Intron Health

SPONSORED RESEARCH
12/08/2020

# Hansa Biopharma

## A Rare Gem

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## INITIATION - A Rare Gem

## Sponsored Research

**Price: SEK262**
**Target Price: SEK385**


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**Hansa is a Swedish rare disease biotech whose lead asset, Idefirix, recently received a positive CHMP opinion for use in highly sensitised kidney transplant patients. Idefirix's highly elegant & effective profile makes it a pipeline & a platform technology in itself. Hansa's recent successes have made it big enough to be within most investors' investment universe and we see 50% upside. There are multiple S-T catalysts, numerous sources of upside to our valuation, commercial-isation could be aided by kidney transplant guideline updates & mgmt have expertise in shifting treatment paradigms. Bone marrow transplant indication could add SEK32/share to cons.**

### Idefirix In Kidney Transplant Alone Accounts for Current Mkt Cap

An EU7 launch in Q4 & the ongoing pivotal US trial could generate peak sales of $500m. We expect a slow sales ramp but believe updated clinical guidelines would materially accelerate revenues above our forecasts.

### Material Upside from Future Gene Therapy Deals

We estimate the Sarepta deal is worth SEK37/share. There are 300 gene therapies in development & 20 already FDA-approved, with many likely to experience viral vector antibody issues, so this is a large opportunity.

### Many Sources of Upside and Multiple Near-Term Catalysts

We do not include: 1) New gene therapy deals 2) Out-licensing of Idefirix in ROW 3) Any sales from the pipeline. We see multiple catalysts including; 1) Guideline updates, 2) Anti-GBM P2 in 3Q, 3) Oct 29th CMD.

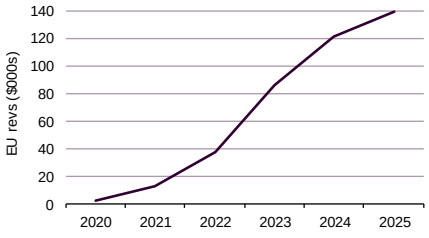
### Hansa Should be Profitable by 2023 and Have Enough Cash

The recent $120m equity raise should see Hansa through to cashflow positive and it should be able to raise debt to fund the US launch. Clinical trials could be accelerated and expanded given the new cash injection.

### SOTP Valuation Implies 50% Upside with Potential for More

EU & US kidney transplant indication is worth SEK257/share & there is S-T upside from gene therapy deals & ROW kidney out-licensing deals.

***Idefirix Sales Trajectory in Europe***




*Source: Intron Health estimates*

***SOTP Valuation***

| Indication | NPV / share (SEK) |
|---|---|
| Kidney transplant | 257 |
| Anti-GBM | 19 |
| Sarepta | 37 |
| AMR | 41 |
| GBS | 50 |
| Bone marrow | 32 |
| Costs (SG&A, R&D) | -79 |
| Net cash | 28 |
| **Total** | **385** |

*Source: Intron Health estimates*

***Summary Financials***

| | 20E | 21E | 22E | 23E |
|---|---|---|---|---|
| Sales $m | 0.9 | 13.0 | 38.1 | 87.3 |
| EPS (SEK) | -10.51 | -9.65 | -6.16 | 1.69 |
| Net cash $m | 145.1 | 96.6 | 59.9 | 56.0 |
| 2025 PE | 11.7x | | | |
| Market cap | $1.3bn | | | |

*Source: Intron Health estimates*

# Contents

# Investment Summary

**Hansa has recently received a positive CHMP opinion for imlifidase in kidney transplant and signed a potentially paradigm-shifting deal with Sarepta for use alongside two gene therapy indications. However, despite the considerable share price surge we see significant upside with multiple catalysts in the coming 12 months.**

## Idefirix – A Pipeline in a Drug

**Idefirix (imlifidase) is such an effective drug with a very elegant mode-of-action that it is in itself a pipeline & a platform encompassed within a drug. Idefirix's ability to almost completely deplete IgG for an optimal length of time allows it to be applied to many different indications. In addition to Kidney transplants, we believe gene therapy & bone marrow transplants will be big value drivers.**

## Conservative Assumptions & Still Above Consensus

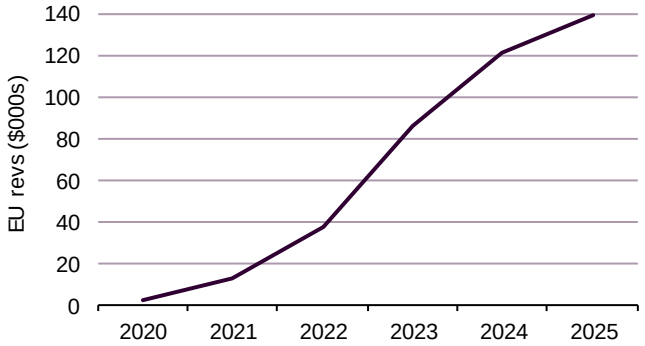
**We are 40% above consensus on 2023 sales despite assuming a slow ramp and 15% lower volume in 2024. However, we are also above consensus for Idefirix pricing, with $200k per patient in the US and $163k in the EU; this drives our higher sales.**

*Table 1: Key Assumptions and Intron Health Vs Consensus*

| USD (000s) | 2020 | 2021 | 2022 | 2023 | 2024 |
|---|---|---|---|---|---|
| **EU penetration rate** | | | | | |
| Highly sensitised (cPRA>80%) | 0% | 4% | 12% | 25% | 34% |
| Moderately sensitised | 0% | 0% | 1% | 2% | 4% |
| **Moderate-highly sensitised** | **0%** | **2%** | **6%** | **14%** | **19%** |
| **EU kidney revenues** | **1** | **13** | **38** | **86** | **121** |
| | | | | | |
| **Sales - Intron vs consensus** | **-81%** | **-16%** | **23%** | **41%** | **-15%** |
| Group EPS (SEK) | -10.51 | -9.65 | -6.16 | 1.69 | 8.98 |
| | | | | | |
| ***No. of pts treated in 2024*** | ***Intron*** | ***899*** | | *Cons.* | *1,056* |
| ***US Idefirix Price*** | ***Intron*** | ***$250k*** | | *Cons.* | *$199k* |
| ***EU Idefirix Price*** | ***Intron*** | ***$163k*** | | *Cons.* | *$127k* |

*Source: Intron Health estimates*

*Chart 1: S-Shaped Sales Forecasts for EU Kidney Transplants*




*Source: Intron Health estimates*

## Gene Therapy Opportunity

**Imlifidase can solve a major problem for many gene therapies – antibodies to the AAV vectors that many gene therapies use (and potentially also lentiviral vectors). Currently, there is no solution to this problem and patients who are seropositive for AAV antibodies are generally ineligible to receive gene therapy.**

**The Sarepta deal extracted significant value from imlifidase and we estimate it is worth 14% to Hansa's market cap. We expect more deals to be signed with other gene therapy players given management are in active discussions with other interested parties. There are currently 20 gene products already FDA approved & over 300 pipeline therapies with most likely to see the same problem, with many patients having antibodies to the viral vector.**

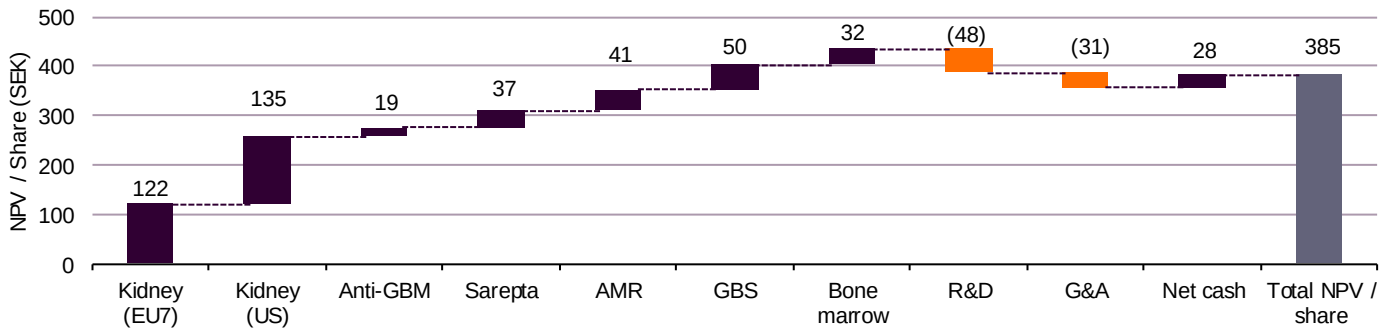
## Bone Marrow Upside Not in Numbers

**Whilst Hansa is yet to initiate trials in this indication, given the ability to move straight into P2 and potentially even a pivotal P2, this could be material upside to the valuation. Patient numbers for allogenic bone marrow transplants are similar to kidney transplant. We see >$400m of potential peak sales by c.2030. Moreover, the adoption rate would likely be higher as oncologists usually adopt new technologies faster than in other therapeutic areas.**

## Multiple Sources of Upside to SEK385 Price Target

**There are multiple sources of upside to our valuation: We assume: 1) no out-licensing deals in ROW/Japan 2) no more gene therapy deals 3) a slow uptake in Kidney 4) the pipeline of 2 assets is worth zero 5) we heavily risk-adjust P2 trials 6) EU price could be higher.**

***Chart 2: NPV/share waterfall chart, by indication***




*Source: Intron Health estimates*

## Plethora of Near-term Catalysts

**Biotech companies often lack catalysts but Hansa has a significant number in the coming months:**

- EU approval
- Updated kidney transplant guidelines which would accelerate uptake
- More gene therapy deals – Sarepta was worth c.14% upside
- Anti-GBM P2 data in Q320
- Capital Markets Day highlighting multiple sources of upside – 29th Oct

## Cash Can Accelerate Development – Profitable by 2023

**In June, Hansa raised ~$120m. This cash will allow it to invest more aggressively behind the pipeline and accelerate clinical timelines (which in orphan diseases are notoriously slow and further hampered by COVID). Moreover, on our numbers, Hansa is profitable by 2023, ahead of the likely US launch. Thus, they may be able to raise debt rather than equity making it now self-sufficient.**

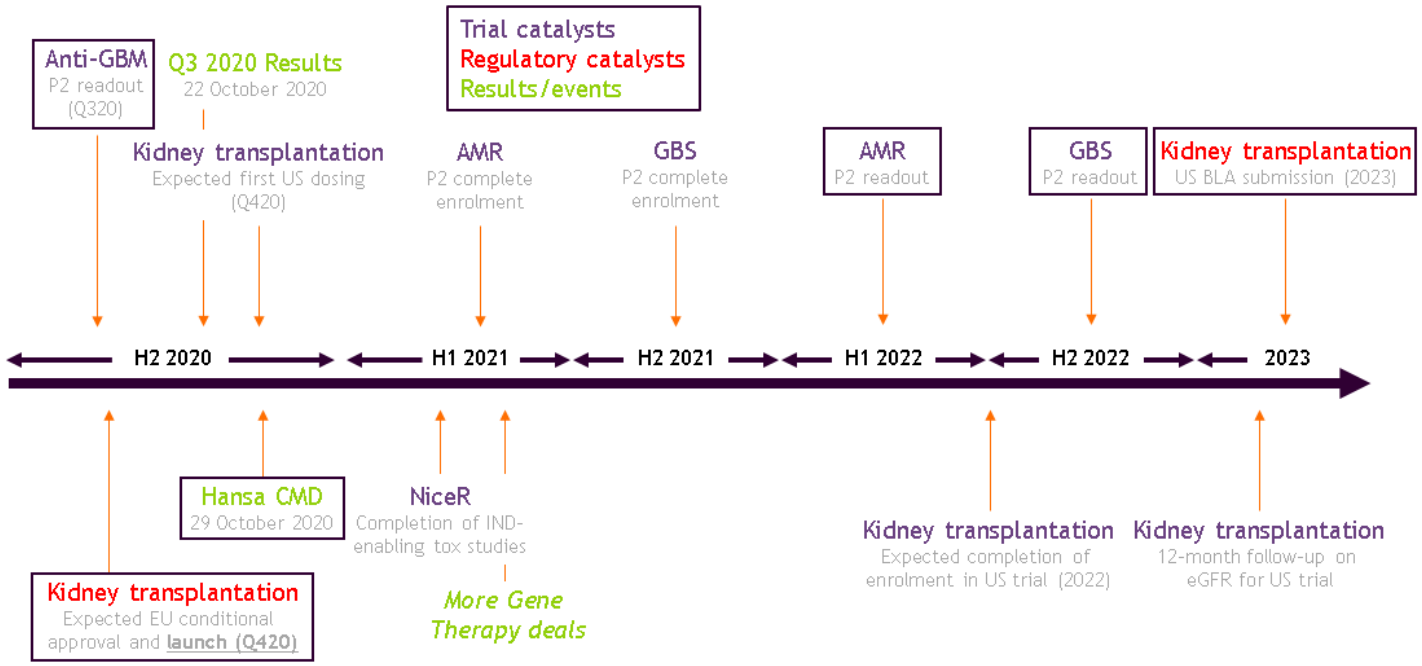
***Table 2: Imlifidase has a broad range of indications***

| Disease | Disease Description | Imlifidase mechanism in disease | Patient Numbers | Clinical Data | Future Data Readouts |
|---|---|---|---|---|---|
| **Sensitised patients requiring kidney transplantation** | Patients have numerous anti-human leukocyte antigen (HLA) antibodies in their bloodstream.<br><br>This makes it difficult to find appropriate HLA-matching kidneys for transplantation.<br><br>These IgG antibodies are likely to stimulate an immune attack on a transplanted organ that leads to rejection. | Imlifidase is a bacterial enzyme that specifically and rapidly cleaves human IgG antibodies.<br>This provides a 7-day window to perform transplantation, provided other conditions are met.<br><br><u>Mechanism</u><br>• Cleaves the hinge region of the IgG antibody heavy chains, eliminating Fc region dependant complement binding<br>• Cleaves the receptors of circulating B-cells and impairs antigen-specific B-cell IgG responses<br>• Preventing complement-mediated and antibody dependant cell cytotoxicity | EU7<br>3,700<br><br>US<br>4,000 | Phase 1- Favourable safety profile with efficacious removal of IgG at 0.12 and 0.24 mg/kg doses<br>Phase 2 - EU and US trials<br>2016- 10 ESRD patients at median cPRA 90%. Single dose permitted all to undergo transplantation. 100% graft survival at 6 months.<br>2018- 17 ESRD patients at median cPRA 99.6%. Single dose permitted transplantation in all. At 6 months, graft survival was 94%. At 3-years, one death and 2 further graft losses occurred. ABMR in 41% of patients but all responded to treatment.<br>2018- HighDes- 18 ESRD patients at CPRA 99.9%, single dose converted positive crossmatches to negative. At 2 years (N=31), graft survival was 90%, patient survival 100%. | Long-term observational prospective study of Phase 2 participants in progress, with data expected at yearly intervals.<br><br>A randomised controlled trial will take place in the US.<br><br>A post-approval efficacy study will also take place in the EU. |
| **Guillain Barre Syndrome** | Autoimmune disease of the peripheral nerves and nerve roots. The synthesis of IgG antibodies activates inflammatory cells that damage the myelin sheath of nerves, impairing their conduction. This leads to neuromuscular paralysis. | Imlifidase would cleave these IgG antibodies, preventing further damage to the myelin sheath. This would improve nerve conduction and paralysis. | EU5, US<br><br>9,300 | 2019- Phase II trial in 30 GBS patients initiated.<br>Protocol- single 0.25mg/kg dose followed by five consecutive days of IVIG treatment<br>Objectives - safety, functional outcome at 4 weeks, functional capability up to 1-year. | Trial recruitment completed in H2 2021<br><br>Results available in H2 2022 |
| **Anti-Glomerular Basement Membrane Disease** | Form of autoimmune vasculitis of the kidneys and lungs. IgG antibodies bind to the basement membranes of these capillaries and cause inflammation. | Imlifidase administration would cleave the antibodies responsible for causing this lung and kidney damage. | EU7<br>550<br><br>US<br>525 | In a preclinical mouse model of anti-GBM, imlifidase prevented severe albuminuria, cleaved IgG and diminished the deposition of protein complexes that promote leukocyte recruitment and inflammation. | Phase-2 trial in progress.<br><br>Data expected Q3 2020 |
| **AMR** | AMR is the rejection of a graft due to antibodies targeted against blood group antigens, HLA or endothelial cell antigens on the transplant.<br>These antibodies activate the classical complement pathway, inducing inflammatory cell recruitment that results in graft injury. | Imlifidase would cleave the functional regions of the antibodies, preventing activation of the complement pathway that causes this graft rejection. | EU5, US,<br><br>2,700 | 2019- Phase II trials for acute AMR commenced and aim to recruit 30 candidates.<br>Protocol- single 0.25mg/kg imlifidase dose or PLEX sessions.<br>Objectives- reduction of DSA 5-days post-treatment, secondary outcomes of efficacy e.g. DSA levels and eGFR levels at 6-months. | Study data is anticipated to be released in H2 2022. |
| **Gene Therapy** | Therapies that utilise AAV vectors are hindered by anti-AAV antibodies. These prevent AAV entry to target cells and activate responses that eliminate AAV delivered transgene expressing cells. | Imlifidase could degrade these anti-AAV antibodies to create a 1-week window to administer/re-dose a therapy. This would maximise vector delivery/ transduction and so increase therapeutic efficacy | 100k's potentially | 2020- A pre-clinical study revealed imlifidase depleted anti-AAV antibodies in human plasma samples and enhanced AAV vector transduction in NHPs. | We expect further Sarepta-like deals to be announced in the coming months |
| **Bone marrow transplantation** | Allogenic bone marrow transplants are hindered by the presence of IgG antibodies. These recognise DSAs and stimulate inflammation that leads to graft rejection. | Imlifidase cleaves any DSAs, enabling partially-HLA matching transplants. This could improve transplantation outcomes and graft functioning. | Europe<br>2,900<br>US<br>1,600 | Clinical data for the potential use of imlifidase is expected to be initiated in 2021. | |

*Source: Intron Health; Hansa Biopharma AB; Jordan et al, 2017; Lin et al, 2020; Yang et al, 2010; Leborgne et al, 2020;*

# Catalyst-Rich 12 Months Upcoming

***Chart 3: Catalyst timeline***




*Source: Company reports*

# Kidney Transplants - Main Value Driver

**In June 2020, imlifidase (Idefirix) received CHMP positive opinion on the granting of a marketing authorisation in the EU, which will likely precede a full approval in September. This will be imlifidase's first approval, with the label expected to be for the desensitisation of highly sensitised patients needing kidney transplantation but unlikely to receive a compatible transplant. Clinical data looks extremely strong: all highly sensitised patients across four phase II trials were successfully desensitised by imlifidase such that they became transplant eligible. In those that received kidney transplants, graft survival rates have ranged from 89-100%. The US BLA submission is expected by 2023, with the first US pivotal trial patient expected to be dosed in Q420.**

**We have researched the potential market in considerable detail and estimate that the addressable market in Europe consists of 3.7k patients. We assume ~24% penetration of these sensitised patients at peak (40% for highly sensitised, 8% for moderately sensitised) and have established that global peak sales could be >$500m. We calculate an NPV for the European market of $624m, with another potential $689m for the US market, though US commercialisation now becomes one of the biggest risks for Hansa. We see the US and EU kidney transplant opportunities alone as supporting Hansa's current share price, with an NPV/share of SEK257. There could also be upside from licensing deals outside these regions.**

## CKD Causes ESRD

The kidneys are essential organs that not only filter waste products and toxins from the blood, but also regulate plasma osmolarity and stimulate red blood cell synthesis.

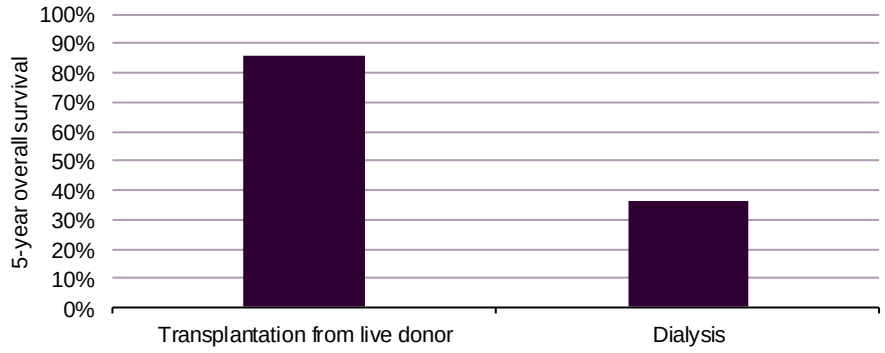
Chronic kidney disease (CKD) is a major health affliction with a prevalence of 697.5 million cases worldwide. It is a progressive disease that eventually leads to kidney failure, also known as end-stage renal disease (ESRD). This is fatal in the absence of dialysis or transplantation.

## Transplantation is the Optimal Treatment For ESRD

Kidney transplantation is the ideal form of renal replacement treatment and has superior outcomes to dialysis. Although dialysis serves as a life-saving artificial kidney, patients have a decreased quality of life and worse survival rate. Dialysis patients require 6-hour clinical visits 3-4 times weekly for the remainder of their life or until transplantation is performed. Long term dialysis patients are also commonly afflicted by complications like cardiovascular disease, peripheral neuropathy and parathyroid adenoma. Therefore, it is unsurprising that kidney transplant

recipients have a significantly higher 5-year survival rate than those on dialysis, 86% vs 36% respectively:

***Chart 4: Five-year overall survival for transplant recipients vs dialysis patients***




*Source: US Department of Health*

Established research has also displayed that kidney allografts function significantly longer in pre-emptively transplanted patients (those transplanted without previous dialysis).

Individuals on dialysis for greater than 2-years pre-transplantation are three times more likely to experience loss of transplant functioning than patients that wait less than 6-months on dialysis. This highlights the urgent need for a solution that would allow greater transplantation and decrease the average wait time on dialysis of 3.6 years in the US.

## Transplant Volume is Limited: Demand > Supply

There is a significant shortage of kidneys available for transplantation worldwide, with transplant waiting lists far exceeding supply from the donor pool of both deceased and the living. In the US alone, approximately 94,000 patients are awaiting transplantation but only 23,000 organs are transplanted annually. This chronic lack of available organs is exacerbated by donor populations suffering from an increased incidence of diabetes and high blood pressure. These are deleterious to donor kidney integrity and render organ donation ineligible. Therefore, less suitable organs are available for use and so approximately 5,000 Americans die awaiting a kidney every year.

***Table 3: Kidney waiting list and organs transplanted by region***

| Region | Kidney Waiting List | Kidneys Transplanted |
|---|---|---|
| US | 94,315 | 23,401 |
| UK | 4,730 | 3,647 |
| France | 8,065 | 3,567 |
| Germany | 6,850 | 2,291 |
| Italy | 6,770 | 2,124 |
| Spain | 3,993 | 3,310 |

*Source: International Registry in Organ Donation and Transplantation 2018, Global Observatory on Donation and Transplantation; National registries*

This is further complicated by organ match suitability (HLA), which takes us to next section.

## HLA Sensitisation Hinders Organ Match Suitability

HLAs are cell surface glycoproteins present on the major histocompatibility complex (MHC) of every cell. **They permit the immune system to distinguish between self and foreign material** and so protect the body from harmful invaders such as pathogens.

Organ suitability is assessed primarily according to blood type and Human Leukocyte Antigens (HLA – see margin).

Post-transplantation, the immune system can use HLAs to recognise the transplanted organ as foreign, leading to the secretion of antibodies from plasma B cells to attack it. This antibody-mediated rejection (AMR) can lead to graft loss (kidney loss) and/or impaired functioning of the kidneys. **Therefore, to mitigate against this risk, donor and recipient must have as closely matching HLA antigens as possible.**

Patients with anti-HLA antibodies (known as donor-specific antibodies, or DSA), to a large proportion of the donor population are classed as sensitive and are at an increased risk of AMR.

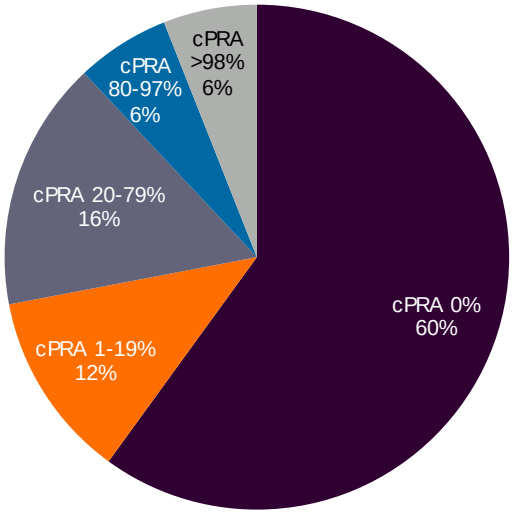
DSAs are usually secreted in response to a previous immunogenic event, such as 30-50% of women who experience multiple pregnancies, 50% of people who undergo blood transfusions and 90% who had had a previous transplantation. Individuals can also unknowingly have DSAs from previous infections. The generation of DSAs is usually asymptomatic but they present a significant immunological barrier to transplant recipients.

## HLA Sensitisation is Measured by cPRA

Patient sensitisation to organ transplantation is assessed via the calculated Panel Reactive Antibody (cPRA) score. This ascertains the percentage of the general population against whose HLAs a potential transplant recipient with pre-existing DSAs would have a positive crossmatch. A positive crossmatch signifies the presence of reactive antibodies against a particular donor kidney and **so the likely rejection of that graft.**

As shown in the chart below, sensitised patients are defined as possessing a cPRA greater than 20% and make up 28% of the kidney wait-list. Those with a cPRA score greater than 80% are classified as highly sensitised and comprise 12% of the total US waitlist.

***Chart 5: Proportion of cPRA scores across US waiting lists***




*Source: Organ Procurement and Transplant Network, Advanced Report as of March 2020*

The higher the percentage score, the lower the probability of a transplant candidate receiving an appropriate donor organ. For example, someone with a cPRA of 80% would be ineligible to receive a transplant from 80% of the general population. As shown in the table, the likelihood of finding a suitable organ match decreases exponentially as cPRA increases.

***Table 4: Estimated number of match runs needed for a suitable donor organ***

| cPRA score | Theoretical number of match runs |
|---|---|
| 10% | 2 |
| 20% | 2 |
| 30% | 3 |
| 40% | 4 |
| 50% | 5 |
| 60% | 6 |
| 70% | 9 |
| 80% | 14 |
| 85% | 19 |
| 90% | 29 |
| 95% | 59 |
| 99% | 300 |
| 99.50% | 600 |
| 99.90% | 3,000 |
| 99.99% | 30,000 |
| 99.999% | 300,000 |

*Source: Clinical Journal of the American Society of Nephrology, 2016, 11 (4): p684-693*

The avoidance of donor kidneys that harbour these specific antigens decreases an already small donor pool for these individuals. Sensitized patients wait four times longer than unsensitized patients for a compatible donor. These patients therefore remain on dialysis and have a mortality rate double those who receive transplantation. Hence, this is a prominent issue that requires addressing.

## Desensitisation Permits Sensitised Transplantation

Sensitised patients can undergo immunomodulatory therapies pre-transplantation that sufficiently diminish DSAs to permit successful organ engraftment, a process termed desensitisation. Desensitisation prevents immediate AMR, with this risk of graft rejection not exacerbated even after IgG antibodies return.

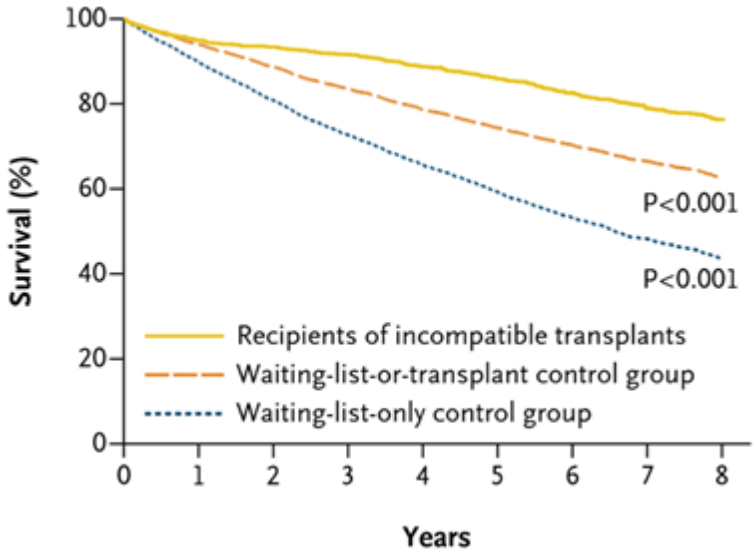
There is a significant survival benefit for highly sensitised individuals that are desensitised and transplanted instead of remaining on the waitlist for an ideal compatible donor. A 2016 major multi-centre study of 1,025 transplant recipients conducted by Orandi *et al* affirmed this. Desensitised recipients of HLA-incompatible live donor organs had a superior survival rate than those who remained on the waiting list or waited for a compatible deceased donor organ at 1,3,5, & 8 years (see table and chart below). This survival benefit was significant across 8 years regardless of levels of donor specific antibodies.

***Table 5: Survival statistics for recipients of kidney transplants from incompatible live donors and matched controls***

| Year | Survival Rate | | |
|---|---|---|---|
| | **Desensitised recipients of incompatible transplants N=1,025** | **Wait-listed and deceased donor transplant group N=5,125** | **Waitlisted Group N=5,125** |
| 1 | 95.0% | 94.0% | 89.6% |
| 3 | 91.7% | 83.6% | 72.7% |
| 5 | 86.0% | 74.4% | 59.2% |
| 8 | 76.5% | 62.9% | 43.9% |

*Source: Orandi et al, 2016*

***Chart 6: Survival statistics for recipients of kidney transplants from incompatible live donors and matched controls***




*Source: Orandi et al, 2016*

## Current Methods of Desensitisation

Currently, there are no specifically approved therapies for HLA desensitisation, but the most commonly utilised protocol combinations consist of plasmapheresis (PLEX), high-dose intravenous immunoglobulin therapy and off-label use of pharmaceuticals like Rituxan. However, these procedures have varying efficacy patient-to-patient and are only employed by select treatment centres in the US and Europe.

### Intravenous Immunoglobulin Therapy (IVIG)

Immunoglobulins are antibodies naturally secreted by the immune system. Intravenous immunoglobulin therapy consists of the infusion of healthy donor antibodies, which may cause a recipient to be desensitised by decreasing IgG half-life through FcRn occupation, or by modulating their circulating anti-HLA antibodies.

This has been the cornerstone of all desensitisation protocols for decades, with this procedure seen to improve transplantation rates for highly sensitised, ABO-incompatible and crossmatch-positive patients. However, this procedure is slow with one cycle taking a month and is associated with post-transplantation antibody rebound and AMR of the graft further down the line.

### Plasmapheresis

Plasmapheresis involves the exchange of patient plasma with fresh plasma to remove serum antibodies and the co-administration of IVIG to inhibit the return of these antibodies. Treatment is required a week prior to transplantation and so is not appropriate for deceased donor transplantation (due to the prolonged ischaemia the donor organ would be subjected to).

However, essential blood components like coagulation factors are also depleted during this process and there is a material infection risk. High residual levels of IgG remain even after treatment and often there is a rapid rebound of anti-HLA antibodies. This also limits its usage to living donor transplantation which is rarely appropriate for highly sensitised patients.

### Rituxan

This monoclonal antibody is specific for CD20, a specific membrane spanning protein on the surface of B-lymphocytes. Upon binding to CD20, Rituxan stimulates the immune destruction and depletion of these B-cells. It is used in conjunction with IVIG and has been observed to improve transplantation in sensitised patients. However, this protocol is slow and some patients may not be able to tolerate such a regimen.

Peng *et al* found the wait time for deceased donor recipients decreased significantly from 95 ± 46 months to 4.2 ± 4.5 months after Rituxan treatment. Patient and graft survival at 24 months were 95% and 84% respectively and infusion was well tolerated.

### Current Desensitisation Therapies Have Many Drawbacks

Current desensitisation protocols are slow, inefficient and often result in graft injury and rejection. There is an urgent need for a desensitising antibody-removing agent that is efficacious, reliable and can act rapidly. This would enable greater transplantation rates for highly sensitised individuals that largely rely on deceased donor organs that require minimal ischaemic time.

## Imlifidase is a Better Solution for DSAs

### Imlifidase is a novel agent to cleave Immunoglobulin G (IgG), the key antibody responsible for transplant rejection.

The human immune system is a complex and multifaceted system that is built to protect the body from harmful stimuli such as foreign pathogens, damaged cells and toxic substances. A key immunological response is the secretion of specific antibodies from plasma B cells that recognise foreign antigens (surface protein molecules) on non-self-entities.

Immunoglobulin G (IgG) comprises 80% of antibodies in the blood and is an essential part of the adaptive immune system. When IgG antibodies bind to an antigen, various immune responses are stimulated such as: neutralisation, engulfment of foreign material by phagocytes and activation of the complement system to destroy pathogens by lysis. In various autoimmune diseases and organ transplantation, the immune system malfunctions and attacks self-antigens of its own tissues or non-self-antigens of the allograft. This can detrimentally impact the individual and lead to allograft (kidney transplant) rejection. IgG antibodies are the main mediator of this response. Hence, depleting IgG under these conditions provides significant therapeutic benefit.

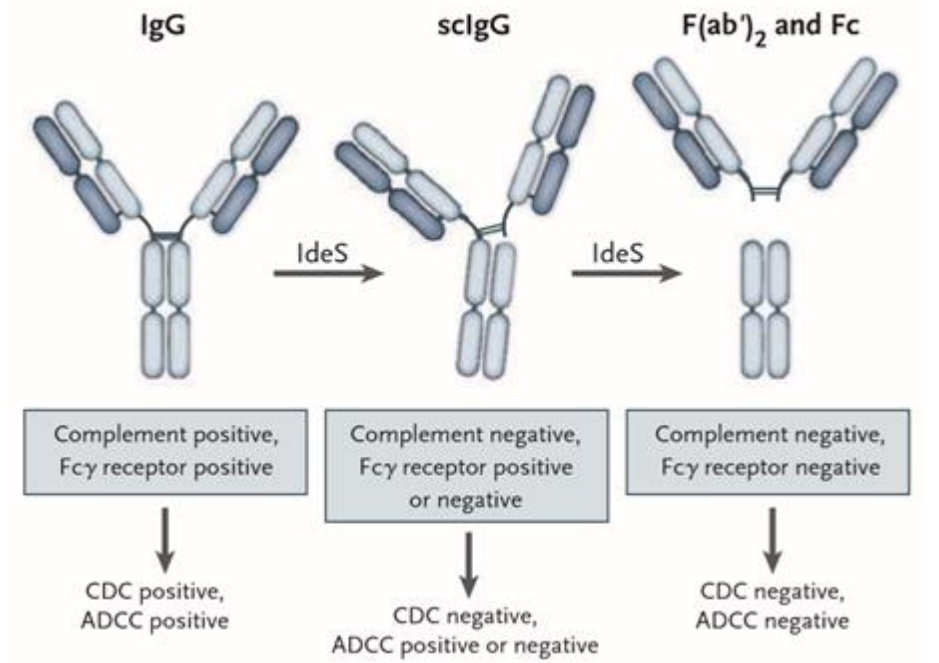
Imlifidase is a bacterial enzyme from *Streptococcus pyogenes* that specifically cleaves IgG antibodies, leaving other immunoglobulins unaffected, allowing other immune responses to continue to fight infections. This protease is recombinantly synthesised in *E. coli* and infused intravenously to have a therapeutic effect.

Imlifidase rapidly inactivates all subclasses of IgG (free, antigen and membrane bound). It also degrades IgG in circulating blood and within human tissue within 6 hours. Thus, if a donor is found but DSAs are detected, then an administration of imlifidase would enable the transplant to go ahead. The elimination of DSAs in highly sensitised patients creates a window of 7 days to perform the transplant. IgG antibodies return after this period, because the antibody secreting B-cells are unaffected. It is hypothesised that as the patient is able to adjust to the kidney graft, even when IgG rebounds, it does not provoke an immediate rejection.

Imlifidase administration results in the complete inactivation of IgG-mediated immunity by two mechanisms: the prevention of Fc dependant

effector functions and compromised IgG type memory B-cell activation. Imlifidase cleaves the hinge region of the IgG antibody heavy chains, eliminating Fc region dependant complement binding (see diagram below). Therefore, it prevents complement-mediated and antibody-dependant cell cytotoxicity (ADCC) from occurring, which is how antibody mediated rejection happens. Imlifidase also cleaves the receptors of circulating B-cells and impairs antigen-specific B-cell IgG responses. This further reduces the impact of DSAs and may facilitate transplantation and counteract allograft rejection.

***Chart 7: Cleavage of IgG by imlifidase (IdeS)***




*Source: Jordan et al , 2017*

- Imlifidase removes interstitial (tissue) IgG, not just IgG from the blood. After 7-10 days, the antibodies return because the B cells are still there and produce more antibodies.
- When IgG levels return, AMR may occur. This happened in 35% of patients in an imlifidase phase II trial, but all were successfully treated (usually by plasma exchange to remove antibodies although there is no consensus as to how to remove the antibodies).
- The other 65% do not get AMR and there are multiple theories for why this may be. One popular theory is that patients develop “accommodation”: a one-week window with no IgG means your body adjusts to the kidney graft, so when IgG returns there is no reaction against it. The antibodies can still bind to the kidney, but nothing happens. Over time, these antibodies against the kidney may fall naturally.

- We do not need to worry about IgA/D/E antibodies as they don't recruit the complement system, which is what causes the damage to the kidney
- We also do not need to worry about IgM antibodies. Whilst they do have some effect when it comes to organ rejection, it is very small compared to IgG, which binds at 10x the affinity of IgM. IgM antibodies are also less effective at activating the complement system.

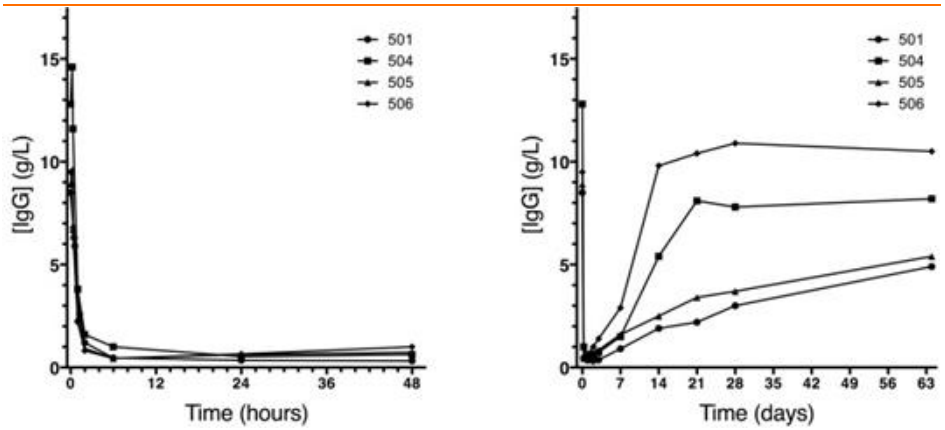
# Imlifidase Clinical Data is Very Strong

**At present, Hansa Biopharma has completed one phase I and four phase II clinical studies of imlifidase in HLA-sensitised kidney transplantation, which have generated encouraging outcomes. Additionally, an observation follow-up study of 46 previously treated and transplanted patients is currently in progress to ascertain the long-term efficacy and safety profile of imlifidase.**

## First-in-Man Study

The phase I study was a double-blind randomised study of single ascending doses of imlifidase in 26 healthy subjects. It demonstrated impressive plasma IgG cleavage efficacy within minutes after dosing at 0.12mg/kg and 0.24mg/kg body-weight. The phagocytic capacity of IgG/IgG fragments was significantly reduced after 2 hours with near complete IgG depletion in 6 hours (see below). Imlifidase exhibited a favourable safety profile without reported serious adverse effects and dose limiting toxicity.

***Chart 8: Graphs showing serum IgG levels from 4 subjects dosed with imlifidase 0.24mg/kg body weight. The left graph displays the rapid degradation of IgG over 48 hours. The right graph displays the antibody recovery over 63 days.***




*Source: Winstedt et al, 2015 . Data was quantified via a validated ELIZA method performed by Covance Laboratories Ltd, UK*

## Phase II Studies Strong Enough For Approval

Phase II trials have affirmed favourable drug safety and the ability of imlifidase to sufficiently degrade anti-HLA antibodies to permit kidney transplantation in highly sensitised candidates.

The Swedish 2014/2015 trial presented largely positive outcomes, with HLA antibody levels in all patients falling to acceptable levels to receive a transplant. The one recipient of a transplant post-imlifidase treatment reported stable graft functioning at the 36-month follow-up. Treatment was well tolerated, with myalgia experienced by one candidate and no serious adverse events reported. Likewise, in 2016, all ten sensitised patients that received imlifidase were able to successfully undergo transplantation. These recipients did not experience delayed graft function and exhibited good renal functioning.

Studies in the US also found imlifidase permitted successful transplantation in highly sensitised patients refractory to previous desensitisation. These individuals had undertaken IVIG and Rituxan treatment but failed to sufficiently lower their DSAs to an acceptable level. These candidates would not be expected to have successful engraftment, yet imlifidase administration facilitated transplantation in all. Cases of AMR did occur, but all responded to treatment. These studies affirmed the imlifidase mechanism of action and therapeutic potential for highly sensitised and refractory patients.

The HighdeS study was pivotal in evaluating the efficacy of imlifidase. Eighteen patients who were refractory and unlikely to respond to desensitisation were successfully converted to a negative cross match, when previously testing positive. Imlifidase successfully enabled transplantation in all patients and fulfilled the secondary endpoints of an appropriate level of DSA, good kidney function and an acceptable safety profile.

***Table 6: Summary of clinical studies of imlifidase***

| Trial | Status | Design | Regimen | Key Findings |
|---|---|---|---|---|
| **Phase I** NCT01802697 (Sweden) | Completed 2014 | Single centre, double blind, randomised, 29 healthy subjects | Since IV infusion of imlifidase at doses of 0.01, 0.04, 0.12, 0.24 mg/kg BW or placebo | Favourable safety profile. Efficacious removal of IgG at 0.12 and 0.24 mg/kg doses. |
| **Phase II** NCT02224820 (Sweden) | Completed 2015 | Single centre, open-label 8 ESRD patients on transplant waitlist, median cPRA 93% | IV imlifidase at 0.12 or 0.25mg/kg doses administered once or twice (within 48hrs) | Resulted in HLA antibody levels acceptable for transplantation in all patients. One patient received a transplant post-imlifidase treatment. Follow-up at 36 months reported stable graft functioning. |
| **Phase II** NCT02475551 (Sweden) | Completed 2016 | Single centre, open label | IV imlifidase at dose 0.25mg/kg pre-transplantation, horse ATG induction immunosuppression.<br>10 ESRD patients on transplant waitlist, median cPRA 90% | All patients were able to undergo transplantation. Favourable safety profile reported, with 100% graft survival at 6 months. |
| **Phase II** NCT02426684 (US) | Completed 2018 | Single centre, open-label, 17 ESRD patients on transplant waitlist, median cPRA 99.6% | IVIG + rituximab pre transplantation<br>IV imlifidase 0.24mg/kg administered pre-transplant, alemtuzumab induction immune suppression<br>IVIG + rituximab post-transplantation | Imlifidase permitted transplantation in all patients. At 6 months, graft survival was 94%, with one graft loss. At 3-years, one death and 2 further graft losses occurred. AMR occurred in 41% of patients but all cases responded to treatment. |
| **Phase II** NCT02790437 HighdeS (US, France, Sweden) | Completed 2018 | Multi-centre, open-label, 18 ESRD patients on transplant waitlist, median cPRA 99.9% | IV imlifidase at dose 0.25mg/kg pre-transplant, alemtuzumab induction immunosuppression, IVIG + rituximab post-transplant | Achieved primary endpoint of imlifidase converting positive crossmatch to negative in all patients. At 6-months, graft survival was 89%. Patient survival was 100%. |

*Source: Intron Health*

### Longer-term follow-up data to be released

Hansa has initiated a long-term observational prospective study expected to last 5 years for all 46 imlifidase-permitted transplants that took place in the phase II trials. The primary objective is to ascertain graft-survival and to evaluate overall patient survival, measures of kidney function (like creatinine levels and estimated mean glomerular filtration rate), quality of life and comorbidities.

Interim follow up data for six-months and two years from the four pooled phase II trials was presented at the European Society for Organ Transplantation annual conference in 2019 and the American Transplant Congress in May 2020 respectively (see table below). As this study progresses, the data generated over five years is expected to solidify a foundation for imlifidase as a desensitisation agent.

***Table 7: Interim follow up data from long-term observational study***

| Demographics of study population | Characteristics post-imlifidase and transplantation | Follow-up data at 6-months | Follow-up data at 2 years |
|---|---|---|---|
| 46 Patients (6-months) | All candidates were cross match negative. | Episodes of AMR occurred in 38% (5% were subclinical, detected by a biopsy taken at 6 months). Incidence rate is consistent with 20-60% of patients experiencing AMR with standard desensitisation protocols. All cases successfully resolved. | 31 patients assessed. Despite varying levels of patient DSA rebound, the AMR frequency was comparable with those reported in studies with less sensitised patients. Only 1 AMR occurred later than 6 months post-transplantation. |
| 70%- re-transplant patients | All transplanted successfully | Kidney functioning was positive and stable. Patients had estimated glomerular filtration rate (eGFR) of 60 ml/min/1.73m², consistent with historical post-kidney transplantation data. | 92% of patients had satisfactory or good kidney function (≥30 mg/min/1.73m2) At 2 years, the median eGFR was 61.5 (range 22.4-106.7) |
| 85% were crossmatch positive | DSA levels recovered post-transplantation but no significant association with cases of AMR. | Graft survival - 94% | Graft survival - 91% |
| 50% had a cPRA of 100% pre-treatment with imlifidase | | Patient survival - 100% | Patient survival - 91% |

*Source: Company reports*

## Imlifidase is Better Than Standard of Care

The four phase II trials of imlifidase have exhibited its rapid efficacy in desensitising severely sensitised patients. This is highly impressive considering the very mixed outcomes generated by standard regimens.

***Table 8: Summary of the efficacy outcomes of standard regimens***

| Study | Regimen | N | cPRA | Transplant Rate |
|---|---|---|---|---|
| 4x Hansa Pooled Data | Imlifidase | 46 | 99% | 100% |
| Jordan, 2004, J Am Soc Nephrol | IVIG | 98 | 80% | 35% |
| Vo, 2008, NEJM | IVIG + Rituxan | 20 | 77% | 80% |
| Marfo, 2012, Transplantation | IVIG+ Rituxan | 13 | >90% | 18% |
| Alachkar, 2012, Transplantation | IVIG+ Rituxan | 27 | 100% | 41% |

*Source: Company reports, NEJM, JASN, Transplantation, Intron Health*

### IVIG alone does not measure up

IVIG is the cornerstone of the current desensitisation protocols but has limited efficacy for patients with severe sensitisation. In 2004, the American Society of Nephrology found that IVIG alone reduced DSAs in sensitised individuals (cPRA 80%), enabling 35% to undergo transplantation (vs 17% of the placebo group). However, the two-year graft survival was not significantly different between the IVIG (80%) and placebo group (75%). Furthermore, allograft rejection episodes occurred in 9 of the 17 IVIG candidates in comparison to 1 in 10 of the placebo group. **These outcomes are sub-par in comparison to imlifidase.**

### IVIG + Rituxan still compares unfavourably to imlifidase

Combinations of IVIG and Rituxan may be no better than IVIG alone, with varying efficacy outcomes reported for this combination across different studies. Marfo *et al* observed transplantation rates of 18% in those given IVIG + Rituxan vs 52% in the placebo group. In addition to not increasing transplantation rates, the IVIG + Rituxan group also had higher cPRA levels post-dosing in comparison to the 14 patients that received placebo. This suggests this regimen was wholly ineffective at desensitising patients and actually performed worse than placebo.

This finding was supported by evidence in 2012 which demonstrated the failure of high-dose IVIG + Rituxan to lower DSAs in 27 highly sensitised patients with a cPRA of 100%. Although a higher proportion of IVIG + Rituxan treated individuals underwent transplantation than a similarly sensitised historical control cohort (41% and 12.8% respectively), there were no significant changes in DSA profiles post-IVIG/Rituxan treatment. Retrospective cross-matching tests of the pre-treatment sera of these transplant recipients revealed these patients would have still been eligible for transplantation with their respective deceased donor organs irrespective of IVIG/Rituxan treatment. It was deduced that the higher rate of transplantation was achieved independently of IVIG/Rituxan treatment and likely resulted from frequent crossmatching and improved medical readiness for transplantation.

Considering the 2017 conclusions of Jordan *et al*; imlifidase is likely to be utilised in conjunction with IVIG and rituximab in-order to maintain a longer window of IgG antibody suppression.

## Safety Looks Very Clean

**Although Hansa had initially feared that imlifidase may cause infection, they have not seen any evidence for this in the clinical trials. Antibiotics were used prophylactically against the possibility of upper respiratory tract infections, given for just 4 weeks orally. With this regimen, imlifidase has a favourable safety profile, with further follow-up data to be generated over the next 5 years.**

The most frequent adverse effects reported from imlifidase treatment included cases of headaches and myalgia (see table below). Out of a total of 73 patients that received imlifidase across multiple trials, one had an infusion reaction. This was rapidly resolved within 11 minutes.

Reassuringly, there was not an increase in opportunistic upper respiratory tract infections and immune vulnerability that are associated with other desensitisation techniques. This is attributed to the preservation of function of other Ig antibodies and immune cells like T and NK cells. A low risk of infection was maintained even under combinations of pre-dosing with rituximab and IVIG therapy prior to imlifidase treatment.

Imlifidase is contraindicated for patients with thrombotic thrombocytopenic purpura, as there were two cases of grade 4 serum sickness-like reactions, but it is believed these reactions were specific to the disease.

***Table 9: Safety data summary from clinical trials***

| Trial | Adverse Events Reported | Conclusion |
|---|---|---|
| **Phase I NCT01802697** | 39 AEs classified as probably related to imlifidase: | AE similar incidence to placebo |
| | - 35/39 were of Grade 1 | Safe and well tolerated |
| | - 4x Grade 2 AEs | |
| | All from one subject that experienced a probable infusion reaction. This was resolved in 15 mins with antihistamine treatment and infusion was not interrupted. | |
| | - No serious reported AEs | |
| | - No dose limiting criteria met | |
| | - No cases of withdrawal of study drug | |
| | AEs experienced by imlifidase (I) vs placebo (P): | |
| | Nasopharyngitis – 50% (I) vs 67% (P) | |
| | Fatigue – 25% (I) vs 0% (P) | |
| | Headache – 35% (I) vs 11% (P) | |
| **Phase II NCT02224820** | Combined Data for 25 patients: | Safe and well tolerated |
| | - 0% Patient mortality | |
| **Phase II NCT02475551** | No significant infectious complications | |
| **Phase II NCT02426684** | Possibly related AE: | |
| | - Parvovirus B19 viremia - 4% (1 case) | |
| | - Persistent myalgia 4% - (1 case) | |
| | - Abdominal Infection - 4% (1 case) | |
| | - Blood infection - 4% (1 case) | |
| | - Catheter site infection - 4% (1 case) | |
| **Phase II NCT02790437** | - No treatment related safety concerns | Favourable safety profile |

*Source: NEJM, company reports*

# Global Kidney Sales Could Be >$500m

**We show that the number of kidney transplants that take place will likely rise, driven by underlying conditions such as CKD as well as government policies. In recent years, some governments have put greater emphasis on the need to find kidney transplants for highly sensitised patients, which we also think will provide a favourable backdrop to help Hansa build out the market. We estimate peak sales could hit over $500m in the US and EU7 by 2030 and value this opportunity at $1.3bn, or ~100% of the value of the company.**

## Need For Kidney Transplants is Increasing

Chronic Kidney Disease (CKD) is a progressive disease that eventually leads to end-stage renal disease (ESRD), or kidney failure. ESRD is defined as an irreversible decline in kidney function which is fatal in the absence of dialysis or transplantation. The table below shows the large numbers of patients that currently exist by region and we expect this number to continue to rise, reflecting an increasing incidence of diabetes, hypertension and an ageing population. This is turn will fuel the waiting list for kidney transplants in the US and Europe.

***Table 10: CKD is the primary driver of the kidney transplant market***

| Region | CKD* Cases | ESRD Cases | Dialysis Patients |
|---|---|---|---|
| US | 15.4 million | 746,557 | 525,352 |
| EU7 | 17.9 million | 304,944 | 245,250 |

*Source: PubMed, BMJ, Briggs et al (2000) * Estimates for stages 3, 4 and 5*

## Highly Sensitised Patients Now Being Prioritised

Kidney transplantation systems vary by country, but as we show in the table below, in the US and several European countries, highly sensitised patients are being prioritised.

***Table 11: Kidney transplant policy by country***

| US | Europe | UK |
|---|---|---|
| In 2014, the US Organ Procurement and Transplantation Network (OPTN) implemented a new kidney allocation system (KAS). One of the objectives was to increase transplant opportunities for those with cPRA scores at or near 100%. Following these changes, transplant statistics do suggest that KAS improved organ access for highly sensitised patients, but lengthy wait times still persist. The percentage of transplants allocated to patients with a cPRA >99% increased from 2-3% in 2013-2014 to 11-18% in 2015. As a result, the number of very highly sensitised patients on the US waitlist decreased by 13% from 2013-2014 to 2015. | The Eurotransplant* kidney allocation system (EKTAS) has attempted to prioritise highly sensitised patients via allocation of organs to those in the “Acceptable Mismatch Programme”. These individuals have undertaken dialysis for at least 2-years and present a cPRA greater than 85%. This has led to HLA-sensitised patients gaining a greater likelihood of receiving a kidney, though there is currently no significant evidence that the most severely sensitised patients with a cPRA> 99.9% have yet benefited from this policy. | The 2019 framework utilises a two-tiered system to allocate deceased donor kidneys to recipients. In Tier A, candidates are ranked by a matchabilility score that considers blood type, HLA type and antigens. Patients with 100% chronic renal failure and those that have waited greater than 7 years on dialysis are also prioritised under this tier. Tier B encapsulates all other eligible patients and allocates points according to donor-recipient risk index combinations, waiting time, HLA match and age, patient locality to donor, donor recipient age difference, blood group and total HLA mismatch. This scheme has improved effective matching of graft life expectancy and recipient life expectancy but it does not prioritise highly sensitised patients. |

*Source: Stewart et al, 2016, Lee et al, 2018, Heidt et al, 2019 * Austria, Belgium, Croatia, Germany, Hungary, Luxembourg, the Netherlands and Slovenia*

- This shift towards prioritising highly sensitised patients is important because it will help Hansa to build market share, as they provide a solution to the problem of sensitisation
- Recent data from the Organ Procurement & Transplantation Network (US) revealed that 30% of candidates with cPRA > 98% had been on the waitlist for greater than 5-years, compared to just 14% of candidates with a cPRA<98%
  - Although many of these patients are now prioritised, a significant unmet medical need remains, which Hansa can address
- Those patients at the most highly sensitised end will benefit the most from imlifidase as transplantation is currently exceedingly difficult to achieve for this group
  - Candidates with a cPRA greater than 99.95% comprise 34% of those on the US waitlist with a cPRA between 99-100%. Yet, only 8% of transplants carried out in those with a cPRA 99-100% were in patients with a cPRA above 99.95%.
  - Analysis of data from 2016-2017 also revealed only 9.7% of patients with a cPRA>99.9% received a transplant. This is significantly lower than the average transplant rate of 18.9%.

**We would expect Hansa to target imlifidase at the areas of highest unmet medical need in the early stages of the launch, where it can have the biggest impact and where market gains should be easiest. In the next section we explain our key assumptions which give rise to our peak sales estimates in the kidney transplant space.**

## Revenue Opportunity is >$500m

**We calculate that the addressable market is 3-4k patients in both the EU7 and US. With a ~40% penetration of the most highly sensitised patients per year (and <10% of the more moderately sensitised), we believe this addressable market can continue to replenish itself given 40% of the waiting list receive transplants in Europe each year, yet the waiting list continues to grow. We forecast US net pricing as likely to be around $250k based on the cost saved from negating the need for dialysis, with pricing 35% cheaper in the EU7. From this, we calculate peak sales could approach $500m by 2030 despite not including any sales from regions outside the US or EU7. We think it likely that following the positive CHMP opinion, Hansa will seek partners for other countries which will be upside to our valuation.**

## Addressable market is 3-4k patients in each of US and EU7

Although 16k and 24k kidney transplants take place in the EU7 and US respectively each year, we estimate that the addressable market for imlifidase is likely 3-4k in each region, based on our calculations. The line "Imlifidase-eligible transplants by cPRA" in the table below is the number of transplants we would expect to happen in each cPRA band if sensitisation were not a barrier to transplantation (i.e. this becomes our addressable market once imlifidase is available).

***Table 12: Addressable market in EU7***

| EU7 | 2018 | 2019 | 2020 |
|---|---|---|---|
| Dialysis patients | | | 245,250 |
| growth | | | |
| Waiting list for transplant | | 40,410 | 40,814 |
| growth | | | 1% |
| Transplants | 15,640 | 15,953 | 16,272 |
| growth | | 2% | 2% |
| Transplants at leading centres | 11,730 | 11,965 | 12,204 |
| **Imlifidase-eligible transplants by cPRA** | | | |
| of which cPRA >80% | 1,760 | 1,795 | 1,831 |
| of which cPRA 20-80% | 1,760 | 1,795 | 1,831 |
| **Total addressable market** | **3,519** | **3,589** | **3,661** |

*Source: Intron Health estimates, Company reports*

***Table 13: Addressable market in US***

| US | 2018 | 2019 | 2020 |
|---|---|---|---|
| Dialysis patients | 515,000 | 520,150 | 525,352 |
| Growth | | 1% | 1% |
| Waiting list for transplant | 97,466 | 98,441 | 99,425 |
| Growth | | 1% | 1% |
| Transplants | 22,500 | 23,401 | 23,869 |
| Growth | | 2% | 2% |
| Transplants at leading centres | 13,500 | 14,041 | 14,321 |
| **Imlifidase-eligible transplants by cPRA** | | | |
| of which cPRA >98% | 870 | 888 | 905 |
| of which cPRA 80-98% | 807 | 823 | 839 |
| of which cPRA 20-80% | 2,199 | 2,243 | 2,288 |
| **Total addressable market** | **3,876** | **3,954** | **4,033** |

*Source: Intron Health estimates, Company reports, AstraZeneca epidemiology*

- Transplant growth over the past 5 years has been around 2-3%
- In the EU7, around 40% of the waiting list receive a transplant each year, whereas in the US it is only 24% (though the US aims to double the kidney supply by 2030)
- Hansa are targeting transplants at the leading centres in the EU7, which account for 70-80% of transplants performed
- We have assumed that the US transplant market is more fragmented, with leading centres accounting for 50-70% of volume
- In the EU7, around 15% of the waiting list has cPRA>80% and a further 15% have cPRA 20-80%
- In the US, around 29% of the waiting list have a cPRA>20%

## 8-50% annual penetration for imlifidase in eligible patients

With imlifidase expected to launch in the EU from H220, we forecast an S-shaped uptake curve owing to the difficulty in building out a new market where there have been few and inadequate treatment options historically. Also, for this reason, we have not forecasted a "bolus" effect in kidney transplant despite the high unmet medical need. Our forecasts imply fairly modest but realistic uptakes for imlifidase at peak – around 5% of all kidney transplants in the EU7 and 4% in the US. Given the high unmet need, clearly there could be upside to our forecasts.

*Table 14: Imlifidase market share forecasts by region and cPRA band*

| EU7 | 2020 | 2021 | 2022 | 2023 | 2024 | 2025 | 2026 | 2027 | 2028 | 2029 | 2030 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Eligible transplants with cPRA >80% | 1,831 | 1,867 | 1,905 | 1,943 | 1,981 | 2,021 | 2,062 | 2,103 | 2,145 | 2,188 | 2,231 |
| Treated with imlifidase | 5 | 77 | 222 | 493 | 667 | 745 | 803 | 841 | 858 | 875 | 893 |
| Share | 0% | 4% | 12% | 25% | 34% | 37% | 39% | 40% | 40% | 40% | 40% |
| Eligible transplants with moderately sensitised | 1,831 | 1,867 | 1,905 | 1,943 | 1,981 | 2,021 | 2,062 | 2,103 | 2,145 | 2,188 | 2,231 |
| Treated with imlifidase | 0 | 4 | 10 | 35 | 77 | 110 | 134 | 148 | 165 | 168 | 172 |
| Share | 0% | 0% | 1% | 2% | 4% | 5% | 7% | 7% | 8% | 8% | 8% |
| **Total EU7 patients treated with imlifidase** | **5** | **80** | **231** | **528** | **745** | **855** | **937** | **989** | **1,023** | **1,044** | **1,064** |
| *as % of total transplants* | *0%* | *0%* | *1%* | *3%* | *4%* | *5%* | *5%* | *5%* | *5%* | *5%* | *5%* |
| **US** | | | | | | | | | | | |
| Eligible transplants with cPRA >98% | 905 | 924 | 942 | 961 | 980 | 1,000 | 1,020 | 1,040 | 1,061 | 1,082 | 1,104 |
| Treated with imlifidase | 0 | 0 | 0 | 0 | 16 | 53 | 161 | 342 | 447 | 498 | 537 |
| Share | 0% | 0% | 0% | 0% | 2% | 5% | 16% | 33% | 42% | 46% | 49% |
| Eligible transplants with cPRA 80-97% | 839 | 856 | 873 | 891 | 909 | 927 | 945 | 964 | 984 | 1,003 | 1,023 |
| Treated with imlifidase | 0 | 0 | 0 | 0 | 13 | 40 | 131 | 247 | 299 | 327 | 349 |
| Share | 0% | 0% | 0% | 0% | 1% | 4% | 14% | 26% | 30% | 33% | 34% |
| Eligible transplants with cPRA 20-79% | 2,288 | 2,334 | 2,381 | 2,428 | 2,477 | 2,526 | 2,577 | 2,628 | 2,681 | 2,735 | 2,789 |
| Treated with imlifidase | 0 | 0 | 0 | 0 | 5 | 13 | 46 | 103 | 146 | 178 | 196 |
| Share | 0% | 0% | 0% | 0% | 0% | 1% | 2% | 4% | 5% | 7% | 7% |
| **Total patients treated with imlifidase** | **0** | **0** | **0** | **0** | **34** | **105** | **339** | **692** | **892** | **1,004** | **1,082** |
| *as % of total transplants* | *0%* | *0%* | *0%* | *0%* | *0%* | *0%* | *1%* | *3%* | *3%* | *4%* | *4%* |

*Source: Intron Health estimates*

- For patients with lower sensitisation rates, they are more likely to be able to find a matching transplant without the need for imlifidase use, hence the lower market penetration in those patients
- The US kidney transplant market is also more fragmented which will make it harder for imlifidase to build its market share

### Pricing of $250k would be justified in the US

We believe that imlifidase pricing of $250k in the US is a reasonable level given that:

- It treats severe and rare diseases and has orphan drug designation in several indications (AMR, kidney transplantation, GBS and GBM)
- It is highly effective and there are no other competing treatments that come close to its level of efficacy
- Imlifidase use can enable a kidney transplant that would be expected to save $500k of dialysis costs (over 5 years)
  - Transplantation costs ~$180-200k over 5 years, implying a saving to the healthcare system of c.$300k in costs

In the EU7, we forecast pricing to be around 35% lower, so $163k per course of treatment.

### Peak Sales Approaching $500m by 2030

Putting all the above together, we forecast almost $500m in sales by 2030 (note that the latest patent protection family extends to 2035 with some going in 2030).

***Table 15: Imlifidase in kidney transplant - sales forecasts by region***

| **EU7** | **2020** | **2021** | **2022** | **2023** | **2024** | **2025** | **2026** | **2027** | **2028** | **2029** | **2030** |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Total patients treated | 5 | 80 | 231 | 528 | 745 | 855 | 937 | 989 | 1,023 | 1,044 | 1,064 |
| Price ($) | 162,500 | 162,500 | 162,500 | 162,500 | 162,500 | 162,500 | 162,500 | 162,500 | 162,500 | 162,500 | 162,500 |
| growth | N/A | 0% | 0% | 0% | 0% | 0% | 0% | 0% | 0% | 0% | 0% |
| Sales ($m) | 1 | 13 | 38 | 86 | 121 | 139 | 152 | 161 | 166 | 170 | 173 |
| **Sales (SEKm)** | **8** | **114** | **328** | **748** | **1,054** | **1,210** | **1,327** | **1,400** | **1,448** | **1,477** | **1,507** |
| *growth* | *N/A* | *1362%* | *188%* | *128%* | *41%* | *15%* | *10%* | *5%* | *3%* | *2%* | *2%* |
| **US** | | | | | | | | | | | |
| Total patients treated | 0 | 0 | 0 | 0 | 34 | 105 | 339 | 692 | 892 | 1,004 | 1,082 |
| Price ($) | 250,000 | 252,500 | 255,025 | 257,575 | 260,151 | 262,753 | 265,380 | 268,034 | 270,714 | 273,421 | 276,156 |
| growth | N/A | 1% | 1% | 1% | 1% | 1% | 1% | 1% | 1% | 1% | 1% |
| Sales ($m) | 0 | 0 | 0 | 0 | 9 | 28 | 90 | 185 | 241 | 274 | 299 |
| **Sales (SEKm)** | **0** | **0** | **0** | **0** | **77** | **240** | **783** | **1,615** | **2,102** | **2,391** | **2,603** |
| *growth* | *N/A* | *N/A* | *N/A* | *N/A* | *N/A* | *211%* | *226%* | *106%* | *30%* | *14%* | *9%* |
| | | | | | | | | | | | |
| Global sales ($m) | 1 | 13 | 38 | 86 | 130 | 167 | 242 | 346 | 408 | 444 | 472 |
| **Global sales (SEKm)** | **8** | **114** | **328** | **748** | **1,131** | **1,450** | **2,110** | **3,015** | **3,550** | **3,868** | **4,109** |
| *Growth* | | *1362%* | *188%* | *128%* | *51%* | *28%* | *45%* | *43%* | *18%* | *9%* | *6%* |

*Source: Intron Health estimates*

## The NPV of the Kidney Opportunity Alone is ~$1.3bn

Assuming mature EBIT margins of 85%, a tax rate of 20% and a discount rate of 9%, we calculate that the NPV of imlifidase revenues over 2020-35 is approximately $625m in the EU7 and $700m in the US, giving a total value of $1.3bn. At a share price of SEK257, the kidney transplant opportunity alone is worth 100% of the market cap.

***Table 16: Imlifidase in kidney - NPV calculation***

| **Item** | |
|---|---|
| Global NPV ($m) | 1,313 |
| Global NPV/share (SEK) | 257.13 |
| Share price (SEK) | 257.00 |
| **Kidney transplant indication value as % of share price** | **100%** |

*Source: Intron Health estimates*

# Commercialisation Plans

**One of the key issues for investors will be whether Hansa can successfully commercialise imlifidase in the kidney transplant setting. We have discussed in detail the launch plans with management and feel more confident than we would with most small biotechs that Hansa can commercialise Idefirix by themselves and extract the value the market is placing on the indication. However, it is very clear to us that sales will be slow to take off as many changes in behaviour are required to get Idefirix to all the patients that need it. Investors (and analysts) will need to be patient and track non-sales related data points to assess whether Idefirix is on track to reach its full potential.**

## Hansa to Use Highly Targeted Launch Tactics

Hansa intend to build out their own sales force in Europe to sell in the 5 main countries (plus Sweden and Norway). However, the launch will be with a small number of sales reps (low double digits) and medical sales liaisons. It will focus on leading transplantation centres in Europe (3-5 in each country), which account for 70-80% of all kidney transplants. Hansa will thus be targeting a small number of high-volume centres which are also the most innovative and likely to be willing to try imlifidase. Moreover, many of the doctors in those centres will have been involved in the imlifidase trials and are therefore already familiar with the data. Hansa's approach will be so targeted that they will go centre by centre rather than country by country.

## Sales Will Ramp Very Slowly

**As we discussed in an earlier section, the US and Europe have a very prescriptive approach to kidney allocation. However, both regions have implemented changes as to how they allocate kidneys to try to enable more sensitised patients to receive donor kidneys. These changes have only come within the last 5 years and in Europe seemed to have made little difference for highly sensitised patients. Therefore, we believe that Hansa will have to change behaviours materially to increase the propensity for highly sensitised patients to receive a kidney. They will have to stop doctors viewing a kidney allocation to a highly sensitised patient as being a risky option with the kidney potentially being used less effectively.**

Despite these challenges we believe that Hansa can shift mindsets given that they are only targeting 3-5 key centres per country in the EU7 and all the centres will know of the existence of Idefirix even if they have not tried it. Today, some kidneys that are donated are lost because a suitable recipient can't be found (1k in the US a year). If a sensitised-only patient can be found to receive one of those, that will be an easy win. There are

also highly sensitised patients who will die without receiving a kidney, so this is another area where Hansa can rapidly convert patients.

### CEO Has Changed Clinical Behaviours Before

In our discussions with management, the CEO's prior experience at Vifor in trying to convince doctors to use IV iron despite the availability of an oral substitute (but a vastly inferior one) should help Hansa here.

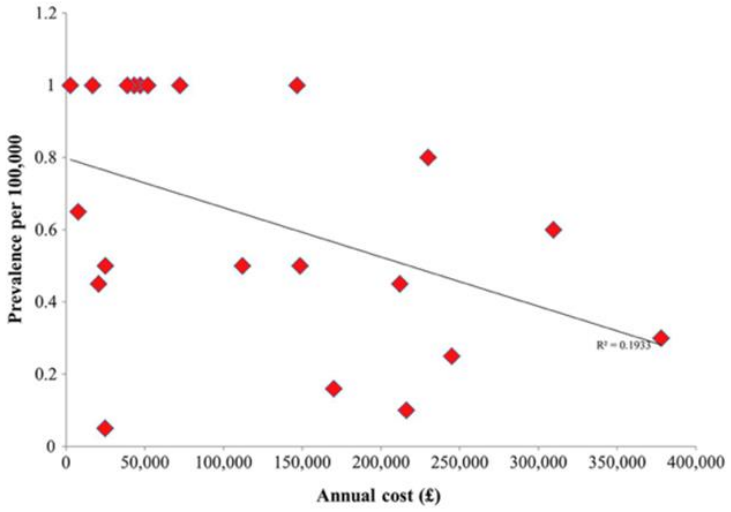
## Commercial Launch to Be Relatively Inexpensive

**Hansa will require very few reps on the ground (in the low double digits), limited commercial activity given the very small transplant community and target 3-5 transplant centres per country, which account for 70-80% of all transplants in the EU7. Consequently, we forecast just $5m of marketing costs in 2020, rising to $10m by 2021. Clearly, US approval will warrant higher commercial spend.**

## Idefirix to Be Priced as Orphan Drug

Management have indicated that Idefirix should achieve orphan drug pricing levels and that they are more than comfortable with current analyst assumptions of $200k pricing/course in the US. In terms of passing Europe's stringent health economics boards (NICE/IQWIG), Hansa will be able to point to the fact that dialysis costs $60-70k per year in Europe ($100k in the US) and hence 4-5 years without dialysis should allow major savings ($300-500k, less drug cost) for the health system. We assume net pricing of $163,000 in Europe and $250,000 in the US given that the cost of the operation and potential other desensitisation treatments may also need to be incorporated into the health economics filing.

***Chart 9: Scatter plot of ultra-orphan disease prevalence against annual cost***




*Source: Igho J Onakpoya et al, BMJ (2015)*

# Gene Therapy Opportunity

**We believe that gene therapy presents a transformational opportunity for Hansa. Imlifidase can solve a major problem for many gene therapies – antibodies to the AAV vectors that many gene therapies use (and likely lentiviral vectors). Currently, there is no solution to this problem and patients who are seropositive for AAV antibodies are generally ineligible to receive gene therapy, as it is unlikely to work.**

**By signing the Sarepta deal, Hansa has shown a new way to extract value from imlifidase which is replicable and could be worth more than the kidney transplant indication if they are able to sign multiple deals.**

**We estimate that the Sarepta deal itself is worth 14% to Hansa's market cap, which gives an indication of the future upside that could come from this opportunity. Hansa is already in talks with a number of potential gene therapy partners and we show how active the space is likely to be in the next few years. Despite the huge potential for imlifidase and the follow-on pipeline cousins, there is no obvious acquirer for Hansa. This is because most gene therapy companies are too small and there is no Big Pharma strategic buyer given the highly niche indications with very small numbers of patients.**

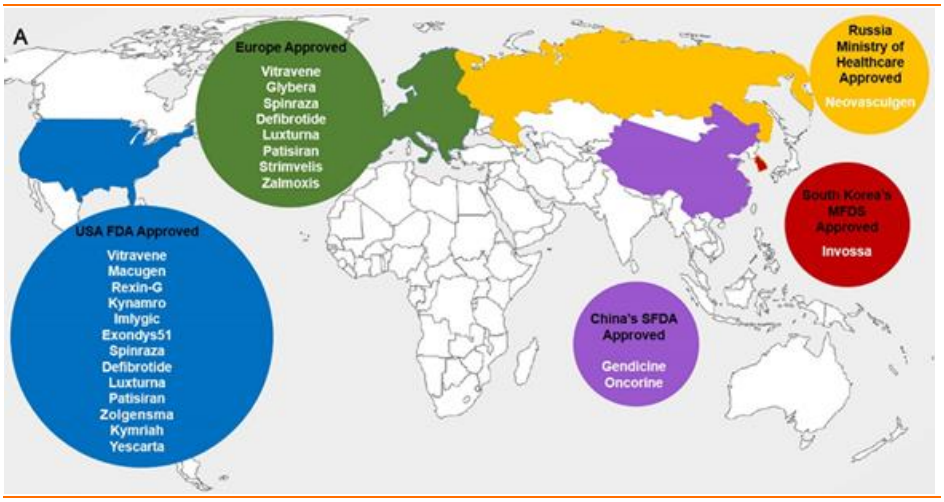
## Gene Therapy - A Rapidly Growing Area of Medicine

The gene therapy field has grown rapidly over the past 10 years, with 20 gene products already approved and over 300 product candidates currently under development for human gene therapy. These treatments are generally used where a single genetic mutation is the cause of disease – so by delivering a healthy copy of the gene, it is possible to cure the disease.

In North America and Europe, 13 and 8 gene therapies are already approved, respectively, as of 2019 (see map below). Two recent approvals include:

- Spark Therapeutics's Luxturna in 2018, which uses an AAV vector to deliver the RPE65 gene to patients with retinal dystrophy
- Novartis' Zolgensma in 2019, which uses an AAV9 vector to deliver SMN1 for the treatment of SMA

***Chart 10: Map of approved gene therapies***




*Source: Frontiers, 2019*

## Exciting Pipeline of Near-Term Assets

There are over 300 gene therapies currently in development, with 58% in phase II and 9% in phase III. The gene therapy pipeline for 2020-2022 notably includes therapeutics for various cancers, paediatric patients and haematological conditions (see below).

***Table 17: Selection of Gene Therapy Pipeline 2020-2022***

| Therapy Name | Manufacturer | Indication | Phase of Development | Projected Launch Year |
|---|---|---|---|---|
| Valoctocogene roxaparvovec | BioMarin Pharmaceutical | Severe haemophilia A in adult patients | Pending FDA approval 21/08/20 | **2020** |
| Instiladrin | FKD Therapies/ Ferring Pharmaceuticals | High-grade, non-muscle invasive, bacillus Calmette-Guérin refractory bladder cancer in adults | Received CRL*, likely to resubmit | **2021** |
| OTL-200 | Orchard Therapeutics | Late infantile or early juvenile metachromatic leukodystrophy | Phase I/II | **2021** |
| AAVhAADC | Agilis Biotherapeutics/ PTC Therapeutics | Aromatic L-amino acid decarboxylase deficiency in paediatrics | Phase II | **2021** |
| AT132 | Audentes Therapeutics | X-linked myotubular myopathy in pediatrics | Phase I/II | **2021** |
| Engensis (donaperminogene seltoplasmid) | Helixmith | Diabetic foot ulcers in adults with peripheral artery disease | Phase III | **2021** |
| Etranacogene dezaparvovec | Uniqure | Haemophilia B in adults | Phase III | **2021** |
| OTL-101 | Orchard Therapeutics | adenosine deaminase severe combined immunodeficiency in paediatrics aged 1 month and older | Phase I/II | **2021** |
| SPK-8016 | Spark Therapeutics | Haemophilia A adult patients with inhibitors | Phase I/II | **2021** |
| Lumevoq | GenSight Biologics | Leber's hereditary optic neuropathy, in adults with the ND4 mutation | Phase III | **2022** |
| ProstAtak (aglatimagene besadenovec) | Advantagene | First-line treatment of adults with intermediate to high-risk, localized, prostate cancer, in combination with external beam radiation therapy and valacyclovir | Phase III | **2022** |
| LentiGlobin (beta-globin gene therapy) | Bluebird Bio | Sickle cell disease in adult and paediatric patients | Phase III | **2022** |
| Fidanacogene elaparvovec | Spark Therapeutics | Haemophilia B in adult patients | Phase III | **2022** |
| OTL-103 | Orchard Therapeutics | Wiskott Aldrich syndrome in paediatrics | Phase II | **2022** |
| BIIB112 | Biogen/ Nightstar Therapeutics | X-linked retinitis pigmentosa in males aged 10 years and older. | Phase II/III | **2022** |
| SPK-8011 | Spark Therapeutics | Haemophilia A in adult patients | Phase III | **2023** |

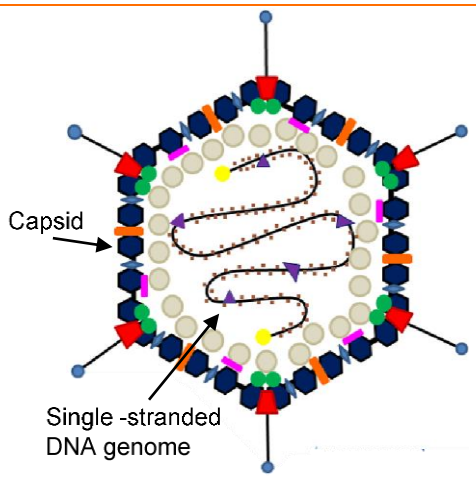
*Source: US National Library of Medicine * CRL was for manufacturing issue, so resubmission seems likely within 1 year*

## AAVs are the Most Popular Choice of Vector

Viral vectors such as AAV are most frequently used to deliver healthy genes to patients due to their limited capacity to induce an immune response (relative to other viruses) coupled with their efficient ability to invade cells and enable episomal expression of the DNA they carry.

AAVs consist of a protein shell (called a capsid), which encapsulates a small single-stranded DNA genome (as below). It is possible to manufacture recombinant AAVs that have been engineered to have no viral genes and instead contain a copy of the healthy gene that patients lack. This AAV vector is then able to deliver the healthy gene into the cell, allowing the body to use it to transcribe healthy protein.

***Chart 11: Image of an AAV vector***




*Source: Waye et al, 2010*

AAV vectors are divided into different serotypes according to the amino acid sequence of their capsid. These serotypes differ in the cell-types they can infect and so can preferentially transduce specific cell types. The table below indicates the optimal serotypes for the transduction of various organs:

***Table 18: Optimal serotypes for transduction of various organs***

| Serotype | Tissue |
|---|---|
| AAV1 | Skeletal muscle, lung, CNS, retina, pancreas, |
| AAV2 | Smooth muscle, skeletal muscle, CNS, liver and kidney |
| AAV3 | Hepatocarcinoma, skeletal muscle, inner ear |
| AAV4 | CNS, retina |
| AAV5 | Skeletal muscle, CNS, lung, retina, liver |
| AAV6 | Skeletal muscle, heart, lung, bone marrow |
| AAV7 | Skeletal muscle, retina, CNS |
| AAV8 | Liver, skeletal muscle, CNS, retina, pancreas, heart |
| AAV9 | Liver, heart, brain, skeletal muscle, lungs, pancreas, kidney |
| AAV10 | Liver |

*Source: Verdera et al, 2020*

## But AAV Antibodies Cause a Problem…

Although AAV viruses have relatively low immunogenicity, elements such as the capsid and the delivered nucleic acid sequence can still trigger an immune response. This, coupled with the finding that 50-90% of the human population have been previously exposed to AAV and so may have developed a pre-existing adaptive response to that particular AAV variant, results in the presence of neutralising antibodies (NAbs) against capsid proteins in a significant proportion of the population.

The presence of pre-formed NAbs can dramatically impair the clinical efficacy of AAV therapies by:

- Binding to and preventing gene therapies from entering the target cell, thereby reducing the expression of that gene in the target tissues
- Activating adaptive responses that eliminate cells that express AAV delivered transgenes

The prevalence of any level of neutralising antibodies towards AAV serotypes ranges from 40-70% across the general population and is higher in some serotypes than others. As there is broad cross-reactivity between AAV serotypes, neutralising antibodies to one serotype is likely to be at least partially reactive against another.

***Table 19: Prevalence of neutralising antibodies towards differing serotypes***

| Serotype | Prevalence in the general population |
|---|---|
| AAV1 | 67% |
| AAV2 | 72% |
| AAV5 | 40% |
| AAV6 | 46% |
| AAV8 | 38% |
| AAV9 | 48% |

*Source: Boutin et al, 2010*

### Other factors also matter

Whether a powerful immune response occurs against an AAV vector is determined by several factors, not just whether a patient is seropositive. These other factors include:

- Target Cell Type
  - There is a lower risk of an immune response if vectors are administered to isolated organs such as the eye or CNS
- Delivery Cell Type
  - The site of administration can matter, as intramuscular injections or IV infusions can increase the risk of immunogenicity
- Vector Profile
  - The properties of the vector impacts immunogenicity; for example, vectors that possess an inert capsid and do not contain certain triggering sequences of DNA are less immunogenic

- Impurities in Vector from manufacturing
  - The more impurities and the less precise the manufacturing, the more likely it is to be immunogenic

**However, if a patient has a large number of neutralising antibodies, it is very likely that there will be a powerful immune response, regardless of other factors, which will negate the effects of gene therapy. Therefore, most seropositive individuals are ineligible to receive AAV-based treatment or repeated doses of a previously received therapy.**

## …Imlifidase Could Be the Solution

The 1-week window provided by imlifidase is sufficient for the 2 days required for AAV therapy transfection. Cytokine storms do not occur as anti-AAV antibodies are pre-existing.

Hansa's endopeptidase technology could address the limitation of NAbs in gene therapy. Imlifidase could sufficiently degrade these NAbs to create a 1-week window of opportunity to administer or re-dose a gene therapy. This would maximise vector transduction and delivery of the gene product and so increase therapeutic efficacy.

### Imlifidase successfully decreased anti-AAV antibodies

NHPs are natural hosts to AAVs and so naturally have anti-AAVs present.

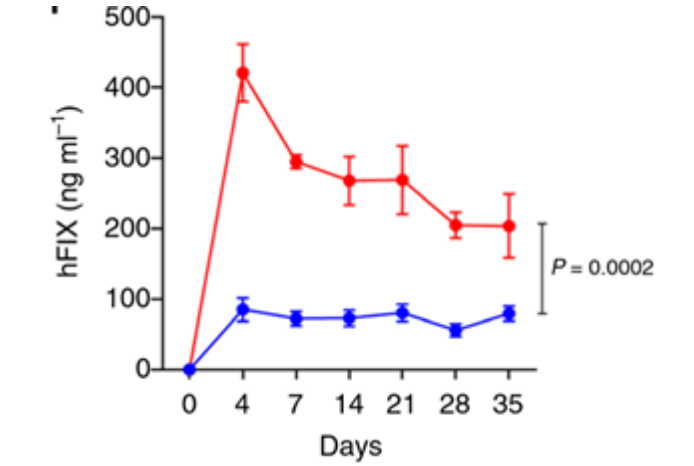
A pre-clinical study published in Nature by Spark Therapeutics has shown that a single *in vivo* administration of imlifidase resulted in decreased anti-AAV antibodies and Nabs, enabling successful liver transduction in both the setting of pre-existing natural immunity to AAVs and vector re-administration in non-human primates (NHPs).

In a therapeutically relevant model of haemophilia B:

- NHPs either received imlifidase or placebo treatment pre-administration of an AAV8 vector delivering human coagulation factor IX (hFIX), which haemophilia B patients lack
- Imlifidase administration decreased anti-AAV8 IgG and permitted significantly higher hFIX transgene expression compared to those given a placebo
- After vector administration, those treated with imlifidase developed lower anti-AAV8 IgG than the control animals

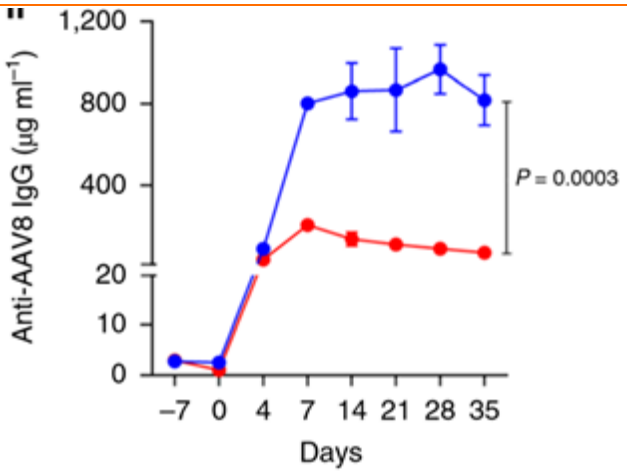
These findings were replicated in another set of NHPs with minimal pre-existing antibodies, with total degradation of IgG and enhanced liver transduction observed in those given imlifidase. **These results suggest that imlifidase administration reduces natural immunity to AAV and enhances AAV vector transduction in NHPs.**

***Chart 12: hFIX transgene plasma levels over 35 days post-AAV administration (Red-imlifidase, Blue- placebo)***




*Source: Nature (Leborgne et al, 2020)*

***Chart 13: Anti-AAV8 IgG at baseline and post AAV8-hFIX vector administration. (Red-imlifidase, blue-placebo)***




*Source: Nature (Leborgne et al, 2020)*

## Imlifidase Can be Re-dosed & Works Well in Humans

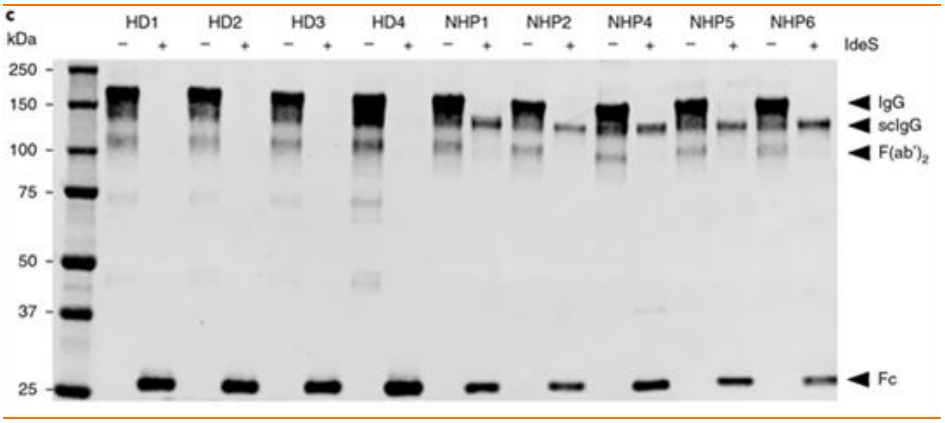
Also investigated in the Nature study, imlifidase was shown to enable *in vivo* gene therapy **after imlifidase and gene therapy had previously been administered.** These findings were then affirmed in a larger NHP study group, in which imlifidase administration and AAV treatment, after a previous AAV infusion, resulted in a higher transgene expression than in the control.

Furthermore, imlifidase administration in *in vitro* human plasma samples of healthy and Crigger-Najjar Syndrome patients (a rare liver disease) affirmed this efficacy.

- Post-incubation with imlifidase, all plasma samples had significantly lower anti-AAV8 IgG levels (see Western blot below)
- The presence of anti-imlifidase antibodies in human subjects did not affect the cleavage of IgG

These results suggest that imlifidase may **efficiently** and **safely** degrade anti-AAV neutralising antibodies in humans, indicating imlifidase may permit seropositive individuals to access viral vector gene therapy.

***Chart 14: Western blot displaying efficient cleavage of plasma IgG in healthy humans (HD1-HD4) and non-human primates (NHP1-NHP6)***




*Source: Leborgne et al , 2020 "+" indicates that imlifidase was added to sample of plasma*

- Blots show presence of IgG in all samples without imlifidase (the "-" columns)
- All human subjects (HD1-HD4) had complete cleavage of IgG, signified by the presence of Fc fragments in the "+" column where imlifidase was added
- Non-human primate (NHP) samples also recorded a blot for scIgG, which indicates the IgG was not fully broken down, showing that imlifidase is more effective in humans than NHPs

### Non-IgG antibodies are not a barrier to gene therapy

Imlifidase only depletes IgG antibodies, leaving others, such as IgM and IgA, untouched. However, the presence of these other antibodies, even if they are neutralising and against AAV, seems not to be a problem. Unlike IgG, IgM does not activate the complement system and thus is much less effective against potential pathogens including AAV. IgG also binds with 10x the affinity of IgM and it is therefore clear that evolution intended for IgG to be the main molecule conferring immunity.

### Antibodies directed towards imlifidase are not an issue

Antibodies to imlifidase from previous exposure to *S.pyogenes* (which naturally produces imlifidase as a defence mechanism against the human immune system) is a potential concern and could mean that imlifidase is unable to deplete IgG sufficiently before being neutralised itself. However, the results of the Nature study (Leborgne *et al*, 2020) and of other imlifidase clinical studies have shown that imlifidase can still be effective despite the presence of neutralising antibodies against it. We would hypothesise that because the amount of imlifidase administered is very large, it does not give enough time for neutralising antibodies to remove it before it can act to deplete IgG.

Furthermore, although anti-imlifidase antibodies develop post-treatment, this appears to be transient and decreases sufficiently over time to permit subsequent doses.

## Sarepta Deal Can be Model For Future Deals

**The Sarepta deal does not preclude Hansa from signing similar deals with other gene therapy companies for different indications. We expect this to be a priority for the company given the near-term gene therapy pipeline that exists and management are currently in active discussions. However, we include zero revenues for any future deals in our base case, so any new deals would be upside to our valuation.**

In July 2020, Hansa and Sarepta announced an agreement that Hansa would grant a global license to Sarepta to develop and promote imlifidase as a pre-treatment for gene therapy in DMD and LGMD patients who have pre-existing antibodies to AAV.

We believe that the structure of the Sarepta deal is favourable to Hansa, allowing them to earn sales, milestones and royalties without paying for development. Sarepta has agreed to fund all preclinical, clinical and regulatory development. Hansa's only obligation is to supply imlifidase to Sarepta free of charge for development purposes. Once they have approval, Hansa will control the price of imlifidase, which it will sell direct to Sarepta, and Sarepta can then choose to bundle it with gene therapy or price separately to suitable patients. The financial terms of the deal are that Hansa:

- Collects a $10m upfront payment
- Books 100% imlifidase sales
- May earn up to $397.5m in milestones, the majority of which are sales milestones (not included in our base forecasts)
- Earn tiered high-single digit to mid-teens royalties on incremental sales of gene therapy

## DMD and LGMD are Serious Genetic Disorders

**Both DMD and LGMD are genetic diseases that cause muscle wasting and are the focus of Sarepta's alliance with Hansa.**

**Duchenne muscular dystrophy (DMD)** is a severe hereditary form of muscular dystrophy that originates from a recessive X-linked mutation of the dystrophin gene. As a result, dystrophin production is limited, which is essential for muscle development. As DMD patients age, muscle is increasingly replaced by fibrous tissue and fat, causing progressive muscle weakness and eventually cardiac and respiratory problems, ultimately causing death, usually in the twenties.

**Limb-girdle muscular dystrophies (LGMD)** are genetic diseases that result in progressive muscle weakness and wasting of the arms and legs. The age of onset, severity and progression of symptoms varies case to case, with childhood-onset cases observed to be more debilitating. Most patients with LGMD will be wheelchair dependant at 30 years of age and will not fulfil their full life expectancy.

## Sarepta Deal is Worth SEK37/share

**Hansa hope that imlifidase in gene therapy will move into the clinic in H2 2021. We expect the first DMD sales in 2024 and forecast highly risk-adjusted peak sales (including royalties) of c. $100m by 2027. Thereafter, we expect sales to fall as the DMD bolus sales decline to zero by 2030. Given the different disease dynamics of DMD and LGMD, we have forecasted imlifidase sales separately for each. With a gross margin of 90% and no OPEX, these sales are very high margin and with the contribution from gene therapy royalties, we value the deal at 14% of the current market cap.**

### DMD Bolus to peak in 2026

Given there is a large prevalent population with DMD, who are inadequately treated, we would expect to see a bolus effect for the sales in this population.

*Table 20: Imlifidase forecast for treatment of DMD prevalence (bolus)*

| US | 2020 | 2021 | 2022 | 2023 | 2024 | 2025 | 2026 | 2027 | 2028 | 2029 | 2030 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| DMD - prevalence (bolus) | 10,000 | 10,300 | 10,609 | 10,927 | | | | | | | |
| growth | | 3.0% | 3.0% | 3.0% | | | | | | | |
| **of which have AAV antibodies** | **1,750** | **1,803** | **1,857** | **1,912** | **1,874** | **1,780** | **1,638** | **1,507** | **1,432** | **1,417** | **1,417** |
| Imlifidase penetration | | | | | 2% | 5% | 8% | 8% | 5% | 1% | 0% |
| **Patients treated (bolus)** | | | | | **38** | **94** | **142** | **131** | **75** | **14** | **0** |

*Source: Intron Health estimates*

- The prevalence is growing at 3% due to better treatments which are extending lifespan
- Around 15-20% of the DMD prevalence have AAV antibodies and thus would be ineligible for gene therapy treatment without using imlifidase
- Our forecasts imply just under 30% of the bolus with AAV antibodies receive imlifidase over 6 years
- The other 70% may be ineligible for gene therapy for other reasons

### Around 50 incident DMD patients treated per year at peak

In the US, we estimate there are around 450 new diagnoses of DMD per year. Of these, 15-20% have AAV antibodies, leaving an eligible population of around 80 patients, of which we assume 60% could be treated with imlifidase at peak.

*Table 21: Imlifidase forecast for treatment of DMD incidence*

| US | 2020 | 2021 | 2022 | 2023 | 2024 | 2025 | 2026 | 2027 | 2028 | 2029 | 2030 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| DMD - incidence | 450 | 453 | 456 | 460 | 463 | 466 | 469 | 473 | 476 | 479 | 483 |
| growth | | 0.7% | 0.7% | 0.7% | 0.7% | 0.7% | 0.7% | 0.7% | 0.7% | 0.7% | 0.7% |
| **Of which have AAV antibodies** | **79** | **79** | **80** | **80** | **81** | **82** | **82** | **83** | **83** | **84** | **84** |
| Imlifidase penetration | | | | | 10% | 30% | 40% | 50% | 60% | 60% | 60% |
| **Patients treated (incident)** | | | | | **8** | **24** | **33** | **41** | **50** | **50** | **51** |

*Source: Intron Health estimates*

### Risk-adjusted imlifidase sales in DMD to be around $10m/year

Hansa cannot afford to erode imlifidase pricing in other indications, so we expect pricing in gene therapy to be similar (~$250k in the US). We risk-adjust our sales down to 40% to account for development and regulatory risk and then scale them up to account for ex-US territories.

*Table 22: Imlifidase global sales from DMD*

| US | 2024 | 2025 | 2026 | 2027 | 2028 | 2029 | 2030 | 2031 | 2032 | 2033 | 2034 | 2035 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Price ($/dose) | 260,151 | 262,753 | 265,380 | 268,034 | 270,714 | 273,421 | 276,156 | 278,917 | 281,706 | 284,523 | 287,369 | 290,242 |
| Imlifidase direct US DMD sales ($m) | 12 | 31 | 47 | 46 | 34 | 18 | 14 | 14 | 14 | 15 | 15 | 15 |
| Risk adjustment | 40% | | | | | | | | | | | |
| **Risk-adjusted US DMD sales ($m)** | **5** | **12** | **19** | **18** | **14** | **7** | **6** | **6** | **6** | **6** | **6** | **6** |
| | | | | | | | | | | | | |
| ROW sales as % of US sales | 70% | 70% | 70% | 70% | 70% | 70% | 70% | 70% | 70% | 70% | 70% | 70% |
| ROW imlifidase DMD sales | 3 | 9 | 13 | 13 | 9 | 5 | 4 | 4 | 4 | 4 | 4 | 4 |
| **Global risk-adj. imlifidase DMD sales ($m)** | **8** | **21** | **32** | **31** | **23** | **12** | **10** | **10** | **10** | **10** | **10** | **10** |

*Source: Intron Health estimates*

### DMD royalties to add $15-40m of profit

Assuming a price of $1m for the gene therapy in the US (Zolgensma, a gene therapy from 2019, was priced at >$2m), we calculate that Hansa would receive $38m at peak in gene therapy royalties, falling to c. $15m as the use in the bolus declines.

*Table 23: Gene therapy royalties to Hansa in DMD*

| US | 2024 | 2025 | 2026 | 2027 | 2028 | 2029 | 2030 | 2031 | 2032 | 2033 | 2034 | 2035 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Gene therapy pricing ($000s/dose) | 1,000 | 1,010 | 1,020 | 1,030 | 1,041 | 1,051 | 1,062 | 1,072 | 1,083 | 1,094 | 1,105 | 1,116 |
| *Growth* | | *1%* | *1%* | *1%* | *1%* | *1%* | *1%* | *1%* | *1%* | *1%* | *1%* | *1%* |
| Hansa royalty rate | 8% | 10% | 11% | 13% | 14% | 15% | 15% | 15% | 15% | 15% | 15% | 15% |
| **Global DMD gene therapy royalties ($m)** | **6** | **19** | **33** | **38** | **31** | **17** | **14** | **14** | **14** | **14** | **15** | **15** |

*Source: Intron Health estimates*

### LGMD sales and royalties could peak at ~$30m.

As we have built a similar sales model for LGMD to DMD, we do not include all the tables here, so please contact us if you would like to have this information. Our total sales and royalties for LGMD are given below.

*Table 24: Imlifidase global sales from LGMD*

| US | 2025 | 2026 | 2027 | 2028 | 2029 | 2030 | 2031 | 2032 | 2033 | 2034 | 2035 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Price ($/dose) | 262,753 | 265,380 | 268,034 | 270,714 | 273,421 | 276,156 | 278,917 | 281,706 | 284,523 | 287,369 | 290,242 |
| Imlifidase direct US LGMD sales ($m) | 5 | 14 | 21 | 20 | 13 | 4 | 2 | 2 | 2 | 3 | 3 |
| Risk adjustment | 40% | | | | | | | | | | |
| **Risk-adjusted US LGMD sales ($m)** | **2** | **5** | **8** | **8** | **5** | **2** | **1** | **1** | **1** | **1** | **1** |
| | | | | | | | | | | | |
| ROW sales as % of US sales | 70% | 70% | 70% | 70% | 70% | 70% | 70% | 70% | 70% | 70% | 70% |
| ROW imlifidase LGMD sales | 2 | 4 | 6 | 6 | 4 | 1 | 1 | 1 | 1 | 1 | 1 |
| **Global risk-adj. imlifidase LGMD sales ($m)** | **4** | **9** | **14** | **13** | **9** | **3** | **2** | **2** | **2** | **2** | **2** |
| **Global LGMD gene therapy royalties ($m)** | **3** | **8** | **15** | **16** | **11** | **4** | **2** | **2** | **2** | **2** | **2** |

*Source: Intron Health estimates*

- The US prevalence of LGMD is around 5.5k and we view this as having a bolus potential (for the 15-20% with AAV antibodies)
- We forecast around 30% of the bolus are treated with imlifidase over 6 years
- We estimate the US incidence at just 75-80 people/year, falling to ~15 with AAV antibodies and assume a peak penetration of 60% of this population
- We forecast a 2025 launch

### Total DMD & LGMD sales of up to $45m and royalties of $52m

Combining our forecasts, we are looking for c. $100m of sales and royalties across both DMD and LGMD, at peak. When the bolus opportunity is spent, we see a longer-term potential for around $30m/year at very high margin (>90%).

***Table 25: Global Imlifidase and royalty forecasts for DMD & LGMD***

| US | 2024 | 2025 | 2026 | 2027 | 2028 | 2029 | 2030 | 2031 | 2032 | 2033 | 2034 | 2035 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Global Sarepta imlifidase sales ($m) | 8 | 25 | 41 | 45 | 36 | 21 | 12 | 11 | 12 | 12 | 12 | 12 |
| Global Sarepta gene therapy royalties ($m) | 6 | 22 | 42 | 52 | 47 | 29 | 18 | 16 | 17 | 17 | 17 | 17 |

*Source: Intron Health estimates*

### NPV of Sarepta is SEK1.6bn, or 14% of market cap

At a WACC of 9% and no terminal value after 2035, we show that the Sarepta deal is still worth 14% of its current share price (SEK257).

***Table 26: NPV calculation of Sarepta deal (in SEKm)***

| SEKm | 2024 | 2025 | 2026 | 2027 | 2028 | 2029 | 2030 | 2031 | 2032 | 2033 | 2034 | 2035 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Sales | 71 | 216 | 356 | 396 | 318 | 180 | 109 | 99 | 100 | 102 | 104 | 105 |
| Gross margin | 90% | 90% | 90% | 90% | 90% | 90% | 90% | 90% | 90% | 90% | 90% | 90% |
| **Gross profit** | **64** | **194** | **321** | **357** | **286** | **162** | **98** | **89** | **90** | **92** | **93** | **95** |
| Royalties | 55 | 192 | 364 | 457 | 409 | 251 | 156 | 142 | 144 | 147 | 149 | 152 |
| **EBIT** | **119** | **387** | **685** | **814** | **696** | **413** | **254** | **230** | **234** | **238** | **242** | **247** |
| Tax (at 20%) | -24 | -77 | -137 | -163 | -139 | -83 | -51 | -46 | -47 | -48 | -48 | -49 |
| **NOPAT** | **95** | **309** | **548** | **651** | **556** | **330** | **203** | **184** | **188** | **191** | **194** | **197** |
| **NPV (SEKm)** | **1,634** | | | | | | | | | | | |
| Number of shares (2020) | 44,468 | | | | | | | | | | | |
| **NPV/share (SEK)** | **36.74** | | | | | | | | | | | |
| | | | | | | | | | | | | |
| Share price (SEK) | 257 | | | | | | | | | | | |
| **Sarepta as % of share price** | **14%** | | | | | | | | | | | |

*Source: Intron Health estimates*

# Bone Marrow Opportunity Could Be Big

**An allogenic bone marrow transplant involves the administration of healthy hematopoietic stem cells (HSC) to patients with depleted or dysfunctional bone marrow and is most commonly used to treat R/R haematological malignancies, such as multiple myeloma, lymphomas and leukaemia. These treatments are often urgently needed, which precludes the time to find a fully matched donor. Therefore, in the past several years, there has been a rise in the use of partially (haploidentical), alternative and HLA-mismatched**

**allogenic bone marrow transplants. Therefore, the presence of donor specific antibodies has become an increasingly prominent barrier to successful bone marrow engraftment, similar to what we have seen with kidney transplants. We believe there is good reason to believe that imlifidase could be the solution to this problem and if so, we could see >$400m of peak sales by the early 2030s. We currently value this opportunity at an NPV of $165m, but if fully de-risked it could be of a similar size to the kidney transplant market. Moreover, the adoption rate would likely be higher as oncologists usually adopt new technologies faster than in other therapeutic areas.**

### Sensitised stem cell transplant patients have worse outcomes

In sensitised patients who undergo an allogenic stem cell transplant, studies have affirmed the increased incidence of primary poor graft function, with 27.3% of sensitised patients experiencing this issue vs 1.9% of non-sensitised patients. The presence of these antibodies (DSAs) has also been linked with lower patient survival. Desensitisation protocols, like those for solid organ transplantation, are therefore deployed to lower DSAs pre-transplantation.

### Current desensitisation methods are inadequate in many patients

Current desensitisation protocols utilise a combination of plasma exchange, adsorption and donor or surrogate platelet therapy. IVIG and Rituxan may also be coupled with these protocols, with standard post-HSCT immunosuppression administered to achieve the most positive outcomes. Unfortunately, these protocols have had varying success in very small patient populations, with mixed rates of DSA-lowering ability and engraftment success.

**Given that IgG is heavily implicated in bone marrow transplant failure, and imlifidase is known to deplete IgG to very low levels, we believe there is a good chance it could be an effective pre-treatment option for these sensitised patients.**

### Around 4.5k patients could benefit from imlifidase in US & Europe

Of the c. 75k stem cell transplants that occur in the US and Europe each year, we estimate that around 4.5k are allogenic transplants in moderate-to-highly sensitised patients. The stem cell transplant CAGR over 2013-17 was 3.8% so we conservatively assume 3% ongoing growth.

*Table 27: Bone marrow transplant market epidemiology - US and Europe*

| US | 2018 | 2019 | 2020 | 2021 | 2022 | 2023 | 2024 | 2025 |
|---|---|---|---|---|---|---|---|---|
| Hematopoietic stem cell transplants | 23,549 | 24,255 | 24,983 | 25,733 | 26,504 | 27,300 | 28,119 | 28,962 |
| growth | | 3.0% | 3.0% | 3.0% | 3.0% | 3.0% | 3.0% | 3.0% |
| of which are allogenic | 9,655 | 9,945 | 10,243 | 10,550 | 10,867 | 11,193 | 11,529 | 11,874 |
| as % | 41% | 41% | 41% | 41% | 41% | 41% | 41% | 41% |
| **Moderately-to-highly sensitised** | **1,510** | **1,555** | **1,602** | **1,650** | **1,700** | **1,751** | **1,803** | **1,857** |
| as % | 16% | 16% | 16% | 16% | 16% | 16% | 16% | 16% |
| **Europe+** | | | | | | | | |
| Hematopoietic stem cell transplants | 46,781 | 48,184 | 49,629 | 51,118 | 52,652 | 54,231 | 55,858 | 57,534 |
| growth | | 3.0% | 3.0% | 3.0% | 3.0% | 3.0% | 3.0% | 3.0% |
| of which are allogenic | 17,670 | 18,200 | 18,746 | 19,308 | 19,887 | 20,484 | 21,098 | 21,731 |
| as % | 38% | 38% | 38% | 38% | 38% | 38% | 38% | 38% |
| **Moderately-to-highly sensitised** | **2,764** | **2,846** | **2,932** | **3,020** | **3,110** | **3,204** | **3,300** | **3,399** |
| as % | 16% | 16% | 16% | 16% | 16% | 16% | 16% | 16% |

*Source: HRSA, Intron Health estimates "Europe+" defined as 40 European countries plus Algeria, Iraq, Iran, Israel, Jordan, Lebanon, Saudi Arabia, South Africa, and Tunisia*

## Sales could exceed $400m by early 2030s

Although Hansa has yet to begin any clinical trials, if they move straight into phase 3, we estimate they could launch from 2026. Due to the lack of clinical data, we risk adjust sales down to 25%, but still forecast sales of >$100m by 2033, implying that if trials are successful, we would anticipate raising this to >$400m.

*Table 28: Bone marrow transplant market epidemiology - US and Europe*

| US | 2026 | 2027 | 2028 | 2029 | 2030 | 2031 | 2032 | 2033 | 2034 | 2035 |
|---|---|---|---|---|---|---|---|---|---|---|
| Allogenic stem cell transplants | 12,231 | 12,598 | 12,976 | 13,365 | 13,766 | 14,179 | 14,604 | 15,042 | 15,494 | 15,958 |
| Moderately-to-highly sensitised | 1,913 | 1,970 | 2,029 | 2,090 | 2,153 | 2,218 | 2,284 | 2,353 | 2,423 | 2,496 |
| **Patients treated** | **38** | **197** | **365** | **523** | **646** | **732** | **799** | **823** | **848** | **874** |
| **Market penetration** | **2%** | **10%** | **18%** | **25%** | **30%** | **33%** | **35%** | **35%** | **35%** | **35%** |
| Price ($/dose) | 265,380 | 268,034 | 270,714 | 273,421 | 276,156 | 278,917 | 281,706 | 284,523 | 287,369 | 290,242 |
| Sales ($m) | 10 | 53 | 99 | 143 | 178 | 204 | 225 | 234 | 244 | 254 |
| *growth* | | *420.2%* | *87.3%* | *44.5%* | *24.8%* | *14.4%* | *10.3%* | *4.0%* | *4.0%* | *4.0%* |
| **Risk-adj. US sales in HSCT ($m)** | **3** | **13** | **25** | **36** | **45** | **51** | **56** | **59** | **61** | **63** |
| **Europe+** | | | | | | | | | | |
| Allogenic stem cell transplants | 22,383 | 23,055 | 23,747 | 24,459 | 25,193 | 25,948 | 26,727 | 27,529 | 28,355 | 29,205 |
| Moderately-to-highly sensitised | 3,501 | 3,606 | 3,714 | 3,825 | 3,940 | 4,058 | 4,180 | 4,305 | 4,435 | 4,568 |
| **Patients treated** | **50** | **258** | **478** | **683** | **844** | **957** | **1,045** | **1,076** | **1,109** | **1,142** |
| **Market penetration** | **1%** | **7%** | **13%** | **18%** | **21%** | **24%** | **25%** | **25%** | **25%** | **25%** |
| Price ($/dose) | 162,500 | 162,500 | 162,500 | 162,500 | 162,500 | 162,500 | 162,500 | 162,500 | 162,500 | 162,500 |
| Sales ($m) | 8 | 42 | 78 | 111 | 137 | 155 | 170 | 175 | 180 | 186 |
| *growth* | | *415.0%* | *85.4%* | *43.1%* | *23.6%* | *13.3%* | *9.2%* | *3.0%* | *3.0%* | *3.0%* |
| **Risk-adj. EU sales in HSCT ($m)** | **2** | **10** | **19** | **28** | **34** | **39** | **42** | **44** | **45** | **46** |
| | | | | | | | | | | |
| **Risk-adj. global sales in HSCT ($m)** | **5** | **24** | **44** | **63** | **79** | **90** | **99** | **102** | **106** | **110** |

*Source: HRSA, Intron Health estimates "Europe+" defined as 40 European countries plus Algeria, Iraq, Iran, Israel, Jordan, Lebanon, Saudi Arabia, South Africa, and Tunisia*

## NPV of $165m factors in heavy discounting and risk-adjustment

Using a WACC of 9% and with no sales beyond 2035, we value the current stem cell transplant opportunity at $165m, but that is despite the high-risk adjustment, the slow ramp and the far-out revenues. This underlines for us how significant the stem cell market could be for Hansa in the long term.

# Anti-GBM Could be $50m Peak Sales

**Anti-GBM phase II topline data is due in Q320 and will be the next validation point of imlifidase's high potential as a pipeline in a drug.**

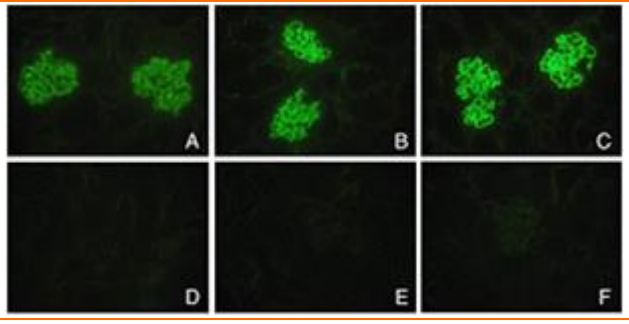
Anti-glomerular basement membrane (anti-GBM) disease is rare life-threatening disorder impacting approximately 1.6 cases per million annually in European populations. It is a form of autoimmune vasculitis that afflicts the glomerular capillaries of the kidney and pulmonary capillaries of the lung. Patients develop auto-IgG antibodies that bind to the basement membranes of these capillaries and stimulate neutrophil dependant inflammation. This can result in high blood pressure, renal failure (66% of patients) and pulmonary haemorrhage.

The aetiology of anti-GBM disease is unknown, but there is a genetic aspect and linkage to environmental factors like infections, certain drugs e.g. alemtuzumab, exposure to metal dust and hydrocarbon fumes.

There are no specific therapies targeted to treat anti-GBM, but plasmapheresis, cyclophosphamide and prednisone administration improves overall mortality and renal survival.

Imlifidase has exhibited positive preclinical results that demonstrate its efficacy in a mouse model of anti-GBM. Yang *et al*, 2010 found imlifidase administration prevented severe albuminuria in mice injected with anti-GBM antibodies. Immunofluorescence revealed imlifidase effectively degraded these IgG antibodies (see imaging below) and diminished deposition of protein complexes that promote leukocyte recruitment and inflammation. This would imply that imlifidase could degrade anti-GBM antibodies sufficiently to prevent renal damage in these patients.

***Chart 15:** Immunofluorescence to detect IgG antibodies in kidneys of positive control group (A-C) and imlifidase-treated group (D-F)*




*Source: Yang et al, 2010*

At present, Hansa is conducting a phase II trial in conjunction with Professor Marten Segelmark at Lund University Hospitals. This open-label trial will evaluate whether the addition of a single 0.25mg/kg dose of imlifidase to standard regimens (PLEX, immunosuppressants and steroids) will improve outcomes for those severely affected and unlikely to respond to conventional treatment. The main objective of this study is

to assess safety, tolerability and the proportion of patients that are dialysis independent six-months post-treatment. Fifteen patients across five European countries are enrolled and the first trial data is expected in Q3 2020.

## Anti-GBM Opportunity Worth $100m to Hansa

We assume an imlifidase peak penetration of around 30% of the incidence of GBM in the US and EU7. This equates to some 400 patients treated annually, for c. $90m of sales. However, due to the current lack of data, we risk-adjust our numbers down by 50%.

***Table 29: Imlifidase sales forecasts in anti-GBM by geography***

| **EU7** | **2020** | **2021** | **2022** | **2023** | **2024** | **2025** | **2026** | **2027** | **2028** | **2029** | **2030** |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Annual incidence | 544 | 555 | 566 | 577 | 589 | 601 | 613 | 625 | 637 | 650 | 663 |
| growth | | 2.0% | 2.0% | 2.0% | 2.0% | 2.0% | 2.0% | 2.0% | 2.0% | 2.0% | 2.0% |
| Patients treated | | | 6 | 17 | 41 | 90 | 129 | 156 | 178 | 189 | 199 |
| Market penetration | | | 1% | 3% | 7% | 15% | 21% | 25% | 28% | 29% | 30% |
| Price ($/dose) | | | 162,500 | 162,500 | 162,500 | 162,500 | 162,500 | 162,500 | 162,500 | 162,500 | 162,500 |
| **Sales ($m)** | | | **1** | **3** | **7** | **15** | **21** | **25** | **29** | **31** | **32** |
| **US** | | | | | | | | | | | |
| Annual incidence | 525 | 535 | 546 | 557 | 568 | 579 | 591 | 603 | 615 | 627 | 640 |
| growth | | 2.0% | 2.0% | 2.0% | 2.0% | 2.0% | 2.0% | 2.0% | 2.0% | 2.0% | 2.0% |
| Patients treated | | | | | | 12 | 30 | 66 | 123 | 157 | 179 |
| Market penetration | | | | | | 2% | 5% | 11% | 20% | 25% | 28% |
| Price ($/dose) | | | | | | 262,753 | 265,380 | 268,034 | 270,714 | 273,421 | 276,156 |
| **Sales ($m)** | | | | | | **3** | **8** | **18** | **33** | **43** | **49** |
| | | | | | | | | | | | |
| **Total sales in anti-GBM ($m)** | | | **1** | **3** | **7** | **18** | **29** | **43** | **62** | **74** | **82** |
| growth | | | | 206% | 138% | 164% | 63% | 50% | 44% | 18% | 11% |
| **Risk adjustment** | **50%** | | | | | | | | | | |
| **Risk-adj. global sales in anti-GBM ($m)** | | | **0** | **1** | **3** | **9** | **14** | **22** | **31** | **37** | **41** |

*Source: Intron Health estimates*

### Anti-GBM market opportunity has NPV of $100m

At a WACC of 9%, tax rate of 20%, risk adjustment of 50% and assuming no revenues after 2035, we value the anti-GBM opportunity for Hansa as being c. $100m.

***Table 30: Imlifidase sales forecasts in anti-GBM by geography***

| **$m** | **2022** | **2023** | **2024** | **2025** | **2026** | **2027** | **2028** | **2029** | **2030** | **2031** | **2032** | **2033** | **2034** | **2035** |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Risk-adj. global sales in anti-GBM | 0 | 1 | 3 | 9 | 14 | 22 | 31 | 37 | 41 | 44 | 45 | 46 | 47 | 49 |
| Margin | 70% | 80% | 85% | 85% | 85% | 85% | 85% | 85% | 85% | 85% | 85% | 85% | 85% | 85% |
| EBIT | 0 | 1 | 3 | 8 | 12 | 18 | 26 | 31 | 35 | 37 | 38 | 39 | 40 | 41 |
| **Profit after Tax** | **0** | **1** | **2** | **6** | **10** | **15** | **21** | **25** | **28** | **30** | **31** | **31** | **32** | **33** |
| **Discounted CF** | **0** | **1** | **1** | **4** | **5** | **7** | **10** | **11** | **11** | **11** | **10** | **9** | **9** | **8** |
| **NPV of Anti-GBM ($m)** | **97** | | | | | | | | | | | | | |

*Source: Intron Health estimates*

# Other Indications

**Imlifidase's two other major opportunities – AMR and GBS – are unlikely to launch until 2025 or beyond. Despite this, we conservatively calculation that they could together be worth an NPV of ~$500m.**

## Antibody Mediated Rejection – Peak Sales of $100m

AMR is defined as the rejection of an organ graft due to antibodies targeted against blood group antigens, HLA or endothelial cell antigens on the transplant. These antibodies activate the classical complement pathway, inducing inflammatory cell recruitment that results in graft injury. AMR is experienced by 10-15% of solid organ transplant recipients and is a prominent factor associated with graft rejection. Conventional treatment such as IVIG, PLEX and steroids have limited efficacy in severe cases and are slow to improve symptoms. However, in terms of pharma pipeline there are several candidates under development so imlifidase would be likely to face more competition in this indication than for the others. Initially, Hansa is targeting approval in kidney AMR, but if this is successful there could be follow-on AMR indications including in heart or lung.

### Clinical data expected in H2 2022

The phase II open-label multicentre trials of imlifidase for the treatment of acute AMR commenced in 2019 and aim to recruit 30 candidates across the US, Australia and Europe. Patients with active AMR will either receive a single imlifidase dose of 0.25mg/kg or 5-10 sessions of PLEX. The primary objective assessed will be the reduction of DSAs five days post-treatment for imlifidase vs PLEX, with the secondary outcomes of efficacy measured six months post-treatment (serum creatine, DSA levels and eGFR levels).

At present, 4 candidates have been recruited with enrolment anticipated to resume in Q320, following a ~6 month recruitment delay due to COVID-19. A readout was originally anticipated to be in H1 2022, but we now look for it in H2 2022.

### Peak sales of >$200m unadjusted for risk; NPV is $210m today

AMR of kidney transplantation occurs with an incidence of around 2,700 new cases a year in the US and EU5. With a peak penetration of 30% and risk adjustment of 50%, we show how risk-adjusted peak sales could be $100m and the NPV is $210m. As we do not include any sales for potential future AMR approvals in organs outside of the kidney, these are not valued in our NPV and can be considered as free upside.

***Table 31: Imlifidase sales and NPV forecasts for AMR***

| US & EU5 | 2024 | 2025 | 2026 | 2027 | 2028 | 2029 | 2030 | 2031 | 2032 | 2033 | 2034 | 2035 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Incident population | 2,776 | 2,796 | 2,815 | 2,835 | 2,855 | 2,875 | 2,895 | 2,915 | 2,936 | 2,956 | 2,977 | 2,998 |
| *growth* | *0.7%* | *0.7%* | *0.7%* | *0.7%* | *0.7%* | *0.7%* | *0.7%* | *0.7%* | *0.7%* | *0.7%* | *0.7%* | *0.7%* |
| Patients treated | | 56 | 282 | 510 | 714 | 819 | 869 | 875 | 881 | 887 | 893 | 899 |
| Market penetration | | 2% | 10% | 18% | 25% | 29% | 30% | 30% | 30% | 30% | 30% | 30% |
| Price ($/dose) | | 212,626 | 213,940 | 215,267 | 216,607 | 217,961 | 219,328 | 220,709 | 222,103 | 223,512 | 224,934 | 226,371 |
| **Sales ($m)** | | **12** | **60** | **110** | **155** | **179** | **190** | **193** | **196** | **198** | **201** | **204** |
| *growth* | | | *407%* | *82%* | *41%* | *16%* | *7%* | *1%* | *1%* | *1%* | *1%* | *1%* |
| **Risk adjustment** | **50%** | | | | | | | | | | | |
| **Risk-adj. global sales in AMR ($m)** | | **6** | **30** | **55** | **77** | **89** | **95** | **97** | **98** | **99** | **100** | **102** |
| Margin | | 70% | 80% | 85% | 85% | 85% | 85% | 85% | 85% | 85% | 85% | 85% |
| EBIT | | 4 | 24 | 47 | 66 | 76 | 81 | 82 | 83 | 84 | 85 | 87 |
| Profit after Tax | | 3 | 19 | 37 | 53 | 61 | 65 | 66 | 67 | 67 | 68 | 69 |
| **Discounted CF** | | **2** | **11** | **19** | **24** | **26** | **25** | **23** | **22** | **20** | **19** | **17** |
| **NPV of AMR ($m)** | **208** | | | | | | | | | | | |

*Source: Intron Health estimates*

## Guillain-Barré Syndrome - Peak Sales of $115m

Guillain-Barré Syndrome (GBS) is a rare and potentially fatal autoimmune disease of the peripheral nerves and nerve roots. It is characterised by nerve damage that induces rapid onset muscle weakness to the extremities and is the most common cause of acute neuromuscular paralysis in the US. The disease is induced by the synthesis of IgG antibodies and activation of inflammatory cells that infiltrate the nerve myelin sheath. The compromised integrity of the myelin sheath impairs the conduction ability of these nerves, preventing transmission to the brain. The cause of GBS is unknown but is believed to originate from aberrant immune responses to infections that lead to peripheral nerve damage. Its incidence is estimated to be 1-2 per 100,000 people annually, with this increasing during infectious outbreaks such as the Zika virus. There are no specific drug therapies indicated for treating GBS, with PLEX and IVIG normally used. However, these treatments are substandard, with 20-30% of patients requiring mechanical ventilation and 3-5% dying.

### Clinical data expected in H2 2022

In 2019, Hansa initiated a phase II open-label multi-centre study of imlifidase in GBS patients. The trial will assess the efficacy of a single 0.25mg/kg dose followed by five consecutive days of 0.4g/kg IVIG treatment in 30 GBS patients across the UK, France and the Netherlands. The objectives include a safety assessment as well as an efficacy investigation using a number of GBS related outcome measures. The trial is expected to complete recruitment in H2 2021, with results available in H2 2022. With the possibility of COVID-19 disruption, this may be delayed into early 2023.

### Peak sales of >$200m unadjusted for risk; NPV is $250m today

We estimate there was an incidence of roughly 9.3k cases of GBS in the US and EU5 in 2020. Given the difficulty in identifying these patients early enough to have a beneficial impact on their course of disease, we have

assumed a peak penetration of just 10% for imlifidase. Nevertheless, if Hansa can execute on this indication it would be a major opportunity and we show how it is worth $250m of NPV today even with a risk adjustment of 50%. There would also be potential upside from out-licensing this drug in Japan to Takeda, who already have a large rare disease franchise (inherited from the Shire acquisition).

***Table 32: Imlifidase sales and NPV forecasts for GBS***

| **US & EU5** | **2024** | **2025** | **2026** | **2027** | **2028** | **2029** | **2030** | **2031** | **2032** | **2033** | **2034** | **2035** |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Incident population | 9,544 | 9,610 | 9,678 | 9,745 | 9,814 | 9,882 | 9,952 | 10,021 | 10,091 | 10,162 | 10,233 | 10,305 |
| *growth* | *0.7%* | *0.7%* | *0.7%* | *0.7%* | *0.7%* | *0.7%* | *0.7%* | *0.7%* | *0.7%* | *0.7%* | *0.7%* | *0.7%* |
| Patients treated | | 192 | 484 | 682 | 883 | 988 | 995 | 1,002 | 1,009 | 1,016 | 1,023 | 1,030 |
| Market penetration | | 2% | 5% | 7% | 9% | 10% | 10% | 10% | 10% | 10% | 10% | 10% |
| Price ($/dose) | | 212,626 | 213,940 | 215,267 | 216,607 | 217,961 | 219,328 | 220,709 | 222,103 | 223,512 | 224,934 | 226,371 |
| **Sales ($m)** | | **41** | **104** | **147** | **191** | **215** | **218** | **221** | **224** | **227** | **230** | **233** |
| *growth* | | | *153%* | *42%* | *30%* | *13%* | *1%* | *1%* | *1%* | *1%* | *1%* | *1%* |
| **Risk adjustment** | **50%** | | | | | | | | | | | |
| **Risk-adj. global sales in AMR ($m)** | | **20** | **52** | **73** | **96** | **108** | **109** | **111** | **112** | **114** | **115** | **117** |
| Margin | | 70% | 80% | 85% | 85% | 85% | 85% | 85% | 85% | 85% | 85% | 85% |
| EBIT | | 14 | 41 | 62 | 81 | 92 | 93 | 94 | 95 | 97 | 98 | 99 |
| Profit after Tax | | 11 | 33 | 50 | 65 | 73 | 74 | 75 | 76 | 77 | 78 | 79 |
| **Discounted CF** | | **7** | **18** | **25** | **30** | **31** | **29** | **27** | **25** | **23** | **21** | **20** |
| **NPV of AMR ($m)** | **256** | | | | | | | | | | | |

*Source: Intron Health estimates*

# Hansa's Pipeline Assets

## The NiceR Programme Could Enable Repeat Dosing

Imlifidase has been developed as a one-off treatment. Although it has high efficacy in degrading IgG, one issue that may preclude repeat dosing which may be needed for some new indications is that it stimulates an immune response itself. As observed in studies, patients develop anti-imlifidase antibodies over 2 weeks after administration. These levels decrease over several months, but their presence potentially prevents the re-treatment of patients in the short-term. Furthermore, naturally occurring neutralising antibodies against imlifidase are naturally present in a significant proportion of the general population anyway due to exposure to *A. streptococcus*.

To counter this potential limitation, Hansa has initiated the NiceR programme - Novel IgG Cleaving Enzymes for Repeat dosing. This aims to develop several novel IgG-inactivating enzymes that have lower immunogenicity and could permit repeated dosing. NiceR has the potential to expand to applications beyond imlifidase and meet needs characterised by re-occurring flare-ups induced by IgG antibodies.

In March 2019, Hansa selected a leading candidate for clinical development. This candidate is an IgG cysteine endopeptidase based on the amino acid sequence of an imlifidase homologue but with lower immunogenicity than imlifidase. GMP-manufacturing process has been initiated for the candidate, with toxicology studies and a clinical phase I trial currently underway. This is anticipated to be completed by H1 2021.

### The EnzE Programme

EnzeE (Enzyme-based antibody enhancement) is a pre-clinical research and development programme that is exploring the combined use of approved antibody-based cancer therapies with IgG modulating enzymes.

Most antibody-based cancer treatments utilise antibody-dependant cell-mediated cytotoxicity to fight against cancer. Therapeutic antibodies bind to the surface antigens of cancerous cells - this highlights malicious cells to the immune system and promotes phagocytosis and other cell-mediated immune destruction. High plasma levels of IgG impair the efficacy of antibody treatments as they can saturate the Fc region of the patient's immune cells. This prevents immune cells from binding to the Fc region of the therapeutic antibody. Therefore, treatments that decrease IgG plasma concentrations have the potential to increase the efficacy of these existing therapeutics.

Early preclinical data looks promising: *in vitro* and *in vivo* data has been generated in a mouse model of lymphoma, in which the IgG-eliminating ability of imlifidase unblocked cellular antibody receptors and significantly potentiated the efficacy of several therapeutic antibody treatments for lymphomas, breast and colon cancer.

Monoclonal antibody treatments dominate the pharmaceutical market with global sales exceeding $122 billion per year. This is projected to increase to more than $200 billion in 2024. Hence, there is a substantial opportunity for Hansa and their antibody enhancing developments.

## Limited Competition for Imlifidase

### Imlifidase is Unique From Other New Therapies

**Although there are several therapies in the pipeline that seek to treat diseases that imlifidase is also targeting, imlifidase stands alone as the only IgG cleaving agent in development. Moreover, only Lemtrada is targeting imlifidase's core market indication (desensitisation pre-kidney transplant), but shows limited efficacy and has known safety concerns. FcRn-blockers are also known to reduce IgG levels, but as they take ~1 week to work and only reduce IgG levels down by ~50% (imlifidase almost completely depletes IgG), we do not see them as strong competitors. Drugs targeting other imlifidase indications (AMR, GBS, GBM) such as Annexon's ANX005 or Sanofi's sutimlimab have different mechanisms of action, typically targeting the complement system. Even if they are effective, the IgG antibodies will still be present so it is likely there would still be a place for imlifidase in patients whose disease is driven by IgG.**

## Other Therapies Not Direct Competitors

Imlifidase is the only IgG cleaving agent in development. Competitor candidates may target the initiating C1 complex of the complement system, but IgG antibodies will remain. Although imlifidase would be utilised in 100% of pre-graft patients, these C1 inhibitor candidates could be administered post-transplantation to alleviate the AMR that afflicts 35% of imlifidase treated patients.

## Lemtrada - Sensitised Kidney Transplant Recipients

Alemtuzumab (Lemtrada) is a humanised monoclonal antibody against CD52 that depletes various immune cells including B and T lymphocytes, monocytes and natural killer cells. It is already approved for the treatment of multiple sclerosis (MS) and chronic lymphocytic leukaemia (CLL). It is also used off-label for the prevention and treatment of acute allograft rejection in kidney transplantation.

Clinical data has revealed that superiority of alemtuzumab as an induction agent for kidney transplantation is restricted to low-risk patients with no significant difference observed vs rabbit anti-thymocyte globulin (a control immunosuppressant, standard of care) in highly sensitised patients. A Cochrane systematic review also re-iterated this, with no significant difference in graft-loss and overall survival.

Safety is a prominent issue with alemtuzumab, with its use dwindling in MS. Due to its profound immunosuppression, patients are significantly pre-disposed to opportunistic infection for 12-months. Alemtuzumab administration is also associated with an increased risk of viral related cancers including non-Hodgkin lymphoma, human papilloma virus-related, liver and colorectal cancer. Secondary autoimmune events including thyroid issues and immune thrombocytopenia have also been reported.

Some physicians use alemtuzumab instead of thymoglobulin for T-cell depletion in transplantation and as such, **it should be viewed as complementary to imlifidase, rather than as a competitor. In the imlifidase clinical trials, it was administered to many of the patients who also received imlifidase.**

## Sutimlimab For Antibody-Mediated Rejection

This drug is an anti-C1 antibody that impairs activation of the classical complement system of the immune system by C1. The activation of this pathway contributes to the pathogenesis of antibody-mediated rejection (AMR), a major contributor to graft rejection. Significantly, sutimlimab preserves the activity of the alternate and lectin complement pathways that mediate the humoral surveillance of pathogens unlike other drug candidates such as Soliris. This should result in a less toxic drug profile,

which coupled with its high efficacy and rapid action at target makes it a candidate to watch.

In 2017, sutimlimab was assessed in a phase 1B study of 10 stable kidney transplant recipients with late active AMR and DSA-mediated complement pathway activation. Multiple weekly treatments over the 7-week trial duration were found to profoundly inhibit overall and DSA-triggered complement pathway activation. However, there were no changes in kidney function, DSA levels or microcirculation inflammation at early follow-up. Although this trial was limited by parallel-group control, short treatment duration and small sample size, it was concluded that sutimlimab has potential efficacy and was well-tolerated.

Sutimlimab has also been granted Breakthrough Therapy Designation by the FDA and orphan drug status by the FDA and EMA for the treatment of cold agglutin disease (CAD). CAD is a rare chronic autoimmune disease where activation of the complement pathway leads to haemolysis (red blood cell destruction) and ultimately severe anaemia. It is currently undergoing phase III trials for this disease. In May 2020, the US FDA granted priority review with a decision expected by 13th November 2020. Whilst this is promising for sutimlimab, we do not believe it will have any bearing on its likely efficacy in AMR where it may come into competition with imlifidase one day.

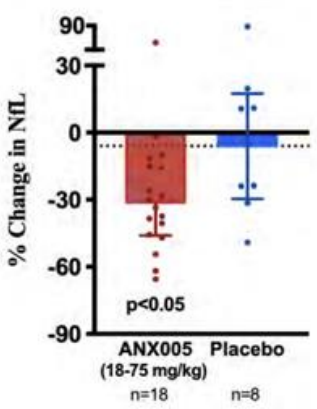
## ANX005 For Guillain Barré Syndrome

ANX005 is a monoclonal antibody that inhibits C1q, the initiating molecule of the classical complement pathway. This prevents antibody-mediated autoimmune and complement-mediated neurodegeneration.

Annexon has completed a phase 1B placebo-controlled study in 31 Guillain-Barré Syndrome (GBS) patients. ANX005 was found to be well tolerated, successfully inhibiting C1q and the classical complement pathway in serum and cerebrospinal fluid. Patients also had a significant reduction in neurofilament light chain (NfL), a predictive biomarker of nerve damage in neurodegenerative disease that correlates with disease severity. Treated patients also exhibited early dose-dependent improvements in muscle strength and their disability score (see table below, which shows that 28% of ANX005-treated patients improved by greater than 3 points on a scale of disease severity by Week 8, vs 0% on placebo). These outcome measures correlate with the prognosis for long-term functional recovery and so are a promising indication of the therapeutic efficacy of ANX005.

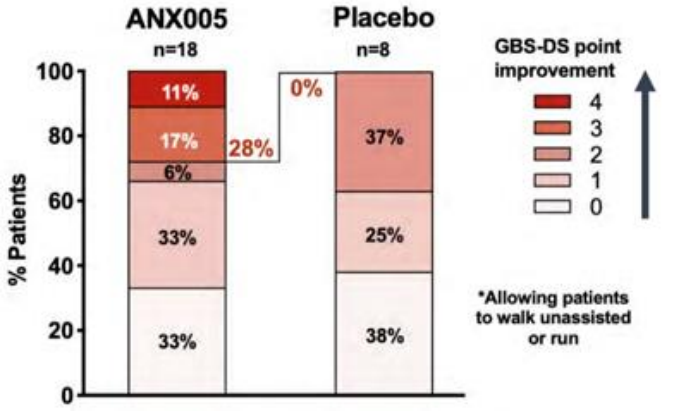
The drug has been advanced to later stage clinical trials based on these promising results, with data anticipated in H1 2021. It has also received Fast Track and Orphan Drug designations from the FDA.

*Chart 16: Changes in Nfl in ANX005 vs placebo*




*Source: Company reports*

*Chart 17: GBS-Disability Score improvements for high-dose ANX005 vs Placebo at 8 weeks*




*Source: Company reports*

## CK0801 For Guillain Barré Syndrome

Cellenkos is undertaking a phase I trial of cord blood-derived T-regulatory cell product CK0801 for Guillain Barré Syndrome (GBS). This open-label trial of 18 patients with treatment resistant GBS will assess safety, efficacy in improving GBS symptoms and determine the highest possible dose that is safe to be administered.

## CSL842 For AMR

CSL-Behring has developed a human plasma-derived C1-esterase inhibitor for the treatment of refractory antibody mediated rejection.

In 2015, CSL842 was assessed in a phase I/II trial for the prevention of AMR in 20 highly sensitised patients. These patients were desensitised with IVIG, Rituxan and plasmapheresis prior to either the administration of CSL842 or a placebo intraoperatively then weekly for 7 doses. CSL842 was found to reduce ischaemia perfusion injury and to significantly reduce levels of C1q and HLA antibodies, leading to the conclusion that CSL842 may prove useful in the prevention of AMR.

At present, CSL842 is undergoing a phase III trial to assess its efficacy and safety as an add on to the standard of care (IVIG) in 90 adult kidney transplant patients in a double-blind trial. Data from this trial is not expected until 2026.

## Soliris (eculizumab) For GBS and AMR

Soliris is a first in class terminal complement pathway inhibitor. It exerts this effect by impairing the activation of the C5a and C5b proteins of the complement system. This pathway is essential to the pathogenesis of GBS and AMR. The drug is currently indicated for anti-acetylcholine receptor antibody positive generalised Myasthenia Gravis (GMG), anti-aquaporin-4 antibody positive neuromyelitis optica spectrum disorder patients (NMOSD), atypical haemolytic uremic syndrome (AHUS) and

paroxysmal nocturnal haemoglobinuria (PNH). It has also exhibited promise as a novel treatment for GBS and AMR.

In 2018, a Japanese manufacturer-funded phase II trial observed an improvement in GBM patients given eculizumab, but this was not significant enough to conclude its efficacy (see table below). Adverse events occurred in all eculizumab recipients with two severe adverse events of anaphylaxis and intracranial abscess recorded. This could not be ruled out as resulting from treatment so larger studies would be required to ascertain safety.

Eculizumab may also have potential therapeutic value in incidences of AMR in sensitised kidney transplant recipients. Various case studies in established cases of AMR have suggested that eculizumab may provide benefit, with patients resistant to standard AMR protocols exhibiting rapid and drastic improvement with eculizumab. Stabilisation and improvements in renal functioning have also been reported post-eculizumab in a small cohort of severely sensitised patients unresponsive to standard treatment. A phase II trial also affirmed this, with eculizumab concluded to have therapeutic potential (see table below).

Patients treated with Soliris have a significantly increased risk of serious infection. All must receive vaccination including the meningococcal vaccine at least 2 weeks prior to therapy and antibiotic treatment to mitigate this risk. This risk can persist for 3 months after the last dose.

***Table 33: Eculizumab has also exhibited promise as a novel treatment for GBS and AMR, but with safety issues***

| Disease | Study | Results | Conclusion |
|---|---|---|---|
| **GBS** | 2018- 24 week, multicentre, double-blind, manufacturer-funded phase II trial.<br>34 GBS patients at functional grade 3-5.<br>Assigned 4-weeks of IVIG with either 900mg of eculizumab or placebo | 65% of eculizumab cohort were able to function independently vs 45% of placebo group.<br>At 24-weeks, a greater proportion of patients could run and walk compared to those given a placebo, 91.6% and 74% of those given eculizumab vs 71.9% and 18% of the placebo group respectively. | Greater improvement in eculizumab group. Not significant enough to reach the predefined response rate. |
| **AMR** | 2019 – A phase II 9-week multi-centre trial to evaluate efficacy of eculizumab in sensitised kidney transplant recipients that required desensitisation.<br>102 patients, 51 received eculizumab treatment. | Eculizumab found to be safe and well tolerated<br>Improvement in rates of treatment failure reported in the treatment group vs the placebo (11.8% vs 21.6% respectively) | Eculizumab may have therapeutic potential |

*Source: Misawa et al, 2018; Marks et al, 2019*

# IP Issues Are a Small Concern

**Whilst imlifidase has very significant potential across multiple indications and various modalities, there is one small concern that we have - the imlifidase IP position. Imlifidase is a naturally occurring enzyme from the bacterium *Streptococcus pyogenes*. Genovis, a Swedish-based supplier of enzymes sells a product called FabRICATOR (IdeS) which is the same enzyme as imlifidase.**

**Our concerns have arisen following a Nature publication in which Spark therapeutics recently used IdeS in a pre-clinical study to show that imlifidase was effective at removing AAV vector antibodies. Not only have Spark/Janssen used an off-the-shelf copy of imlifidase, they have also filed a patent for the use of imlifidase in gene therapy. As yet, this patent has not been granted, with the ISA (International Searching Authority) having declared Spark/Genethon/Inserm application non-inventive. Hansa do not believe that they will succeed in getting the patent granted as they already have prior art, including a patent for the medical use of imlifidase in gene therapy. Moreover, Hansa believe that clinical or commercial development of imlifidase in gene therapy would infringe several of their approved and pending patents.**

**Hansa have protected imlifidase with 7 patent families covering method-of-use and process patents, including a method-of-use patent in gene therapy (patent pending). Whilst Spark's filing could be a material issue, we make a number of observations that limit the risk for Hansa and thus, investors:**

- Hansa already hold existing patents for imlifidase
- Hansa has clinical data in the crucial kidney transplant setting and hence an unassailable position here
- No other company could replicate their early clinical and pre-clinical data that quickly which would allow Hansa to partner with other gene therapy players
- Sarepta will have had their patent attorneys look at the patents and clearly were not materially concerned by the situation
- The ISA say that the Spark/Genethon/Inserm application is non-inventive and the relevant patent granting courts will use ISA's opinion
- Hansa cannot yet file against Spark as its patent has not been granted
- The worst case for Hansa would be that they lose the gene therapy setting but we believe this to be unlikely

Hansa currently have patents that cover:

- Use of purified IdeS for IgG cleaving – method-of-use
- Use of nucleotide – method-of-use
- Use of IgG cleaving enzymes in gene therapies – method-of-use – pending
- Imlifidase has no composition of matter patent as you cannot patent molecules that occur naturally in nature
  - However, we note that Hansa have applied for compound patents for the NiceR molecules, as they do not occur naturally

# Financials – Could Be Profitable By 2023

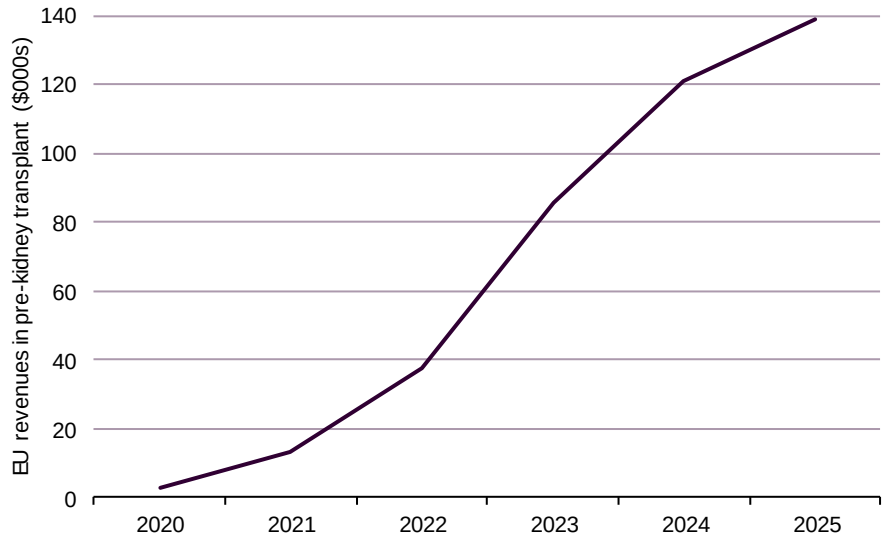
**We anticipate Hansa reaching profitability by 2023 and expect the cash runway to last until at least that year, meaning that the US launch in 2024 could be debt-funded, rather than having to carry out another equity raise. This is despite us forecasting a slow start to revenues in 2020-21 as it will take time to change physician behaviour – there is no precedent for a drug like imlifidase in the kidney transplant space. Consequently, we see the EU kidney transplant uptake curve being S-shaped, as shown in the chart below.**

***Table 34: Key Assumptions and Intron Health Vs Consensus***

| USD (000s) | 2020 | 2021 | 2022 | 2023 | 2024 | 2025 |
|---|---|---|---|---|---|---|
| **EU penetration rate** | | | | | | |
| Highly sensitised (cPRA>80%) | 0% | 4% | 12% | 25% | 34% | 37% |
| Moderately sensitised | 0% | 0% | 1% | 2% | 4% | 5% |
| **Moderate-highly sensitised** | **0%** | **2%** | **6%** | **14%** | **19%** | **21%** |
| **EU kidney revenues** | **1** | **13** | **38** | **86** | **121** | **139** |
| | | | | | | |
| Sales – Intron Vs Consensus | -81% | -16% | +23% | +41% | -15% | |
| Group EPS (SEK) | -10.51 | -9.65 | -6.16 | 1.69 | 8.98 | 21.94 |
| Number of pts treated in 2024 | Intron | 899 | Consensus | 1,056 | % Diff | -15% |

*Source: Intron Health estimates*

***Chart 18: We forecast an "S" shape revenue curve for EU imlifidase kidney sales***




*Source: Intron Health estimates*

## Incremental Sales at High Gross Margin

We forecast the gross margin rising to 84% by 2024-25, which we believe is reasonable and in line with other biologic-focused companies such as Roche. Hansa are using CDMOs to manufacture imlifidase, which should be flexible and ensure management stay focused on ramping up sales. In the table below, we show our total sales forecasts for the group, split by indication as well as the royalties we expect from the Sarepta deal.

*Table 35: Hansa Group global sales forecasts by indication*

| $m | 2020 | 2021 | 2022 | 2023 | 2024 | 2025 | 2026 | 2027 | 2028 | 2029 | 2030 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Kidney transplantation | 1 | 13 | 38 | 86 | 130 | 167 | 242 | 346 | 408 | 444 | 472 |
| Anti-GBM | 0 | 0 | 0 | 1 | 3 | 9 | 14 | 22 | 31 | 37 | 41 |
| Guillain-Barré Syndrome | 0 | 0 | 0 | 0 | 0 | 20 | 52 | 73 | 96 | 108 | 109 |
| Antibody-mediated rejection (kidney) | 0 | 0 | 0 | 0 | 0 | 6 | 30 | 55 | 77 | 89 | 95 |
| Bone marrow transplant | 0 | 0 | 0 | 0 | 0 | 0 | 5 | 24 | 44 | 63 | 79 |
| Sarepta deal revenues (ex-royalties) | 0 | 0 | 0 | 0 | 8 | 25 | 41 | 45 | 36 | 21 | 12 |
| **Total sales ($m)** | **1** | **13** | **38** | **87** | **141** | **227** | **384** | **565** | **692** | **762** | **808** |
| **Total sales (SEKm)** | **8** | **114** | **332** | **760** | **1,232** | **1,973** | **3,344** | **4,923** | **6,030** | **6,636** | **7,041** |
| *growth* | *131%* | *1362%* | *192%* | *129%* | *62%* | *60%* | *69%* | *47%* | *22%* | *10%* | *6%* |
| | | | | | | | | | | | |
| Sarepta deal royalties to Hansa ($m) | 0 | 0 | 0 | 0 | 6 | 22 | 42 | 52 | 47 | 29 | 18 |
| **Sarepta deal royalties to Hansa (SEKm)** | **0** | **0** | **0** | **0** | **55** | **192** | **364** | **457** | **409** | **251** | **156** |

*Source: Intron Health estimates*

## Cash Runway to 2023

The recent equity issuance raised SEK1.1bn of cash, which we forecast as lasting until at least 2023. We also expect Hansa to break even for the first time in 2023, meaning there is a good chance they could become self-funding (including debt) from this time.

We have carefully forecast our cost lines to take account of all the moving parts:

- Pre-clinical projects will move into the clinic next year and the US kidney trial will start at the end of this year
- We include >$5m of new costs this year for the commercial launch of imlifidase in the EU and an additional $5m in 2021

Our SG&A and R&D lines are shown in the table below (in USD for ease of comparison):

*Table 36: Opex cost forecasts*

| $ (000s) | 2018 | 2019 | 2020 | 2021 | 2022 | 2023 | 2024 | 2025 |
|---|---|---|---|---|---|---|---|---|
| **SG&A** | **-10,377** | **-19,209** | **-24,936** | **-29,923** | **-31,419** | **-32,990** | **-37,939** | **-41,732** |
| growth | | 85% | 30% | 20% | 5% | 5% | 15% | 10% |
| as % of sales | N/A | N/A | N/A | -229% | -83% | -38% | -27% | -18% |
| **R&D** | **-17,745** | **-22,153** | **-26,554** | **-29,209** | **-30,670** | **-27,603** | **-28,983** | **-30,432** |
| growth | | 25% | 20% | 10% | 5% | -10% | 5% | 5% |
| as % of sales | N/A | N/A | N/A | -291% | -99% | -39% | -25% | -16% |

*Source: Intron Health estimates*

# Valuation Supports SEK385/Share

We believe a sum-of-the-parts valuation is the most appropriate way of valuing Hansa given the "pipeline in a drug" potential of imlifidase. As we have already shown, our NPV estimates for each indication are conservative, applying high risk adjustments and assuming a slow ramp up and no revenues after 2035. In addition, we assume:

- WACC of 9%
- Tax of 20% with no relief for past losses
- Expenses not included in our indication NPVs have been capitalised and deducted from our valuation (G&A and R&D)

- We have added back net cash
- We use a SEK/USD rate of 8.71

**Overall, we value Hansa at SEK385 / share, which implies 50% upside from the current share price of SEK261.**

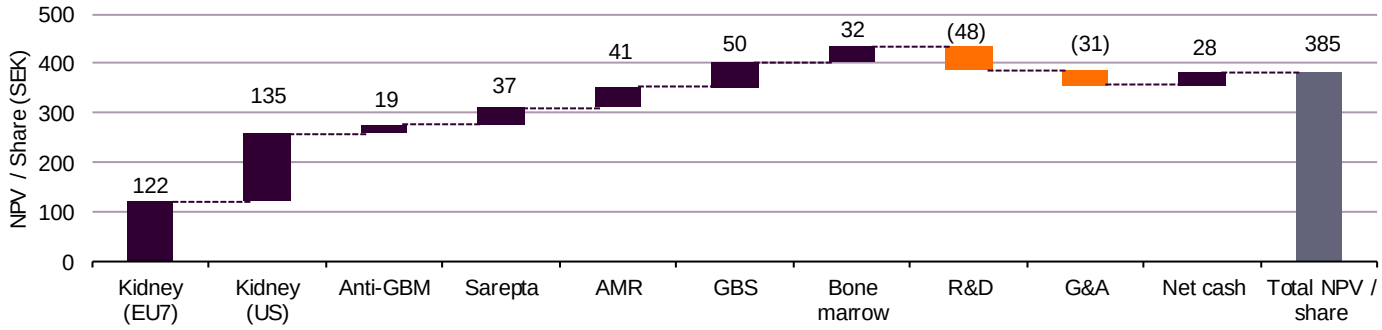
***Table 37: Sum of the parts valuation***

| $m | Risk adjustment | NPV ($m) | NPV / share (SEK) |
|---|---|---|---|
| Kidney - EU7 | 100% | 625 | 122 |
| Kidney - US | 100% | 689 | 135 |
| Anti-GBM - EU7 & US | 50% | 97 | 19 |
| Sarepta (global) | 40% | 188 | 37 |
| AMR (US & EU5) | 50% | 208 | 41 |
| GBS (US & EU5) | 50% | 256 | 50 |
| Bone marrow (US & Europe+) | 25% | 165 | 32 |
| R&D | | -246 | -48 |
| G&A | | -160 | -31 |
| Net cash | | 144 | 28 |
| **Total ($m)** | | **1,965** | |
| **Total (SEKm)** | | **17,118** | **385** |
| | | | |
| Share price SEK | | 257 | |
| **Upside to our valuation** | | **50%** | |

*Source: Intron Health estimates*

*Note: We do not risk adjust the kidney transplant indication in the US despite the ongoing trial because we believe the trial will work given data seen to date and the fact that the control arm is "watch & wait" which is unlikely to beat an active arm where a kidney is transplanted*

***Chart 19: NPV/share waterfall chart, by indication***




*Source: Intron Health estimates*

## There Are Numerous Potential Upsides to Valuation

We would like to highlight that there are numerous potential sources of upside to our valuation. These come not only from risk-adjustments to sales, but from opportunities for which we currently forecast no sales due to lack of data or the early stage of development. Nevertheless, some of these opportunities have a good chance of eventually making it to market. Sources of upside include:

- Price – we have assumed $250k/course for the US and $163k in the EU, but due to orphan status and the money it saves the healthcare system, it could feasibly be higher than this

- We have not included revenues for most indications outside of the US or EU (e.g. kidney, GBM, GBS, AMR, bone marrow)
  - Hansa may choose to out-license the drug in these regions and could receive upfronts, milestones and royalties
  - For example, it would make sense for Hansa to out-license GBS rights in Japan to Takeda, whose rare disease franchise would be a good fit with imlifidase
- We have only included the kidney opportunity in AMR sales forecasts, but imlifidase could also be used for heart and lung transplants
- There is a good potential for further gene therapy deals to be struck
- The $397.5m of milestones from the Sarepta deal are not included in our forecasts
- If the anti-GBM P2 reads out positively in Q320 then our risk adjustment can be lowered

# Board and Management

### Chief Executive Officer - Soren Tulstrup

Mr. Soren Tulstrup is an accomplished senior global biopharmaceutical industry executive, with diverse and extensive industry experience having assembled and led high-performance biopharma companies and country operations in both the US and Europe.

Recently, he served as CEO of Vifor Pharma AG, a market leading global company in chronic kidney disease with annual sales of 1 billion USD. His previous roles have included Senior Vice President and Global Franchise Head of MPS, both at Shire Pharmaceuticals, during which time he helped achieve a strong market performance of Elaprase for the rare disorder Hunter Syndrome. Furthermore, Soren has served as CEO of Santaris Pharma (presently part of Roche) and held senior commercial roles within Merck & Co. Inc. and Sandoz Pharma AG. He holds a Master of Science, Economics and Business Administration from Copenhagen Business School.

### Chief Financial Officer - Donato Spota

Mr Donato Spota is a senior executive with more than 20 years of international pharmaceutical experience, including investor relations, strategic finance and international capital markets transactions. Prior to joining Hansa, Mr Spota was with Basilea Pharmaceuticals for 16 years, serving as CFO for the past 5. He holds a Master's degree in Business Administration from the Hochschule für Wirtschaft und Umwelt.

### COO & Chief Scientific Officer - Christian Kjellman

Dr. Christian Kjellman joined Hansa Biopharma in 2008 after serving at BioInvent AB as a Senior Scientist focusing on antibody technology and novel target evaluation. Previously, he served as Head of Research at Cartela AB. Dr Kjellman has extensive research experience in cell and molecular biology and is an Assistant Professor in Molecular Genetics at Lund University. He holds an MSc in Chemical Biology and a PhD in Tumour Immunology from Lund University.

### Chief Commercial Officer - Henk Doude van Troostwijk

Mr. Henk Doude van Troostwijk, the Chief Commercial Officer, has extensive management experience in sales and marketing in the areas of transplantation and orphan drugs. Prior to joining Hansa Biopharma in 2016, he served as General Manager of European Commercial Operations and Emerging Markets at Raptor Pharmaceuticals. Before that, he held the position of Business Unit Director Oncology and Transplantation at Genzyme Europe BV. Mr. van Troostwijk holds an MBA from the University of Reading, UK.

### VP of Corporate Strategy – Max Sakajja

Mr Sakajja joined Hansa in 2017 and has a comprehensive corporate development background having previously worked in corporate finance at Biovitrum/SOBI as the Director of Mergers & Acquisitions. Prior to joining Hansa, Mr Sakajja worked in strategy and business development as the Global Product and Service Development Manager at Envirotainer. He holds an MSc in Biotechnology from the Royal Institute of Technology.

### Chairman of the Board – Ulf Wiinberg

Mr Wiinberg is an experienced healthcare industry professional that has served on the boards of several healthcare industry associations. Ulf has extensive experience from holding the positions of President of the global consumer healthcare business at Wyeth and CEO of H Lundbeck A/S for several years. At present, he holds several biotech and pharmaceutical board positions including Alfa Laval and Nestle Health and Science.

# Financial Statements

## Group P&L

*Table 38: Hansa Group P&L (SEK000s)*

| SEK (000s) | 2018A | 2019A | 2020 | 2021 | 2022 | 2023 | 2024 | 2025 |
|---|---|---|---|---|---|---|---|---|
| **Revenue** | **3,358** | **3,364** | **7,773** | **113,640** | **331,525** | **760,134** | **1,231,831** | **1,973,116** |
| **growth** | | **0.2%** | **131.1%** | **1362.0%** | **191.7%** | **129.3%** | **62.1%** | **60.2%** |
| Cost of revenue | -916 | -866 | -2,021 | -26,137 | -62,990 | -136,824 | -203,252 | -315,699 |
| growth | | -5% | 133% | 1193% | 141% | 117% | 49% | 55% |
| as % of sales | -27.3% | -25.7% | -26.0% | -23.0% | -19.0% | -18.0% | -16.5% | -16.0% |
| **Gross profit** | **2,442** | **2,498** | **5,752** | **87,503** | **268,535** | **623,310** | **1,028,579** | **1,657,418** |
| **Gross margin** | **73%** | **74%** | **74%** | **77%** | **81%** | **82%** | **84%** | **84%** |
| SG&A | -90,387 | -167,310 | -217,191 | -260,629 | -273,661 | -287,344 | -330,445 | -363,490 |
| growth | | 85.1% | 29.8% | 20.0% | 5.0% | 5.0% | 15.0% | 10.0% |
| as % of sales | -2692% | -4974% | -2794% | -229% | -83% | -38% | -27% | -18% |
| R&D | -154,558 | -192,949 | -231,285 | -254,413 | -267,134 | -240,421 | -252,442 | -265,064 |
| growth | | 24.8% | 19.9% | 10.0% | 5.0% | -10.0% | 5.0% | 5.0% |
| as % of sales | -6329% | -7724% | -4021% | -291% | -99% | -39% | -25% | -16% |
| Other operating income | 725 | 166 | 0 | 0 | 0 | 0 | 54,896 | 192,305 |
| Other operating expenses | -4,720 | -2,073 | -810 | -1,000 | -1,000 | -1,000 | -1,000 | -1,000 |
| **EBIT** | **-246,498** | **-359,668** | **-443,534** | **-428,540** | **-273,259** | **94,546** | **499,589** | **1,220,169** |
| **EBIT margin** | **-7341%** | **-10692%** | **-5706%** | **-377%** | **-82%** | **12%** | **41%** | **62%** |
| Net financial expense | -1,516 | 76 | -473 | -473 | -473 | -473 | -473 | -473 |
| Profit before tax | -248,014 | -359,592 | -444,007 | -429,013 | -273,732 | 94,073 | 499,116 | 1,219,696 |
| Tax | 40 | -417 | 0 | 0 | 0 | -18,815 | -99,823 | -243,939 |
| Effective tax rate | 0.0% | 0.1% | 0.0% | 0.0% | 0.0% | -20.0% | -20.0% | -20.0% |
| **Net income** | **-247,974** | **-360,009** | **-444,007** | **-429,013** | **-273,732** | **75,258** | **399,293** | **975,757** |
| growth | | 45.2% | 23.3% | -3.4% | -36.2% | -127.5% | 430.6% | 144.4% |
| **Earnings per share (diluted)** | **-6.47** | **-9.00** | **-10.51** | **-9.65** | **-6.16** | **1.69** | **8.98** | **21.94** |
| **growth** | | **39.0%** | **16.8%** | **-8.2%** | **-36.2%** | **-127.5%** | **430.6%** | **144.4%** |
| Number of shares (000s, diluted) | 38,326 | 40,020 | 42,244 | 44,468 | 44,468 | 44,468 | 44,468 | 44,468 |

*Source: Intron Health estimates*

*Table 39: Hansa Group P&L (USD 000s)*

| USD (000s) | 2018A | 2019A | 2020 | 2021 | 2022 | 2023 | 2024 | 2025 |
|---|---|---|---|---|---|---|---|---|
| **Revenue** | **386** | **386** | **892** | **13,047** | **38,063** | **87,271** | **141,427** | **226,535** |
| **growth** | | **0.2%** | **131.1%** | **1362.0%** | **191.7%** | **129.3%** | **62.1%** | **60.2%** |
| Cost of revenue | -105 | -99 | -232 | -3,001 | -7,232 | -15,709 | -23,335 | -36,246 |
| growth | | -5% | 133% | 1193% | 141% | 117% | 49% | 55% |
| as % of sales | -27.3% | -25.7% | -26.0% | -23.0% | -19.0% | -18.0% | -16.5% | -16.0% |
| **Gross profit** | **280** | **287** | **660** | **10,046** | **30,831** | **71,563** | **118,092** | **190,289** |
| **Gross margin** | **73%** | **74%** | **74%** | **77%** | **81%** | **82%** | **84%** | **84%** |
| SG&A | -10,377 | -19,209 | -24,936 | -29,923 | -31,419 | -32,990 | -37,939 | -41,732 |
| growth | 0.0% | 85.1% | 29.8% | 20.0% | 5.0% | 5.0% | 15.0% | 10.0% |
| as % of sales | -2692% | -4974% | -2794% | -229% | -83% | -38% | -27% | -18% |
| R&D | -17,745 | -22,153 | -26,554 | -29,209 | -30,670 | -27,603 | -28,983 | -30,432 |
| growth | 0.0% | 24.8% | 19.9% | 10.0% | 5.0% | -10.0% | 5.0% | 5.0% |
| as % of sales | -6329% | -7724% | -4021% | -291% | -99% | -39% | -25% | -16% |
| Other operating income | 83 | 19 | 0 | 0 | 0 | 0 | 6,303 | 22,079 |
| Other operating expenses | -542 | -238 | -93 | -115 | -115 | -115 | -115 | -115 |
| **EBIT** | **-28,301** | **-41,294** | **-50,922** | **-49,201** | **-31,373** | **10,855** | **57,358** | **140,088** |
| **EBIT margin** | **-7341%** | **-10692%** | **-5706%** | **-377%** | **-82%** | **12%** | **41%** | **62%** |
| Net financial expense | -174 | 9 | -54 | -54 | -54 | -54 | -54 | -54 |
| Profit before tax | -28,475 | -41,285 | -50,977 | -49,255 | -31,427 | 10,801 | 57,304 | 140,034 |
| Tax | 5 | -48 | 0 | 0 | 0 | -2,160 | -11,461 | -28,007 |
| Effective tax rate | 0.0% | 0.1% | 0.0% | 0.0% | 0.0% | -20.0% | -20.0% | -20.0% |
| **Net income** | **-28,470** | **-41,333** | **-50,977** | **-49,255** | **-31,427** | **8,640** | **45,843** | **112,027** |
| growth | 0.0% | 45.2% | 23.3% | -3.4% | -36.2% | -127.5% | 430.6% | 144.4% |
| **Earnings per share (diluted)** | **-0.74** | **-1.03** | **-1.21** | **-1.11** | **-0.71** | **0.19** | **1.03** | **2.52** |
| **growth** | **0.0%** | **39.0%** | **16.8%** | **-8.2%** | **-36.2%** | **-127.5%** | **430.6%** | **144.4%** |
| Number of shares (000s, diluted) | 38,326 | 40,020 | 42,244 | 44,468 | 44,468 | 44,468 | 44,468 | 44,468 |

*Source: Intron Health estimates*

# Group Balance Sheet

***Table 40: Hansa Group balance sheet***

| SEK (000s) | 2018A | 2019A | 2020 | 2021 | 2022 | 2023 | 2024 | 2025 |
|---|---|---|---|---|---|---|---|---|
| Intangible assets | 33,197 | 33,348 | 32,514 | 31,701 | 30,909 | 30,136 | 29,383 | 28,648 |
| PP&E | 5,876 | 6,035 | 4,065 | 6,749 | 9,500 | 11,656 | 13,782 | 15,269 |
| Leased assets | 0 | 9,109 | 9,109 | 9,109 | 9,109 | 9,109 | 9,109 | 9,109 |
| Financial assets | 39,528 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| **Non-current assets** | **78,601** | **48,492** | **45,688** | **47,559** | **49,517** | **50,901** | **52,274** | **53,026** |
| | | | | | | | | |
| Accounts receivable | 8,033 | 522 | 1,278 | 18,680 | 54,497 | 124,954 | 202,493 | 324,348 |
| Inventory | 0 | 0 | 1,065 | 15,567 | 45,414 | 104,128 | 168,744 | 270,290 |
| Prepaid expenses & accrued income | 0 | 2,979 | 2,979 | 2,979 | 2,979 | 2,979 | 2,979 | 2,979 |
| Other receivables | 0 | 11,149 | 11,149 | 11,149 | 11,149 | 11,149 | 11,149 | 11,149 |
| Short term investments | 418,746 | 419,397 | 419,397 | 419,397 | 419,397 | 419,397 | 419,397 | 419,397 |
| Cash and cash equivalents | 439,441 | 181,697 | 853,671 | 431,101 | 111,467 | 77,499 | 367,904 | 1,162,163 |
| **Current assets** | **866,220** | **615,744** | **1,289,539** | **898,873** | **644,904** | **740,105** | **1,172,666** | **2,190,326** |
| | | | | | | | | |
| **Total assets** | **944,821** | **664,236** | **1,335,227** | **946,432** | **694,422** | **791,007** | **1,224,940** | **2,243,352** |
| | | | | | | | | |
| Share capital | 40,682 | 41,448 | 41,448 | 41,448 | 41,448 | 41,448 | 41,448 | 41,448 |
| Share premium | 1,400,512 | 1,413,447 | 2,484,623 | 2,484,623 | 2,484,623 | 2,484,623 | 2,484,623 | 2,484,623 |
| Treasury shares | -722 | -1,421 | -1,421 | -1,421 | -1,421 | -1,421 | -1,421 | -1,421 |
| Reserves | 31,216 | 81,163 | 81,163 | 81,163 | 81,163 | 81,163 | 81,163 | 81,163 |
| Retained earnings | -611,812 | -971,821 | -1,415,828 | -1,844,841 | -2,118,573 | -2,043,315 | -1,644,023 | -668,266 |
| **Total shareholders' equity** | **859,876** | **562,816** | **1,189,985** | **760,972** | **487,239** | **562,497** | **961,790** | **1,937,547** |
| | | | | | | | | |
| Deferred tax liabilities | 511 | 507 | 507 | 507 | 507 | 507 | 507 | 507 |
| Provisions | 10,948 | 818 | 818 | 818 | 818 | 818 | 818 | 818 |
| Lease liabilities | 476 | 4,827 | 4,827 | 4,827 | 4,827 | 4,827 | 4,827 | 4,827 |
| Contingent consideration | 679 | 730 | 730 | 730 | 730 | 730 | 730 | 730 |
| **Non-current liabilities** | **12,614** | **6,882** | **6,882** | **6,882** | **6,882** | **6,882** | **6,882** | **6,882** |
| | | | | | | | | |
| Lease liabilities | 101 | 4,632 | 4,632 | 4,632 | 4,632 | 4,632 | 4,632 | 4,632 |
| Accounts payable | 40,426 | 50,573 | 86,397 | 118,615 | 132,336 | 145,663 | 172,304 | 206,959 |
| Other liabilities | 5,562 | 6,940 | 6,940 | 6,940 | 6,940 | 6,940 | 6,940 | 6,940 |
| Accrued expenses and deferred income | 26,242 | 32,393 | 40,392 | 48,392 | 56,392 | 64,392 | 72,392 | 80,392 |
| **Current liabilities** | **72,331** | **94,538** | **138,361** | **178,579** | **200,300** | **221,627** | **256,268** | **298,923** |
| | | | | | | | | |
| **Total shareholders' equity and liabilities** | **944,821** | **664,236** | **1,335,227** | **946,432** | **694,422** | **791,007** | **1,224,940** | **2,243,352** |

*Source: Intron Health estimates*

# Group Cash Flow

***Table 41: Hansa Group cash flow***

| SEK (000s) | 2018A | 2019A | 2020 | 2021 | 2022 | 2023 | 2024 | 2025 |
|---|---|---|---|---|---|---|---|---|
| **EBIT** | **-246,498** | **-359,668** | **-443,534** | **-428,540** | **-273,259** | **94,546** | **499,589** | **1,220,169** |
| D&A | 1,837 | 7,463 | 8,607 | 4,222 | 4,439 | 5,334 | 5,681 | 6,654 |
| Incentive programme costs | 11,675 | 7,246 | 8,000 | 8,000 | 8,000 | 8,000 | 8,000 | 8,000 |
| Pension contributions | 0 | 85 | 0 | 0 | 0 | 0 | 0 | 0 |
| Unrealised FX differences | -68 | -181 | 0 | 0 | 0 | 0 | 0 | 0 |
| Interest paid | -210 | -337 | -473 | -473 | -473 | -473 | -473 | -473 |
| Income taxes paid | 0 | -123 | 0 | 0 | 0 | -18,815 | -99,823 | -243,939 |
| **CFO before change in WC** | **-233,264** | **-345,515** | **-427,400** | **-416,791** | **-261,293** | **88,592** | **412,973** | **990,411** |
| Accounts receivable | 450 | -464 | -756 | -17,403 | -35,817 | -70,456 | -77,539 | -121,855 |
| Inventory | 0 | 0 | -1,065 | -14,502 | -29,847 | -58,714 | -64,616 | -101,546 |
| Operating receivables | -362 | -6,157 | 0 | 0 | 0 | 0 | 0 | 0 |
| Accounts payable | 36,653 | 10,146 | 35,824 | 32,218 | 13,722 | 13,327 | 26,641 | 34,655 |
| Operating liabilities | -8,037 | 7,215 | 0 | 0 | 0 | 0 | 0 | 0 |
| **Total change in WC** | **28,704** | **10,740** | **34,003** | **313** | **-51,943** | **-115,843** | **-115,514** | **-188,746** |
| **Cash flow from operations** | **-204,560** | **-334,775** | **-393,397** | **-416,478** | **-313,235** | **-27,251** | **297,459** | **801,665** |
| | | | | | | | | |
| Acquisition of intangible assets | -127 | -729 | 0 | 0 | 0 | 0 | 0 | 0 |
| Acquisition of PP&E | -2,366 | -2,699 | -5,803 | -6,093 | -6,398 | -6,718 | -7,053 | -7,406 |
| Proceeds from equipment sales | 0 | 87 | 0 | 0 | 0 | 0 | 0 | 0 |
| Purchase of short term investments | -493,984 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Sale of short term investments | 109,000 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Proceeds from sales of shares in Genovis AB | 0 | 89,125 | 0 | 0 | 0 | 0 | 0 | 0 |
| **Cash flow from investing** | **-387,477** | **85,784** | **-5,803** | **-6,093** | **-6,398** | **-6,718** | **-7,053** | **-7,406** |
| | | | | | | | | |
| Issue of shares | 453,075 | 0 | 1,111,837 | 0 | 0 | 0 | 0 | 0 |
| Cost of share issue | -20,712 | -7,646 | -40,661 | 0 | 0 | 0 | 0 | 0 |
| Sale of treasury shares | 4,473 | 877 | 0 | 0 | 0 | 0 | 0 | 0 |
| Issue of warrants | 13,514 | 2,309 | 0 | 0 | 0 | 0 | 0 | 0 |
| Dividends | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Repayment of lease liabilities | -44 | -4,424 | 0 | 0 | 0 | 0 | 0 | 0 |
| **Cash flow from financing** | **450,306** | **-8,884** | **1,071,176** | **0** | **0** | **0** | **0** | **0** |
| | | | | | | | | |
| **Net change in cash & cash equivalents** | **-141,731** | **-257,875** | **671,975** | **-422,571** | **-319,633** | **-33,969** | **290,406** | **794,259** |
| **Cash & cash equivalents, beginning of year** | **581,078** | **439,440** | **181,696** | **853,671** | **431,101** | **111,467** | **77,499** | **367,904** |
| Effects of FX on cash | 93 | 131 | 0 | 0 | 0 | 0 | 0 | 0 |
| **Cash & cash equivalents, end of year** | **439,440** | **181,696** | **853,671** | **431,101** | **111,467** | **77,499** | **367,904** | **1,162,163** |

*Source: Intron Health estimates*

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