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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 introducer 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.

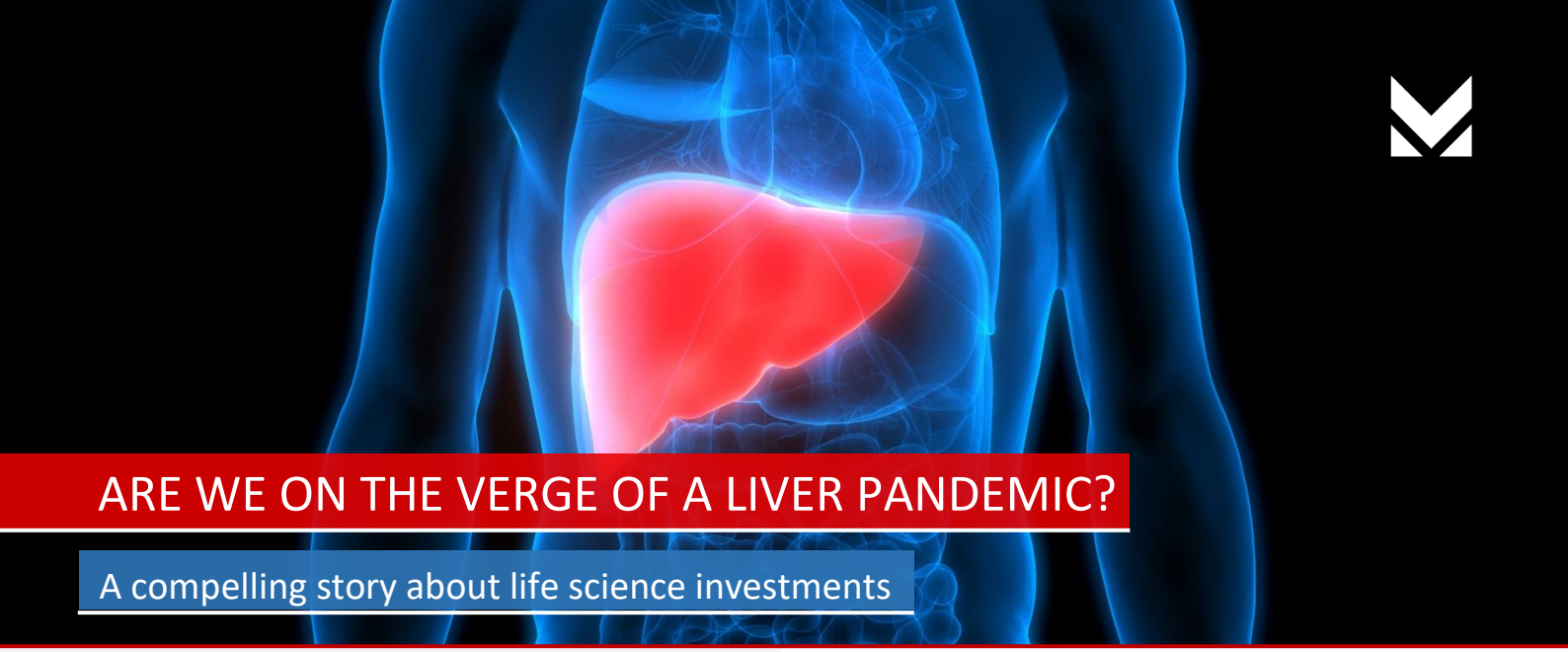
Our value proposition is attributable to our world class team and their proven track record in the life-science sector, plus the strong emphasis that we place upon due diligence and first-hand experience. Our goal is to offer attractive and diverse investments to both high net worth private clients and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

In this edition of our newsletter –Melior Insights, we review the role of the liver, the complexity of liver disease and its economic costs, provide some examples of the liver disease market and share with our readership an exciting and innovative project developing novel treatments for liver disease.

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

Melior Capital Management

MELIOR CAPITAL MANAGEMENT



ARE WE ON THE VERGE OF A LIVER PANDEMIC?

A compelling story about life science investments

Liver disease is a growing problem with both rising costs and investments, yet the gap between the current state-of-the-art and demand for solutions is ever widening. Subsequent sections of this report review in detail the depth and breadth of liver function, illnesses, as well as the economic costs associated with liver disease. This article describes a unique and innovative project developing sustainable solutions for the treatment of liver disease. This project not only has an experienced team, exceptional vision, proven scientific data and intellectual property, but also presents a real opportunity to change the paradigm of liver disease treatment.

A billion people have liver disease. Yet only recently have targeted treatments begun to appear. How can this be so? And what has changed to make treatment possible?

Liver disease has many causes, ranging from viral infection to alcohol abuse and obesity. It can take decades to develop liver disease, often without the patient noticing. For example, a patient treated recently at one of the largest hospitals in the UK was a typical case: a middle-aged man who drank two large glasses of wine a day. He was not diagnosed with liver cirrhosis until a routine health check-up was conducted. Five years later he was first admitted to hospital and five days after that he died, becoming the latest of the two million people dying of liver disease each year.

What do liver disease patients have in common? What links excess alcohol intake, obesity and viral infections? Why does the disease take so long to progress? And why is it so lethal?

These are the questions that one of the leading global experts in liver disease and co-founder of the Melior investee company, has dedicated his career to answering. Over 20 years, the research group headed by this expert has published over 400 papers, been cited over 25,000 times and has created a global alumni network of over 60 research fellows.

At the heart of this expert's deep understanding of liver disease is the connection between a patient's digestive system and their liver.

The story begins with the gut microbiome, the trillions of bacteria that live happily within each of us. In liver disease patients – of ANY cause – the lining of the intestine becomes leaky. Even gastroenterologists call it a 'leaky gut'. This means that waste products from gut bacteria leak out of the gut instead of being flushed away. It is the liver's job to deal with these waste products, and normally it does an excellent job.

The problems arise if this leakiness lasts for months or years. These waste products are called endotoxins or lipopolysaccharides (LPS). When the liver detects LPS it alerts the immune system. In dealing with LPS, the immune system kills local liver cells, and the leftover fragments of these dead cells triggers a further immune response. This vicious cycle eventually kills so many cells in the liver that it fails. Without the liver doing its job, LPS circulates throughout the body damaging other organs such as the kidneys, brain and lungs.

At this stage, many of these patients are in intensive care. Death rates are high: if just one additional organ fails, then the patient has a 25% chance of dying in less than a month.

If two other organs fail, the number rises to around 50% and with three extra organs failing, mortality is in excess of 80%.

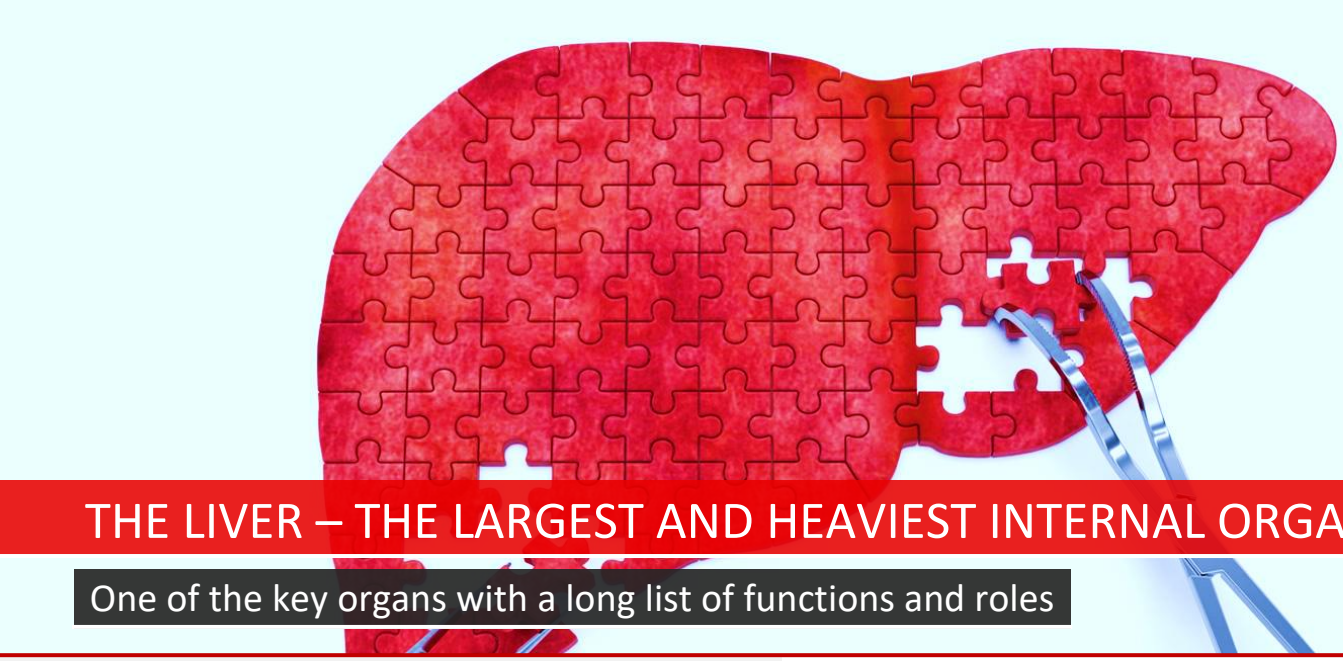
Fortunately, the investee project team have used this understanding to devise three new products. All three are now in clinical trials run by the investee company and its partners.

Each of these products targets LPS present in different parts of the body and each product targets patients at different stages of the multi-year evolution of liver disease.

The investee has now completed mid-stage clinical trials with the first and third products and has agreed a partnership with one of the world's largest pharmaceutical companies to develop the second product.

The high degree of diversification of this investee project places it in a favourable position, with a de-risked product portfolio. The company's therapies have the ability to prevent many of those two million deaths a year from liver disease through development, testing, refining and commercialization.

	The first product	The second product	The third product
Description of the product	An oral adsorbent taken daily to remove LPS from the gut	A pharmaceutical that has been repurposed from a different disease, and in liver patients reduces their sensitivity to LPS by binding to the molecule that detects LPS	A double filtration system that removes LPS from the blood and replaces part of the body's natural defences against LPS
Development stage	The first randomised controlled clinical trial has been successfully completed	In phase 2 clinical trials	The first randomised controlled clinical trial has been successfully completed
Usage	For home use	For hospitalised patients	For intensive care use



THE LIVER – THE LARGEST AND HEAVIEST INTERNAL ORGAN

One of the key organs with a long list of functions and roles

The liver, weighing about 1.5 kg, is the largest and heaviest internal organ in the human body and has a number of key vital functions. It is a triangular-shaped solid organ, located in the upper right abdomen, just below the diaphragm and behind the ribs. It is the only organ with two blood supplies – the hepatic artery, bringing blood from the heart and the hepatic portal vein, bringing blood from the intestines. It is also the only organ that can regenerate. At a microscopic level, the liver is composed of individually functioning units called lobules containing areas with blood vessels, ducts and intervening cords of liver cells, called hepatocytes. These cells process everything that is eaten or drunk and either repackages it for future use or eliminates it. In addition, the liver stores vitamins and is essential in the process of detoxification of the body.

If the liver is damaged, it is likely that the body is not absorbing, storing and utilising the nutrients received during digestion. Furthermore, an unhealthy liver might result in disturbances in metabolism, blood circulation and the production of unwanted hormones.

Functions of liver

The liver is an indispensable organ as it conducts essential activities which are estimated to be more than 500 in number, including functions executed in combination with other systems and organs. There are currently no artificial organs capable of sustaining all of these functions and only a small number can be replaced by liver dialysis. The most reliable solution for a failed liver is a liver transplant.

In the table below some of the key functions of the liver are reviewed:

Function	Role of Function
Bile production and excretion	Essential in the process of food digestion, in particular fats and absorption of vitamins A, D, E and K
Storing and reverse-conversion of glucose	The extra sugar, or glucose, is converted into glycogen, which serves as a reserve of energy and is converted back to glucose when it is needed by the body
Production of blood coagulation factors	The liver produces most of the coagulation factors, as well as being responsible for the absorption of Vitamin K needed for their synthesis
Synthesis of plasma proteins, such as albumin	Albumin is a key protein that regulates blood volume and fluid distribution in the body
Production of amino acids (the building block for proteins)	The liver synthesises proteins like ferritin (responsible for the storage of iron in the body), lipoproteins (involved in the transport of cholesterol), acute phase proteins (involved in infection and inflammation) and proteins that bind to hormones
Aiding hormonal processes	The liver participates in numerous hormonal processes – e.g. it is involved in the conversion of the thyroid hormone into its most active form, angiotensinogen, a hormone that regulates sodium and potassium levels and produced by the liver
Detoxification and breaking-down toxic poisons	The liver breaks down old red blood cells into products which are eliminated via urine and stools, as well as breaking down drugs, alcohol, waste products and toxic poisons

Causes of liver disease

Due to the many roles the liver plays in the human body, it is essential to maintain its health and functions intact. However, there are a number of factors that affect the health of this crucial organ and can cause liver disease:

Alcohol

The most well-known toxin of the liver. Alcohol creates acetaldehyde - a toxin which is evacuated from our bodies by the liver. Excess alcohol consumption often results in significant liver issues, cirrhosis and liver failure

Excess Sugar

Excess sugar can lead to the accumulation of fatty tissue in the liver which may result in liver disease, even in cases of normal body weight. Studies show that sugar is just as damaging as alcohol

Obesity

Increased body weight and accumulation of fat can lead to hardening and swelling of the liver, as well as formation of scar tissue resulting in malfunction of the liver. This can lead to non-alcoholic fatty liver disease (NAFLD)

Prescription Medications

The majority of oral medications pass through the liver and some of them, particulaly those containing substances that are difficult to absorb, or toxins can have damaging consequences

Infections

Parasites and viruses can infect the liver causing inflamation that reduces liver function. There are a number of viruses that can significantly affect the health of the liver: Hepatitis A, Hepatitis B, Hepatitis C, Hepatitis D, Hepatitis E, Epstein–Barr, etc.

Some common types of liver disease

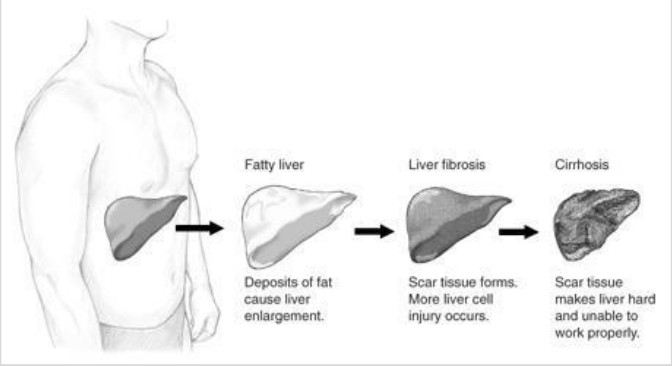
Fatty liver disease

Fatty liver disease (FLD), also known as hepatic steatosis, is a condition where excess fat accumulates in the liver. This disease often has no or few symptoms, such as tiredness and pain in the upper right side of the abdomen. Complications may include cirrhosis, liver cancer, and oesophageal varices. There are two types of FLDs: non-alcoholic fatty liver disease (NAFLD) and alcoholic liver disease (ALD). As the name suggests, the difference between them is the cause of the fat accumulation – alcohol or otherwise.

FATTY LIVER DISEASE (FLD)

- Non-alcoholic fatty liver disease (NAFLD)
  - *Non-Alcoholic Fatty Liver (NAFL)*
  - *Non-Alcoholic SteatoHepatitis (NASH)*
- Alcoholic liver disease (ALD)

NAFL is a milder form of non-alcoholic fatty liver and usually does not progress into NASH or liver cirrhosis, while NASH can include severe liver inflammation. NAFLD can still progress to severe conditions like liver cancer, liver failure or in some cases, cardiovascular disease. ALD is a serious condition and develops in more than 90% of heavy drinkers, while about 25% develop more severe alcoholic hepatitis and about 15% end up with liver cirrhosis.



Stages of NAFLD, progressing from healthy, to steatosis (fat accumulation), inflammation, fibrosis and cirrhosis.

Liver Cirrhosis

Cirrhosis is a condition in which the liver does not function properly due to long-term damage. This damage results in the replacement of normal tissue with scar tissue. Typically, the disease develops slowly over months or years with no symptoms early on. However, as the disease worsens, a person may become tired, weak, itchy, have swelling in the lower legs, develop yellow skin, bruise easily, have fluid accumulation in the abdomen, or develop spider-like blood vessels on the skin.

Hepatitis

Hepatitis is the inflammation of liver tissue. In some cases, there are no symptoms, whereas others develop yellow discoloration of the skin and whites of the eyes (jaundice). If hepatitis resolves within six months it is acute, and the liver can heal on its own. If it takes longer than six months, it is chronic and might result in cirrhosis, liver cancer or even liver failure.

The most common causes of the hepatitis are the hepatitis A, B, C, D and E viruses. Other causes are excessive alcohol use, certain toxins and medications, as well as autoimmune diseases. A short overview of the five viral hepatitis diseases is presented below:

The stages of liver disease

Similar to the stages of NAFLD, liver diseases can be divided into four steps that describe the degradation of the liver condition.

Stage 1 - Inflammation

As outlined before, there are a number of factors that might lead to inflammation of the liver – excess fat in the liver (alcoholic and non-alcoholic), excess toxins or viruses. This leads to enlargement of the liver and deterioration of its functions, especially the detoxification of the blood.

Stage 2 - Fibrosis

If inflammation is not properly addressed and treated, it will cause the liver to start forming scars. Scar tissues will expand and replace the healthy tissues and thus significantly reduce liver function – this process is called fibrosis. Once fibrosis has started and the functions of the liver decrease, fat and toxins start to accumulate in the liver. Furthermore, scar tissue affects normal blood flow to the organ. At this stage, it is possible to save and reverse the negative effects through lifestyle management and medication.

Name of virus	HAV	HBV	HCV	HDV	HEV
Classification	Picornavirus	Hepadnavirus	Flavivirus	Deltavirus	Hepevirus
Viral genome	ssRNA	dsDNA	ssRNA	ssRNA	ssRNA
Transmission	Fecal-oral	Parenteral, sexual	Parenteral, sexual	Parenteral, sexual	Fecal-oral
Incubation period, days	15-45	45-160	15-150	30-60	15-60
Usual onset	Abrupt	Insidious	Insidious	Abrupt	Abrupt
Chronic Hepatitis	No	Yes 10% chance	Yes >50% chance	Yes, <5% of coinfections, >80% of superinfections	No
Mortality rate	< 0.5%	1% - 2%	~ 4%	High to very high	Low, 20% in pregnant women
Cure	No cure. Treatments usually tackle the symptoms. HCV is an exception – there are therapies that can cure it (95% chance), but they are very costly				

Stage 3 - Cirrhosis

If the process of fibrosis is not stopped, it leads to a condition which is much more dangerous, the severe scarring of the liver, called cirrhosis. At this point, the liver is no longer capable of healing itself. It might take as long as 20 to 30 years for a person to develop cirrhosis, but it is often the case that the symptoms of liver degradation are only seen and identified at this late stage. Cirrhosis can lead to a number of complications, including liver cancer. There is no treatment for cirrhosis, just management and control of further scarring and treatment of associated complications and symptoms.

Stage 4 - Liver Failure

At this stage, the liver has lost its function and is unable to heal. There are three forms of liver failure: chronic, acute-on-chronic and acute.

Acute liver failure strikes in as little as 48 hours as a reaction to a drug overdose or poison. Chronic liver failure is slower to develop and might take years. The only solution in cases of liver failure is a liver transplant. In addition to the previously mentioned symptoms of liver disease, liver failure can also have effects on mental health, causing confusion and disorientation. At this stage it is too late to salvage anything from the liver, this is why it is so important to perform regular medical check-ups, as the inflammatory and fibrosis stages can be identified through ultrasound or X-ray, and with appropriate treatment can result in full recovery of the liver.

A few liver facts

- It contains 300 billion hepatocytes (specialised cells)
- In normal conditions, the liver filters about 1.7 litres of blood per minute
- At any given moment, about 13% of the body's blood supply is held by the liver
- The liver regenerates and is capable of fully recovering, from as little as 25% of healthy liver
- The liver is the largest and the most functionally complex organ
- A healthy liver holds the required amount of Vitamin A for about two years
- The first successful human liver transplant occurred in 1967
- In 1989, a portion of a living adult's liver was successfully transplanted into a child resulting in both having normal liver function. This procedure results in two fully functional livers over time from the partial donation of one ht carries significant risks.

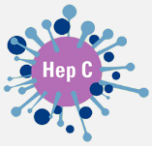
Source: Canadian Gastrointestinal Society, MedicineNet, The WHO, Mayo Clinic, Melior Insights Team

THE ECONOMICS OF LIVER DYSFUNCTION

How much does it cost us?

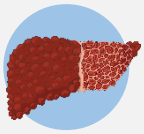
NASH

Market size:
$2.23bn (2018) to **$61.6bn** (2028)
27.62x growth in 10 years



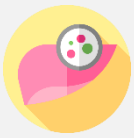
HEPATITIS C

Market size:
$30bn (2017) to **$80bn** (2037)
2.67x growth in 20 years



CIRRHOSIS

hospitalisation costs alone:
$7.4bn (2014)



LIVER CANCER

- 5th most common cancer among men
- 9th most common among women
- 3rd leading cause of cancer death

Liver cancer accounts for **841,000 new cases** and **782,000 deaths globally** (2018)

Liver cancer diagnostics market:
$8.93bn (2018) to **$15.4bn** (2025)
1.72x growth in 7 years

Liver cancer treatment market:
$1.01bn (2020) to **$3.9bn** (2027)
3.86x growth in 7 years

As outlined in previously, two of the main causes of liver disease are alcohol and obesity. A 2018 study from the UK's Foundation for Liver Research looked at these causes and estimated their overall societal costs, which are significant:

These costs are based on the UK alone and include costs associated with liver disease. The global numbers are similar and the effects on liver disease are also comparable. In the subsequent sections, a more comprehensive review of financial data per condition is analysed.

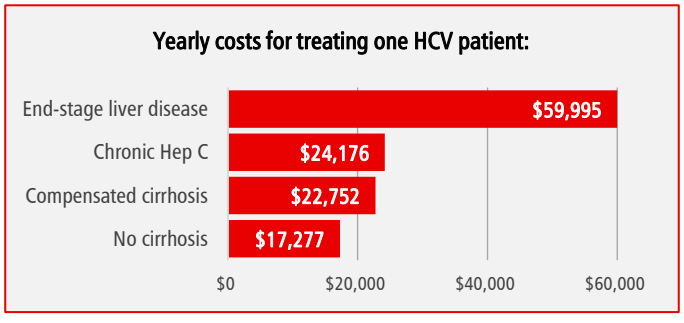
Cause	Statistics	Yearly Costs
Alcohol	**31% of men** and **16% of women** drink more than **14** units of alcohol each week (1 unit = 10 ml of pure alcohol)	**£21bn-£52bn**
Obesity	In 2017, obesity was the primary or secondary cause of **617,000 hospital admissions**, **+191% compared to 2011** Over **25%** of adults and **20%** of school year six children are classified as obese	**2016 - £6.1bn** **2025 ~ £37.2bn**

Fatty liver disease

FLD is the most common chronic liver disease in the world and its global prevalence has been growing rapidly for several decades, being estimated in a 2017 report, at 20-45% in the general population, 70% in diabetic patients and 50-90% in obese people. The two main drivers of the FLD are alcohol consumption and obesity. Confirming the stringency of FLD, in 2017 there were more than 173 products in development targeting FLD, almost a fifth of the pipeline for the gastrointestinal therapy area. The global NASH market, one of the gravest forms of FLD, was estimated at $2.23bn in 2018 and according to some estimations is expected to grow at a CAGR of 39.36% to reach $61.6bn in 2028.

Hepatitis C and B costs

Studies suggest that the number of infected people in the UK range from 216,000 to 466,000, with 86% unaware that they are infected. There is limited information on the financial costs of Hepatitis C in the UK, but lost productivity alone is worth up to £367m per year. Furthermore, a study of five European countries found that hepatitis C treatment resulted in overall savings of £435m annually due to improvements in work productivity, with absenteeism and presenteeism seeing a 16.28% and 19.53% improvement respectively in the study.



The situation is similar in the US, where 80% of HCV positive individuals are not aware of their situation. The Institute of Medicine estimates that 150,000 Americans could die from end-stage liver disease or liver cancer associated with HBV or HCV, while the death rate might triple in the next 10 to 20 years. One research report indicates that the total yearly medical costs for HCV patients could more than double over the next 20 years from $30bn to $80bn.

The fact that a significant number of people with HCV are not aware of the disease and that they do not take any measures to eradicate the virus, may lead to aggravations, including cirrhosis, liver cancer and liver failure, which leads to even higher associated healthcare costs as illustrated in the chart above.

Cirrhosis

Cirrhosis is a condition whereby the liver can no longer be treated, but it can be managed and this is most often done through hospitalisation. The costs associated with cirrhosis hospitalisation in the US have increased 30.2% from 2008 to 2014, reaching $7.4bn. Cirrhosis usually results in complications, such as renal infections, which often lead to death.

Liver Cancer

There were nearly 841,000 new cases of liver cancer diagnosed and 782,000 attributable deaths globally in 2018, according to the World Cancer Research Fund. Liver cancer is considered the fifth most common cancer among men and the ninth most common among women. Liver cancer is also the third leading cause of cancer death. In the US alone, there are about 33,000 diagnoses of liver cancer and 26,000 deaths every year. The costs of the first year of liver cancer treatment can be higher than $62,000, while the first-year cost of a liver transplant can be more than $267,000.

The global liver cancer diagnostics market size was estimated at $8.93bn in 2018 and is expected to grow to $15.4bn by 2025, at a CAGR of 8.1%. The global liver cancer treatment market size is estimated to be $1.01bn in 2020, and is expected to grow to $3.9bn in 2027, at a CAGR of 21.3%.

Source: Royal College of General Practitioners, Clinical and Translational Gastroenterology, GBI Research, Melior Insights Team

THE R&D INVESTMENTS FOCUSED ON LIVER DISEASE

Who is leading research and development in liver disease?

Due to the key importance of the liver in the human body and the prominence of liver disease, there are numerous companies competing for the liver disease market, including the top global pharma. However, as suggested in previously, the liver disease market is continuing to grow and there continues to be significant research and development efforts and investments by governments, big pharma as well as life science start-ups. A few illustrative examples are presented in the subsequent sections.

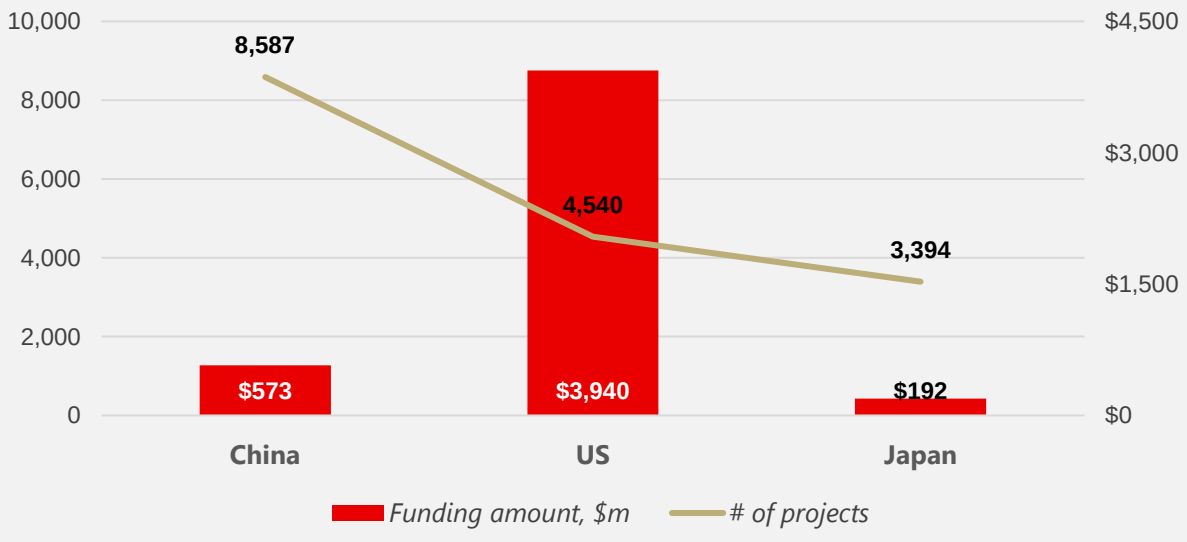
On the basis of treatment, there are a number of areas that are explored for liver disease:

- Anti-viral drugs
- Chemotherapy drugs
- Corticosteroids
- Immunoglobulin
- Immunosuppressant drugs
- Targeted Therapy

Government sponsored research into liver disease

Due to the rising cost of liver disease, both direct and indirect, there has been significant investment from governments sponsoring research and development efforts to find treatments for liver disease.

Below is the data that compares the funding amount and number of projects sponsored by the National Natural Science Foundation of China (NSFC), the US National Institutes of Health (NIH) and Japan's National Grants-in-Aid for Scientific Research (KAKENHI) between 1986 and 2017.



Big Pharma and liver disease

Bayer reported sales of EUR 706m in 2019 for Nexavar, EUR 411m for Stivarga, both being kinase inhibitors used in the treatment of primarily liver cancer, as well as kidney cancer and certain types of thyroid cancers.

Gilead is one of the leading pharma companies producing and selling liver disease drugs with a portfolio of seven leading hepatitis drugs. The global sales of these seven drugs totalled $3.88bn in 2019. The company has also a number of other liver disease drug candidates at different stages of research and development.

Drug	Condition	Global Sales, $m
Epclusa	chronic hepatitis C	1,965
Harvoni	chronic hepatitis C	643
Vemlidy	chronic hepatitis B	488
Viread	hepatitis B / HIV-1	243
Vosevi	chronic hepatitis C	257
Hepsera & Sovaldi	chronic hepatitis B / chronic hepatitis C	285

In January 2020, AstraZeneca received Orphan Drug Designation in the US for two of its drug candidates Imfinzi (an anti-CTLA4) and tremelimumab (potential new medicine), targeting hepatocellular carcinoma (HCC), the most common type of liver cancer.

Initial Public Offerings

In October 2012, Intercept Pharmaceuticals, a clinical stage biopharmaceutical company focused on the development and commercialization of novel therapeutics to treat chronic liver diseases, raised $75m in its IPO. The current market capitalisation of the company is $2.38bn, with worldwide net sales of $249.6m in 2019 for its sole approved drug – Ocaliva, a 40% growth over the prior year.

In June 2018, Madrigal Pharmaceuticals, a clinical-stage biopharmaceutical company focused on the development and commercialization of innovative therapeutic candidates for the treatment of cardiovascular, metabolic and liver diseases, was listed on Nasdaq and raised $200m. In December 2019, the company raised a further $129.42m in a secondary public offering and its current market capitalisation is estimated at $1.79bn.

In March 2019, Genfit, a French biopharmaceutical company focused on discovering and developing drug candidates and diagnostic solutions targeting liver diseases, listed on Euronext Paris and Nasdaq. The company publicly offered 6,650,000 ordinary shares at $20.32, which raised a total of $135.13m. This public offering was for approximatively 17.58% of the company, which values the company at $768.79m.

Licensing deals, merger & acquisitions

In September 2016, Allergan acquired Tobira Therapeutics, a clinical-stage biopharmaceutical company focused on developing and commercialising therapies for NASH and other liver diseases. The deal was estimated at $1.7bn.

In December 2016, Novartis signed a licensing deal to co-develop a FLD drug with Conatus Pharmaceuticals, under the term of the deal Conatus received $50m upfront. The agreement allowed the companies to jointly develop Conatus, a first-in-class oral treatment for NASH.

In November 2018, Roche purchased the preclinical start-up company Jecure Therapeutics, founded in 2015 and developing NLRP3 inhibitors targeting NASH. The financial terms of the deal were not disclosed, but it is known that one year prior to the acquisition, Jecure raised $20m in its Series A funding round.

In August 2019, GlaxoSmithKline exercised its option to license Ionis Pharmaceuticals' antisense medicines for people with chronic hepatitis B virus infection following positive Phase 2 results. As part of the licensing agreement, Ionis is eligible to receive license fees and milestone payments of up to $262 million, as well as tiered royalties in the low double digits on net sales. GSK being responsible for all development, regulatory and commercialization activities and costs.

In October 2019, Novartis paid $80m to obtain the global license to Pliant Therapeutics' preclinical NASH asset and three additional candidates. Novartis has also agreed to fund research and development activities.

In January 2020, Boehringer Ingelheim and Enleofen announced a deal, whereby Boehringer acquired worldwide exclusive rights to Enleofen's preclinical interleukein-11 (IL-11) platform, which is being tested for NASH treatment. No financial details were disclosed, although the companies mentioned that Enleofen could be eligible for payments in excess of $1bn per product in upfront and success-based development and commercialization milestones

Source: Journal of Hepatology, GlobeNewsWire, Annual Reports and websites of the Pharma companies, Melior Insights Team

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I. Investors and their advisers must be prepared that some investments could fail. Melior is only available through professional advisers for qualified investors who genuinely understand and accept risk. Investors should only invest money they do not need access to, and which they can afford to lose. No investment may be entered into, neither in part nor in whole, on the basis of this newsletter. This newsletter is not an offer nor an invitation to subscribe. Melior does not provide or imply investment advice.

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III. Members of the Melior Scientific Team have worked on and taken to market a large number of life science projects during their careers, which spans over the past forty years. Some projects added additional revenue streams to an existing big pharma patent portfolio, some were trade-sales and some were IPOs.

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