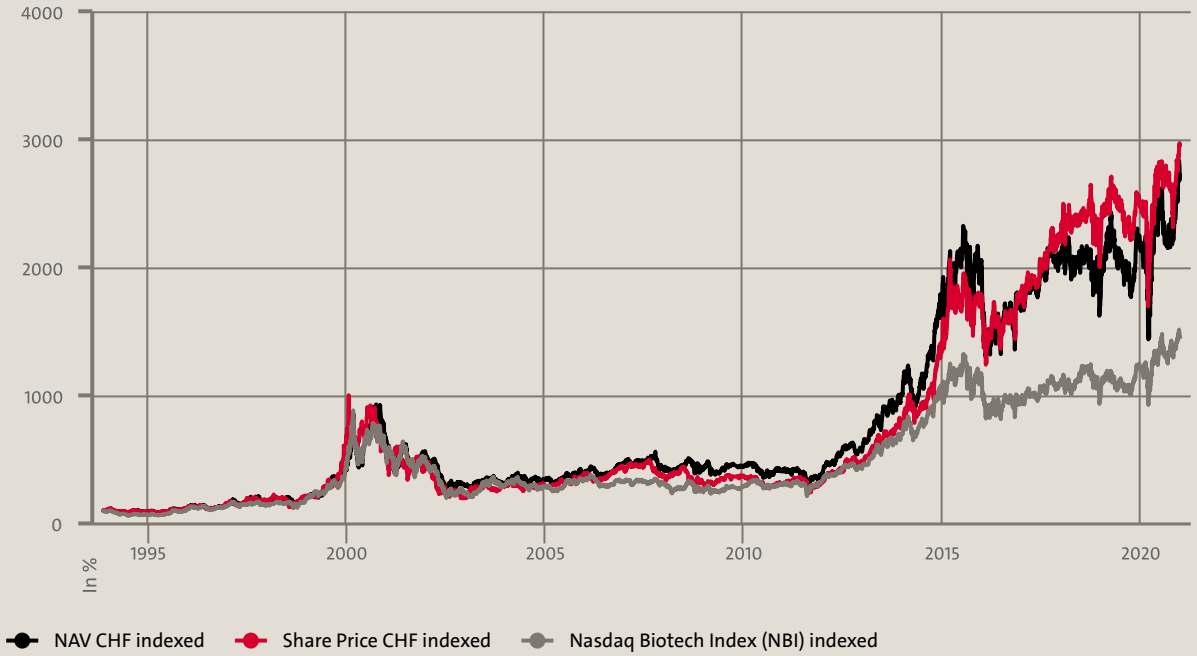
BUSINESS REPORT

PERFORMANCE / MULTI-YEAR COMPARISON

Indexed performance since launch (in CHF)

BB Biotech AG (SIX)-CHF



Annual performance

12/31/2020

	SHARE	NAV	NBI TR
2020	19.3%	24.3%	15.8%
2019	18.5%	23.4%	23.0%
2018	(5.2%)	(14.5%)	(8.0%)
2017	22.9%	23.4%	16.4%
2016	0.2%	(19.3%)	(19.8%)

Cumulated performance

12/31/2020

	SHARE	NAV	NBI TR
YTD	19.3%	24.3%	15.8%
1 year	19.3%	24.3%	15.8%
3 years	34.1%	31.1%	31.1%
5 years	65.1%	30.6%	22.1%
since inception [1)]	2 849%	2 585%	1 353%

[1] 11/09/1993

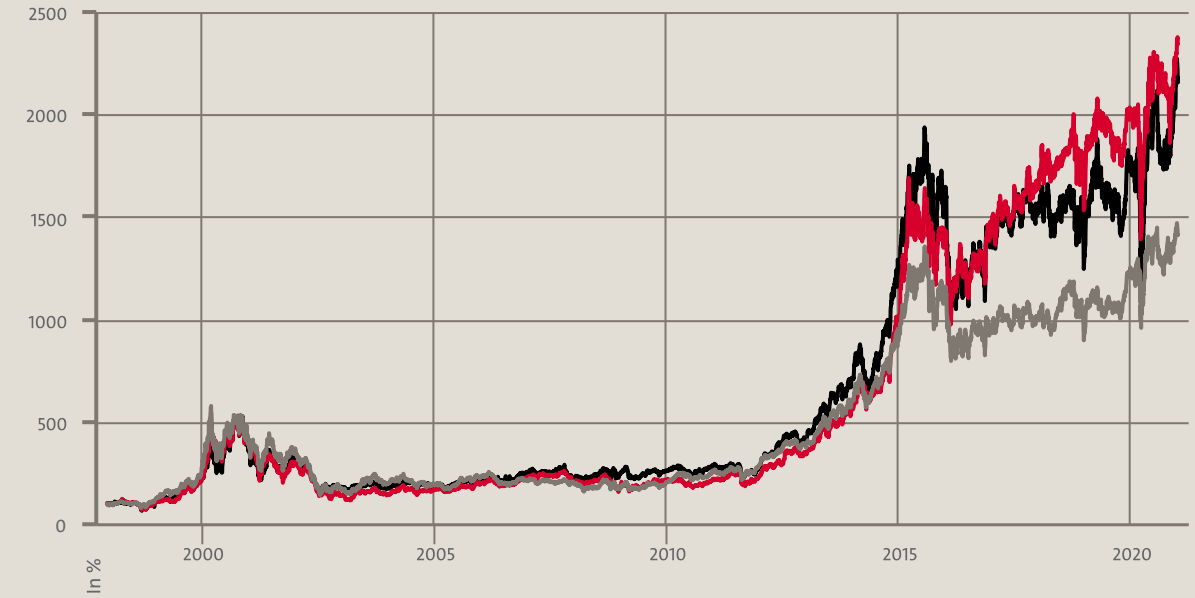
Annualized performance

12/31/2020

	SHARE	NAV	NBI TR
1 year	19.3%	24.3%	15.8%
3 years	10.3%	9.5%	9.4%
5 years	10.6%	5.5%	22.1%
since inception [1)]	13.3%	12.9%	10.4%

[1] 11/09/1993

BB BIOTECH AG (XETRA)-EUR



Annual performance

12/31/2020

	SHARE	NAV	NBI TR
2020	18.1%	24.8%	16.1%
2019	23.4%	28.1%	27.6%
2018	(2.2%)	(11.1%)	(4.3%)
2017	12.9%	12.5%	6.7%
2016	1.7%	(17.8%)	(19.0%)

Cumulated performance

12/31/2020

	SHARE	NAV	NBI TR
YTD	18.1%	24.8%	16.1%
1 year	18.1%	24.8%	16.1%
3 years	42.5%	42.0%	41.8%
5 years	63.7%	31.4%	22.6%
since inception [1)]	2 243%	2 057%	1 365%

[1] 12/10/1997

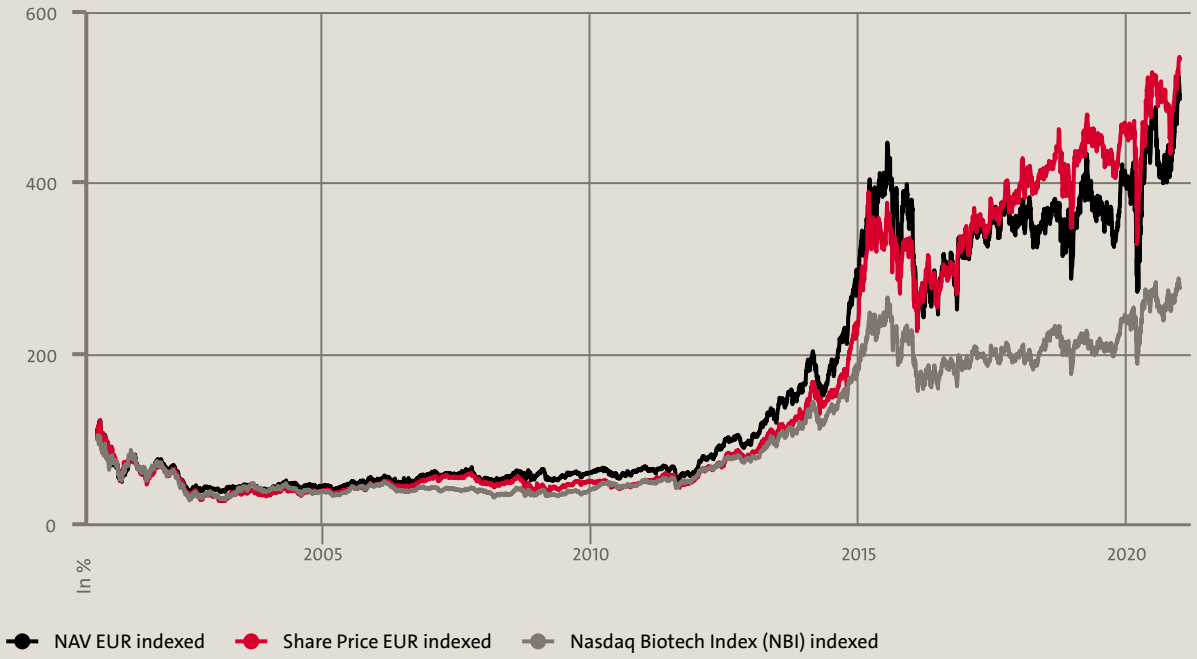
Annualized performance

12/31/2020

	SHARE	NAV	NBI TR
1 year	18.1%	24.8%	16.1%
3 years	12.5%	12.4%	12.3%
5 years	10.4%	5.6%	4.2%
since inception [1)]	14.6%	14.2%	12.4%

[1] 12/10/1997

BB BIOTECH AG (MILAN)-EUR



Annual performance

12/31/2020

	SHARE	NAV	NBI TR
2020	19.7%	24.8%	16.1%
2019	22.6%	28.1%	27.6%
2018	(1.3%)	(11.1%)	(4.3%)
2017	12.2%	12.5%	6.7%
2016	1.2%	(17.8%)	(19.0%)

Cumulated performance

12/31/2020

	SHARE	NAV	NBI TR
YTD	19.7%	24.8%	16.1%
1 year	19.7%	24.8%	16.1%
3 years	44.8%	42.0%	41.8%
5 years	64.4%	31.4%	22.6%
since inception [1)]	445%	398%	177%

[1] 10/19/2000

Annualized performance

12/31/2020

	SHARE	NAV	NBI TR
1 year	19.7%	24.8%	16.1%
3 years	13.1%	12.4%	12.3%
5 years	10.5%	5.6%	4.2%
since inception [1)]	8.8%	8.3%	5.2%

[1] 10/19/2000

Multi-year comparison

	2020	2019	2018	2017	2016
Market capitalization at the end of the period (in CHF mn)	4 107.9	3 670.3	3 235.4	3 576.1	3 052.5
Net Asset Value at the end of the period (in CHF mn)	3 887.5	3 393.0	2 884.5	3 538.7	3 003.0
Number of shares (in mn) [1]	55.4	55.4	55.4	55.4	55.4
Trading volume (in CHF mn)	2 315.6	2 004.2	2 610.7	2 864.7	3 204.5
Profit/(loss) (in CHF mn)	691.2	677.4	(471.3)	687.5	(802.1)
Closing price at the end of the period in CHF [1]	74.15	66.25	58.40	64.55	55.10
Closing price (G) at the end of the period in EUR [1]	68.00	61.40	52.00	55.68	51.70
Closing price (I) at the end of the period in EUR [1]	68.50	61.00	52.00	55.20	51.60
Stock performance (incl. distributions) [2]	19.3%	18.5%	(5.2%)	22.9%	0.2%
High/low share price in CHF [1]	74.70/45.44	73.20/59.35	74.10/56.10	67.80/52.10	58.20/40.78
High/low share price in EUR [1]	69.00/43.04	64.70/52.10	64.80/48.60	59.10/48.42	53.98/36.74
Premium/(discount) (annual average)	9.2%	11.8%	9.7%	(2.5%)	(5.1%)
Cash distribution / dividend in CHF (*proposal) [1]	3.60*	3.40	3.05	3.30	2.75
Degree of investment (quarterly figures)	106.8%	109.1%	108.4%	103.1%	109.9%
Total Expense Ratio (TER) p.a. [3]	1.25%	1.26%	1.25%	1.27%	1.30%

1 Five-for-one share split as at March 29, 2016 considered
2 All figures in CHF %, total return-methodology
3 Based on market capitalization

SHAREHOLDER LETTER

BB Biotech performed well in 2020 in a volatile market environment. The biotech sector made significant strides, leading the effort against the SARS-CoV-2 virus pandemic through approved mRNA vaccines and therapeutic antibodies. M&A activity picked up substantially in H2 2020, further driving solid performance as the year came to a close. The Board of Directors will propose an ordinary dividend of CHF 3.60 at the Annual General Meeting.

«BB Biotech performed well in 2020 in a volatile market environment»

Dr. Erich Hunziker
Chairman

Dear Shareholders

During the last quarter of the year major global equity indices extended their 2020 gains. Many markets achieved new all-time highs even though the SARS-CoV-2 infection rates reaccelerated in the final weeks of 2020. The Dow Jones (+9.7% in USD), the Dax (+3.5% in EUR), and the SPI (+3.8% in CHF) indices all showed gains for the year with the technology dominated Nasdaq Composite outperforming (+45.1% in USD) the broader equity markets. The Nasdaq Biotech Index (NBI) rallied into the year-end, resulting in a 2020 total return of 26.4% in USD and a significant outperformance of the broader markets.

Although the SARS-CoV-2 situation remained front and center for regulatory authorities in 2020, an impressive number of drug approvals was achieved by the US FDA – releasing 13 new drugs in the fourth quarter 2020, driving the total drug approvals to 53 for 2020. Additionally, two SARS-CoV-2 prophylactic vaccines and multiple drugs received emergency use authorization (EUA) during 2020.

For 2020, BB Biotech's total share return of 19.3% in CHF and 18.1% in EUR was slightly below the underlying portfolio performance. Weakening of the USD versus the CHF and EUR throughout the

year created additional headwind for CHF and Euro-denominated performance. The portfolio Net Asset Value (NAV) gained 24.3% in CHF, 24.8% in EUR and 35.9% in USD.

For the fourth quarter, BB Biotech's share price was up 10.9% in CHF and 9.0% in EUR. BB Biotech shares were unable to track the portfolio's upward trend. BB Biotech's Net Asset Value (NAV) for the same period tracked NBI index gains – increasing 20.6% in CHF, 20.4% in EUR and 25.5% in USD.

The consolidated fourth quarter 2020 data for BB Biotech indicates a net gain of CHF 665 mn versus 2019 fourth quarter net gain of CHF 505 mn. The consolidated full year 2020 data showed a net gain of CHF 691 mn compared to a net gain of CHF 677 mn for 2019.

Annual General Meeting on March 18, 2021

DIVIDEND 2021
CHF 3.60
(Proposed)

At the scheduled upcoming Annual General Meeting, all five existing board members will stand for re-election by the shareholders on March 18, 2021. The Board of Directors will propose a regular dividend of CHF 3.60 per share at the AGM on March 18, 2021. Applied to the average share price of December 2020 and consistent with the dividend policy introduced in 2013, this corresponds to a 5% dividend yield.

Portfolio adjustments in the fourth quarter 2020

In the fourth quarter, BB Biotech exited four holdings: Myokardia was acquired by Bristol-Myers Squibb at USD 225 per share, valuing the company at USD 13.1 bn. The position was tendered in November, generating approximately USD 248 mn in cash for the portfolio, and a profit of more than USD 205 mn for the investment cycle. The positions in G1 Therapeutics, Intercept and Sangamo were sold because the investment case for these stocks was no longer viable.

During the fourth quarter, profits were also taken on investments including Halozyme, Moderna, Myovant, Crispr Therapeutics and Scholar Rock. The cash was reinvested in targets associated with the strategic portfolio reallocation – focusing on smaller and mid cap portfolio companies. BB Biotech took advantage of market conditions by investing more in Molecular Templates, Arvinas, Generation Bio and Relay Therapeutics.

«Three new investments were made in the fourth quarter – Mersana, Biogen and Beam Therapeutics»

Three new investments were made in the fourth quarter – Mersana, Biogen and Beam Therapeutics. Mersana is a company which focuses on antibody drug conjugates, with the company's lead program, XMT-1536 in clinical development for ovarian cancer. The basis for a tactical investment in Biogen was provided by the FDA reviewing Division medical reviewer's highly positive stance toward Biogen's aducanumab for Alzheimer's disease despite reservations from the FDA statistical reviewers and the overwhelmingly negative vote of an FDA advisory panel. The final action of the Agency on aducanumab in the face of these conflicting viewpoints will be consequential for the entire biotech sector. A position in Beam Therapeutics was initiated to increase BB Biotech's portfolio exposure to the genetic medicine field. Beam Therapeutics utilizes base editing – a technology that allows for a specific corrective nucleotide change without cutting the genome. Beam's lead programs are being developed for hemoglobinopathies such as sickle cell disease and beta thalassemia as well as for liver diseases such as alpha-1 antitrypsin deficiency.

Fourth-quarter portfolio update

The fourth quarter 2020 provided multiple milestones for our portfolio holdings such as M&A activity, licensing deals, clinical news and regulatory action. Highlights in the fourth quarter were driven especially by licensing deals.

TO THE HIGHLIGHTS

Outlook for 2021 with exciting sector fundamentals and expected transaction momentum to continue – even in a new political US environment

BB Biotech believes that 2021 will include the successful first wave of the roll-out of SARS-CoV-2 vaccines, led by Moderna's mRNA-1273 and Pfizer/Biontech's bnt162b2. Further, subsequent approval of adenovirus-vector based vaccines and traditional recombinant protein subunit vaccines are expected. It also anticipates that the industry will continue to deliver significant technology progress and new products that address important unmet medical needs. The BB Biotech investment team's asset allocation will continue to focus on established areas – such as orphan diseases, oncology and neurological indications – and also on rapidly emerging technologies which promise the best therapeutic profile and economic value.

«BB Biotech also anticipates that the industry will continue to deliver significant technology progress and new products that address important unmet medical needs»

Set against exciting technological developments, the stance of the US government regarding healthcare access and healthcare costs will be of importance. The new administration of President Elect Biden includes HHS Secretary nominee Xavier Becerra, currently serving as attorney general of California. Mr. Becerra is well-known for his defense of the Affordable Care Act. The Administration will also include Jeffrey D. Zients, an entrepreneur and management consultant who served as the head of President Obama's National Economic Council, as coronavirus czar in the White House. The nominations for FDA and CMS leadership have not yet been made. In view of the tied Senate with a deciding vote from Vice President Elect Harris, and narrowly Democratic House, President Elect Biden may be pressed to push on with reform of drug pricing. But in a year in which their major focus is to get the SARS-CoV-2 pandemic under control, the emphasis is likely to be on improving access to care (including vaccines) and supporting those with inadequate insurance, rather than chopping cancer or rare disease drug prices. BB Biotech believes the new Administration and Congress are aware of the astonishing value, health improvements and hope being created by the biotechnology sector.

With some areas in the biotech sector such as genetic medicines currently attracting significant investor attention, which drove valuations impressively in 2H 2020, BB Biotech continues to see attractive valuations for select smaller and mid cap biotech firms. Further, M&A activity picked up in the second half of 2020 and will likely continue in the sector in 2021. The takeover of Alexion by AstraZeneca for USD 39 bn demonstrates that larger cap firms may also be at play at these

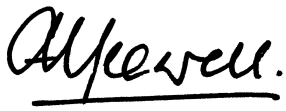
valuation levels. Remote deal making has become a normal approach so social distancing and lockdowns are unlikely to limit strategic activities in the biotech sectors.

BB Biotech's long-term horizon makes it an effective investor and partner for many biotechnology firms – and the investment team believes that the growth case for biotechnology and the company itself is as compelling as ever. This means management is confident it can continue to offer potentially sector-leading returns moving forward. The investment team anticipates that 2021 will be another banner year for new products worldwide and looks forward to more exciting news flow from its portfolio companies.

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

The Board of Directors of BB Biotech AG

Dr. Erich Hunziker
Chairman



Dr. Clive Meanwell

Dr. Susan Galbraith

Prof. Dr. Mads Krogsgaard Thomsen

Dr. Thomas von Planta

PORTFOLIO UPDATE Q4 2020

The fourth quarter 2020 provided multiple major milestones for our portfolio holdings such as clinical results, regulatory decisions, licensing deals and M&A transactions. The highlight in the fourth quarter was the high efficacy and good safety profile of mRNA-1273, Moderna's prophylactic mRNA vaccine against SARS-CoV-2, leading to an emergency use authorization (EUA) by FDA in late December. Moderna has announced to deliver around 20 mn doses in December alone and in the meantime has increased its delivery capacity by upping the lower capacity range from 500 mn to 600 mn, with a continued 1 bn as peak capacity for 2021.

Promising clinical trial results

Next to the positive vaccine update, many clinical trial read-outs reported by our portfolio holdings were convincing and positive. Agios reported that 40% of patients with pyruvate kinase deficiency who are not regularly transfused achieved a sustained hemoglobin increase of more/equal 1.5 g/dl compared to 0 placebo patients. In January 2021, the company reported a second positive study in patients with pyruvate kinase deficiency being transfusion-dependent. These two studies are the basis for a regulatory filing in the first half of 2021.

Incyte reported top line results for Ruxolitinib (Jakafi) with significant improved outcomes in patients with steroid-refractory or steroid-dependent chronic graft-versus-host disease. These results complement previously reported results in steroid-refractory acute graft-versus-host disease, added to the Jakafi label in 2019. Subsequently, Incyte has raised its 2027 Jakafi US revenue guidance to above USD 3 bn.

Promising proof-of concept data was reported by Scholar Rock, Arvinas and Crispr Therapeutics, with Vertex reporting disappointing news regarding its first oral development candidate VX-814 targeting patients with alpha-1 antitrypsin deficiency. Scholar Rock announced positive interim analysis for the Phase II trial testing SRK-15, a selective inhibitor of the activation of myostatin, in patients with spinal muscle atrophy. Motor function improvement were observed at the 6-month interim analysis, with data for the 12-month treatment expected in the second quarter of 2021. Arvinas announced a robust efficacy signal for ARV-471 in heavily pretreated breast cancer patients. ARV-471 is an investigational orally bioavailable PROTAC protein degrader designed to selectively target and degrade the estrogen receptor (ER). Responses in heavily pretreated breast cancer patients support Arvinas to initiate a Phase II dose expansion of ARV-471 in the first half of 2021.

Progress has been achieved and reported for our holdings developing genetic medicines. Crispr Therapeutics presented updated results for its investigational Crispr/Cas9 gene-editing therapy CTX001. The company together with its development partner Vertex disclosed now seven beta thalassemia patients treated and transfusion-independent with 3 to 18 months of follow-up after a single CTX-001 infusion. In sickle cell patients, all three patients were free of vaso-occlusive crisis with 3 to 15 months of follow-up after the CTX-001 infusion. The companies expect to enroll the last patients per end of 2021 and will continue the dialogue with regulatory authorities to set out the registration path.

Numerous milestones with regard of regulatory decisions

BB Biotech's portfolio holdings updated on multiple regulatory decisions in the fourth quarter 2020 such as

- Margenza (margetuximab) from Macrogenics was approved by the FDA for patients pretreated metastatic HER2-positive breast cancer
- Orgovyx (relugolix) from Myovant was approved by FDA for adult patients with advanced prostate cancer
- mRNA-1273 from Moderna received an emergency use authorization (EUA) as prophylactic vaccine for SARS-CoV-2.
- Oxlumo (lumasiran) from Alnylam was approved by the FDA and the EMA for primary hyperoxaluria type 1 patients
- Agios withdrew its EMA marketing authorization application of Tibsovo (ivosidenib) to treat acute myeloid leukemia patients with IDH1 mutations

Accelerating M&A activities and beneficial collaboration in the second half of 2020

With M&A as well as business development activities slowing down in the first half of 2020, a clear re-acceleration was observed for the second half of the year. In the fourth quarter alone, four of BB Biotech's portfolio holdings reported substantial transactions. The Myokardia takeover by Bristol Myers Squibb was completed in November in an all-cash transaction for approximately USD 13.1 bn. In late November, Sage and Biogen announced a global collaboration to develop and commercialize Zuranolone, a next-generation positive allosteric modulator of the gamma-aminobutyric acid (GABAA) receptor that is developed as an antidepressant. The deal includes as well SAGE-324, a next-generation positive allosteric modulator of GABAA receptors in Phase II development for essential tremor. A large takeover was announced in December, with AstraZeneca acquiring Alexion, with a total consideration of USD 60 per share in cash plus 2.1243 shares (AZN US), in total USD 39 bn or USD 175 per share. The companies recently updated the timelines for the deal expected to close in the third quarter of 2021. In late December, Servier agreed to acquire Agios oncology business for up to USD 2 bn plus future royalties. Agios announced to use around two thirds of these proceeds to repurchase shares and around one third to invest into its remaining genetically defined disease franchise.

PORTFOLIO AT A GLANCE

Securities as at December 31, 2020

Company	Number of securities	Change since 31.12.2019	Local currency	Share price	Market value in CHF mn	In % of securities	In % of shareholders' equity	In % of company
Ionis Pharmaceuticals	8 220 000	225 045	USD	56.54	411.4	10.4%	10.6%	5.9%
Moderna	2 854 963	(1 962 818)	USD	104.47	264.0	6.7%	6.8%	0.7%
Neurocrine Biosciences	3 035 000	(193 074)	USD	95.85	257.5	6.5%	6.6%	3.2%
Argenx SE	921 332	(23 407)	USD	294.09	239.8	6.1%	6.2%	1.9%
Incyte	2 900 000	(500 000)	USD	86.98	223.3	5.6%	5.7%	1.3%
Vertex Pharmaceuticals	900 000	(340 000)	USD	236.34	188.3	4.8%	4.8%	0.3%
Alexion Pharmaceuticals	1 294 428	(20 000)	USD	156.24	179.0	4.5%	4.6%	0.6%
Arvinas	2 176 903	935 000	USD	84.93	163.7	4.1%	4.2%	4.6%
Fate Therapeutics	2 030 000	2 030 000	USD	90.93	163.4	4.1%	4.2%	2.3%
Agios Pharmaceuticals	4 158 902	261 948	USD	43.33	159.5	4.0%	4.1%	6.0%
Halozyme Therapeutics	3 970 000	(3 993 056)	USD	42.71	150.1	3.8%	3.9%	3.0%
Alnylam Pharmaceuticals	1 155 000	(445 000)	USD	129.97	132.9	3.4%	3.4%	1.0%
Crispr Therapeutics	900 884	170 422	USD	153.11	122.1	3.1%	3.1%	1.2%
Sage Therapeutics	1 540 104	260 000	USD	86.51	117.9	3.0%	3.0%	3.0%
Radius Health	7 455 714	574 029	USD	17.86	117.9	3.0%	3.0%	16.0%
Biogen	537 000	537 000	USD	244.86	116.4	2.9%	3.0%	0.3%
Myovant Sciences	4 757 039	(58 070)	USD	27.62	116.3	2.9%	3.0%	5.3%
Intra-Cellular Therapies	3 538 419	1 238 419	USD	31.80	99.6	2.5%	2.6%	4.4%
Macrogenics	4 815 564	296 405	USD	22.86	97.4	2.5%	2.5%	8.4%
Scholar Rock Holding	2 255 651	(378 815)	USD	48.53	96.9	2.5%	2.5%	6.7%
Esperion Therapeutics	3 947 964	220 000	USD	26.00	90.9	2.3%	2.3%	14.2%
Generation Bio Co.	2 333 180	2 333 180	USD	28.35	58.6	1.5%	1.5%	5.0%
Molecular Templates	6 380 331	5 084 644	USD	9.39	53.0	1.3%	1.4%	12.8%
Relay Therapeutics	1 409 357	1 409 357	USD	41.56	51.8	1.3%	1.3%	1.6%
Exelixis	2 835 000	–	USD	20.07	50.4	1.3%	1.3%	0.9%
Mersana Therapeutics	1 885 000	1 885 000	USD	26.61	44.4	1.1%	1.1%	2.8%
Nektar Therapeutics	2 620 676	–	USD	17.00	39.4	1.0%	1.0%	1.5%
Black Diamond Therapeutics	1 390 000	1 390 000	USD	32.05	39.4	1.0%	1.0%	3.9%
Beam Therapeutics	396 821	396 821	USD	81.64	28.7	0.7%	0.7%	0.7%
Kezar Life Sciences	4 533 148	2 982 479	USD	5.22	20.9	0.5%	0.5%	9.8%
Wave Life Sciences	2 602 858	200 000	USD	7.87	18.1	0.5%	0.5%	5.3%
Homology Medicines	1 737 122	125 000	USD	11.29	17.4	0.4%	0.4%	3.8%
Voyager Therapeutics	2 680 283	–	USD	7.15	17.0	0.4%	0.4%	7.2%
Cidara Therapeutics	2 822 495	527 223	USD	2.00	5.0	0.1%	0.1%	6.4%

Alder Biopharmaceuticals – Contingent Value Right	2 766 008	–	USD	0.88	2.2	0.1%	0.1%	
Bristol-Myers Squibb – Contingent Value Right	800 000	–	USD	0.00	0.0	0.0%	0.0%	
Total securities					**3 954.7**	**100.0%**	**101.7%**	
Other assets					8.4		0.2%	
Other payables					(75.6)		(1.9%)	
Net asset value					**3 887.5**		**100.0%**	
BB Biotech registered shares [1)]	114 662	114 662			8.5			0.2%

[1] Correspond to the total of all own shares held including the second trading line

Exchange rate as at 31.12.2020: USD/CHF: 0.8852

OUTLOOK

The global corona pandemic continues to keep the world on tenterhooks. With the first approved vaccines, such as the mRNA vaccines, the biotech industry has emerged as a player. The challenge now is to overcome manufacturing capacity and logistical challenges to ensure widespread introduction of the vaccines. Only then it will be possible to boost population immunity to SARS-CoV-2 and its variants. In addition, new technologies, such as gene editing, are likely to come into focus in 2021. Thanks to increased technological advances and growing capital flows, the biotech sector's momentum will continue to accelerate. In terms of policy, the newly elected US government's main goal is to enable more citizens to access the healthcare system. A well-organized healthcare ecosystem makes innovation affordable for patients in need. BB Biotech assumes that the existing price structure can be maintained.

The COVID-19 pandemic continues to challenge global healthcare infrastructures as well as societies and economies. Under intense pressure and with a substantial upside opportunity, the drug development industry moved quickly to identify technologies and compounds with potential to be used prophylactic or therapeutic against the virus. Unprecedented efforts and collaboration in 2020 between scientists, the drug development industry and regulatory authorities has led to the development of multiple effective and safe prophylactic vaccines. Following approvals with the mRNA vaccines in the lead, the focus now has turned towards manufacturing capacities and logistical challenges to allow broad vaccine roll-out and adoption leading to an increase in population immunity. The national differences in investing and gaining access to vaccine capacity has so far led to highly dispersed vaccination rates in different countries, allowing the virus to spread in unprotected areas of the world, and more worrisome the surfacing and spread of novel virus strains. To win this race, an effective global vaccination strategy is required, additional novel prophylactic vaccines to help increase capacity and continued efforts to convince the population to participate. The new strains such as the UK, the Brazilian or the South African strain already prove that not all the vaccines can maintain their high protection levels to all variants in circulation. The leading vaccine players such as Moderna have already outlined their plans to adapt the vaccine's make-up to specifically improve the protection levels for these resistance strains, being it through a booster strategy such as a third injection or by developing novel versions of the vaccine as a booster that encode for the respective variant. The challenge to quickly adapt to a changing situation proves that the messenger RNA technology and platform is ideally suited to respond faster than historic vaccine technologies and platforms.

«Unprecedented efforts and collaboration in 2020 between scientists, the drug development industry and regulatory authorities has led to the development of multiple effective and safe prophylactic vaccines»

LEARN MORE ABOUT MODERNA IN OUR TOP STORY

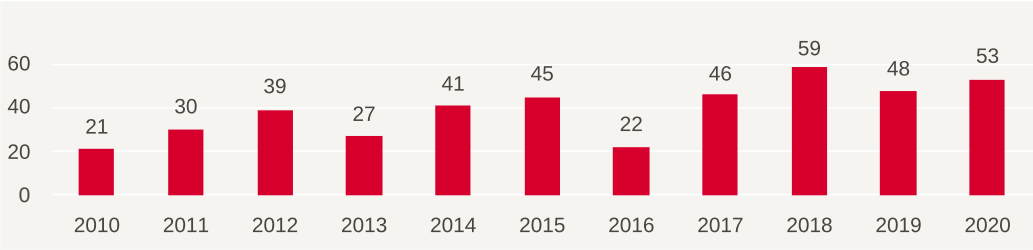
Moderna

The leading vaccine players such as Moderna have already outlined their plans to adapt the vaccine's make-up to specifically improve the protection levels for these resistance strains, being it through a booster strategy such as a third injection or by developing novel versions of the vaccine as a booster that encode for the respective variant. The challenge to quickly adapt to a changing situation proves that the messenger RNA technology and platform is ideally suited to respond faster than historic vaccine technologies and platforms.

The key questions that we are currently engaged with are 1) whether the dynamic between natural immunity, vaccine-induced immunity and viral resistance will necessitate a continuous update of vaccine valency similar to what is common procedure in the seasonal flu protocols and 2) if so how often a boost will be required, 3) in which subpopulations and 4) over what timeframe. The scenario of seasonal influenza with its characteristic traversal between northern and southern hemispheres may be the only but in fact poor proxy as a long-term model if one considers the relatively low average vaccine efficacy (30-50% in most years) and the substantially higher mutation rate in comparison to SARS-CoV-2 owing to the former's lack of genetic repair mechanisms.

We are surprised by the emergence of a strain partially resistant to vaccines at such an early timepoint, though it likely is a mutational pressure reaction to the broader natural immunity acquired by some populations such as in South Africa. It seems very difficult to assess the variety of possible conformational spaces the spike protein could occupy through mutational variation, avoiding prior antibodies induced through natural infection or vaccination while retaining the ability to efficiently bind to the human ACE2 receptor.

Number of FDA drug approvals



Source: Bellevue Asset Management, December 2020

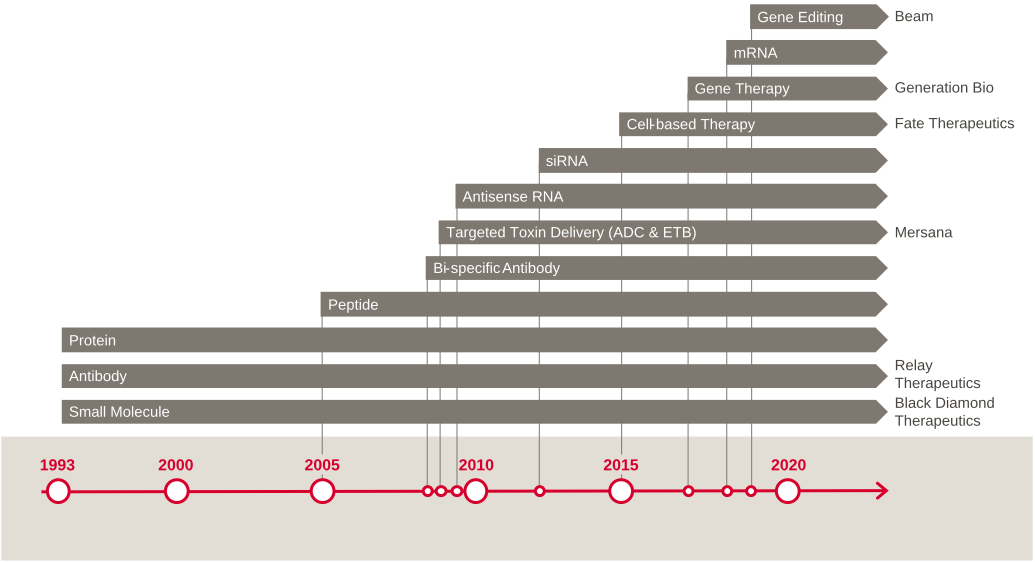
Overall, the pandemic situation continues to be a substantial strain on the healthcare system, with many areas of healthcare continued being underserved and financially constrained. The consequences of that will become more evident in the coming years such as the implications due to late diagnosis and a lack of initiation of important medical therapies. During the pandemic FDA and other regulatory bodies around the world have worked quite efficiently and we saw more than 50 new drug approvals in the US in 2020. We are expecting to see a significant number of approvals in 2021 with several of those coming from BB Biotech´s portfolio companies. For regulators and the drug development industry the learning curve has been steep during the pandemic and we hope that some of these learnings can be leveraged to in the future.

New technologies are expected to prove their disruptive potential

Progress for the newest drug modalities will be a focal point for biotech investors in 2021 and beyond. With important and highly promising results presented in 2020, further proof for technologies such as gene editing, next generation gene therapy and cell therapy technologies are expected. Exemplary of such success is the gene editing treatment CTX001 by Crispr Therapeutics and Vertex to treat sickle cell and beta thalassemia patients. A one-time treatment, still a rather invasive procedure requiring transplantation so far has resulted in de facto functional cures in all treated patients. Increasing knowledge driving efficacy and maintaining a clean long term safety

data will allow that the gene editing companies to move from rare and severe diseases towards broader and large chronic diseases. To achieve this, further technological advancements are required to improve ease of use and administration routes, lower manufacturing costs and growing safety database.

BB Biotech's investments in new technologies



Source: Bellevue Asset Management, December 2020

A similar trajectory, substantially further than the gene editing technology can be observed for the RNA-based and RNA-targeting drug modalities. With first drugs approved years ago, the improved next generation chemistry and improved delivery options allow to go through these expansion steps, following what has been achieved with recombinant proteins and antibody therapeutics in the last two decades.

Development speed – adaption of our S-curved investment strategy

Deeper understanding of the genotypic and phenotypic differences between cells in normal and diseased states, substantially improved computational approaches in drug screening, identification and selection all the way to smarter and adaptive clinical trial programs are contributing to an acceleration of the innovation cycle. The most obvious examples can be found in genetically defined rare diseases and targeted oncology with development timelines from the lab to the patient in record time, often achieved in two to three years. The acceleration of the development cycle is appealing for investors, allowing smaller companies to raise and deploy capital efficiently and in many cases aspire to develop and commercialize first in class or best in class therapies all on their own. This again results in improved return on invested capital for investors to attract capital and re-invest into the next generation of companies.

BB Biotech Investment Strategy

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

LEARN MORE ABOUT THE STRATEGY

Important milestones will support the positive industry momentum

The momentum of the biotech industry will remain strong, even accelerate due to the increased technological advancements, growing capital flow supporting innovation from the venture investors to public investors, all the way through an increasing number of clinical development projects leading up to a growing number of product approvals. Product approvals have grown from the 20's per year in the early 2000s, increasing to 30-40 products approved per year in the last decade to 50-ish in recent years. Even though the pandemic impacted the industry and regulatory authorities, 53 approvals were awarded in 2020, excluding emergency use authorizations such as those for SARS-CoV-2 vaccines. 2021 shall be no exception to this trend, with regulatory authorities continuing their COVID response but supporting innovative technology progress and clinical projects and by reviewing important registration filings. A substantial investor focus will be on the regulatory decisions for aducanumab for the treatment of Alzheimer disease that could set precedents and shape future interactions between the drug development industry and regulatory authorities.

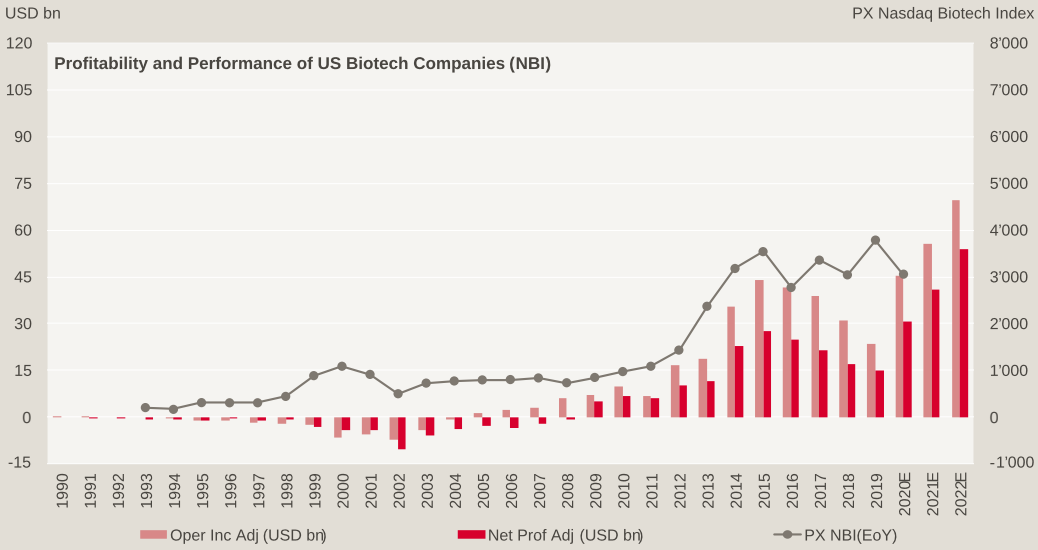
We expect important progress for many clinical development projects such as targeting oncogenes and oncogenic mutations and a host of immune oncology programs is inching towards major readouts that will impact future enthusiasm and investment behavior from both industry and investors in this area. For central nervous system disorders, substantial progress is ongoing for many of the genetically driven diseases such as Huntington disease (HD) or amyotrophic lateral sclerosis (ALS). In cardiovascular disease, novel lipid and triglyceride lowering agents are advancing in late-stage clinical trials and in cardiovascular outcomes trials. Another important area that is experiencing renewed investments is in the regenerative medicine field driven by an increasing tool box to modify cells accordingly, such as with the Crispr/Cas9 gene editing approach.

Politics and healthcare reform – US administration expanding access to the healthcare system

The newly elected US administration has outlined its healthcare plans, with core priorities being to maintain and even broaden access to healthcare insurances. This includes a push for the individual mandate, to limit the costs of such healthcare insurance all the way to lowering prescription drug prices by changing laws currently banning Medicare from negotiating lower drug prices with manufacturers. A clear positive for the science driven and innovative biotechnology industry is the role of a newly appointed presidential science advisor Eric Lander, a decorated geneticist who was a key figure in the Human Genome Project – the race to sequence the human genome.

A well-managed healthcare ecosystem will make innovation affordable for patients in need. Access to the newest and often more expensive treatment options require an insurance model. We expect that orphan drugs and targeted oncology drugs will maintain their price premium and that the general model for high volume drugs at lower price points allows to maintain this price model. In this context and with the global pandemic leading historical record levels of volume and demand for the prophylactic vaccines, we agree with industry that the price range from USD single digit to high 30's offer tremendous value for societies.

30 years biotechnology – shift to a sustainable growth industry



Source: Bellevue Asset Management; Bernstein Research, March 2020

VIDEO INTERVIEW

Dr. Daniel Koller, Head Investment Team, is looking back on the challenging pandemic year 2020 in a video interview. First he discusses the groundbreaking success of the biotech industry. It has developed successful and safe vaccines in record time and is leading the fight against the SARS-CoV-2 virus pandemic with these vaccines and therapeutic antibodies. It is therefore not surprising that the biotech sector has become the focus of investors. In addition, he explains why BB Biotech had already had invested in Moderna in 2018 and what opportunity he sees for the mRNA technology in the future. Finally he gives an insight into the portfolio and tells why he has added an «evergreen company», namely Biogen, in the portfolio.

«We had already invested in Moderna in 2018, when people didn't know about Corona yet»

Dr. Daniel Koller
Head Investment Team BB Biotech

MRNA TECHNOLOGY

The global coronavirus pandemic put the biotech sector squarely in the focus of the investment community. Having produced the very first vaccines for coronavirus disease, the biotechnology sector has emerged as a key player in the race to overcome the grave medical and economic challenges the world now faces. Moderna, the US company that has developed an mRNA-based COVID-19 vaccine, is the latest shining example of the progress biotech companies are making for the good of society.

Less than 11 months after the SARS-CoV-2 genome was decoded the first two vaccine candidates that could help to bring the global coronavirus pandemic under control were already submitted to regulatory authorities for approval. «The mRNA technology used by Moderna is a good example of how innovative technologies developed and applied in the labs of biotech companies are driving medical progress,» explains Dr. Daniel Koller, Head of BB Biotech's Investment Team.

«mRNA technology is representative of the innovative power of the entire biotech industry»

MRNA technology – preferred method for future vaccine development

«Our vision is to develop a new generation of medicines,» explained Stéphane Bancel, CEO of Moderna, in his presentation for an online investor conference organized by BB Biotech in December 2020. Full regulatory approval of Moderna's mRNA-1273 vaccine against COVID-19 will clear the way for other applications with mRNA vaccines. In clinical trials, Moderna's vaccine was 94.1% effective across all age groups. This vaccine was first authorized by the FDA for emergency use in the US and has since been granted emergency use authorizations by many other regulatory agencies, including the EU and Swiss regulators.

The COVID-19 vaccine is being manufactured by the Swiss company Lonza, among others. One billion doses could be produced in 2021.

«Our vision is to develop a new generation of medicines»

Stéphane Bancel
CEO Moderna

Given all the advantages mRNA offers, Bancel is sure it will establish itself as the technology of choice for vaccine development. The higher probability of response will be a crucial factor here, Bancel believes. Because human mRNA has the same chemical structure in all molecules, and mRNA-based drugs differ only in the coded genetic information they contain, mRNA platforms can be used to develop a variety of drugs in shorter periods of time. In the case of the SARS-CoV-2 virus, Moderna took just a few days to select the sequence for the vaccine from the virus's gene sequence. The huge advantage of this technology is that it is quickly adaptable to new variants of a virus. Another bonus of the mRNA mechanism is that all vaccines are packaged in the same molecular envelopes, which makes it easier to produce large volumes. Moreover, unlike the rival BioNTech/Pfizer product, the vaccine can be stored for a period of up to six months at minus 20 degrees Celsius, 30 days at refrigerator temperatures of six to eight degrees, and six hours at room temperature.

«BB Biotech invested in Moderna in 2018, before the company even went public»

Dr. Daniel Koller
Head Investment Team BB Biotech

Through its investment in robotics, IT and production processes, Moderna has, in the words of Bancel, created the conditions for scaling up all clinical products that the biotech company brings to the market in the future. Management had initially planned to reach this milestone in 2023 but that time frame was shortened by three years thanks to the successful development and the government funding of its COVID-19 vaccine program.

Moderna has 24 development candidates, 13 of which are currently in clinical testing, and six of them are vaccines, including the SARS-CoV-2 vaccine that was granted emergency use authorization in January 2021. BB Biotech invested in Moderna in 2018, before the company even went public.

PORTFOLIO WEIGHTING IN %

6.7%

As at 12/31/2020

mRNA

This novel approach allows the manufacture of proteins that patients are unable to make themselves because of genetic defects in their genome. mRNA therapies introduce a messenger RNA from outside to make specific proteins. Moderna has the broadest R&D pipeline in the field of mRNA. Its most advanced product is the COVID-19 vaccine that was just recently approved by regulatory authorities. Other Moderna clinical candidates are undergoing trials as mRNA therapeutics in immuno-oncology and as vaccines for cancers and viral diseases like Zika virus infection.

TO MODERNA

RELAY THERAPEUTICS & CRISPR THERAPEUTICS

Spotlight on two promising companies

BB Biotech anticipates that 2021 will bring significant technology progress and new products that address important unmet medical needs. In addition to established treatment areas such as oncology, orphan diseases and neurological indications, attention will increasingly center on rapidly developing promising technologies that offer tremendous economic value thanks to their excellent therapeutic profile. Bearing that in mind, we cast a spotlight on two companies that investors should be following.

Relay Therapeutics: On-screen molecular design

An innovative treatment approach emerging from biotech laboratories is called molecular design. Relay Therapeutics, which was floated on the stock exchange in July 2020, is a leader in rational drug design. The process involves studying the movement of protein molecules to understand the role of protein motion in causing disease. Relay uses a computational platform instead of conventional three-dimensional crystal structures. Machine learning is used for digital simulation and visualization of chemical and biophysical processes that occur on a timescale of milliseconds. This is a faster and cheaper way to identify molecules with potential to be developed as drugs. What's more, molecule design allows more customized mechanisms of action because properties like pharmacodynamics, effective dose, bioavailability and toxicity can all be tweaked much more precisely.

«Relay Therapeutics will present topline data for two products in 2021»

Relay Therapeutics is using this technology to develop oral medications to treat cancer. The most advanced candidate, RLY-1971, is an SHP2 inhibitor mainly being tested for use in combination with other drugs. RLY-1971 is currently in the Phase I clinical trial stage. Relay will present topline data for two products in 2021.

BB Biotech added Relay Therapeutics to its portfolio in the third quarter of 2020 by participating in its successful IPO and bought more of the company's shares on the open market immediately after they were listed.

Crispr Therapeutics: Crispr fixes genetic defects for good

The awarding of the Nobel Prize in Chemistry to Emmanuelle Charpentier and Jennifer A. Doudna in October 2020 underlines the importance of genome editing as a disruptive technology for future drug development. This molecular biological tool is used to make targeted changes in the human genome to cure diseases permanently. Genome editing is already being used with success in cell-based cancer therapies. In contrast, Crispr Therapeutics is a leading exponent of ex-vivo applications of the Crispr/Cas9 approach. This involves taking cells from a patient, modifying them in a lab and

re-administering them to the patient. The novelty of the approach is that fragments of human DNA identified as genetic triggers of disease are cut out and repaired using genetic replacement parts. The Crispr/Cas9 enzyme activates the genetic repair mechanism which every somatic cell possesses.

«The genetically modified stem cells that were administered back to the patients led to a complete cure»

BB Biotech has been invested in Crispr Therapeutics since the first quarter of 2019. The company is pursuing two clinical trials in beta thalassemia and sickle cell anemia in cooperation with Vertex Pharma, a core position in BB Biotech's portfolio. Both diseases are inherited genetic disorders that result in the defective formation of blood cells with severe progression. The genetically modified stem cells that were administered back to the patients led to a complete cure. In addition to these two clinical trials, Crispr Therapeutics is pursuing three cell-based projects in immuno-oncology on its own.

COVID-19 VACCINES AS A WAY OUT OF THE CRISIS

Prof. Dr. med. Daniel Paris, Director, Department of Medicine at the Swiss Tropical and Public Health Institute, University of Basel, held a talk about the COVID-19 pandemic, including his views regarding the potential implications of the new virus variants first identified in the United Kingdom, South Africa and Brazil and what measures should be taken, during a webinar hosted by BB Biotech in early February. Below is a summary of his remarks:

What we have observed so far is that the mutations are mostly concentrated in spike proteins on the surface of the SARS-CoV-2 virus, which is significant because these spike proteins are also the main target of the currently approved vaccines. Such mutations can make it easier for the SARS-CoV-2 virus to evade the body's immune response because antibodies (especially neutralizing antibodies) can longer bind as easily to the virus and then eliminate it. Such escape mutations could weaken the immune response and allow the coronavirus to spread more easily. Higher viral loads are often associated with increased transmissibility. The first Phase III vaccine studies based on data/samples taken from regions with a higher incidence of viral variants have already revealed a decrease in the vaccines' rate of effectiveness. Consequently, the concept of herd immunity via vaccine-induced immune responses will have to be reconsidered. To neutralize a higher infectivity and achieve natural herd immunity, a higher immunity threshold might be necessary. Up to now this threshold has been calculated to range between 60% and 65% of the population. Future vaccination strategies against COVID-19 could display a cyclical or seasonal pattern, as already is the case regarding the seasonal flu. This would mean redesigning a vaccine to match the currently circulating strains of the virus.

«Future vaccination strategies against COVID-19 could display a cyclical or seasonal pattern, as already is the case regarding the seasonal flu»

Diagnostic testing plays a critical role in the rapid identification of emerging hot spots of coronavirus infection. In the context of COVID-19, three main types of tests are being used: molecular PCR tests, antigen tests and antibody tests. The currently employed PCR and antigen test samples, however, must be processed in a lab. Antibody tests require a blood sample. The market potential for easy-to-use diagnostic test kits for self-testing at home, or in senior care facilities, schools or at large events, or when traveling, for example, is far from tapped. The DAVINCI consortium in Switzerland was formed by academic institutions and private-sector partners to develop a complete at-home test for COVID-19. Saliva samples are tested for antigens and antibodies and the results are processed by a simple smartphone app. After a successful proof-of-concept study in 2020, development of the test kit is expected to be completed by the end of 2021. The test kit could also be used as a testing platform for other infectious diseases such as influenza.

«Another advantage of the mRNA vaccines is that they can be quickly redesigned to match new seasonal variants and they have minor side effects»

The development of prophylactic vaccines for COVID-19 over the past twelve months was quite impressive. In early February there were 63 clinical vaccine trials underway, including 22 pivotal Phase III studies. Ten vaccines have already been granted marketing authorization. Three basic technologies are being used to develop these vaccines. Viral vector vaccines, using modified viral vectors as a delivery system, can trigger a strong immune response. The single-shot vaccines developed by AstraZeneca and Janssen have efficacy percentages of 70% and 66%, respectively, but they are much less effective against the emerging virus variants. The two mRNA vaccines developed by Moderna and Biontech/Pfizer that were the very first vaccines to be approved by regulators demonstrated very high efficacy of 94% and 95%, respectively. Another advantage of the mRNA vaccines is that they can be quickly redesigned to match new seasonal variants and they have minor side effects. A disadvantage is that they must be stored at very cold temperatures of minus 20° to minus 70° C. The authorized protein-based vaccines consisting of proteins and adjuvants have proven to be effective against influenza and human papilloma viruses and also demonstrated a high efficacy against COVID-19, but they are likewise not as effective against the recently identified coronavirus variants.

Data available so far does not yet allow for a conclusive analysis of the durability of the immune responses induced by vaccines. A comparison of data from placebo and treatment groups after the first injection of an mRNA vaccine has indicated that with this type of vaccine there might be a latency period of up to twelve weeks for the second dose. Effective, durable immunity to COVID-19 will largely depend on how quickly vaccines can be redesigned to match mutated protein spikes on the surface of the coronavirus. Inhalers and nasal sprays are likely to figure prominently as a means of making the administration of the vaccine more patient-friendly.