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ERIK PENSER BANK

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Modus Therapeutics Holding

High potential at high risk

Major unmet medical need

Modus Therapeutics is a Swedish biotech company that is developing sevuparin – a potentially ground-breaking treatment for sepsis (or blood poisoning, as it was previously known). The company has chosen an indication with a major unmet medical need that currently lacks a treatment alternative – hence the potential for this to achieve blockbuster-level revenues. Approximately 50 million people are affected by sepsis each year, and 11 million sepsis-related deaths occur worldwide, representing almost 20% of all deaths in a year. Modus is not alone in selecting this indication, but competitors are few, suggesting the possibility to take a significant market share.

Planned phase II study in sepsis and other opportunities

According to the top-line data from a ph Ib study, sevuparin has been proven to be safe and tolerable – an encouraging sign for further studies. In addition, sevuparin has shown clinically relevant and immunomodulatory effects. Modus now plans to initiate a ph II study before year-end to evaluate the efficacy of sevuparin and confirm its safety profile in sepsis patients. The company is actively working to broaden its IP through collaborations and is evaluating sevuparin in other forms of systemic inflammation (a clinical study with paediatric patients with severe malaria and studies in anaemia/chronic kidney disease).

High potential at high risk

An investment in Modus offers unique exposure to research into an important, challenging, and potentially lucrative area that has not yet seen success. As with many early-stage biotech companies, Modus still faces a great deal of risk, including clinical trial failures, regulatory setbacks, financial risks, and competition from other companies. The most imminent at present is financing risk, as the company needs to take in capital to carry out its important ph II study. The potential is high, though, and despite these risks, Modus has a low valuation versus other biotech companies at a similar development phase. Should the company succeed with its planned studies and attract one or more licensing partners, the upside to our estimates is high.

Change in estimates

	23e	24e	25e
Total revenue	-	-	-
-	-	-	-
-	-	-	-

Upcoming events

Q2 - report	23 August 2023
Q3 - report	22 November 2023

Company facts (SEK m)

Number of shares	16m
Market capitalization	37
Net debt	0
EV	37
Free float	33%
Daily trading volume, average	25k
Bloomberg Ticker	MODTX SS EQUITY

Analyst

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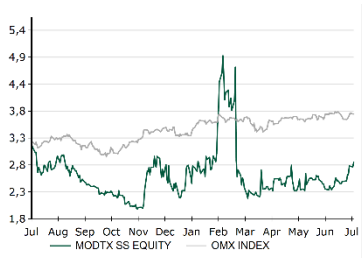
Forecast (SEK m)

	2022	2023e	2024e	2025e
Revenue growth	N.m.	N.m.	N.m.	N.m.
EBITDA, adj.	-18	-24	-49	-52
EBIT, adj.	-18	-24	-49	-52
EPS, adj.	-1,1	-1,5	-3,1	-3,3
EPS growth, adj.	N.m.	N.m.	N.m.	N.m.
BV/share	-	1,4	3,3	0,1
EBIT margin	Neg.	Neg.	Neg.	Neg.
ROE, adj.	Neg.	Neg.	Neg.	Neg.
ROCE, adj.	Neg.	Neg.	Neg.	Neg.
P/BV	-	1,6x	0,7x	32,5x
Net debt / EBITDA	-0,1x	1,0x	1,1x	0,1x

Rating

Potential	5
Risk	5
Financial position	1
History & track record	3
Share price	SEK 2,9

Price Performance 12 months



Conflicts of interest

	Yes	No
Liquidity provider		✓
Certified adviser		✓
Transactions 12m		✓

Investment case

Modus Therapeutics has a skilled management team and support from the company's major shareholders in the form of extensive research and development experience and knowledge of the financing and commercialisation of pharma and medical device projects. Its goal is to develop a treatment specifically for sepsis, while it is evaluating its lead drug candidate, sevuparin, at the research stage in anaemia/chronic kidney disease and in clinical studies in malaria through a partner. An investment in Modus offers unique exposure to the challenging but lucrative market for sepsis drugs, but the path to possible market approval can be long and the risks are high.

There are no approved treatments for sepsis, Modus's chief indication, on the market today, and the unmet medical need is substantial. Every year, millions of people around the world are affected by sepsis and the death rate is high. It is a considerable public health issue, and the World Health Organization has cited management of sepsis as a global health priority. The global burden of sepsis is difficult to determine, but an estimated some 48.9 million people are affected by sepsis each year and 11 million sepsis-related deaths occur around the world annually, representing almost 20% of all deaths in a year.

Because of this unmet medical need for sepsis treatment, there is potential for sevuparin to obtain accelerated approval from agencies such as the FDA and EMA, which would speed up its route to market and allow Modus to generate revenues sooner. Modus has reported positive top-line data from the recently completed clinical ph Ib study, indicating that sevuparin is safe and well-tolerated. Moreover, clinically relevant and immunomodulatory effects on systemic inflammation were observed with sevuparin. This is an encouraging signal for investors and suggests the drug has a decent likelihood of success in subsequent tests. Sevuparin has also demonstrated a comprehensive tolerability and safety profile in previous trials in other indications.

Direct competitors in this area are few, meaning that if Modus succeeds in taking sevuparin all the way to market, the company can potentially capture a significant share of the market. The market potential is difficult to determine, since there is a large unrecorded number of patients with sepsis. We estimate the market potential reaching at least USD 5–10bn by 2028. Crucial to the potential is the timing of treatment – early in the course of sepsis or in septic shock.

As with many early-stage biotech companies, Modus still faces a great deal of risk, including clinical trial failures, regulatory setbacks, financial risks, and competition from other companies. Sepsis as an indication has largely flown under the research world's radar in the past and has been a challenging indication in which to conduct studies because of factors like the historically inconsistent definition of the condition and various ethical considerations. Investing in Modus Therapeutics is high risk, but we believe the potential is also high and could include blockbuster potential. As the company's resources are limited, commercialisation deals with partners will play a key role in the company's future development. Should the company succeed with its planned studies and attract one or more licensing partners, the upside to our estimates is high.

Company description

Modus Therapeutics is a research and development company in the clinical phase of developing a treatment for sepsis and septic shock. It also considers sevuparin, its drug candidate, to have the potential to address other forms of systemic inflammation; it is being evaluated in another study (SEVUSMART*) in paediatric patients with severe malaria and in studies into anaemia/chronic kidney disease. The SEVUSMART study is being carried out and financed by Imperial College London/Wellcome, but Modus retains all commercial rights. This broadening of the drug candidate's areas of use is, of course, positive and provides more opportunities to generate revenues in the long term.

Overview of the project portfolio

Projects	Indication	Pre-clinical	Phase I	Phase II	Phase III	NDA	Marketing
Sevuparin	Sepsis/septic shock		Undertaken	Planned for 2023			2028
	Severe malaria		Ongoing				
	Anaemia/chronic kidney disease	Ready for potential ph IIa study					

Source: Company

Our valuation

We use four key areas across which to assess the company: potential, financial position, risks, and history and track record.

- **Potential (5 points)**

Modus aims to meet the enormous unmet medical need by developing a treatment specifically for sepsis. The sepsis market is challenging to value, with the lack of approved drugs making our estimates highly uncertain. On the other hand, the market potential is extensive, given the enormous patient burden – regardless of which source is used. We thus expect that if Modus can successfully take sevuparin all the way to market with the help of a possible partner and be among the first players to do so, the product has blockbuster potential. As a result, we see the potential as high and thus award 5 points.

- **Risk (5 points)**

Significant development risks persist since Modus is still at a relatively early stage and the path to the first complete ph II data readout is not straightforward. There are also regulatory, operational, and financial risks. Thanks to the good safety and tolerability profile, and the observations of clinically relevant and immunomodulatory effects, the project holds lower risk than projects still in pre-clinical or ph I, but the risk level remains elevated, and so we award 5 points.

- **Financial position (1 point)**

Our assessment of the financial position is based on the reported history. At the end of Q1, cash and cash equivalents totalled SEK 6.6m. The company does not have enough capital right now to conduct the planned ph II study, and it needs to draw in additional capital beyond that announced with the bridge financing. It is positive that Modus has a strong owner in the form of Karolinska Development, which has supported the company with financing over the years. When the ph II study is completed, Modus will probably need to enter into a licensing agreement to take the project all the way to market. If it cannot sign a licensing deal, Modus will need additional financing to push the development project to market or until a commercial partner can take over the development costs. The costs associated with drug development are high and rapidly deplete the coffers. We model the raising of capital in H2 2023 and in 2024 to meet these financing requirements, and we thus award 1 point, given the company's current financial position.

- **History & track record (3 points)**

Modus is a small but dedicated organisation, run with the support of its largest shareholder, Karolinska Development. The board and management possess the necessary knowledge and skills to take the product all the way to market. We also believe members of management are among the largest shareholders, giving them a strong incentive to commit to the company's future development. We currently award 3 points on history and track record.

Probability assumptions

Below, we present the likelihoods of probability used in our models for valuing the company. The probability adjustment is mainly based on existing empirical data on the likelihood of a drug project reaching the market.

This should be seen only as a benchmark. As the company moves ahead in its clinical development, there can be opportunities to seek accelerated approval, for example, as well as the risk that further studies will need to be carried out. Sepsis and septic shock are severe systemic inflammation conditions, and data for such indications is not available. Historically, only one drug candidate has gone all the way to market, but its approval was subsequently withdrawn. For this reason, we use average probabilities for all indications, as shown below. This data and our assumptions suggest **the likelihood of sevuparin reaching the market is 10%.**

	Ph I to Ph II	Ph II to Ph III	Ph III to NDA	Approval	Cumulative
All indication	-	25,0%	45,0%	85,0%	**10%**
Assumed probability					
Sevuparin		25%	45%	85%	**10%**

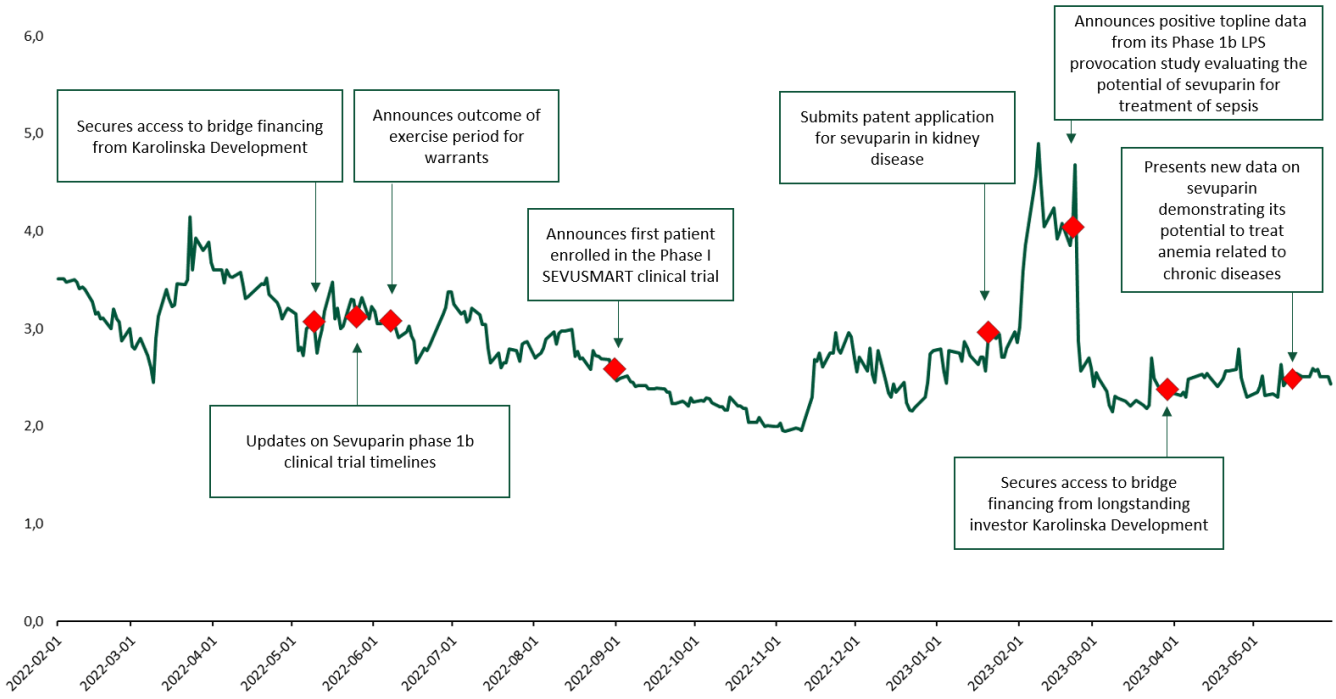
Source: QLS and PharmaIntelligence

History

Modus Therapeutics was founded as Dilaforette AB in 2011 and is a biotech company with its roots in Karolinska Institutet. In 2016, the company renamed itself Modus Therapeutics, and it was listed on Nasdaq First North Growth Market in 2021.

During 2022, it expended considerable focus on its clinical ph Ib study with sevuparin. Much time last year was spent securing financing and managing COVID-19-related delays that affected the development of the clinical study. Recruitment to the ph Ib study ended in September 2022. This year has already seen positive news, with the company's most important sevuparin milestone to date: positive top-line data from the ph Ib study in February. All three dosing levels of sevuparin were assessed as being safe and tolerated across the entire study period, confirming the drug candidate's favourable safety profile. Moreover, treatment with sevuparin demonstrated a statistically significant and dose-dependent increase in white blood cells in certain populations, along with a dose-dependent reduction in the LPS-induced increased respiratory rate. These observations imply clinically relevant and immunomodulatory effects with sevuparin in systemic inflammation conditions.

Significant events and share price development over the past year



Source: Company, MFN

Share price development

The share price has been affected over the past year both by the general negative market sentiment and the announced delays and uncertainties regarding the company's financial situation. The upturns seen have not been lasting, and we believe a deal and more clinical data are needed for a more sustainable effect on the share price. The large drop in February 2023 came, we believe, as market expectations were built up ahead of the quarterly report after the positive top-line data was presented.

Expected news flow

The single most important near-term triggers, in our view, relate to the development of sevuparin projects in sepsis/septic shock. At the same time, the company is working with sevuparin in a project in anaemia/chronic kidney disease for which it filed a patent application in early 2023. We would expect news related to this project to have less of a share price impact in the short term but possibly a significant effect on valuation in the long term. Modus is not running the malaria project itself and so news on this would be positive, but we would not expect it to have a lasting effect on the share price.

Events	Period	Price impact
First patient recruited (sevuparin for sepsis)	2023	High
Data readout (sevuparin for sepsis)	2024	High
Indication selection announced for the anaemia/chronic kidney disease project	-	Medium
Announcement of non-dilutive financing solutions	-	High
Licensing partner announced	-	High
Success in the malaria project	-	Medium

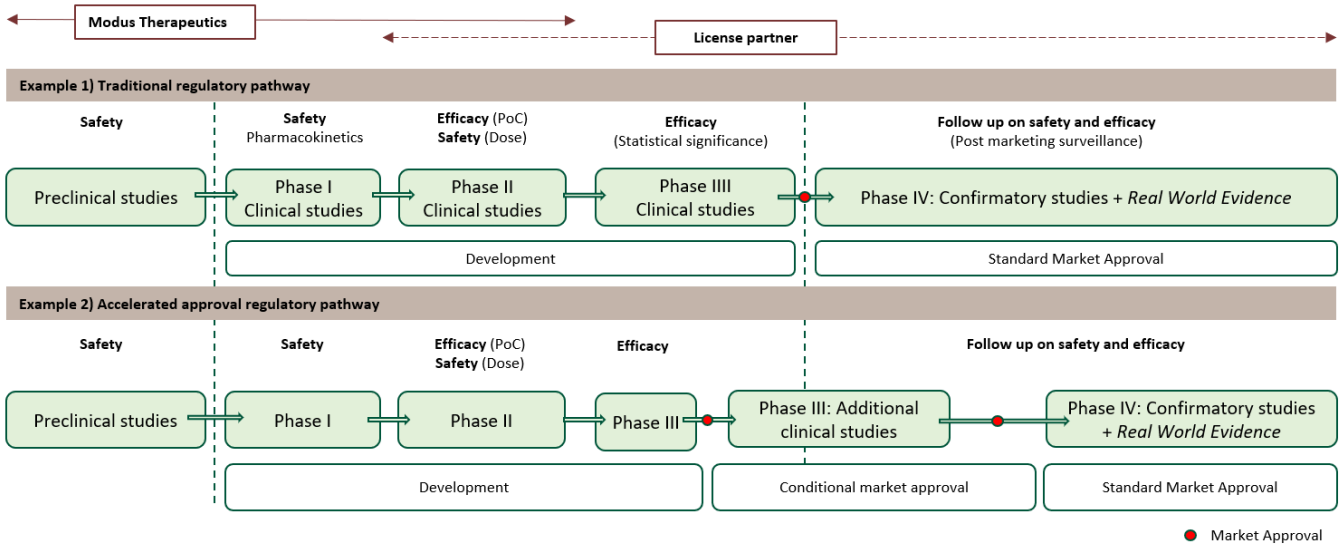
Source: EPB

Business strategy

A drug development company and its product candidates need to undertake all the traditional development steps to begin registration and pre-clinical and clinical studies, along with the approval process in the respective countries where the company intends to sell a drug. The most common business strategies among smaller biotech companies include licensing and partnerships. Companies often seek partnerships and collaborations with major pharma companies, academic institutions, and other stakeholders to access resources, expertise, and financing.

The goal for Modus is either to successfully complete the planned ph II study with sevuparin in sepsis/septic shock and then establish a partnership to take the project all the way to market, or to forge a co-operation before the planned ph II ends. Since there is no approved drug to specifically treat sepsis at present, the route to market could prove far shorter. The opportunities to reduce the regulatory hurdles include *accelerated approval* and *breakthrough therapy* classification. Such approvals can allow for earlier commercialisation of sevuparin while the ph III study to confirm the expected results is conducted (*the company*).

Traditional vs. accelerated authorisation process



Source: Frontiers in Pharmacology; adapted from Detela & Lodge (2019)

Accelerated approval: a rule allowing for drug candidates for serious conditions that fulfil an unmet medical need to be approved based on *surrogate endpoint* or *intermediary endpoints.* This makes it possible for the FDA to approve these drugs more quickly.

A surrogate endpoint used for accelerated approval is a marker – a laboratory measurement, X-ray, physical sign, or other measure – that is believed to predict clinical benefit, but it is not itself a measure of such. Likewise, an intermediary clinical endpoint is a measure of a therapeutic effect considered able to predict the clinical benefit of a drug, such as an effect on irreversible morbidity and mortality.

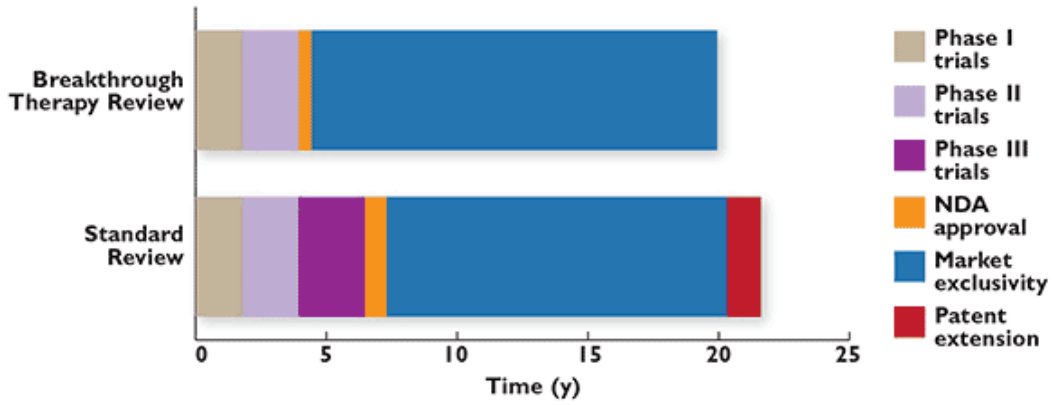
Using surrogate or intermediary clinical endpoints can save valuable time in the drug approval process. The company still needs to carry out studies to further confirm the effect. Received approval can be withdrawn or a drug's labelled indication changed if the studies fail to confirm a clinical benefit or do not demonstrate sufficient clinical benefit to justify the risks associated with the drug.

Breakthrough therapy: a process designed to accelerate the development and review of a drug intended to treat a serious condition where preliminary clinical evidence suggests the drug can have a significant improvement compared with available therapy on one or more clinically significant endpoints.

Source: Läkartidningen magazine, FDA

Data from *Pharmacist* suggests the time to market for a medicine classified as a *breakthrough therapy* differs widely from the standard approval process (see diagram below).

Standard review vs. review for drugs classified as breakthrough therapies



Source: US Pharmacist

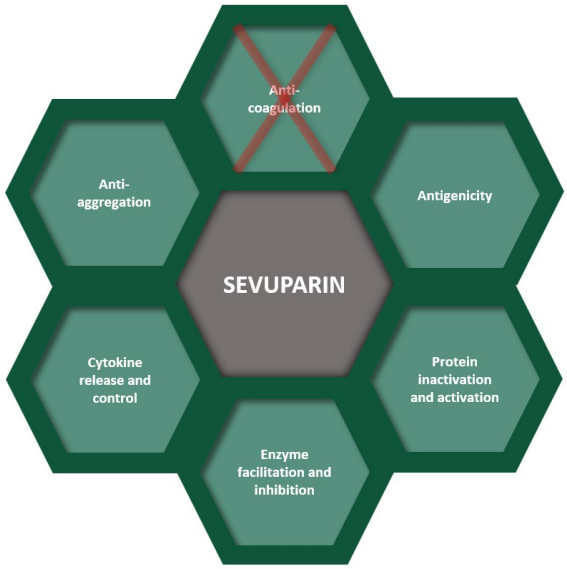
For Modus, this means the time it could take sevuparin to reach the market could be significantly shorter than for a drug candidate undergoing the traditional approval process. This potentially provides several years for the company to benefit from market exclusivity with sevuparin, in terms of patent validity, leading to higher revenues.

Sevuparin – a unique molecule

Sevuparin, the company's drug candidate, is a unique molecule based on heparin – a naturally occurring substance found in the body and produced by the liver and certain cells in blood vessels. Heparin is an anticoagulant (i.e., it prevents blood from clotting) that is often used to prevent or treat blood clots in various medical settings, such as during surgery, with dialysis, and to treat clots in the veins and lungs.

Sevuparin is a chemically modified heparin molecule that has been changed from a typical heparinoid – with anticoagulant properties – to a molecule with a far lower anticoagulant effect. The chemically modified sevuparin molecule makes it possible to provide a substantially greater dose compared with regular anticoagulants on the market without the risk of unwanted bleeding, but still with immunomodulatory properties (*the company*).

Immunomodulatory and other properties of sevuparin



- antigenicity (ability to specifically bind to antigen receptors);
- ability to counteract the aggregation of cells;
- control and release of cytokines;
- stimulation and inhibition of enzymes;
- activation and deactivation of proteins.

Source: Company

Thanks to its unique profile of highly reduced blood-thinning properties and its confirmed safety profile, sevuparin has the potential to use these favourable properties in sepsis/septic shock and other conditions of systemic inflammation. Examples of such conditions are severe trauma, burns, major surgery, and severe malaria (*the company*).

Completed studies and results

Modus Therapeutics has undertaken two preclinical in-vivo studies in mice that have indicated favourable effects in several disease models – including sickle cell anaemia and malaria. Other preclinical studies in mice and in-vitro human testing have also indicated favourable effects in septic conditions. In the ph I trial with healthy volunteers, sevuparin was shown to be safe and tolerated in intravenous single and multiple doses within clinically relevant dose ranges.

Malaria and sickle cell anaemia

Two patient studies (ph Ib and II) demonstrated sevuparin's inhibitory effects on the malaria parasite's ability to bind to blood cells and vascular walls. At present, Modus is participating in a malaria project in collaboration with Imperial College London. Sevuparin is being evaluated in paediatric patients with severe malaria in a clinical ph I study called SEVUSMART. The study will evaluate the safety and tolerability profiles at escalating doses of sevuparin in up to 20 paediatric patients aged between three months and 12 years old with severe malaria. The project is financed through a research grant from Wellcome to Professor Maitland's research group in the KEMRI-Wellcome Trust Programme, Kilifi Kenya, and to an international consortium "*Severe Malaria Africa – a consortium for Research and Trials*" (SMAART), which aims to identify and research new treatments for severe malaria (the company).

In a patient study to treat acute sickle cell anaemia, sevuparin showed a favourable safety profile for use in humans, although no improvement in the disease was seen compared with placebo.

Sepsis

The most recently published data included the top-line results from the ph Ib induction study. The study tested the effects of sevuparin on systemic inflammation triggered by bacterial endotoxin in healthy volunteers (LPS induction study*). Sevuparin doses were investigate in three areas:

1) **Systemic LPS induction**: the endotoxin was injected directly into the bloodstream. Different aspects of using three different doses of sevuparin were compared with placebo: the safety of induced systemic inflammation, any relevant effects on clinical symptoms, and the relevance of the selected doses of sevuparin to the preclinical model.

2) **Local LPS induction**: the endotoxin was injected into the skin (i.e., locally). This part of the study investigated the effects of the three different sevuparin doses on the response to an injection of LPS into the skin.

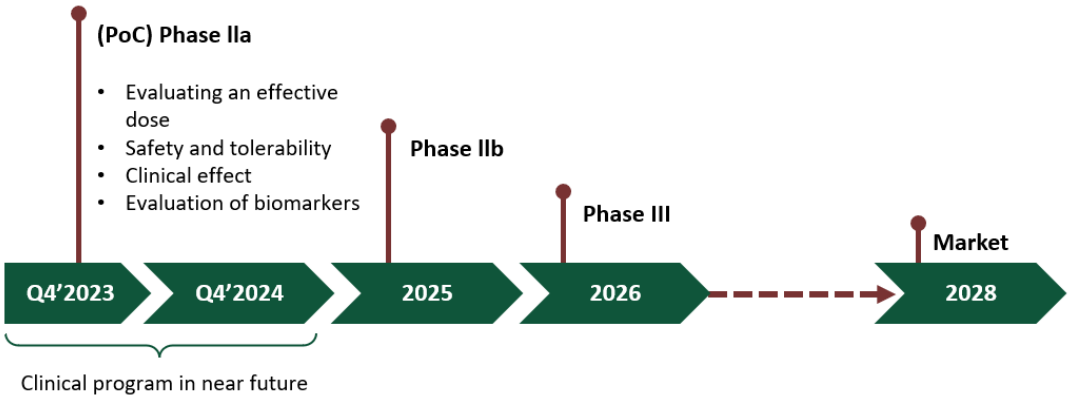
3) **Combined with regular heparin** (enoxaparin): the third part of the study evaluated the potential interaction between enoxaparin (a common form of heparin medication) and sevuparin. Critically ill patients can have an increased risk of blood clots and are often prescribed a low-dose heparin prophylaxis.

***LPS:** Bacterial endotoxins are lipopolysaccharides (LPS), components of gram-negative bacterial cell walls, known to cause fever and diseases when they are injected into the bloodstream. Induction with LPS is a well-established model used to characterise the early stages of septic inflammation by producing a number of measurable symptoms.

As stated above, data showed the drug candidate could modulate levels of certain types of white blood cells and counteract the increased respiratory rate, a characteristic symptom of sepsis and signs in humans induced by this bacterial endotoxin. Both the levels of certain white blood cells and the breathing frequency are important parameters for measuring and are key components in most scales to evaluate systemic inflammation and sepsis. All three tested sevuparin dosing levels were judged to be safe and tolerated throughout the study period, confirming the drug candidate's favourable safety profile in induced inflammatory conditions and in combination with the blood thinner heparin.

Plans for future studies

A clinical ph IIa study is planned to start at the end of 2023, in which the dose of sevuparin that brought the results in the ph Ib study will be used in addition to the standard of care (*SoC*), with SoC as the control. The multi-centre study is expected to include 30–60 sepsis patients. The purpose of this proof-of-concept study is to confirm sevuparin's safety profile in sepsis patients and to assess the relevant clinically beneficial effects. Safety and tolerability can potentially vary, depending on the studied populations, whether these are different types of patients or LPS-induced healthy volunteers. It is thus important to ensure observations correlate with earlier safety and tolerability data before expanding to a larger ph II study. Data from the ph Ib study demonstrates clinical effects early in the clinical pathway. Even in the early hours of systemic inflammation, sevuparin showed a tangible effect. These insights are valuable when considering the assessment of relevant clinical effects in the coming ph IIa study.



Source: Company

Sepsis – an enormous unmet medical need

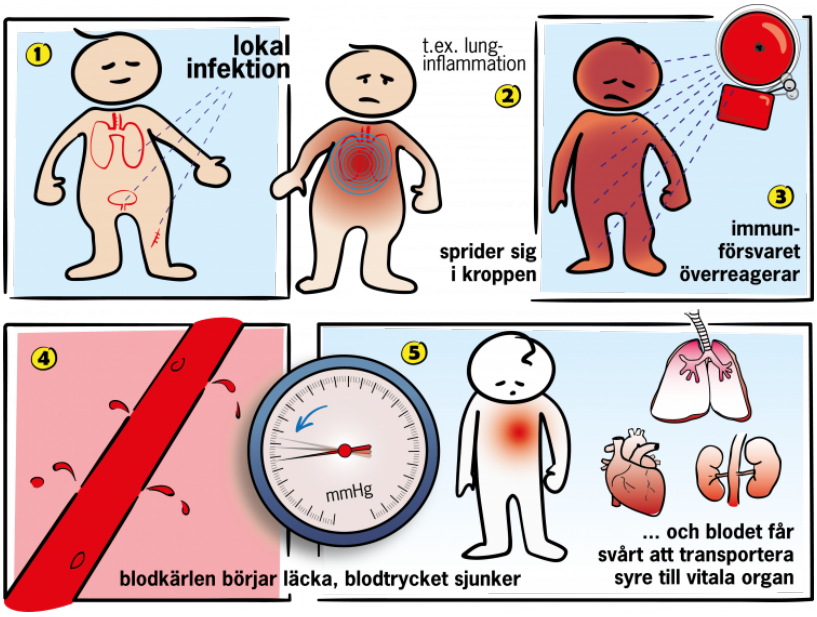
What is sepsis?

Sepsis – previously known as blood poisoning – is a life-threatening condition that occurs when the immune system overreacts to an infection in the body. Sepsis is when the infection spreads to the entire body and affects vital organs like the heart, lungs, and kidneys *(Sepsisfonden).* In 20% of cases, sepsis can develop into septic shock – a subset of sepsis in which underlying circulatory and cellular/metabolic disorders are sufficiently pronounced and significantly increase the risk of death. Every year, millions of people around the world are affected by sepsis. In the US, sepsis contributes to between one-third and half of deaths among hospitalised people, making it the leading cause of death in hospitals *(JAMA, 2014).* The annual cost for treating sepsis patients is USD 24bn in the US alone *(Crit Care Med, 2018).*

A key driving force in the progression of sepsis is the increasing loss of endothelial barrier function; that is, the loss of vascular integrity *(JAMA, 2016)*. This leads to uncontrolled leakage of fluids, proteins, and cells to the surrounding tissue. Patients suffer a rapid drop in blood pressure (*hypotension*) and severe abnormalities in circulatory, cellular, and metabolic function. The drop in blood pressure, which further restricts the supply of oxygen to organs (*hypoperfusion*), contributes to multi-organ failure and death.

90% of all sepsis cases in Sweden and the western world are the result of a bacterial infection, but sepsis can also be caused by fungal or viral infections.

Sepsis disease progression



Simply put, sepsis is when an infection in the body becomes life-threatening. The body's immune system overreacts to the infection, and this can damage the body's organs.

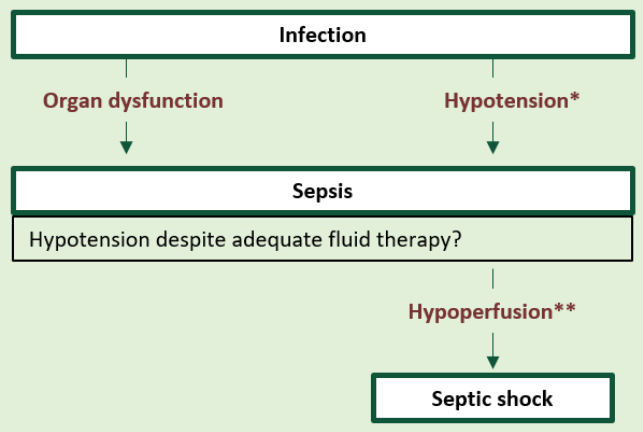
From Swedish: Local infection, for instance pneumonia, is spreading throughout the body; leading to the immune defence system overreaction. Blood vessels begin leaking fluids and blood pressure drops, which makes it difficult for blood to transport oxygen to vital organs.

Source: Vetenskap & hälsa magazine

Around the world, sepsis has particularly high incidence and mortality rates, representing a major public health issue. The global burden from sepsis is difficult to determine, but there were approximately 48.9 million cases of sepsis and 11 million sepsis-related deaths around the globe in 2017, which represents almost 20% of all deaths globally *(The Lancet)*. During 2017, nearly half of all incidents of sepsis around the world were among children, at an estimated 20 million cases. There are, however, significant regional differences in sepsis prevalence and death rates – some 85.0% of sepsis cases and sepsis-related deaths globally are in low- and middle-income countries *(WHO)*. Because of the high incidence and death rates, the WHO has cited management of sepsis as a global health priority.

Recently, a new definition of sepsis has been introduced – sepsis-3 – which now includes organ dysfunction and replaces the older term of *"severe sepsis"*. The diagnostic criteria for sepsis have also been clarified and are now based on a grading of organ dysfunction using SOFA scores.

Structure of the definition of sepsis



***Hypotension** = abnormally low blood pressure

****Hypoperfusion** = reduced blood flow through an organ, which can lead to tissue damage or cell death

Source: LiU

The *SOFA score* (*Sequential Organ Failure Assessment*) grades coagulation and cardiovascular, CNS, liver, lung, and kidney function on a four-point scale. According to sepsis-3 definitions, sepsis occurs when an acute infection causes organ dysfunction corresponding to an increase of ≥ 2 SOFA scores versus pre-sepsis values. Septic shock is when mean arterial pressure that, despite fluid administration, requires drugs for circulatory support *(vasopressors)* to maintain blood pressure at levels >65 mm Hg and elevated lactate ≥2 mmol/L. Three clinical parameters (a quickSOFA (qSOFA)) are proposed as screening tools: affected mental status, systolic blood pressure of ≤100 mm Hg, and a respiratory rate of ≥22/minute. Two of these indicate a deterioration in the prognosis (*Läkartidningen, Sepsis på akuten*).

SOFA points

Organ system/parameter	Score (points)				
	0	1	2	3	4
Respiratory					
PaO2/FIO2 (kPa)	e53.5	<53.3	<40	<26.7	<13.3
Coagulation					
Platelets, x10^9/L	e150	<150	<100	<50	<20
Liver					
Billirubin	<20	20-32	33-101	102-204	>204
Cardiovascular					
Blood pressure	MAP >= 70 mm Hg	MAP <70 mm Hg			
Vasopressors	-	-	Low dose	Medium dose	High dose
CNS					
GCS (Glasgow Coma Scale)	15	13-14	10 - 12	6 - 9	<6
Renal					
Creatinine (µmol/L)	<110	110-170	171-299	300-440	>440
and/or urine output (ml/day)				<500	<200

FIO2: fraction of inspired oxygen
PaO2: partial pressure of oxygen in arterial blood
MAP: mean arterial pressure
Vasopressors: class of drugs that induce vasoconstriction and thereby elevate mean arterial pressure (MAP)

Source: Adapted from the Sepsis and Septic Shock Care Programme (2018)

This new formulation of the concept of sepsis broadens the scope compared to the previous, stricter inflammation-centred approach, better reflecting the current state of knowledge.

One challenge is that many hospitals around the world apply different triage and *"early warning"* systems for timely identification of failing vital signs. Examples are RETTS *(Rapid Emergency Triage and Treatment System),* and MEWS and NEWS (*Modified Early Warning Score* and *National Early Warning Score*). These likely contribute to more rapid detection of sepsis, but use of multiple scoring systems risks creating ambiguity and reducing patient safety.

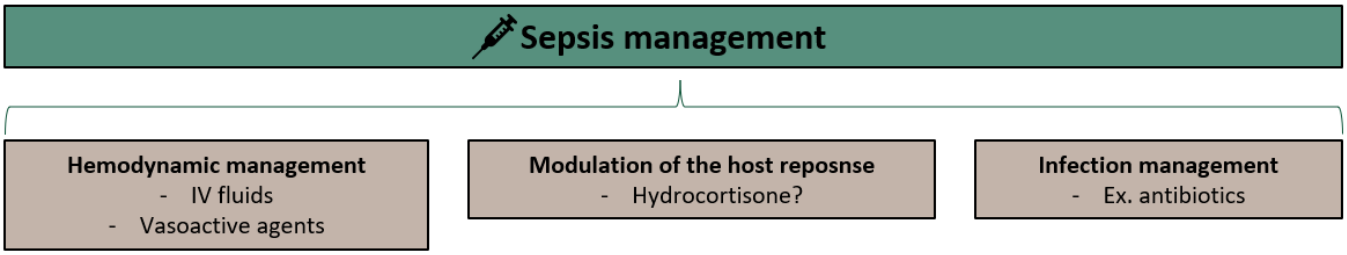
New definitions and diagnostic criteria for sepsis and septic shock, according to Sepsis-3

	Sepsis	Septic shock
Definition	Life-threatening organ dysfunction caused by a dysregulated host response to infection	A subset of sepsis in which particularly profound circulatory, cellular, and metabolic abnormalities are associated with a greater risk of mortality than with sepsis alone
Diagnostic criteria	Organ dysfunction can be identified as an acute change in total SOFA score ≥2 points consequent to the infection	Patients with septic shock can be identified with a clinical construct of sepsis with persisting hypotension requiring vasopressors to maintain MAP ≥65 mm Hg and having a serum lactate level >2 mmol/L (18 mg/dL) despite adequate volume resuscitation

Source: Sepsis and septic shock care programme (2018)

Treatment

Since there is no specific treatment for sepsis, successful initial treatment consists of two key principles: **organ support** and **infection management (i.e., antimicrobial treatment)**. With organ support, treatment is intravenous fluid, given early on, other intravenous therapy to support the circulatory system, and early effective oxygen therapy. Antimicrobial treatment is the early introduction of adequate antibiotics in sufficient doses.



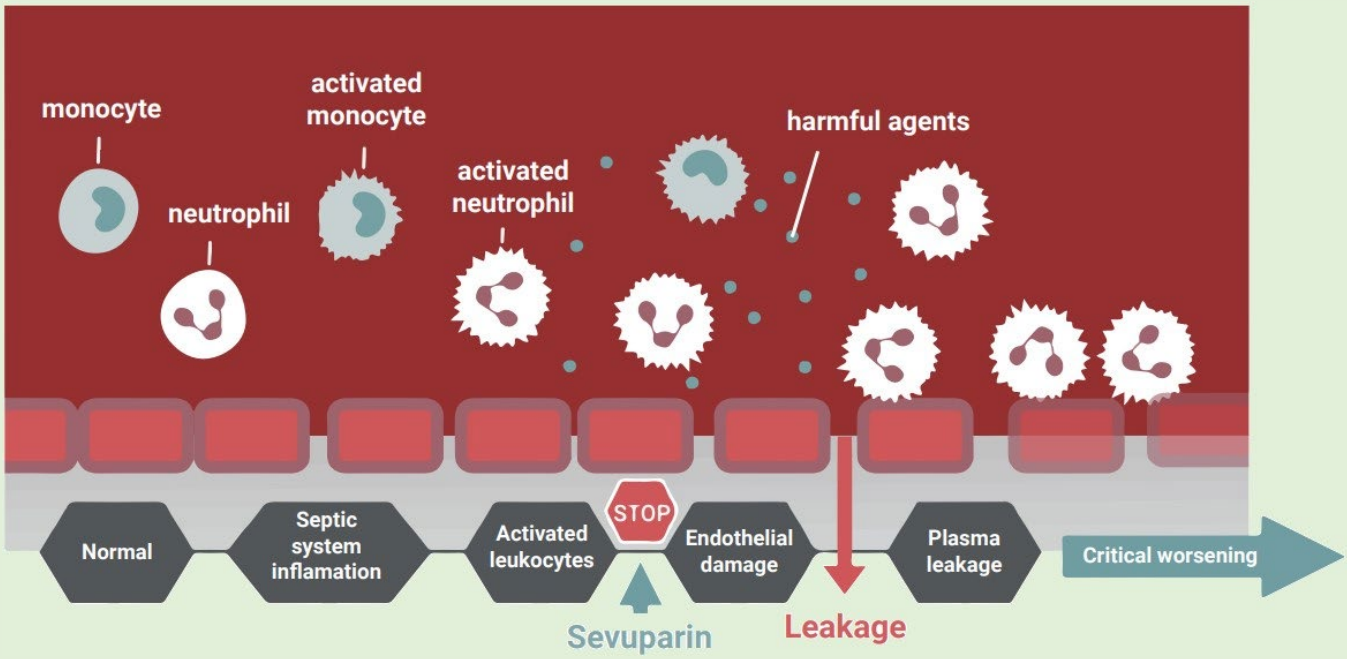
Source: Intensive Care Med

How does sevuparin work against sepsis?

Results from preclinical research shoes that sevuparin counteracts systemic inflammation by binding and neutralising harmful substances released by white blood cells in sepsis and septic shock. This provides robust vessel protection, which is key for blood vessels in the lungs – organs particularly vulnerable to sepsis.

Sevuparin helps to protect the endothelium – the layer of cells covering the inside of the blood vessels – in septic and systemic inflammation. In a normal situation, the threat can be identified and managed through careful regulation of the white blood cells of the immune system and endothelium. In some cases, bacteria that has infiltrated into the blood over-activates the white blood cells while the endothelium loses its protective surface. The white blood cells react by releasing active substances that not only threaten the bacteria but also risk damaging the exposed endothelial lining of blood vessels. This sets in motion a destructive chain of events with ongoing endothelial damage and white blood cells stuck in the vessel walls, which can eventually lead to organ failure, meaning respiratory care in the case of the lungs.

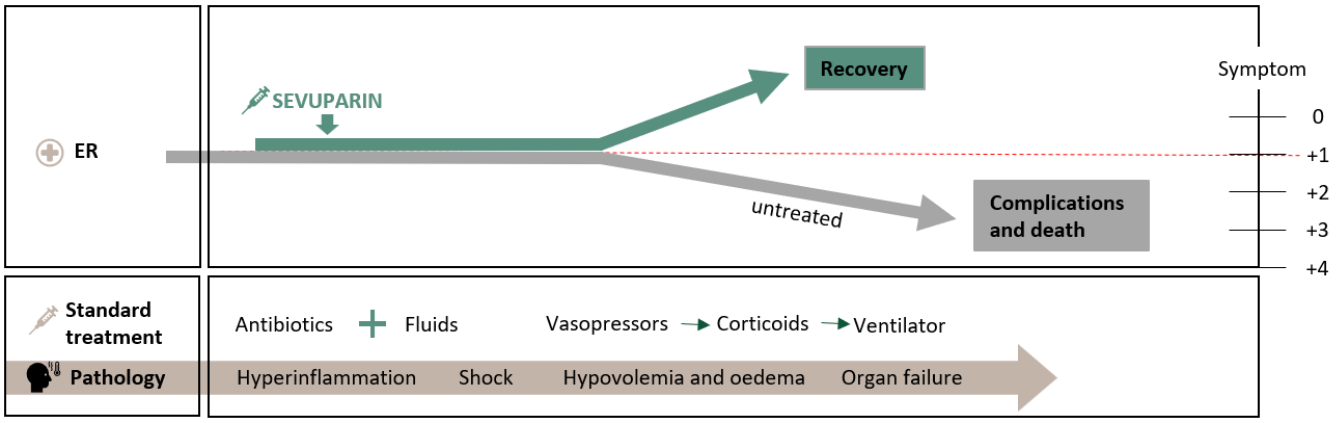
Sevuparin has been shown to bind and neutralise the potentially damaging substances released by the white blood cells and that threaten the chain structure of the blood vessels during systemic inflammation. This can break the destructive molecular chain of events that leads to vascular damage, depletion of white blood cells, and plasma leakage in patients with sepsis/septic shock and other conditions involving systemic inflammation.



Source: Company

Using sevuparin, Modus aims to treat sepsis patients at an early stage. Early prevention of progression to this very serious condition, with its complications and potential death, is crucial when treating sepsis and other systemic inflammations. One further aspect is that the mechanism of sepsis is likely to be similar in a number of different systemic inflammations, which provides an opportunity to broaden the scope. Examples could be severe malaria or serious viral infections, such as COVID-19, but also systemic inflammatory conditions following major trauma or extensive surgical procedures.

At what stage does sevuparin treatment play a role?



Source: Company, adapted

Challenges in the field of sepsis

Despite the enormous unmet medical need, there is still no specific treatment for sepsis. In recent decades, only one product for treating sepsis has been approved and taken to market, despite a painfully long list of new drug candidates being evaluated in clinical trials. Xigris is the only product specifically for treating sepsis that has successfully completed a ph III study. The drug candidate was a human recombinant activated protein C and was used to treat adult patients with severe sepsis with failure of two or more organs. The drug was given as a supplement to standard treatment, such as antibiotics and fluids. Xigris was later withdrawn from the market after a follow-up, placebo-controlled study failed to replicate the results of the first registration study undertaken ten years earlier *(Crit Care Med, EMA).*

Another product used to treat sepsis is GIAPREZA, a drug intended for treatment of persistent low blood pressure in adults with sepsis when other antihypertensive measures are not effective. The product is thus not marketed as a specific sepsis treatment.

In recent decades, there have been in excess of 100 ph II and ph III studies, and *Evaluate Pharma* specifies more than 100 actives projects in research and development in sepsis and septic shock. The number of ongoing and completed studies in sepsis is relatively low compared with other indications, and sepsis can be considered a condition that still flies under the research world's radar. One of the leading causes of death in the world has so far been of limited interest to researchers, not least because of the challenges listed below. Thanks to progress and more understanding over the years, the indication has, however, started to receive more attention.

Sepsis/septic shock	Number of products
Phase III	5
Phase II	14
Phase I	15
Preclinical	51
Research projects	39
Total	**124**

Source: Evaluate Pharma

Strategies tested in the clinic include:

- use of corticosteroids;
- use of anti-tumour necrosis factor (TNF), interleukin-1 (IL-1), platelet-activating factor, and nitric oxide;
- non-selective targeting of inflammatory mediators;
- administration of proteins that stimulate certain aspects of immune system function;
- administration of anticoagulant molecules like activated protein C (APC)

Clinical tests of sepsis have encountered challenges and limitations that can have contributed to the failures or lack of definitive results. Some of the reasons for this include:

- **Heterogeneity**
  Sepsis is a complex condition with various underlying causes, clinical presentations, and patient populations, making it challenging to identify a single intervention or method that is universally effective for all.
- **Lack of standardised definitions and endpoints**
  There have been several amendments to definitions and the criteria to diagnose sepsis over time, leading to variations in patient populations and outcomes across different studies. The lack of standardised endpoints can make it difficult to compare results between trials and to draw clear conclusions.
- **Ethical considerations**
  Sepsis is a life-threatening condition, and conducting randomised controlled trials with placebo-controlled groups can raise ethical questions, since refraining from potentially life-saving interventions may not be ethically justifiable in many cases.
- **Timing and complexity of interventions**
  Starting treatment in time is crucial with sepsis, and delays to treatment start can affect the outcome. Management of sepsis often involves complex interventions, which can be difficult to standardise across different settings and patient populations.
- **Recruitment difficulties**
  It has been difficult with a condition as serious as sepsis to recruit a sufficient number of patients, which can limit the statistical power and generalisability of results.
- **Translation of ph II study results into ph III**
  Key problems persist regarding the translation of clinical results from the ph II to the ph III study. The first attempts to find a treatment for sepsis date back almost 30 years, when a ph II study showed an improvement in 28-day survival, but this could not be replicated in the subsequent ph III trial.

How to respond to these challenges?

- **Standardised definitions and endpoints**
  The establishing of standardised definitions and endpoints for sepsis can ensure stringency across different trials. It remains to be seen what effect the implementation of the sepsis-3 framework will have on future clinical studies. Unlike previous definitions, sepsis-3 has been built upon a scientific approach, a well-described work process, systematic literature reviews, and analysis of electronic health databases. This should aid comparisons between results and make meaningful conclusions possible.
- **Early and aggressive intervention**
  Assurance of rapid and consistent implementation can contribute to successful clinical trials.
- **Collaborations and multi-centre trials**
  The involvement of several institutions and patient populations can increase the sample size and diversity of participants, leading to more robust and generalisable results.
- **Ethical considerations**
  Considerations including appropriate informed consent procedures and the balancing of potential benefits and risks with intervention measures should be carefully managed in clinical trials with sepsis.

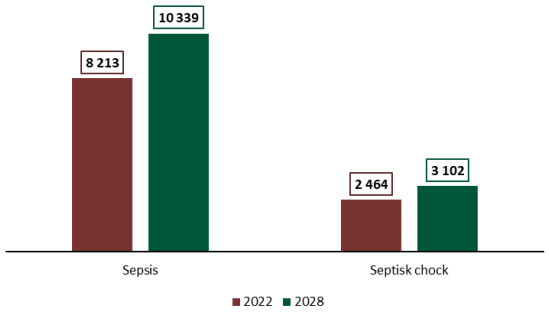
Source: Crit Care Med

Sepsis market

How the market for sepsis drugs is valued varies widely depending on which source is used, and data is generally scarce. As there is no approved drug specifically to treat sepsis at present, we must rely on forecasts for as yet unapproved drugs and sales data for drugs used to manage sepsis but not specifically designed for that purpose.

We assume a market size of USD 10bn for sepsis and USD 3bn for septic shock in 2028. One benchmark we use is *Vantage Market Research*'s USD 3.2bn estimate for the septic shock market in 2022, which it expects to grow by a CAGR of 7% until 2030. Given the above-mentioned challenges, investor should keep in mind the considerable uncertainty in these estimates. On account of the great uncertainty about the market value for both sepsis and septic shock, we have undertaken a sensitivity analysis to consider the total market potential for sevuparin in 2028, based on different levels of incidence and global average pricing. We have assumed that incidence grows by 4% a year. The pricing assumptions are based on the average of our assumed price scenarios for sevuparin in Europe and the US, in turn based on Xigris's price per treatment session (for more on this, see the Pricing section).

The market for sepsis-related drugs by value (USDm)



Source: EPB

Sensitivity analysis: market size for sepsis and septic shock – per year

Sepsis

	Newly diagnosed patients (USA and EU4+UK) (millions)				
Assumed global pricing	3,8	4,2	4,6	5,0	5,4
$500	1 900	2 100	2 300	2 500	2 700
$1 000	3 800	4 200	4 600	5 000	5 400
$2 250	8 550	9 450	10 350	11 250	12 150
$4 000	15 200	16 800	18 400	20 000	21 600
$6 000	22 800	25 200	27 600	30 000	32 400

Septic shock

	Newly diagnosed patients (USA and EU4+UK) (millions)				
	3,8	4,2	4,6	5,0	5,4
$1 500	855	945	1 035	1 125	1 215
$3 000	1 710	1 890	2 070	2 250	2 430
$4 500	2 565	2 835	3 105	3 375	3 645
$6 000	3 420	3 780	4 140	4 500	4 860
$7 500	4 275	4 725	5 175	5 625	6 075

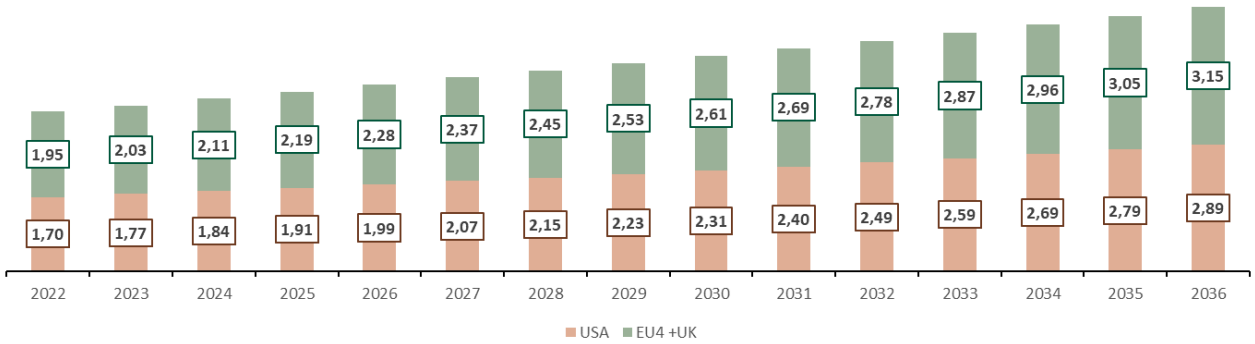
Source: EPB

Growth in the market is expected to depend on the increasing incidence of sepsis, as well as growing awareness of early diagnosis and treatment, plus a focus on improving outcomes for sepsis patients in terms of cost-effectiveness.

Our estimates consider two scenarios: early treatment of sepsis patients and treating patients in septic shock. We have analysed the markets in the US and EU4+UK, using incidence data from the US and the EU.

We estimate the number of newly diagnosed sepsis patients at 1.7 million a year in the US and 2.0 million a year in the EU for 2022, and we expect this to expand by an average of 4% a year. In addition, we assume that some 75% of these patients are treated at acute care hospitals, representing the addressable population for sevuparin, while the remaining patients receive treatment outside the acute inpatient setting *(CDC)*. In scenario two, we assume around 20% of these patients progress to septic shock (*American Journal of Respiratory & Critical Care; Global Sepsis Alliance; JAMA).*

Number of newly diagnosed sepsis patients (millions)



Source: *American Journal of Respiratory & Critical Care; Global Sepsis Alliance; JAMA*

Pricing

Market launch of sevuparin would take place in 2028 at the earliest, we believe, which is in line with the company's timetable for trials. In terms of pricing, we start with the price for the no longer approved Xigris, which was priced at about USD 6,800–8,000 per treatment session in the US (*Scientific American, PharmaIntelligence*). For scenario one, we assume a price of USD 3,000 in the US and USD 1,500 in the EU, while for scenario two, we assume USD 6,000 in the US and USD 3,000 in the EU. Market penetration is 15% in scenario one and 30% in scenario two.

We expect the company can enter into a licensing deal after the clinical ph II study at the earliest, once data has been summarised, which we believe would be in 2026. We model a deal value of USD 185m for scenario one and USD 110m for scenario two, with USD 15m in a one-off payment and high single-digit royalties (8%). Our deal value assumptions are above both mean and median levels for completed deals in sepsis-related areas in recent decades. As there is no approved treatment for sepsis, we instead rely on previous agreements for drugs with blockbuster potential.

Based on the above assumptions, we estimate sevuparin can reach peak sales of just under USD 2bn in scenario one and some USD 1.6bn in scenario two, with sales starting in 2028 at the earliest.

Selection of completed deals in sepsis and related indications

Date	Company	Deal partner	Deal value (mUSD)	Upfront payment (mUSD)	Phase when signing	Phase now
2021-03-05	TTY Biopharm	PAION	1	1	Approved	Active
2005-05-23	Merck & Co	BioXell	3	3	Pre-clinical	Inactive
2013-09-21	Tenax Therapeutics	Orion	5	N/A	Phase II	Active
2015-05-20	China Medical System	Faron Pharmaceuticals	6	N/A	Phase II	Inactive
2005-10-03	ENZON PHARMACEUTICALS	NatImmune	10	10	Phase I	Inactive
2009-08-12	Pfizer	Forest Laboratories	40	40	Phase III	Active
2007-11-29	Sanofi	Regeneron Pharmaceuticals	68	68	Pre-clinical	Active
2005-12-08	AstraZeneca	Protherics	340	28	Phase II	Inactive
Average			**59**	**25**		
Median			**8**	**19**		

Source: Evaluate Pharma

Addressable population for scenario one: early treatment of sepsis

		2022	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036
USA																
Sepsis incidense																
Newly diagnosed patients with sepsis (millions)	4%	1,7	1,8	1,8	1,9	2,0	2,1	2,1	2,2	2,3	2,4	2,5	2,6	2,7	2,8	2,9
Source: American journal of Respiratory & Critical care; Global Sepsis Alliance; JAMA																
Number of patients admitted to emergency care	75%															
Adressable population for sevuparin *(millions)*		1,3	1,3	1,4	1,4	1,5	1,6	1,6	1,7	1,7	1,8	1,9	1,9	2,0	2,1	2,2
								START						PEAK		
Launch curve		0	0	0	0	0	0	0,03	0,15	0,25	0,45	0,75	0,8	1	1	1
Market penetration	15%															
Number of patients		0	0	0	0	0	0	7 246	37 606	65 058	121 554	210 289	232 832	302 099	313 579	325 495
Netto price per treatment (USD)	3 000						3 000	3 090	3 183	3 278	3 377	3 478	3 582	3 690	3 800	3 914
Change in price	3%															
Sales (mUSD)		**0**	**0**	**0**	**0**	**0**	**0**	**22**	**120**	**213**	**410**	**731**	**834**	**1 115**	**1 192**	**1 274**
EU4 + UK																
Sepsis incidense	1,95kk/år															
Newly diagnosed patients with sepsis (millions)	4%	**2,0**	**2,0**	**2,1**	**2,2**	**2,3**	**2,4**	**2,4**	**2,5**	**2,6**	**2,7**	**2,8**	**2,9**	**3,0**	**3,1**	**3,2**
Source: Intensive care medicine; Critical Care; Eurostat																
Number of patients admitted to emergency care	75%															
Adressable population for sevuparin *(millions)*		**1,5**	**1,5**	**1,6**	**1,6**	**1,7**	**1,8**	**1,8**	**1,9**	**2,0**	**2,0**	**2,1**	**2,1**	**2,2**	**2,3**	**2,4**
								START						PEAK		
Launch curve		0	0	0	0	0	0	0,03	0,15	0,25	0,45	0,75	0,8	1	1	1
Market penetration	15%															
Number of patients		0	0	0	0	0	0	8 263	42 639	73 339	136 234	234 322	257 942	332 745	343 393	354 382
Netto price per treatment (USD)	1 500						1 500	1 545	1 591	1 639	1 688	1 739	1 791	1 845	1 900	1 957
Change in price	3%															
Sales (mUSD)		**0**	**0**	**0**	**0**	**0**	**0**	**13**	**68**	**120**	**230**	**407**	**462**	**614**	**652**	**694**
Total sales **EU4+UK+USA (mUSD)**		**0**	**0**	**0**	**0**	**0**	**0**	**35**	**188**	**333**	**640**	**1 139**	**1 296**	**1 728**	**1 844**	**1 968**

Revenue estimates for scenario one (not risk-adjusted)

		2022	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036
Total sales EU4+UK+USA (mUSD)		**0**	**0**	**0**	**0**	**0**	**0**	**35**	**188**	**333**	**640**	**1 139**	**1 296**	**1 728**	**1 844**	**1 968**
Royalty (mUSD)	8%	0	0	0	0	0	0	3	15	27	51	91	104	138	148	157
			Q3'24	*Q4'24*												
			Fas IIa	*Fas IIb*		*Fas III*		*Lansering*								
Milestone payments (mUSD)						15		15		30		50		75		
Revenue for Modus Tx (mkr)	10,49	**0**	**0**	**0**	**0**	**157**	**0**	**187**	**157**	**595**	**537**	**1480**	**1088**	**2 237**	**1 548**	**1 651**

Addressable population for scenario two: treatment of septic shock

		2022	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036
USA																
Sepsis incidense	1,7 kk/år															
Newly diagnosed patients with sepsis (millions)	4%	**1,7**	**1,8**	**1,8**	**1,9**	**2,0**	**2,1**	**2,1**	**2,2**	**2,3**	**2,4**	**2,5**	**2,6**	**2,7**	**2,8**	**2,9**
Source: American journal of Respiratory & Critical care; Global Sepsis Alliance; JAMA																
Number of patients admitted to emergency care	75%															
Number of patients with septic shock	20%															
Adressable population for sevuparin *(millions)*		**0,3**	**0,3**	**0,3**	**0,3**	**0,3**	**0,3**	**0,3**	**0,3**	**0,3**	**0,4**	**0,4**	**0,4**	**0,4**	**0,4**	**0,4**
								START						PEAK		
Launch curve		0	0	0	0	0	0	0,03	0,15	0,25	0,45	0,75	0,8	1	1	1
Market penetration in septic shock	30%															
Number of patients		0	0	0	0	0	0	2 898	15 042	26 023	48 622	84 116	93 133	120 840	125 432	130 198
Netto price per treatment (USD)	6000						6 000	6 180	6 365	6 556	6 753	6 956	7 164	7 379	7 601	7 829
Price change	3%															
Sales (mUSD)		**0**	**0**	**0**	**0**	**0**	**0**	**18**	**96**	**171**	**328**	**585**	**667**	**892**	**953**	**1 019**
EU																
Sepsis incidense	1,95kk/år															
Newly diagnosed patients with sepsis (millions)	4%	**2,0**	**2,0**	**2,1**	**2,2**	**2,3**	**2,4**	**2,4**	**2,5**	**2,6**	**2,7**	**2,8**	**2,9**	**3,0**	**3,1**	**3,2**
Source: Intensive care medicine; Critical Care; Eurostat																
Number of patients admitted to emergency care	75%															
Number of patients with septic shock	20%															
Adressable population for sevuparin *(millions)*		**0,3**	**0,3**	**0,3**	**0,3**	**0,3**	**0,4**	**0,4**	**0,4**	**0,4**	**0,4**	**0,4**	**0,4**	**0,4**	**0,5**	**0,5**
								START						PEAK		
Launch curve		0	0	0	0	0	0	0,03	0,15	0,25	0,45	0,75	0,8	1	1	1
Market penetration in septic shock	30%															
Number of patients		0	0	0	0	0	0	3 305	17 056	29 335	54 494	93 729	103 177	133 098	137 357	141 753
Netto price per treatment (USD)	3000						3 000	3 090	3 183	3 278	3 377	3 478	3 582	3 690	3 800	3 914
Price change	3%															
Sales (mUSD)		**0**	**0**	**0**	**0**	**0**	**0**	**10**	**54**	**96**	**184**	**326**	**370**	**491**	**522**	**555**
Total sales EU4+UK+USA (mUSD)		**0**	**0**	**0**	**0**	**0**	**0**	**28**	**150**	**267**	**512**	**911**	**1 037**	**1 383**	**1 475**	**1 574**

Revenue estimates for scenario two (not risk-adjusted)

		2022	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036
Total sales EU4+UK+USA (mUSD)		**0**	**0**	**0**	**0**	**0**	**0**	**28**	**150**	**267**	**512**	**911**	**1 037**	**1 383**	**1 475**	**1 574**
Royalty (mUSD)	8%	0	0	0	0	0	0	2	12	21	41	73	83	111	118	126
			Q3'24	*Q4'24*												
			Fas IIa	*Fas IIb*		*Fas III*		*Lansering*								
Milestone payments (mUSD)						15		15			30			50		
Revenue for Modus Tx (mkr)	10,49	**0**	**0**	**0**	**0**	**157**	**0**	**181**	**126**	**224**	**745**	**765**	**870**	**1 685**	**1 238**	**1 321**

Source: EPB

Our estimates are highly dependent on the chosen penetration rate and pricing once the product is on the market. Below, we present a scenario analysis with the impact of the penetration rate and pricing on peak sales levels for sevuparin in both scenarios for the US.

Sensitivity analysis: sepsis

Top sales dependent on assumed price and market penetration level (USDm)

Price USA (USD)	Market penetration 5%	10%	15%	20%	25%
500	109	219	328	437	547
1 500	328	656	984	1 312	1 640
3 000	656	1 312	1 968	2 624	3 279
5 000	1 093	2 186	3 279	4 373	5 466
6 000	1 312	2 624	3 935	5 247	6 559

Sensitivity analysis: septic shock

Top sales dependent on assumed price and market penetration level (USDm)

Price USA (USD)	Market penetration 10%	20%	30%	35%	40%
2 000	175	350	525	612	700
4 000	350	700	1 049	1 224	1 399
6 000	525	1 049	1 574	1 836	2 099
8 000	700	1 399	2 099	2 449	2 798
10 000	875	1 749	2 624	3 061	3 498

Source: EPB

Competitors

As far as we are aware, there are only two companies ready for ph III with specific sepsis and septic shock projects: **Adrenomed** and **Inotrem**.

Adrenomed is a privately financed German biotech company in the clinical phase that aims to develop precision medicine to restore vascular integrity in septic shock. Its key product candidate is Adrecizumab, a monoclonal antibody in clinical development for sepsis and septic shock. Adrecizumab targets the vascular protective peptide adrenomedullin, which is an important regulator of vascular integrity. Its strategy is to develop biomarker-driven approaches that make it possible to identify patients likely to benefit from treatment with Adrecizumab.

Adrenomed has successfully undertaken a ph II proof-of-concept (PoC) study and plans to start clinical ph III. Results showed that relative mortality was significantly reduced by more than 50% after day 28 (*MedNous, 2023*; *Adrenomed).*

Inotrem is also a privately financed biotech company, and it was founded in 2013 in France. The company has developed a concept for immunomodulation that targets TREM-1 to control unbalanced inflammatory responses. TREM-1 is an innate immune enhancer, the use of which aims to restore a balanced response in inflammatory diseases. The drug candidate is called nangibotide and is a peptide and *first-in-class* TREM-1 inhibitor with applications in severe conditions, such as septic shock and COVID-19. During 2019, Inotrem gained fast track designation for its sepsis project, supporting our argument that this is also possible for Modus, given the lack of other specific treatment options for sepsis.

Inotrem has also successfully concluded its ph IIb study, ASTONISH, in septic shock. The study showed a therapeutic effect with nangibotide in patients with high levels of the immuno-activating marker sTREM-1. ASTONISH also showed that nangibotide boosts respiratory, heart, and kidney function and offered evidence of an improvement in mortality at day 28 (*Inotrem*).

Unlike Modus, both Inotrem and Adrenomed are applying the strategy of using biomarkers in the treatment of sepsis patients. Precision medicine can be both positive and negative from a number of aspects: pricing, the time taken to carry out sampling, and population size. Modus's drug candidate sevuparin holds a clear advantage in that it can be applied across a broader patient population. If Inotrem or Adrenomed were to succeed in taking their products to market, it would, of course, limit the market for sevuparin. Another factor is which of the companies can reach the market first – since being the first to launch a drug for a patient group has historically been something to strive for. According to data from *McKinsey & Company* that investigated the importance of being the first to market, the first drugs out have an average of 6% higher market share than subsequent drugs out for ten years after launch.

Other indications – anaemia caused by chronic kidney disease

Earlier in May, the company announced data from a collaboration with Professor Maura Poli and her research group in Brescia that showed sevuparin has the potential to be developed as a treatment for anaemia in patients with certain chronic diseases. The full results will be presented at the European Hematology Association's annual meeting in June. The study was carried out in mice and healthy volunteers, and the results indicate that sevuparin strongly suppresses the iron-regulating hormone hepcidin. Should the company decide to progress with the new indication of anaemia caused by chronic kidney disease, the next step could be a ph IIa study, since there is already extensive safety and tolerability data for sevuparin.

This broadening of the drug candidate's areas of use is, of course, positive, providing more opportunities to generate revenues in the long term. For the time being, we do not calculate potential revenues from sevuparin in anaemia caused by chronic kidney disease in our models, but our view could change should the company progress further in planning for this indication.

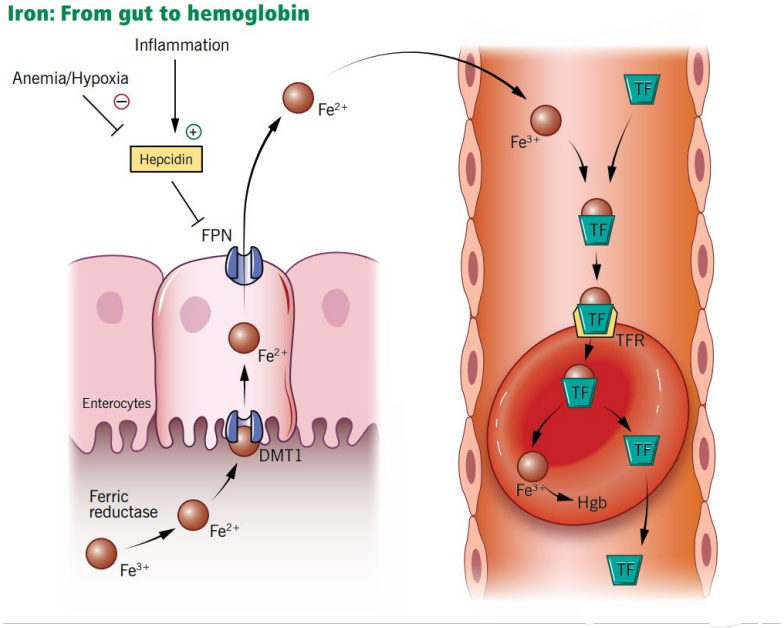
Anaemia/chronic kidney disease

Over the past decade, increasing attention has been paid to chronic kidney disease (CKD) and chronic kidney failure as potential health issues around the world. Incidence of chronic kidney disease has risen for various reasons, including an ageing population and ever more people affected by cardiovascular diseases and type 2 diabetes. Several research studies have shown that the number of people with chronic kidney disease can be as high as 15% (or more) of the adult populations in countries including Norway, the UK, the US, China, Canada, Australia, and Japan *(Läkartidningen)*.

Anaemia is one of the most serious complications of chronic kidney disease. The kidneys play a key role in the production of erythropoietin, a hormone that stimulates bone marrow to produce red blood cells. In CKD, production of erythropoietin is reduced as kidney function worsens, leading to lower production of red blood cells.

This reduced red blood cell production with CKD can result in anaemia, which is characterised by a lower-than-normal level of haemoglobin in the blood. As haemoglobin's role is to transport oxygen to the body's tissues, a lower haemoglobin level can cause symptoms including fatigue, weakness, breathlessness, dizziness, and pale skin. There are other factors that can also contribute to anaemia in CKD. These include deficiencies of iron, folic acid, and vitamin B12 – essential to the production of red blood cells. Moreover, CKD can bring about changes to bone marrow and reduce the lifespan of red blood cells.

Iron absorption is controlled by several proteins

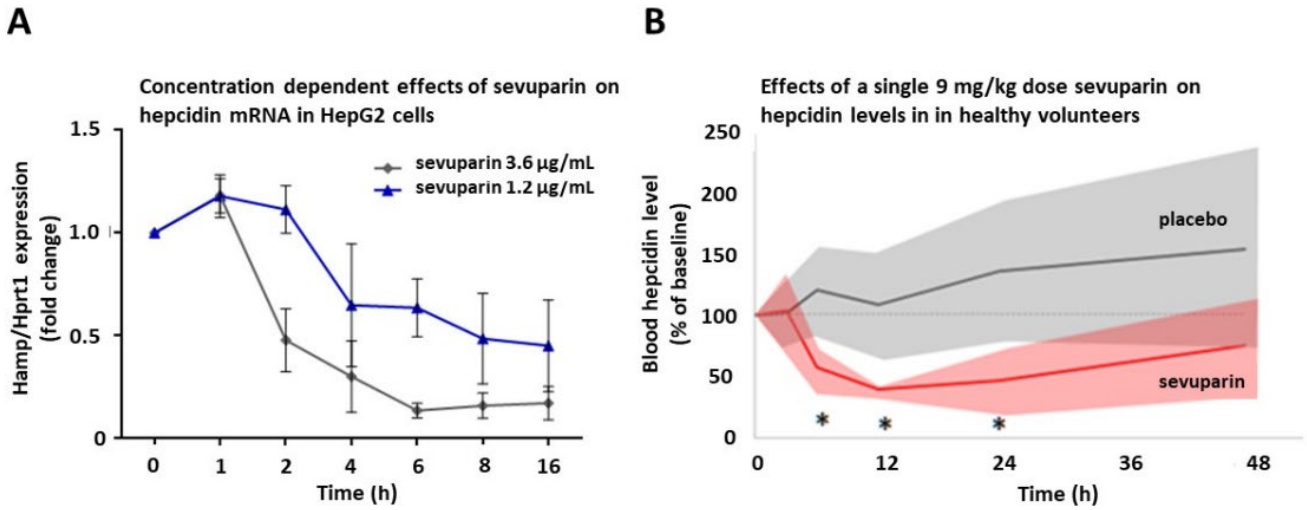


Source: Cleveland Clinic Journal of Medicine

Fact box: Hepcidin
Hepcidin is the body's iron regulator. It determines how much iron is absorbed from food by inhibiting the release of iron from the intestinal epithelial cells, and it controls how much iron is available in the blood by inhibiting its release from iron stores in the bone marrow and liver. Hepcidin synthesis increases with the availability of iron and in inflammation. A rise in hepcidin during inflammation explains the onset of secondary anaemia (anaemia resulting from inflammatory disease). The inflammatory cells, mainly monocytes and lymphocytes, release IL-6, which stimulates hepcidin synthesis. The released hepcidin blocks the export of iron from macrophages to erythroblasts. Erythroblasts cannot produce haemoglobin without iron and do not develop into erythrocytes.
Source: Region Skåne

Modus announced in May that it has generated data showing its drug candidate sevuparin has the ability to strongly suppress hepcidin at doses not considered as carrying the risk of causing side effects. The research findings support the possibility of developing sevuparin as a new treatment for hepcidin-related disorders such as anaemia caused by chronic kidney disease and other chronic inflammatory diseases. High levels of hepcidin are considered a factor in causing and aggravating the anaemia that often complicates chronic kidney disease and chronic inflammatory diseases. Elevated hepcidin is also believed to play a role when patients do not respond as expected to current standard anaemia treatments, as its action can be a potential resistance mechanism in these cases *(the company)*.

Preliminary results



Source: EHA

Ongoing activity in the field

Disc Medicine is a company on an interesting journey, with its discovery that reducing hepcidin levels can help to raise iron levels, thus treating anaemia caused by inflammation. It is a biotech company focused on developing therapies for haematological diseases. By identifying and targeting biological mechanisms that affect haematopoietic stem cells and their microenvironment, Disc Medicine aims to create new treatments in haematology.

Its drug candidate DISC-0974 (anti-HJV mAb) is a monoclonal antibody against haemojuvelin (HJV) that is intended to suppress hepcidin production and increase iron levels to treat anaemia caused by various types of inflammation in the body. Disc Medicine has investigated the level above hepcidin and identified HJV, which plays a key role in iron metabolism and is required for hepcidin production. The company believes a focus on HJV offers a unique, selective, and potent approach to suppressing hepcidin and normalising iron metabolism *(Disc Medicine)*.

Disc Medicine had already entered into a licensing agreement with AbbVie in the preclinical phase. The company conducted a clinical ph I study in healthy volunteers in 2021 and plans to develop DISC-0974 to treat several forms of anaemia caused by inflammation. It has initiated a ph Ib/II study in patients with anaemia caused by myelofibrosis (MF) and plans further studies in patients with anaemia caused by CKD as well as other indications. Should Disc Medicine begin clinical trials in anaemia caused by CKD, it would be a direct competitor to Modus, while its licensing agreement with AbbVie gives hope for interest in the field from Big Pharma.

Financial position and overall financial forecasts

Modus is in early-stage development and has not yet reported any revenues. Its 2022 operating expenses were lower y/y, but they were affected by delays to clinical studies and reduced R&D spending. Cash and cash equivalents were around SEK 10m as of year-end. Given cash flows from operating activities at just over SEK -18m and its planned clinical study, we believe the company will need to secure additional financing to complete this crucial ph II study. Bearing this in mind, we have included the raising of capital in our model.

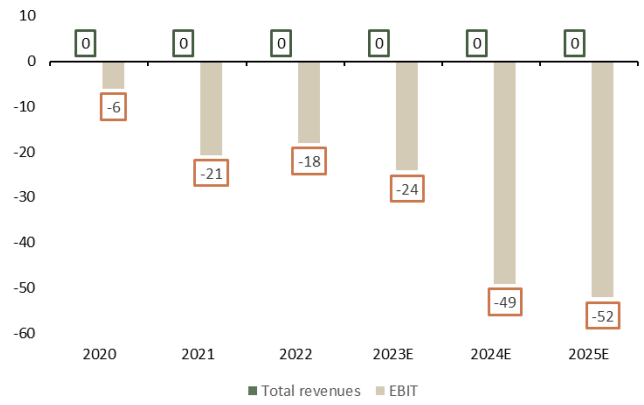
The listing issue took place in June-July 2021, after which the company received around SEK 33m before issue costs. The exercise period of the series TO1 warrants ended in June 2022, but no such warrants were exercised. The share price was lower than the subscription price throughout the exercise period, which likely contributed to the lack of interest in the TO1. Since its listing, the company has secured financing from KDEV on two occasions, and the latest bridge financing was announced at the end of March 2023.

Date		Capital injection (SEKm)
2021	Stock exchange listing	33
2022	TO1	0
2022	Bridge financing	11
2023	Bridge financing	7

Source: MFN

We expect the operating losses to increase owing to the clinical studies to be conducted and the high associated R&D costs. Operating costs are expected to comprise R&D costs for the various development programmes, overheads and fixed costs, and other external expenses for consultancy work, etc. The future revenues we model consist of one-off payments, milestones, and royalties from future potential licensing partners.

Sales and operating results: historical figures and forecasts



Source: Company, EPB

Valuation of peer companies

As Modus Therapeutics has not yet achieved profitability in its operations, we do not consider the standard key figures as particularly useful for a relative valuation. In their place, we use the technology value (EV) to evaluate Modus in relation to comparable companies at a similar development stage. We also look at the number of active projects and whether there are announced collaborations with larger pharma companies.

Company	Stock price (kr)	Market cap (mkr)	EV (mkr)	EBIT (mkr)	# of projects	Leading project	Partnership
Modus Therapeutics	2,6	41	42	-18	1	Fas II	
Active Biotech	0,8	215	164	-57	6	Fas II	NeoTX; AstraZeneca
Cyxone	0,7	67	28	-54	2	Fas II	-
Initiator Pharma	5,7	297	248	-60	5	Fas IIb	-
Abliva	0,2	249	104	-85	3	Fas IIb	-
Kancera	3,2	252	183	-53	7	Fas II	-
Mendus	1,8	358	395	-134	7	Fas II	-
Alligator Bioscience	1	224	151	-194	5	Fas II	-
Average		**237**	**182**				
Median		**249**	**164**				

Source: FactSet (data as of 24 April 2023)

The valuation of Modus is low compared with listed Swedish peers at a similar clinical development stage. We believe the market has reacted to the delays to the ph Ib study, caused by pandemic-related effects that hindered recruitment to the study. Test subjects have been unable to participate if they have contracted Covid-19 or received a Covid-19-vaccination during the screening/enrolment period, hence the delays. Moreover, we believe the market is uncertain regarding the financing of the ph II study, prompting a wait-and-see attitude towards the share. Challenges and risks with the chosen indications may also discourage investors and overshadow the high potential we see in the company.

Risks

Clinical development risk

The greatest risk for companies at an early clinical development stage is them not succeeding with planned clinical studies or failing to receive approval to initiate clinical studies. Modus currently has an active project in the clinic for its development programme in sevuparin for sepsis/septic shock and one preclinical project with the same drug candidate in anaemia/chronic kidney disease. There is a risk the authorities will not approve the initiation of these clinical studies. Both preclinical and clinical studies are associated with substantial uncertainty and risks related to the timing and outcome of the studies. We believe the likelihood of the risks stated above is high, as with other R&D companies at a relatively early development stage.

Risks related to patient recruitment and delays

The planned ph II study with sevuparin is expected to include 30–60 patients to be recruited and treated. The study design has not yet been published and we do not know the stage at which the company will choose to enter and evaluate its treatment – sepsis or septic shock. Should it opt for septic shock, there will be challenges with patient recruitment in the form of contact with family members and carers, as well as several ethical considerations.

The company's other preclinical programme awaits a decision on indication and an application for regulatory authorisation before the first clinical study can begin. Here, likewise, there is risk in patient recruitment and of delays. We see the risks associated with these as high.

Risks related to key personnel

The company has a tight management structure and is highly dependent on senior executives. Should the company lose any of its key personnel, it would hurt its future development. Several people in senior management and on the board hold shares in Modus and are among the ten largest shareholders, which we consider a sign of confidence in the company's business concept and potential. We see the risk associated with these key personnel as medium.

Financial risks

The company plans to begin a clinical ph IIa study this year. Given the current cash position, we believe it will need to take in capital to bring this to fruition while the preclinical research continues in the other project with anaemia/chronic kidney disease.

There are no guarantees that the company can raise the necessary capital on favourable terms, or that this capital can even be raised. Should it not be able to raise this capital, it would risk the company's ongoing operations. We consider the risk associated with its financial position to be high in the short term.

Other risks

Other risks include those associated with the competitive environment and regulatory changes. For now, we can only identify two direct competitors to Modus, but this could change quickly. The changing legislative landscape also poses a risk. We see the risks associated with this as medium.

Ownership and management

The largest shareholders in the company in terms of both capital and votes are Karolinska Development and KDev Investments with 55% combined. CEO John Öhd holds around 11% of both capital and votes.

Shareholder	Equity	Votes	Country	Verified
Karolinska Development AB	37,9%	37,9%	Sweden	29-03-2023
KDev Investments AB	17,1%	17,1%	Sweden	29-03-2023
John Öhd	10,7%	10,7%	Sweden	29-03-2023
Hans Wigzell	4,6%	4,6%	Sweden	29-03-2023
Anders Bladh	2,2%	2,2%	Sweden	29-03-2023
Avanza Pension	1,8%	1,8%	Sweden	29-03-2023
Nordnet Pensionsförsäkring	1,5%	1,5%	Sweden	29-03-2023
Ellen Donnelly	1,2%	1,2%	US	2022-12-31
Per Lindqvist	0,9%	0,9%	Sweden	29-03-2023
AB Wigzellproduktion	0,8%	0,8%	Sweden	29-03-2023

Source: MFN Holdings

Board of directors

Viktor Drvota, chair of the board

Chair since 2016. Viktor Drvota is a qualified doctor, lecturer, and associate professor in cardiology at Karolinska Institutet. He was responsible for life science at SEB Venture Capital in 2002–2016 and has many years' experience of board positions at biotech and medtech companies. He is currently CEO of Karolinska Development, chair of the board at Umecrine Cognition, and board member at UC Research AB, Dilafor AB, and Dilafor Incentive AB. Viktor Drvota is independent of the company and its management but has a relationship to the company's major shareholders.

Torsten Goesch, board member

Board member since 2014. Torsten Goesch is a qualified doctor who holds a Doctor of Medicine, as well as an MBA from the Kellogg School of Management, Chicago. He has more than 25 years of life science sector experience, including as a senior executive at Biogen and Merck KGaA. Torsten Goesch also has experience of successful divestments, including Cytochroma, Enobia, and STI Technologies. His current roles include chair of the board at Dilafor, board member at Biosergen, EyeSense, Forward Pharma, and ProMore, and partner at Rosetta Capital. Torsten Goesch is independent of the company, its management, and its major shareholders.

Ellen K. Donnelly, board member

Board member since 2020. Ellen Donnelly holds a doctorate in neuroscience from Yale School of Medicine. Her experience includes management positions in life science, including previously as CEO of Modus and in senior positions at Pfizer and Combinato Rx. Her current roles include being CEO of Abliva AB and as a board member at Alzecure Pharma AB. Ellen Donnelly holds 195,073 shares in the company and is independent of the company and its management, plus the major shareholders.

Management

John Öhd, CEO

CEO since 2020, and before that, CMO since 2018. John Öhd is a qualified doctor and holds a Doctor of Medicine. He has experience in drug development and has previously worked in a variety of indication areas, including CNS, cancer, and haematological diseases. His earlier roles include senior positions in research at AstraZeneca and Shire, and as Chief Medical Officer at biotech company Medivir. John Öhd's other assignments include as CSO at Karolinska Development AB and board member at Umecrine Cognition and Svenska Vaccinfabriken Produktion AB. He holds 1,730,591 shares and 86,000 series 2021/2024 warrants.

Claes Lindblad, CFO

CFO since 2021. Claes Lindblad has a Masters in chemistry and economy from Karlstads universitetet. He has more than 25 years' broad experience in key positions in the life science sector. Claes Lindblad has been CFO at medtech company OssDsign, where he managed the company's financial and administrative functions and played a key role in its listing on Nasdaq First North Growth Market in 2019. Before that, he held several senior roles, including as Head of Sweden for global market-leading medtech company ConvaTec and as sales manager for the OTC and generic portfolios at Nycomed/Takeda. Claes Lindblad holds 10,812 shares and 86,000 series 2021/2024 warrants.

Appendix 1: Patents and market protection

Modus holds patents until 2032 in the US and 2033 in Europe, with the standard option to extend them for up to five years in each market. We assume market exclusivity for sevuparin until 2034 at the very least, meaning we expect the patents to be extended.

Modus has also recently submitted a patent application with the potential, if granted, to broaden and further expand sevuparin's IP portfolio. It submitted additional patents in 2023 to widen the usage, supported by data from the ph Ib induced endotoxaemia study *(the company)*.

Leading candidate	Year of application	Patent granted	Giltighetstid
Sevuparin*	2013	USA	2032
		Europe	2033
Chronic kidney disease (CKD)	2023		
Kidney diseases with anemia			

*Possibility of a patent extension of up to five years in each market

Source: Company

Income statement

	2020	2021	2022	2023e	2024e	2025e
Administrative Expenses	-2	-7	-7	-7	-7	-7
R & D Expenses	-4	-14	-11	-17	-42	-45
EBITDA	**-6**	**-21**	**-18**	**-24**	**-49**	**-52**
EBITDA, adjusted	**-6**	**-21**	**-18**	**-24**	**-49**	**-52**
EBITA, adjusted	**-6**	**-21**	**-18**	**-24**	**-49**	**-52**
EBIT	**-6**	**-21**	**-18**	**-24**	**-49**	**-52**
EBIT, adjusted	**-6**	**-21**	**-18**	**-24**	**-49**	**-52**
Profit before tax	**-6**	**-21**	**-18**	**-24**	**-49**	**-52**
Profit before tax, adjusted	**-6**	**-21**	**-18**	**-24**	**-49**	**-52**
Net income	**-6**	**-21**	**-18**	**-24**	**-49**	**-52**
Net income, adjusted	**-6**	**-21**	**-18**	**-24**	**-49**	**-52**
Sales Growth	-	*N.m.*	*N.m.*	*N.m.*	*N.m.*	*N.m.*
Gross Margin	*Neg.*	*Neg.*	*Neg.*	*Neg.*	*Neg.*	*Neg.*
EBIT Margin, Adjusted	*Neg.*	*Neg.*	*Neg.*	*Neg.*	*Neg.*	*Neg.*
EPS, Adjusted	-	*-1,29*	*-1,14*	*-1,52*	*-3,07*	*-3,26*
EPS Growth, Adjusted	-	*N.m.*	*N.m.*	*N.m.*	*N.m.*	*N.m.*

Source: Modus Therapeutics Holding, EPB

Cash flow statement

	2020	2021	2022	2023e	2024e	2025e
EBIT	-6	-21	-18	-24	-49	-52
Changes in working capital	-1	5	-4	0	0	0
Cash flow from operating activities	**-7**	**-16**	**-22**	**-24**	**-49**	**-52**
Free cash flow	**-7**	**-16**	**-22**	**-24**	**-49**	**-52**
New share issue / repurchase	3	29	0	50	80	0
Change in liabilities	10	0	12	-5	-7	0
Cash flow from financing	**13**	**29**	**12**	**46**	**73**	**0**
Cash flow	**6**	**13**	**-10**	**21**	**24**	**-52**
Net debt	**-7**	**-21**	**1**	**-25**	**-55**	**-3**

Source: Modus Therapeutics Holding, EPB

Balance sheet

	2020	2021	2022	2023e	2024e	2025e
ASSETS						
Other current assets	0	0	1	1	1	1
Cash and cash equivalents	7	21	10	32	55	3
Total current assets	**7**	**21**	**11**	**32**	**56**	**3**
TOTAL ASSETS	**7**	**21**	**11**	**32**	**56**	**4**
EQUITY AND LIABILITIES						
Equity	7	16	-3	23	54	1
Total equity	**7**	**16**	**-3**	**23**	**54**	**1**
Short-term interest-bearing liabilities	0	0	12	7	0	0
Accounts payable	0	4	1	1	1	1
Other current liabilities	0	1	1	1	1	1
Total current liabilities	**0**	**5**	**14**	**9**	**2**	**2**
TOTAL EQUITY AND LIABILITIES	**7**	**21**	**11**	**32**	**56**	**4**

Source: Modus Therapeutics Holding, EPB

Growth and margins

	2020	2021	2022	2023e	2024e	2025e
Revenue growth	-	N.m.	N.m.	N.m.	N.m.	N.m.
EBITDA growth, adjusted	-	N.m.	N.m.	N.m.	N.m.	N.m.
EBIT growth, adjusted	-	N.m.	N.m.	N.m.	N.m.	N.m.
EPS growth, adjusted	-	N.m.	N.m.	N.m.	N.m.	N.m.
Gross margin	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.
EBITDA margin	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.
EBITDA margin, adjusted	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.
EBIT margin	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.
EBIT margin, adjusted	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.
Profit margin, adjusted	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.

Source: Modus Therapeutics Holding, EPB

Return

	2020	2021	2022	2023e	2024e	2025e
ROE, adjusted	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.
ROCE, adjusted	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.
ROIC, adjusted	Neg.	>100%	>100%	>100%	>100%	>100%

Source: Modus Therapeutics Holding, EPB

Capital efficiency

	2020	2021	2022	2023e	2024e	2025e
Total short-term liabilities / total cost	8%	26%	77%	39%	5%	5%
Working capital / total revenue	-17500%	-	-	-	-	-

Source: Modus Therapeutics Holding, EPB

Financial position

	2020	2021	2022	2023e	2024e	2025e
Net debt	-7	-21	1	-25	-55	-3
Equity ratio	93%	74%	-23%	71%	96%	33%
Net debt / equity	-1,1x	-1,3x	-0,4x	-1,1x	-1,0x	-2,3x
Net debt / EBITDA	1,2x	1,0x	-0,1x	1,0x	1,1x	0,1x

Source: Modus Therapeutics Holding, EPB

Per share data

	2020	2021	2022	2023e	2024e	2025e
EPS	-	-1,29	-1,14	-1,52	-3,07	-3,26
EPS, adjusted	-	-1,29	-1,14	-1,52	-3,07	-3,26
FCF per share	-	-1,00	-1,35	-1,52	-3,07	-3,26
Book value per share	-	0,98	-0,16	1,43	3,33	0,07
Number of shares, m	-	16,1	16,1	16,1	16,1	16,1
Number of shares after dilution, average	-	16,1	16,1	16,1	16,1	16,1

Source: Modus Therapeutics Holding, EPB

Valuation

	2020	2021	2022	2023e	2024e	2025e
P/E, adjusted	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.
P/BV	Neg.	3,9x	Neg.	1,6x	0,7x	32,5x
P/FCF	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.
FCF-yield	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.
Dividend yield	Neg.	0,0%	0,0%	0,0%	0,0%	0,0%
Payout ratio, adjusted	-	0,0%	0,0%	0,0%	0,0%	0,0%
EV/Sales	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.
EV/EBITDA, adjusted	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.
EV/EBIT, adjusted	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.
EV	Neg.	41	46	37	37	37
Share price, year end	-	3,8	2,8	2,3	2,3	2,3

Source: Modus Therapeutics Holding, EPB

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