



Quarterly Update: Q4 2021

The Year in Review and What is Coming Up

Looking back at 2021 we saw sharp declining biotech share prices as of mid-February 2021 around the so-called 'Turn out of Tech'. Due to a first signal of increasing interest rates, share prices of technology companies that were not profitable yet were hit hard as they use debt to finance themselves. For no good reason non-profitable biotech companies, although they do not (or hardly) use debt, were taken down as well. Even COVID-19 vaccine companies BioNTech and Moderna saw their share prices decrease 55% from their 2021 peak.

The biotech sector had been in the spotlight due to the pandemic and the IPO window for biotech companies was wide open already since mid-2020. This continued in 2021, heavily pushed by the banks involved, which resulted in a record of biotech IPOs (105) over 2021, even when share prices were declining rapidly. The median share price development of IPOs in 2021 was negative, at -25%. Aescap did not participate in any of the IPOs.

The declining share prices moved generalist investors out of the market which resulted in further decreasing share prices.

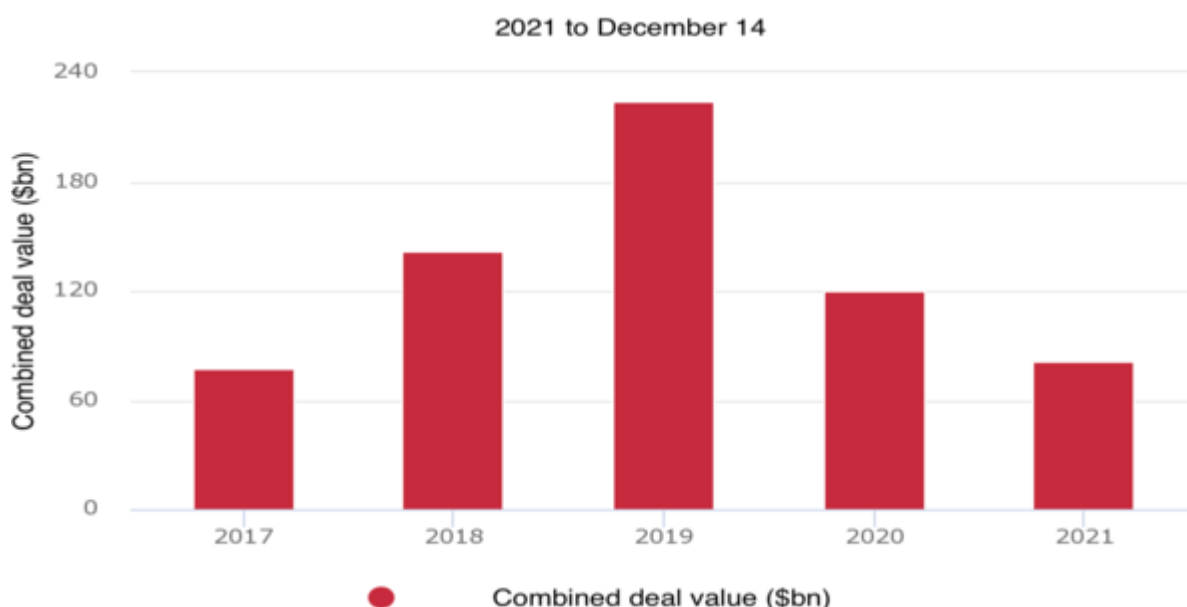
The market also suffered from further delays in clinical studies due to hospitals still dealing with too many COVID-19 patients, on top of a long period of uncertainty around who the new head (commissioner) of the FDA would be. US President Biden eventually nominated Robert Califf, a former FDA commissioner, who is expected to be endorsed soon by the Senate.

On a positive note, revenues and profits of biotech companies over 2021 did increase, even when the promotion of products was challenged as many doctors couldn't be visited, due to the pandemic. Many companies adapted quickly and moved forward with innovative solutions such as advanced online promotion tools that have shown amazing positive results for several firms.

What Could Trigger Change

Decreased company valuations for small- and mid-cap biotech typically trigger mergers and acquisitions (M&A) activity. The graph below shows the low amount of biotech M&A in 2021. An approval of one or more multibillion blockbuster medicines, of which several are lined up for 2022, could also help switch sentiment positively. Our portfolio company Argenx received approval for such a medicine on December 17th.

Even the start of a new year, when investors typically review their portfolio looking for new opportunities, could change the sentiment. Looking at the average price/earnings ratio versus other sectors we see a historic low for biotech at around half of the general industry. This in contrast with the fundamentals for the biotech industry that are widely perceived as stronger than ever.

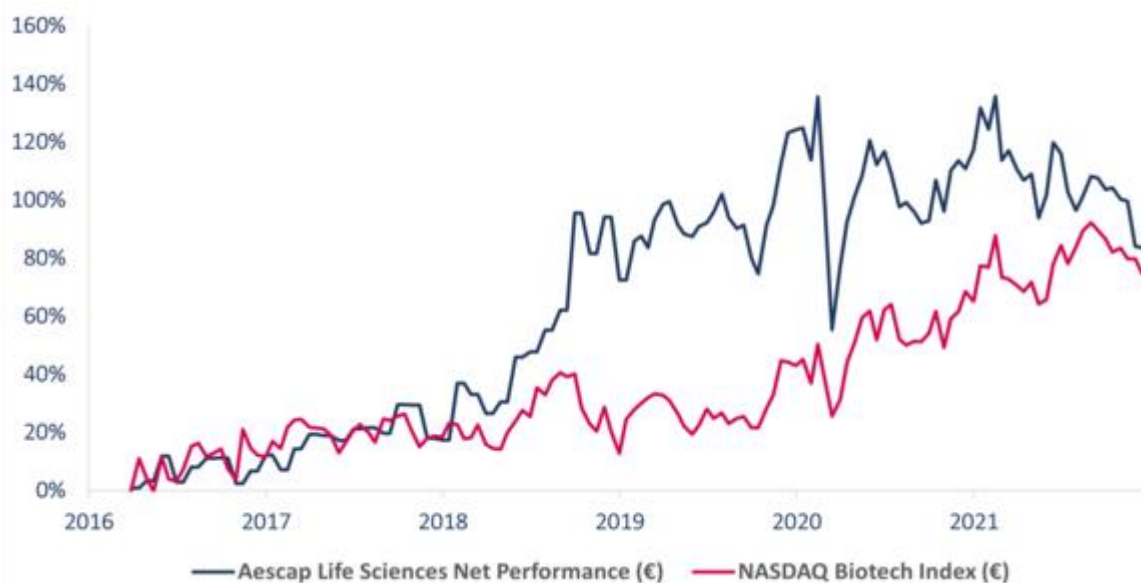


Biotech M&As during the past five years ([Evaluate Pharma](#), 2021)

Net Performance (since inception at March 28, 2016)

**Unit Value per December 31, 2021:
€ 1.858,0425**

Net IRR	2021	1 month	1 year	3 years	5 years
+ 11,4%	- 14,5%	+ 0,9%	- 14,5%	+ 7,7%	+ 65,6%



Fund Breakdown per December 31st

Assets under Management:
€ 167.232.654

Location (based on value):

US: 49,8%
Europe: 42,5%
Asia: 7,7%

Invested per Currency:

USD: 88,6%
EUR: 5,2%
DKK: 4,3%
GBP: 1,5%
SEK: 0,4%

Top-5 Performers

- 1. Dicerna Pharmaceuticals + 90%**
- 2. Apellis Pharmaceuticals + 43%**
- 3. Argenx + 19%**
- 4. Amicus Therapeutics + 18%**

Portfolio Highlights

The share prices of our portfolio companies for sure did not move in line with their increase in intrinsic value / earning power. Therefore, the undervaluation of our portfolio over 2021 increased significantly. We made use of the depressed share prices by swapping some companies in our portfolio with others that are further matured / already profitable but still have a large upside potential. As a result, the average market cap of our portfolio went up from around \$5 billion to \$13,6 billion in December. Below please find the most important Q4 company highlights.

Apellis Pharmaceuticals (+43%)

Apellis' fourth quarter was rich in positive developments. Mid-December it received approval for its medicine, Aspaveli, for the treatment of a life-threatening blood disease. This followed the US FDA's approval earlier in 2021, where the product is called Empaveli. Apellis arranged sales & distribution of Aspaveli outside of the USA through a deal with Swedish biotech company SOBI, a company founded by our portfolio advisor Bo Jesper Hansen. Apellis is testing the medicine in different formulations in another 5 diseases, two of which clinical studies can potentially directly lead to approval, on top of other exciting products in their pipeline.

The company also announced that after receiving feedback from the FDA, it plans to proceed with the filing for approval of the same medicine for the treatment of a common yet untreatable eye disease, known as geographic atrophy (GA). Normally, an announcement on the possibility to file would not be a noticeable value inflection point for biotech companies. However, Apellis' share price was under strong pressure because of the negative expectations investors had regarding the possibility for the company to file with the whole clinical data package it had at hand. Therefore, this announcement on FDA feedback lifted such overhang from the stock and allows the company to move one step further and potentially receive approval for the treatment of GA as well. The disease has a remarkably high unmet medical need with millions of people suffering from it and represents a market potential of around \$5 billion.

Right after the FDA feedback, Apellis conducted a successful public offering, raising over \$400 million, allowing the company to continue executing the launch of its lead medicine while also providing the resources to continue the expansion of its clinical pipeline.

Argenx (+19%)

Belgium biotech Argenx got its first medicine, Vyvgart, approved in the US in December for the treatment of a muscle-weakening disease that can be life-threatening. We expect the product will be approved in at least another 10 autoimmune diseases and will become a top-20 selling global medicine. Analysts are expecting annual sales of \$5 billion for this first marketed product of Argenx. Approval in Japan is awaited in Q1 and in the EU later in 2022. The product will be marketed in China by license partner Zai Lab, who is planning to file for approval in that territory later this year. The company has \$2,5 billion in the bank, so it is well-positioned to test Vyvgart in an additional 14 diseases as planned. It also has other products in clinical development on top of a few products that are out-licensed to big pharma companies.

Argenx is ranked in the top-3 of Bloomberg's M&A list based on a survey amongst 59 biotech fund managers, but we invested in the company for other reasons.

Arrowhead Pharmaceuticals (+6%)

Arrowhead negotiated a deal with top-10 pharma GlaxoSmithKline out-licensing a product for the treatment of nonalcoholic steatohepatitis (NASH) and will receive \$120 million immediately and up to potentially \$910 million in milestone payments plus royalties. Arrowhead is making good use of its RNA technology platform as it also out-licensed a product to Johnson&Johnson (J&J) for the treatment of another subset of NASH patients earlier on. The company also has another important licensing deal with J&J which is targeting a disease with no sufficient treatment available today, hepatitis B, with over 200 million cases worldwide. In Q4 J&J presented strong clinical data for this medicine-candidate. These deals come on top of several other licensing deals the company concluded in the past.

In Q4, Arrowhead presented compelling new or additional clinical trial data for three products in liver, cardiac and metabolic diseases either being out-licensed or fully owned.

Dicerna Pharmaceuticals (+90%)

Dicerna was acquired on December 28 by Novo Nordisk at a share price premium of 80%. You might recall the intention of the deal was [announced](#) mid-November.

Ionis Pharmaceuticals (-9%)

Ionis closed yet another licensing deal in Q4 with AstraZeneca, bringing in \$200 million directly plus a potential \$3,4 billion in milestone payments on top of royalties. This brings the total number of out-licensed products to 22. The company is not profitable yet but with \$2 billion in the bank and a burn rate of around \$100 million per year they are in a good financial position to further advance their broad pipeline of medicine candidates. In 2021 alone, they brought 6 new products into clinical testing to provide better treatments for serious diseases or even first treatment options for diseases with no options available. This very productive RNA technology platform has been built for more than 30 years now and is really starting to pay off. Ionis' biggest commercial success is the medicine, Spinraza, which is generating around \$2 billion in sales annually for license partner Biogen, from which Ionis receives around \$300 million yearly in royalties. A few days ago, Biogen closed an additional deal for a product from Ionis' platform to treat SMA, paying \$60 million immediately plus an undisclosed amount of potential milestone payments and royalties.

Zai Lab (-40%)

Zai Lab's share price has been under pressure further in the fourth quarter, however, the causes of such downturn had no impact on the value of the company itself. Zai Lab again achieved several milestones, see below, but the threat of US sanctions against Chinese companies led to a generalized negative sentiment towards Chinese companies.

In response to China's handling of the Uyghur situation, the US placed several tech companies on an investment blacklist to prevent US investors from investing in those companies. Zai Lab is not on this list but the chance that it could have been included drove the share price down. Even though sentiment around Chinese firms has been grim in 2021, we believe that the US and China greatly need each other and therefore will have to sit at the table together to work things out.

We believe the underlying fundamentals for Zai Lab have not changed and the share price pullback is a long-term buying opportunity.

On top of this, the Chinese Party has stated biotech as a focus area for Chinese investment. We believe the China biopharma industry will continue to flourish and transition out of a largely genericized market as recent medicine regulations in China benefit innovative companies with novel best/first-in-class products like Zai Lab is bringing to the market.

Zai Lab continued to deliver on promises with the most significant event in Q4 being the approval in the US of Vyvgart from Argenx. Zai Lab licensed this product for the Chinese market and can now file for approval. Zai Lab received approval from Chinese authorities for Nuzyra, an antibiotic that will help fight bacterial resistance in China. The company continued expanding its product portfolio with the addition of two products licensed from Blueprint Medicines as well as a new medicine for the treatment of schizophrenia from partner Karuna therapeutics.

Royalty Pharma (-6% from entry date)

New in our portfolio is Royalty Pharma plc (Nasdaq: RPRX), the largest buyer of pharmaceutical royalties globally. The company is delivering a steady increase in revenues and profit year after year. The company published their Q3 financial results with total royalty receipts of \$712 million, an increase of 21%, compared to \$588 million in the same period of 2020. Royalty Pharma also raised its financial guidance for 2021 and now expects adjusted cash receipts to be around \$2,12 billion (18% growth year/year). During Q4 it concluded an extension of a royalty deal totaling \$350 million with biotech company BioCryst.

Especially now that P/E ratios of biotech companies are at a historic low, Royalty Pharma has a very interesting proposition. Instead of raising money through the stock market, biotech companies rather sell a part of their royalty income in return for cash, to finance, for example, an acquisition or license deal. Many biotech companies have royalty income from non-core products they have out-licensed to another company for which the product suits their existing sales & distribution channels in a specific disease area.

Royalty Pharma claims over 50% market share in the biotech/pharma royalty business and only has a few competitors. The company went public in June 2020 and was founded in 1996 by its CEO Pablo Legoretta.

Vertex Pharmaceuticals (+17% from entry date)

During the fourth quarter, we added Vertex Pharmaceuticals. The company is constantly increasing its dominant position in the Cystic Fibrosis market. Cystic fibrosis is a disease that causes severe damage to the lungs, digestive system, as well as other organs. Vertex has been at the forefront of the development of novel therapies for this disease for many years. In 2020 it had a net income of \$2,7 billion on \$6,2 billion in revenues. Revenue guidance for 2021 is \$7,5 billion. In November the company received a positive opinion from the European Committee for Medicinal Products for Human Use (CHMP) for the use of its products in

even younger patients in need, which typically leads to an approval of a medicine in Europe within a few months.

In October the company announced early yet promising results for the treatment of type 1 diabetes using a cell therapy approach. The first patient treated showed a restoration of insulin production, leading to a 91% decrease in daily insulin requirement and strong improvements in glucose control. Early December Vertex also announced positive results from a novel medicine for the treatment of a disease that damages the filtration function of the kidneys, eventually leading to kidney failure. These positive results clearly indicate that Vertex is on course to expand and differentiate its medicine portfolio to create more value beyond its very profitable cystic fibrosis franchise.

Outlook

In biotech most years with a negative performance have been followed by a strong rebound. Since the start of the XBI/S&P Biotech index in 2006, the index has never been down two years in a row. Let's look at the facts. An industry with such good fundamentals for future growth and profits ended 2021 with price/earnings levels at around 50% of the S&P 500. The Aescap Life Sciences portfolio with high-growth companies is undervalued at around 100% and many value-creating events across the portfolio are ahead of us in 2022.

Wishing you an inspiring and fruitful 2022 in good health.

Best regards on behalf of the Aescap team,

Patrick J. H. Krol
Portfolio Manager Aescap Life Sciences

About Aescap Life Sciences

Aescap Life Sciences is an open-end fund investing in public biotech companies that develop and market next generation medical treatments. Within its focused portfolio of around 20 companies it diversifies over different diseases, development phases and geographies. Companies are selected for their growth potential ('earning power') and limited risk (technological and financial). Investors can enter and exit the fund twice per month.

The selection of companies in our portfolio is based on 'high conviction' - extensive fundamental analyses combined with intense interaction with management and relevant experts. The fund's performance is fueled by

stock picking and an active buy and sell discipline. Biotech stocks are known for their very low correlation and high volatility, caused by media, macro-events and short-term speculative investors. This creates an ideal setting for a high conviction fund manager to invest in undervalued companies with a great mid- and long-term earning power. The fund has an average annual net performance target of 20% over the mid-term (4-5 years)

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