LSP Life Sciences Fund – Interim Report

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CONNECTING INVESTORS TO INVENTORS

Dear Investor,

Following two recent and important positive developments in the portfolio of the LSP Life Sciences Fund, the fund is up **+21%** year-to-date and **+278%** since inception.

Our overall track record since starting to invest in small- and mid-cap biotech stocks back in 2008, currently stands at +1,100% on a gross basis (or +21% per annum over a 12-year period). This compares quite favorably to the performance of any equity market index over the same period. For instance, if one would have invested over the same period in the MSCI Europe Pharma & Biotech Index, one would have generated a return of 224% since 2008.

What happened recently and what drove the LSP Life Sciences Fund outperformance year-to-date?

1. On November 2nd 2020 Sanofi, made an all cash offer for portfolio company **Kiadis Pharma** at a 272% premium; the highest premium ever paid for a Euronext listed biotech.
2. On November 12th 2020 portfolio company **Calliditas** announced positive Phase 3 data for its lead product.

These two milestones in November added to a growing list of positive portfolio developments achieved over the course of the past few months:

3. **Aimmune** was acquired by Nestle in July at a 174% premium;
4. **Albireo** announced positive pivotal data in PFIC, an orphan disease which leads to liver failure;
5. **Intra-Cellular** announced positive pivotal data for Caplyta in the treatment of bi-polar disorder; Caplyta is being launched as a new treatment option for schizophrenia with a very benign safety profile.
6. **Arrowhead** was added to the portfolio in September, for its leading platform technology RNA interference which has a broad range of applications.

We identified cell therapy as a focus area having successfully invested in the first-generation autologous cell therapy (personalized therapy) companies Juno and Kite:

7. We made investments in second generation cell therapy companies (off-the-shelf product) **Allogene** and **Fate Therapeutics**. These investments were also successful which lead us to invest in **Kiadis** and more recently **Precision Biosciences** and **TCR2 Therapeutics**.

And finally, we participated in 4 equity offerings this year: **Kiadis**, **Oncopeptides**, **Calliditas** and **Abivax** and each of these companies has seen positive developments

The above developments are credit to our consistent strategy of investing in a highly concentrated portfolio of undervalued, yet high growth innovation plays that are difficult to select for, without knowing the life sciences market as we do.

Kiadis Pharma, for example, targets the development of a therapy that triggers a patient's own immune system to recognize the cancer cells, attack those cells and clear them out. It does this by making use of a specific type of blood cells - NK Cells or Natural Killer Cells – that are part of the human immune system.

What are NK Cells? The immune system's task is to protect the human body against diseases. It does so through a highly complex and sophisticated system, making use of all kind of unique and specific cells that jointly make up an extraordinarily effective system. NK cells are part of this system and make up the body's first line of defense against infections and diseases. NK cells can rapidly seek and destroy "abnormal cells", meaning cells that are not "normal" to the human body - hence their "killer" name.

Why are NK cells interesting for drug development? While the immune system does a spectacular job in fighting diseases, it does not always succeed. In fact, in the case of cancer, it never does. This can be attributed to one of two reasons: the immune system is either not able to recognize the abnormal cancer cells or – when the cancer cell is detected, it changes and adapts to escape and remain invisible to the immune system. As a result, cancer is a disease that is not attacked by a patient's own immune system. Instead, all type of drugs are being prescribed to effectively take over that task.

To make things more complicated, there are literally hundreds of different kinds and types of cancer, all of which require the development of drugs specific to the type of cancer. Would it therefore not be great to be able to trigger a patient's own immune system to recognize the cancer cells, attack them and clear them?

This question is being studied and addressed by scientists and researchers active in the Immune-Oncology field of drug development. This is where NK cells and the NK cell technologies, come into play.

How does this work? Scientific advancements made over the past decades by academia and businesses, have led to the development of so-called CAR-T therapies. At its most basic level, these are therapies that make use of white blood cells or more specifically T-cells – also important cells that are part of the immune system – drawn from a patient's own blood and then re-engineered using advanced bio-molecular techniques, such that they do recognize certain cancer types.

This re-engineering allows certain structures - called Chimeric Antigen Receptors or CARs - to establish on the surface of T-Cells (hence the name CAR-T cells). These re-engineered cells are then reinjected into the patient, which then help T cells identify and attack cancer cells throughout the body. The fact that these T cells divide and multiply in a patient's body, strengthens the efficacy of the treatment.

Spectacular clinical results have been obtained with this approach and as recently as 2017, the very first CAR-T therapy gained market approval. This allowed doctors to treat some of their cancer patients. The approval was given for the treatment of an advanced form of leukaemia, both in children and adults. A second CAR-T therapy has been approved only months after the first, treating patients that would otherwise not have survived their specific cancer type (diffuse large cell lymphoma).

However, although proven to be highly efficacious and considered to be a breakthrough in cancer treatment, CAR-T therapies also have their drawbacks. Apart from potentially triggering very harmful

side effects for the patient (known as cytokine release syndrome or cytokine storm), also the production of these CAR-T therapies is a highly complex endeavor. Essentially, the treatment is patient specific, meaning that for every patient a specific drug needs to be produced. This obviously carries a high price.

What is their advantage? The next generation of cell therapies are being developed as off-the-shelf products. This means that a batch of cells can be prepared in advance and given to a number of patients when needed rather than being a patient specific product. Portfolio companies, **Allogene Therapeutics**, **Precisions BioSciences** and **TCR2 Therapeutics** are each using different T-cell technologies to achieve this goal.

Kiadis is one of a small number of companies focused on NK cells rather than T-cells. The big advantage of NK cells is that they do not recognize self and could be the ideal off-the-shelf cell type. Patients should not cross react to the engineered NK cells allowing the NK cells to seek and destroy the cancer cells. In addition, NK cells have an inherent ability to target tumor cells without needing genetic alteration. In theory, this would mean that the side effect profile of NK therapies, should be better than CAR-Ts. Sanofi clearly saw the potential of this technology and signed a license agreement with the Company in July of this year. They then quickly moved to acquire the company just a few months later. Sanofi announced on November 2nd that it has acquired **Kiadi**s for a consideration of EUR 308 million. The deal is expected to close in 1Q21.

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