. For the full year 2024, we recorded a net profit of CHF 76 mn compared to a net loss of CHF 207 mn in 2023.

Full-year Performance	2024		2023	
	CHF	EUR	CHF	EUR
BB Biotech share price	-13.5%	-14.1%	-18.1%	-15.2%
BB Biotech NAV	3.0%	1.7%	-7.4%	-1.3%
NBI Index	7.6%	6.3%	-4.8%	1.3%
Net profit/loss	76 mn		-207 mn	

At the close of 2024, BB Biotech's share price was trading at a 15.2% discount to NAV in CHF, a notable shift from the 0.9% premium at the beginning of the year. This change reflects the ongoing volatility and subdued sentiment within the biotech sector. The Board remains committed to addressing this by balancing share buybacks and marketing strategies to enhance shareholder value.

Discount to NAV	February 18, 2025	YE 2024	YE 2023
Premium (+) / Discount (-), CHF	-10.9%	-15.2%	+0.9%

<sup>\*</sup>Editorial deadline

#### Outlook: opportunities amid challenges

As we look ahead to 2025 and beyond, it is important to step back and re-examine the forces shaping the biopharmaceutical industry. While fundamental drivers fuel innovation and growth, governing forces define its trajectory, determining how and when progress translates into real-world impact.

Fundamental drivers continue to propel biopharma's innovation and growth. Unmet medical needs, aging populations, and demographic shifts are increasing demand for novel therapies, particularly for cancer, cardiovascular, and neurodegenerative diseases. However, these must align with value-based pricing and sustainability, as healthcare systems prioritize affordability. Capital markets remain selective, favoring differentiation and clear commercialization strategies.

Meanwhile, regulatory frameworks, reimbursement models, and supply chain constraints shape market access. Policies like the Inflation Reduction Act (IRA) and Medicare drug price negotiations are altering pricing dynamics, while intellectual property protections face scrutiny as governments balance affordability with R&D incentives.

As these forces interact, the defining advantage in biopharma is not simply size or scale, but true innovation. The next wave of breakthrough medicines will not come from incremental improvements, but from differentiated therapies addressing high unmet medical needs in ways that traditional approaches alone cannot. Al-driven drug discovery, gene and cell

therapy, targeted protein degradation, RNA therapeutics, synthetic biology, and precision medicine are not just expanding the drug development toolbox – they are redefining treatment paradigms. The intersection of these technologies improves success rates, shortens development timelines, and creates entirely new market opportunities.

BB Biotech remains focused on investing in companies pursuing high-impact, differentiated medicines rather than incremental advancements. While optimizing existing therapies can provide commercial success, the greatest long-term value in biotech lies in platforms and approaches that redefine standards of care. The companies that successfully harness these technologies will be the leaders of the next decade, and this is where we aim to be positioned.

While optimizing existing therapies can provide commercial success, the greatest long-term value in biotech lies in platforms and approaches that redefine standards of care.

As biopharma continues to evolve, industry consolidation remains a natural response to innovation gaps and market pressures. The 20 largest biopharma companies collectively hold over USD 1 tr in deal-making capacity, with at least USD 200 bn in revenues at risk from patent expirations over the next five years, rising to at least USD 400 bn over the next decade as blockbusters like Keytruda, Darzalex, and Eliquis approach the end of their exclusivity. M&A is not simply a financial decision – it is a necessity for companies facing declining revenue streams and internal R&D limitations.

While 2024 saw a slowdown in biotech M&A, 2025 is shaping up to be a stronger year for deals. Some speculate that a more lenient FTC may ease restrictions, but valuation – not regulation – has been the primary constraint. As bid-ask spreads normalize and sellers adjust expectations, acquisitions should accelerate. Most acquisitions will likely be sub-USD 20 bn, where BB Biotech's core holdings are strong strategic fits. A recent example is Johnson & Johnson's USD 14.6 bn acquisition of Intra-Cellular Therapies, reinforcing the ongoing need for innovation in neuropsychiatry and validating our investment approach. Beyond strong returns, liquidity from such transactions provides the flexibility to reinvest in new opportunities across both public and crossover markets.

Against this backdrop, the current biotech investment landscape presents a rare opportunity. Many biotech companies with clinical differentiation are trading well below their intrinsic value, despite delivering pipeline progress, regulatory approvals, and commercial execution. After a prolonged period of underperformance relative to broader markets, biotech valuations have corrected sharply, particularly when compared to the continued expansion in technology stocks. This disconnect between scientific advancement and market valuation allows us to increase exposure to high-quality, mid to late-stage biotech at compelling prices, while selectively allocating capital to earlier-stage opportunities with asymmetric upside.

As the patent cliff looms and industry pressures mount, M&A will remain a key industry mechanism for growth, efficiency, and sustained innovation across biopharma. However, true value creation will come from companies developing novel, differentiated therapies that address significant unmet needs. This evolving landscape reinforces the need for a disciplined, high-conviction investment strategy that prioritizes scalable innovation, sustainable business models, and long-term value creation.

#### Strategy and process evolution: building for long-term success

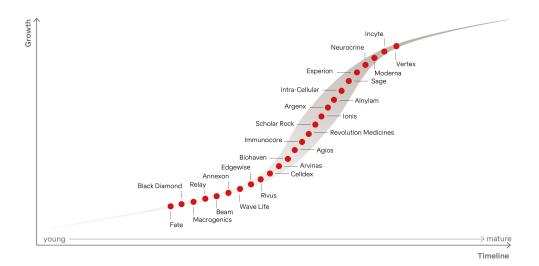
BB Biotech's structure as an investment company remains ideally suited to the unique dynamics of the biotech sector. We continue to emphasize a high-conviction portfolio, a long-term investment horizon of three or more years, and a focus on identifying transformational companies at the forefront of innovation. However, the challenges of recent years have underscored the importance of evolving our processes to enhance returns while mitigating risk.

We have implemented key adjustments in our valuation framework, making it more dynamic and responsive to market conditions. By emphasizing valuation scenarios, the impact of catalysts on these scenarios, and risk-adjusted returns, we are better equipped to allocate capital effectively, balancing upside potential with downside protection in an increasingly volatile environment.

We have implemented key adjustments in our valuation framework, making it more dynamic and responsive to market conditions.

Our approach to portfolio management is also evolving. We have refined our entry and exit strategies, exercising greater caution in the pace of capital deployment when investing in earlier-stage companies at the lower end of our S-curve. With investors increasingly prioritizing clinical validation and strong commercial positioning over early-stage plays, we further refined our focus toward high-conviction, differentiated assets. The tempering of the crossover boom and the higher cost of capital reinforce our selective approach to private investments, ensuring capital is deployed into late-stage companies with near-term public market prospects. This shift reflects both assumptions around long-term interest rates and cost of capital, as well as empirically higher volatility and uncertainty in risk-reward dynamics at the lower end of the S-curve.

#### BB Biotech's S-curve model



At the same time, we have enhanced discipline in divesting from both successful and underperforming investments. In the fourth quarter of 2024, we exited five positions:

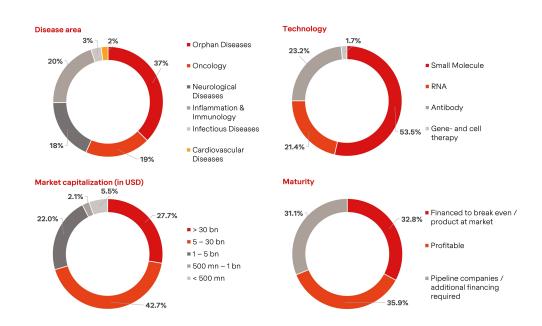
- Crispr Therapeutics and Exelixis delivered positive returns, but we lacked conviction in their long-term pipeline strength.
- Molecular Templates, Essa Pharma, and Generation Bio were exited following disappointing clinical outcomes or significant platform and business uncertainties.

These decisions reflect our commitment to maintaining a high-conviction portfolio while actively managing risk. Consequently, our portfolio ended 2024 with 26 positions, reflecting deliberate and disciplined resource allocation. Following the acquisition of Intra-Cellular Therapies, this number will further decline. However, we remain actively engaged in new investment opportunities, closely tracking the renewed IPO market and follow-on offerings. Given the shifting financing landscape, we are placing greater emphasis on differentiated assets with strong clinical data, rather than early-stage platform plays. New investment cases are actively being evaluated, and capital deployment is already underway. These investments will be reflected in our Q1 2025 results.

Over time, we aim to expand toward the upper limit of our investment guidelines, targeting 35 holdings. This expansion will focus on identifying transformative companies across the biotech lifecycle, ensuring a robust and adaptable portfolio.

In addition to listed companies, crossover investments remain an area of strategic interest. With a capacity to deploy up to 10% of the portfolio (currently at 2%) in private companies, these investments offer unique advantages, particularly greater information arbitrage potential and relatively lower competition from market participants. However, our approach remains consistent with our public investment strategy – we prioritize new investments in companies that have or are close to key clinical or commercial inflection points, ensuring a comparable risk profile. Moreover, we focus on investments where we can actively support a path to the public markets within 12–18 months, leveraging our expertise and networks to facilitate successful transitions. Given current capital market conditions, we are highly selective in private investments, prioritizing opportunities with clear paths to public listings or partnerships.

Portfolio breakdown as at December 31, 2024



# Substantial fundamental progress in the portfolio throughout 2024

In 2024, BB Biotech's portfolio advanced through critical clinical and regulatory milestones, reflecting both opportunities and challenges. The final quarter brought particularly strong performance from smaller positions, reinforcing confidence in the long-term investment strategy.



#### Team evolution: strengthening expertise for the future

Leadership and team evolution have been key themes in 2024. We extend our heartfelt gratitude to Dr. Daniel Koller for his dedication over the past 20 years and his leadership over the last 13 years. His commitment has been instrumental in shaping BB Biotech's investment strategy and success. With Daniel's decision to step down, we are pleased with the appointment of one of his deputies, Dr. Christian Koch, as the new Head of the dedicated investment team within Bellevue Asset Management, which manages BB Biotech's investments. Christian has built deep expertise across therapeutic areas and drug technologies over more than a decade. He has played a pivotal role in leading our private investments, including Moderna and Rivus Pharmaceuticals, while spearheading the data science initiatives. In his new role as Head, Christian ensures both continuity and a clear strategic vision for disciplined growth.

Dr. Maurizio Bernasconi remains a pillar of stability, ensuring continuity as Deputy Head. Over the past decade, he has played a key role in driving many of our successful autoimmune investments and has enriched the team's capabilities in chemistry, particularly in understanding novel chemical modalities. As part of his Deputy Head function, he serves as the lead within the analyst team in Switzerland, guiding and driving research efforts.

As the leading hub for biotech innovation, commercialization, and financing, the US remains our focal point. We are committed to strengthening and expanding our presence in this critical market.

As the leading hub for biotech innovation, commercialization, and financing, the US remains our focal point. We are committed to strengthening and expanding our presence in this critical market. In this regard, the addition of Dr. Wendy Lam brings fresh perspectives and further strengthens the team with her deep expertise. With over a decade of biotech investment experience, she has a proven track record and an extensive network spanning both private and public markets. Since joining as Deputy Head on December 1, 2024, Wendy will lead the US office in New York, rebuilding our global research efforts and enhancing access to high-quality investment opportunities. Her deep relationships across the biotech

ecosystem – including executives, investors, bankers and thought leaders – will be instrumental in shaping our investment pipeline and providing broader strategic insights.

In Switzerland, Dr. Anna Guinot Aguado joined the investment team, bringing valuable expertise in oncology and biotech venture capital to deepen our insights in these areas. The team is actively evaluating opportunities to further expand specialized functions, for example in trading and legal. Recognizing the interconnected nature of biotech innovation, the investment team works across therapeutic areas, leveraging cross-sector insights to identify synergies and new opportunities. This collaborative approach sharpens the ability to invest in companies developing truly differentiated therapies with multi-indication potential, reinforcing BB Biotech's position at the forefront of biotech innovation.

#### Innovation pipeline: delivering transformative therapies

Our portfolio is positioned to benefit from high-impact advances across diverse therapeutic areas, with many of our holding reaching registrational clinical and regulatory milestones in 2025.

#### Immunology and inflammation

- Argenx Expanding Vyvgart with a new pre-filled syringe formulation (Q2), driving broader adoption in chronic inflammatory demyelinating polyneuropathy (CIDP) and earlier use in myasthenia gravis (MG), key to securing its status as a multibillion-dollar blockbuster.
- Incyte Phase III data for povorcitinib in hidradenitis suppurativa (Q1), offering an oral
  alternative to biologics. While povorcitinib won't offset Jakafi's loss of exclusivity later this
  decade, it provides a bridge to Incyte's more ambitious disease-modifying programs
  targeting CALR and JAKV617F mutations in myeloproliferative neoplasms (e.g.,
  myelofibrosis, polycythemia vera).
- Biohaven Updates on its MODE degrader platform, advancing next-generation therapies targeting reductions in IgG, IgA, and beyond.
- Annexon Early data on an oral C1q inhibitor for cold agglutinin disease (CAD).

#### Oncology

- Incyte Initial data for disease-modifying therapies targeting mCALR and JAKV617F mutations (Q4), with potential transformative impact on myeloproliferative neoplasms.
- Arvinas Phase III readout for vepdegestrant, an estrogen receptor degrader in breast cancer. The key question is whether it can differentiate by demonstrating efficacy in the overall population. Partner Pfizer is positioning it for frontline and adjuvant use as an antihormonal standard-of-care backbone.
- Black Diamond Therapeutics First results from its study targeting frontline non-classical EGFR mutations in NSCLC. Given its market cap and cost of capital, success hinges on response quality and depth in first-line treatment.

#### Rare diseases

- Ionis Pharmaceuticals Approvals and launches anticipated for its hereditary angioedema (HAE) and familial chylomicronemia syndrome (FCS) programs.
- Neurocrine Biosciences Launch of Crenessity for congenital adrenal hyperplasia (CAH), an overlooked market with significant price and volume potential.
- Agios Pharmaceuticals Mitapivat approval for thalassemia (Q3), following Phase III data and prior liver safety signals. Additional registrational data for sickle cell disease expected in Q4.
- Scholar Rock FDA approval and launch of apitegromab for spinal muscular atrophy (SMA) (Q3).
- Wave Life Sciences Key updates on its Duchenne muscular dystrophy (DMD) and RNAediting program for alpha-1 antitrypsin deficiency, with potential for accelerated approval.
- Beam Therapeutics First-in-human liver gene editing data via its base-editing platform (A1ATD), a key milestone for expansion into other rare diseases.

#### Cardiometabolic

- Alnylam Pharmaceuticals Market launch of Amvuttra for ATTR cardiomyopathy (H1), following stellar Helios-B data. This underscores Alnylam's push into broader diseases beyond rare conditions. The evolution toward (semi-)annual treatments could unlock a multibillion-dollar opportunity.
- Scholar Rock Following a successful Phase III trial in SMA, tracking approval and launch alongside proof-of-concept data for potential use in obesity. The goal is to mitigate muscle loss seen with incretin therapies when combined (Q2).
- Edgewise Therapeutics Proof-of-concept data for repeat doses of EDG-7500 in obstructive and non-obstructive hypertrophic cardiomyopathy (HCM).
- Rivus Pharmaceuticals (private) Large Phase II proof-of-concept study in metabolicallyassociated steatohepatitis (MASH), focusing on liver fat loss and weight loss over 6 months.

#### Central nervous system disorders

Vertex Pharmaceuticals – Launch of Journavx (VX-548) for acute pain (Q1), the first non-opioid pain treatment in 20 years. While initially positioned for acute pain, a potential expansion into chronic pain could transform this into a significant franchise alongside its cystic fibrosis business.

#### Infectious diseases

 Moderna – Final results for its pivotal cytomegalovirus (CMV) vaccine trial expected in 2025. Following positive interim data, this is a crucial step in restoring confidence in Moderna's latent virus vaccine platform. Additionally, approval and launch of the COVID+flu combination vaccine could help expand its respiratory franchise.

#### Regulatory environment: navigating policy shifts

The 2024 US presidential election introduced significant market volatility, reflecting the biotech sector's sensitivity to political shifts. Markets initially reacted positively to Donald Trump's return, expecting pro-business policies, deregulation, and tax incentives. However, optimism was tempered by the controversial nomination of Robert F. Kennedy Jr. as Secretary of Health and Human Services (HHS), whose skepticism toward vaccines and regulatory policies has raised concerns. His leadership could disrupt key agencies –including the FDA, CDC, and CMS – impacting drug approvals, reimbursement structures, biomedical research funding, and public health initiatives.

Regulatory uncertainty remains a valuation overhang, particularly in vaccines, where shifting FDA, CDC, and CMS policies create approval and reimbursement risks. While macroeconomic factors are priced into biotech valuations, policy-driven risks – especially around vaccine innovation and pandemic preparedness – remain underpriced, creating both risks and opportunities. This is particularly relevant for Moderna, which is expanding its respiratory vaccine franchise and exploring latent virus vaccines. Changes in public health funding, pandemic preparedness, and reimbursement could materially impact pipeline prioritization and commercial execution for vaccine leaders.

The appointment of Dr. Martin Makary as FDA Commissioner has provided stability. Known for his pragmatic, data-driven approach, he is expected to maintain rigorous standards while streamlining regulatory pathways. The FDA remains the global benchmark for drug approvals, with 50 novel drugs approved in 2024, slightly below 55 in 2023 but above 37 in 2022 – averaging 47 approvals per year over the past decade.

Broader regulatory shifts present both challenges and opportunities. The Inflation Reduction Act (IRA) continues to reshape pricing dynamics, with Medicare's drug price negotiations introducing pressures but also favoring companies with strong value propositions. The

industry needs to remain engaged with policymakers to ensure that pricing reforms encourage innovation without stifling access to life-saving therapies.

Leadership changes at HHS and the FDA will shape regulatory timelines and industry priorities in the years ahead. The newly formed government efficiency institution remains a wild card, with an unclear impact on agency operations and industry oversight. This evolving policy landscape reinforces the need for strategic adaptability. BB Biotech is well-positioned to navigate these shifts, leveraging our disciplined investment approach to align with regulatory developments and support our portfolio companies in achieving key milestones.

#### Commitment to shareholders

At BB Biotech, we place great emphasis on alignment with shareholder interests. Since introducing our dividend policy in 2013, we have consistently prioritized delivering tangible returns while maintaining a long-term focus on portfolio growth. In 2024, the dividend once again proved to be a key component of shareholder value, offering an attractive yield amid heightened market uncertainty.

Beyond capital returns, shareholder engagement remains a cornerstone of our approach. Over the past year, we have conducted hundreds of meetings with investors, incorporating their valuable insights into our decision-making processes. Additionally, we recognize the growing importance of environmental, social, and governance (ESG) factors. In 2024, BB Biotech received an A rating from MSCI, underscoring our commitment to sustainable investing and responsible portfolio management.

As we look ahead, BB Biotech remains anchored by its core principles – long-term investing, disciplined capital allocation, and an unwavering commitment to shareholder value. The challenges of recent years have tested our resolve, but they have also reinforced the importance of adaptability and innovation in navigating the evolving biotech landscape.

We are optimistic about the opportunities ahead, driven by transformative advances in science, a revitalized M&A landscape, and renewed growth potential across our portfolio. Our team is committed to executing a strategy that balances stability with bold action, ensuring BB Biotech delivers sustainable value for years to come.

We appreciate your continued support and look forward to discussing our vision and strategy at the Annual General Meeting on March 19, 2025, at the Pavillon im Park, Steigstrasse 26, 8200 Schaffhausen, Switzerland. Proxy voting forms will be available for those unable to attend.

Together, we will chart a path toward a bright future for BB Biotech and the broader biotech industry to support the development of breakthrough medicines for patients.

Sincerely,

The Board of Directors of BB Biotech AG

**Dr. Thomas von Planta** Chairman

Laura Hamill Member

Camilla Soenderby

Member

Dr. Clive Meanwell
Vice-Chairman
Dr. Pearl Huang
Member

Prof. Dr. Mads Krogsgaard Thomsen

Member

# Substantial fundamental progress in the portfolio throughout 2024

In 2024, BB Biotech's portfolio advanced through critical clinical and regulatory milestones, reflecting both opportunities and challenges. The final quarter brought particularly strong performance from smaller positions, reinforcing confidence in the long-term investment strategy.

#### Q12024

**Vertex Pharmaceuticals** reported encouraging Phase III results for VX-548, the first non-opioid pain treatment in two decades. While it did not outperform hydrocodone in acute pain, the company is now focusing on more promising chronic pain studies, with results expected in 2026. Chronic pain affects approximately 50 million US adults, presenting a substantial market opportunity for effective non-opioid alternatives. The shift away from opioids is particularly relevant amid the ongoing opioid crisis, reinforcing the strong commercial potential of VX-548 if successful. This program is now a key growth driver for Vertex, expanding its pipeline beyond cystic fibrosis.

**Celldex Therapeutics'** barzolvolimab showed strong Phase II data in chronic spontaneous urticaria (CSU), demonstrating significant efficacy, including in patients unresponsive to standard-of-care treatments like Xolair. The drug is positioned as a best-in-class therapy, but its safety profile requires monitoring due to risks of neutropenia and hypopigmentation. Currently in Phase III, barzolvolimab faces competition from «me-too» drugs and oral KIT inhibitors but retains strong commercial potential.

**Argenx** achieved a major milestone with positive Phase II data for efgartigimod in Sjögren's disease, representing its largest potential indication and more than doubling Vyvgart's current label. With 330 000 US patients, Sjögren's offers a substantial opportunity, and the company has already initiated Phase III trials. Despite anticipated FcRn competition, Vyvgart continues to lead the field.

**Crispr Therapeutics** and **Vertex Pharmaceuticals** secured the first-ever FDA approval for a gene-editing therapy, Casgevy, in transfusion-dependent beta thalassemia. However, the commercial opportunity remains limited due to a small eligible US patient population. Given strategic concerns over Crispr's pipeline, BB Biotech exited its position after concluding that their approach to allogeneic CAR-T therapies and widespread disease targeting lacked long-term viability.

#### Q2 2024

**Alnylam Pharmaceuticals'** HELIOS-B Phase III trial for vutrisiran in ATTR cardiomyopathy delivered one of the most significant biotech milestones of 2024. The therapy demonstrated a 30-35% relative risk reduction in all-cause mortality, a transformative clinical outcome in a high-value cardiovascular market. With over 100 000 US patients and Pfizer's Vyndaqel/Vyndamax already generating multi-billion-dollar sales, vutrisiran is positioned to become a dominant therapy upon its anticipated 2025 approval. Alnylam is also advancing ALN-SC04, a

next-generation RNA therapy with a lower royalty burden and potential for annual dosing, reinforcing its leadership in RNAi-based cardiometabolic disease treatment. This result strengthens our conviction in Alnylam's ATTR franchise and marks an inflection point in its evolution from a rare disease company to a broader RNAi-based biotech leader with multi-therapeutic area ambitions.

**Agios Pharmaceuticals** reported positive Phase III data for mitapivat in transfusion-dependent thalassemia (TDT), reinforcing its first-in-class position as a pyruvate kinase activator. However, safety concerns arose with liver injury observed in a small number of patients, requiring label updates. Agios is also developing mitapivat for sickle cell disease, where competitors have struggled. We expect approval for TDT in Q3 2025, and for sickle cell disease in 2026 if the upcoming Phase III data are positive.

Intra-Cellular Therapies' Caplyta (lumateperone) reported some of the strongest Phase III data in major depressive disorder (MDD), showing a significant MADRS score improvement across two consistent studies. MDD is a massive market, and Caplyta's peak sales are projected to exceed USD 5 bn, with Johnson & Johnson acquiring the company for USD 14.6 bn. A key driver of value was a patent litigation settlement extending exclusivity until ~2040, removing major IP risks.

**Macrogenics'** vobra duo (B7-H3 ADC) was discontinued following five treatment-related deaths in the Phase II TAMARACK study in prostate cancer. The company has pivoted to a next-generation ADC with a novel payload and linker, now in Phase I clinical trials. However, competition has intensified, and Macrogenics is now trading near cash levels, relying on non-dilutive funding sources from partner milestones.

**Sage Therapeutics** suffered another setback as SAGE-718 (dalzanemdor) failed all Phase II trials in Alzheimer's, Parkinson's, and Huntington's disease. This latest failure compounds issues stemming from SAGE-217 (Zurzuvae), which was only approved for postpartum depression (PPD) and not MDD, with questionable efficiency of economics for Sage given the profit sharing with partner Biogen.

**Argenx** secured FDA approval for Vyvgart Hytrulo (SC formulation) in CIDP, further strengthening its immunology franchise. CIDP is expected to be a similarly large or larger opportunity than myasthenia gravis (MG), with potential for higher dosing frequency, leading to increased revenue per patient. The subcutaneous formulation improves convenience, but competition from FcRn inhibitors is expected.

#### Q3 2024

**Ionis Pharmaceuticals** reported promising Phase I/II data for ION582 in Angelman syndrome, demonstrating consistent improvements in cognition, communication, and motor function. With 330 000 potential patients, Angelman is a sizable, rare disease market. A Phase III trial will begin in H1 2025, positioning ION582 as a strong contender against Ultragenyx's gene therapy (GTX-102).

**Neurocrine Biosciences** reported Phase II data for NBI-568, a muscarinic receptor agonist in schizophrenia, which fell short of expectations. Given last year's Karuna and Cerevel acquisitions, there was heightened anticipation around the disclosure, though Cerevel's asset has since failed. Our investment thesis remains centered on Ingrezza's continued growth and the launch of Crenessity, while we see the psychiatry pipeline – including AMPA and muscarinic programs – as high risk but optional value. These modalities face historically high placebo responses and clinical variability. Neurocrine recently advanced its AMPA program into Phase III after Takeda declined co-commercialization, making it a higher-risk, higher-spending, but potentially higher-reward asset.

**Biohaven's** troriluzole delivered an unexpected Phase III win in spinocerebellar ataxia (SCA), achieving a 50–70% reduction in disease progression over three years. BB Biotech's primary investment thesis in Biohaven remains the MoDE degrader platform for IgG-lowering diseases, but this success validates the company's broader neurology pipeline.

**Rivus Pharmaceuticals'** HU6 (controlled metabolic accelerator) reported positive Phase IIa data in obesity-related heart failure (HFpEF), showing significant weight loss while preserving muscle mass. A large Phase II proof-of-concept study in MASH (metabolic dysfunction-associated steatohepatitis) is expected in 2025, and BB Biotech continues to view Rivus as a high-potential private investment.

**Edgewise Therapeutics'** EDG-7500 demonstrated the strongest pharmacodynamic effects ever seen in hypertrophic cardiomyopathy (HCM). Unlike myosin inhibitors (mavacamten, aficamten), which reduce LVEF and require REMS monitoring, EDG-7500 selectively targets the sarcomere, maintaining LVOT reductions without impacting systolic function. A Phase II study in both obstructive and non-obstructive HCM will read out in Q1 2025, with potential expansion into HFpEF, a multi-million-patient market.

**Wave Life Sciences** reported promising interim results for WVE-N531 in Duchenne muscular dystrophy, with dystrophin expression levels on par with the best available data, though cross-exon and assay comparisons remain challenging. The therapy's favorable safety and potential for monthly dosing could differentiate it, while regulatory clarity on accelerated approval in Q1 2025 would further derisk the asset. We stepped onto Wave based on stereopure chemistry where first generations of exon skipping and ASOs disappointed, later shifting toward RNA editing and the GSK-partnered alpha-1 program. However, with WVE-N531's progress and the potential for a broader DMD franchise, exon skipping is becoming a more tangible value driver within Wave's RNA-based platform.

#### Q4 2024

Scholar Rock's apitegromab met its primary endpoint in the Phase III SAPPHIRE trial for non-ambulatory spinal muscular atrophy (SMA) types 2 and 3, validating BB Biotech's investment thesis. As the first muscle-directed therapy for SMA, apitegromab has the potential to enhance motor function beyond existing SMN-targeting treatments and could see broad adoption as an add-on to Spinraza and Evrysdi. With a Biologics License Application (BLA) filing expected in Q1 2025, regulatory clarity is a near-term catalyst. Additionally, its exploration in obesity-related muscle loss (Phase II EMBRAZE trial, Q2 2025 readout) could expand its market potential beyond SMA. Scholar Rock's TGF- $\beta$  signaling platform strengthens its M&A appeal for neuromuscular players, positioning it as a high-value strategic asset.

Argenx's decision to advance efgartigimod SC in the Phase II/III ALKIVIA trial for idiopathic inflammatory myopathies (IIM) reinforces its leadership in FcRn-targeted therapies and confirms expansion potential beyond myasthenia gravis (MG) and CIDP. While FcRn inhibitors are facing increased competition from novel entrants (e.g., nipocalimab, rozanolixizumab), Argenx remains ahead with multiple label expansions, best-in-class pharmacology, a subcutaneous formulation advantage, and long-term physician adoption. IIM is a high-value orphan opportunity, and if successful, efgartigimod SC could unlock a meaningful new commercial market. This progress aligns with our investment in companies executing well on franchise expansion and leadership in rare diseases.

**Wave Life Sciences** achieved a first-in-human proof-of-mechanism for RNA editing with WVE-006 in alpha-1 antitrypsin deficiency (AATD), nearly reaching the therapeutic threshold at the lowest dose, validating its A-to-I RNA editing approach. With GSK set to take over registrational development, this derisks the path to late-stage clinical trials and potential commercialization. Beyond AATD, Wave is expanding its RNA editing pipeline, while advancing exon-skipping, ASOs, and siRNA programs in obesity and neuromuscular diseases, reinforcing its position as a leading RNA therapeutics platform.

**Essa Pharma** terminated its Phase II trial for masofaniten in metastatic castration-resistant prostate cancer (mCRPC) after a pre-specified interim analysis showed insufficient efficacy and safety concerns. The trial tested masofaniten in combination with enzalutamide, aiming to improve on standard-of-care outcomes, but the results did not support further development. Given the lack of late-stage assets and increased competition in the mCRPC space, Essa now faces strategic uncertainty and may need to pivot or seek external partnerships. BB Biotech exited its position during the event-driven high liquidity, mitigating further downside risk.

Incyte's decision to pause patient enrollment in the Phase II study of MRGPRX2 in chronic spontaneous urticaria (CSU) due to preclinical toxicology concerns and to terminate MRGPRX4 (CP) after disappointing Phase II efficacy data raises questions about the strategic rationale behind its USD 750 mn acquisition of Escient Pharmaceuticals. This outcome reinforces Incyte's suboptimal track record in business development, as previous acquisitions have yet to deliver meaningful late-stage pipeline additions. Furthermore, even if successful, these programs would not have meaningfully addressed Incyte's looming Jakafi loss-of-exclusivity (LOE) challenge, given their early-stage nature and extended commercialization timelines. Instead, we see Incyte's best path forward in its disease-modifying CALR and JAKV617F myeloproliferative neoplasm (MPN) programs, which could provide a longer-term strategic solution to sustain its hem-onc franchise.

**Revolution Medicines'** RAS(ON) inhibitors (RMC-6236, RMC-9805) are delivering the best pancreatic cancer data ever seen. The multi-selective inhibitor (6236) already outperforms chemo in late-line disease, with a Phase III 2L study underway. The company is also exploring combo with chemo and a doublet regimen with the G12D-specific inhibitor (9805) to enter frontline treatment. Beyond pancreatic cancer, expansion into lung and colorectal cancer remains the major upside driver.

**Vertex Pharmaceuticals** reported Phase II results for suzetrigine (VX-548) in lumbosacral radiculopathy (LSR), meeting its primary endpoint with statistically significant pain reduction. However, a high placebo response complicated data interpretation, raising uncertainty about its differentiation in neuropathic pain. Despite this, Vertex is advancing a Phase III trial in diabetic peripheral neuropathy (DPN) and planning a broader registrational program that includes LSR, signaling continued commitment to its non-opioid pain strategy. Beyond suzetrigine, Vertex is developing a pipeline of selective sodium channel inhibitors, aiming to create a differentiated pain portfolio. The success of this franchise will determine whether Vertex can extend its leadership in a new therapeutic area.

**Neurocrine Biosciences** secured FDA approval for Crenessity as an adjunctive treatment for congenital adrenal hyperplasia (CAH), reinforcing its leadership in rare endocrine disorders. With no existing FDA-approved medical therapy for CAH, Crenessity fills a significant unmet need by offering glucocorticoid replacement therapy while managing androgen levels, aiming to reduce long-term steroid exposure risks. While the primary investment thesis for Neurocrine remains centered on Ingrezza's continued growth, the approval of Crenessity strengthens the company's endocrine franchise and adds a durable revenue stream. Meanwhile, Neurocrine's psychiatry pipeline remains high risk but optional. The AMPA program recently entered Phase III after Takeda declined co-commercialization, increasing investment costs but also potential upside. Muscarinic approaches, while mechanistically interesting, remain at an early stage with historically high failure rates in CNS.

Overall, 2024 showcased significant progress across BB Biotech's portfolio, balancing expansion in high-conviction franchises with disciplined exits in underperforming assets. The year's milestones reinforce our commitment to long-term value creation through fundamental-driven biotech investing.

# Portfolio at a glance

#### Securities as at December 31, 2024

Company	Number of securities	Change since 31.12.2023	Local currency	Share price	Market value in CHF mn	In % of securities	In % of shareholders' equity	In % of company
Argenx SE	591 000	(234 000)	USD	615.00	329.8	13.7%	14.4%	1.0%
Ionis Pharmaceuticals	7 850 000	(740 000)	USD	34.96	249.0	10.3%	10.9%	5.0%
Neurocrine Biosciences	1820 000	(590 000)	USD	136.50	225.4	9.4%	9.9%	1.8%
Intra-Cellular Therapies	2 425 000	(615 000)	USD	83.52	183.8	7.6%	8.0%	2.3%
Revolution Medicines	4 374 300	(672 400)	USD	43.74	173.6	7.2%	7.6%	2.4%
Vertex Pharmaceuticals	475 000	(165 000)	USD	402.70	173.6	7.2%	7.6%	0.2%
Alnylam Pharmaceuticals	760 000	(99 700)	USD	235.31	162.3	6.7%	7.1%	0.6%
Incyte	2 150 000		USD	69.07	134.7	5.6%	5.9%	1.1%
Agios Pharmaceuticals	3 515 150	(484 850)	USD	32.86	104.8	4.4%	4.6%	6.2%
Scholar Rock Holding	2 486 707	353 982	USD	43.22	97.5	4.1%	4.3%	2.7%
Celldex Therapeutics	3 071 615	655 319	USD	25.27	70.4	2.9%	3.1%	4.6%
Biohaven	2 040 853	965 853	USD	37.35	69.2	2.9%	3.0%	2.0%
Moderna	1600 000	(291 075)	USD	41.58	60.4	2.5%	2.6%	0.4%
Wave Life Sciences	4 094 458	(400 000)	USD	12.37	46.0	1.9%	2.0%	2.7%
Arvinas	2 380 000	(114 531)	USD	19.17	41.4	1.7%	1.8%	3.5%
Rivus Pharmaceuticals 1)			USD		37.4	1.6%	1.6%	
Edgewise Therapeutics	1 428 929	1 428 929	USD	26.70	34.6	1.4%	1.5%	1.5%
Beam Therapeutics	1 518 121	825 000	USD	24.80	34.2	1.4%	1.5%	1.8%
Immunocore	1 205 464	239 810	USD	29.50	32.3	1.3%	1.4%	2.4%
Macrogenics	9 929 963	_	USD	3.25	29.3	1.2%	1.3%	15.8%
Relay Therapeutics	7 375 000	1 450 000	USD	4.12	27.6	1.1%	1.2%	4.4%
Annexon	5 157 290	5 157 290	USD	5.13	24.0	1.0%	1.0%	4.8%
Sage Therapeutics	4 460 693	955 693	USD	5.43	22.0	0.9%	1.0%	7.3%
Esperion Therapeutics	9 944 064	5 750 000	USD	2.20	19.9	0.8%	0.9%	5.0%
Black Diamond Therapeutics	8 517 839	_	USD	2.14	16.5	0.7%	0.7%	15.1%
Fate Therapeutics	4 839 779		USD	1.65	7.2	0.3%	0.3%	4.2%
Molecular Templates – Warrants, 2.4.29	769 334	769 334	USD	0.00	0.0	0.0%	0.0%	
Radius Health – Contingent Value Right	8 733 538		USD	0.00	0.0	0.0%	0.0%	
Total securities					2 406.9	100.0%	105.3%	
Other assets					0.5		0.0%	
Other payables					(121.1)		(5.3%)	
Net Asset Value					2 286.3		100.0%	

<sup>&</sup>lt;sup>1</sup> Unlisted company

Exchange rate as at 31.12.2024: USD/CHF: 0.9074