BB Biotech
Bellevue Investments

In Focus
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Marketing document

BB Biotech sharpens its focus on gene therapies

Dr. Daniel Koller
Head Investment Team

Getting in early when an investment opportunity starts taking off with massive upside potential is every investor's dream, but often that also exposes investors to unexpectedly high risk. In the health industry, gene therapies seem to be up and coming, but many of these approaches are in early clinical development and will take years to reach the market, if they even get that far.

The big blockbuster drugs dominating the pharmaceutical market for much of its history have clearly been based on chemical substances. In the last two decades, these agents have increasingly been displaced by biologics (therapeutic agents manufactured in a living system such as microorganisms, plants, or animal cells) – evident from the fact that eight of the current top ten best-selling drugs were developed on the basis of antibodies and therapeutic proteins.

Although last year saw a record 59 new drug approvals in the United States, gene therapies accounted for a very small proportion of that figure. However, the low approval quota for the new technologies is only because drug development cycles always tend to be long.

An upswing in investment in gene therapy candidates in the development pipeline is apparent in the large number of clinical trials now being done and in statements by recently resigned FDA Commissioner Scott Gottlieb, who expects an increase in the number of gene therapy product approvals in the coming years. Besides the promising potential and incentives to provide tangible, long-lasting benefits to patients with serious diseases after just one treatment, pharmaceutical companies have been offering hefty premiums to take over these medical pioneers, which has been drawing additional investor interest to these new fields of medicine. In 2018 Novartis acquired gene therapy company Avexis for USD 8.7 bn, while Roche has just announced its intention to buy Spark Therapeutics for USD 4.3 bn.

New therapeutic indications have potential for patients and the biotech industry

1 x day	$ - $$$ per tablet	Chemical substance
1 x week/month	$$$ - $$$ $$$ per injection	Biologics RNA-based therapies
1 x year/life	$$$ $$$ - $ $$$ $$$ per infusion	Cell-based therapies Gene therapies Gene editing

Source: Bellevue Asset Management

Clinical research into new technologies is forging ahead

While most of the drugs available to date are designed to block certain disease-causing proteins temporarily, the aim with gene therapies is the opposite: to durably replace a missing or faulty function with a single dose of treatment. The most common vector used to carry the gene material is viruses, often adeno-associated viruses but also retroviruses. The viruses transport the desired gene into the cell, where the information is read and implemented. Gene therapy achieves a stable effect, lasting for years in some cases, but without integrating in the human genome. The even more complex technology of gene editing also uses viruses to transport the genetic material, but aims to permanently change the human genome in cells and organs and thus correct existing errors or replace missing information.

«BB Biotech is investing successfully in the pioneers of cell and gene therapy»

Alongside the potential, there are also risks and challenges, with issues ranging from long-term safety, the dosage of the single treatment and efficiency in reaching target organs and cells to unintended effects of gene editing on the human genome, not to mention the high initial cost of gene-editing techniques.

BB Biotech is increasing its investment in gene therapies

BB Biotech's first gene therapy investment was Avexis, which ended very successfully in 2018 when Novartis acquired the company. Afterwards Voyager Therapeutics was the only other gene therapy company in the portfolio until the fourth quarter of 2018, when several new positions were opened, in Audentes, Sangamo and other companies.

GENE THERAPIES IN CLINICAL TRIALS

2 805
(as of August 2018)

Audentes is developing AT132 for the treatment of X-linked myotubular myopathy, a serious genetic disorder. Infants with mutations in the MTM1 gene cannot produce a functioning version of the protein myotubularin, leading to serious musculoskeletal abnormalities. Sangamo develops gene therapy projects with partners while itself focusing on gene editing in serious genetic inherited disorders that require life-long enzyme replacement therapy.

RNA therapies are several steps ahead of gene therapies

Not to be forgotten is another important product category – RNA-based therapies – which we believe have been wrongly neglected as a result of the hype generated by the acquisition activity in the gene therapy area. This technology uses various genetic building blocks to reduce or raise the production of specific proteins in a controlled fashion without affecting the human genome. 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 Pharma has established itself as a global pioneer in antisense technology with more than 30 candidates in its proprietary development pipeline. The company's sales partner Biogen Idec achieved one of the most successful sales trajectories for orphan drugs with the Ionis product Spinraza for the treatment of spinal muscular atrophy, a rare muscular disorder. Another investment, Alnylam, was granted approval for Onpattro, the first drug to be developed on the basis of siRNA 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 rare bleeding disorders. In addition, Alnylam is collaborating with The Medicines Company to develop a cholesterol-lowering drug.

ANTISENSE CANDIDATES IN THE PIPELINE

>30
(Ionis)

Share facts

Board of directors	Dr. Erich Hunziker (Präsident) Dr. Clive A. Meanwell Prof. Dr. Dr. Klaus Strein Thomas von Planta
Management	Bellevue Asset Management
Legal structure	Incorporated company
Foundation	November 9, 1993
Share type	Registered shares
Nominal value	CHF 0.20
Share structure	55.4 mn shares
Listing	Swiss Stock Exchange German Stock Exchange Italian Stock Exchange
ISIN number	CH0038389992
Security number (CH)	3 838 999
WKN (D/I)	A0NFN3
Investor relations	Dr. Silvia Siegfried-Schanz: Phone +41 44 267 72 66 E-Mail ssc@bellevue.ch Claude Mikkelsen: Phone +41 44 267 67 26 E-Mail cmi@bellevue.ch E-Mail Maria-Grazia Iten-Alderuccio: Phone +41 44 267 67 14 E-Mail mga@bellevue.ch
Media relations	Tanja Chicherio: Phone +41 44 267 67 07 E-Mail tch@bellevue.ch

Contact

BB Biotech AG
Schwertstrasse 6
CH - 8200 Schaffhausen
T +41 52 624 08 45
www.bbbiotech.com