

Market commentary, December 9, 2021

## Cancer medicine improves the chances of a cure

**Oncology is the therapeutic area with the greatest weighting in BB Biotech's portfolio and it could deliver the most significant commercial breakthroughs in the not all-too-distant future, alongside its investments in the field of mRNA technology.**

Oncology is the therapeutic area with the greatest weighting by far in BB Biotech's investment portfolio, followed by rare hereditary diseases and central nervous system disorders. Some of the companies in the portfolio have recently made remarkable clinical progress on cancer therapies. With the attention of the general public and investors focusing on breakthroughs in COVID-19 vaccines and treatments this year, these successes have gone largely unnoticed except by industry experts.

The highlights include immunotherapies to treat blood cancers such as acute and chronic leukemia, lymphatic system cancers, and diffuse large B-cell lymphoma (DLBCL). Incyte, a long-standing position in our/OR/BB Biotech's portfolio, and its German biotech partner MorphoSys jointly launched Monjuvi, a new treatment for DLBCL. DLBCL has historically been managed by a combination of antibodies, chemotherapies and steroids, but about one-third of patients fail to respond to this treatment strategy. DLBCL is the most common type of non-Hodgkin lymphoma, accounting for 30% to 40% of all cases. It is characterized by rapidly growing masses in the lymph nodes, spleen, liver and bone marrow. Novel second-line therapies include MorphoSys's and Incyte's Monjuvi in combination with lenalidomide, an agent from the class of immunomodulators that has been used to date to treat multiple myeloma. The goal in future clinical trials is to establish Monjuvi as the standard of care in this indication.

In the category of cell-based therapies, former BB Biotech positions Kite Pharma and Juno Therapeutics – both companies having been acquired – were pioneers in first-generation autologous therapies, which work by mobilizing the patient's own immune system to attack the tumor cells. Genetically modified T cells – i.e., taken from patients, engineered and then returned to the hosts – increase the number of tumor-specific cells for an immune response.

Second-generation CAR T therapies use allogeneic T cells modified by gene editing technology. The precision and efficiency of multiplex editing with CRISPR/Cas9 is designed to help overcome the challenges of current-generation CAR T cell therapies. The advantage of allogeneic cells from healthy donors is that they are quicker to produce, available immediately, and promise higher efficacy. Another portfolio investment, CRISPR Therapeutics, developed a CRISPR/Cas9-edited CAR T cell therapy based on the novel genome editing process. Initial clinical trials in lymphoid malignancies demonstrated complete response to treatment twelve months after a single infusion.

Fate Therapeutics is focusing on a third generation of development with stem cell-based candidates using renewable iPSC master cell lines. These constitute a renewable cell source that can be used repeatedly, facilitating low-cost production. Two agents, FT516 and FT596-101, are being developed in Phase I trials as cancer immunotherapies suitable for combination with any approved cancer antibody such as Rituxan or Gazyva. In contrast, MacroGenics is pursuing a monoclonal antibody-based approach with the development of flotetuzumab for acute myeloid leukemia, a form of blood cancer that relapses after treatment in about half of patients.

### Portfolio structure and outlook

The aforementioned four companies pursuing oncology research are representative of BB Biotech's strategy of investing in new technologies and treatment approaches as soon as sound data of a medical breakthrough is presented. As in previous years, the Investment Team of BB Biotech firmly believes that its strategy will continue to deliver market-beating returns going forward. Moderna, currently the largest position in the portfolio, is a prime example of an early-stage investment that was made as soon as convincing evidence of an innovative technology's future commercial success was presented. This portfolio position was expanded during the ensuing three years in step with the regulatory approval of its COVID-19 vaccine and its post-launch sales trajectory.

The regulatory delays that have held back clinical trials and approval procedures as regulators focused their attention on containing COVID-19 have so far had an only marginal impact on BB Biotech's portfolio companies. CRISPR Therapeutics reported compelling Phase I data for CTX-110 in lymphoid malignancies in 2021. Radius Health and Menarini also announced convincing Phase III results for elacestrant for the treatment of advanced or metastatic breast cancer.

Radius Health, a long-standing investment in our portfolio, is expected to announce pivotal Phase III data on abaloparatide-TD in the treatment of postmenopausal osteoporosis by the end of this year. In neurology, Neurocrine Biosciences will soon present Phase III data for valbenazine to treat Huntington's disease, an inherited degenerative and ultimately fatal brain disorder for which no treatments currently exist. Arvinas and collaboration partner Pfizer are to present efficacy data for ARV-471. Administered as a tablet, this estrogen receptor PROTAC degrader is being developed for patients with a locally advanced or metastatic type of breast cancer. Macrogenics is expected to announce initial clinical data for MGD006 in acute myeloid leukemia. BB Biotech's portfolio contains a considerable number of companies that could be a positive trigger for BB Biotech shares in the near future if the various data readouts are positive.

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##### **Company profile**

BB Biotech AG is an investment company registered in Schaffhausen/Switzerland and listed on the Swiss, German and Italian stock exchanges. It has invested in innovative drug developers headquartered primarily in the US and Western Europe. BB Biotech is one of the world's largest investors in this sector. BB Biotech relies on the long-standing experience of its distinguished Board of Directors and the investment research skills of the experienced investment management team of Bellevue Asset Management AG when making its investment decisions.

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