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NEWSLETTER

MELIOR INSIGHTS

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Melior
CAPITAL MANAGEMENT



Introduction to Melior Capital Management

MELIOR

/me'ljor/
(from Latin)

BETTER, SOUNDER, SUPERIOR

Melior Capital Management is a Swiss domiciled company investor and advisory firm focused exclusively on the global life science sector.

We specialise in finding funding for medtech, biotech and pharmaceutical companies by applying institutional quality service and process to raise capital.

Our investment approach is to find qualified innovative projects, with proven management teams, promising data, robust IP, strong corporate governance and a likely opportunity for significant commercial upside in a three to five-year horizon.

In the current environment, many existing companies seeking capital for medical trials have encountered a diminishing supply of funding from governments, private equity firms, investment banks and research foundations in favour of start-ups. At Melior, we combine the global reputation of our scientific, management and advisory members to select best in class investment opportunities with credible upside potential.

Our value proposition is attributable to our world class team and their proven track record in the life-science sector, plus the strong emphasis that we place upon due diligence and first-hand experience. Our goal is to offer attractive

and diverse investments to both high net worth private clients and larger corporates through their professional advisers. For our business to be truly successful, we consider the needs of all parties, including our investees, investors and professional advisers at introduction and throughout the life of the investment. Our financial success depends on funds raised and the financial return of our investees as we share a common goal.

Our previous editions show how the global pandemic resulted in growing interest and increased funding for life sciences. In this edition of our Melior Insights newsletter, we review three Melior investees, the conditions they address, their impact and how COVID influenced these market niches. Innovative ideas, bold approaches and hard work bring the changes needed to shift the paradigm for the treatment of these life-threatening diseases. Each of these projects comes as an opportunity to revolutionise the approach to solving an unmet need and impacting millions of lives.

Melior does not accept enquiries from members of the general public, but we welcome enquiries from professional intermediaries.

Melior Capital Management

MELIOR CAPITAL MANAGEMENT



THE HEART IMPLANT TREATING ATRIAL FIBRILLATION

THE CONDITION

Two devastating cardiovascular diseases (CVD) are atrial fibrillation and heart failure. Atrial fibrillation is the condition when the heart's two upper chambers (the atria) beat irregularly and/or out of sync with the two lower chambers (the ventricles). It comes with symptoms like heart palpitations, weakness and shortness of breath, and can lead to strokes, heart complications and heart failure. Heart failure occurs when the heart is not capable of maintaining a healthy blood flow, which requires significant lifestyle compromises, medications and often implants or heart surgeries, including bypass surgery and heart transplant.

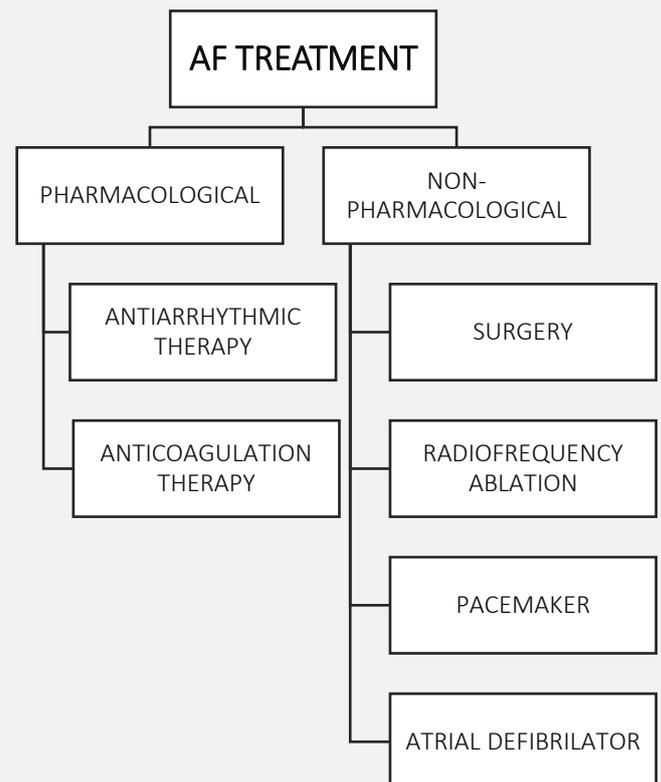
THE IMPACT

The WHO reports that cardiovascular disease (CVD) is the number 1 global cause of death, with more than 17.3 million attributable deaths occurring yearly. The global costs of managing chronic CVD, including atrial fibrillation, is estimated as \$149 billion for the next 5 years, just covering medical technologies, not accounting for the additional significant costs of medication. In the US alone, direct and indirect healthcare expenditure, including lost productivity, is estimated as being more than \$317 billion, with 647,000 Americans dying each year from heart disease, or one person every 37 seconds, or 1 of every 4 deaths. By 2030, over 40% of the US population is projected to have CVD, while the direct medical costs are anticipated to triple, approaching \$1 trillion. Similarly, the prevalence of atrial fibrillation is expected to increase 2-4 fold, to over 12 million US patients in the next decade. The demand for treatment is also expected to grow due to rising rates of obesity and diabetes, while the level of

physical activity is decreasing. The global market for atrial fibrillation medical devices in 2020 was estimated at \$6.9 billion, while the market for heart failure devices was estimated at \$12.9 billion.

THE SOLUTIONS

The dominant treatment for many heart conditions, including atrial fibrillation, is currently pharmacological in nature. These are often of a lengthy duration, with various side effects and furthermore are expensive. In addition, for many patients with atrial fibrillation, often the only possible therapeutic outcome is lifelong control rather than cure of the condition.



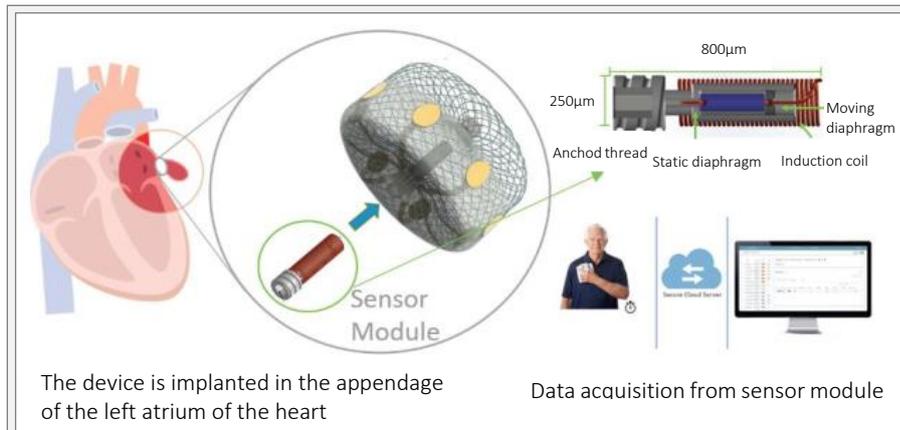


In recent years, there has been growing interest in non-pharmacological measures for treating atrial fibrillation. Surgeries, like the Maze operation, are considered major heart surgery and come with an expected 1-2% perioperative mortality, thus it is cautiously performed. Radiofrequency ablation is estimated to yield success in 90% of the cases, with few complications, but is not feasible for many of the more advanced atrial fibrillation cases.

Pacemakers tend to reduce the number of grave atrial fibrillation events by bringing the rhythm of the heart to a more harmonious equilibrium. Alternatively, atrial defibrillation uses implants to reduce the level of arrhythmia, however, it comes with a steep price and patients feel pain and anxiety when the defibrillator is intervening to synchronise the rhythm of the heart.

THE INNOVATION

A Melior investee has developed a device that is implantable in the appendage of the left atrium and is able to ablate when the heart rhythm is unbalanced. This solution will be superior to pharmacological options as it does not affect the body chemically. In addition, it only requires one procedure, which has lasting therapeutic effects. Another major advantage of this option is the capability of the device to capture valuable data concerning performance of the heart using smart sensors. This allows doctors to monitor and detect even insignificant changes, thus permitting early intervention, improvement of quality of life and survival, while also minimising expensive hospitalisations.



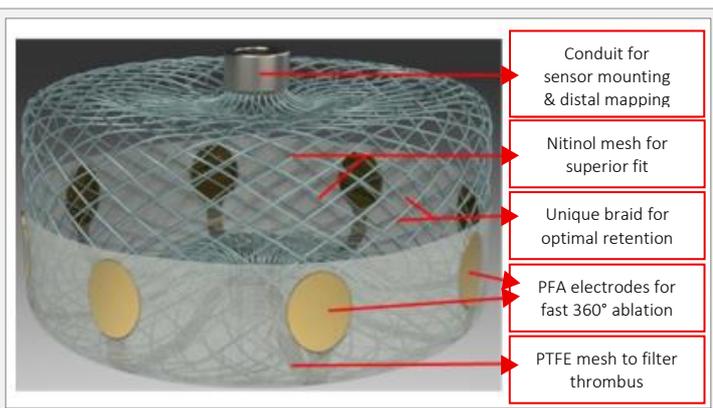
The device combines three important technologies into a single platform:

- a. Intra-cardiac non-thermal ablation
- b. Stroke prophylaxis
- c. Heart failure / intra-cardiac monitoring

The company is led by an experienced team, with a qualified track record, with the device having already passed proof of concept studies in animal models and having attracted significant grant funding and recognition.

THE COVID IMPACT

The lingering effects, lack of herd immunity and the emergence of new variants of the SARS-CoV-2 virus that causes COVID-19 means that the pandemic will not disappear, but will require careful public health monitoring. This will affect many people who are in various health risk groups such as the immunosuppressed. One other such group are people with atrial fibrillation (AFib). The ongoing seven-decade long Framingham Heart Study has shown that the lifetime risk of AFib in the US is as high as one in four. For patients with AFib and other heart conditions, the likelihood of grave COVID-19 outcomes is much higher, as has been proven by multiple studies in China, the EU and US. In addition, studies have shown that some patients have developed AFib after they have suffered from COVID-19. Initially, this tended to be older patients with several risk factors, like hypertension. However, more recently, more and more cases are occurring, and the number ending in heart failure is growing. A device that is capable of not only intervening to reduce and manage the health effects of AFib, but also reports on the health of the heart in real time will benefit millions of patients, not just those with AFib but also other heart conditions.





A REVOLUTIONARY TREATMENT FOR SEVERE KIDNEY DISEASE

THE CONDITION

Kidneys are an important organ in our bodies, being responsible for a number of functions, with their main role being the filtration of the blood and removal of metabolic waste products. When their capacity to filter blood is disrupted, which can happen quickly in cases of acute kidney injury (AKI) or acute renal failure, abnormal levels of salts and chemicals build up and affect other organs, and can lead to complete shutdown of the kidneys, which, without dialysis, leads to death. Another condition that affects this organ is chronic kidney disease (CKD), which is a long-term condition where there is deviation from the normal functioning of the kidneys. This is a common condition associated with older people, but it can affect younger people too, especially those with high blood pressure, increased cholesterol levels or diabetes.

THE IMPACT

Approximately 13.3 million cases of AKI are diagnosed every year, with the majority being in emerging countries. Of the 1.7 million yearly deaths caused by AKI, around 1.4 million occur in low- and middle-income countries, many of which could be prevented if the condition could be identified earlier and treated. AKI is a common condition in hospitalisations, ranging from 8-16% of hospital admissions, with a fourfold risk of hospital mortality. In the US alone, more than 35 million hospitalisations are associated with AKI yearly, with each case ranging in cost from \$11,016 to \$42,077, with an overall, estimated, accountable sum of up to \$24 billion per year in the US alone. In the UK, more than 1% of health service expenditure is attributed to AKI.

More than 1 in 7 adults, accounting for approximately 37 million people in the US are estimated to have CKD, with as many as 9 in 10 not even being aware of their condition. Every month, 10,000 new chronic patients start dialysis. The costs of the condition are estimated to be over \$100 billion per year in the US alone. The global CKD rate is slightly lower at 10%, but this condition drastically increases the risk of a number of other diseases, including cardiovascular and bone disease, a weakened immune system, as well as depression and a decreased quality of life significantly intensifying the overall impact of CKD on health and healthcare costs.

THE SOLUTIONS

Solutions for the treatment of AKI and CKD remain elusive, with the problem increasing in magnitude and cost every year, both in the US and the rest of the world. CKD has been "branded" a US epidemic, with an Executive Order being signed by the US President on July 10th 2019, dedicated to "advancing American kidney health". The current treatment of AKI ranges from increased intake of water and minerals for early forms of disease together with avoidance of drugs that might increase kidney toxicity, and ultimately to dialysis. Treatments often require close monitoring by doctors, multiple clinical investigations and often hospitalisations.

Conversely, there are no available treatments for CKD, although the condition can be prevented from worsening through lifestyle changes, including consuming a healthy and balanced diet, taking regular exercise, weight management, no smoking and limitation of alcohol consumption. In addition to these lifestyle changes, CKD management usually involves the treatment of associated



conditions – high blood pressure, high cholesterol levels, water retention and anaemia. Many CKD patients eventually require dialysis or a kidney transplant, which often has a waiting list of at least 2 years.

these patients often have a weaker immune system, which makes them an easier COVID target. All of these factors highlight the importance of novel treatments for kidney conditions like AKI and CKD.

THE INNOVATION

A Melior investee is developing a platform of 3 biotech products addressing AKI and CKD:

1. A prophylactic treatment for patients with a heightened risk of AKI which has passed the preclinical stage of development, has completed a Phase I trial, and has commenced a Phase II trial in the first half of 2021.
2. A small molecule capable of reducing the progression of CKD by restoring cellular homeostasis, reducing inflammation and fibrosis. Protective effects have been observed in the heart too, and the medication is effective in CKD patients with diabetes.
3. A product developed to treat iron deficiency anaemia without inducing nephrotoxicity and cardiotoxicity. Positive preclinical studies were presented at the beginning of the year and Phase II studies are expected to begin in the first half of 2022.

The company has an experienced team, strong data, well protected intellectual property and is advancing towards regulatory approvals.

THE COVID IMPACT

The effect of the COVID pandemic has been significant for both AKI and CKD patients. First, several studies have shown that COVID can cause AKI in addition to affecting the respiratory system in vulnerable patients hence they suffer from more severe forms of the disease with prolonged hospitalisations, kidney failure, slower recovery and a higher morbidity rate. Second, COVID patients with pre-existing kidney conditions have, in general, experienced worse symptoms, with a 3-fold increase in severe COVID amongst this population of patients. Third, there have been significant delays and complications associated with dialysis and kidney transplant procedures;



A SAFER WAY TO PREVENTING PULMONARY EMBOLISM

THE CONDITION

Pulmonary embolism (PE) is a blockage of one of the arteries in the lungs. These are caused most of the time by blood clots and can be life-threatening. When the artery is blocked, the portion of the lung it serves is prevented from receiving oxygen-rich blood, and the lung tissue may die. This then diminishes the capacity of the lung to provide oxygen to the body. Half of all people who have a pulmonary embolism do not have any symptoms and therefore are not aware of the condition which can lead to sudden death. Those with symptoms experience shortness of breath, chest pain or coughing-up blood which presents an opportunity for quick intervention.

THE IMPACT

Pulmonary embolism is the third most common cause of cardiovascular death and is associated with multiple inherited and acquired risk factors as well as advanced age. The number of PE-related hospital admissions more than tripled in less than ten years (1999: 60,000 to 2012: 202,000) in the US, this evolution maintaining the same trend in the last decade. Estimates show that 5-10% of in-hospital deaths are a direct result of PE. The condition claims the lives of over 100,000 Americans and 300,000 Europeans every year. In the US, PE occurs in approximately 1 in every 1,000 adults yearly, with an estimated annual cost of about \$8 billion.

THE SOLUTIONS

The first option in treating PE are anticoagulants (blood thinners) which represents a \$25 billion annual market. However, this approach cannot be used following trauma or major surgical procedures due to collateral bleed risk,

thus leaving many PE patients vulnerable. Secondly, when anticoagulants cannot be used, patients face surgery where a metal blood filter is inserted into the inferior vena cava, which prevents clots from reaching the lungs. Doctors recommend that these filters be removed within weeks of deployment and once the risk of PE decreases, as they can create damage by migration or fragmentation and can in themselves result in death; however, many patients never return for the extraction surgery.

THE INNOVATION

A Melior investee came up with an original approach, developing a filter made of absorbable material that is capable of collecting and facilitating resorption of clots for 12 weeks before breaking down into carbon dioxide and water – natural components of our bodies. Thus, the device helps deal with PE while not affecting coagulation of the blood and does not require any extraction surgery as do metal filters. These extraction surgeries are extremely challenging interventions that have resulted in numerous lawsuits. Use of the new absorbable filter is estimated to save about \$12,000 on the extraction procedure alone, while being a much safer option for patients with PE.

The company has already secured 10 patents and grant funding, completed a randomised controlled animal study, and finalised the first successful human study which received remarkable recognition from key specialists.

COVID IMPACT

Similar to kidney complications, PE commonly occurs in COVID patients, with a 14.2% incidence, with a higher prevalence of 26.6% in COVID patients in intensive care



units. Even though the long-term effects of COVID are not yet completely clear, the chance of a PE is increased in patients that had moderate to severe COVID. Patients with pre-existing PE predisposition remain a high-risk group that can develop blood clots, face more severe forms and can die of COVID. These factors increase the attractiveness of a solution that can be easily implanted as an out-patient, does not require extraction, and does not interfere with the ability of blood to coagulate.

Sources

The heart implant treating atrial fibrillation

Mayo Clinic, The WHO, The Global Market Insights, National Center for Biotechnology Information 1, National Center for Biotechnology Information 2, Diagnostic and Interventional Cardiology, BMJ Journal and the Melior Insights Team

A revolutionary treatment for severe kidney disease

International Society of Nephrology, Nephron, Advances in Chronic Kidney Disease, Centers for Disease Control and Prevention, The NHS 1, The NHS 2, American Society of Nephrology, National Kidney Foundation, Karger, MedScape, Yale News, Nephrology, Dialysis, Transplantation, Clinical Journal of the American Society of Nephrology and the Melior Insights Team

A safer way to preventing pulmonary embolism

MedlinePlus, Mayo Clinic, Seminars in Interventional Radiology, American Heart Association, Annals of Intensive Care, European Respiratory and the Melior Insights Team



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