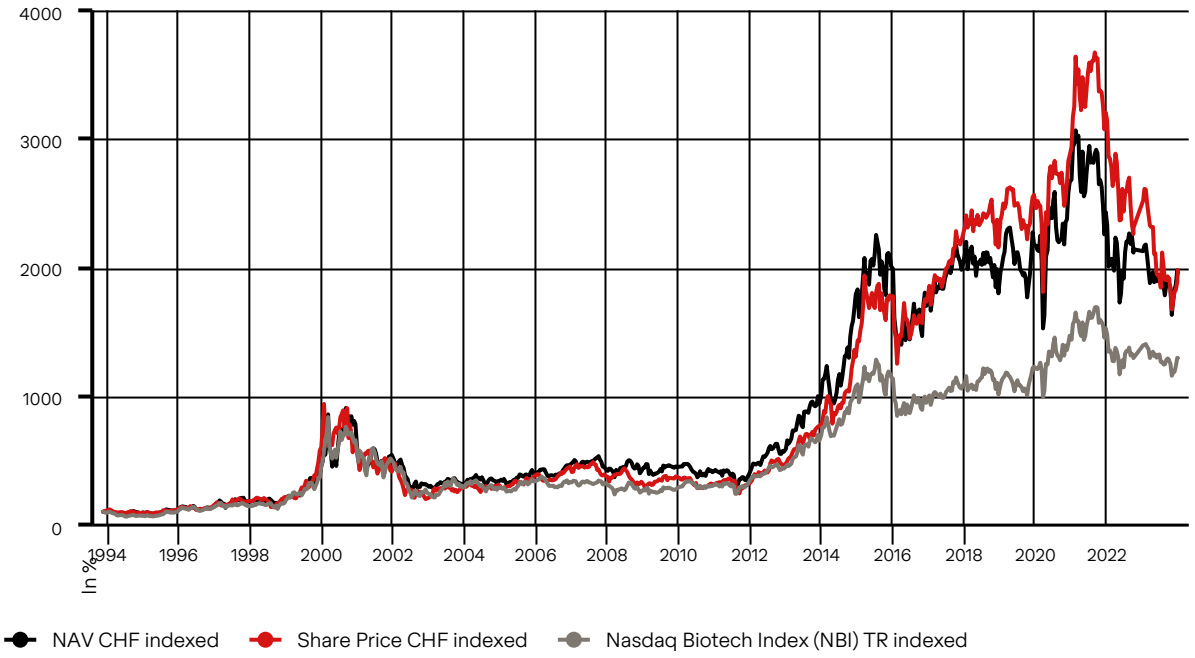
Business report

Performance/Multi-year comparison

Indexed performance since launch

BB Biotech AG (SIX)-CHF



Annual performance

31.12.2023

	SHARE	NAV	NBI TR
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%
2019	18.5%	23.4%	23.0%

Cumulated performance

31.12.2023

	SHARE	NAV	NBI TR
1 year	(18.1%)	(7.4%)	(4.8%)
3 years	(32.9%)	(27.0%)	(10.9%)
5 years	(5.0%)	11.9%	27.0%
10 years	149%	96%	84%
since inception [1)]	1 880%	1 860%	1 196%

[1] 09.11.1993

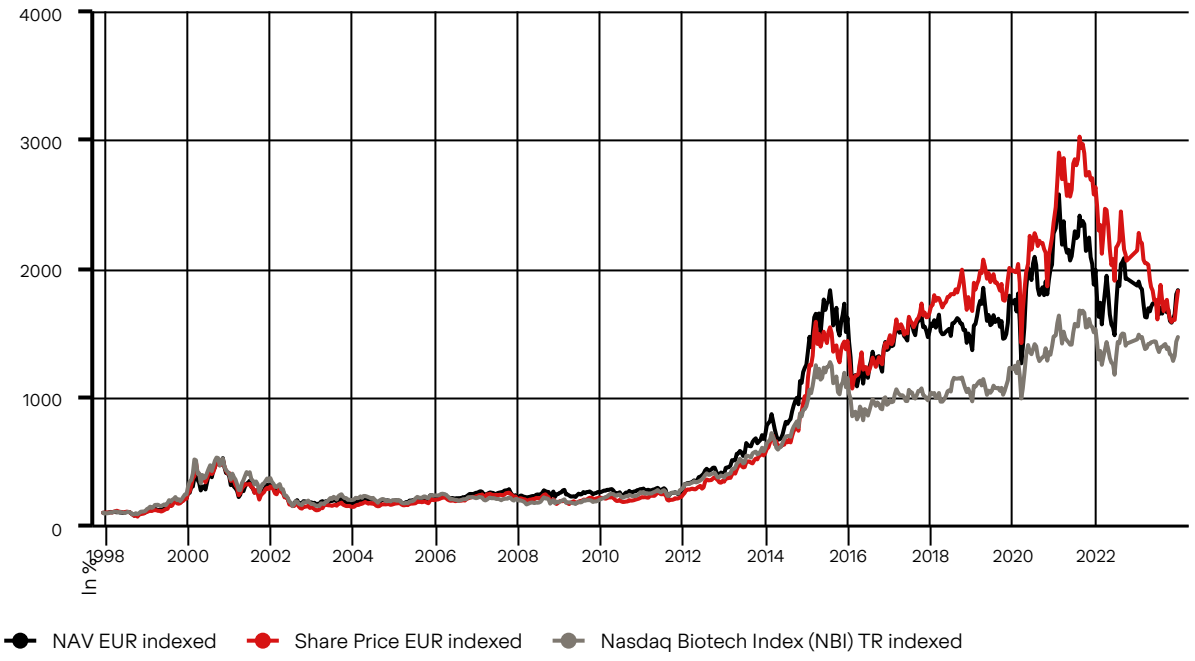
Annualized performance

31.12.2023

	SHARE	NAV	NBI TR
1 year	(18.1%)	(7.4%)	(4.8%)
3 years	(12.4%)	(10.0%)	(3.8%)
5 years	(1.0%)	2.3%	4.9%
10 years	9.5%	6.9%	6.3%
since inception [1)]	10.4%	10.4%	8.9%

[1] 09.11.1993

BB BIOTECH AG (XETRA)-EUR



Annual performance

31.12.2023

	SHARE	NAV	NBI TR
2023	(15.2%)	(1.3%)	1.3%
2022	(19.0%)	(6.7%)	(4.5%)
2021	13.3%	(7.8%)	7.4%
2020	18.1%	24.8%	16.1%
2019	23.4%	28.1%	27.6%

Cumulated performance

31.12.2023

	SHARE	NAV	NBI TR
1 year	(15.2%)	(1.3%)	1.3%
3 years	(22.2%)	(15.1%)	3.9%
5 years	13.4%	35.7%	53.9%
10 years	223%	159%	143%
since inception [1)]	1 724%	1 731%	1 367%

[1] 10.12.1997

Annualized performance

31.12.2023

	SHARE	NAV	NBI TR
1 year	(15.2%)	(1.3%)	1.3%
3 years	(8.0%)	(5.3%)	1.3%
5 years	2.5%	6.3%	9.0%
10 years	12.4%	10.0%	9.3%
since inception [1)]	11.8%	11.8%	10.8%

[1] 10.12.1997

Multi-year comparison

	2023	2022	2021	2020	2019
Market capitalization at the end of the period (in CHF mn)	2 368.4	3 058.1	4 274.1	4 107.9	3 670.3
Net Asset Value at the end of the period (in CHF mn)	2 323.2	2 686.1	3 283.5	3 887.5	3 393.0
Number of shares (in mn)	55.4	55.4	55.4	55.4	55.4
Trading volume (in CHF mn)	906.3	1 482.0	2 101.0	2 315.6	2 004.2
Profit/(loss) (in CHF mn)	(206.6)	(357.8)	(404.8)	691.2	677.4
Closing price at the end of the period in CHF	42.75	55.20	77.15	74.15	66.25
Closing price at the end of the period in EUR	45.50	56.70	74.05	68.00	61.40
Stock performance (incl. distributions) [1)]	(18.1%)	(24.3%)	8.3%	19.3%	18.5%
High/low share price in CHF	60.70/35.60	78.15/51.00	92.20/73.40	74.70/45.44	73.20/59.35
High/low share price in EUR	60.50/37.10	75.40/49.60	86.20/67.80	69.00/43.04	64.70/52.10
Premium/(discount) (annual average)	7.5%	20.5%	19.5%	9.2%	11.8%
Dividend in CHF (*proposal)	2.00*	2.85	3.85	3.60	3.40
Degree of investment (quarterly figures)	113.7%	112.8%	108.6%	106.8%	109.1%
Total Expense Ratio (TER) p.a. [2)]	1.34%	1.27%	1.22%	1.25%	1.26%

[1] All figures in CHF %, total return-methodology
[2] Based on market capitalization

Shareholder letter

In 2023, global equity performed better than anticipated by many. The US central bank moderated and then paused interest rate hikes. These developments resulted in a year-end bond market rally and encouraged equity markets further – but led to a noticeable devaluation of the USD, particularly relative to the CHF. Additionally, the year witnessed an uptick in takeover activities. The biotech sector made strong gains as the year closed. BB Biotech achieved significant gains in the fourth quarter.

Dear Shareholders

During the last quarter of 2023, global equity indices extended their 2023 gains. The US central bank held rates steady in the fall, lifting market sentiment in the last two months of 2023.

The US markets traded to all-time highs: The S&P 500 gained 26.3% in USD for the year, the Nasdaq 100 gained 55.1% in USD. European equities followed: The Euro Stoxx 50 was up 23.2% in EUR and the Dax was up 20.3% in EUR. Healthcare markets nevertheless underperformed in 2023, with total returns for the MSCI World Healthcare Index of +4.3% in USD and for the Nasdaq Biotech Index of +4.6% in USD – up slightly for the full year 2023.

The central bank action devalued the USD against most international currencies in 2023, particularly (and of central importance for BB Biotech's reporting currency), the Swiss franc, which strengthened 9% versus the US Dollar.

BB Biotech's fourth quarter share return was +3.4% in CHF and +7.1% in EUR. This was encouraging but not enough to reverse earlier 2023 losses. The total return for 2023, including the dividend payment of CHF 2.85 in March 2023, was –18.1% in CHF, –15.2% in EUR.

Fourth quarter net asset value performance started badly in October but saw a rally of almost 30% (in USD) from October lows to the end of year. Net asset value performance in the last quarter of 2023 was +14.2% in USD, respectively +5.0% in CHF. Fourth quarter gains of CHF 109 mn compare to the net loss of CHF 35 mn for the fourth quarter 2022. This may be signaling a strengthening biotech market.

Nevertheless, for full year 2023, NAV performance including the dividend was +1.8% in USD but –7.4% in CHF thanks to the USD devaluation. Consolidated full year 2023 data showed a net loss of CHF 207 mn for 2023 compared to a net loss of CHF 358 mn for 2022.

A proposed dividend of CHF 2.00 per share

Dividend 2024

CHF 2.00

(proposed)

The Board of Directors will propose a regular dividend of CHF 2.00 per share at the AGM. A 5% dividend yield will be applied to the average share price of December 2023, consistent with the dividend policy introduced in 2013.

Changes to the Board of Directors

Dr. Erich Hunziker has informed the Board of Directors that he will not stand for re-election at the upcoming Annual General Meeting and will step down after the AGM. The Board expresses its deepest gratitude for the remarkable leadership, strategic insights, and excellent governance which Dr. Hunziker has brought to BB Biotech. In the 10 years of his Chairmanship the Board increased its diversity, the Investment Management Team successfully entered neuroscience and the whole BB Biotech team was strengthened with data scientists to leverage the potential of artificial intelligence.

Dr. Thomas von Planta, a highly active member of the Board of Directors since 2019, will be proposed to the Annual General Meeting on March 21, 2024 as Dr. Hunziker's successor as chairman. In addition to many contributions to BB Biotech, Dr. von Planta has profound experience in corporate finance and capital markets and is familiar with the healthcare industry. He is also the chairman of Baloise Holding AG.

Ms. Camilla Soenderby will be proposed as a new Member at the AGM. Ms. Soenderby has held executive roles at leading biopharmaceutical companies in the EU, the US and Asia and is also a board member of F2G (UK/US) and Affibody AB (Sweden), advisor to the private equity group EQT and a member of the Novo Advisory Group.

Portfolio adjustments in the fourth quarter 2023

During the fourth quarter, we exited the portfolio holding Mersana, and made two new investments in Immunocore, an immune oncology company, and Biohaven with activities in immunology and neuroscience. These two new positions plus further investments in Arvinas and Celldex were financed through select profit taking from the successful long-term investments in Vertex, Incyte, Ionis, Neurocrine and Argenx. BB Biotech's investment levels were steady in 2023, closing the year at 113.4%.

We made two new investments: Immunocore, an immune oncology company, and Biohaven with activities in immunology and neuroscience.

Fourth-quarter portfolio update

The fourth quarter of 2023 marked significant progress for our portfolio companies, characterized by key clinical results, regulatory approvals, and licensing agreements. Despite not capitalizing on the heightened merger and acquisition activity in late 2023, our performance was largely influenced by successes in mid-stage clinical trials and proof-of-concept studies. On the other hand, outcomes of late-stage trials were varied. Notably, US and EU regulators granted approvals for several products, including the groundbreaking gene editing therapy, Casgevy, in December 2023. In response to tighter capital markets and rising capital costs, our portfolio companies strengthened their financial positions through additional capital raises and licensing deals.

2024: Exciting sector fundamentals and continued M&A activity leading to improved sector performance

During 2023, the US FDA approved 55 new medicines – up from 37 in 2022. This pace is expected to continue – driven by new platform technologies and continued investment in research and clinical development. Innovative biotechnology companies continue to invest substantially more into R&D than SGA, even though more and more biotech firms are commercializing their own products.

We believe that 2024 will include multiple catalysts for the sector and for BB Biotech's portfolio companies, including product launches, important clinical trial results, licensing deals and M&A activity.

Many clinical trial read-outs are eagerly anticipated from portfolio companies in 2024. The focus will be on Vertex VTX-548 pain program, Alnylam's vutrisiran for patients with transthyretin-mediated amyloidosis with cardiomyopathy, Ionis' donidalorsen for hereditary angioedema and Intra-Cellular's Caplyta data in major depression disease. Many proof of concept studies are also due, including for Revolution Medicines' RMC-6236, for Relay's RLY-2608 and Macrogenics' B7H3 ADC vobramitamab duocarmazine. Argenx will report on proof of concept data for primary Sjogren's syndrome for efgartigimod and Agios will report on transfusion dependent thalassemia patients for its PK activator mitapivat.

We expect multiple product approvals and label expansions to drive future revenue and profit opportunities:

- Incyte with axatilimab for chronic graft versus host disease
- Ionis with olezarsen for patients with familial chylomicronemia syndrome
- Moderna with its RSV vaccine mRNA-1345
- Argenx with efgartigimod for patients with chronic inflammatory demyelinating polyneuropathy
- Crispr and Vertex with Casgevy for beta thalassemia patients

Capital markets appear to have opened up in the last months of 2023, mainly geared towards the large-cap biopharma sector. In contrast to the broad investor base favoring large caps, many of them continue to bolster their pipeline and technology access by acquiring smaller to mid-cap companies. The recently accelerated take-over activity combined with an

improved capital market allowing companies to raise working capital again, supports both the sector but as well our view that valuations are highly attractive and the innovation power to reside in the smaller and mid-cap segment.

We continue to seek attractive investments – applying ever more stringent methodologies including big, wide, and deep data and AI to support the diligence processes. We continue to hold a strong conviction that fundamental progress in biosciences and commercialization of superior new drugs from biotechnology will yield attractive investment returns.

We thank you for the trust you have placed in the Company.

The Board of Directors of BB Biotech AG

Dr. Erich Hunziker
Chairman
Laura Hamill
Member
Prof. Dr. Mads Krogsgaard Thomsen
Member
Dr. Clive Meanwell
Vice Chairman
Dr. Pearl Huang
Member
Dr. Thomas von Planta
Member

Portfolio Update Q4 2023

The fourth quarter of 2023 marked significant progress for our portfolio companies, characterized by key clinical results, regulatory approvals, and licensing agreements. Despite not capitalizing on the heightened merger and acquisition activity in late 2023, our performance was largely influenced by successes in mid-stage clinical trials and proof-of-concept studies. On the other hand, outcomes of late-stage trials were varied. Notably, US and EU regulators granted approvals for several products, including the groundbreaking gene editing therapy, Casgevy, in December 2023. In response to tighter capital markets and rising capital costs, our portfolio companies strengthened their financial positions through additional capital raises and licensing deals.

Key clinical data milestones in proof-of-concept studies as well as late-stage trials
Neurocrine Biosciences' Phase III study of crinecerfont, aimed at treating congenital adrenal hyperplasia (CAH) in children and adolescents, marked a significant achievement. The drug demonstrated efficacy by lowering serum androstenedione levels and enabling reduced glucocorticoid dosage while effectively controlling androgen. This significant breakthrough led to the US FDA awarding crinecerfont a breakthrough therapy designation, acknowledging the urgent need for new treatments in CAH. Neurocrine Biosciences is preparing to file a new drug application in 2024.

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Argenx, after a period of consistent success, faced setbacks in late 2023 with the failure of two Phase III studies. The subcutaneous formulation of Efgartigimod, branded as Vyvgart Hytrulo, was tested in primary immune thrombocytopenia (ITP) patients but failed to meet the primary endpoint of sustained platelet count response and secondary endpoints. Additionally, the same formulation in pemphigus patients also did not achieve the clinical endpoints. Despite the demonstrated pharmacodynamic effect of Efgartigimod in reducing total immunoglobulin G (IgG) and autoantibodies, the control arm with low-dose steroids showed a comparable impact on reducing disease-causing autoantibodies. Argenx plans to conduct further analysis of the ITP study results to determine future steps, while discontinuing the development of Efgartigimod for pemphigus treatment. These consecutive clinical trial failures were unexpected, leading to a significant decline in Argenx's valuation in Q4 2023.

The Phase II results of Vertex's VX-548 for treating painful diabetic peripheral neuropathy led to a rally in its stock. Patients with chronic pain showed improvement over twelve weeks at varying doses of VX-548, an investigational oral NaV1.8 inhibitor. This positive outcome bolstered investor confidence in the VX-548 program, currently undergoing registrational studies for the expansive chronic pain management market. It also enhanced the anticipated success of multiple acute pain trials slated for the first half of 2024.

Arvinas, in collaboration with Pfizer, revealed results for vepdegestrant combined with palbociclib in breast cancer patients. The treatment showed a 42% overall response rate and a median progression-free survival of 11.1 months in heavily pre-treated patients, alongside an acceptable tolerability profile. Following these results, the companies have decided to broaden the development profile of vepdegestrant. Additionally, Arvinas has bolstered its financial position with a USD 350 mn private placement, which included participation from BB Biotech.

Moderna, alongside its development partner Merck, provided an update on their ongoing personalized cancer vaccine program, mRNA-4157, in combination with Keytruda. This update covers patients with complete resections who have been followed for three years. The combination therapy has shown a 49% reduction in the risk of recurrence or death and a 62% decrease in the risk of distant metastasis or death. Both companies are significantly investing in the development of mRNA-4157 through extensive, randomized Phase III trials. They are also considering seeking accelerated approval for stage III/IV melanoma patients, contingent on the establishment of adequate manufacturing and logistics to meet potential patient and market demands. Additionally, Moderna is making notable advancements in its prophylactic vaccine business for respiratory viruses. The company announced promising early results for mRNA-1083, their combination vaccine against influenza and COVID-19, and initiated a Phase III program in Q4 2023.

Celldex revealed encouraging topline results for barzolvolimab, a c-kit targeting antibody, in chronic spontaneous urticaria (CSU) patients. The treatment led to significant reductions in urticaria disease activity, evidenced by lower disease scores (UAS) and up to half of the patients achieving complete control, as indicated by a UAS7 score of zero. In response to these updates and the positive reception from investors, Celldex strengthened its financial position through a public offering, raising approximately USD 200 mn. This funding will support the initiation of registrational trials for barzolvolimab, anticipated to begin in 2024.

Investor attention is keenly directed towards Alnylam's HELIOS-B study of vutrisiran, with its data readout anticipated in the first half of 2024. Meanwhile, Alnylam has reported significant advancements in other major indications, such as hypertension treatment. Their subcutaneous RNAi therapeutic, Zilbesiran, targeting angiotensinogen (AGT), has demonstrated effective and sustained blood pressure reduction in treatment-naive hypertension patients, administered either once every three or six months. Alnylam has entered into a partnership with Roche, sharing the development costs and co-commercializing Zilbesiran in the US. Additionally, Roche has acquired exclusive rights for commercializing Zilbesiran outside the US.

Revolution Medicines provided a notable update on RMC-6236, their RAS-multi (ON) inhibitor, within a landscape of intriguing early clinical programs in the industry and our portfolio. This drug was evaluated in non-small cell lung cancer (NSCLC) and pancreatic ductal adenocarcinoma (PDAC) patients with various KRAS-mutant genotypes (G12D, V, and R). In NSCLC, RMC-6236 demonstrated a 38% objective response rate (ORR) and an 85% disease control rate, while PDAC patients experienced a 20% ORR and a 87% disease control rate. Subsequently, Revolution Medicines completed a merger with EQRx, adding approximately USD 1.1 bn to its balance sheet, a move that positions the company for substantial investment in the registrational program for RMC-6236.

Numerous regulatory decisions milestones

Regulatory decisions in Q4 2023 significantly impacted BB Biotech's portfolio holdings, including:

- Ionis, in partnership with AstraZeneca, announced FDA approval in the US for Wainua (eplontersen) to treat adults with polyneuropathy of hereditary transthyretin-mediated amyloidosis. Wainua will be available in the US from January 2024, with further regulatory reviews for global markets ongoing.
- Vertex and Crispr Therapeutics celebrated the US FDA approval of Casgevy (exagamglogene autotemcel) for sickle cell disease (SCD) treatment. This pioneering gene editing therapy, now available for curative one-time use, will initially be offered in select centers of excellence, expanding to more transplant centers over time. Additionally, treatment for transfusion-dependent beta-thalassemia was added as a second indication in early 2024.
- Argenx reported the European Commission's approval of subcutaneous Vyvgart Hytrulo for general myasthenia gravis. This offers patients in Europe the option of both intravenous and self-administered subcutaneous forms.
- Alnylam received a complete response letter (CRL) from the US FDA for the supplemental new drug application for patisiran, aimed at treating cardiomyopathy of ATTR amyloidosis. This decision followed a divided FDA advisory panel opinion, citing limited data from the 12-month APOLLO-B study involving 360 adults. Notably, Alnylam's subsequent molecule, vutrisiran, is undergoing a more extensive HELIOS-B study involving double the patient count over three years, with top-line results expected in the first half of 2024.

Participation in licensing deals and partnerships, none in an escalating M&A environment

During 2023, a year marked by escalating M&A activity with several deals emerging late in the year, BB Biotech did not directly benefit from these takeover events. The M&A focus in both the entire year and particularly the fourth quarter was on oncology, specifically targeting developers in radiotherapies and antibody drug conjugation (ADC), alongside major indications in autoimmune diseases and psychiatry, such as inflammatory bowel disease, schizophrenia, and depression. While our holdings saw indirect benefits through increased valuations in similar disease areas and technologies, our lack of participation in high-premium transactions was a notable factor in our performance relative to the benchmark NBI. Despite the benchmark including most announced takeovers, the NBI's consolidation in 2023 suggests increasing performance pressures for its constituents.

Non-dilutive capital contributions continue to be an appealing funding source for companies, along with securing commercial partners for international markets. Ionis, aspiring to be a commercial entity and initially focusing on the US market, struck a European licensing deal with Otsuka for donidalorsen in hereditary angioedema. Ionis stands to receive an upfront payment of USD 65 mn and is eligible for milestone payments and tiered royalties of 20% to 30%.

A significant move in our midcap portfolio was Revolution Medicine's merger with EQRx. Despite EQRx's setbacks in pipeline development, their substantial cash reserve of over USD 1.1 bn was merged into Revolution Medicines, enhancing their financial strength for the advanced development of RAS(ON) inhibiting drugs.

Given our portfolio strategy's focus on innovation and pipeline, intellectual property litigation and settlements hold lesser importance. However, our more established midcap and large-cap companies must navigate mature business franchises and impending patent expirations.

Neurocrine resolved all patent litigations related to Ingrezza, allowing four companies to sell its generic versions in the US starting March 1, 2038, under certain conditions. This resolution enhances Neurocrine's long-term financial outlook, supporting further investments in its pipeline. Exelixis, facing similar litigation with Teva over Cabometyx, reached a settlement for a generic US version available from January 1, 2031. However, its litigation with MSN Laboratories was unexpectedly extended into the first half of 2024.

Portfolio at a glance

Securities as at December 31, 2023

Company	Number of securities	Change since 31.12.2022	Local currency	Share price	Market value in CHF mn	In % of securities	In % of shareholders' equity	In % of company
Ionis Pharmaceuticals	8 590 000	(1 045 000)	USD	50.59	365.6	13.9%	15.7%	6.0%
Neurocrine Biosciences	2 410 000	(320 000)	USD	131.76	267.2	10.1%	11.5%	2.5%
Argenx SE	825 000	(67 503)	USD	380.43	264.1	10.0%	11.4%	1.4%
Vertex Pharmaceuticals	640 000	(290 523)	USD	406.89	219.1	8.3%	9.4%	0.2%
Intra-Cellular Therapies	3 040 000	(251 479)	USD	71.62	183.2	7.0%	7.9%	3.2%
Moderna	1 891 075	389 124	USD	99.45	158.2	6.0%	6.8%	0.5%
Alnylam Pharmaceuticals	859 700	(30 300)	USD	191.41	138.5	5.3%	6.0%	0.7%
Revolution Medicines	5 046 700	269 138	USD	28.68	121.8	4.6%	5.2%	3.1%
Incyte	2 150 000	(741 077)	USD	62.79	113.6	4.3%	4.9%	1.0%
Arvinas	2 494 531	358 119	USD	41.16	86.4	3.3%	3.7%	3.7%
Celldex Therapeutics	2 416 296	616 296	USD	39.66	80.6	3.1%	3.5%	4.4%
Macrogenics	9 929 963	1 000 000	USD	9.62	80.4	3.1%	3.5%	16.0%
Agios Pharmaceuticals	4 000 000	(30 792)	USD	22.27	75.0	2.8%	3.2%	7.2%
Sage Therapeutics	3 505 000	554 722	USD	21.67	63.9	2.4%	2.8%	5.8%
Immunocore	965 654	965 654	USD	68.32	55.5	2.1%	2.4%	2.0%
Relay Therapeutics	5 925 000	1 804 280	USD	11.01	54.9	2.1%	2.4%	4.8%
Crispr Therapeutics	880 000	(8 605)	USD	62.60	46.4	1.8%	2.0%	1.1%
Essa Pharma	7 879 583	–	USD	6.60	43.8	1.7%	1.9%	17.9%
Exelixis	2 000 000	(654 500)	USD	23.99	40.4	1.5%	1.7%	0.6%
Biohaven	1 075 000	1 075 000	USD	42.80	38.7	1.5%	1.7%	1.3%
Scholar Rock Holding	2 132 725	–	USD	18.80	33.7	1.3%	1.5%	3.0%
Black Diamond Therapeutics	8 517 839	3 140 000	USD	2.81	20.1	0.8%	0.9%	16.5%
Wave Life Sciences	4 494 458	–	USD	5.05	19.1	0.7%	0.8%	3.8%
Beam Therapeutics	693 121	–	USD	27.22	15.9	0.6%	0.7%	0.9%
Fate Therapeutics	4 839 779	–	USD	3.74	15.2	0.6%	0.7%	4.9%
Rivus Pharmaceuticals [1)]			USD		14.7	0.6%	0.6%	
Esperion Therapeutics	4 194 064	–	USD	2.99	10.6	0.4%	0.5%	3.7%
Generation Bio Co.	3 608 280	–	USD	1.65	5.0	0.2%	0.2%	5.5%
Molecular Templates [2)]	1 029 820	283 686	USD	3.73	3.2	0.1%	0.1%	19.2%
Radius Health – Contingent Value Right	8 733 538	–	USD	0.00	0.0	0.0%	0.0%	
Total securities					**2 634.7**	**100.0%**	**113.4%**	
Other assets					2.4		0.1%	
Other payables					(313.9)		(13.5%)	
Net Asset Value					**2 323.2**		**100.0%**	

[1] Unlisted company
[2] Share split 1:15 as at August 14, 2023

Exchange rate as at 31.12.2023: USD/CHF: 0.8414

2024: Rebuilding investor trust by translating fundamental progress into capital returns

Heading into 2024, BB Biotech AG finds itself in a swiftly changing environment, shaped by pivotal shifts in capital markets, technological breakthroughs and healthcare regulations. Our strategy aims to respond adeptly to these dynamics, refining our investment approaches and seizing new opportunities that arise. We will closely track the market reception of innovative products like Casgevy, the pioneering gene editing therapy, and anticipate key proof of concept results from cutting-edge technologies, including in vivo gene editing. Moreover, the surge in M&A activities observed in 2023 is poised to continue, playing a crucial role in driving biotech industry growth and delivering value to investors.

Biotechnology industry adapting to higher cost of capital

2024 is set to be a pivotal year for biotech equities, heavily influenced by the US Federal Reserve's policy direction. The critical issue is the trajectory of the Fed's interest rate policy over the year and its impact on the biotech sector, especially regarding companies' financing costs. Navigating these monetary policy changes is essential for our investment strategies and portfolio management. Despite the rising interest rates over the past two years, BB Biotech has focused on its core holdings, cautiously expanding its portfolio. The addition of two new mid-cap companies in Q4 2023, with plans for more development stage company investments in 2024, marks a strategic shift.

We expect a more dynamic financing environment for biotech in 2024, with increased capital raising activities, PIPEs, and potentially more IPOs. Monitoring public biotech investment fund flows will be key, as we anticipate a shift from the recent trend of outflows to potential inflows, driven by renewed market confidence and promising returns. Notably, venture capital funding has decreased, reaching a multi-year low, presenting a complex but potentially rewarding scenario for performance turnaround.

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Engagements with management teams reveal a strategic focus on navigating volatile capital markets, with companies bracing for prolonged higher capital costs and bolstering their financials for sustained investment in pipeline projects and product launches. Partnerships and M&A activity, which picked up in late 2023, are expected to play significant roles in meeting the sector's capital needs.

Technology serving as basis to transform standards of care across therapeutic areas

The coming year is poised to bring groundbreaking developments in biotechnology, with our focus intensifying on the clinical advancement of cutting-edge gene editing techniques, including base and in vivo editing. A notable highlight is the launch of Casgevy, a pioneering gene editing therapy developed by Crispr Therapeutics and Vertex, now approved as a curative treatment for sickle cell disease and beta thalassemia. While its administration remains complex, Casgevy represents a transformative «once and done» solution for severe genetic disorders. Its premium pricing is justified by the potential to circumvent lifelong medical expenses and significantly enhance patient quality of life. As the field evolves, gene editing treatments must become more user-friendly, capable of addressing intricate genetic corrections, and more affordable to address widespread diseases effectively.

The coming year is poised to bring groundbreaking developments in biotechnology, with our focus intensifying on the clinical advancement of cutting-edge gene editing techniques, including base and in vivo editing.

In the realm of RNA-based medicines, substantial opportunities for expansion are on the horizon. Notably, Moderna's second prophylactic vaccine is on track for approval in 2024, with its RSV vaccine expected to receive full clearance. We are keenly monitoring progress in therapeutic vaccines, including personalized cancer vaccines, and Moderna's endeavors to target various tissues through innovative delivery routes or sophisticated mRNA packaging. For Alnylam, our RNAi-centric entity, we anticipate crucial data from a late-stage trial of vutrisiran in TTR cardiomyopathy patients, potentially broadening its market from ultra-rare to more common diseases and reaching a larger patient demographic. Similarly, Ionis Pharmaceuticals is set to embark on a parallel commercial path with its latest antisense oligonucleotide (ASO) therapy, aiming for a wider disease target range in the forthcoming years.

Emerging chemical modalities, such as PROTACs and LYTACs, are making strides in clinical development, targeting intracellular and extracellular protein degradation, respectively, and showing promise as orally administered therapies. Meanwhile, cell-based treatments, including CAR-T therapies, are being explored beyond oncology to address severe autoimmune disorders, with early clinical results spurring investment in clinical development, as seen with Fate Therapeutics.

In summary, we anticipate significant advancements and additional product approvals in 2024 and beyond, and expect biotechnology and platform-based products will have a clearly positive impact on patient benefit and sales potential.

New targets for diseases with limited to no progress over past decades

For many years, numerous diseases have faced a stagnation in the development of new drug modalities, due to high hurdles in surpassing established standards of care, a lack of new pathways and drug modalities, or a shift in the pharmaceutical industry's focus towards other areas. However, 2024 is set to be a year of significant progress, with expectations for multiple data readouts spanning from early human studies to registrational trials.

Vertex is set to release initial top-line data from several registrational clinical studies evaluating VX-549, a small molecule aimed at voltage-gated sodium channels such as NaV1.7 and NaV1.8, for the management of acute pain. This molecule is under investigation for its potential to block pain signals from reaching the brain. Additional trials in 2025 will explore VX-549 in chronic pain settings, where not only efficacy but also the drug's side effect profile will be critically assessed, especially considering the prevalence of addiction issues in current chronic pain treatments using opioids.

Recent mergers and acquisitions have spotlighted psychiatric medications, with Neurocrine Biosciences, a company within our portfolio, advancing a diverse pipeline for schizophrenia, major depression, and other central nervous system disorders. The company is exploring drug candidates across various neurotransmitter systems, including muscarinic receptors and pathways such as NMDA, AMPA, and DAAO, while also developing a next-generation VMAT2 inhibitor with potential improvements over valbenazine.

Incyte, known for its JAK1/2 inhibitor Jakafi – a first-in-class and standard of care in myeloproliferative neoplasms like myelofibrosis, essential thrombocythemia, and polycythemia vera – is investing in the next wave of treatments for these conditions. Beyond combination strategies with Jakafi, Incyte is exploring novel approaches with particular interest in the progress of INCA33989, an anti-mutant calreticulin (mCALR) monoclonal antibody, and a targeted therapy for the JAK V617F mutations, a key driver in various MPNs. These innovations hold promise for disease-modifying potential beyond the capabilities of current standard treatments.

BB Biotech Investment Strategy

BB Biotech's long standing investment strategy is to invest capital in promising technology platforms and early clinical assets, follow these companies through their clinical development, regulatory approval, commercial launches, sustainable revenue and profit growth to ultimately become more mature companies. Upon such a long term cycle, BB Biotech would divest and reinvest into the next promising candidates. The same trend will continue to make smaller and mid-cap companies attractive licensing partners for large pharmaceutical and large-cap biotech companies, either signing attractive business development deals or ultimately through consolidation.

M&A cycle has started to roll – more to be expected in 2024

The M&A landscape in 2024 is anticipated to be dynamic, with particular emphasis on sectors such as obesity, autoimmune disorders, and oncology. In oncology, the spotlight on antibody-drug conjugates (ADCs), radiotherapies, and intellectual property (IP) and immuno-oncology (IO) considerations has intensified activity, surpassing that of targeted small molecule development. The ADC sector, having seen many of its focused companies acquired or licensed, presents a unique scenario for the remaining entities, posing questions of exclusion or advantage due to scarcity. Recent trends also show an increased interest in addressing widespread diseases, including psychiatric and autoimmune disorders. However, the potential of these large markets is tempered by the complexities of market launches, often characterized by larger patient volumes and lower annual drug prices.

The looming patent cliff, with numerous loss of exclusivities (LOEs) expected by 2028, compels large pharmaceuticals and biotech firms to pursue strategic acquisitions to secure future revenue growth, pipeline diversity, and technological advancements. Industry analysts highlight the substantial financial capacity of these large entities, a fusion of existing leverage opportunities and projected robust cash flows, positioning virtually every company in our portfolio as a potential acquisition target. Given continued attractive valuations and the allure of smaller and mid-cap companies with promising drugs and technologies, the momentum for acquisition activity is expected to persist, reflecting a strategic pursuit of growth and innovation in the biotech and pharmaceutical sectors.

Healthcare politics with the focus on the IRA implementation

The healthcare sector, notably the pharmaceutical and biotechnology industries, is consistently influenced by political shifts in major markets, including the US. With the presidential election scheduled for November 2024, healthcare investors are particularly attentive to the US Congress and the potential policy directions that could significantly alter the healthcare framework. A critical focus will be on discussions surrounding the Inflation Reduction Act (IRA) and proposed Senate reforms targeting pharmacy benefit managers (PBMs).

As we move into 2024, BB Biotech is on the cusp of a period marked by substantial transition and potential. Our strategy is to navigate these changes proactively, ensuring our investments not only align with the evolving landscape but are also optimally positioned to benefit from forthcoming innovations in the biotech sector.