As it is the first month of the new year, we wanted to take a moment to review the past 12 months, particularly considering the recent general market volatility. Was 2018 a good year for the LSP Life Sciences Fund? Yes and no. It was not our greatest year in terms of share price performance especially not in comparison to the stellar performance in 2017, but it was – again - an excellent year in terms of news flow and advancements made by our portfolio companies. The irony of this anomaly is not lost on us. In assessing the fund performance for the year - we cannot come to any other conclusion than that the portfolio is in great shape and the intrinsic value of our holdings has significantly increased, even if this has not been reflected in the share price; not yet at least.

Here we review the highlights of 2018 for the markets in general and for the Fund in particular.

The Markets: As there is no relevant index for the European healthcare sector, let alone for our small- & mid-cap biotechnology subsegment – we tend to look at several indices to assess the general healthcare market trends, such as the Nasdaq Biotechnology Index, the MSCI World Healthcare Index, the STOXX 600 Healthcare Index amongst others. In all cases, when comparing performances, one needs to compromise either on geography, market cap, concentration, sector, segment or any combination thereof. Looking at the NBI: following a relatively volatile start to the year, it peaked at about +12% towards the end of September. The MSCI World Healthcare Index had a similar performance up to that time point (+10%). Since then, the NBI has fallen dramatically, along with most other general indices. For instance, one such general index - the Nasdaq Composite - fell 9% in October and again 9% in December, losing almost 24% between September 1st and December 24th. Such a drop is exceptional. In fact, not seen since the financial crisis hit in late 2008, over a decade ago. This sell off was swift and unforeseen and not sector specific. It would appear trade wars, Brexit and elections, budget concerns and the FED's (anticipated) interest policy, have increased market uncertainty and reduced investor appetite for equities. At least for the time being. Quite astoundingly, the markets rebounded in the first two weeks of the new year even faster than they fell in the months before. We do not wish to speculate about the reasons for such a rebound.

The Fund: Turning to the LSP Life Sciences Fund itself, throughout 2018, the Fund held a portfolio of between 15 and 20 companies. Exactly in line with our strategy to hold an ultra-concentrated portfolio and not – as most Funds and indices do – build a large and diversified portfolio. During the year, we have exited 8 positions with an additional 2 exits through M&A. Both **Juno Therapeutics** and **Ablynx** were acquired in January, getting the LSP Life Sciences fund off to an excellent start for the year. Other positions were sold for a variety of reasons. For example, we invested in UK company **Clinigen** for the first time in mid-2014. At that time, we believed it to be undervalued, with a strong management team in place, with a clear vision for the future direction of the company. By mid-2018, we considered that this strategy had mostly played out and decided to switch to better opportunities and liquidate our holding in Clinigen.

There were two exits in the portfolio where the investment case played out, but not the way we had expected. Early in the year we invested in **Prothena** based on excellent Phase 2 clinical data in a rare and very serious blood disorder called AL Amyloidosis. Unfortunately, and contrary to what we had expected, the company announced further clinical data from another follow-on trial, that unfortunately were not strong enough. Also, at the same time, Prothena announced that its ongoing Phase 3 trials would be stopped for reasons of futility. This – frankly - was the worst possible outcome for the company and its shares sold off dramatically as a result. We liquidated our entire holding following these negative developments back in April 2018. The second exit of a holding that did not deliver on its investment case, was antibiotics company **Tetraphase**. They announced negative trial results in the treatment of urinary tract infections and we liquidated our position as a result back in February of 2018. The only other negative news in the portfolio in the entire year 2018 was from French cancer company, **Erytech**. While their lead program, and the focus of our investment, was – and still is - in Phase 3 trials for prostate cancer, the shares were crushed when the company announced that a study in AML would be stopped. While this was a minor part of the valuation, it would have provided the only significant news flow anticipated for the company in 2018 and the shares were punished. We liquidated our position in mid-July, 2018. So, looking back, these were the three companies we should not have invested in in 2018. Still, these were the only three and interestingly, they all happened in the first half of the year. In fact, as per the end of July 2018, the Fund stood at a net return of +13%. This was *after* we liquidated and realized a loss on the positions we held in Prothena, Tetraphase and Erytech. So indeed, in the first six months of the year, that loss was more than compensated by significant *gains* made in the rest of the portfolio. Indeed, it is fair to say that positive developments and good news in the portfolio, significantly out weighted the relatively few negative developments in the past 12 months.

For instance – right at the start of the year - two companies were acquired at significant premiums, **Juno** and **Ablynx**. Juno got acquired by Celgene for USD 9 bln in cash (at the start of 2019 Celgene in turn got acquired by BMS for a whopping USD 74 bln – the largest healthcare deal in history) and Ablynx got acquired by Sanofi for almost USD 5 bln in cash. In addition, four companies in the portfolio received marketing approval from the FDA and three have launched important new treatments: **Dova Pharmaceuticals** (no longer in portfolio), **Verastem, Stemline and GW Pharmaceuticals** (no longer in portfolio); **Aerie Pharmaceuticals** launched its new treatment for Glaucoma, an eye disease, and is reporting an impressive initial market response to the treatment. Aerie also filed for approval of a combination treatment for glaucoma, Roclatan, and will hear from the FDA in 1Q19; cancer company **Stemline Therapeutics** filed its lead drug for FDA approval and the FDA approved the drug ahead of its February 2019 PDUFA, giving the company an early Christmas present.

As most of our readers know, before any new treatment can be launched – it goes through a series of tests or clinical trials. The reporting of such data is critically important for all healthcare companies, big or small, pharma or biotech. Simply because the value of a product and a proprietary technology increases in line with clinical progress made. In other words: the stronger the clinical data (efficacy and safety) that has been proven in well controlled clinical trials – the higher the likelihood of a new drug reaching the market and in turn, the higher the value of that drug (the drug will be meaningfully differentiated from the competition, assuming all other metrics are positive as well of course). This metric typically dictates the premium paid in M&A transactions. In 2018, the vast majority of our portfolio companies presented or published great clinical data – significantly increasing the intrinsic value of the assets – if not the share price.

In fact, during the period **September 1st and December 31st 2018**, the period of near unprecedented sell off in the equity markets, our portfolio companies indeed announced so much good news, like we have not seen in any such 4-months period in the past 10 years.

In summary all the major developments since September 1st 2018:

+ we had an impressive 7 companies come out with positive Phase 3 results (**Foamix, Galapagos, Amarin, Obseva, Genmab, Zogenix and Fibrogen – see note on Amarin published by us here**),
+ we had another 6 companies in the portfolio that reported positive Phase 2 results (**Zogenix, Galapagos, argenx, Viking Therapeutics (2x), UniQure and Obseva**),
+ we had **Cocrystal** finalizing its enrollment in its Phase 2 trial in Hep C (data expected in January 2019), **Obseva** complete enrollment for its other Phase 3 trial and **Foamix** announce positive Phase 3 data in both acne and rosacea. **Galapagos** also announced results of the first Phase 3 study for its arthritis drug.

- we had both **Verastem and Stemline** see their drugs approved for marketing in the US by the FDA, **Aerie** see its Glaucoma drug dossier being accepted by EMA, **Dova** see its sNDA for its main drug accepted by the FDA, **Stemline** see its main drug receiving accelerated assessment for marketing approval and **Foamix** submitting a New Drug Application to the FDA for its Acne drug. **Clementia** announced FDA would allow them to file for early approval of their breakthrough treatment for a rare disease.

- we had **CytomX** reporting positive clinical data showing proof-of-mechanism of its highly innovative cancer technology platform,

- we had **Morphosys, Genmab and Fibrogen** see their abstracts being accepted for late breakers at ASH and **Galapagos** see clinical results of its main drug being published in The Lancet,

- we had **Merus** settle - to its benefit - its important patent litigation with Regeneron,

- we had 7 companies jointly raise an impressive USD 1.5 bln through new equity offerings to allow for further investments in their innovative R&D pipelines (**Zogenix, Foamix, Galapagos, Viking, argenx, Verastem and Amarin**),

- and we had **argenx** strike a deal with J&J on one of its products for a total deal value of USD 1.6 billion, including a USD 300 mln equity investment by J&J into argenx;

Triggered by these many positive developments in our portfolio companies, we have seen over 200 research reports being published by banks such as Jefferies, Cowen, Goldman, JP Morgan, Morgan Stanley etc, *only in the past 4 months*. As per the end of the year, every single portfolio company was trading far below consensus analyst ratings. As per January 7th 2019, 50% - or 9 out of 18 - of our portfolio companies, had more than 100% upside according to the analysts covering these companies (**Verastem, Foamix, Cocrystal, Viking, Stemline, Obseva, Amarin, Aerie and CytomX**). Out of these 9 companies, 4 having more than 200% upside according to the Analysts (**Verastem, Foamix, Cocrystal and Viking**). For what it is worth, Wall Street seems to believe these companies have become ridiculously cheap.

Given the overwhelmingly positive news flow within the Fund's portfolio, it is disappointing that there was not a positive return for the year for the Fund. After a stellar 2017, in which the Fund generated a net return of +39%, outperforming all markets by a very significant margin, it closed at a net return of -9% in 2018. Is that performance a worry to us? Or, better still, should it be a worry to our investors? We believe it should not. Why not? Because we focus solely on the fundamental investment cases underlying the various portfolio companies that we hold, and do not try to "play" or "time" the markets. In fact, as the famous investor Peter Lynch has said[1]: "*Far more money has been lost by investors trying to anticipate corrections than has been lost in corrections themselves.*".

Since we focus on the fundamentals - and the fundamentals only - selecting for those companies that we believe are attractively valued – given risk profile and upside potential – and based on the due diligence which we perform in-house supported by a global LSP network of advisors and experts, we would worry only if our analyses prove to be wrong too often. That has not been the case. In fact, the opposite is true as described above.

The markets in 2018 have been heavily impacted by short term political and macro-economic trends and events. In particular during the second part of the year. Trump's rather unorthodox approach to running his political-, economic-, and foreign- & internal-affairs agendas, are – at best – unpredictable, leading to uncertainty, in turn leading to market volatility. This volatility – down and up – does impact the share *price* of the companies we invest in, it has no real impact on their *value*. Volatility in the portfolio due to non-

[1] *Kapitale Verhalen, Jaargang 5, 2018, Hans Betlem, Chief Investment officer, IBS Capital Allies*

company specific events, are beyond our control. What we can and do control, is the make-up of our portfolio. It was in great shape in 2018 and still is at the start of the new year.

The intrinsic value of the existing portfolio has increased due to the events of the past months. The share prices have shown an inverse trend. This value however should be priced in if - and when - the markets start to correct.

Furthermore, in the coming months, important investor, scientific and medical conferences will take place. Several of the companies in the portfolio will be announcing and presenting new data at these conferences. Positive data and progressing innovative new treatments towards the market is the life blood of this industry. Bringing new treatments to patients in need is the core purpose of these companies. The main markets may remain volatile but launching new drugs will ultimately benefit everyone – including our investors, like we have shown in the past 10 years.

On behalf of all at LSP, we wish all our readers and all our investors a good and healthy 2019.

Mark Wegter

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