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Molecular strike force for the immune system

The increasing number of market-ready new therapies for previously incurable and hard-to-treat autoimmune diseases is creating attractive investment opportunities.

Autoimmunity is an area rich in scope for the delivery of innovative therapies by the biotech industry. More than 100 autoimmune diseases affecting nerves, organs or muscle tissue are currently known to medical science. Autoimmune diseases are the most common form of chronic disease after heart disease and cancer, affecting 5% to 8% of the global population.

The reasons for the rise in autoimmunity are manifold. Environmental factors, overactive immune responses, and genetic causes may be factors in triggering autoimmune disease. Unmet medical need is greatest in niche autoimmune disease indications due to the complete absence of treatment options. That is not the case for chronic diseases like rheumatoid arthritis, psoriasis, and multiple sclerosis (MS) that affect millions of people worldwide. With so many approved medicines already available for these indications, including generics and biosimilars of off-patent drugs, it is much harder to develop an innovative product that works better than existing options.

Multiple sclerosis, a hotbed of innovation

For an example of how progress can be made in treating and controlling an autoimmune disease, one need only look at the advances in MS treatment over the last 30 years. More than 20 MS drugs are now on the market. Initially, medicines were only available by infusion at hospital outpatient clinics. Now patients can take their medication as tablets or by injection pen for subcutaneous administration at home. At the same time, the goal of treatment has shifted to preventing and delaying relapses. Two-thirds of all MS patients begin medical treatment no later than one year after diagnosis. A look at disease progression statistics highlights the benefit of using this window of opportunity. In the 1980s, disability progression in MS typically put patients in a wheelchair within ten years after disease onset. That interval is now as long as 30 years, during which patients enjoy sustained and stable quality of life.

As medical science continues to evolve, therapeutic approaches targeting underlying metabolic processes are filling research and development pipelines. The last two years have seen a major breakthrough in myasthenia gravis, a rare neuromuscular disease in which misdirected antibodies disrupt nerve-muscle communication and damage the muscle membrane. The result is muscle weakness with difficulty breathing, swallowing and speaking.

Big breakthrough at Argenx …

We acted early on to gain exposure to companies making clinical and commercial progress with autoimmune therapies. There are currently three companies focused on autoimmune disease indications in our portfolio. The Belgian company Argenx is currently the second-largest position in the portfolio and had a weighting of 10.3% at the end of the third quarter of 2022. We first opened a position in Argenx in early 2018 and added to it during the following twelve months. In the meantime the market capitalization of

Argenx has increased more than five-fold to EUR 20 bn. At the end of September 2022, BB Biotech had achieved a paper gain of USD 277.6 mn on this investment.

We were confident that efgartigimod, an antibody for treating generalized myasthenia gravis, would be a commercial success when we first invested in Argenx. Sold under the brand name Vyvgart, efgartigimod is now the first drug ever approved in the US, Europe and Japan for the treatment of this neuromuscular disease. Vyvgart is a biological drug with immunomodulatory activity derived from the Fc fragment of human immunoglobulin G1 (IgG1). Because it is three times smaller than conventional antibodies, it penetrates tissues more easily and is effective at lower doses. Recent clinical trial results show that the subcutaneous version of Vyvgart is not less effective than intravenous dosing, which has been the basis for marketing authorization to date.

Argenx has reported strong sequential quarterly sales growth so far this year. Total sales in the third quarter amounted to USD 227.3 mn, an increase of 76% from the preceding quarter. At the current growth rates, Vyvgart will pass the billion-dollar mark in 2023. What's more, this incredible start might only be the beginning of a long-lasting growth story. The big opportunity with efgartigimod is to use the same mechanism of action to treat five other autoimmune diseases, including immune thrombocytopenia (ITP), a bleeding disorder caused by platelet decline. If Argenx receives marketing authorization in all of these additional indications, we estimate that the drug's annual sales potential could range between USD 8 and 10 bn.

… and two promising newcomers

Celldex Therapeutics, a US company, has been in BB Biotech's portfolio since the second quarter of 2022. Celldex is exciting because of its most advanced clinical candidate, barzolvolimab (CDX -0159). Barzolvolimob is the first antibody agent designed to inhibit mast cell activation. Mast cells store chemical messengers such as histamine in the body's natural immune system. Mast cells promote the stimulation of IgE (immunoglobulin E) receptors by the IgE produced by B cells. By attaching to the surface of mast cells, especially in the mucous membranes, IgE can trigger allergies, angioedema and hives (urticaria). CDX-0159 is currently in Phase II clinical trials for the treatment of chronic urticaria. If clinical trial outcomes are favorable, the drug might be approved for other skin conditions and for some gastrointestinal disorders as well.

We first invested in Kezar Life Sciences in 2018. It most advanced product candidate is KZR-616 for the management of three autoimmune diseases for which no adequate treatment options currently exist. KZR-616, a first-in-class immunoproteasome inhibitor, is thought to prevent the production of pro-inflammatory cytokines while increasing the activity of regulatory T cells. Clinical trials exploring the drug's efficacy in autoimmune hepatitis, dermatomyositis, polymyositis, and lupus nephritis are underway. Lupus nephritis is a potentially life-threatening autoimmune disease of the kidneys. The only treatment options currently available are immunosuppressants, which are ineffective in many cases. Kezar has reported positive topline data on renal response in this indication.

We expect that targeted new drugs will go some way to addressing the high unmet medical need in autoimmune diseases in the near future. Clinical news flow and a steady high number of product approvals are leading the entire biotech sector higher and sustained strong sales and profit growth is expected to continue in 2023. Stock valuations remain at attractive levels, and we see interesting investment opportunities.

Author

Dr. Daniel Koller has been with Bellevue Asset Management since 2004 as a Portfolio Manager and was appointed Head of Investment Management Team BB Biotech AG in 2010. From 2001 to 2004 he was an investment manager at equity4life Asset Management AG and from 2000 to 2001 an equity analyst at UBS Warburg. He studied biochemistry at the Swiss Federal Institute of Technology in Zurich (ETH) and earned his doctorate in biotechnology at the ETH and Cytos Biotechnology AG, Zurich.

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Company profile

BB Biotech AG is an investment company with its registered office 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. The competent Board of Directors with its long-standing experience set the investment strategy and guidelines. Investment decisions are taken by the experienced investment management team of Bellevue Asset Management AG based on their extensive investment research.