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Dr. Daniel Koller, Head Investment Management Team, BB Biotech at Bellevue Asset Management

Moderna was just the beginning

RNA-based drugs will revolutionize the application of gene therapy to treat a growing number of diseases and disorders during the coming years.

Alnylam, a stock in BB Biotech's portfolio, made its biggest one-day gain since the company went public in June of 2004. Alnylam shares were marked up 60%, reaching a new all-time high, in reaction to the publication of promising data from a pivotal trial of patisiran, an active substance the company is testing on patients with transthyretin amyloid cardiomyopathy. ATTR cardiomyopathy (ATTR-CM) is a rare inherited disease which is characterized by a buildup of faulty amyloid deposits, causing irreversible damage to the heart and nerves, as well other organs or tissues. The life expectancy of a typical patient is less than five years from diagnosis.

Alnylam will present detailed trial results at a medical conference in September and plans to file for regulatory approval in this indication by the end of the year.

The euphoric reaction of financial markets to this news reflects consensus expectations that patisiran will deliver billions in annual peak sales in this indication. Patisiran was already approved for the treatment of the polyneuropathy of ATTR amyloidosis four years ago and is sold under the brand name Onpattro. Alnylam reported annual sales of USD 475 mn from this drug in 2021. Some 50 000 individuals worldwide are affected by ATTR amyloidosis, and Onpattro could be prescribed to treat an additional 300 000 adults with ATTR-CM.

Commercial breakthrough a reality

Alnylam is considered to be one of the most promising takeover candidates in the biotech industry today. The company is marketing four authorized products and will present pivotal clinical trial data on five pipeline candidates by the end of 2023, including Phase III data for fitusiran, an investigational RNA interference treatment for people with hemophilia that Alnylam is developing in collaboration with Sanofi. However, the most compelling takeover argument from an acquirer's perspective is Alnylam's status as a pioneer and market leader in the field of small interfering RNA (siRNA) technology. This is a therapeutic approach that utilizes double-stranded RNA molecules to block the mechanisms of target proteins that have been identified as triggers for certain diseases. Simply put, messenger RNA (mRNA), i.e., the genetic blueprint encoding disease-causing proteins, is effectively suppressed to inhibit the production of those proteins.

RNAi (RNA interference) is a natural biological process for silencing or inhibiting gene expression. siRNAs are one class of RNAi mediators. Antisense technology is a related field where scientists are utilizing short single-stranded nucleic acids, or antisense oligonucleotides, to detect and eliminate disease-causing proteins. Ionis Pharma, a US biotech company, is a pioneer in the field of antisense that has been a core fixture of BB Biotech's portfolio for years. Messenger RNA, or mRNA for short, on the other hand, is a different therapeutic approach that instructs cells to make certain proteins. mRNA technology achieved a major commercial breakthrough with the development and marketing approval of COVID-19 vaccines in less than a year's time. These mRNA vaccines train the body's immune system to detect viral proteins and

develop an effective response without actually getting sick. The two COVID-19 vaccines developed by Moderna and Pfizer/Biontech were crucial in containing the coronavirus pandemic.

RNA technology enters a new chapter

BB Biotech recognized the medical potential of RNA technology early on. There are a total of four RNA-focused companies, including two core shareholdings, Moderna and Ionis, in its portfolio with an aggregate weighting of around 25%. The double-digit price gains of these companies in response to the breakthrough at Alnylam also helped BB Biotech's share price to gain 10% during the same period. In addition to Alnylam's gains, the value of our stake in Wave Life Sciences rose by 50%. This markup was triggered by the company's announcement that clinical trials of drugs in genome-editing therapies would begin next year.

Looking ahead to the next few years, we expect RNA-based drugs to enter a new market phase. Under the assumption, of course, that the later-stage testing is likewise successful, the range of potential applications for RNA-based therapeutics would grow to include diseases that affect large patient populations, for example cardiovascular diseases, metabolic disorders, cancer and organ fibrosis. Innovative products that make it to the market will generate billions in revenues.

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 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.