

# Your investment opportunity

Despite remarkable progress in the research and development of new drugs and treatments in the global healthcare system, many severe diseases still have no real cure to this day. These include various types of cancer and chronic infectious diseases. Demographic transition toward a higher life expectancy and an increasing proportion of elderly people in the population are factors contributing to a rising prevalence of age-related diseases. The result is a massive increase in healthcare spending, which in turn emphasizes the need for efficient and effective medicines. Whereas the strength of pharmaceutical companies tends to lie in the global marketing and sale of medicinal products, biotech companies' biggest asset is their high innovation capabilities. Biotech products target the root causes of disease and in some cases have come up with new therapeutic approaches for diseases that may only have been amenable to symptom control in the past. Another trend favoring the biotech industry is the fact that many big pharma players are facing sharp revenue losses as a result of patent expirations. To fill their product pipelines, they are buying innovative biotech products for which they are prepared to pay high premiums. With increasing numbers of biotech companies, launching drugs on the market and reaching profitability, the industry is maturing steadily and managing to do so without disappointing expectations regarding innovative drug development activities and growth potential. This is what makes the biotech sector an attractive and fundamentally strong, high-growth sector for investors.

# Our investment skills

BB Biotech is one of the largest and most experienced biotech investors worldwide and can look back on a track record of 25 years. The challenging task of picking the right stocks within the dynamic, constantly changing field of biotechnology is met by BB Biotech's competent Investment Management Team consisting of biochemists, molecular biologists, doctors, and economists. Bringing together scientific and financial professionals facilitates the evaluation of complex issues and ensures a sound assessment of the prospects that drug candidates have as they move through the R&D pipeline and into the market. Drug development entails risks that are difficult to assess for investors with a broader focus. BB Biotech's portfolio managers are supported in their daily work through regular meetings with the highly qualified medical and financial experts on its Board of Directors.

# Our investment solution – BB Biotech

BB Biotech invests in carefully screened and selected biotechnology firms with a long-term time horizon. It focuses on companies with products that are already in the marketplace and generating income and on companies with promising drug candidates in advanced stages of development. During the past years a number of new product-launches by biotech companies attracted widespread attention and buoyed the entire sector. BB Biotech was able to profit from these developments through its carefully constructed investment portfolio. We expect to see a growing number of launches of innovative products in the coming year and have positioned ourselves accordingly, so BB Biotech can keep up the momentum and generate more value for its shareholders. Besides its investments in large, fast-growing biotech companies, BB Biotech holds numerous interests in smaller biotech companies and provides them with the necessary capital to pursue their research projects.

#### **General information**

**Board of Directors** Dr. Erich Hunziker (Chairman

Dr. Clive Meanwell Prof. Dr. Dr. Klaus Strein

Investment Management Dr. Daniel Koller (Head

Dallas Webb Felicia Flanigan Dr. Stephen Taubenfeld Dr. Christian Koch Dr. Maurizio Bernasconi

Portfolio Management Jan Bootsma

Nathalie Isidora-Kwidama Hugo van Neutegem Rudy Le Blanc

Legal structure Incorporated company

Listing Swiss stock exchange (BION SW)

talian stock exchange (BB IM)

Foundation November 9, 1999

**Share structure** 55.4 mn registered shares

 ISIN
 CH003838999

 Security number (CH)
 3 838 999

 Security number (G/I)
 AONFN3

Investor Relations Dr. Silvia Siegfried-Schanz

Claude Mikkelsen

Maria-Grazia Iten-Alderuccio

Media Relations Tanja Chicherio

### Multi-year comparison

|   | 2018        | 2017        | 2016        | 2015        | 2014        |
|---|-------------|-------------|-------------|-------------|-------------|
| Market capitalization at the end of the period (in CHF mn)      | 3 235.4     | 3 576.1     | 3 052.5     | 3 463.2     | 2 799.0     |
| Net Asset Value at the end of the period (in CHF mn)            | 2 884.5     | 3 538.7     | 3 003.0     | 3 978.2     | 3 492.5     |
| Number of shares (in mn) 1)                                     | 55.4        | 55.4        | 55.4        | 59.3        | 59.3        |
| Trading volume (in CHF mn)                                      | 2 610.7     | 2 864.7     | 3 204.5     | 6 265.2     | 3 186.6     |
| Profit/(loss) (in CHF mn)                                       | (471.3)     | 687.5       | (802.1)     | 652.8       | 1 470.1     |
| Closing price at the end of the period in CHF 1)                | 58.40       | 64.55       | 55.10       | 58.45       | 47.24       |
| Closing price (G) at the end of the period in EUR <sup>1)</sup> | 52.00       | 55.68       | 51.70       | 53.99       | 39.60       |
| Closing price (I) at the end of the period in EUR 1)            | 52.00       | 55.20       | 51.60       | 54.18       | 39.34       |
| Stock performance (incl. distributions) 2)                      | (5.2%)      | 22.9%       | 0.2%        | 28.1%       | 75.3%       |
| High/low share price in CHF 1)                                  | 74.10/56.10 | 67.80/52.10 | 58.20/40.78 | 70.25/46.48 | 48.16/26.74 |
| High/low share price in EUR <sup>1)</sup>                       | 64.80/48.60 | 59.10/48.42 | 53.98/36.74 | 66.02/39.39 | 39.98/21.82 |
| Premium/(discount) (annual average)                             | 9.7%        | (2.5%)      | (5.1%)      | (17.6%)     | (22.1%)     |
| Cash distribution/dividend in CHF (*proposal) 1)                | 3.05*       | 3.30        | 2.75        | 2.90        | 2.32        |
| Degree of investment (quarterly figures)                        | 108.4%      | 103.1%      | 109.9%      | 101.0%      | 104.6%      |
| Total Expense Ratio (TER) p.a. <sup>3)</sup>                    | 1.25%       | 1.27%       | 1.30%       | 1.29%       | 1.41%       |
|   |             |             |             |             |             |

- $^{1)}$  Five-for-one share split as at March 29, 2016 considered
- 2) All figures in CHF %, total return-methodology
- based on market capitalization

### Indexed performance since launch (in CHF)

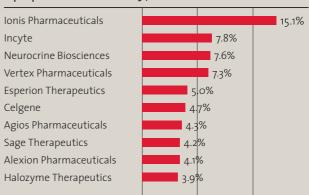


■ BB Biotech share

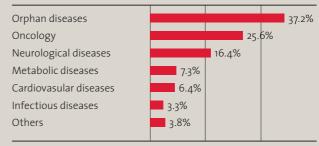
■ BB Biotech Net Asset Value

#### ■ Nasdaq Biotechnology Index

### Top 10 positions as of December 31, 2018



### Breakdown by sector as of December 31, 2018

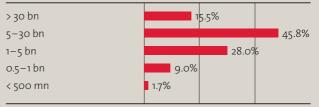


# **Cumulated performance**

| As of 12/31/2018 | 1 year | 3 years | 5 years  | since<br>inception |
|------------------|--------|---------|----------|--------------------|
| Switzerland      | (5.2%) | +16.7%  | + 162.0% | +1984%             |
| Germany          | (2.2%) | +12.3%  | + 184.6% | + 1 507%           |
| Italy            | (1.3%) | +12.0%  | + 184.3% | + 271.5%           |

Source: Bloomberg, 12/31/2018, all figures in %

# Breakdown by market capitalization (USD) as of December 31, 2018



# Strong backing from shareholders

BB Biotech's total stock return of -5.2% in CHF and -2.2% in EUR during a turbulent year for stock markets was much better than the underlying portfolio's NAV performance thanks to the enduring confidence of its shareholders. Portfolio performance stood at -14.5% in CHF and -11.1% in EUR. Performance in EUR benefited from the euro's depreciation against the dollar.

# Record number of drug approvals

We witnessed tremendous progress on the drug development front and throughout the entire biotechnology industry in 2018. The FDA approved 18 new drugs in the fourth quarter 2018, bringing the total number of approvals for the year to a record 59. More than half of these new drugs originated from biotech firms.

# Attractive dividend yield of 5% maintained for 2018

The Board of Directors will propose a regular dividend of CHF 3.05 per share at the Annual General Meeting on March 21, 2019. This corresponds to a 5% return on the volume-weighted average closing price of BB Biotech shares in December of 2018 – consistent with the dividend policy introduced in 2013.

# Inclusion in index

BB Biotech AG has been part of the SMIM Index and the SPI Index (sub-index SPI Mid) of the SIX Swiss Exchange since September 24, 2018. The blue-chip SMI Index is the most prestigious index of stocks listed in Switzerland and comprises the 20 largest stocks from the SPI. The SMIM Index comprises the 30 most liquid and heavily capitalized stocks in the mid-cap segment. BB Biotech was already admitted to the Stoxx Europe 600 Index in 2014.

# M&A as growth driver in 2019

The decline in valuations during 2018 could make smaller and mid-cap biotech firms more willing to embrace M&A as a means of addressing their funding requirements. Bidders might even be attracted to large cap biotech companies earning good profits, lured by the enticing valuations.

#### PERFORMANCE BB BIOTECH SINCE INCEPTION (11/15/1993)

1984%

(in CHF)

**MARKET CAPITALIZATION AS OF 12/31/2018** 

CHF 3.2 bn

(2017: CHF 3.6 bn)

**DISTRIBUTION FOR FISCAL YEAR 2018 (PROPOSED)** 

**CHF 3.05** 

(2017: CHF 3.30)

NUMBER OF PORTFOLIO COMPANIES

34

(as at 12/31/2018)

**NUMBER OF APPROVALS 2018** 

**59** 

(USA, 2017: 46)

NUMBER OF TAKEOUTS IN PORTFOLIO 2018

3

(Tesaro, Avexis, Juno)

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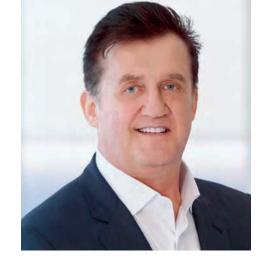


**Dr. Erich Hunziker** Chairman of the Board of Directors since 2013

Member of the Board since

Previously CFO of Roche, various executive positions at Corange, Boehringer Mannheim and Diethelm-Keller-Gruppe

Ph.D. in Industrial Engineering from the Swiss Federal Institute of Technology in Zurich



**Dr. Clive Meanwell**Vice-Chairman of the Board of
Directors since 2003

CIO and founder of The Medicines Company

Previously managing director of MPM Capital L.P., various positions at Hoffmann-La Roche

M.D. and Ph.D. from the University of Birmingham, UK

#### **Dear Shareholders**

All major global equity indices declined in 2018, due to fears of a global economic slowdown associated with US-China trade disputes and concern about tightening of the US monetary conditions. The European Union endured Brexit woes and government budget concerns practically all year long.

conducted under unfavorable conditions. Nevertheless, most of the proposed transactions were successfully completed because the fundamental progress of new technologies and the underlying market needs remain exciting and valuable. The correction in the valuations of almost all biotechnology companies may bring new opportunities for value growth and dispositions in 2019.

# 5% Dividend yield

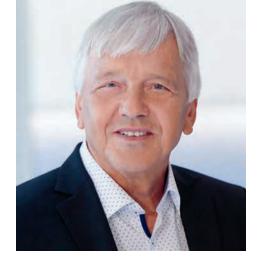
The Dow Jones (–3.5% in USD), Nasdaq Composite (–2.8% in USD), DAX (–18.3% in EUR), and SPI (–8.6% in CHF) indices all fell, while the Nasdaq Biotech Index (NBI) lost around –8.9% in USD in 2018. Most of these losses came from a very weak fourth quarter, when most of these benchmarks fell double-digit percentages.

Notwithstanding the general market landscape and the very pessimistic mood as the year came to an end, management observed many positive developments in 2018. Fundamental progress was made on the drug development front and across the biotechnology industry during the year. The FDA approved 18 new drugs in the fourth quarter 2018, bringing the total number of approvals for the year to a record 59. The capital many companies sought to raise, either through IPOs or rights issues, exceeded the inflow of funds into investment vehicles focused on the biotechnology industry. Consequently, many of the capital-raising transactions in 2018 were

# Strong shareholder support underpins BB Biotech's relative stability in FY 2018

For 2018, BB Biotech's total return of –5.2% in CHF and –2.2% in EUR was less than the underlying portfolio due to continued strong shareholder support. Weakening of the EUR over the USD created a tailwind for Euro-denominated performance. The portfolio Net Asset Value (NAV) declined –14.5% in CHF, –11.1% in EUR, and –15.0% in USD.

For the fourth quarter, BB Biotech's share price declined –18.8% in CHF and –17.2% in EUR. Since the inclusion into the SPI and SMIM Index on September 24, 2018, additional demand for BB Biotech shares has amplified short-term volatility, which added to the effects of weak market conditions. BB Biotech's portfolio NAV for the same period traced the overall market decline at –18.2% in CHF, –17.3% in EUR and –18.2% in USD. The portfolio performance was favorable relative to the overall broad NBI benchmark in this most difficult fourth quarter.



**Prof. Dr. Dr. Klaus Strein**Member of the Board of
Directors since 2013

Various positions with Roche including head of global pharma research

Previously at Boehringer Mannheim

Post-graduate degrees in chemistry and medicine, University of Heidelberg

Consolidated and audited fourth quarter 2018 data indicate a net loss of CHF 643 mn versus last year's loss of CHF 156 mn. Consolidated and audited full year 2018 data showed a net loss of CHF 471 mn compared to a net gain of CHF 688 mn for the full year of 2017.

### A proposed dividend of CHF 3.05 per share

The Board of Directors will propose a regular dividend of CHF 3.05 per share at the general assembly on March 21, 2019. This is computed as a 5% dividend yield applied to the average share price of December 2018 – consistent with the dividend policy introduced in 2013.

#### Fourth quarter portfolio update

The fourth quarter 2018 provided multiple milestones for our portfolio holdings such as clinical news, regulatory action, and updates on important product launches. Vertex reported two highly positive clinical studies of the triple combination of VX-659, a next generation corrector, together with tezacaftor and ivacaftor. People with cystic fibrosis with one F508deletion mutation and one minimal function mutation showed a mean absolute improvement in ppFEV1 of 14 percentage points from baseline to week 4 of treatment compared to placebo. In people with two F508 deletion mutations, the addition of VX-659 in patients already receiving tezacaftor and ivacaftor resulted in a mean absolute improvement in ppFEV1 of 10 percentage points from baseline at week 4 of treatment compared to the placebo group that received tezacaftor and ivacaftor. Vertex is awaiting Phase III results in early 2019 for its second next generation corrector VX-445 and will decide to file for a triple combination regimen with either VX-659 or VX-445. Importantly for Vertex and its shareholders, the triple combination will substantially expand the addressable CF population for Vertex medications and has increased the efficacy and safety hurdle for potential competitors in earlier clinical development.

Esperion reported another positive Phase III study evaluating the LDL-C lowering efficacy and the safety and tolerability for 180 mg daily bempedoic acid in patients with

atherosclerotic cardiovascular disease (ASCVD) and/or heterozygous familial hypercholeresterolemia (HdFH). On-treatment LDL-C lowering of an additional 18% over placebo was confirmatory to the drug candidates profile seen in the earlier clinical trials. These results completed the company's pivotal program with Esperion guiding for a first quarter 2019 filing to the US FDA followed by filing in Europe in the second quarter 2019.

Alnylam initiated its rolling submission for Givosiran, an investigational RNAi therapeutic for the treatment of acute hepatic porphyria. Data from the company's openlabel extension trial confirmed the effectiveness of Givosiran dosed monthly at 2.5 mg/kg leading to a substantial lowering of aminolevulinic acid (ALA) and porphobilinogen (PBG) by 87 and 83%, respectively, and thus toward normal levels. More importantly, patients receiving Givosiran experienced a mean reduction in annualized attack rate of 93% and annualized hemin use of 94% compared to the patients pre-treatment results. The company is guiding for topline results from the ENVISION phase III pivotal study in early 2019.

Neurocrine announced topline data from the Phase IIb T-Force GOLD study demonstrating that Ingrezza (Valbenazine) did not meet the primary endpoint in pediatric patients with Tourette syndrome. Tourette syndrome was expected to become an important market expansion for Ingrezza, already very successfully launched for treating adult patients with tardive dyskinesia, an involuntary movement disorder. As often, Wall street reacted overly harsh with the reset valuation of Neurocrine offering an attractive level to re-allocate more assets post the disappointing update.

Two larger portfolio holdings of BB Biotech received important product approval by the US FDA. Ionis, together with its distribution subsidiary Akcea, announced the US FDA approval of Tegsedi (inotersen) for the treatment of the polyneuropathy of hereditary transthyretin-mediated amyloidosis in adults. The antisense product, required regular monitoring allow patients a once-weekly subcuta-

neous injection — suited for self-administration — will compete with Alnylam's Onpattro, an intravenous delivered RNAi product. Alexion, using its FDA voucher, received an early FDA approval for Ultomiris (ravulizumab-Cwvz) in adults with paroxysmal nocturnal hemoglobinurea. Ultomiris is a long-acting C5 complement inhibitor administered intravenously every eight weeks, a substantial improvement for patients and over Soliris administered bi-weekly. Ultomiris proved to be highly effective in treatment naïve patients as well as allowing Soliris treated patients to effectively transition from Soliris to Ultomiris.

Next to clinical trial results and regulatory product approvals, investors carefully monitor initial market uptake of novel medicines to assess potential profit trajectories. Our portfolio has significant exposure into multiple important products with four of them being important severe neurological disorders. Ingrezza, for the treatment of tardive dyskinesia, continues to grow strongly with Neurocrine guiding for USD 130 mn for the fourth quarter. Ionis benefits from Spinraza, for patients with spinal muscular atrophy, generating USD 468 mn in revenues in the third quarter 2018. Alnylam's Onpattro and Akcea/ Ionis' Tegsedi for treating hereditary transthyretin-mediated amyloidosis are in the early market adoption. Alnylam launched Onpattro in the third quarter, with the company announcing an update regarding very early launch metrics such as over 200 patients on the drug per year end and unaudited global net revenues of 11–12 mn. Ionis, receiving FDA approval of Tegsedi in the fourth quarter will update on the launch progress throughout 2019.

Radius continued to gain market share against Eli Lilly's Forteo for the treatment of postmenopausal women with osteoporosis at high risk for fracture. The company announced that it has reached 40% share in new patients by year end 2018 and to surpass its 2018 full-year guidance of USD 95 to 98 mn. The steady growth of Tymlos is expected to continue in 2019, with the company reaching profitability for its subcutaneous Tymlos franchise in the second half of 2019. Tesaro, initially disappointing investors by reducing its 2018 full year revenue goals for Zejula from USD 255 to 275 mn to USD 225 to 235 mn on its second quarter 2018 call, has regained its footing with a solid third quarter update. Zejula, successfully launched for treating women with recurrent ovarian cancer ultimately led to GSK's offer of USD 5 bn in the fourth quarter 2018.

#### Portfolio adjustments in the fourth quarter 2018

In the fourth quarter, BB Biotech exited three positions. First, after building a stake in Tesaro at distressed valuation levels, it gained from Glaxo Smith Kline's acquisition price of USD 75 per share (approximately USD 5 bn for the company). The entire position was sold at the time the transaction documents were released, which generated

approximately 8% cash for the portfolio, and a substantial profit at a time when equity markets were under substantial pressure. Second and third, the remaining holdings in Novo Nordisk and Achillion were sold. Early in the fourth quarter, further profits were taken on other large cap investments, Celgene, Gilead and Regeneron, which were then reinvested as part of the announced strategic portfolio reallocation – focusing more on existing smaller and mid cap portfolio companies and some promising new positions. BB Biotech took advantage of market conditions by investing more in existing mid cap companies such as Neurocrine, Agios, Alnylam and Sage at attractive valuations, and by increasing the stake in Argenx, Nektar, Myokardia and G1 Therapeutics. It also invested capital in Moderna Therapeutics, both in their record-breaking IPO of USD 600 mn and in the post-IPO opportunity created by a sell-off that drove share prices lower.

An investment was made in Kezar, a company new to BB Biotech, focusing on autoimmune disorders. The company's lead program, KZR-616, is a first-in-class immunoproteasome inhibitor about to be tested in Phase II trials in lupus nephritis patients.

Following a comprehensive review of the genetic therapy landscape, in line with BB Biotech's strategy to reinvest more in earlier stage leaders, capital was invested in Sangamo and Audentes. Sangamo has improved zinc finger nuclease technology for gene therapy over more than two decades and is advancing multiple fully-owned projects as well as partnered programs. Audentes has four gene therapies in clinical development. Their lead program is AT-132, an adeno-associated virus carrying the MTM1 gene for long-term expression of myotubularin in muscle cells for newborns with X-linked myotubular myopathy disease.

# Outlook for 2019 – sector fundamentals exciting, very attractive valuation levels

BB Biotech believes that 2019 will continue to bring important technology progress allowing new drug modalities to address many unmet medical needs in future years. Thus, the Management Team's asset allocation will not only center around established areas — such as oncology, orphan diseases and neurological indications — but will also focus on rapidly emerging technologies which can offer novel drug modalities which promise the best therapeutic profile and economic value.

For example, BB Biotech believes that RNA-based medicines – currently in early adoption for rare and serious diseases — will broaden into larger patient populations in the coming years. On the other hand, one-time potentially curative genetic medicines are likely to be applied for the foreseeable future to rare, monogenetic diseases. As it has already done successfully in the past, BB Biotech will continue to add companies performing early-stage clinical

development in these areas. With this strategy, BB Biotech's current focus on small molecules and biologics will evolve over time to include newer drug modalities based on technologies its portfolio managers expect to provide high-value medical solutions to seriously sick patients over the coming decade.

With respect to the biotechnology environment, continued debate around value assessment and structural change in the US healthcare system can be expected. This debate has impacted the profit outlook for large and profitable biotechnology and pharmaceutical companies. The decline in valuations during 2018 may force smaller and mid cap biotechnology companies requiring further financing to turn to M&A more readily than before. The surprising takeover of Celgene by Bristol-Myers Squibb for USD 70 bn underpins that even the large capitalized and highly profitable biotechnology companies can become acquisition targets thanks to their very attractive valuation levels. With the transaction expected to consummate in the

third quarter of 2019, BB Biotech would close out another long-term and highly successful investment.

These dynamics are welcomed by BB Biotech as a demonstration of the vibrancy of the investment cycle in biotechnology — and the need to remain diligent and focused on value creation for the future. Critically then, the growth case for the biotechnology industry and for BB Biotech's highly selective portfolio companies is as compelling as ever. Management anticipates that 2019 will be another banner year for product approvals as the FDA continues its quest to support innovation. BB Biotech looks forward to exciting news flow from its portfolio companies and believes that mid- and long-term growth in biotechnology will continue to provide an excellent case for investment.

Prof. Dr. Dr. Klaus Strein

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

The Board of Directors of BB Biotech AG

Dr. Erich Hunziker, Chai man

Dr. Clive Meanwell

BB Biotech **Shareholder letter** 

Eventful year for BB Biotech ahead: new product launches will be one of the focal point for biotech investors in 2019, as the resulting cash flows enable continued investments in the companies' research pipelines and catapult them to the next level of their life cycle. For larger biopharma companies, acquisitions and licenses will continue to serve as an additional source of diversification and subsequent growth, and this dynamic will be boosted by the 2018 US tax reform, which lowered corporate tax rates and encourages the repatriation of ex-US cash.

On the flip side, as partisan behavior seemingly manifests in the US Congress towards the 2020 election, key political topics such as the debate on drug pricing as well as changes to the Affordable Care Act will remain. However, we continue to fundamentally believe that – despite the political situation having the potential to cause market uncertainty – innovation provided by the industry will improve the quality as well as cost of individual care for society, thus justifying adequate pricing.

cystic fibrosis, Alexion's next-gen complement inhibitor Ultomiris for patients with paroxysmal nocturnal hemo-globinuria and Sage's brexanolone for women with severe post-partum depression. The plethora of approvals fortifies our confidence in the double-digit revenue growth potential of BB Biotech's portfolio.

# Research pipeline investment supports future value creation

In 2018 alone, 59 new products were approved in the US, more than in any of the previous 20 years. Of these, 30 products were developed by biotech companies, 19 by large pharmaceutical companies and 10 by speciality pharmaceuticals and generics companies. The EU CHMP recommendations for approval totaled 42 new active substances in 2018, with 17 stemming from biotech companies and 25 from the large and speciality pharmaceutical industry. We are particularly excited about development stage companies that are investing in new technology

# **Biotechnology** Outlook

# Recent and expected product approvals highlight significant revenue growth opportunity

Investors continue to be heavily focused on the market success of newly introduced individual products and product classes. Categories of interest include the CGRP products Aimovig (Amgen/Novartis), Ajovy (Teva) and Emgality (Lilly), CAR-T products Yescarta (Gilead) and Kymriah (Novartis), and the newly launched TTR amyloidosis products Onpattro (Alnylam) and Tegsedi (Ionis) prior to the expected US entry of Tafamidis (Pfizer) in summer 2019.

Recently launched products that will be closely monitored to determine whether they will meet full-year sales expectations include Agios/Celgene's Idhifa and Tibsovo for acute myeloid leukemia (AML), Ionis/Biogen's Spinraza for spinal muscular atrophy, Neurocrine's Ingrezza for tardive dyskinesia and Radius' Tymlos for osteoporosis. Further, we expect a number of key approvals and launches in 2019, including Vertex's triple therapy products for

platforms that provide the foundation for generating multiple candidates that could treat a variety of unique indications. These include RNA-focused companies such as Ionis Pharmaceuticals, Alnylam Pharmaceuticals, Wave Life Sciences and Moderna Therapeutics as well as other technology platform companies such as Macrogenics and Sangamo. Companies with individual products that find clinical and market success in multiple indications over time are also of great interest, as this will provide them with a sustained source of future growth following revenue stabilization in initial indications.

Sage's 217 molecule is a prime example. It is expected to be filed and initially approved for treating women with a severe form of post-partum depression (PPD) but the company is also testing 217 in larger indications such as major depression disorder (MDD) and other CNS disorders such as bipolar depression and insomnia. Argenx, a European biotechnology company, is deploying a similar strategy for its lead development candidate efgartigimod, a novel FcRn antagonist developed for different autoim-

mune disorders such as myasthenia gravis (MG), immune thrombocytopenia (ITP), pemphigus vulgaris (PV), and chronic inflammatory demyelinating polyneuropathy (CIDP). Further examples include Incyte's Jakafi, currently approved for treating patients with myelofibrosis (MF) and polycythemia vera (PV), which is expected to receive FDA approval for acute graft versus host disease (GvHD), and Intercept's Ocaliva, approved for primary biliary cholangitis (PBC) and in multiple clinical trials for patients with nonalcoholic steatohepatitis (NASH).

### Industry consolidation remains a key driver of growth

Not only smaller- and mid-cap companies are potential acquisition targets. Large biotechnology companies – due to depressed and attractive valuations – received takeover offers as well. Three takeovers affected our portfolio in 2018. Avexis was taken over by Novartis for USD 12 bn, Juno by Celgene for USD 9 bn and Tesaro was valued at USD 5 bn in GlaxoSmithKline's offer. Early 2019 started with the surprising announcement that Bristol-Myers Squibb was offering more than USD 70 bn for Celgene. The deal terms include USD 50 per Celgene share in cash, one BMS share per Celgene share and a contingent value right of USD 9 per Celgene share if three key candidates in Celgene's pipeline are approved in the next few years. Further consolidation in the industry is likely to continue.

# Drug prices still in focus, regulatory environment remains favorable

BB Biotech expects continued debate around drug pricing as list prices for existing medications remain on the rise and companies with highly novel medicines are expected to seek premium prices after their approval. However, we believe investor concerns that prices will ultimately be restricted will prove to be more sporadic than systematic. We will closely follow changes sought by Alex Azar, who has been appointed Secretary of Health and Human Ser-vices and has highlighted reduced drug prices and outcomes-based pricing for the Medicare segment as priorities as head of HHS. We also anticipate continued debate over the US Affordable Care Act, changes which will likely reduce the pool of insured individuals through the repeal of the individual mandate. Indeed, repeal of the individual mandate will allow healthy and younger individuals to opt out of healthcare insurance plans without a financial penalty, which may exert pressure on premiums for those remaining on the plans.

A supportive regulatory environment remains critical to the continued success of the biotech industry. During 2018, new PDUFA guidelines, PDUFA VI, were finalized and approved by Congress. The new law ensures the consistent funding of the FDA during fiscal years 2018–2022, enabling the agency to continue to bring important new medicines to the market.

# Key approvals and clinical trial results provide ample newsflow

One of the highlights within the BB Biotech portfolio is the expected approval and launch of products such as Vertex, which will report trial results from its second triple (VX-455 containing regimen) combination therapy tested in patients who have one F508deletion mutation and one minimal functional mutation not likely to respond to tezacaftor and/or ivacaftor. The company will then decide to file either the VX-659 or the VX-455 three-drug cocktail with an expected successful launch in late 2019.

Companies in our portfolio expected to receive their first product approval include Sage — for Brexanolone treating women with post-partum depression — and for Intra-Cellular Therapies — for Lumateperone, which treats schizophrenia patients. Investors will carefully monitor Alexion's launch success with Ultomiris, the company's next-generation and long-acting C5 complement inhibitor for ultrarare disorders such as for adults with paroxysmal nocturnal hemoglobinuria (PNH).

«Companies with individual products that fin clinical and market success in multiple indications over time are of great interest»

On the clinical data front, many important late-stage readouts will impact the valuation of our holdings. These include results from both Intercept (Ocaliva) and Gilead (Selonsertib) for non-alcoholic steatohepatitis NASH patients; Macrogenics with survival data for Margetuximab to treat Her2+ metastatic breast cancer patients who have received prior anti-Her2 therapies and Myovant reporting on multiple Phase III studies for Relugolix to treat women's diseases such as uterine fibroids and endometriosis as well as men with advanced prostate cancer.

The team of experienced biotech specialists has established an enviable track record in identifying and managing investment opportunities in the biotech sector. Its academic expertise, many years of experience and collaboration, and a broad interest in all areas of medicine, biochemistry, and economics ensure an inspiring and constructive interdisciplinary dialogue.



# Access to fast since 1993





Biotechnology is one of the most attractive of any sector today with estimated annual growth in the double-digits. Megatrends such as increasing life expectancy and a westernized lifestyle are powerful growth drivers.





BB Biotech invests in companies in the fast growing market of biotechnology and is one of the world's largest investors in this sector with 25 years of experience. The shares of BB Biotech are listed on the SIX Swiss Exchange, the Frankfurt Stock Exchange and the Stock Exchange in Milan. Its investments are focused on listed companies that are developing and commercializing novel drugs that offer sound value for the health-care system.

# growing biotechs













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Since 2006 with the BB Biotech Investment Management Team MBA Texas Christian University of Fort Worth BS in microbiology and zoology, Louisiana State University

**New York** 











**Rudy LeBlanc** 

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# Jan Bootsma

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BB Biotech Team, London



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#### **Dr. Daniel Koller**

Since 2004 with the BB Biotech Investment Management Team and its head since 2010 Master's degree in biochemistry of the Swiss Federal Institute of Technology (ETH) Zurich PhD in Biotechnology of the Swiss Federal Institute of Technology (ETH) Zurich, and Cytos Biotechnology Ltd, Zurich

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#### Michael Hutter

Since 2008 responsible for Finance & Compliance Swiss Chartered Accountant

#### Tanja Chicherio

Since 2013 responsible for Marketing & Communication
Degree in media and communication sciences with a minor in business administration
from the University of Zurich



# Idea generation and pre-screening

The investment universe for BB Biotech comprises about 800 companies in the biotech industry worldwide. It includes large caps to microcaps and even later-stage private companies. The portfolio management team monitors this industry actively.

In an initial phase the team identifies disease areas where major progress is being made, technological advances are promising, new mechanisms of action are being discovered or technology platforms that could be leveraged for multiple therapies are being developed.

To stay highly informed, the team talks to analysts, conducts interviews with doctors and specialists, attends medical conferences, reviews scientific literature, and visits companies on-site. The team also regularly evaluates the geographical allocation of its investments by visiting countries or areas that show interesting developments.

Once promising investment themes (disease area, technology, etc.) are identified, the universe is reduced from 800 companies to about 300.

# Due Diligence

With the due diligence process the focus switches from themes to individual companies and products. Qualitative as well as quantitative screening criteria are applied. Again, doctors and specialists are consulted to learn more about different drug candidates. The objective is to understand the innovation behind a product, to see what benefit the product could provide for the patient, but also if the product makes sense from a health economic standpoint.

BB Biotech tries to focus on products that are novel and essentially reduce healthcare costs because of their higher efficiency or better safety. The time horizon for these investments is mid- to long-term. Another important point is the quality of the management, which is assessed in discussions during company meetings.

For about 100 companies the team has created and maintains financial models that help to assess the financial position of the company and get a sense of market opportunities or to review the clinical data companies have produced and presented. At the end of this phase the team discusses the investment cases and selects the most promising ideas.

INVESTMENT UNIVERSE

800

(number of companies)

FINANCIAL MODELS BB BIOTECH

100

(number of companies)





# Investment decision and portfolio construction

If the team feels comfortable with an investment idea, the analyst that covers the company prepares a detailed investment proposal. This includes a financial model, a summary of the clinical data the company has presented, the investment rationale with potential upside and downside as well as the proposal of the size of the investment and at what price range the investment should be built up. This proposal is then presented to the Board during the monthly calls, where the Board of Directors and the team engage in an active discussion about the potential investment.

BB Biotech also holds a biannual strategy meeting, where the Board and the Investment Management Team review strategic developments in the biotech industry and meet with the management of the portfolio holdings or of potential investments.

Once the Board has approved a proposal, the portfolio managers build the position in a relatively short time, provided that the price levels are within the approved range for investment. This results in a biotech portfolio of around 20 to 35 companies.

# IV

# Monitoring and risk management

Once the portfolio is established, the monitoring and risk management processes begin. The development of the drug candidates is monitored closely with new clinical data becoming available at medical conferences. The validity of the investment case is continuously assessed as the team regularly meets with management and keeps the financial model updated.

If there is a substantial change in the underlying value of a company that requires action, the team will present a proposal to the Board to increase the position, or to exit it, depending on what the reasons for the change are.

Additionally, the portfolio managers may adjust the positions in the portfolio by buying when prices are lower than the Net Asset Value estimated with the help of financial modeling or by selling a part of the position on strength, if a stock looks relatively overvalued. However, the Board is always involved in major changes. The portfolio is also monitored with the help of risk management software.

POSITIONS IN THE PORTFOLIO

20 - 35

(number of companies)

NUMBER OF COMPANY MEETINGS

> 100

(2018)

BB Biotech invests in fast-growing biotechnology companies that are developing and marketing innovative drugs. It focuses on biotech companies whose products address areas of significant unmet medical needs and thus have above-average sales and profit-growth potential. Besides profitable large cap companies, BB Biotech is building up its investments in promising small and mid cap companies

The team of investment experts is concentrating not only on established target areas such as oncology, orphan diseases and neurological indications, but also on the technologies of tomorrow that could lead to novel treatment methods with attractive therapeutic profiles and substantial economic rewards. These future technologies include RNA platforms and cell and gene therapies. A total return of 15% p.a. over a medium- to longer-term investment horizon is targeted.

The asset classes available to BB Biotech are direct investments in the shares of listed companies, equity interests in unlisted companies, corporate bonds, and options on a range of underlying assets. BB Biotech invests almost

Team of Bellevue Asset Management Group when making its investment decisions. It can also turn to an extensive international network of physicians and specialists in individual sub-segments of the biotech industry for further support and advice. The Investment Management Team creates detailed financial models for all portfolio holdings and they must provide compelling arguments that these holdings have the potential to double in value over a fouryear time frame. The team is guided by its convictions, not by benchmark considerations. Upside potential is driven in most cases by the power of innovation, the launch of new products for serious or significant illnesses, and successful company management. Each investment case is constantly monitored and evaluated within the scope of our stringent and disciplined risk management process and corrective action will be taken if and when necessary.

BB Biotech's investment portfolio will usually consist of 20 up to a maximum of 35 biotechnology companies. There are established, large cap companies as well as small and mid cap companies in the portfolio. No single core position will have a weighting of more than 25%, however. Smaller positions will be taken in innovative biotech

# Investment Strategy

exclusively in stocks for liquidity and risk/return reasons. At least 90% of its shareholdings must be in listed companies, while always holding more than 50% of its assets in equity investments. Corporate bonds are an alternative primarily when stock market trends are negative. Options on the stocks of portfolio companies will be bought and sold at opportune times and as a means of hedging currency exposure.

Exhaustive, multi-stage due diligence precedes the selection of individual investments. We must have a thorough understanding of every company we invest in. Before an investment is made, the team analyzes a company's financial statements in detail and assesses its competitive environment, R&D pipeline, and patent portfolio as well as its customers' perceptions of its products and services. Close contact with company executives is of high importance to us in this due diligence process, but also afterwards, as we believe that it takes strong leaders to achieve strong results.

BB Biotech relies on the long-standing experience of its distinguished Board of Directors and on the fundamental analysis of the experienced Investment Management

companies with promising R&D pipelines. From a regional perspective, the US biotech sector has displayed a high level of innovation and so this regional bias is also reflected in BB Biotech's portfolio. The predominance of the US biotech industry can be traced to the country's stellar research clusters, industry-friendly regulatory frameworks and myriad financing options, among other factors.

New investments in small and mid-cap companies will have a weighting of between 0.5% and a maximum of 4% to ensure that both upside potential and R&D risks are adequately addressed. Because it is an investment company, BB Biotech has the flexibility to increase portfolio weightings considerably over time as a position increases in value. Smaller positions may become a top holding as their business develops and milestones such as positive Phase III outcomes, drug approvals, the successful marketing of products, and a sustainable flow of profits are achieved. All positions and their valuations are continually monitored, taking into account their growth potential and other aspects, and will be reduced if and when appropriate

# Participations as at December 31, 2018

| Company                                    | Number of<br>securities | Change since<br>12/31/2017 | Local<br>currency | Share<br>price | Market value<br>in CHF mn | In % of securities | In % of<br>shareholders'<br>equity | In % of<br>company |
|--|-------------------------|----------------------------|-------------------|----------------|---------------------------|--------------------|------------------------------------|--------------------|
| Ionis Pharmaceuticals                      | 8 741 334               | 605 000                    | USD               | 54.06          | 463.9                     | 15.1%              | 16.1%                              | 6.4%               |
| Incyte                                     | 3 808 322               | 110 000                    | USD               | 63.59          | 237.7                     | 7.8%               | 8.2%                               | 1.8%               |
| Neurocrine Biosciences                     | 3 343 090               | (109 663)                  | USD               | 71.41          | 234.3                     | 7.6%               | 8.1%                               | 3.7%               |
| Vertex Pharmaceuticals                     | 1 370 445               | (105 000)                  | USD               | 165.71         | 222.9                     | 7.3%               | 7.7%                               | 0.5%               |
| Esperion Therapeutics                      | 3 392 964               | 1 030 000                  | USD               | 46.00          | 153.2                     | 5.0%               | 5.3%                               | 12.7%              |
| Celgene                                    | 2 303 875               | (1 120 423)                | USD —             | 64.09          | 144.9                     | 4.7%               | 5.0%                               | 0.3%               |
| Agios Pharmaceuticals                      | 2 878 134               | 158 136                    | USD               | 46.11          | 130.3                     | 4.3%               | 4.5%                               | 4.9%               |
| Sage Therapeutics                          | 1 375 229               | 332 790                    | USD               | 95.79          | 129.3                     | 4.2%               | 4.5%                               | 2.9%               |
| Alexion Pharmaceuticals                    | 1 314 428               | (40 000)                   | USD               | 97.36          | 125.6                     | 4.1%               | 4.4%                               | 0.6%               |
| Halozyme Therapeutics                      | 8 322 860               | (197 277)                  | USD               | 14.63          | 119.5                     | 3.9%               | 4.1%                               | 5.8%               |
| Alnylam Pharmaceuticals                    | 1 571 389               | 520 051                    | USD               | 72.91          | 112.5                     | 3.7%               | 3.9%                               | 1.6%               |
| Radius Health                              | 6 710 276               | 1 011 477                  | USD               | 16.49          | 108.6                     | 3.5%               | 3.8%                               | 14.9%              |
| Argenx SE                                  | 884 739                 | 884 739                    | USD               | 96.07          | 83.4                      | 2.7%               | 2.9%                               | 2.5%               |
| Gilead                                     | 1 332 204               | (1 442 392)                | USD               | 62.55          | 81.8                      | 2.7%               | 2.8%                               | 0.1%               |
| Moderna Therapeutics 1) 2)                 | 4 785 681               | 4 785 681                  | USD               | 15.27          | 71.7                      | 2.3%               | 2.5%                               | 1.5%               |
| Akcea Therapeutics                         | 2 386 471               | 1 137 821                  | USD               | 30.14          | 70.6                      | 2.3%               | 2.4%                               | 2.7%               |
| Wave Life Sciences                         | 1 465 002               | 608 906                    | USD               | 42.04          | 60.5                      | 2.0%               | 2.1%                               | 5.0%               |
| Myovant Sciences                           | 3 597 882               | 90 000                     | USD               | 16.41          | 58.0                      | 1.9%               | 2.0%                               | 5.3%               |
| Intercept Pharmaceuticals                  | 575 719                 | 90 000                     | USD               | 100.79         | 57.0                      | 1.9%               | 2.0%                               | 1.9%               |
| Exelixis                                   | 2 835 000               | 2 835 000                  | USD               | 19.67          | 54.7                      | 1.8%               | 1.9%                               | 0.9%               |
| Nektar Therapeutics                        | 1 380 975               | 1 380 975                  | USD               | 32.87          | 44.6                      | 1.5%               | 1.5%                               | 0.8%               |
| Myokardia                                  | 877 266                 | 877 266                    | USD               | 48.86          | 42.1                      | 1.4%               | 1.5%                               | 2.2%               |
|  | 3 283 272               | 682 860                    | USD               | 12.70          | 40.9                      | 1.4%               | 1.4%                               | 7.8%               |
| Macrogenics                                |                         | 1 279 978                  | USD —             | 22.97          | 28.9                      | 0.9%               | 1.0%                               | 5.1%               |
| Scholar Rock Holding                       | 1 279 978               |                            |                   | 10.25          | 27.8                      | 0.9%               | 1.0%                               | 4.0%               |
| Alder Biopharmaceuticals                   | 2 766 008               | 500 000                    | USD               |                |                           |                    |                                    |                    |
| Voyager Therapeutics                       | 2 865 841               | 1 326 321                  | USD               | 9.40           | 26.4                      | 0.9%               | 0.9%                               | 8.8%               |
| Regeneron Pharmaceuticals                  | 68 156                  | (136 844)                  | USD               | 373.50         | 25.0                      | 0.8%               | 0.9%                               | 0.1%               |
| Intra-Cellular Therapies                   | 2 200 000               |                            | USD               | 11.39          | 24.6                      | 0.8%               | 0.9%                               | 4.0%               |
| Kezar Life Sciences                        | 818 432                 | 818 432                    | USD               | 23.60          | 19.0                      | 0.6%               | 0.7%                               | 4.3%               |
| Audentes Therapeutics                      | 769 404                 | 769 404                    | USD               | 21.32          | 16.1                      | 0.5%               | 0.6%                               | 1.8%               |
| Sangamo Therapeutics                       | 1 350 000               | 1 350 000                  | USD               | 11.48          | 15.2                      | 0.5%               | 0.5%                               | 1.3%               |
| Novavax                                    | 8 330 000               |                            | USD               | 1.84           | 15.0                      | 0.5%               | 0.5%                               | 2.2%               |
| G1 Therapeutics                            | 671 925                 | 671 925                    | USD               | 19.15          | 12.6                      | 0.4%               | 0.4%                               | 1.8%               |
| Cidara Therapeutics                        | 2 295 272               |                            | USD               | 2.35           | 5.3                       | 0.2%               | 0.2%                               | 8.3%               |
| Radius Health warrants,<br>02/19/2019      | 71 409                  |                            | USD               | 2.90           | 0.2                       | 0.0%               | 0.0%                               |                    |
| Total securities                           |                         |                            |                   |                | 3 064.2                   | 100.0%             | 106.2%                             |                    |
| Other assets                               |                         |                            |                   |                | 22.6                      |                    | 0.8%                               |                    |
| Other payables                             |                         |                            |                   |                | (202.3)                   |                    | (7.0%)                             |                    |
| Net asset value                            |                         |                            |                   |                | 2 884.5                   |                    | 100.0%                             |                    |
| BB Biotech registered shares <sup>3)</sup> | _                       | _                          |                   |                | _                         |                    |                                    |                    |

Exchange rates as at 12/31/2018: USD/CHF: 0.98160

Share split 1:2.18 as at December 6, 2018
 IPO of Moderna Therapeutics Inc. as of December 6, 2018
 Correspond to the total of all own shares held including the second trading line



# The biotech sector is fascinating

Dr. Daniel Koller has worked as an analyst and portfolio manager for the investment company for almost 15 years and has been head of the investment team since 2010. In this interview, the biochemist talks about the investment opportunities of small and medium-sized drug developers, important milestones, highlights and failures from the past decades and explains the success factors of his work.

# BB Biotech was launched as an investment vehicle 25 years ago. What were the reasons?

This was during the early years of Bellevue Group and at that time neither Switzerland nor the EU offered access to the very young and dynamic biotech sector in the United States. In Switzerland, there were only three big pharma players — Ciba, Sandoz, and Roche. At the same time, financial experts recognized that the sector had huge potential and they wanted to provide investors ways of tapping that potential. So we set up a special investment company that people could use to invest in the US biotech industry. BB Biotech was born.

# What kind of environment did the founders encounter at launch? The biotech sector was very different in those days, after all.

I started studying biotechnology in 1993. Special areas like genetic engineering were exciting and new, but so was biotechnology and the industrialization of the technology.

«Our first portfolio consisted of seven investments»

# Do you remember the composition of the first portfolio back then?

There were just a handful of listed companies, including today's industry giants like Amgen, Vertex, Biogen, and Genentech. They were just starting out back then and had just one or two marketable products, if any. We only had seven companies in our portfolio, with the three biggest accounting for more than three-quarters of our holdings. To compare: at the end of 2018, BB Biotech's portfolio comprised 34 positions.

# Where is the biggest unmet medical need today?

What we're seeing in the pipeline on Alzheimer's still gives little grounds for optimism. And other serious neurological disorders are incurable to this day, one example being Huntington's chorea, a genetic brain disorder. Then you have lots of cancers with few and/or fairly ineffective treatment options. And finally, only about 400 of the

approximately 7000 rare diseases – called orphan diseases in the trade – are addressable with an approved drug or potential treatment in late-stage clinical development. Despite these issues, we have reason to be hopeful because development is moving forward at a fast rate: 59 new drugs were approved in the US last year alone – more than ever before, which is an indication of the sector's strong momentum.

# Highly effective and technologically innovative drugs cost a lot of money. Is healthcare becoming a two-tier system, one for the rich, one for the poor?

I don't share that opinion. In established markets like the US, Europe, and Japan, the bulk of the population has access to public and private health insurance that covers even the costliest treatments. Plus, even though some medicines may be expensive, they all go through the life cycle typical of this business. The makers earn a profit with their product during the patent exclusivity period. When the patent eventually expires, imitators enter the market and squeeze the price. Many of the drugs that get top dollar today will be available at a much lower price in the coming 10 to 15 years when their product cycle ends. Apart from that, I would still not call it a two-tier system, even with the very high priced drugs, because many of these products help to tackle very serious and rare diseases that affect very small numbers of people. Price levels are much lower for drugs with large patient populations.

# You joined BB Biotech in 2004 and have headed portfolio management since 2010. What do you think were the key milestones during that time?

In 2010, after consultation with the Board of Directors and the portfolio Management Team, we decided to change the structural composition of the portfolio and to invest more in small and medium caps. Among other advantages, this allowed to benefit from at least one acquisition during each of the past several years. The acquisition of Actelion by Johnson & Johnson in 2017 was a highlight that clearly boosted our performance. Even more importantly, looking back over the years, we were able to support a wide range of outstanding medical treatment successes and thrilling launches that helped to make serious diseases treatable or even curable, ranging from the hepatitis C treatment revolution to cell-based therapies, novel cystic fibrosis drugs and innovations in the treatment of spinal muscular atrophy.

### What companies surprised you the most, in a good way?

II'd like to single out Vertex Pharmaceuticals as a prime example. It has now been listed on the stock exchange for more than two decades and hasn't always had it easy. Vertex was the first company to succeed in launching a novel direct acting antiviral to treat hepatitis, but their product was crowded out of the market by rivals soon after. To their great credit, Vertex developed a number of cystic fibrosis drugs all the way to approval. What's more, we expect a triple combo to be approved in 2019. While it

#### **POSITIONS IN PORTFOLIO**

**34** 

(2018)

does not cure cystic fibrosis, taking the tablet daily helps patients with the condition to reach the status of a healthy person. Other portfolio companies have also been raising the bar and dominating their markets, such as Incyte with Jakafi for the treatment of myelofibrosis and Celgene with Revlimid for the treatment of multiple myeloma. This brings me back to Actelion, which developed a number of dominant products for the treatment of pulmonary hypertension – which is ultimately what led to the Johnson & Johnson acquisition with the USD 30 bn price tag.

«We have accompanied a whole series of outstanding drug successes and launches that make illnesses treatable or curable»

# What were the biggest disappointments?

One of the most disappointing areas has been antimicrobial drug development. We made investments in the past based on the high unmet medical need in this area. The outcome was sobering at the end of the day, especially since many of the products failed to convince in clinical practice because they lacked true innovation and did not stand out much from existing older generations of antibiotics.

# Were there ever periods in which you wished you'd picked a different job?

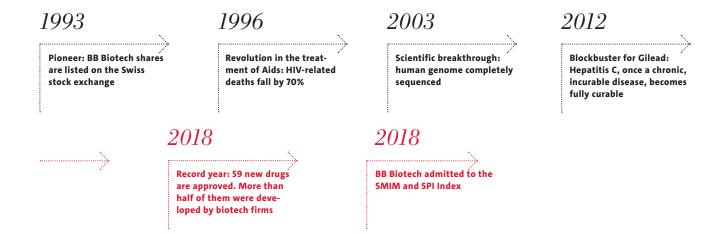
The first two years as Head Portfolio Management at BB Biotech were challenging, especially because pushy investors and some banks were urging us to convert to a fund. All in all, though, it's always been hugely exciting and I am still absolutely convinced that we are investing not just in one of the most promising but also one of the most fascinating sectors.

# You're a biochemistry PhD managing a stock portfolio worth billions. How did you learn the financial expertise you needed for the job?

It was a big step for me to change sides after handing in my dissertation at the turn of the millennium. I started in investment banking as a sell-side analyst at UBS. A year and a half later I switched to the buy side at a venture fund and was lucky to start working for BB Biotech at Bellevue Asset Management in 2004, initially as an analyst and portfolio manager and then as team leader since 2010. One of the main skills you need to be a successful investor in the biotechnology sector is the ability to judge whether a drug will develop successfully. The subject-area expert knowledge is more important than the financial arithmetic aspect.

# You initiated another portfolio restructuring last year: small and medium caps are attracting more attention again while the weighting of large caps is declining. What motivated this move?

Many of the large caps we have already shed or plan to shed are very solid businesses. But they no longer meet our criteria in terms of sales and profit growth to achieve our target return of about 15% per annum. What's more, our focus on new technologies means it makes sense to keep coming back to small and medium-sized firms, given their success in pursuing RNA-based, cell-based or genebased technologies and products, for example.



# Most of the investments in your portfolio are US-based. Is the European biotech sector less interesting?

Our portfolio structure is multi-tier. The first level is our medical areas such as oncology, orphan diseases, and neurological disorders. At level two, development status is relevant. We exclude both large US companies and very young and very small firms - and focus squarely on companies with a sound position in the clinical development of new therapies. Our third tier relates to new technologies. Putting all these criteria on top of each other, you invariably end up in the US market, which moreover is much broader and generally further developed than the European market. Argenx, which is Belgian, is the only European representative in our portfolio right now. Nevertheless, we are always screening European and Asian companies as well. But for the foreseeable future, BB Biotech's portfolio will continue to be US-heavy. That is also reflected in the investment candidates we have our eyes on at the moment, the majority of which are based in the US.

# Many investors are wary of buying biotech stocks because they seem too risky. What's your response?

I think the challenge for most investors is to be able to accurately assess the scientific novelty and the medical and clinical development risks involved. Then you have regulatory obstacles – the regulatory agencies FDA (US) and EMA (Europe) – followed by the pricing negotiations between the drug developers and the health insurance providers. And finally, the products need to be able to compete against existing products. That's why individual investments in smaller and younger firms are high-risk. Our response to this is diversification; we are currently invested in 34 biotech stocks. Volatility in the biotech sector is higher than average, true, but significantly higher overall returns make up for that.

# You have earned average annual returns of about 15% since starting out at BB Biotech. Do you think you can continue to add value at that rate in future?

If you include the medium to long-term cycle and the current valuations and analyze it all with our internal financial models, I am perfectly confident of that. Another factor is the courage to go against market trends in a given situation. When markets are down, we tend to buy more. When they bubble up as they did in 2015, we raise the cash allocation so we can take advantage of new investment opportunities further down the road. However, we really can't predict short-term trends. Think of the past few months, for example. While December was extremely tough, BB Biotech share prices have recovered since the start of the year.

«The judgement of whether a drug is successful is a critical success factor in our work»

### What are your three personal favorites for 2019?

In large caps, we think Vertex is ideally positioned. It's an extremely profitable company with a pipeline that promises a doubling or even trebling of sales over the coming years. In the mid-cap space, Argenx is a strong contender with a new approach to the treatment of autoimmune disorders. Its finances are sound and the company is heading in a very promising direction. Our largest investment, Ionis Pharmaceuticals, has a very strong balance sheet with about USD 2 bn in cash, owns three-quarters of Akcea, which is listed; it's a leader in antisense therapy and has more than 30 new drug entities in the pipeline based on this technology. We believe Ionis is only just starting to grow in value and expect it to make big strides in the foreseeable future.

# Biotechnology: driving innovation in medicine

There were 59 new drug approvals in 2018 in the United States, the world's largest drugs market. This was the highest number since 1996, when a record 53 new drugs were approved. More flexibility on the clinical and regulatory front in combination with an acceleration of new technology developments enabled the trend.

In the medical innovation journey from laboratory bench to market-ready medicines, drug developers are focusing their efforts on five main areas of medicine. In cancer medicine, the goal is to prolong patients' lives while improving their quality of life with better-tolerated drugs.

In rare inherited diseases, new therapies are targeting molecular switches in the human genome. These genetic engineering methods aim to eliminate the genetic defect and bring about a lasting cure. In the wide-ranging area of neurology, new therapeutic modalities affect the transfer of neurotransmitters involved in disease processes. New products have recently entered the market in a few therapeutic areas, but the causes of other diseases such as Alzheimer's are still not fully understood.

By contrast, doctors have plenty of approved drugs to choose from in the treatment of metabolic diseases. New products therefore need to stand out by being easier to administer to patients or by having fewer side effects. On the other hand, new medicines to treat infectious diseases need to be more effective, less resistant and better tolerated than today's standard treatments.

A growing number of these new products are biologics. While medicines made from chemical substances need to be taken daily, medicinal products made from antibodies, proteins or other biological molecules are administered by injection or infusion weekly, monthly or at longer intervals. This makes it easier for patients to adhere to their treatment regimens.

# Market-ready technologies in BB Biotech's portfolio

BB Biotech opened positions in some companies as soon as they published evidence demonstrating the efficacy of their investigational therapeutics in clinical trials. One example of such an investment is Ionis Pharmaceuticals, which is now a core portfolio position. Ionis has established itself as a leader in the field of antisense technology. More than 30 compounds currently being evaluated

**PRODUCT APPROVALS 2018** 

**59** 

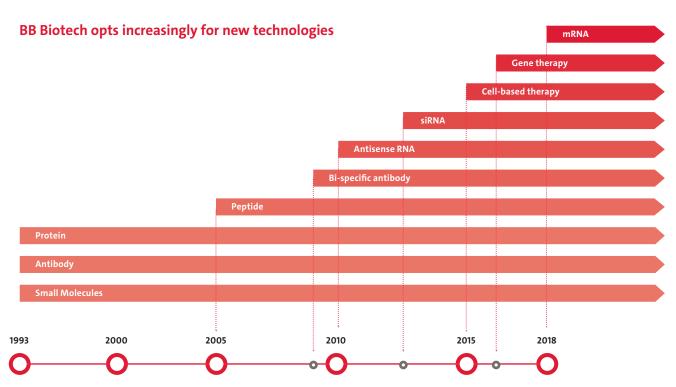
(USA)





# «Spinraza is one of the most successful orphan diseases product launches»

**Dr. Daniel Koller** Head Investment Management Team



Source:Bellevue Asset Management

in preclinical and clinical trials, either by Ionis itself or by third-parties through licensing agreements, originated from the company's proprietary technology platform. Spinraza, a drug for treating spinal muscular atrophy, a rare muscle disorder in infants, was launched in 2017 in the US and Europe and has since enjoyed one of the most successful post-launch sales curves ever witnessed in the field of orphan diseases (estimated 2018 sales through Ionis' partner Biogen: USD 1.5 bn).

Vertex Pharma is another prime example of a biotech company that has snagged a commercially lucrative niche market. The company has three products in the marketplace for treating patients with cystic fibrosis, a disease caused by a defective gene that prevents bodily secretions in the respiratory tract, for example, from being cleared out. It is fatal if left untreated. The drugs that Vertex has launched thus far target about 60% of all the different genotypes associated with this disease and they allow the people afflicted with this condition to have an almost normal life expectancy. That percentage will climb above 80% if a new product combining all three substances is approved in 2020, which we expect will be the case.

SPINRAZA SALES

**USD 1.5 bn** 

(2018, estimated)

# Gene therapies

Gene therapies aim to provide a permanent cure rather than just managing a disease. Specifically, the goal is to fix an inherited genetic defect. The trigger of disease is an error in the genetic information that may for instance cause a certain protein to be non-functioning. Treatments such as enzyme replacement therapy remedy this deficiency. Certain virus types such as adeno-associated viruses or retroviruses act as messengers by inserting the desired gene into the cell so that the information is read and implemented.

| Voyager Therapeutics  | 0.9% |
|-----------------------|------|
| Audentes Therapeutics | 0.5% |
| Sangamo Therapeutics  | 0.5% |

#### APPROVED GENE THERAPIES

7

(3 USA, 4 Europe)

In conventional gene therapies, a gene is inserted either episomally (not integrating in the genome) or randomly into the genome. In gene editing, the patient's genome is cut at precisely the right location and corrected or embellished. A variety of «gene scissors» (endonucleases) are used for this purpose, including CRISPR, zinc finger nucleases, meganucleases and TALEN (transcription activator-like effector nuclease). An advantage of this approach is that integration of the genetic material means that only one treatment would be required for a potential cure, so a treatment's long-term sustainability or tolerability would not be an issue.

After decades of research, a variety of gene therapy approaches have made it to market. CAR-T-cell therapies make use of the fact that our bodies are trained to automatically attack pathogens or cancer cells. The basic aim of this approach is the genetic reprogramming of T-cells. T-cells are taken from the patient, equipped with the gene for a specific artificial (chimeric) receptor in a laboratory and then replicated. These new CAR-T-cells are then infused back into the patient, where they track down the defined antigens on cancer cells and initiate their destruction.

Pioneers in the field of CAR-T therapy include our former portfolio investments Juno Therapeutics (2017 acquired by Gilead) and Kite Pharma (2018 acquired by Celgene). Kite received US regulatory approval for its Yescarta product in 2017 and EU approval in 2018.

While T-cells are engineered in these CAR-T therapies ex vivo, in vivo gene therapies are delivered directly by the intravenous or intrathecal route. BB Biotech opened a position in Avexis, an in vivo gene therapy company, in September 2016 that yielded a handsome return. The US company, which is working on a gene therapy to permanently cure spinal muscular atrophy, was acquired by Novartis in April 2018.





# «We are investing successfully in the pioneers of cell and gene therapy»

**Dallas Webb**Investment Management Team

# New therapeutic indications have potential for patients and the biotech industry

| 1 x day       | \$ per tablet – \$\$\$ per tablet                            | Chemical substance                                     |
|---------------|--|--|
| 1x week/month | \$\$\$ per injection — \$\$\$ \$\$\$ per injection           | Biologics<br>RNA based therapies                       |
| 1 x year/life | \$\$\$ \$\$\$ per infusion — \$ \$\$\$ \$\$\$\$ per infusion | Cell-based therapies<br>Gene therapies<br>Gene editing |

Source: Bellevue Asset Management

# Gene therapy in numbers

Medical experts believe that the new gene therapy approaches will be useful in treating a growing number of diseases. Since tumor growth often has genetic causes, approximately two-thirds of all gene therapies are being tested for use in cancer medicine, according to recent estimates of the Journal of Gene Medicine. Other therapeutic areas are monogenic disorders caused by a single gene defect (>11%), infectious diseases (>5%), cardiovascular diseases (>5%) and neurological disorders (>1%). Many inherited diseases have a prevalence of 1 000 to 10 000 patients. Three gene therapies are currently approved in the USA and four in the EU. Approximately 2 800 such therapies are undergoing clinical trials worldwide. More than half of these candidates are in the first phase of clinical development, with only a few being tested in pivotal regulatory studies. The time-consuming and costly treatment process, which generally involves prolonged hospitalization, and the small patient population have their price. As an example, treatment with Luxturna, which transfers a functioning version of the RPE65 gene into the retina, comes with a price tag of USD 825 000 per patient per year.

GENE THERAPIES IN CLINICAL TRIALS

2805

(as of August 2018)

# RNA therapies

While most drugs so far are designed to block certain proteins that cause disease, RNA therapies intervene at an earlier stage. They target human DNA in the nucleus where enzymes produce these proteins, either by blocking the production of these proteins or by promoting gene expression. The substances thus developed can be tailored specifically for use in many therapeutic indications, ranging from metabolic disorders and rare genetic diseases to cancer, infectious diseases and neurological disorders.

| Ionis Pharmaceuticals   | 15.1% |
|-------------------------|-------|
| Alnylam Pharmaceuticals | 3.7%  |
| Moderna Therapeutics    | 2.3%  |
| Akcea Therapeutics      | 2.3%  |

#### ANTISENSE CANDIDATES IN PIPELINE

**>30** (lonis)

Antisense, RNAi and small interfering RNA (siRNA) technologies have become established as genetic engineering techniques in drug development. They all work by blocking certain steps in the transfer and coding of genetic information. The antisense approach acts on the expression of certain genes that trigger disease in one of two ways: either by blocking gene expression, or by promoting gene expression through interference with the splicing apparatus that joins the substances to make fully-fledged mRNA. Our core holding lonis Pharmaceuticals is a world leader in this technology with more than 30 candidates in its proprietary development pipeline. siRNA technology is used to block the synthesis of certain proteins that trigger the onset of certain diseases. By contrast, substances based on the mRNA approach work by introducing a messenger RNA from outside to make specific proteins.

2018 was a very exciting year for the RNA specialists in BB Biotech's portfolio. Akcea is an antisense specialist and its Tegsedi therapeutic was approved late in the year by the US FDA for hATTR, an inherited rare disease. Akcea is a spinoff of Ionis Pharmaceuticals and focused on developing antisense therapies for rare lipid disorders. The market capitalization of Akcea doubled during the course of 2018.

Alnylam received regulatory approval for Onpattro, the first drug ever to be developed using RNAi technology. Alnylam has more products in late-stage clinical trials, Fitusiran, for example, with which it is taking a completely new approach in the treatment of hemophilia and rare bleeding disorders. In addition, Alnylam is collaborating with The Medicines Company to develop a cholesterol-lowering drug.



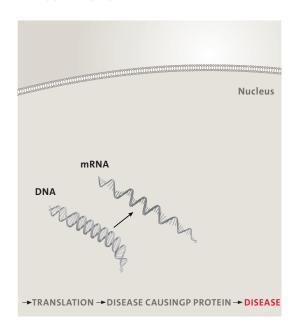


# «In 2018 we saw trailblazing RNA based product approvals»

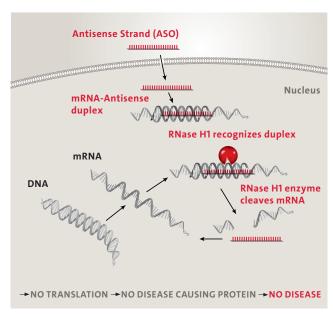
**Dr. Christian Koch** Investment Management Team

# Mechanism of action antisense therapy

#### WITHOUT ANTISENSE



#### **WITH ANTISENSE**



Source: Ionis Pharmaceuticals/Bellevue Asset Management

# A GRAPHIC GUIDE TO ANTISENSE

The antisense approach is about inactivating or at least significantly downregulating the transfer of genetic information from the human genome in order to stop the production of the abnormal proteins that cause a particular disease. This intervention always takes place after the DNA has been transcribed to messenger RNA (mRNA). Specifically, this method uses short fragments of DNA (antisense oligonucleotides, ASOs) to bind to messenger RNA and thus stop the mRNA from being translated into abnormal proteins.

Wave Life Sciences, which has been publicly traded since the end of 2015, presented initial clinical data in December for its most advanced product candidate, which targets Huntington's disease, an inherited progressive brain disorder. The company is investigating a proprietary stereochemistry technology that enables the precise three-dimensional arrangement of molecular structures so to modify their chemical and pharmacologic properties.

Moderna Therapeutics is a pioneer in the new class of mRNA therapeutics. This US company raised USD 606 mn through its IPO on December 6, 2018, making it the largest IPO in the history of the biotech industry. However, the ten vaccines in Moderna's pipeline targeting various indications are still in very early stages of development.

# Neurology

Neurological diseases span a broad spectrum of brain and peripheral nervous system dysfunction, including conditions such as Alzheimer's, Parkinson's, depression, migraine and multiple sclerosis. Rapid aging of the global population poses growing challenges to healthcare systems. On top of the increasing cost of medicines, the cost of residential care adds to the burden. The demand for new therapies that modify disease outcome instead of just relieving symptoms is all the more urgent.

| Neurocrine Biosciences   | 7.6% |
|--------------------------|------|
| Sage Therapeutics        | 4.2% |
| Alder Biopharmaceuticals | 0.9% |
| Scholar Rock             | 0.9% |
| Voyager Therapeutics     | 0.9% |

**COST OF NEUROLOGICAL DISEASES** 

> USD 800 bn

(annually, USA)

New drugs to treat conditions such as depression, schizophrenia and Alzheimer's commonly require clinical trial programs involving large patient populations. These medical areas continue to be the domain of primarily large pharma and biotech firms because of the associated high costs. Exceptions include two BB Biotech portfolio companies. Intra-Cellular Therapeutics owns lumateperone, an investigational medicinal product that has successfully completed two Phase III trials for the treatment of schizophrenia. The substance is novel in being able to simultaneously target multiple pathways for neurotransmitters like serotonin and dopamine. The target action date for a decision by the relevant FDA panel on approval of the drug in this therapeutic indication is September 2019. Voyager Therapeutics develops gene therapies, one of which is VY-AADC, an agent to treat Parkinson's. It works by promoting the synthesis of an enzyme designed to promote the production of an important neurotransmitter, dopamine, in the brains of patients with advanced disease.

A migraine drug developed by Alder Biopharmaceuticals is in the final preapproval stage. The antibody eptinezumab is the only drug from the class of CGRP inhibitors that involves just four infusions a year. Alder plans to file a new drug application for approval in the US in the first quarter of 2019. Sage Therapeutics made for another highlight in 2018 with its drug Zulresso for the management of postpartum depression. Up to 20% of mothers experience this psychological disorder to a greater or lesser degree. It occurs immediately after childbirth and is attributable to hormonal changes. The agent stands out from all the other treatments available through its combination of rapid efficacy and good tolerability. The FDA's decision on approval of the injectable version is expected by March 2019. In January, the company also presented good data from its study of SAGE-217 in postpartum depression. SAGE-217 is a next-generation product for oral use.





# «Neurological diseases are the most common cause of work disability»

**Dr. Stephen Taubenfeld**Investment Management Team

# Yearly economic burden of major neurological diseases (in USD bn)

| USD 800   | Traumatic Spinal Cord Injury |                               | Parkinsons         |
|-----------|------------------------------|-------------------------------|--------------------|
| USD 700   |                              | Epilepsy                      | Multiple Sclerosis |
| UCD 600   |                              | Migraine Headache             |                    |
| USD 600   |                              | Traumatic Brain Injury        |                    |
| USD 500   |                              | Stroke                        |                    |
| USD 400 — |                              |                               |                    |
|           |                              | Chronic Low Back Pain         |                    |
| USD 300   |                              |                               |                    |
| USD 200   |                              |                               |                    |
| USD 100   |                              | Alzheimer's + other dementias |                    |
|           |                              |                               |                    |
| USD 0     |                              |                               |                    |

Source: ANNALS of Neurology, Analysis 2017, Dollar figures converted into 2014 values using the all items consumer price index for nonmedical (indirect) costs

# **Neurology in figures**

Neurological diseases increase in frequency with age and are the most common cause of work disability. In the United States alone, neurological diseases affect one-quarter of the population and cost the country an estimated USD 800 billion a year. Approximately 15% of people in the world today can expect to experience neurological injury of one kind or another during their lifetime. The biopharmaceutical industry is correspondingly keen in its efforts to develop new forms of treatment. 537 agents for the treatment of neurological disorders were under clinical development in 2018, according to surveys by PhRMA, the trade group representing the pharmaceutical industry in the US. That is the third highest number after cancer (1 120) and rare diseases (566).

The growing costs of health care for neurological and other diseases were the major impetus for the implementation of the Affordable Care Act, but it is not clear the proposed measures of this program will be sufficient to meet the daunting fiscal challenges of the near future. Given the extraordinary and rapidly growing costs of neurological disorders themselves, a concrete strategy is urgently needed to reduce the burden of neurological disease.

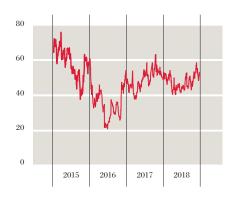
**SUBSTANCES IN CLINICAL TRIALS** 

**537** 

(2018)

# 7.4 bn

(In USD as at 12/31/2018)



#### **Ionis Pharmaceuticals**

lonis Pharmaceuticals is the leader in the space of antisense, with over 40 compounds in development using this technology. Antisense allows for the control of protein production at the genetic level. Our focus and investment strategy revolve around the technology platform, which has demonstrated significant progress. Spinraza (partnered with Biogen) was approved in late 2016 following two positive Phase III studies in spinal muscular atrophy, and had a very strong launch throughout 2017 and 2018. Tegsedi, partnered with Akcea, for hereditary transthyretin amyloidosis polyneuropathy, was approved in the US and EU in 2018. Our focus going forward is on the company's next-generation technologies such as 2.5 and LICA. Thus, Ionis remains an important and truly innovative investment in our portfolio.

#### MARKET CAPITALIZATION

# 13.5 bn

(In USD as at 12/31/2018)



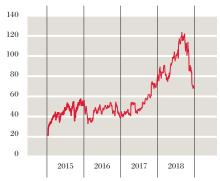
### Incyte

Incyte is focused on hematologic disorders, inflammatory disorders, and cancer. Their marketed product is Jakafi, an oral JAK-2 inhibitor that received approval for myelofibrosis (MF) and polycythemia vera (PV) in 2011 and 2014, respectively. We estimate that MF and PV represent a USD 3+ bn market opportunity in the US and Europe. Phase III trials in graft-versus-host-disease (GvHD) are also ongoing and could add another USD 500+ mn in sales if approved in 2019. In November 2009, Novartis licensed ex-US rights to Jakafi. A second-generation JAK-2 inhibitor, Baracitinib, posted positive data from several Phase III trials in rheumatoid arthritis and the product was launched as Olumiant in 2018. Incyte will receive royalties from partner Eli Lilly. Progress on other cancer compounds in its pipeline, including an FGFR inhibitor for cholangiocarcinoma and bladder cancer and a c-Met inhibitor for lung cancer, continues.

#### MARKET CAPITALIZATION

# 6.5 bn

(In USD as at 12/31/2018)



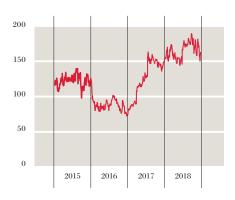
Source: Bloomberg

### **Neurocrine Biosciences**

Neurocrine is a biopharmaceutical company with a focus on women's health and CNS disorders. Neurocrine received approval for Ingrezza (Valbenazine) for tardive dyskinesia in mid-2017 and launched the product in the US with continued growth driven by underlying patient and physician demand. Tardive dyskinesia is a condition where patients have involuntary movements that cannot be controlled. Its second product is Elagolix, which is an oral GnRH antagonist approved for endometriosis and uterine fibroids. Endometriosis is a condition where part of the endometrium grows outside of the uterus leading to severe pain, painful intercourse, and bleeding. Uterine fibroids is a condition that can lead to painful menstruation and excessive bleeding, and potentially surgical removal of the uterus. Partner AbbVie will file for approval in uterine fibroids in 2019.

# 42.3 bn

(In USD as at 12/31/2018)



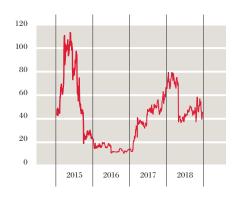
#### **Vertex Pharmaceuticals**

Vertex's core focus is cystic fibrosis. CFTR potentiator Kalydeco was launched in the US and Europe in 2012 for a subgroup of patients with cystic fibrosis. While the initial market opportunity is limited to around 5% of the patient population, we believe that sales could reach USD 1.0 bn with the inclusion of other small patient populations on the label. Positive Phase III results with the combination of Kalydeco and CFTR corrector VX-809, released in June 2014, enabled Vertex to begin to target the roughly 45% of patients who are homozygous for the most common mutation in the US and Europe in 2015. With this label inclusion, we expect sales of Kalydeco and the Kalydeco/VX-809 combination to reach approximately USD 4.0 bn. The company is also developing correctors that can be combined with Kalydeco and VX-661 to target the remaining patients who are heterozygous for the mutation. Data from Phase III trials announced in november were highly positive and we expect approval to follow in 2019.

#### MARKET CAPITALIZATION

# 1.2 bn

(In USD as at 12/31/2018)



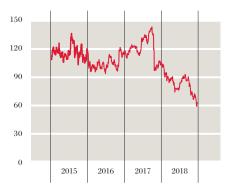
### **Esperion Therapeutics**

Esperion Therapeutics is focused on the development of treatments for cardio-metabolic diseases. Bempedoic acid is the only clinical asset and has now completed its registrational Phase III program. ETC-1002's main target ATP citrate lyase is located upstream of where statins work and ultimately reduces LDL cholesterol by upregulation of the LDL receptor. Bempedoic acid has shown LDL cholesterol reduction levels of around 20% on top of statins, up to 30% as monotherapy and up to 50% in combination with ezetimibe. In contrast to the recently approved subcutaneously administered PCSK9 antibodies, bempedoic acid poses a convenient and more economic once-daily oral solution. In parallel Esperion will submit an NDA for a fixed-dose combination with ezetimibe. Primary markets for both the mono- as well as fixed dosed combination therapy will be the statin-intolerant population as well as additional treatment for patients whose LDL cholesterol levels are not sufficiently controlled with a maximum tolerated statin. Regulatory submission in the US and in Europe are expected in the first and second quarter 2019.

# MARKET CAPITALIZATION

# 44.8 bn

(In USD as at 12/31/2018)



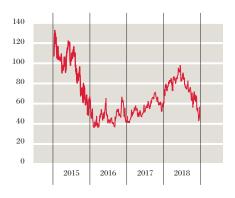
Source: Bloomberg

# Celgene

Celgene specializes in oncology and inflammatory diseases and has very strong fundamentals and positive long-term prospects based on products such as Revlimid, Pomalyst, Otezla and its robust pipeline of early-stage products. We expect Revlimid US revenue to continue to grow until loss of exclusivity in the 2024/25 timeframe, driven by the combined effects of increased prevalence, penetration and duration of treatment. The company's acquisition of Receptos broadened their immunology and inflammation franchise beyond Otezla by gaining access to ozanimod, which we expect to be approved in multiple sclerosis late this year and continues to be developed for inflammatory bowel disease (IBD). Celgene's acquisition of Juno in 2018 as well as their strategic collaboration with Bluebird has established the company as a leader in the CAR-T space. In January of 2019, Bristol-Myers Squibb entered into a definitive merger agreement to acquire Celgene in a cash and stock transaction with an equity value of approximately USD 74 bn. The deal is expected to close in the third quarter of 2019.

# 2.7 bn

(In USD as at 12/31/2018)



#### **Agios Pharmaceuticals**

The two most advanced oncology programs of Agios Pharmaceuticals are targeting mutations in the isocitrate dehydrogenase 1 and 2 (IDH1 and IDH2) enzymes, which are implicated in hematologic malignancies and solid tumors. Data with IDH2 inhibitor Idhifa (AG-221) were compelling and due to the high response rate and well-defined group of patients who benefited, the drug was given an accelerated approval in August 2017. We estimate the worldwide market opportunity for Idhifa at USD 750 mn for acute myeloid leukemia (AML). Celgene has worldwide rights to Idhifa, and Agios will receive milestones and an estimated 15% royalty on sales. Data with IDH1 inhibitor AG-120 in AML were also promising and the product was approved in July 2018. Results with AG-120 in rare solid tumors were not as compelling as hoped, and we include little revenue potential from these indications despite continued development. Finally, the company is developing AG-348, a novel compound for the treatment of pyruvate kinase deficiency that reported compelling proof-of-concept data, and Phase III trials are now underway.

#### MARKET CAPITALIZATION

# 4.5 bn

(In USD as at 12/31/2018)



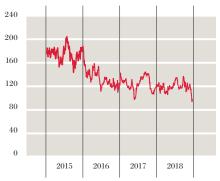
### Sage Therapeutics

Sage Therapeutics is a clinical-stage biopharmaceutical company focused on developing therapies for CNS disorders utilizing their GABA-A receptor-targeted proprietary platform. The company's lead therapy, Zulresso (brexanolone), is expected to be approved in March 2019 as an intravenous treatment for post-partum depression (PPD). Zulresso has shown rapid and durable efficacy, which sets it apart from all classes of drugs currently used in the field of depression and mood disorders. Sage is also developing an oral, follow-on version of Zulresso, called SAGE-217, which recently delivered positive Phase III data in PPD, and further supported by a successful Phase II study in major depressive disorder (MDD). An ongoing Phase III trial in MDD is expected to read out in 2020, after which the company plans to file a complete application for approval in both PPD and MDD. Sage is also investigating SAGE-217 in essential tremor and Parkinson's disease and owns an NMDA program with SAGE-718, targeting several orphan neurological indications.

# MARKET CAPITALIZATION

# 21.7 bn

(In USD as at 12/31/2018)



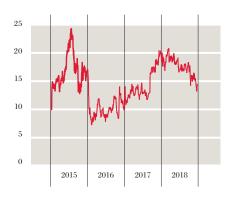
Source: Bloomberg

#### **Alexion Pharmaceuticals**

Alexion is developing drugs for rare disorders. Its lead product Soliris was approved in the US and Europe in 2007 for paroxysmal nocturnal hemoglobinuria (PNH) and we expect sales in PNH to reach about USD 2.0 bn. Atypical hemolytic uremic syndrome (aHUS) is the next indication for which Soliris gained approval in the US and Europe in 2011. We estimate it adds another USD 2.0 bn market opportunity for Soliris. Other indications such as myasthenia gravis and neuromyelitis optica could add an additional USD 1.0 to 2.0 bn in sales. To maintain its dominance, Alexion is in advanced development with a next-generation Soliris, ALXN-1210, which has an improved dosing profile and showed positive Phase III results. To diversify the revenue base away from Soliris, the company received approval of a novel compound for hypophosphatasia, Asfotase Alfa, in March 2015 and sales to date have exceeded expectations. In addition, Alexion gained Kanuma for lysosomal acid lipase (LAL) deficiency via its May 2015 acquisition of Synageva, and while the launch has been slow, the product should eventually be a more meaningful contributor to revenue. In 2018, the company acquired two additional rare disease companies, Wilson Therapeutics and Syntimmune.

# 2.1 bn

(In USD as at 12/31/2018)



# **Halozyme Therapeutics**

Halozyme Therapeutics is a biopharmaceutical company with a business model consisting of two platforms. Enhanze is based on partnerships with pharmaceutical companies that use Halozyme's rHuPH20 to prepare subcutaneous formulations of intravenous therapies. The company receives upfront milestone payments as well as a steady flow of royalties. Partnered products include blockbusters such as Herceptin and Rituxan as well as future products such as Darzalex, Opdivo or AXLN-1210. The second platform is based on PegPH20, which is being tested for the treatment of pancreatic cancer in combination with chemotherapy and in many other cancers in combination with Roche's anti-PD-L1 Tecentriq. A Phase III study in pancreatic cancer has almost completed enrollment and is expected to read out on the Overall Survival (OS) endpoint by year-end 2019.

#### MARKET CAPITALIZATION

# 7.4 bn

(In USD as at 12/31/2018)



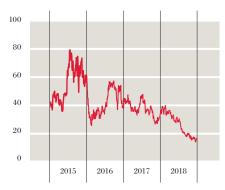
### **Alnylam Pharmaceuticals**

Alnylam Pharmaceuticals is the market leader in RNA interference (RNAi) therapeutics. This treatment approach selectively blocks the synthesis of specific disease-causing proteins. Their first marketed therapy, Onpattro (patisiran), received approval in 2018 for TTR amyloidosis, a rare and serious disorder in patients diagnosed with familial amyloidotic polyneuropathy (FAP). In addition to Onpattro, Alnylam has a broad pipeline of candidates, including four programs that have advanced to the clinical development stage. These include Fitusiran, which pursues a revolutionary approach in the treatment of hemophilia and rare bleeding disorders, Givosiran for the treatment of acute hepatic porphyrias, and Lumisiran, which received breakthrough status for primary hyperoxaluria. Alnylam continues to support its collaboration with The Medicines Company in their advancement of inclisiran into Phase III studies, which investigates RNAi disruption of PCSK9 for the treatment of hypercholesterolemia. Data thus far have been supportive of a once-quarterly and possibly biannual subcutaneous administration, which has obvious advantages over other PCSK9 antibody therapies.

# MARKET CAPITALIZATION

# 751 mn

(In USD as at 12/31/2018)



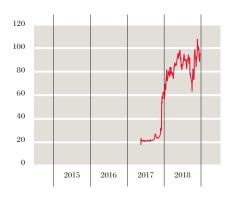
Source: Bloomberg

#### **Radius Health**

Radius Health is a company focused on women's health and oncology. The company currently markets Tymlos (abaloparatide), a synthetic human PTHrP analogue. Tymlos' faster onset of action and reduction in fractures in nonvertebral sites like the hip and wrist versus Eli Lilly's Forteo are differentiating and should allow it to capture significant market share. Radius received approval in 2017, and we expect 2019 to be a year of continued Tymlos growth and reimbursement as well as pipeline execution. Importantly, Radius is developing a transdermal patch formulation which could greatly enhance the outcomes in women with osteoporosis. Transdermal data presented to date has shown a meaningful improvement in its profile, and we expect a pivotal study to begin in mid-2019. Furthermore, the company has elacestrant, a selective estrogen receptor degrader (SERD), in Phase III development for estrogen-receptor-positive breast cancer. Elacestrant diversifies Radius' portfolio and strengthens its focus on women's health.

# 3.5 bn

(In USD as at 12/31/2018)



#### **Argenx SE**

Argenx is a Belgian clinical stage small cap biotechnology company developing targeted antibody therapies through its multiple antibody platforms. The company has a variety of mid-to-late stage clinical drug candidates with ARGX-113 (efgartigimod) being the lead asset. This molecule has proven to be efficacious in Phase II proof of concept in two IgG-mediated autoimmune diseases (myasthenia gravis and ITP) with two other indications (pemphigus vulgaris and CIDP) being currently evaluated. Important clinical trial read-outs from this program are expected in the coming 12 to 18 months. A solid balance sheet and experienced management rounds the company's profile. Argenx can be considered an antibody platform company targeting novel scientific pathways in indications with high unmet medical need with little competition and innovation in the last decades.

#### MARKET CAPITALIZATION

# 80.9 bn

(In USD as at 12/31/2018)



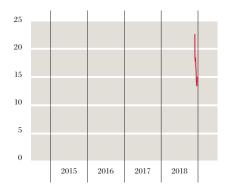
#### Gilead

Gilead develops drugs primarily for infectious diseases such as HIV and hepatitis, as well as cancer. The first product, Viread, was launched in 2001 and is a key component in treatment regimens for HIV. Most recently, it launched regimens that include a replacement for Viread with a better long-term safety profile, which should enable it to maintain its leadership when Viread goes generic. The introductions of Hepsera and Viread established Gilead as an important player in the treatment of hepatitis B infection. Gilead's acquisition of Pharmasset enabled it to become the market leader in the USD 20+ bn hepatitis C (HCV) space. Indeed, peak sales in 2016 of its lead products, Sovaldi and Harvoni, were followed by a precipitous decline, and we expect a continued decline in future years due primarily to pricing and competition. To offset the declining HCV sales, the company purchased Kite Pharmaceuticals, a leader in CAR-T therapy, in October 2017. The first product, Yescarta, was approved in October 2017 for diffuse large B-cell lymphoma (DLBCL) and we expect label expansions for other hematologic indications to follow. Meanwhile, Phase III data on development candidates for rheumatoid arthritis and NASH are expected in 2019.

# MARKET CAPITALIZATION

# 5.0 bn

(In USD as at 12/31/2018)



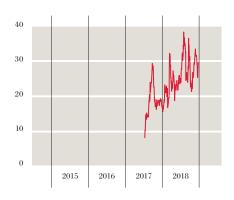
Source: Bloomberg

# **Moderna Therapeutics**

Moderna Therapeutics is pioneering a new class of medicine made of messenger RNA. Moderna recently gathered a lot of attention through the record-breaking IPO, which raised over USD 600 mn in December 2018. A substantial amount of the USD 3 bn of total capital raised since inception in 2011 has been invested in what is now the leading mRNA technology platform in order to be able to quickly drive development candidates into the clinic on a broad front of therapeutic and prophylactic applications. Their pipeline now includes 19 development candidates, with 10 of them in the clinic, for mRNA-based vaccines as well as treatments in diverse therapeutic areas. In our view, the key programs that will be reading out clinical data within the next few years include the rare liver disease MMA and PPA, the proprietary vaccines in congenital CMV and hMPV+PIV3, the intra-tumorally injected cytokine cocktail OX40L+IL23+IL36 gamma, the personalized cancer vaccine and early data on the VEGF Phase II during CABG-surgery.

# 2.7 bn

(In USD as at 12/31/2018)



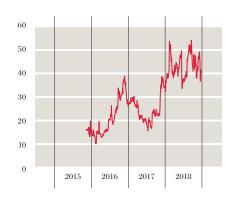
## **Akcea Therapeutics**

Akcea was spun out of Ionis Pharmaceuticals and is developing antisense drugs to treat rare and severe diseases. Its lead product is Tegsedi which was launched in late 2018 for the treatment of hereditary transthyretin amyloidosis, a rare and severe disease. The company received a complete response letter for Waylivra for the treatment of familial chylomicronemia syndrome, a rare lipid disorder, and is pursuing a path forward with the FDA. Akcea also has a pipeline of next generation lipid products based on its LICA technology which allows for much lower dosing and higher potency. ANGPTL3-Lrx is in a Phase I/II study for rare hyperlipidemias and is also being evaluated in fatty liver diseases such as NAFLD and NASH. Akcea has two LICA programs partnered with Novartis for larger diseases, APO(a)-Lrx and APOCIII-Lrx for patients with elevated risk factors for cardiovascular disease. Ionis remains a majority shareholder.

#### MARKET CAPITALIZATION

# 1.2 bn

(In USD as at 12/31/2018)



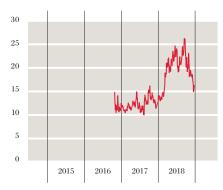
#### **Wave Life Sciences**

Wave is a leader in the space of stereochemistry, with an initial focus on antisense oligonucleotides (ASOs) and exon skipping. In simple terms, stereochemistry refers to the three-dimensional structure of a molecule and how this affects its chemical properties. Current ASOs can contain hundreds to hundreds of thousands of various enantiomers (stereomixture), many of which do not contribute to efficacy, but could be causing toxicity. Wave is able to specifically design their individual molecules (stereopure) to contain the desired properties, thus potentially enhancing potency and minimizing toxicity. The company's lead product is in Phase I/II development for Huntington's disease and targets very specific point mutations in order to knock down the mutant protein. We expect data in early 2019. Wave's second program recently entered Phase I development for Duchenne muscular dystrophy (DMD) and acts by skipping exon 51.

## MARKET CAPITALIZATION

# 1.1 bn

(In USD as at 12/31/2018)



Source: Bloomberg

## **Myovant Sciences**

Myovant is a biopharmaceutical company with a focus on endocrinology in women's and men's health. Its lead candidate, Relugolix, is an oral GnRH antagonist in Phase III development for three indications, endometriosis, uterine fibroids, and advanced prostate cancer. Endometriosis is a condition where part of the endometrium grows outside of the uterus leading to severe pain, painful intercourse, and bleeding. Uterine fibroids is a condition that can lead to painful menstruation and excessive bleeding, and potentially surgical removal of the uterus. Advanced prostate cancer is cancer of the prostate that continues to grow despite castration and/or radiation. Partner Takeda announced positive data from two Phase III trials in uterine fibroids in Japanese women, further validating Relugolix's mechanism of action. We expect data from all three Phase III trials in the US in 2019. Myovant owns worldwide rights outside of Asia.

# 3.0 bn

(In USD as at 12/31/2018)



#### **Intercept Pharmaceuticals**

Intercept Pharmaceuticals is focused on the development of bile acid analogs for the treatment of cholestatic liver diseases. This disease area primarily includes highly prevalent non-alcoholic steatohepatitis (NASH) as well as the orphan diseases primary biliary cirrhosis (PBC) and primary sclerosing cholangitis (PSC). Intercept's lead product is Ocaliva, a first-in-class farnesoid X receptor (FXR) agonist, was approved in the US and Europe for PBC in 2016. As a second and commercially far more attractive indication, Intercept also started a pivotal trial for NASH that is expected to read out in the first half-year 2019. NASH, being an obesity and metabolic syndrome-linked disease, has the potential to take on epidemic proportions in western and emerging societies over the coming years. It is projected to be the leading cause of costly liver transplants and liver cancer by 2020. With currently no drug approved, there clearly is an unmet medical and health economic need for new treatments. Intercept's Ocaliva is the drug furthest in development for NASH and the first to show an anti-fibrotic effect on liver histology.

#### MARKET CAPITALIZATION

# 5.9 bn

(In USD as at 12/31/2018)



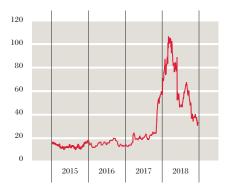
#### **Exelixis**

Exelixis is a biotechnology company focused on oncology. The company has one of the most potent tyrosine kinase inhibitors (TKI) on the market. Cabozantinib is approved for the treatment of all stages of renal cell carcinoma (RCC; kidney cancer). Additionally, a Phase III study in second-line hepatocellular carcinoma (HCC; liver cancer) was stopped early due to a positive survival benefit, and we expect this new indication to add incremental value to the cabozantinib franchise. Cabozantinib is also approved for medullary thyroid cancer. Importantly, the drug is being tested in various tumor settings with immune-oncology agents, which can add further, substantial value. Exelixis partnered a second TKI, cobimetinib, with Roche and is approved for the treatment of metastatic melanoma. Finally, having reached profitability, Exelixis is now at a point where it can invest more aggressively in its internal pipeline, which should create value in the future.

## MARKET CAPITALIZATION

# 5.7 bn

(In USD as at 12/31/2018)



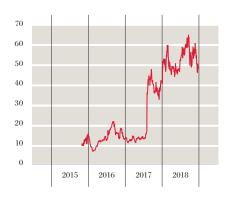
Source: Bloomberg

## **Nektar Therapeutics**

Nektar Therapeutics is focused on developing novel drugs for oncology, autoimmune disease, and chronic pain. The most important product in the pipeline is NKTR-214, a CD122-biased agonist designed to achieve broader efficacy, better safety, and an improved dosing schedule than IL-2 with its prodrug design and sustained signaling. Initial results from the dose-escalation portion of the Phase I/II trial with NKTR-214 plus PD1 inhibitor Opdivo, as well as data from an extension cohort of melanoma patients, showed evidence of activity and a favorable safety profile. Specifically, there was a 53% overall response rate and a 24% complete response rate in first-line melanoma patients who received the combination. Encouraging results were also shown in kidney, lung, and bladder cancer, and data from larger cohorts of patients with these tumor types are due in 2019. Meanwhile, a large pivotal program targeting these tumors, as well as others, is underway with partner Bristol-Myers. Terms of the partnership include total upfront payments of USD 1.85 bn, USD 1.8 bn in potential milestones, and a cost and profit sharing agreement.

# 2.0 bn

(In USD as at 12/31/2018)



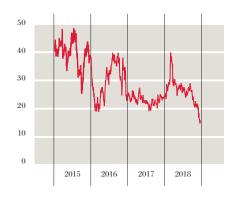
## Myokardia

Myokardia is one of only a few small biotech companies in the cardiovascular disease area. The company's initial focus is on the treatment of inheritable cardiomyopathies, a group of rare, genetically driven forms of heart failure that result from biomechanical defects in cardiac muscle contraction. The most advanced pipeline asset is MYK-461 (mavacamtem), an allosteric inhibitor of cardiac beta myosin function that is being investigated in obstructive hypertrophic cardiomyopathy (oHCM or HoCM). The company posted intriguing Phase II results not only showing direct improvement in biomarkers (up to 15% reduction in ejection fraction, up to 90% reduction in LVOT gradient) but also an increase of up to 17% in exercise capacity and an improvement in symptoms (1 Class NYHA improvement on average). A single Phase III trial aiming at exercise capacity and symptom improvement has been initiated with an expected readout in 2020. Further studies include a Phase II study in non-obstructive HCM as well as early dose escalation data in H2-18 for their second asset (MYK-491) that is being developed for DCM (dilated cardiomyopathy).

#### MARKET CAPITALIZATION

# 537 mn

(In USD as at 12/31/2018)



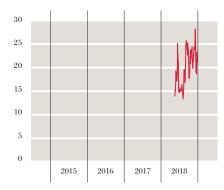
## Macrogenics

Macrogenics has multiple compounds in clinical development that were generated using its propriety Fc-optimization technology that simultaneously reduces resp. enhances binding to inhibitory resp. activating FcyRs, thus dramatically increasing antibody-dependent cellular cytotoxicity (ADCC), and its DART (dual-affinity re-targeting) platform. The company believes its DART platform has overcome the challenges of construct instability and short half-lives encountered by other dual-specific antibodies by incorporating proprietary covalent disulfide linkages and particular amino acid sequences that efficiently pair the chains of the DART molecule. This results in a structure with enhanced manufacturability, long-term structural stability, and the ability to tailor the half-lives of the DARTs to their clinical needs. Data from clinical trials with multiple products are expected throughout 2019.

## MARKET CAPITALIZATION

# 580 mn

(In USD as at 12/31/2018)



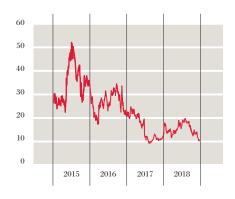
Source: Bloomberg

## **Scholar Rock Holding**

Scholar Rock is a biotech company with a platform based on the understanding of the extracellular activation of growth factors. By targeting the pro and latent forms of the growth factors with antibodies, not the active/mature factor (given the very high degree of similarity in amino acid sequences in the active sites across the TGF-beta superfamily), the company believes it can avoid the off-target toxicities that have plagued this field historically. Its lead compound is SRK-015, a monoclonal antibody targeting pro myostatin and latent myostatin, is designed to inhibit the activation of myostatin thereby promoting muscle growth and function. The initial indication is later onset spinal muscular atrophy (Type 2 and 3) where it can potentially be used in combination with Spinraza and other therapeutics as its mechanism is complimentary, not competitive. Phase II, interim proof-of-concept data are expected in the second half-year 2019. SRRK also plans on announcing a second muscle wasting indication in 2019. The platform technology is also focused on TGF-beta 1 in the IO space as well as fibrosis. The fibrosis indications have been partnered with Gilead.

# 700 mn

(In USD as at 12/31/2018)



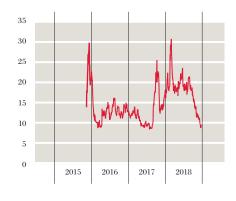
### **Alder Biopharmaceuticals**

Alder is a clinical-stage company with a differentiated antibody discovery and manufacturing platform to design and select antibodies that have the potential to maximize efficacy in various therapeutic indications including inflammatory and neurological conditions. Their clinical candidate, eptinezumab, is an antibody that inhibits calcitonin gene-related peptide (CGRP), a well-validated molecular target shown to trigger migraine attacks. Eptinezumab has recently completed Phase III clinical testing for the prevention of both chronic and frequent episodic migraines. Data were highly significant and notable for achieving rapid, robust, and durable efficacy. Alder is the only company with an anti-CGRP therapeutic that could be marketed as a durable, intravenous formulation administered by neurologists in-office — an infusion that could be given every three months, compared to monthly or biweekly self-administered subcutaneous injections at home. The company expects to apply for FDA approval in early 2019.

#### MARKET CAPITALIZATION

# 306 mn

(In USD as at 12/31/2018)



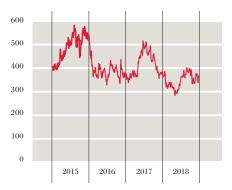
## **Voyager Therapeutics**

Voyager is a clinical-stage biotech company focused on developing novel genetically targeted therapies to treat CNS diseases. The company's lead asset, VY-AADC, is an AAV-based gene therapy with the objective of increasing the expression of the enzyme responsible for converting levodopa to dopamine (AADC, L-amino acid decarboxylase) in the brains of Parkinson's disease patients. VY-AADC is currently enrolling patients in a Phase II trial, which will serve as the first of two sham-controlled studies for registration. A Phase III study to begin in 2020 will serve as the second pivotal trial. The company is also developing other AAV vectors targeted at increasing expression of a key gene in Friedreich's ataxia, delivering monoclonal antibodies, or silencing/knocking down genes using microRNA delivery in diseases like monogenic SOD1 familial ALS and Huntington's disease. Voyager's discovery engine has generated programs in five CNS indications, and in the next 18 to 24 months, they plan to initiate at least three other clinical programs.

# MARKET CAPITALIZATION

# 40.4 bn

(In USD as at 12/31/2018)



Source: Bloomberg

## **Regeneron Pharmaceuticals**

Regeneron focuses on developing monoclonal antibodies. The blockbuster success of Eylea, a VEGF inhibitor indicated for ophthalmic disorders, has been the primary driver of growth for the company. We expect near-term growth to continue in 2019 as Eylea gains broader adoption in wet AMD and expands into DME. Regeneron holds a partnership with Bayer Healthcare for the development, marketing, and sale of Eylea outside of the US. Regeneron also holds a partnership with Sanofi, with whom they have commercialized four products thus far and, more importantly, have a deep pipeline of assets the two partners are co-developing. Praluent for hypercholesterolemia is approved by the FDA for heterozygous familial hypercholesterolemia or clinical atherosclerotic cardiovascular disease patients who need additional lowering of LDL cholesterol. In addition, Kevzara is approved for rheumatoid arthritis, Dupixent is marketed for both atopic dermatitis and adult asthma, and Libtayo recently launched in advanced cutaneous squamous cell carcinoma. With Teva and Mitsubishi Tanabe, the company is also developing Fasinumab, an antibody against nerve growth factor for pain therapy. Regeneron also has collaboration agreements with Intellia Therapeutics to advance CRISPR/Cas gene-editing technology.

# 623 mn

(In USD as at 12/31/2018)



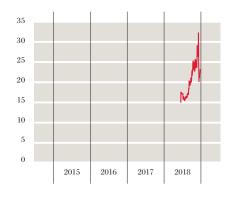
## **Intra-Cellular Therapies**

Intra-Cellular Therapies is a biopharmaceutical company developing treatments for disorders that affect the central nervous system. Their wholly owned lead product candidate is Lumateperone, a 5-HT2A serotonin receptor antagonist that also modulates dopamine and serotonin transporters, which was filed for FDA approval in late 2018 for the treatment of schizophrenia. Lumateperone could prove highly differentiated from other anti-psychotics due to its ability to modulate multiple neurotransmitter pathways simultaneously. This was demonstrated in their first pivotal Phase III trial which showed strong efficacy and placebo-like safety. Tolerability and compliance on current schizophrenia therapies is challenging due to a range of motor and metabolic side effects, which is where Lumateperone has proven to be differentiated. Intra-Cellular is also evaluating Lumateperone in two Phase III trials for the treatment of bipolar depression to be completed in 2019. The company also has a PDE-1 inhibitor, ITI-214, in Phase II trials evaluating its role in Parkinson's disease and other indications.

#### MARKET CAPITALIZATION

# 451 mn

(In USD as at 12/31/2018)



#### **Kezar Life Sciences**

Kezar Life Sciences is a development-stage biotechnology company focused on developing novel small molecule therapeutics targeting immunoproteasome inhibition for the treatment of autoimmune disorders. KZR-616, Kezar's lead product candidate, is currently in Phase Ib dose escalation in patients with systemic lupus erythematosus (SLE) with or without active nephritis. Following the conclusion of this trial in H1 2019, the company plans to start four Phase II trials in autoimmune disorders with high unmet medical need where proteasome inhibitors like Velcade have proven efficacious but too toxic for chronic treatment.

# MARKET CAPITALIZATION

# 910 mn

(In USD as at 12/31/2018)



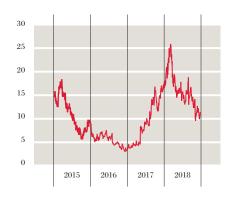
Source: Bloomberg

## **Audentes Therapeutics**

Audentes is a clinical stage gene therapy company focused on rare diseases. The company has two clinical stage programs and importantly, commercial scale, in-house manufacturing capability that is GMP-approved. AT132 is the lead product in Phase I/II for the treatment of X-linked myotubular myopathy (XLMTM). The second clinical compound is AT342 in Phase I/II for the treatment of Crigler-Najjar syndrome (CN), but the drug needs to be dosed higher as the first patient data at the lowest dose saw a return to baseline following a reduction in the target. Beyond the two lead assets, there are two preclinical compounds and a yet to be named compound. Given the data seen so far with the lead asset, the company will discuss the regulatory path with the FDA and present the data, which we believe have established proof of concept thus far, with durability being the main question. The manufacturing facility has 2 500 liters bioreactors with additional capacity of up to 5 000 liters. The same process, facility, and scale have been used from the beginning which is a very important factor in the regulatory process. The manufacturing process uses a mammalian, serum-free suspension culture which allows for increased scalability versus adherent cultures.

# 1.2 bn

(In USD as at 12/31/2018)



## Sangamo Therapeutics

Sangamo Therapeutics is uniquely positioned as the dominant and almost exclusive holder and developer of Zinc-finger-based genomic editing (ZFN) IP. One of the key achievements of the new CEO on the pharmacological side was the manifold improvement in selectivity of the ZFN platform (100x), thereby pushing off-target cutting below the limit of detectability, which enables the company to conduct the first in vivo gene-editing clinical trial (MPS II). Further the company now also pursues classic gene therapy approaches through the formulation expertise (that they gained while delivering ZFN) and IP around AAV2/6 (AAV6 capsid with AAV2 promotor/genome), e.g. in haemophilia A (Phase I/II running) as well as Fabry's disease (IND). It will be key for Sangamo to successfully develop their ZFN platform for their first proprietary projects (MPS I, MPS II, hemophilia B) and based thereon deploy that or newer generations of ZFN into further liver albumin locus targeting applications, while reaping the optionality from partnered projects (hemophilia A with Pfizer, ex vivo collaborations with Bioverativ and Kite, gene regulation ZFP without nucleases with Shire and Pfizer).

#### MARKET CAPITALIZATION

# 704 mn

(In USD as at 12/31/2018)



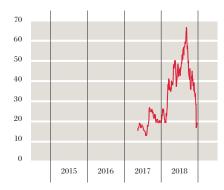
#### Novavax

Novavax is a company specializing in the development of novel vaccines. The most advanced program is a vaccine to prevent RSV infections in infants and older adults. Respiratory syncytial virus (RSV) is a respiratory tract infection which may be fatal in infants, older adults, and people with compromised immune systems. In a Phase II study in older adults, Novavax showed that its vaccine results in 44% fewer symptomatic RSV infections and a more than 60% reduction in severe RSV infections. However, in 2016, the company announced that the Phase III study in the elderly failed due to a much lower event rate than expected. In its Phase II study in pregnant women, Novavax showed that the antibodies are transferred effectively from the mothers to their infants. A corresponding Phase III study has been initiated in pregnant women with data expected in early 2019. Novavax also has a seasonal influenza vaccine, an Ebola vaccine, and a pandemic influenza vaccine in its pipeline.

## MARKET CAPITALIZATION

# 712 mn

(In USD as at 12/31/2018)



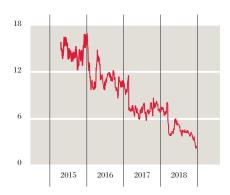
Source: Bloomberg

## **G1** Therapeutics

G1 Therapeutics is a clinical-stage small cap biotechnology company focused on the discovery and development of cancer treatment therapeutics. The company has two distinct clinical-stage selective inhibitors of cyclin-dependent kinases 4/6 (CDK4/6i) in its pipeline, trilaciclib and G1T38, both being evaluated in combination with multiple regimens. Whereas trilaciclib could become the first CDKi to be used as a myelosparing agent, the second asset, G1T38, is a fast follower and is currently being evaluated in yet untapped indications by the other CDKi already on the market. The strong scientific rationale coupled with the available clinical data and the proven mode of action gives us confidence that the upcoming multiple readouts in several indications over the coming twelve months for both assets will confirm their clinical profile.

# 65 mn

(In USD as at 12/31/2018)



## **Cidara Therapeutics**

Cidara is a biotechnology company focused on treating severe and resistant microbial infections. Its lead product, Rezafungin (in a Phase III study for candidemia and invasive candidiasis), is from the echinocandin class of antifungals but is dosed as a onceweekly infusion, versus daily for the current echinocandins. This would provide the option of treating patients with the best antifungal on an outpatient basis, thus offering significant advantages to both patients and the healthcare system. Initial Phase II data have demonstrated a strong safety profile and confirmed the once-weekly dosing potential along with a favorable efficacy profile. Data from an extension of the Phase II study will read out in 2019. Following a constructive meeting with the FDA, a smaller than expected Phase III study was possible allowing Cidara to also conduct a prophylaxis study in bone marrow transplant patients. Finally, Cidara is the only company developing an immunotherapy platform for serious infections.

Source: Bloomberg



# **Consolidated financial statements**

## Consolidated balance sheet as at December 31

(in CHF 1 000)

|   | Notes | 2018      | 2017      |
|---|-------|-----------|-----------|
| Current assets                                  |       |           |           |
| Cash and cash equivalents                       |       | 22 072    | 10 730    |
| Receivables from brokers                        |       | 334       | _         |
| Securities at fair value through profit or loss | 4     | 3 064 175 | 3 627 069 |
| Other assets                                    |       | 263       | =         |
|   |       | 3 086 844 | 3 637 799 |
| Total assets                                    |       | 3 086 844 | 3 637 799 |
| Current liabilities                             |       |           |           |
| Short-term borrowings from banks                | 5     | 185 000   | 95 000    |
| Payables to brokers                             | -     | 13 139    | _         |
| Other short-term liabilities                    | 6     | 4 056     | 4 049     |
| Tax liabilities                                 | -     | 137       | 75        |
|   |       | 202 332   | 99 124    |
| Total liabilities                               |       | 202 332   | 99 124    |
| Shareholders' equity                            |       |           |           |
| Share capital                                   | 7     | 11 080    | 11 080    |
| Retained earnings                               | 7     | 2 873 432 | 3 527 595 |
|   |       | 2 884 512 | 3 538 675 |
| Total liabilities and shareholders' equity      |       | 3 086 844 | 3 637 799 |
| Net asset value per share in CHF                |       | 52.05     | 63.90     |

The notes on pages 46 to 57 are an integral part of these consolidated financial statements.

 $The \ consolidated \ financial \ statements \ were \ approved \ by \ the \ Board \ of \ Directors \ of \ BB \ Biotech \ AG \ on \ February \ 12, \ 2019.$ 

# Consolidated statement of comprehensive income for the year ended December 31

(in CHF 1 000)

|   | Notes | 2018      | 2017     |
|---|-------|-----------|----------|
| Operating income                        |       |           |          |
| Net gains from securities               | 4     | -         | 723 256  |
| Interest income                         |       | 29        | _        |
| Dividend income                         |       | 5 458     | 6 783    |
| Foreign exchange gains net              |       | -         | 6        |
| Other income                            |       | 290       | 4        |
|   |       | 5 777     | 730 049  |
| Operating expenses                      |       |           |          |
| Net losses from securities              | 4     | (427 090) | _        |
| Finance expenses                        |       | (1 086)   | (542)    |
| Foreign exchange losses net             |       | (2 544)   | _        |
| Administrative expenses                 | 8     | (41 849)  | (37 508) |
| Other expenses                          | 9     | (4 480)   | (4 419)  |
|   | -     | (477 049) | (42 469) |
| Operating income before tax             | 12    | (471 272) | 687 580  |
| Income taxes                            | 10    | (71)      | (77)     |
| Net income for the year                 |       | (471 343) | 687 503  |
| Total comprehensive income for the year |       | (471 343) | 687 503  |
| Income per share in CHF                 | 11    | (8.51)    | 12.42    |
| Diluted income per share in CHF         |       | (8.51)    | 12.42    |

The notes on pages 46 to 57 are an integral part of these consolidated financial statements.

# Consolidated statement of changes in equity for the year ended December 31

(in CHF 1 000)

| Share<br>capital | Treasury<br>shares | Retained<br>earnings  | Total  |
|------------------|--------------------|---|--|
| 11 850           | (119 332)          | 4 085 640   | 3 978 158  |
| =                | =                  | (160 489)   | (160 489)  |
| (770)            | 133 294            | (132 524)   | _  |
| =                | (14 821)           | 2 118   | (12 703)   |
| -                | _                  | 118   | 118  |
| -                | =                  | (802 065)   | (802 065)  |
| 11 080           | (859)              | 2 992 798   | 3 003 019  |
|                  |                    | (152 066)   | <b>3 003 019</b> (152 066)   |
| _                |                    | (152 066)   | (152 066)  |
| ·                |                    | ` '   | 194  |
|                  |                    |   | 25   |
|                  |                    |   | 687 503  |
| 11 080           |                    | 3 527 595   | 3 538 675  |
|                  |                    |   |  |
| 11 080           | -                  | 3 527 595   | 3 538 675  |
| -                | _                  | (182 820)   | (182 820)  |
| -                | -                  | (471 343)   | (471 343)  |
| 11 080           | _                  | 2 873 432   | 2 884 512  |
|                  | 11 080             | capital         shares           11 850         (119 332)           -         -           (770)         133 294           -         (14 821)           -         -           -         -           11 080         (859)           -         -           -         -           11 080         -           -         -           11 080         -           -         - | capital         shares         earnings           11 850         (119 332)         4 085 640           —         —         (160 489)           (770)         133 294         (132 524)           —         —         (14 821)         2 118           —         —         —         (802 065)           11 080         (859)         2 992 798           —         —         (152 066)           —         —         25           —         —         687 503           11 080         —         3 527 595           —         —         (182 820)           —         —         (471 343) |

The notes on pages 46 to 57 are an integral part of these consolidated financial statements.

# Consolidated statement of cash flow for the year ended December 31

(in CHF 1 000)

|  | Notes   | 2018      | 2017      |
|--|---------|-----------|-----------|
| Cash flows from operating activities                   |         |           |           |
| Proceeds from sales of securities                      | 4       | 1 078 776 | 907 095   |
| Purchase of securities                                 | 4       | (930 168) | (608 694) |
| Dividend receipts                                      |         | 5 458     | 6 783     |
| Interest receipts                                      |         | 29        |           |
| Payments for services                                  |         | (46 299)  | (41 577)  |
| Income taxes paid                                      |         | (4)       | (139)     |
| Total cash flows from operating activities             |         | 107 792   | 263 468   |
| Cook flows from from the activities                    |         |           |           |
| Cash flows from financing activities                   |         | (102.020) | (152.066) |
| Cash distribution/dividend                             |         | (182 820) | (152 066) |
| Proceeds from sales of treasury shares                 |         |           | 18 718    |
| Purchase of treasury shares                            |         | -         | (19 083)  |
| Borrowing/(Repayment) of bank loans                    | 5       | 90 000    | (110 000) |
| Interest payments                                      |         | (1 086)   | (542)     |
| Total cash flows from financing activities             | <u></u> | (93 906)  | (262 973) |
| Foreign and an at 100 and                              |         | (2.544)   |           |
| Foreign exchange difference                            |         | (2 544)   | 6         |
| Change in cash and cash equivalents                    |         | 11 342    | 501       |
| Cash and cash equivalents at the beginning of the year |         | 10 730    | 10 229    |
| Cash and cash equivalents at the end of the year       |         | 22 072    | 10 730    |

The notes on pages 46 to 57 are an integral part of these consolidated financial statements.

## 1. The Company and its principal activity

BB Biotech AG (the Company) is listed on the SIX Swiss Exchange, in the «Prime Standard Segment» of the German Exchange as well as in the «Star Segment» of the Italian Exchange and has its registered office in Schaffhausen, Schwertstrasse 6. Its principal activity is to invest in companies active in the biotechnology industry for the purpose of capital appreciation. The investments are held through its wholly owned subsidiaries.

| Company                      | Capital<br>in CHF 1 000 | Capital and<br>voting interest<br>in % |
|------------------------------|-------------------------|--|
| Biotech Focus N.V., Curação  | 11                      | 100                                    |
| Biotech Growth N.V., Curaçao | 11                      | 100                                    |
| Biotech Invest N.V., Curação |                         | 100                                    |
| Biotech Target N.V., Curaçao | 11                      | 100                                    |

## 2. Accounting policies

### General

The consolidated financial statements of the Company and its subsidiary companies (the Group) have been prepared in accordance with International Financial Reporting Standards (IFRS), as well as the provisions of the rules of the SIX Swiss Exchange for Investment Companies. The consolidation is prepared from the financial statements of the Group companies using uniform accounting principles. With the exception of financial assets and liabilities (incl. derivative instruments), which are held at fair value through profit or loss, the financial statements are prepared under the historical cost convention. This requires management to make assumptions and estimates that have an impact on the balance sheet values and items of the income statement in the current financial year. In certain circumstances, the actual values may differ from these estimates.

The following new standards and interpretations, valid since January 1, 2018, have been applied in these annual consolidated financial statements:

- IFRS 7 (effective January 1, 2018) Financial instruments Disclosure Additional disclosures on transition from IAS 39 to IFRS 9
- IFRS 9 (effective January 1, 2018) Financial instruments
- IFRS 15 (effective January 1, 2018) Revenue from contracts with customers
- IFRIC 22 (effective January 1, 2018) Foreign Currency Transactions and Advance Consideration

The Group assessed the impact of the above-mentioned new standards and interpretations. Based on the analysis, the Group concludes that these new standards have no material impact on the Group's accounting policies and overall results and financial position. This also applies to IFRS 9 as all securities are valued at fair value through profit or loss. The first-time adoption of IFRS 9 does not result in an adjustment of the previous year's figures.

The following new standards and interpretations were approved, but will only be applicable for the Group prospectively and were not early adopted in these annual consolidated financial statements:

- IFRS 3 (amended, effective January 1, 2020) Definition of a Business
- IFRS 16 (effective January 1, 2019) Leases
- IFRIC 23 (effective January 1, 2019) Uncertainty over Income Tax Treatments

The Group assessed the potential impact of the above-mentioned new standards and interpretations. Based on the analysis, the Group concludes that these new standards and interpretations have no material impact on the Group's accounting policies and overall results and financial position.

## Basis of consolidation

The consolidated financial statements include the Company and the subsidiary companies which are controlled by it. Control is the ability to influence the financial and operating activities of an entity so as to benefit from its activities. Subsidiaries are fully consolidated from the date on which control is transferred to the Company and are deconsolidated from the date that control ceases. The consolidation is performed using the acquisition method. All intercompany transactions and balances with companies included in the consolidation are eliminated. All Group companies have a December 31 year-end.

## Foreign currency translation

Based on the economic environment (primary listing, investors, costs and performance measurement) in which the Company and its subsidiaries operate, the consolidated financial statements of the Group are presented in Swiss francs, which is the Company's and its subsidiaries functional currency. Transactions in foreign currencies are converted at exchange rates as at transaction dates. Assets and liabilities in foreign currencies at year-end are translated at rates of exchange prevailing as at the balance sheet date. Exchange differences are reflected in the statement of income. Translation differences on marketable securities held at fair value through profit or loss are reported as part of the net gains/(losses) from marketable securities.

The following exchange rates have been used for the preparation of these consolidated financial statements:

| Currency | 12/31/2018 | 12/31/2017 |
|----------|------------|------------|
| USD      | 0.98160    | 0.97420    |
| DKK      | 15.07690   | 15.71020   |
| EUR      | 1.12751    | 1.16995    |
| GBP      | 1.25330    | 1.31690    |
| SEK      | 11.07800   | 11.90140   |

## Cash and cash equivalents

Cash and cash equivalents comprise current accounts and call money at banks which have a maturity of three months or less. These are stated at the notional amount as this is a reasonable approximation of fair value due to the short-term maturity.

## Receivables/payables against brokers

Receivables/payables against brokers result from security transactions and do not bear any interest. These are stated at amortized cost which is a reasonable approximation of fair value due to the short-term maturity.

### Financial assets

The Group classifies its financial assets in the following categories: at fair value through profit or loss as well as loans and receivables. Financial assets at fair value through profit or loss comprise marketable securities which are classified as current assets.

Loans and receivables are non-derivative financial assets with fixed or determinable payments that are not quoted in an active market. They are included in current assets, except when they have maturities of greater than twelve months after the balance sheet date they are classified as non-current assets. The balance sheet items cash and cash equivalents, receivables from brokers and other assets comprise this category.

## Marketable securities

Marketable securities consist of securities, designated at fair value through profit or loss, and derivatives. Initially, securities and derivatives are valued at fair value and are subsequently remeasured at market values based on stock exchange prices or generally accepted valuation models that are based on market conditions existing at each balance sheet date, such as Black-Scholes, earnings multiple and discounted cash flow model. Purchases and sales of marketable securities are accounted for at trade date. Realized gains and losses on security trading are recognized in the statement of income as net realized gains/losses from marketable securities at the day of the transaction. Changes in fair value of securities are recognized as net unrealized gains/losses from marketable securities in the statement of income in the period in which they arise. Marketable securities are derecognized when the rights to receive cash flows from marketable securities have expired or where the Group has transferred substantially all risks and rewards of ownership.

## Income taxes

Current income taxes are calculated on the basis of the applicable tax laws in individual countries and recognized as an expense in the period in which the related profits are made.

Assets or liabilities related to current income taxes are reported in the balance sheet in the items "Current tax assets" or "Current tax liabilities". Tax effects arising from temporary differences between the carrying amounts of assets and liabilities in the Group's balance sheet and their corresponding tax values are recognized, respectively, as "Deferred tax assets" and "Deferred tax liabilities". Deferred tax assets arising from temporary differences and from loss carry-forwards eligible for offset are capitalized if it is likely that sufficient taxable profits will be available against which those temporary differences or loss carry-forwards can be offset. Deferred tax assets and deferred tax liabilities are calculated at the tax rates expected to apply in the period in which the tax assets will be realized, or the tax liabilities settled.

Earnings per share Basic earnings per share are calculated by dividing the net profit/loss attributable to shareholders by the weighted average number of registered shares in issue during the year, less treasury shares. For the diluted earnings per share, the weighted average number of registered shares in issue and the net profit is adjusted to assume conversion of all dilution potential registered shares. The potential registered shares include all registered shares, which will be issued by exercising warrants or options.

## Short-term borrowings from banks

Short-term borrowings are recognized initially at fair value, net of transaction costs incurred. Borrowings are subsequently stated at amortized cost; any difference between the proceeds (net of transaction costs) and the redemption value is recognized in the income statement over the period of the borrowings using the effective interest method. Borrowings are classified as current liabilities unless the Group has an unconditional right to defer settlement of the liability for at least twelve months after the balance sheet date.

## Treasury shares

Treasury shares are deducted from shareholders' equity. All profits and losses arising from trading in treasury shares are directly credited/debited to retained earnings. Treasury shares may be acquired and held by the Company or by other members of the consolidated Group.

## Net asset value per share

The net asset value per share is calculated by dividing the shareholders' equity by the number of shares outstanding less treasury shares held.

#### Dividend income

Dividends on marketable securities are recognized in the income statement when the Group's right to receive payment is established.

#### **Pension funds**

BB Biotech AG maintains for its employee a defined benefit plan. Due to the immateriality of any potential pension liability or potential pension asset, no disclosures according to IAS 19 are made within these consolidated financial statements.

## Commitments, contingencies and other off-balance sheet transactions

The operations of the Group are affected by legislative, fiscal and regulatory developments for which provisions are made where a legal or constructive obligation has been incurred which will probably lead to an outflow of resources that can be reasonably estimated.

## Critical accounting estimates and judgments

The fair value of financial instruments that are not traded in an active market is determined by using valuation techniques. The Group makes estimates and assumptions that are mainly based on market conditions to value these financial instruments. Since these financial instruments are not traded in an active market, inherent difficulties exist to value these financial instruments. These difficulties cannot be eliminated. The difference between the proceeds from sale of these financial instruments and the carrying amount may be material.

IFRS 10 «Consolidated Financial Statements» require, that investment companies no longer consolidate their subsidiaries, which themselves are investment companies. Instead they should be accounted for using the fair value. In the analysis of the first-time adoption of IFRS 10, the Company came to the conclusion that the subsidiaries do not meet the criteria for investment entities under IFRS 10 and acts as an extension of the parent (providing of investment-related services). Thus, the Group continues to consolidated its subsidiaries. The fair value accounting would not have a material impact on the net income and equity.

## 3. Financial risk management

Within the framework of the law, articles of incorporation and regulations, the asset manager carries out currency and marketable security forward transactions, buys, sells and makes use of options as well as fulfills all necessary obligations that result from these businesses.

## Credit risk

The Group is exposed to credit risk, which is the risk that a counterparty will be unable to pay amount in full when due. Impairment provisions are provided for losses that have been incurred by the balance sheet date, if any. The Group maintains business relations only with counterparties with an acceptable credit rating. All transactions in listed securities are settled/paid for upon delivery using approved brokers. The risk of default is considered minimal, as delivery of securities sold is only made once the broker has received payment. Payment is made on a purchase once the securities have been received by the broker. The trade will fail if either party fails to meet its obligation. Other assets consist of prepayments. The Group's credit positions, if any, are monitored on a daily basis by the asset manager and are reviewed on a regular basis by the Board of Directors.

### Market risks

Risk associated with changing market prices

Due to its business activity and the resulting high portion of marketable securities in relation to total assets, the Group is exposed to market price risk arising from uncertainties and fluctuations on the financial and foreign exchange markets.

The Group participates partially, but to a substantial extent, in the capital of its investments. In the case of sales of large parts of these investments, it may be able to influence the market price. The Group's marketable securities positions are monitored on a daily basis by the asset manager and are reviewed on a regular basis by the Board of Directors.

The annual volatility of registered shares BB Biotech AG (reference volatility for the marketable securities) for 2018 is 25.32% (2017: 18.26%). At December 31, 2018, had the value of listed securities increased or decreased by 25.32% (2017: 18.26%) with all other variables held constant, the increase or decrease respectively in net income/loss as well as shareholders' equity would amount to CHF 775.8 mn (2017: CHF 661.7 mn).

At December 31, 2018, and 2017 the Company holds no unlisted shares.

#### Interest risk

Interest rates on liquid funds are based on market rates. The funds are due on demand.

Short-term borrowings from banks are on current and short-term loan accounts with interest, based at market rates. Due to the high level of own funds, the effect of interest payable on the statement of income is insignificant. The majority of the Group's marketable securities are non-interest bearing; as a result, the Group is not subject to significant amounts of risk due to fluctuations in the prevailing levels of market interest rates.

The Group's interest sensitivity is monitored on a daily basis by the asset manager and reviewed on a regular basis by the Board of Directors.

## **Currency risk**

The Company and its subsidiaries hold assets denominated in currencies other than the Swiss franc, the functional currency. They are therefore exposed to currency risk, as the value of the securities denominated in other currencies will fluctuate due to changes in exchange rates. Depending on the market situation the Group could use foreign currency options and/or forward contracts to reduce the currency risk.

The following table summarizes the Group's exposure to currency risks:

| 2018 | Net exposure<br>12/31/<br>(in CHF 1 000) | Annual<br>volatility<br>(in %) | Potential<br>impact<br>(in CHF 1 000) <sup>1)</sup> |
|------|--|--------------------------------|---|
| USD  | 3 064 292                                | 6.47                           | 198 168   |
| 2017 |  |                                |   |
| USD  | 3 463 700                                | 7.14                           | 247 274   |
| DKK  | 143 209                                  | 4.91                           | 7 032   |
| EUR  | 13 039                                   | 4.94                           | 644   |
| SEK  | 4  | 6.89                           |   |

<sup>10</sup> Potential impact on total comprehensive income as well as shareholders' equity with all other variables held constant

The Group's currency position is monitored on a daily basis by the asset manager and is reviewed on a regular basis by the Board of Directors.

## Liquidity risk

The Group invests the majority of its assets in investments that are traded in an active market and can be readily disposed of. The Group's treasury shares, with the exception of shares purchased under a share buy-back program, are considered readily realizable as they are listed on three stock exchanges. The Group could invest a minor part of its portfolio in marketable securities, which are not traded on a stock exchange and may be illiquid. As a result, the Group may not be able to liquidate quickly its investments in these instruments. In addition, the Group has access to a credit line (note 13).

The tables below analyze the Group's financial liabilities into relevant maturity groupings based on the period between the balance sheet date and the contractual maturity date (in CHF 1 000):

| Less than<br>1 month | 1-3 months  | More than 3 months/<br>no stated maturity                                 |
|----------------------|---|---|
| 185 000              | -   | -   |
| 13 139               | -   | -   |
| 3 563                | 493   | -   |
| 201 702              | 493   | -   |
|                      |   |   |
| 95 000               | _   | -   |
| 3 652                | 397   |   |
| 98 652               | 397   | _   |
|                      | 1 month  185 000  13 139  3 563  201 702  95 000  3 652 | 1 month  185 000 —  13 139 —  3 563 493  201 702 493  95 000 —  3 652 397 |

The Group's liquidity position is monitored on a daily basis by the asset manager and is reviewed on a regular basis by the Board of Directors.

## Diversification

The investment portfolio usually consists of 20 to 35 investments. This includes five to eight large core positions, which together will account for up to two-thirds of the portfolio. The maximum share of companies without a stock market listing is 10%.

As per December 31, 2018, the Group held five core investments, representing 43% (2017: six core investments, 48%) of the portfolio. The portfolio is – in line with the strategy – concentrated on a limited number of investments. Risk diversification is therefore limited.

## Fair values

The following table presents the Group's assets that are measured at fair value at December 31 (in CHF 1000):

| 2018  | Level 1   | Level 2 | Level 3 | Total     |
|---|-----------|---------|---------|-----------|
| Assets  |           |         |         |           |
| Securities at fair value through profit or loss |           |         |         |           |
| - Shares  | 3 063 972 | -       | -       | 3 063 972 |
| – Derivative instruments                        | _         | 203     | -       | 203       |
| Total assets                                    | 3 063 972 | 203     | -       | 3 064 175 |
| 2017  |           |         |         |           |
| Assets  |           |         |         |           |
| Securities at fair value through profit or loss |           |         |         |           |
| – Shares  | 3 623 929 | _       | -       | 3 623 929 |
| – Derivative instruments                        |           | 3 140   |         | 3 140     |
| Total assets                                    | 3 623 929 | 3 140   |         | 3 627 069 |

The fair value of financial instruments traded in active markets is based on quoted market prices at the balance sheet date. A market is regarded as active if quoted prices are readily and regularly available and those prices represent actual and regularly occurring market transactions on an arm's length basis. The quoted market price used for financial assets held by the Group is the closing price. These instruments are included in level 1.

The fair value of financial instruments that are not traded in an active market is determined by using valuation techniques. These valuation techniques maximize the use of observable market data where it is available. The options are valued on the basis of the Black-Scholes model which is based on market conditions existing at each balance sheet date. These instruments are included in level 2.

If one or more of the significant inputs is not based on observable market data, the instrument is included in level 3. The valuation of level 3 instruments is regularly reviewed. As soon as new or adjusted parameters are available the valuation models (earnings multiple model) of unlisted shares are adjusted accordingly. The valuations are reviewed at least once a year. As of December 31, 2018 and 2017, no valuation is necessary as there are no more level 3 investments.

The table below summarizes the transactions in level 3 instruments (in CHF 1 000):

|  | 2018     | 2017 |
|--|----------|------|
| Opening balance  | -        | _    |
| Purchases  | 65 408   | _    |
| Reclassification   | (69 356) | _    |
| Income included in income from securities                              | 3 948    | _    |
| Closing balance  | -        | _    |
| Total income on level 3 instruments included in income from securities | 3 948    | _    |

Due to the IPO of Moderna Therapeutics Inc. as of December 6, 2018, a reclassification of the Moderna Therapeutics shares from level 3 to level 1 (CHF 69 356) took place in the period.

For assets and liabilities carried at amortized cost, their carrying values are a reasonable approximation of fair value.

## 4. Financial assets

## Marketable securities

The changes in value of securities at fair value through profit or loss by investment category are as follows (in CHF 1000):

|   | Listed<br>shares | Unlisted<br>shares | Derivative<br>instruments | Total       |
|---|------------------|--------------------|---------------------------|-------------|
| Opening balance as at 01/01/2017 at fair values | 3 201 135        | -                  | 4 721                     | 3 205 856   |
| Purchases                                       | 594 901          | _                  | _                         | 594 901     |
| Sales   | (896 944)        |                    | _                         | (896 944)   |
| Net gains/(losses) from securities              | 724 837          |                    | (1 581)                   | 723 256     |
| Realized gains                                  | 263 537          | _                  | _                         | 263 537     |
| Unrealized gains                                | 749 236          | _                  | _                         | 749 236     |
| Unrealized losses                               | (287 936)        | _                  | (1 581)                   | (289 517)   |
| Closing balance as at 12/31/2017 at fair values | 3 623 929        |                    | 3 140                     | 3 627 069   |
| Opening balance as at 01/01/2018 at fair values | 3 623 929        | -                  | 3 140                     | 3 627 069   |
| Purchases                                       | 877 899          | 65 408             | -                         | 943 307     |
| Sales   | (1 076 876)      | -                  | (2 235)                   | (1 079 111) |
| Reclassification <sup>1)</sup>                  | 69 356           | (69 356)           | -                         | -           |
| Net gains/(losses) from securities              | (430 336)        | 3 948              | (702)                     | (427 090)   |
| Realized gains                                  | 209 613          | -                  | 371                       | 209 984     |
| Realized losses                                 | (64 769)         | -                  | -                         | (64 769)    |
| Unrealized gains                                | 154 039          | 3 948              | -                         | 157 987     |
| Unrealized losses                               | (729 219)        | _                  | (1 073)                   | (730 292)   |
| Closing balance as at 12/31/2018 at fair values | 3 063 972        | -                  | 203                       | 3 064 175   |

<sup>1)</sup> IPO of Moderna Therapeutics Inc. as of December 6, 2018

| Company   | Number<br>12/31/2017 | Change               | Number<br>12/31/2018 |     | larket price in<br>ginal currency<br>12/31/2018 |         | Valuation<br>CHF mn<br>12/31/2017 |
|---|----------------------|----------------------|----------------------|-----|---|---------|-----------------------------------|
| Ionis Pharmaceuticals                                 | 8 136 334            | 605 000              | 8 741 334            | USD | 54.06   | 463.9   | 398.7                             |
| Incyte  | 3 698 322            | 110 000              | 3 808 322            | USD | 63.59   | 237.7   | 341.2                             |
| Neurocrine Biosciences                                | 3 452 753            | (109 663)            | 3 343 090            | USD | 71.41   | 234.3   | 261.0                             |
| Vertex Pharmaceuticals                                | 1 475 445            | (105 000)            | 1 370 445            | USD | 165.71  | 222.9   | 215.4                             |
| Esperion Therapeutics                                 | 2 362 964            | 1 030 000            | 3 392 964            | USD | 46.00   | 153.2   | 151.6                             |
| Celgene   | 3 424 298            | (1 120 423)          | 2 303 875            | USD | 64.09   | 144.9   | 348.1                             |
| Agios Pharmaceuticals                                 | 2 719 998            | 158 136              | 2 878 134            | USD | 46.11   | 130.3   | 151.5                             |
| Sage Therapeutics                                     | 1 042 439            | 332 790              | 1 375 229            | USD | 95.79   | 129.3   | 167.3                             |
| Alexion Pharmaceuticals                               | 1 354 428            | (40 000)             | 1 314 428            | USD | 97.36   | 125.6   | 157.8                             |
| Halozyme Therapeutics                                 | 8 520 137            | (197 277)            | 8 322 860            | USD | 14.63   | 119.5   | 168.2                             |
| Alnylam Pharmaceuticals                               | 1 051 338            | 520 051              | 1 571 389            | USD | 72.91   | 112.5   | 130.1                             |
| Radius Health   | 5 698 799            | 1 011 477            | 6 710 276            | USD | 16.49   | 108.6   | 176.4                             |
| Argenx SE   |                      | 884 739              | 884 739              | USD | 96.07   | 83.4    |                                   |
| Gilead  | 2 774 596            | (1 442 392)          | 1 332 204            | USD | 62.55   | 81.8    | 193.6                             |
| Moderna Therapeutics 1) 2)                            |                      | 4 785 681            | 4 785 681            | USD | 15.27   | 71.7    |                                   |
| Akcea Therapeutics                                    | 1 248 650            | 1 137 821            | 2 386 471            | USD | 30.14   | 70.6    | 21.1                              |
| Wave Life Sciences                                    | 856 096              | 608 906              | 1 465 002            | USD | 42.04   | 60.5    | 29.3                              |
| Myovant Sciences                                      | 3 507 882            | 90 000               | 3 597 882            | USD | 16.41   | 58.0    | 43.2                              |
| Intercept Pharmaceuticals                             | 485 719              | 90 000               | 575 719              | USD | 100.79  | 57.0    | 27.6                              |
| Exelixis  |                      | 2 835 000            | 2 835 000            | USD | 19.67   | 54.7    |                                   |
| Nektar Therapeutics                                   |                      | 1 380 975            | 1 380 975            | USD | 32.87   | 44.6    |                                   |
|   |                      | 877 266              | 877 266              | USD | 48.86   | 42.1    |                                   |
| Myokardia   | 2 600 412            | 682 860              | 3 283 272            | USD | 12.70   | 40.9    | 48.1                              |
| Macrogenics   |                      |                      |                      | USD |   |         | -                                 |
| Scholar Rock Holding                                  |                      | 1 279 978<br>500 000 | 1 279 978            |     | 22.97   | 28.9    |                                   |
| Alder Biopharmaceuticals                              | 2 266 008            |                      | 2 766 008            | USD | 10.25   | 27.8    | 25.3                              |
| Voyager Therapeutics                                  | 1 539 520            | 1 326 321            | 2 865 841            | USD | 9.40  | 26.4    | 24.9                              |
| Regeneron Pharmaceuticals                             | 205 000              | (136 844)            | 68 156               | USD | 373.50  | 25.0    | 75.1                              |
| Intra-Cellular Therapies                              | 2 200 000            |                      | 2 200 000            | USD | 11.39   | 24.6    | 31.0                              |
| Kezar Life Sciences                                   |                      | 818 432              | 818 432              | USD | 23.60   | 19.0    |                                   |
| Audentes Therapeutics                                 |                      | 769 404              | 769 404              | USD | 21.32   | 16.1    |                                   |
| Sangamo Therapeutics                                  |                      | 1 350 000            | 1 350 000            | USD | 11.48   | 15.2    |                                   |
| Novavax   | 8 330 000            |                      | 8 330 000            | USD | 1.84  | 15.0    | 10.1                              |
| G1 Therapeutics                                       |                      | 671 925              | 671 925              | USD | 19.15   | 12.6    |                                   |
| Cidara Therapeutics                                   | 2 295 272            |                      | 2 295 272            | USD | 2.35  | 5.3     | 15.2                              |
| Novo Nordisk  | 2 724 775            | (2 724 775)          |                      | DKK | n.a.  |         | 143.2                             |
| Juno Therapeutics                                     | 1 925 000            | (1 925 000)          |                      | USD | n.a.  | -       | 85.7                              |
| Tesaro  | 1 046 193            | (1 046 193)          |                      | USD | n.a.  | _       | 84.5                              |
| AveXis  | 402 800              | (402 800)            |                      | USD | n.a.  | -       | 43.4                              |
| Five Prime Therapeutics                               | 827 500              | (827 500)            |                      | USD | n.a.  |         | 17.7                              |
| Probiodrug  | 1 050 784            | (1 050 784)          |                      | EUR | n.a.  | -       | 13.0                              |
| Prothena Corp.  | 350 000              | (350 000)            |                      | USD | n.a.  | -       | 12.8                              |
| Idorsia   | 323 606              | (323 606)            |                      | CHF | n.a.  | _       | 8.2                               |
| Achillion Pharmaceuticals                             | 1 279 340            | (1 279 340)          |                      | USD | n.a.  | -       | 3.6                               |
| Listed shares   |                      |                      |                      |     |   | 3 063.9 | 3 623.9                           |
| Total shares  |                      |                      |                      |     |   | 3 063.9 | 3 623.9                           |
| Radius Health, warrants, USD 14, 02/19/2019           | 71 409               | =                    | 71 409               | USD | 2.90  | 0.2     | 1.3                               |
| Radius Health, warrants, USD 14, 04/23/2018           | 107 114              | (107 114)            |                      | USD | n.a.  | _       | 1.9                               |
| Total derivative instruments                          |                      |                      |                      |     |   | 0.2     | 3.2                               |
| Total securities at fair value through profit or loss |                      |                      |                      |     |   | 3 064.2 | 3 627.1                           |

The marketable securities are deposited with Bank Julius Baer & Co. Ltd., Zurich.

Share split 1:2.18 as at December 6, 2018
 IPO of Moderna Therapeutics Inc. as of December 6, 2018

## 5. Short-term borrowings from banks

At December 31, 2018, a CHF 185 mn short-term loan is outstanding, with interest payable at 0.40% p.a. (2017: CHF 95 mn at 0.40% p.a.).

## 6. Other short-term liabilities

(in CHF 1 000)

Other short-term liabilities comprise the following:

|                                      | 12/31/2018 | 12/31/2017 |
|--------------------------------------|------------|------------|
| Payables to the asset manager        | 3 196      | 3 400      |
| Payables to the market maker         | 28         | 91         |
| Total liabilities to related parties | 3 224      | 3 491      |
| Other liabilities                    | 832        | 558        |
| Total liabilities to third parties   | 832        | 558        |
|                                      | 4 056      | 4 049      |

Liabilities to related parties represent unpaid fees, commissions as well as administration costs. Further information on transactions with related parties are disclosed in note 16, «Related party transactions».

## 7. Shareholders' equity

The share capital of the Company consists of 55.4 mn fully paid registered shares (2017: 55.4 mn registered shares) with a par value of CHF 0.20 each (2017: CHF 0.20). CHF 2.2 mn of the retained earnings (2017: CHF 2.2 mn) are undistributable.

|   | Par value<br>per share<br>in CHF | Nominal value of<br>the share capital<br>in CHF 1 000 | Number of shares | Treasury shares<br>number | Outstanding<br>shares<br>number |
|---|----------------------------------|---|------------------|---------------------------|---------------------------------|
| January 1, 2017                           | 0.20                             | 11 080  | 55 400 000       | 15 715                    | 55 384 285                      |
| Purchases of treasury shares at an        |                                  |   |                  |                           |                                 |
| average price of CHF 57.76                |                                  |   |                  | 316 553                   | (316 553)                       |
| Sales of treasury shares at an            |                                  |   |                  |                           | _                               |
| average price of CHF 58.99                |                                  |   |                  | (317 308)                 | 317 308                         |
| Share allocation Board of Directors (net) |                                  |   |                  | (14 960)                  | 14 960                          |
| December 31, 2017                         | 0.20                             | 11 080  | 55 400 000       |                           | 55 400 000                      |
| January 1, 2018                           | 0.20                             | 11 080  | 55 400 000       | -                         | 55 400 000                      |
| December 31, 2018                         | 0.20                             | 11 080  | 55 400 000       | -                         | 55 400 000                      |

At December 31, 2018 and 2017, the Company has neither an authorized nor a conditional capital.

The General Shareholders' Meeting held on March 17, 2016, has approved a share buy-back program, whereby up to 5 540 000 shares may be repurchased by the Company. Until December 31, 2018, no shares had been repurchased under this share buy-back program.

## 8. Administrative expenses

(in CHF 1 000)

Administrative expenses comprise the following:

|   | 2018   | 2017   |
|---|--------|--------|
| Fund manager                                |        |        |
| – Management fees (incl. VAT)               | 40 810 | 36 454 |
| Personnel                                   |        |        |
| – Board of Directors remuneration           | 910    | 935    |
| – Wages and salaries                        | 73     | 64     |
| – Social insurance contributions and duties | 56     | 55     |
|   | 41 849 | 37 508 |

The remuneration model of BB Biotech AG is determined by the Board of Directors.

Since 2014, the remuneration paid to the asset manager is based upon a 1.1% p.a. all-in fee on the average market capitalization without any additional fixed or performance-based elements of compensation, which is paid on a monthly basis. The compensation of the Board of Directors consists since 2014 of a fixed compensation in the amount of CHF 910 per annum (excluding social insurance contributions and duties).

At the General Shareholders' Meeting held March 19, 2014, the variable, share-based remuneration of the Board of Directors for the business year 2013 was approved. Therefore, the vesting period of the performance-based remuneration ended on March 18, 2017. During the three-year vesting period, all performance targets were met. Therefore, 18 445 shares (gross) were due. The payment in lieu was carried out in treasury shares on April 24, 2017. In the financial year 2018 no costs have been recognized for equity compensation plans (2017: CHF 25). The cost is included in the position «Administrative expenses».

## 9. Other expenses

(in CHF 1 000)

Other expenses comprise the following:

|                                   | 2018  | 2017  |
|-----------------------------------|-------|-------|
| Bank charges                      | 596   | 552   |
| Marketing and financial reporting | 2 122 | 2 266 |
| Legal and consulting expenses     | 409   | 132   |
| Other expenses                    | 1 353 | 1 469 |
|                                   | 4 480 | 4 419 |

## 10. Taxes

(in CHF 1 000)

|  | 2018      | 2017    |
|--|-----------|---------|
| Operating income before tax  | (471 272) | 687 580 |
| Expected tax rate (Federal tax Switzerland)                                  | 7.8%      | 7.8%    |
| Expected income tax  | -         | 53 631  |
| Difference between effective local tax rates and the expected Swiss tax rate | (71)      | 53 554  |
| Total income tax   | 71        | 77      |

In the current year, the average effective income tax rate on a consolidated basis was less than 1% (2017: <1%). This low rate is mainly attributable to the fact that a large proportion of operating income was generated by a company situated in Curação. As at December 31, 2018, there is no nettable loss carry forward (2017: none).

## 11. Earnings per share

|   | 2018       | 2017       |
|---|------------|------------|
| Total comprehensive income for the year (in CHF 1 000)            | (471 343)  | 687 503    |
| Weighted average number of shares in issue                        | 55 400 000 | 55 345 790 |
| Income per share in CHF   | (8.51)     | 12.42      |
| · · · · · · · · · · · · · · · · · · ·                             |            |            |
| Income used to determine diluted income per share (in CHF 1 000)  | (471 343)  | 687 503    |
| Dilution potential (share-based payments) in shares               | -          | 5 675      |
| Weighted average number of shares in issue following the dilution | 55 400 000 | 55 351 465 |
| Diluted income per share in CHF                                   | (8.51)     | 12.42      |

## 12. Segment information

(in CHF 1 000)

The Group has only one business segment, namely the holding of investments in companies active in the biotechnology industry.

The geographical analysis of the operating income before tax is as follows – all income from financial assets are attributed to a country based on the domiciliation of the issuer of the instrument:

| Operating income before tax | 201     | 8 2017      |
|-----------------------------|---------|-------------|
| Netherlands                 | 14.88   | -           |
| Great Britain               | 12 87   | (921)       |
| Singapore                   | 6 84    | 7 (1611)    |
| Sweden                      |         | 9 314       |
| Germany                     | (7 30   | 5) (7 183)  |
| Switzerland                 | (8 05   | 66 748      |
| Ireland                     | (9 73   | 6) (4 778)  |
| Denmark                     | (15 06  | 56 186      |
| Curação                     | (41 75  | 2) (36 857) |
| USA                         | (423 96 | 7) 606 682  |
|                             | (471 27 | 2) 687 580  |

## 13. Assets pledged

At December 31, 2018, the securities in the amount of CHF 2 782.9 mn (2017: CHF 3 097.7 mn) are a collateral for a credit line of CHF 700 mn (2017: CHF 400 mn). At December 31, 2018, a CHF 185 mn short-term loan is outstanding (2017: CHF 95 mn).

## 14. Commitments, contingencies and other off-balance sheet transactions

The Group had no commitments or other off-balance sheet transactions open at December 31, 2018 (2017: none).

The operations of the Group are affected by legislative, fiscal and regulatory developments for which provisions are made where deemed necessary. The Board of Directors concludes that as at December 31, 2018, no proceedings existed which could have any material effect on the financial position of the Group (2017: none).

# 15. Financial assets and liabilities

Financial assets and liabilities are allocated to categories as follows (in CHF 1 000):

| At December 31, 2018             | Loans and receivables                                  | Assets at<br>fair value through<br>profit or loss | Total     |
|----------------------------------|--|---|-----------|
| Assets as per balance sheet      |  |   |           |
| Cash and cash equivalents        | 22 072   | -   | 22 072    |
| Receivables from brokers         | 334  | -   | 334       |
| Marketable securities            | -  | 3 064 175   | 3 064 175 |
| Other assets                     | 263  | -   | 263       |
|                                  | 22 669   | 3 064 175   | 3 086 844 |
|                                  | Liabilities at<br>fair value through<br>profit or loss | Other<br>financial<br>liabilities                 | Total     |
| Liabilities as per balance sheet |  |   |           |
| Short-term borrowings from banks | _  | 185 000   | 185 000   |
| Payables to brokers              | _  | 13 139  | 13 139    |
| Other short-term liabilities     | _  | 4 056   | 4 056     |
|                                  | -  | 202 195   | 202 195   |
| At December 31, 2017             | Loans and receivables                                  | Assets at<br>fair value through<br>profit or loss | Total     |
| Assets as per balance sheet      |  |   |           |
| Cash and cash equivalents        | 10 730   | =   | 10 730    |
| Marketable securities            |  | 3 627 069   | 3 627 069 |
|                                  | 10 730   | 3 627 069   | 3 637 799 |
|                                  | Liabilities at<br>fair value through<br>profit or loss | Other<br>financial<br>liabilities                 | Total     |
| Liabilities as per balance sheet |  |   |           |
| Short-term borrowings from banks |  | 95 000  | 95 000    |
| Other short-term liabilities     |  | 4 049   | 4 049     |
|                                  | _  | 99 049  | 99 049    |

Profit and loss from financial assets and liabilities are allocated to categories as follows (in CHF 1 000):

| 2018  | Loans and receivables | Financial<br>instruments<br>at fair value<br>through profit<br>or loss | Other<br>financial<br>liabilities | Total     |
|---|-----------------------|--|-----------------------------------|-----------|
| Profit and loss from financial instruments      |                       |  |                                   |           |
| Interest income                                 | 29                    | -  | -                                 | 29        |
| Dividend income                                 | _                     | 5 458  | -                                 | 5 458     |
| Losses from marketable securities               | _                     | (427 090)  | -                                 | (427 090) |
| Finance expenses                                | _                     | -  | (1 086)                           | (1 086)   |
| Foreign exchange losses net                     | (2 544)               | -  | -                                 | (2 544)   |
| 2017 Profit and loss from financial instruments |                       |  |                                   |           |
| Gains from marketable securities                |                       | 723 256  |                                   | 723 256   |
| Dividend income                                 | _                     | 6 783  |                                   | 6 783     |
|   |                       |  |                                   |           |
| Foreign exchange gains net                      | 6                     |  |                                   | 6         |

## 16. Related party transactions

The asset management and administration of the Company has been delegated to Bellevue Asset Management Group. Based on the 1.1% p.a. all-in fee model, no additional costs incurred at Bellevue Asset Management Group were charged to the BB Biotech Group (2017: none). Purchases and sales of shares traded in Switzerland are partly processed and settled via Bank am Bellevue AG. In addition, Bank am Bellevue AG was mandated with a market making mandate. The commissions for these transactions amount to 0.15%, 0.20%, and 0.25% respectively. The amounts outstanding at the balance sheet date are disclosed in note 6, «Other short-term liabilities».

Detailed information regarding the remuneration model for the Board of Directors and the asset manager are mentioned under note 8, «Administrative expenses».

## 17. Significant shareholders

The Board of Directors is not aware of any major shareholder with a holding exceeding 3% of all votes as at December 31, 2018 and 2017.

## 18. Subsequent events

There have been no events subsequent to December 31, 2018, which would affect the 2018 consolidated financial statements.



Report of the statutory auditor to the General Meeting of BB Biotech AG Schaffhausen

## Report on the audit of the consolidated financial statements

#### Opinion

We have audited the consolidated financial statements of BB Biotech AG and its subsidiaries (the Group), which comprise the consolidated balance sheet as at 31 December 2018 and the consolidated statement of comprehensive income, consolidated statement of changes in equity and consolidated statement of cash flow for the year then ended, and notes to the consolidated financial statements, including a summary of significant accounting policies.

In our opinion, the consolidated financial statements (pages 42 to 57) give a true and fair view of the consolidated financial position of the Group as at 31 December 2018 and its consolidated financial performance and its consolidated cash flows for the year then ended in accordance with the International Financial Reporting Standards (IFRS) and comply with the provisions of article 14 of the Directive on Financial Reporting (DFR) of the SIX Swiss Exchange and with Swiss law.

## Basis for opinion

We conducted our audit in accordance with Swiss law, International Standards on Auditing (ISAs) and Swiss Auditing Standards. Our responsibilities under those provisions and standards are further described in the "Auditor's responsibilities for the audit of the consolidated financial statements" section of our report.

We are independent of the Group in accordance with the provisions of Swiss law and the requirements of the Swiss audit profession, as well as the IESBA Code of Ethics for Professional Accountants, and we have fulfilled our other ethical responsibilities in accordance with these requirements. We believe that the audit evidence we have obtained is sufficient and appropriate to provide a basis for our opinion.

# Our audit approach

## Overview

Overall Group materiality: CHF 28 845 000



We concluded full scope audit work at all of the reporting units, which are located in Switzerland and Curacao.

Our audit scope therefore addressed 100% of the Group's assets, equity, income, expenses and cash flows.

As key audit matters the following areas of focus have been identified:

- Valuation of securities
- Ownership of securities
- All-in fee calculation

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## Materiality

The scope of our audit was influenced by our application of materiality. Our audit opinion aims to provide reasonable assurance that the consolidated financial statements are free from material misstatement. Misstatements may arise due to fraud or error. They are considered material if, individually or in aggregate, they could reasonably be expected to influence the economic decisions of users taken on the basis of the consolidated financial statements.

Based on our professional judgement, we determined certain quantitative thresholds for materiality, including the overall Group materiality for the consolidated financial statements as a whole as set out in the table below. These, together with qualitative considerations, helped us to determine the scope of our audit and the nature, timing and extent of our audit procedures and to evaluate the effect of misstatements, both individually and in aggregate, on the consolidated financial statements as a whole.

| Overall Group materiality                       | CHF 28 845 000  |
|---|---|
| How we determined it                            | 1% of total consolidated shareholders' equity   |
| Rationale for the materiality benchmark applied | We chose shareholders' equity as the benchmark because, in our view, it is the most relevant benchmark for investors and it is a generally accepted benchmark for investment companies. |

## Audit scope

We tailored the scope of our audit in order to perform sufficient work to enable us to provide an opinion on the consolidated financial statements as a whole, taking into account the structure of the Group, the accounting processes and controls, and the industry in which the Group operates.

The Group consists of a holding company located in Switzerland and four reporting entities located in Curacao, which hold investments in companies in the biotechnology industry. Full scope audit work was performed on each reporting entity.

## Key audit matters

Key audit matters are those matters that, in our professional judgement, were of most significance in our audit of the consolidated financial statements of the current period. These matters were addressed in the context of our audit of the consolidated financial statements as a whole, and in forming our opinion thereon, and we do not provide a separate opinion on these matters.

## Valuation of securities

## Key audit matter

The investment portfolio comprises investments in marketable securities.

We consider this area to be a key audit matter because of the significant value of the securities in the consolidated financial statements.

As set out in note 4 (Schedule of securities) securities amount to CHF 3'064 million or 99.3% of total assets.

The valuation of the securities is prepared by the Investment Manager using the valuation methods disclosed in note 2 (Accounting policies). The Board of Directors approves the valuation of the investment portfolio.

## How our audit addressed the key audit matter

We verified the design and implementation of the controls relating to the valuation of securities in order to determine whether the Investment Manager has appropriate controls in place.

We verified the quoted prices of marketable securities by reconciling the prices applied to an independent source different to the source used by the Investment Manager.

We obtained sufficient audit evidence to conclude that the valuation methods were both appropriate and consistently applied by the Board of Directors.

## Ownership of securities

#### Key audit matter

The securities are safeguarded by an independent custodian.

There is a risk that BB Biotech AG may not have sufficient legal entitlement to the securities.

We consider this area to be a key audit matter because of the significant value of the securities in the consolidated financial statements.

## How our audit addressed the key audit matter

We examined the ownership of the securities by requesting a confirmation of the security position directly from the custodian.

We obtained sufficient audit evidence to conclude that there is sufficient legal entitlement to the security positions.

## All-in fee calculation

## Key audit matter

BB Biotech AG has delegated the administration and asset management activities to Bellevue Asset Management AG and its subsidiary. The remuneration is calculated based on the average market capitalisation of the company.

We consider this area to be a key audit matter because it represents a significant expense in the consolidated financial statements.

## How our audit addressed the key audit matter

We verified that the calculation method complies with the contractual agreements.

We verified the average market capitalisation on a sample basis.

We obtained sufficient audit evidence to conclude that the all-in fee charged to the company complies with the contractual arrangements.

## Other information in the annual report

The Board of Directors is responsible for the other information in the annual report. The other information comprises all information included in the annual report, but does not include the consolidated financial statements, the stand-alone financial statements and the remuneration report of BB Biotech AG and our auditor's reports thereon.

Our opinion on the consolidated financial statements does not cover the other information in the annual report and we do not express any form of assurance conclusion thereon.

In connection with our audit of the consolidated financial statements, our responsibility is to read the other information in the annual report and, in doing so, consider whether the other information is materially inconsistent with the consolidated financial statements or our knowledge obtained in the audit, or otherwise appears to be materially misstated. If, based on the work we have performed, we conclude that there is a material misstatement of this other information, we are required to report that fact. We have nothing to report in this regard.

Responsibilities of the Board of Directors for the consolidated financial statements

The Board of Directors is responsible for the preparation of the consolidated financial statements that give a true and fair view in accordance with IFRS, article 14 of the Directive on Financial Reporting (DFR) of the SIX Swiss Exchange and the provisions of Swiss law, and for such internal control as the Board of Directors determines is necessary to enable the preparation of consolidated financial statements that are free from material misstatement, whether due to fraud or error.

In preparing the consolidated financial statements, the Board of Directors is responsible for assessing the Group's ability to continue as a going concern, disclosing, as applicable, matters related to going concern and using the going concern basis of accounting unless the Board of Directors either intends to liquidate the Group or to cease operations, or has no realistic alternative but to do so.

Auditor's responsibilities for the audit of the consolidated financial statements

Our objectives are to obtain reasonable assurance about whether the consolidated financial statements as a whole are free from material misstatement, whether due to fraud or error, and to issue an auditor's report that includes our opinion. Reasonable assurance is a high level of assurance, but is not a guarantee that an audit conducted in accordance with Swiss law, ISAs and Swiss Auditing Standards will always detect a material misstatement when it exists. Misstatements can arise from fraud or error and are considered material if, individually or in the aggregate, they could reasonably be expected to influence the economic decisions of users taken on the basis of these consolidated financial statements.

A further description of our responsibilities for the audit of the consolidated financial statements is located at the website of EXPERTsuisse: http://expertsuisse.ch/en/audit-report-for-public-companies. This description forms part of our auditor's report.

## Report on other legal and regulatory requirements

In accordance with article 728a paragraph 1 item 3 CO and Swiss Auditing Standard 89o, we confirm that an internal control system exists which has been designed for the preparation of consolidated financial statements according to the instructions of the Board of Directors.

We recommend that the consolidated financial statements submitted to you be approved.

PricewaterhouseCoopers AG

Daniel Pajer Stephanie Zaugg Audit expert Audit expert

Auditor in charge

Zurich, 14 February 2019



# Financial statements BB Biotech AG

## Balance sheet as at December 31

(in CHF)

|  | Notes | 2018          | 2017          |
|--|-------|---------------|---------------|
| Current assets                             |       |               |               |
| Cash and cash equivalents                  |       | 361 124       | 326 967       |
| Other current receivables                  |       | 262 533       | 203           |
|  |       | 623 657       | 327 170       |
| Non-current assets                         |       |               |               |
| Investments                                |       | 1 177 069 500 | 1 177 069 500 |
|  |       | 1 177 069 500 | 1 177 069 500 |
| Total assets                               |       | 1 177 693 157 | 1 177 396 670 |
| Current liabilities                        |       |               |               |
| Other current liabilities                  | 2.1   | 710 933 499   | 603 619 920   |
| Accrued expenses                           |       | 413 472       | 135 230       |
|  |       | 711 346 971   | 603 755 150   |
| Total liabilities                          |       | 711 346 971   | 603 755 150   |
| Shareholders' equity                       |       |               |               |
| Share capital                              | 2.2   | 11 080 000    | 11 080 000    |
| Legal capital reserves                     |       |               |               |
| – Paid-in capital reserve <sup>1)</sup>    |       | 20 579 224    | 20 579 224    |
| Legal profit reserves                      |       |               |               |
| – General legal reserve                    |       | 4 500 000     | 4 500 000     |
| Other reserves                             |       | 226 827 756   | 226 827 756   |
| Retained earnings                          | 5/6   | 203 359 206   | 310 654 540   |
|  |       | 466 346 186   | 573 641 520   |
| Total liabilities and shareholders' equity |       | 1 177 693 157 | 1 177 396 670 |

 $<sup>^{\</sup>mbox{\tiny 1}\mbox{\tiny J}}$  Of which CHF 20 441 000 not confirmed by the Swiss Tax Authorities due to present regulation

The financial statements were approved by the Board of Directors of BB Biotech AG on February 12, 2019.

# Statement of income for the year ended December 31

(in CHF)

|  | Notes | 2018        | 2017        |
|--|-------|-------------|-------------|
| Operating income                                 |       |             |             |
| Income from investments                          |       | 75 000 000  | 300 000 000 |
| Other income                                     | 2.3   | 6 209 320   | 6 092 221   |
|  |       | 81 209 320  | 306 092 221 |
| Operating expenses                               |       |             |             |
| Administrative expenses                          | 2.4   | (1 780 904) | (1 743 583) |
| Other expenses                                   | 2.5   | (3 838 464) | (3 813 778) |
|  |       | (5 619 368) | (5 557 361) |
| Operating income before finance income and taxes |       | 75 589 952  | 300 534 860 |
| Finance income                                   |       | 2 867       | 933         |
| Finance expenses                                 |       | (22 220)    | (23 666)    |
| Operating income before tax                      |       | 75 570 599  | 300 512 127 |
|  |       |             |             |
| Tax expenses                                     | 2.6   | (45 933)    | (68 787)    |
| Net income for the year                          |       | 75 524 666  | 300 443 340 |

## 1. Accounting policies

#### General

The financial statements of BB Biotech AG (the Company) have been prepared in accordance with the provisions of commercial accounting as set out in the Swiss Code of Obligations. The financial statements have been prepared under the historical cost convention.

## Cash and cash equivalents

Cash and cash equivalents includes current accounts at banks. These are stated at the notional amount.

#### Investments

The investments include the subsidiaries over which the Company has control. The Company controls an entity when the Company is exposed to, or has rights to, variable returns from its involvement with the entity and has the ability to affect those returns through its power over the entity. Initially and subsequently, investments are valued at historical cost. An impairment is recognized if the value in use is expected to permanently fall below the book value.

Income from investments is recognized in the income statement when the Company's right to receive the dividend payment is established.

## Receivables/liabilities

Receivables/liabilities are classified as current assets/liabilities if maturity is expected to be within twelve month after the balance sheet date. Else, they are classified as long-term assets/liabilities. Receivables/liabilities are recognized at notional value. Receivables/liabilities against related parties include transactions with the Board of Directors as well as companies and affiliates of the asset manager. Receivables/liabilities against group companies result mainly from cash-pooling activies of the Group. The Group consists of BB Biotech AG and the mentioned subsidiaries under 3.3.

## Treasury shares

Treasury shares are deducted from shareholders' equity. All profits and losses arising from trading in treasury shares are included in the income statement. A reserve for treasury shares is built for treasury shares held by subsidiaries. The reserve is based on cost prices.

## 2. Details and explanations to the financial statements

## 2.1 Other current liabilities

The other current liabilities comprise the following (in CHF):

|                 | 2018        | 2017        |
|-----------------|-------------|-------------|
| Third parties   | 451 957     | 418 551     |
| Related parties | 90 591      | 157 418     |
| Group companies | 710 390 951 | 603 043 951 |
|                 | 710 933 499 | 603 619 920 |

## 2.2 Shareholders' equity

The share capital of the Company consists of 55.4 mn fully paid registered shares (2017: 55.4 mn registered shares) with a par value of CHF 0.20 each (2017: CHF 0.20).

The General Shareholders' Meeting held on March 17, 2016, has approved a share buy-back program, whereby up to 5 540 000 shares may be repurchased by the Company. Until December 31, 2018, no shares had been repurchased under this share buy-back program.

At December 31, 2018 and 2017, the Company has neither an authorized nor a conditional capital.

## 2.3 Other income

Other income comprises the following (in CHF):

|                       | 2018      | 2017      |
|-----------------------|-----------|-----------|
| Income group services | 6 203 000 | 6 088 000 |
| Other income          | 6 320     | 4 221     |
|                       | 6 209 320 | 6 092 221 |

## 2.4 Administrative expenses

Administrative expenses comprise the following (in CHF):

|                                 | 2018      | 2017      |
|---------------------------------|-----------|-----------|
| Board compensation              | 954 033   | 954 033   |
| Investment manager compensation | 742 001   | 714 785   |
| Staff costs                     | 84 870    | 74 765    |
|                                 | 1 780 904 | 1 743 583 |

The remuneration report discloses further details to the Board compensation.

## 2.5 Other expenses

Other expenses comprise the following (in CHF):

|                                   | 2018      | 2017      |
|-----------------------------------|-----------|-----------|
| Marketing and financial reporting | 2 122 012 | 2 266 487 |
| Consulting and audit              | 562 990   |           |
| Bank charges                      | 15 900    | 15 982    |
| Other expenses                    | 1 137 562 | 1 274 525 |
|                                   | 3 838 464 | 3 813 778 |

## 2.6 Tax expenses

Tax expenses comprise the following (in CHF):

|               | 2018   | 2017   |
|---------------|--------|--------|
| Income taxes  | 32 000 | 40 000 |
| Capital taxes | 13 933 | 28 787 |
|               | 45 933 | 68 787 |

## 3. Other information required by law

## 3.1 Name, legal form and registered office

BB Biotech AG is a limited company according to the Swiss Code of Obligation and has its registered office at Schwertstrasse 6 in Schaffhausen.

# 3.2 Declaration of number of full-time equivalents

The number of full-time equivalents did not exceed 10 in the calendar year 2018 (2017: below 10).

## 3.3 Investments

Investments of BB Biotech AG comprise, in the business years 2018 and 2017, the following subsidiaries:

| Company                      | Capital<br>in CHF | Capital and<br>voting interest<br>in % |
|------------------------------|-------------------|--|
| Biotech Focus N.V., Curação  | 10 778            | 100                                    |
| Biotech Growth N.V., Curação | 10 778            | 100                                    |
| Biotech Invest N.V., Curação | 10 778            | 100                                    |
| Biotech Target N.V., Curação | 10 778            | 100                                    |

## 3.4 Treasury shares (balances and change)

Treasury shares are partly held by the Company directly and partly by its 100% subsidiary Biotech Target N.V. indirectly.

|  | BB Biotech AG | Biotech Target N.V. | Total     |
|--|---------------|---------------------|-----------|
| Balance at January 1, 2017                                     | -             | 15 715              | 15 715    |
| Purchases Biotech Target N.V. at an average price of CHF 57.76 |               | 316 553             | 316 553   |
| Sales Biotech Target N.V. at an average price of CHF 58.99     |               | (317 308)           | (317 308) |
| Intercompany transfer  | 14 960        | (14 960)            | _         |
| Share allocation Board of Directors (net)                      | (14 960)      | _                   | (14 960)  |
| Balance at December 31, 2017                                   | _             | _                   | _         |
|  |               |                     |           |
| Balance at December 31, 2018                                   | _             | -                   | -         |

## 3.5 Audit fees

The audit fees comprise the following (in CHF):

|                    | 2018    | 2017    |
|--------------------|---------|---------|
| Audit fees         | 120 000 | 120 000 |
| Audit-related fees | 2 000   | 2 400   |
|                    | 122 000 | 122 400 |

## 3.6 Commitments and contingencies

The Company had no commitments or other off-balance sheet transactions open at December 31, 2018 (2017: none).

The operations of the Company are affected by legislative, fiscal and regulatory developments for which provisions are made where deemed necessary. The Board of Directors concludes that as at December 31, 2018, no proceedings existed which could have any material effect on the financial position of the Company (2017: none).

## 3.7 Subsequent events

There have been no events subsequent to December 31, 2018, which would affect the 2018 financial statements.

## 4. Other information

## 4.1 Significant shareholders

The Board of Directors is not aware of any major shareholder with a holding exceeding 3% of all votes as at December 31, 2018 and 2017.

## 4.2 Statement of holdings of the Board of Directors

As at December 31, the Board of Directors held the following registered shares of BB Biotech AG:

|                                   | 2018      | 2017      |
|-----------------------------------|-----------|-----------|
| Dr. Erich Hunziker, Chairman      | 1 457 884 | 1 457 884 |
| Dr. Clive Meanwell, Vice-Chairman | 5 163     | 5 163     |
| Prof. Dr. Dr. Klaus Strein        | 100 168   | 88 168    |

## 4.3 Management contracts

On behalf of the Company, the Board of Directors has entered into a management contract with Bellevue Asset Management Group (investment manager). In this contract, the investment manager commits to carry out management services relating to the investment activity and management of BB Biotech AG. Under this contract the Company paid in the business year 2018 CHF 742 001 (2017: CHF 714 785) to Bellevue Asset Management AG.

# 4.4 Annual report and cash flow statement

Due to the fact, that BB Biotech AG prepares consolidated financial statements in accordance with a recognized international accounting standard (IFRS), the Company doesn't prepare, in line with the legal requirements, an annual report and cash flow statement.

# 5. Movements on retained earnings

| in CHF   | 2018          | 2017          |
|--|---------------|---------------|
| Retained earnings at the beginning of the year | 310 654 540   | 7 561 200     |
| Appropriation of other reserves                | -             | 155 000 000   |
| Dividend                                       | (182 820 000) | (152 350 000) |
| Net income for the year                        | 75 524 666    | 300 443 340   |
| Retained earnings at the end of the year       | 203 359 206   | 310 654 540   |

# 6. Proposal of the Board of Directors for the appropriation of retained earnings

| in CHF  | 2018<br>Proposal<br>of the Board | 2017<br>Resolution<br>passed at the AGM |
|---|----------------------------------|---|
| Retained earnings at the disposal of the Annual General Meeting | 203 359 206                      | 310 654 540                             |
| Dividend  | 168 970 000                      | 182 820 000                             |
| Carry forward to the next period                                | 34 389 206                       | 127 834 540                             |
|   | 203 359 206                      | 310 654 540                             |



Report of the statutory auditor to the General Meeting of BB Biotech AG Schaffhausen

## Report on the audit of the financial statements

#### Opinion

We have audited the financial statements of BB Biotech AG, which comprise the balance sheet as at 31 December 2018, statement of income and notes for the year then ended, including a summary of significant accounting policies.

In our opinion, the financial statements (pages 64 to 69) as at 31 December 2018 comply with Swiss law and the company's articles of incorporation.

# Basis for opinion

We conducted our audit in accordance with Swiss law and Swiss Auditing Standards. Our responsibilities under those provisions and standards are further described in the "Auditor's responsibilities for the audit of the financial statements" section of our report.

We are independent of the entity in accordance with the provisions of Swiss law and the requirements of the Swiss audit profession and we have fulfilled our other ethical responsibilities in accordance with these requirements. We believe that the audit evidence we have obtained is sufficient and appropriate to provide a basis for our opinion.

# Our audit approach

## Materiality

The scope of our audit was influenced by our application of materiality. Our audit opinion aims to provide reasonable assurance that the financial statements are free from material misstatement. Misstatements may arise due to fraud or error. They are considered material if, individually or in aggregate, they could reasonably be expected to influence the economic decisions of users taken on the basis of the financial statements.

Based on our professional judgement, we determined certain quantitative thresholds for materiality, including the overall materiality for the financial statements as a whole as set out in the table below. These, together with qualitative considerations, helped us to determine the scope of our audit and the nature, timing and extent of our audit procedures and to evaluate the effect of misstatements, both individually and in aggregate, on the financial statements as a whole.

| Overall materiality                             | CHF 4 663 000   |
|---|---|
| How we determined it                            | 1% of total shareholders' equity  |
| Rationale for the materiality benchmark applied | We chose shareholders' equity as the benchmark because, in our view, it is the most relevant benchmark for investors and it is a generally accepted benchmark for investment companies. |

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### Audit scope

We designed our audit by determining materiality and assessing the risks of material misstatement in the financial statements. In particular, we considered where subjective judgements were made; for example, in respect of significant accounting estimates that involved making assumptions and considering future events that are inherently uncertain. As in all of our audits, we also addressed the risk of management override of internal controls, including among other matters consideration of whether there was evidence of bias that represented a risk of material misstatement due to fraud.

Report on key audit matters based on the circular 1/2015 of the Federal Audit Oversight Authority We have determined that there are no key audit matters to communicate in our report.

# Responsibilities of the Board of Directors for the financial statements

The Board of Directors is responsible for the preparation of the financial statements in accordance with the provisions of Swiss law and the company's articles of incorporation, and for such internal control as the Board of Directors determines is necessary to enable the preparation of financial statements that are free from material misstatement, whether due to fraud or error.

In preparing the financial statements, the Board of Directors is responsible for assessing the entity's ability to continue as a going concern, disclosing, as applicable, matters related to going concern and using the going concern basis of accounting unless the Board of Directors either intends to liquidate the entity or to cease operations, or has no realistic alternative but to do so.

## Auditor's responsibilities for the audit of the financial statements

Our objectives are to obtain reasonable assurance about whether the financial statements as a whole are free from material misstatement, whether due to fraud or error, and to issue an auditor's report that includes our opinion. Reasonable assurance is a high level of assurance, but is not a guarantee that an audit conducted in accordance with Swiss law and Swiss Auditing Standards will always detect a material misstatement when it exists. Misstatements can arise from fraud or error and are considered material if, individually or in the aggregate, they could reasonably be expected to influence the economic decisions of users taken on the basis of these financial statements.

A further description of our responsibilities for the audit of the financial statements is located at the website of EXPERTsuisse: http://expertsuisse.ch/en/audit-report-for-public-companies. This description forms part of our auditor's report.

## Report on other legal and regulatory requirements

In accordance with article 728a paragraph 1 item 3 CO and Swiss Auditing Standard 89o, we confirm that an internal control system exists which has been designed for the preparation of financial statements according to the instructions of the Board of Directors.

We further confirm that the proposed appropriation of available earnings complies with Swiss law and the company's articles of incorporation. We recommend that the financial statements submitted to you be approved.

PricewaterhouseCoopers AG

Daniel Pajer Stephanie Zaugg Audit expert Audit expert

Auditor in charge

Zurich, 14 February 2019



# **Corporate Governance**

The following chapter is intended to supplement the annual report with information on corporate governance. As BB Biotech AG is listed on the Swiss, German, and Italian stock exchanges, the Company wishes to be in compliance with the rules and regulations that apply to each of these markets. A great deal of the required information has already been supplied in past sections of the annual report or is available for download on the Internet. In such cases we allow us to refer to the relevant pages in this report or to our website, www.bbbiotech.com.

## Introductory remarks with respect to the specific structure of BB Biotech AG as an investment company

BB Biotech AG is an investment company listed on a stock exchange according to article 2 paragraph 3 of the Swiss Federal Act on Collective Investment Schemes (CISA) in the form of a company limited by shares. As a company limited by shares which is listed on a stock exchange, BB Biotech AG is subject to the supervision and regulation by the SIX Swiss Exchange. Therefore, BB Biotech AG is exempted from the supervision of the Swiss Financial Market Supervisory Authority (FINMA) as well as from the regulation pursuant to the CISA.

As an investment company, the sole purpose of BB Biotech AG is the management of the assets of its investors. The BB Biotech group does not pursue any commercial or operational activity beyond the asset management.

## 2. Group structure and shareholdership

Please refer to note 1 of the consolidated annual financial statements. In addition hereto, we wish to advise that the Board of Directors is not aware of any cross-holdings with other companies exceeding a limit of 5% in terms of capital or the number of votes. Information on key stockholders is listed in note 17 to the consolidated annual financial statements. The notifications which have been notified to the Company and the disclosure office of the SIX Swiss Exchange AG during the fiscal year pursuant to article 20 of the Federal Act on Stock Exchanges and Securities Trading and which have been published on the latter's electronic publication platform may be viewed via the search function on https://www.six-exchange-regulation.com/de/home/publications/significant-shareholders.html.

## 3. Capital structure

The capital structure is as follows: (in CHF 1 000)

|                   | Nominal value of the<br>share capital | Authorized capital | Conditional capital |
|-------------------|---------------------------------------|--------------------|---------------------|
| January 1, 2016   | 11 850                                | _                  | -                   |
| Capital reduction | (770)                                 | =                  | _                   |
| December 31, 2016 | 11 080                                | _                  | _                   |
| January 1, 2017   | 11 080                                | _                  | _                   |
| December 31, 2017 | 11 080                                |                    |                     |
| January 1, 2018   | 11 080                                | -                  | -                   |
| December 31, 2018 | 11 080                                | -                  | -                   |

The share capital of the Company consists of 55.4 mn fully paid registered shares with a par value of CHF 0.20 each (2017 and 2016: 55.4 mn registered shares with a par value of CHF 0.20 each).

The change in equity is disclosed in the statement of changes in equity of the consolidated financial statements on page 44.

#### 4. Board of Directors

## 4.1 Members, nationality, and stock holdings

- Dr. Erich Hunziker, Chairman, Switzerland, 1457 884 registered shares (2017: 1457 884 registered shares)
- Dr. Clive Meanwell, Vice-Chairman, USA, 5163 registered shares (2017: 5163 registered shares)
- Prof. Dr. Dr. Klaus Strein, Germany, 100 168 registered shares (2017: 88 168 registered shares)

The members of the Board of Directors have no executive functions, neither today nor in the last three years. Moreover, no business relations are in place between the Board members and BB Biotech AG. Detailed résumés are available on our website www.bbbiotech.com.

### 4.2 Further mandates of the members of the Board of Directors

- Dr. Erich Hunziker is Chairman of the Board of Directors of Light Chain Biosciences AG and Entsia International AG and a member of the Board of Directors of LamKap Bio alpha AG, LamKap Bio beta AG and LamKap Bio gamma AG.
- Dr. Clive Meanwell is a member of the Board of Directors and CIO of The Medicines Company.
- Prof. Dr. Dr. Klaus Strein is Chairman of the Board of Directors of LamKap Bio alpha AG, LamKap Bio beta AG and LamKap Bio gamma AG
  and a member of the Board of Directors of NovImmune SA.

## 4.3 Number of permissible external mandates

The rule with respect to the number of permissible external mandates of members of the Board of Directors can be found in article 23 of the articles of incorporation of the Company. The articles of incorporation are available for download under the following link: www.bbbiotech.ch/bylaws.

## 4.4 Election and term of office

The Board of Directors is elected by a simple quorum for a term of office of one year. There are no limitations on its tenure. The members of the Board of Directors have first been elected at the following General Meetings:

- Dr. Erich Hunziker: 2011 (Chairman since 2013)
- Dr. Clive Meanwell: 2004 (Vice-Chairman since 2011)
- Prof. Dr. Dr. Klaus Strein: 2013

## 4.5 Internal organization

The Board of Directors consists of a Chairman, Vice-Chairman and a member. In addition, the members of the Board of Directors are appointed in the following committees:

- Dr. Erich Hunziker, Chairman: Chairman of the Audit Committee
- Dr. Clive Meanwell, Vice-Chairman: Member of the Audit Committee and Chairman of the Remuneration and Nomination Committee
- Prof. Dr. Dr. Klaus Strein, Member: Member of the Remuneration and Nomination Committee

The Board of Directors generally meets once per month via video or telephone conference. In addition, two three-day strategy meetings take place each year. These meetings are attended by representatives of the asset manager commissioned. No ordinary board meetings are held in the months of the strategy meetings. In these meetings, the Board of Directors regularly examines the compliance with the investment guidelines. In addition, the representatives entrusted with the asset management present the respective investment and divestiture proposals before their implementation to the Board of Directors. The latter examines the individual investment proposals with respect to the compliance with the investment strategy as well as the investment process. During the fiscal year 2018, nine ordinary board meetings and two strategy meetings took place.

The members of the Audit Committee hold quarterly meetings, the Remuneration and Nomination Committee holds at least one meeting a year. During 2018, four ordinary meetings of the Audit Committee and two meetings of the Remuneration and Nomination Committee took place.

## 4.6 Director's dealing

BB Biotech AG publishes each purchase/sale of BB Biotech AG stocks by members of the Board of Directors as well as by first-degree relatives of such persons within three trading days. This information is made available for 30 days on the website.

#### 5. Asset management

BB Biotech AG as an investment company listed on a stock exchange does not have a management of its own within the meaning of article 716b CO, respectively the Ordinance Against Excessive Compensation in Public Corporations. The Board of Directors of BB Biotech AG has — as it is customary for investment companies — outsourced the asset management based on the management contract to a specialized third company, namely to Bellevue Asset Management Group. The supervision of Bellevue Asset Management Group acting as external asset manager and the taking of core decisions relating to the investment policy remain with the Board of Directors of BB Biotech AG as a non-transferable duty. The management contract is valid for an indefinite period and can be terminated by either party with a notice period of twelve months with effect as per the end of the following calendar year. Detailed information on this mandate and the members of the investment manager involved is available on the website. Since January 1, 2014, the remuneration paid to the asset manager has been based upon a 1.1% p.a. all-in fee on the average market capitalization without any additional fixed or performance-based elements of compensation, which is paid on a monthly basis.

#### 6. Remuneration

See notes 8 and 16 of the consolidated financial statements as well as the remuneration report hereinafter for details relating to the remuneration of the Board of Directors and the process of determining its remuneration.

The rules governing the approval by the General Meeting of the remuneration of the members of the Board of Directors as well as the principles governing the remuneration of the members of the Board of Directors can be found in articles 19–21 of the articles of incorporation of the Company. The articles of incorporation do not contain any provision with respect to loans, credits and pension benefits to the members of the Board of Directors. The articles of incorporation are available for download under the following link: www.bbbiotech.ch/bylaws.

## 7. Stockholders' rights of cooperation

## 7.1 Limitations to voting rights; voting by proxy

There are no limitations to voting rights and no internal rules at variance from the statutory provisions concerning attendance of a General Meeting. The articles of incorporation do not contain any provision with respect to the issuance of directives to the independent voting rights representative or to the electronic participation at a General Meeting.

## 7.2 General Meeting

There are no statutory rules relating to the presence of a majority quorum which differ from the statutory provisions. The convening of a General Meeting as well as the request that items be included in the agenda are governed by article 7 of the articles of incorporation of the Company as well as the statutory provisions of law.

# 7.3 Dividend policy

At present, the Company is pursuing a structured distribution policy. The objective of the Board of Directors is to achieve an annual return of 10% for shareholders via dividends combined with continued share buy-backs. The Board of Directors suggests distributing an annual dividend equivalent to approximately 5% of the average share price in December as well as seeking shareholder authorization for further share buy-backs of approximately 5% p.a.

## 8. Change-of-control and defensive measures

# 8.1 Obligatory offer for sale

An opting-out rule is in place.

## 8.2 Change-of-control clauses

No change-of-control clauses are in place in favor of the Board of Directors.

## 9. Audits

## 9.1 Duration of mandate and term of office of the lead auditor

Since the fiscal year 1994, PricewaterhouseCoopers AG has been the official auditor and group auditor of BB Biotech AG. The lead auditor, Daniel Pajer, has been responsible for auditing the Company's books since the fiscal year 2017.

# 9.2 Fees

The following fees for professional services in the fiscal year ended December 31, 2018, were agreed:

- Audit fees (including interim audit): CHF 120 000
- Fees for audit-related services: CHF 2 000

# 9.3 Instruments of information of the external audit

The asset manager and the auditors are continually in contact with each other. The auditor is consulted by the Board of Directors where necessary. The auditors attend at least two audit committee meetings per year.

## 10. Information policy/diary of Company events

Please refer to «Shareholder information» at page 84.

# 11. Trading in own stocks

BB Biotech AG operates, in line with legal and internal regulations, as an active purchaser/seller of own stocks itself on the market, securing additional liquidity in the process.



# **Remuneration Report**

This remuneration report for the fiscal year 2018 outlines the remuneration system as well as the remuneration of the members of the Board of Directors of BB Biotech AG. The content and scope of the information contained in this report is in accordance with the provisions of the Ordinance Against Excessive Compensation in Public Corporations (the Ordinance) and with the Directive on Information relating to Corporate Governance (DCG) of the SIX Swiss Exchange.

## 1. Responsibilities and authorities with respect to remuneration

## 1.1 Introductory remarks relating to the specific structure of BB Biotech AG as an investment company

The Board of Directors of BB Biotech AG has not made use of its competence to delegate the executive management of all or part of the Company's business pursuant to article 716b CO and therefore manages the business of the Company itself, to the extent it has not been delegated to the investment manager within the framework of the management contract. Accordingly, BB Biotech AG does not have an executive management pursuant to article 716b CO or the Ordinance.

For details, please refer to note 7.

# 1.2 Responsibilities and authorities with respect to the remuneration

The Remuneration and Nomination Committee is responsible for ensuring that the process relating to the determination of the remuneration is held on a fair and transparent basis and that such process is controlled effectively. The adopted remuneration process shall serve as a basis for an adequate decision with respect to services rendered as well as an appropriate incentive to the individual members of the Board of Directors, taking into account the long-term interests of the shareholders and the Company's success. In addition, the Remuneration and Nomination Committee assists the Board of Directors in determining the principles of the remuneration strategy of BB Biotech AG.

The Remuneration and Nomination Committee submits proposals to the Board of Directors for resolution in the following areas:

- Amount and composition of the aggregate remuneration of the Board of Directors;
- Amount and composition of the remuneration of the Chairman of the Board of Directors;
- Amount and composition of the remuneration of the Vice-Chairman as well as the other members of the Board of Directors;
- Amount and composition of the additional remuneration of the members of a Board of Directors Committee.

Furthermore, the Remuneration and Nomination Committee resolves on conclusion, termination, or amendment of contracts entered into with external asset managers and thus in particular on the amount of the compensation to be paid under the respective contracts.

## 2. Remuneration of the members of the Board of Directors

## 2.1 Principles

The remuneration of the members of the Board of Directors is based on the scope of activity and responsibility of the individual members (Chairman of the Board of Directors, Vice-Chairman of the Board of Directors, member of the Board of Directors; involvement in committees: chairmanship of a committee, member of a committee).

The remuneration of the Board of Directors consists of the following elements:

- Fixed remuneration (disbursement by cash compensation);
- Social insurance contributions and duties.

The limitation to a fixed remuneration ensures that the focus of the Board of Directors lies on the long-term success of BB Biotech AG. Its amount takes account of the workload and responsibility of the individual members of the Board of Directors. Therefore, the remuneration of the Board of Directors has been separated from the compensation of the investment manager; thus, the Board of Directors does not have an incentive to take excessively high risks.

Upon request of the Remuneration and Nomination Committee, the entire Board of Directors resolves once a year on the amount of the remuneration of the members of the Board of Directors and the committees.

The Board of Directors had determined the fixed remuneration of its members (as a member of the Board of Directors or a committee) as follows:

|   | 2018<br>in CHF | 2017<br>in CHF |
|---|----------------|----------------|
| - 11 /s 11 lin  |                |                |
| Function/Responsibility                               |                |                |
| Chairman  | 360 000        | 360 000        |
| Vice-Chairman   | 250 000        | 250 000        |
| Member  | 250 000        | 250 000        |
| Chairman of the Remuneration and Nomination Committee | 15 000         | 15 000         |
| Member of the Remuneration and Nomination Committee   | 10 000         | 10 000         |
| Chairman of the Audit Committee                       | 15 000         | 15 000         |
| Member of the Audit Committee                         | 10 000         | 10 000         |
|   | 910 000        | 910 000        |

## 2.2 Remuneration of the individual members of the Board of Directors in the reporting year (audited)

In the reporting year 2018, the three members of the Board of Directors received a total remuneration of CHF 954 033 (2017: CHF 954 033). From this amount, CHF 910 000 (2017: CHF 910 000) have been paid in the form of a fixed remuneration for the work on the Board of Directors and on the committees of the Board of Directors. The social insurance contributions and the duties amounted to a total of CHF 44 033 (2017: CHF 44 033).

The individual members of the Board of Directors were paid the following remuneration:

## Fiscal year 2018

| Name/Function                 | RNC <sup>1)</sup> | AC <sup>2)</sup> | Period F                   | ixed remu-<br>neration | Committee remuneration | Social insurance contributions and duties | Total   |
|-------------------------------|-------------------|------------------|----------------------------|------------------------|------------------------|---|---------|
| Hunziker Erich, Chairman      |                   | Χ                | 01.01.2018 –<br>31.12.2018 | 360 000                | 15 000                 | 27 903                                    | 402 903 |
| Transfer Erren, Gramman       |                   |                  | 01.01.2018 -               |                        |                        |   | .02303  |
| Meanwell Clive, Vice-Chairman | Χ                 | Χ                | 31.12.2018                 | 250 000                | 25 000                 | _   | 275 000 |
|                               |                   |                  | 01.01.2018 -               |                        |                        | <u> </u>                                  |         |
| Strein Klaus, Member          | Χ                 |                  | 31.12.2018                 | 250 000                | 10 000                 | 16 130                                    | 276 130 |

<sup>&</sup>lt;sup>1)</sup> RNC = Remuneration and Nomination Committee

## Fiscal year 2017

| Name/Function                 | RNC 1) | AC <sup>2)</sup> | Period I     | Fixed remu-<br>neration | Committee remuneration | Social insurance contributions and duties | Total   |
|-------------------------------|--------|------------------|--------------|-------------------------|------------------------|---|---------|
|                               |        |                  | 01.01.2017 - |                         |                        |   |         |
| Hunziker Erich, Chairman      |        | Χ                | 31.12.2017   | 360 000                 | 15 000                 | 27 903                                    | 402 903 |
|                               |        |                  | 01.01.2017-  |                         |                        |   |         |
| Meanwell Clive, Vice-Chairman | X      | Χ                | 31.12.2017   | 250 000                 | 25 000                 | _   | 275 000 |
|                               |        |                  | 01.01.2017 - |                         |                        |   |         |
| Strein Klaus, Member          | X      |                  | 31.12.2017   | 250 000                 | 10 000                 | 16 130                                    | 276 130 |

<sup>1)</sup> RNC = Remuneration and Nomination Committee

## 3. Remuneration of related parties at non-market conditions

In the reporting year 2018, no remuneration which was not at arm's length terms was paid to related parties (2017: none).

# 4. Remuneration of former members of the corporate bodies

In the reporting year 2018, no remuneration was paid to former members of the corporate bodies (2017: none).

<sup>2)</sup> AC = Audit Committee

<sup>2)</sup> AC = Audit Committee

### 5. Loans and credits to the members of the Board of Directors

The articles of incorporation of BB Biotech AG do not provide that loans and credits may be granted to the members of the Board of Directors. Accordingly, no loans or credits which BB Biotech AG has granted to current or former members of the Board of Directors or to related parties were outstanding as of December 31, 2018 (December 31, 2017: none).

## 6. Contractual terms at retirement from BB Biotech AG

No member of the Board of Directors has a contract with BB Biotech AG providing for a severance payment in the event of leaving BB Biotech AG

## 7. Management contracts

On behalf of the Company, the Board of Directors has entered into a management contract with Bellevue Asset Management Group (investment manager). In this contract, the investment manager commits to carry out management services relating to the investment activity of BB Biotech AG. The management contract is valid for an indefinite period and can be terminated by either party with a notice period of twelve months with effect as per the end of the following calendar year. The remuneration of the investment manager is determined by the respective contract and corresponds to a fixed fee of 1.1% p.a. on the average market capitalization without any additional fixed or performance-based elements.



Report of the statutory auditor to the General Meeting of BB Biotech AG Schaffhausen

# Report of the statutory auditor on the remuneration report

We have audited the remuneration report of BB Biotech AG for the year ended 31 December 2018. The audit was limited to the information according to articles 14–16 of the Ordinance against Excessive Compensation in Stock Exchange Listed Companies (Ordinance) contained in the tables labeled 'audited' on pages 81 to 82 of the remuneration report.

## Board of Directors' responsibility

The Board of Directors is responsible for the preparation and overall fair presentation of the remuneration report in accordance with Swiss law and the Ordinance against Excessive Compensation in Stock Exchange Listed Companies (Ordinance). The Board of Directors is also responsible for designing the remuneration system and defining individual remuneration packages.

### Auditor's responsibility

Our responsibility is to express an opinion on the remuneration report. We conducted our audit in accordance with Swiss Auditing Standards. Those standards require that we comply with ethical requirements and plan and perform the audit to obtain reasonable assurance about whether the remuneration report complies with Swiss law and articles 14–16 of the Ordinance.

An audit involves performing procedures to obtain audit evidence on the disclosures made in the remuneration report with regard to compensation, loans and credits in accordance with articles 14–16 of the Ordinance. The procedures selected depend on the auditor's judgment, including the assessment of the risks of material misstatements in the remuneration report, whether due to fraud or error. This audit also includes evaluating the reasonableness of the methods applied to value components of remuneration, as well as assessing the overall presentation of the remuneration report.

We believe that the audit evidence we have obtained is sufficient and appropriate to provide a basis for our opinion.

## Opinion

In our opinion, the remuneration report of BB Biotech AG for the year ended 31 December 2018 complies with Swiss law and articles 14–16 of the Ordinance.

PricewaterhouseCoopers AG

Daniel Pajer Stephanie Zaugg Audit expert Audit expert

Auditor in charge

Zurich, 14 February 2019

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### Company profile

BB Biotech AG acquires holdings in companies in the biotechnology growth market and is currently one of the world's largest investors in the sector. The focus of the holdings is on quoted companies that are concentrating on the development and marketing of innovative medicines. For the selection of holdings, BB Biotech AG relies on fundamental analysis by physicians and molecular biologists. The Board of Directors has many years of industrial and scientific experience.

## Official listing and share structure as at December 31, 2018

| Foundation:                           | November 9, 1993; Schaffhausen, Switzerland   |
|---------------------------------------|---|
| Issue price adj. November 15, 1993:   | CHF 4.752   |
| Official listing:                     | December 27, 1993, in Switzerland; December 10, 1997, in Germany;<br>October 19, 2000, in Italy |
| Share structure:                      | CHF 11.08 mn nominal, 55 400 000 registered shares with a par value of CHF 0.20 each            |
| Shareholders, free float:             | Institutional and private investors,<br>100.0% free float                                       |
| Security number Switzerland:          | 3 838 999   |
| Security number in Germany and Italy: | Aonfn <sub>3</sub>  |
| ISIN:                                 | CH0038389992  |

### Shareholder information

The Company publishes its net asset value daily via the major stock market information services and on its website www.bbbiotech.com. The portfolio composition is published at least every three months within quarterly reports.

# Quotes and reports

| Quotes and re | -ports |  |         |   |
|---------------|--------|--|---------|---|
| NAV:          | in CHF | – Datastream: S:BINA   | in EUR  | – Datastream: D:BBNA                          |
|               |        | – Reuters: BABB  |         | – Reuters: BABB                               |
|               |        | <ul><li>Telekurs: BIO resp. 85, BB1</li><li>(Investdata)</li></ul> |         |   |
|               |        | – Finanz & Wirtschaft (CH)   |         |   |
| Stock price:  | in CHF | <ul> <li>Bloomberg: BION SW Equity</li> </ul>                      | in EUR  | <ul> <li>Bloomberg: BBZA GY Equity</li> </ul> |
|               | (SIX)  | – Datastream: S:BIO  | (Xetra) | – Datastream: D:BBZ                           |
|               |        | – Reuters: BION.S  |         | – Reuters: BION.DE                            |
|               |        | – Telekurs: BIO  | in EUR  | – Bloomberg: BB IM Equity                     |
|               |        | <ul><li>Finanz &amp; Wirtschaft (CH)</li></ul>                     | (STAR)  | – Datastream: I:BBB                           |
|               |        | <ul> <li>Neue Zürcher Zeitung (CH)</li> </ul>                      |         | – Reuters: BB.MI                              |
|               |        |  |         |   |

# Corporate calendar 2019

| •                                       |                               |  |
|---|-------------------------------|--|
| Annual General Meeting 2019             | March 21, 2019, 3.00 PM CET   |  |
|   | Park Casino                   |  |
|   | Steigstrasse 26               |  |
|   | CH-8200 Schaffhausen          |  |
| Interim Report as at March 31, 2019     | April 26, 2019, 7.00 AM CET   |  |
| Interim Report as at June 30, 2019      | July 19, 2019, 7.00 AM CET    |  |
| Interim Report as at September 30, 2019 | October 18, 2019, 7.00 AM CET |  |

The BB Biotech annual report is published in English. A translated German and Italian version is also available. In case of any deviations the English shall prevail over the German and Italian text.

## **Investor Relations**



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