Company Update

BUY

29 April 2020

Hansa Biopharma AB

A platform worth digesting

Price	SEK 121.1
Fair value	SEK 190
Market capitalisation	SEK 5.0 billion
Enterprise value	SEK 4.7 billion
12m high/low	SEK 209.8 / SEK 59.3
Avg. daily volume	277,810
Bloomberg / Reuters	HNSA SS / HNSA.ST
Listing	Stockholm
Adviser	Yes
Next results (Q2)	16 July 2020

Top 5 Shareholders

Nexttobe AB	*14.4%*
Invesco	*5.3%*
Consonance Capital Mgmt	*5.2%*
Thomas Olausson	*4.3%*
Gladiator	*3.7%*

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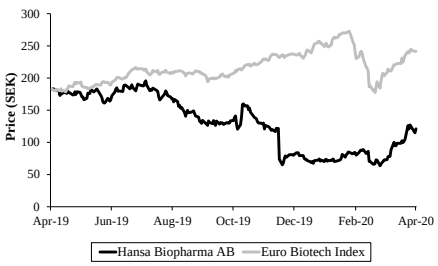
Share price performance (1 year)



Source: R_x Securities

Hansa Biopharma's lead drug imlifidase for HLA desensitisation to enable kidney transplantation is nearing a key inflection point, with the EMA's CHMP expected to provide an opinion later this quarter. If positive, we expect a sequenced launch in Europe, initially targeting the leading centres and physicians, commencing by the end of the year depending on the potential impact of the ongoing COVID-19 pandemic. In the US there is now a clear path to market for imlifidase, which involves a further ~50 patient clinical trial that we believe has a favourable risk profile. We expect positive results would lead to a BLA filing in 2023 under the accelerated approval pathway. We forecast peak sales of imlifidase of ~$400 million in kidney transplantation, but would highlight significant upside from additional indications where it is in Phase II testing – anti-glomerular basement membrane antibody disease (anti-GBM), acute antibody-mediated kidney transplant rejection (AMR) and Guillain-Barré Syndrome (GBS). Furthermore, we believe the Company's endopeptidase technology platform has potentially commercially attractive applications beyond acute autoimmune diseases, in the gene therapy field (as a pre-treatment to broaden access) and in chronic autoimmune diseases (the repeat dosing "NiceR" programme). With a net cash position of SEK 476.9 million at the end of Q1, we project a cash runway for Hansa into H1 2021. We maintain our BUY rating and fair value of SEK 190/share, which is predominantly based on imlifidase in kidney transplantation at this time.

- **Imlifidase CHMP opinion expected in Q2 2020** – in March 2019 the EMA accepted for review Hansa's MAA for imlifidase to enable kidney transplantation in highly HLA sensitised patients. A positive opinion could lead to a European approval in Q3 2020, and we would anticipate first launches before the end of the year. We expect the Company to self-market the drug, capturing its full value and forecast peak sales of ~$140 million in Europe and ~$260 million in the US.
- **Phase II investigator-initiated trial in GBM results slated for Q3 2020** – having finalised enrolment of 15 patients in January. In other indications – 4/30 patients have been enrolled into a Phase II trial in acute AMR, with recruitment slated to close in H1 2021. A Phase II trial in GBS has recruited 4/30 patients and enrolment is expected to be finalised in H2 2021. These timelines consider slower than initially anticipated recruitment due to the COVID-19 pandemic.

Key financial data (SEK'm) - IFRS	**2019A**	**2020E**	**2021E**	**2022E**	**2023E**
Revenue	3.4	13.6	77.9	183.9	378.8
EBITDA	(436.2)	(394.2)	(437.3)	(355.0)	(188.7)
Net Income	(360.0)	(414.2)	(456.3)	(374.9)	(209.6)
EPS (SEK)	(9.0)	(10.3)	(11.4)	(9.4)	(5.2)
Net Cash	600.9	165.6	(275.1)	(633.8)	(826.6)

Source: R_X Securities estimates

Consensus	**2020E**	**2021E**	**2022E**	**2023E**
Revenue	5.4	99.9	210.0	379.0
EBITDA	(474.3)	(212.8)	(514.0)	(188.7)

Source: Bloomberg

Contents

Company Description

Hansa Biopharma AB (Hansa) is a Swedish biotech company developing novel immunomodulatory enzymes which have potentially broad therapeutic application. The Company was founded in 2007 by Bo Håkansson and built upon the research of Professor Lars Björck of Lund University. Today, Hansa employs 78 people with research, both in-house and through long-term co-operation with academic groups. The Company's lead product, imlifidase, is a recombinant bacterial enzyme that cleaves immunoglobulin G (IgG). Hansa's development focus for imlifidase is as a drug to enable kidney transplantation in patients with high human leukocyte antigen (HLA) sensitisation. There are a significant number of patients on transplant waitlists globally who are highly HLA sensitised and are therefore very unlikely to find a compatible donor. These patients face long-term dialysis, which has poor outcomes. We believe imlifidase can change this, as used before a transplant it rapidly degrades the recipient's donor-specific antibodies, the culprits of immediate organ rejection in HLA mismatched transplants. Results from Phase II trials are highly impressive in our view – across four trials, imlifidase enabled 46 kidney transplants in highly HLA sensitised patients, with 94% graft survival at six months and positive longer term data out to three years reported from individual trials. Hansa has filed for approval of imlifidase in kidney transplantation (to be branded IDEFIRIX™) in Europe and expects a decision from the EMA's CHMP in Q2 2020, while in the US the FDA has requested a further clinical study to support a BLA (we anticipate filing in 2023). Imlifidase also has potential in other IgG-mediated autoimmune diseases – Phase II trials in anti-glomerular basement membrane antibody disease (anti-GBM), acute antibody-mediated transplant rejection (AMR) and Guillain-Barré syndrome (GBS) are ongoing. Hansa is also exploring applying its endopeptidase technology in other areas. For example, the Company intends to evaluate its use a pre-treatment to broaden access to gene therapy and is also conducting "NiceR", a project to develop novel IgG-inactivating enzymes for repeat dosing and hence target conditions that lay beyond the remit of imlifidase (which is likely to be a single-use product) such as chronic autoimmune diseases or as a pre-treatment to enhance the efficacy of therapeutic antibodies in cancer therapy (the "EnzE" project). The Company also receives royalties from sales of a heparin-binding protein (HBP) diagnostic for severe sepsis that was developed and then outlicensed to Axis-Shield Diagnostics in 2009. Hansa completed its IPO on NASDAQ's First North market in October 2007 raising SEK 38 million (at SEK 10/share). The Company has raised a total of SEK 1.6 billion since 2007, most recently raising SEK 430 million (at SEK 255/share) in November 2018.

Investment Positives

Imlifidase has generated positive Phase II results; MAA filed in Europe

Imlifidase has generated positive results from four Phase II clinical trials in kidney transplantation of HLA sensitised patients (two trials in very highly sensitised patients, average cPRA of 99.4%). Pooled results from these studies, all of which met their primary endpoints, were presented in September 2019. Imlifidase induced rapid crossmatch conversions and depleted donor-specific antibodies to enable transplantation in all 46 patients. Graft survival six-months post-transplant was 94%, and patients generally had good kidney function with a mean estimated glomerular filtration rate (eGFR) of 60 ml/min/1.73m^2. Furthermore, we believe that three-year results from an investigator-initiated study provide a strong indication that the drug can improve long-term outcomes for difficult-to-treat kidney transplant patients. The results presented at the American Transplant Congress 2019 showed only two graft

losses from 16 transplants occurred, eGFR was 47.5 ml/min/1.73m^2, DSA rebound was low, and the rate of AMR was 44%. These data are in-line with historical results for deceased donor transplantation of non-sensitised patients. Hansa has filed for approval of imlifidase in kidney transplantation in Europe and expects an opinion from the EMA's CHMP in Q2 2020, while in the US the FDA has requested a further clinical study to support a BLA, potentially following the accelerated approval pathway (we anticipate filing in 2023).

Imlifidase has PRIME and Fast Track designations

Our discussions with doctors suggest that there is high unmet medical need for novel HLA desensitisation protocols, as high HLA sensitisation remains a significant barrier to successful transplantation. In the most severely sensitised patients (in the US we estimate ~2,200 patients "active" on the waitlist with cPRA ≥99.9%) existing desensitisation options are ineffective and finding a compatible HLA match is extremely unlikely. In May 2017 the EMA granted the drug access to its PRIME scheme, and in September 2018 the FDA granted it Fast Track designation. Both designations provide enhanced interactions with the agencies and the potential for accelerated regulatory reviews.

Hansa can capture the full value of imlifidase

Hansa retains all development and commercialisation rights to imlifidase and the Company's strategy, which we endorse, is to directly sell the drug and capture its full value. In most countries, kidney transplants occur at a relatively small number of specialised centres (e.g. in the UK 20 transplant centres vs 1,257 hospitals overall and in the US 260 transplant centres vs 6,100 hospitals overall). We believe that Hansa can effectively market and sell the drug with relatively compact sales teams (management has guided towards low double-digit sales personnel numbers in key geographies). Furthermore, Hansa has already made strong links with several KOLs in Europe and the US who are at the forefront of the transplant field, and we anticipate their advocacy for the drug will aid the commercialisation process.

Attractive commercial potential for imlifidase in other acute autoimmune diseases

Having demonstrated clear proof-of-concept in kidney transplantation, we believe that imlifidase has application in various IgG-linked acute autoimmune diseases. An investigator-initiated Phase II trial in anti-GBM completed recruitment in January 2020 and results are slated for Q3 2020, while Phase II trials in acute AMR associated with kidney transplantation and in GBS are ongoing. Currently, plasma exchange or other slow-acting immunodepletion strategies, are treatment options for these diseases, and there remains a clear opportunity for a more rapid and effective method of IgG depletion like imlifidase in our view.We estimate peak sales of imlifidase in kidney transplantation of ~$400 million, but believe progressive label expansion could ultimately lead to peak sales significantly higher.

Hansa's technology could reach beyond acute autoimmune indications

We believe Hansa's endopeptidase technology platform could have applications reaching beyond acute autoimmune diseases. The Company is exploring the possibility of applying its technology to enable broader access to gene therapies and facilitate their re-dosing. Gene therapy is a rapidly growing area of medicine, and we understand that Hansa is in discussions with gene therapy developers to establish a research collaboration. The Company is also developing endopeptidases with lower immunogenicity for repeat dosing, the "NiceR" programme, with a lead candidate selected. A repeat-dose drug could have therapeutic potential in treating regular symptom "flares" that are associated with some chronic autoimmune diseases, or as a treatment to enhance the efficacy of therapeutic antibodies (the "EnzE" project in the oncology field).

Investment Risks

There is a high dependency on imlifidase

Our valuation analysis suggests imlifidase is the key value driver for Hansa. As a result, there is a significant dependency on this single asset – any negative developments are likely to result in a substantial reduction in Hansa's share price, in our view. For example, during 2019, the Company's shares were impacted by the FDA requiring additional clinical data before filing a BLA for imlifidase in the US. While Hansa has additional early-stage pipeline programmes and opportunities (gene therapy, NiceR, EnzE) as well as a marketed HBP diagnostic for which it receives milestones and royalties, there remains a high dependency on imlifidase.

A new study may not support US approval; regulatory risk remains in Europe

In December 2019 Hansa announced that the FDA had requested a randomised, controlled clinical trial of imlifidase in kidney transplantation to support a BLA filing. The Company intends to initiate a trial in Q4 2020 involving ~50 waitlisted patients with a cPRA ≥99.9% to either receive imlifidase and a deceased donor transplant or to remain on the waitlist (control), with a primary endpoint of eGFR (a marker of kidney function) at 6 and 12 months. We are encouraged by imlifidase's clinical data and believe that such a trial has a high probability of success. However, the number of patients transplanted to date is relatively small (46), and there is a risk that the new trial could fail. Graft failure after a successful transplant, an unlikely matched transplant in the control arm, or a previously unseen safety signal are all possible. Regarding its MAA in Europe, Hansa recently submitted responses to the CHMP's Day 180 questions. However, the questions and Hansa's responses are not publically available and as such the likely outcome of the CHMP opinion is unclear at this stage.

Hansa must position imlifidase within kidney transplant allocation schemes

Formal pathways to imlifidase-enabled transplantation must be created within healthcare systems of different countries to enable efficient access to patients. This is complicated by the fact that in Europe, individual countries or groups of countries have different systems for matching and allocating donor organs with recipients based on several factors that include their level of HLA sensitisation. In the US, a new Kidney Allocation System has been in place since late 2014. We expect Hansa will need to work together with the FDA and the United Network for Organ Sharing (UNOS, which administers the Organ Procurement and Transplantation Network in the US) to determine imlifidase's position in the transplant allocation process.

We believe Hansa will require significant additional capital

Hansa reported a net cash position of SEK 476.9 million as at 31 March 2020, which we project finances the Company into H1 2021. We believe if approved, the sequenced EU launch strategy for imlifidase is diligent. Still, we expect a slower ramp in sales than with a conventional drug launch (i.e. not in transplantation) and as such, we believe Hansa will need to raise additional capital to finance the continued construction of European and US commercial infrastructure, the US pivotal trial and other R&D.

NiceR is at an early stage and has yet to achieve proof-of-concept

We are enthusiastic about the commercial potential for NiceR as a repeat dosed IgG-degrading enzyme that has application in autoimmune diseases where imlifidase (likely a single-dose drug due to its immunogenicity) may not be appropriate. However, NiceR is at an early stage, and we would highlight that the Company has not yet presented or published any preclinical results from the project. While imlifidase has validated the NiceR treatment concept, the lead candidate is a different (albeit closely related) molecule. As such, there is a risk that it may not demonstrate efficacy or adequate safety in clinical trials in humans.

Financials (yearly)

Table 1: Earnings Outlook – Annual Forecast Profit and Loss Statement (SEK'm)

Y/E 31 December	2019A	2020E	2021E	2022E	2023E	2024E	2025E	2026E
Revenue	**3.4**	**13.6**	**77.9**	**183.9**	**378.8**	**705.6**	**1,138.2**	**1,594.0**
Imlifidase	-	10.0	74.0	179.6	374.0	700.4	1,132.5	1,587.7
Other revenue	3.4	3.6	3.9	4.3	4.8	5.2	5.8	6.3
Cost of Goods	**(0.9)**	**(2.0)**	**(8.2)**	**(18.8)**	**(38.4)**	**(71.1)**	**(114.4)**	**(160.0)**
Gross Profit	**2.5**	**11.6**	**69.7**	**165.1**	**340.4**	**634.5**	**1,023.8**	**1,434.0**
Expenses	**(360.3)**	**(423.8)**	**(526.0)**	**(540.0)**	**(550.0)**	**(550.0)**	**(750.0)**	**(850.0)**
R&D	(185.9)	(237.5)	(300.0)	(300.0)	(250.0)	(150.0)	(200.0)	(250.0)
SG&A	(174.4)	(185.7)	(226.0)	(240.0)	(300.0)	(400.0)	(550.0)	(600.0)
Other operating inc.	(1.9)	(0.6)	-	-	-	-	-	-
Operating Profit	**(359.7)**	**(412.2)**	**(456.3)**	**(374.9)**	**(209.6)**	**84.5**	**273.8**	**584.0**
EBITDA	**(448.0)**	**(394.2)**	**(437.3)**	**(355.0)**	**(188.7)**	**106.5**	**296.9**	**608.2**
Net financial income	0.1	(2.0)	-	-	-	-	-	-
Profit Before Tax	**(359.6)**	**(414.2)**	**(456.3)**	**(374.9)**	**(209.6)**	**84.5**	**273.8**	**584.0**
Taxation	(0.4)	0.0	-	-	-	-	-	-
Net Income	**(360.0)**	**(414.2)**	**(456.3)**	**(374.9)**	**(209.6)**	**84.5**	**273.8**	**584.0**
EPS (SEK)	**(9.0)**	**(10.3)**	**(11.4)**	**(9.4)**	**(5.2)**	**2.1**	**6.8**	**14.6**
Ave No. of Shares (m)	40.0	40.0	40.0	40.0	40.0	40.0	40.0	40.0
Net cash	**600.9**	**165.6**	**(275.1)**	**(633.8)**	**(826.6)**	**(724.6)**	**(432.7)**	**170.0**

Source: Company data, Rx Securities estimates

Key Model Assumptions

- Our model assumes that Hansa Biopharma is financed into H1 2021 and further capital will be required, though for simplicity our forecasts assume a debt-based model; and
- Our forecasts assume that imlifidase is launched in H2 2020 in Europe and that Hansa Biopharma directly markets the drug, with the initial launch focusing on the leading transplantation centres in Europe. However, there is a risk that the ongoing COVID-19 pandemic could result in a delay to this timeline.

Financials (quarterly)

Table 2: Earnings Outlook – Quarterly Forecast Profit and Loss Statement (SEK'm)

Y/E 31 December	Q1 20A	Q2 20E	Q3 20E	Q4 20E	2020E	Q1 21E	Q2 21E	Q3 21E	Q4 21E	2021E
Revenue	**0.9**	**0.7**	**0.7**	**11.3**	**13.6**	**15.0**	**16.7**	**20.8**	**25.5**	**77.9**
Imlifidase	-	-	-	10.0	10.0	14.0	16.0	20.0	24.0	74.0
Other revenue	0.9	0.7	0.7	1.3	3.6	1.0	0.7	0.8	1.5	3.9
Cost of Goods	**(0.4)**	**(0.1)**	**(0.1)**	**(1.3)**	**(2.0)**	**(1.6)**	**(1.7)**	**(2.2)**	**(2.7)**	**(8.2)**
Gross Profit	**0.5**	**0.5**	**0.6**	**10.1**	**11.6**	**13.4**	**15.0**	**18.6**	**22.8**	**69.7**
Expenses	**(91.8)**	**(97.0)**	**(109.0)**	**(126.0)**	**(423.8)**	**(125.0)**	**(129.0)**	**(133.0)**	**(139.0)**	**(526.0)**
R&D	(52.5)	(55.0)	(60.0)	(70.0)	(237.5)	(75.0)	(75.0)	(75.0)	(75.0)	(300.0)
SG&A	(38.7)	(42.0)	(49.0)	(56.0)	(185.7)	(50.0)	(54.0)	(58.0)	(64.0)	(226.0)
Other operating inc.	(0.6)	-	-	-	(0.6)	-	-	-	-	-
Operating Profit	**(91.4)**	**(96.5)**	**(108.4)**	**(115.9)**	**(412.2)**	**(111.6)**	**(114.0)**	**(114.4)**	**(116.2)**	**(456.3)**
EBITDA	**(85.8)**	**(97.2)**	**(102.0)**	**(109.2)**	**(394.2)**	**(105.8)**	**(114.8)**	**(107.6)**	**(109.1)**	**(437.3)**
Net financial income	(2.0)	-	-	-	(2.0)	-	-	-	-	-
Profit Before Tax	**(93.4)**	**(96.5)**	**(108.4)**	**(115.9)**	**(414.2)**	**(111.6)**	**(114.0)**	**(114.4)**	**(116.2)**	**(456.3)**
Taxation	0.0	-	-	-	0.0	-	-	-	-	-
Net Income	**(93.4)**	**(96.5)**	**(108.4)**	**(115.9)**	**(414.2)**	**(111.6)**	**(114.0)**	**(114.4)**	**(116.2)**	**(456.3)**
EPS (SEK)	**(2.3)**	**(2.4)**	**(2.7)**	**(2.9)**	**(10.3)**	**(2.8)**	**(2.8)**	**(2.9)**	**(2.9)**	**(11.4)**
No. of Shares (m)	40.0	40.0	40.0	40.0	40.0	40.0	40.0	40.0	40.0	40.0
Net cash	**476.9**	**378.7**	**276.3**	**165.6**	**165.6**	**59.7**	**(56.2)**	**(164.3)**	**(275.1)**	**(275.1)**

Source: Company data, R_X Securities estimates

Forecast News Flow

Table 3: Hansa Biopharma's forecast news flow

Timing	Expected News	Programme
Q2 2020	Submission of US pivotal trial in highly HLA sensitised kidney transplantation protocol to FDA	Imlifidase
May/June 2020	CHMP opinion on MAA for desensitisation for kidney transplantation	Imlifidase
16 July 2020	Q2 results	
Q3 2020	Approval by EU Commission (if CHMP opinion positive)	Imlifidase
Q3 2020	Top-line results from the investigator-initiated Phase II trial in anti-GBM disease	Imlifidase
H2 2020*	First launches in Europe	Imlifidase
Q4 2020*	First patient into US registrational trial	Imlifidase
22 October 2020	Q3 results	
H1 2021**	Completion of recruitment into Phase II trial in AMR	Imlifidase
H2 2021**	Completion of recruitment into Phase II trial in GBS	Imlifidase

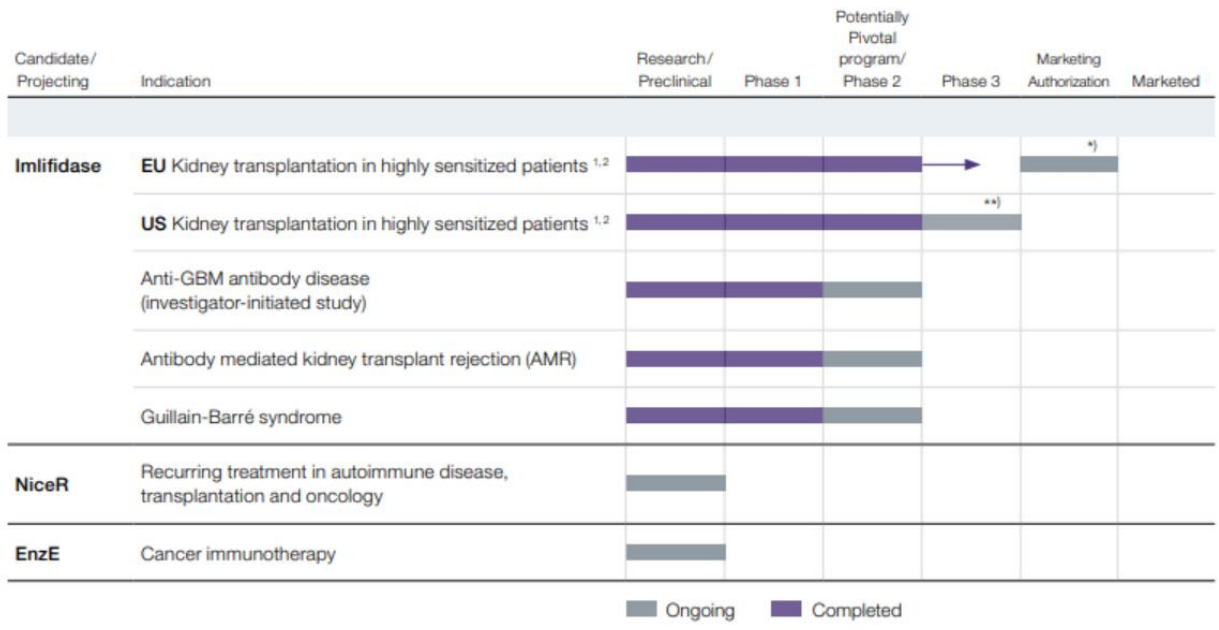
Source: Company data, Rx Securities estimates; * the ongoing COVID-19 pandemic may impact timelines; ** considers 3-6 month delay on previous estimates due to potential COVID-19 pandemic impact

Pipeline

Hansa's pipeline focuses on enzymes that degrade IgG

Hansa's key pipeline drug is imlifidase, a bacterial endopeptidase that degrades IgG antibodies (see Figure 1). Its lead indication is HLA desensitisation to facilitate kidney transplantation. NiceR is a project to develop novel IgG-inactivating enzymes for repeat dosing and hence target conditions that lay beyond the remit of imlifidase (which is likely to be a single-use product). EnzE is a project to use IgG endopeptidases as antibody enhancers for the treatment of cancer.

Figure 1: Hansa Biopharma's pipeline



Source: Hansa Biopharma; 1 = results published in Winstedt el al. (2015) PLOS ONE 10(7); 2 = Lorant et al., American Journal of Transplantation and 03+04 studies (Jordan et al., New England Journal of Medicine); * EMA: imlifidase for kidney transplantation filed for conditional approval after completion of Phase II, a post-approval study would be necessary in case of approval; ** FDA: Agreement with the FDA on a regulatory path forward in the US, a new clinical study could support BLA submission by 2023

Board and Management

Table 4: Key members of the Board and Management

Name	Executive History
Mr Søren Tulstrup *Chief Executive Officer*	Mr Tulstrup has a broad and extensive background as a senior executive in the biopharma industry, most recently serving as CEO of Vifor Pharma AG. His previous roles include Senior VP, Global Franchise Head, MPS at Shire Pharmaceuticals, CEO of Santaris Pharma (now part of Roche) and senior commercial roles within Merck & Co. and Sandoz. He holds a Master of Science, Economics and Business Administration from Copenhagen Business School.
Mr Donato Spota *Chief Financial Officer*	Mr Spota is a senior executive with more than 20 years of international pharmaceutical industry experience, including strategic finance, investor relations and international capital markets transactions. Before joining Hansa, Mr Spota was with Basilea Pharmaceutica for 16 years, serving as CFO for the past five. He holds an MBA from the Hochschule für Wirtschaft und Umwelt.
Dr Christian Kjellman *Chief Operating Officer* *Chief Scientific Officer*	Dr Kjellman joined Hansa Biopharma in 2008 after serving at BioInvent AB as a Senior Scientist. Before that, he was Head of Research at Cartela AB. He 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.
Mr Henk Doude van Troostwijk *Chief Commercial Officer*	Mr van Troostwijk has extensive management experience in sales and marketing in the areas of transplantation and Orphan drugs. Before joining Hansa Biopharma in 2016, he served as General Manager of European Commercial Operations and Emerging Markets at Raptor Pharmaceuticals. Before that, he was Business Unit Director Oncology and Transplantation at Genzyme Europe. Mr van Troostwijk holds an MBA from Henley Management College, UK.
Mr Max Sakajja *VP Corporate Strategy*	Mr Sakajja joined Hansa Biopharma in 2017. He has a broad corporate development background having worked within corporate finance at Biovitrum/SOBI in the position of Director M&A. Before joining Hansa, Mr Sakajja worked in strategy and business development at Envirotainer as the Global Product and Service Development Manager. He holds an MSc in Biotechnology from the Royal Institute of Technology.
Ulf Wiinberg *Chairman of the Board*	Mr Wiinberg is an experienced healthcare industry professional who has served the boards of several healthcare industry associations. At Wyeth, he was President of the global consumer health care and European pharma businesses, and he was also the CEO of Lundbeck for several years. He holds several other board positions in the biotech and pharmaceutical industries.

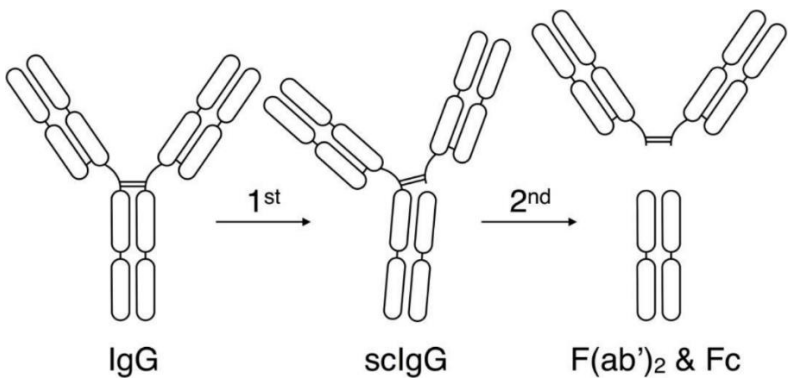
Source: Hansa Biopharma AB

Imlifidase – antibody degrading enzyme

CHMP opinion on Hansa's lead drug imlifidase in kidney transplant due Q2 2020
Imlifidase is an enzyme of the bacterium *Streptococcus pyogenes*. Discovered in 2002, it degrades IgG (the most commonly occurring antibody type that accounts for a vast majority of all antibodies in our body). Imlifidase has generated impressive results from four Phase II studies, in which it removed patients' HLA sensitisation facilitating 46 successful HLA-mismatched kidney transplants. Hansa has filed an MAA with the EMA, and we anticipate a CHMP opinion in Q2 2020, and if this is positive, we would expect approval in Q3 2020. Hansa could then launch imlifidase in Europe before the end of the year, having devised a sequenced strategy focusing initially on leading transplant centres and clinicians to encourage early adoption, which we believe is a diligent approach. In the US, Hansa has agreed with the FDA the regulatory pathway for imlifidase. The Company will conduct a randomised, controlled trial of imlifidase in highly HLA sensitised patients and pending positive results file a BLA in 2023 under the Accelerated Approval pathway. We forecast peak sales of imlifidase in kidney transplantation in the US and Europe of approximately $400 million in 2032. However, we believe the commercial opportunities for imlifidase potentially reach beyond this initial indication and into a range of IgG-mediated autoimmune diseases which could ultimately result in imlifidase achieving peak sales significantly higher. A study in anti-glomerular basement membrane antibody disease (anti-GBM) is fully recruited with results slated for Q3 2020, while trials in acute antibody-mediated kidney transplant rejection (AMR) and Guillain-Barré syndrome (GBS) are also ongoing.

Imlifidase works by degrading IgG antibodies…
Imlifidase specifically degrades IgG antibodies in humans, while sparing the four other classes of antibody (IgA, IgD, IgE and IgM). It cleaves IgG irrespective of whether it is free or bound and without scrutinising how it is bound. The enzyme is also highly efficient, with one molecule of imlifidase estimated to cleave approximately 2,500 IgG molecules. It does this by sequentially cleaving both heavy chains of an IgG antibody, generating fragments that cannot perform the immunomodulatory functions of the intact antibody (see Figure 2). The specificity arises as a function of the requirement of imlifidase to bind to IgG before it can undertake the cleaving process. The process is rapid, with IgG degradation usually occurring within hours. However, imlifidase is immunogenic, restricting its use to where a single dose is sufficient.

Figure 2: Imlifidase binds to and then cleaves IgG into fragments



Source: Winstedt et al., (2015) PLOS One, 10 (7)

…and is protected by a broad patent portfolio

Imlifidase is protected by eleven separate patent families, which include both granted patents as well as pending patent applications (covering the major territories of the US, Europe and Japan). These families cover the use of imlifidase to create antibody fragments, the medical use of imlifidase in IgG-mediated medical conditions including prevention and treatment of transplant rejection and autoimmune diseases, dosing regimens in combination with other treatments such as transplantation as well as of new versions of the drug. The various imlifidase patent families expire between 2021 and 2035, with the possibility of up to five years of supplemental protection.

Imlifidase manufacturing process for commercial supply finalised

Imlifidase is manufactured in *E. coli*, growing a bacterial culture under fermentation conditions, then expressing and purifying the imlifidase protein (microbial fermentation – a relatively cheap process compared to the manufacture of other biological products). Manufacturing of the first GMP batch for clinical studies and commercialisation occurred in late 2017. The drug substance/drug product used for clinical trials was a frozen 10 mg/ml solution. However, optimisation of the manufacturing process means the commercial drug product will be lyophilised, which brings the advantages of easy off-the-shelf use and efficient global distribution. 2018 saw the completion of the full manufacturing process, characterisation and validation for commercial supply of imlifidase. CMOs are now responsible for imlifidase manufacturing and producing commercial supply.

NiceR is a project developing imlifidase-like drugs for repeat dosing

In its "NiceR" programme, Hansa is developing novel IgG cysteine endopeptidases that inactivate IgG with reduced immunogenicity to permit repeat use. Hansa has identified several possible IgG-linked autoimmune diseases characterised by recurring acute exacerbations where a chronically used drug would be of benefit. In March 2019, the Company selected a first drug candidate from the NiceR programme. Preclinical work on this candidate is ongoing, and we believe a first-in-human clinical trial could start in H2 2021.

Imlifidase – for the tough to transplant

With kidney failure, to survive you either need a new kidney or dialysis

Kidney failure, also known as end-stage renal disease (ESRD), is the last stage of chronic kidney disease (CKD). In essence, the kidneys have nearly completely lost function and survival is only possible with dialysis or a kidney transplant. Diabetes is the most common cause of ESRD, followed by high blood pressure. However, autoimmune diseases such as lupus, genetic diseases such as polycystic kidney disease, and urinary tract problems can all lead to ESRD. Today over 2 million people worldwide suffer from ESRD (of which over 750,000 people are in the US). This number is likely to grow rapidly over the next ten years fuelled by the rising prevalence of CKD in emerging markets such as China and India.

Kidney transplantation is preferred to dialysis as it provides better outcomes

Kidney transplantation is preferred to dialysis as it provides better overall outcomes, a better quality of life and longer life expectancy. It is also more cost-effective than dialysis. However, there is a significant shortage of kidneys available for transplant. According to the European Directorate for the Quality of Medicines and Healthcare, there were over 90,000 kidney transplants carried out globally in 2018, including >22,000 in the US and >21,000 in Europe. To put the need in context, there are ~94,000 patients in the US on the kidney transplant waiting list (US Department of Health and Human Services). The median wait time for a kidney transplant in the US is 3.6 years and can vary depending on a patient's health, blood group, HLA compatibility or where they live. Over 3,700 people in the US died in 2019, awaiting a kidney transplant.

Transplantation can be from living donors or deceased donors

Kidney transplants come from either: (1) deceased (or cadaveric) donors; or (2) from a living donor (either related or unrelated). Half of all deceased donor transplants are lost in 10 years, and half of all living donor transplants are lost in 20 years. The wait time for a living donor is significantly shorter than for a deceased donor. According to UNOS/OPTN data, over 23,000 kidney transplants took place in 2019 in the US – ~70% from deceased donors and ~30% from living donors. Due to the chronic shortage of transplantable kidneys, protocols are in place to ensure that when a kidney becomes available, utilisation occurs in patients with the best chance of long-term graft survival. With approximately 12% of the waiting list composed of patients who have previously lost a transplant, extending graft survival would decrease the demand for available organs. While there remains a chronic shortage of kidneys, we note that a large proportion of kidneys recovered for transplant are not transplanted, particularly kidneys from donors aged 50–64 years (30.7% not transplanted); donors aged 65 years and older (58.5%); and donors with diabetes (43.5%), hypertension (34.5%), or terminal creatinine above 1.5 mg/dl (33.6%).

HLA "sensitised" patients are more difficult to transplant

Patients that have antibodies against donor human leukocyte antigens (HLA; also known as donor-specific antibodies, DSAs) have historically poor outcomes following transplant and are known as "sensitised" patients. HLAs are cell surface glycoprotein components of the major histocompatibility complex (MHC) and are crucial for the human immune response. Sensitisation to HLAs occurs when a patient has produced anti-HLA antibodies in response to a previous immunogenic event, usually a prior transplant, blood transfusion, pregnancy or infection. The generation of anti-HLA antibodies usually is harmless but presents a potentially severe problem for people who require a kidney transplant. HLA sensitisation raises the risk of injury to the donor organ, AMR and in severe cases, graft failure.

The cPRA score measures HLA sensitisation

The calculated panel reactive antibody (cPRA) score measures a patient's breadth of sensitisation. This score estimates the percentage of the general population against whose HLA a potential transplant candidate would have a positive crossmatch produced by any pre-existing DSAs. The closer to 100% a candidate's cPRA reaches, the lower the probability of finding an acceptable donor. Table 5 illustrates the significant challenge for transplanting patients with cPRA of 99% and above. Patients with a cPRA of 99% would need approximately 300 "match runs" to have a 95% probability of finding an acceptable donor. This estimate increases exponentially and reaches approximately 300,000 match runs for patients with a cPRA of 100%. To put this statistic in context, the deceased donor pool in 2019 was ~22,200 kidneys, including discarded grafts. In reality, patient matches for cPRA of 100% do happen but are extremely improbable even after many years on the waiting list. We estimate there are approximately 2,200 patients with cPRA ≥99.9% active on the kidney transplant waiting list in the US (an exact cPRA of 99.9% would require ~3,000 match runs to find an acceptable donor). Further details on US kidney transplants and waiting list numbers by cPRA status are available in the Appendix (see page 33).

Table 5: Estimated number of match runs for a 95% probability of finding a donor based on cPRA

cPRA%	Theoretical number of match runs
80	14
85	19
90	29
95	59
99	300
99.5	600
99.9	3000
99.99	30,000
99.999	300,000

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

European countries have different systems that prioritise sensitised patients

There is no common framework for managing organ procurement, allocation and transplantation in Europe. Several European countries (including France, Germany, Italy, Spain and the UK) have systems which seek to increase transplant access for highly HLA sensitised candidates. For example, in the new UK system (introduced in 2019), kidneys from deceased donors are allocated by a computer algorithm based on two ranked tiers of recipients who are eligible to receive a particular donor's organs. Tier A comprises patients with a matchability score of 10 (takes into account blood type, HLA type and unacceptable antigens, 1 = easy to match and 10 = most difficult), patients with cPRA 100% or patients that have accrued seven years of waiting time. Tier B includes all other eligible patients prioritised on a points-based system that considers: waiting time; donor-recipient risk index combinations; HLA match and age combined; location of the patient to the donor; matchability; donor-recipient age difference; total HLA mismatch; and blood group match. On the other hand, the Eurotransplant kidney allocation system (ETKAS), which governs the allocation of donor organs in Germany (and also Austria, Belgium, Croatia, Hungary, the Netherlands, Luxembourg and Slovenia) achieves prioritisation of highly sensitised patients by a different method. In essence, its allocation algorithms first offer deceased donor kidneys to recipients in the "Acceptable Mismatch Program", which increases the chance of highly sensitised kidney transplant candidates receiving a crossmatch

negative offer. To be eligible for the Acceptable Mismatch Program, patients must have been on dialysis for a minimum of two years and have cPRA ≥85%. We believe many European patients who are HLA sensitised have a good chance of receiving a kidney transplant. However, we have seen no evidence to suggest that any of the systems in European countries can help the most severely sensitised patients (we define as cPRA >99.9%). See the Appendix (page 33) for further statistics on European transplants.

In the US, 2014 saw the introduction of a new kidney allocation system…

In December 2014, a new kidney allocation system (KAS) started for deceased donor transplantation in the US. The development of the new KAS was in response to higher than necessary discard rates of kidneys, variability in access to transplants for candidates who are harder to match for biological reasons, inequities resulting from the calculation methodology for waiting times, a matching system that resulted in unrealised life years (i.e. elderly patients dying with functioning kidneys) and high re-transplant rates. The United Network for Organ Sharing (UNOS) operates KAS, which continues to allocate kidneys at a local, regional and national level (there are 11 regions and 58 local donor service areas in total). UNOS uses a national matching computer system that generates optimum recipient lists based on the characteristics of each donated kidney.

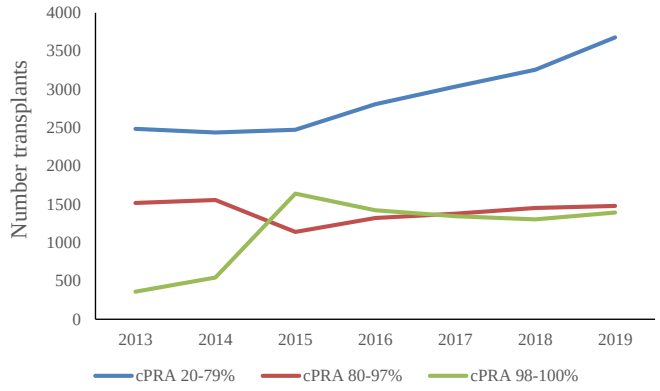
…that uses longevity matching and prioritises HLA sensitised patients

It is the criteria for matching donors and recipients that have changed under KAS compared to the old system. Longevity matching, which is making sure kidneys with the longest expected life go to the patients with the longest expected life, is a crucial element of KAS not incorporated in the old scheme. Longevity matching is achieved by two scoring systems – for donor kidneys the Kidney Donor Profile Index (KDPI) and for recipients the Expected Post-Transplant Survival (EPTS). Their KDPI scores stratify kidneys into four brackets (≤20%; 21–34%; 35–85%; >85%) and match based on their EPTS score. For example, a kidney with a KPDI ≤20% would be preferentially matched to a patient with an EPTS in the top 20th percentile. Within each KDPI class, KAS allocates kidneys in four steps. In contrast to the old system (which put little emphasis on HLA sensitisation), patients in each KDPI bracket with a cPRA of 98%, 99% or 100% (extreme levels of HLA sensitisation) are the first to be considered for transplantation (based on the fact that they are very challenging to match with donor organs) and receive local, regional and national priority respectively. Patients with zero HLA mismatch get the next preference, followed by prior living donors, and then paediatric recipients. If a donor organ with a KDPI ≤20% is still unused after running down the list, it is then offered to candidates with EPTS scores in the bottom 80%. KAS now incorporates a sliding scale for cPRA as opposed to the old system under which only four additional points were awarded for cPRA ≥80%. For example, an extra four points were given to a cPRA score of 100% under the old KAS while under the new system 202.1 points are awarded. The more points accrued by patients on the waiting list, the higher their priority for receiving the next compatible kidney offer. See the Appendix (page 33) for more information on the points system, EPTS, KDPI and other elements of KAS.

KAS has boosted the number of transplants for patients with cPRA 98–100%…

Transplant statistics suggest that KAS is achieving many of its goals, including improving access to transplants for patients with cPRA 98–100%. Transplants in this group rose steeply from 544 in 2014 (~3% of all transplants in HLA sensitised patients) to 1,640 in 2015 (~9% of all HLA sensitised transplants after KAS' introduction) but stabilising subsequently (1,393 in 2019) suggesting a bolus effect (see Figure 3). Conversely, KAS led to an initial decrease in transplant numbers for cPRA 80–97% patients, suggesting that they had disproportionate access to transplants pre-KAS and now transplant numbers have stabilised at a level more proportional to their representation on the waiting list.

Figure 3: KAS has boosted the number of transplants for HLA sensitised patients

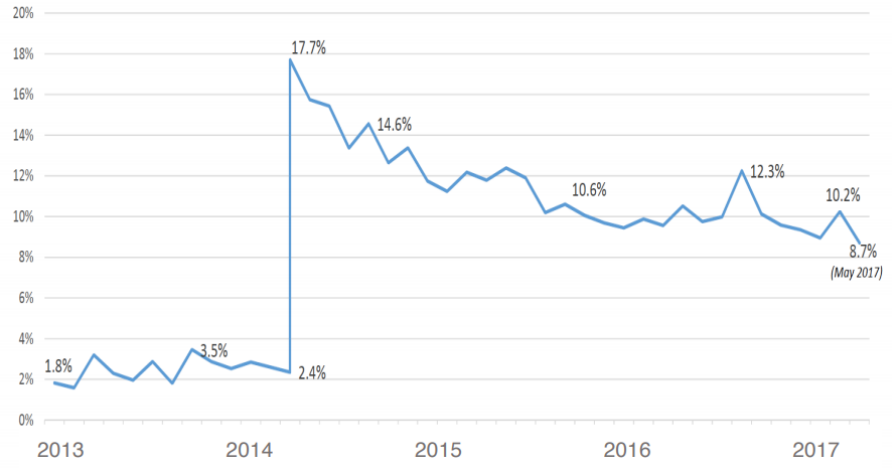


Source: OPTN/UNOS

…though we believe a high unmet need persists for the most severely sensitised

While KAS has improved the transplantation rate in patients with cPRA 98–100% overall, we believe transplantation is still mostly inaccessible to patients at the very top end of this range. The proportion of patients with cPRA >99% who received transplants initially increased dramatically with the introduction of KAS (17.7% in January 2015). However, it has fallen since (8.7% in May 2017, see Figure 4) as the bolus of more easily HLA-matched patients at the bottom end of the range (~600 runs for a match at cPRA 99% vs 3,000 at 99.9% and 300,000 at 99.999%, see Table 5) were quickly transplanted. Indeed, a more granular analysis of the cPRA 99–100% range conducted by Stewart *et al.* (American Journal of Transplantation, 2016, 16 (6): p1834–1847) revealed that not all highly sensitised patients have benefitted to the same degree. Shortly before KAS, patients with cPRA ≥99.95% accounted for 34% of the approximate 8,000 cPRA 99–100% patients on the waiting list in the US. However, in the year following KAS, only 8% of transplants for patients with cPRA 99–100% were performed in cPRA ≥99.95% patients, reflecting the persisting challenge of finding graft matches for these patients. In an analysis of transplant data between June 2016–June 2017, Schinstock *et al.* (2019, Clinical Transplantation, Dec; 33 (12): e13751), found that only 9.7% of candidates with a cPRA >99.9% received a transplant, considerably lower than the overall transplantation rate of 18.9%. As of June 2018, 1,791 actively waitlisted candidates had a cPRA of ≥99.9%, and 34.6% of these had over five years waiting time. Based on these data, we believe the significant number of patients in the US with cPRA ≥99.9% are unlikely to benefit from KAS and have only a very remote chance of transplantation without desensitisation.

Figure 4: Percentage of cPRA >99% patients receiving transplants

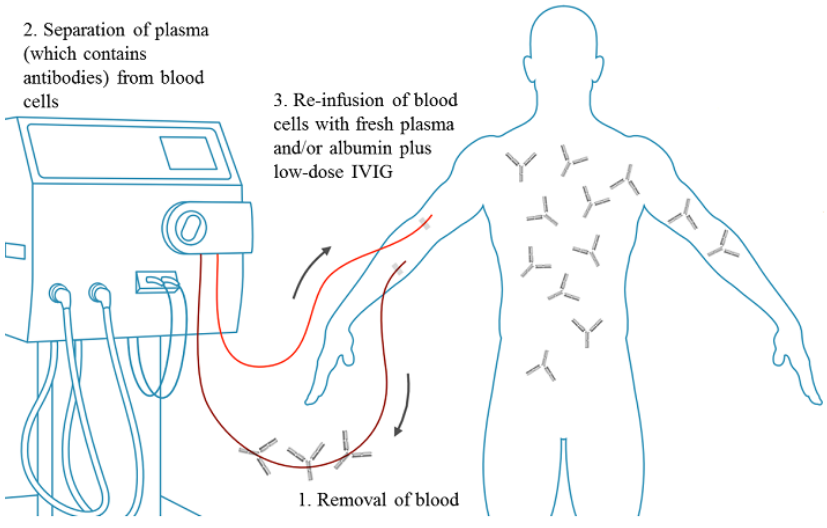


Source: OPTN/UNOS

Current desensitisation treatment involves the use of plasma exchange

With no specifically approved drug therapies for HLA desensitisation, the most common protocols currently employ plasma exchange (PLEX, see Figure 5) and high dose intravenous immunoglobulin (IVIG) therapy. The use of PLEX generally commences a week before transplantation, so it is not appropriate as a desensitisation protocol pre-transplantation utilising a kidney from a deceased donor (too long an ischaemic time). Another disadvantage of the approach is that as well as depleting IgG, PLEX also depletes coagulation factors (not ideal following an invasive surgery) and complement factors. Other approaches to HLA desensitisation include immunoadsorption (does not deplete coagulation factors) and the off-label use of drug immunotherapies such as rituximab (Rituxan®, an anti-CD20 MAb marketed by Roche), bortezomib (Velcade®, a proteasome inhibitor marketed by Takeda/Johnson & Johnson) and eculizumab (Soliris®, an anti-complement component 5 MAb marketed by Alexion Pharmaceuticals).

Figure 5: HLA desensitisation by plasma exchange



Source: Hansa Biopharma AB

PLEX has a high patient burden, is slow, inefficient and associated with high AMR
Protocols employing PLEX with low-dose IVIG were first described by a team at Johns Hopkins University and have been adapted by several other academic groups. These protocols employ multiple rounds of PLEX (one round reduces antibodies by approximately 60%, but they exhibit rapid rebound) and adjuvant low-dose IVIG over weeks to months, which necessitates meticulous planning and timing of transplants. The process has a high patient burden, is slow and expensive. PLEX/low-dose IVIG can also leave significant residual levels of IgG and is often associated with a rapid rebound of anti-HLA antibodies, which limits its use to living donor kidney transplants. Also, the approach is relatively ineffective at preventing a subsequent immune response, with clinical trials of various adaptations of the original protocol reporting acute rejection rates of 24–100% and AMR rates of 12–100% (although graft survival rates after 1–2 years are generally high after subsequent treatment).

IVIG/rituximab for deceased donor transplants, but is also slow with AMR
Professor Stanley Jordan of Cedars-Sinai Medical Center (Los Angeles, US) has developed a desensitisation protocol that permits transplantation of highly sensitised patients using kidneys from *deceased* donors. This procedure is challenging using protocols based on PLEX. The protocol uses alternating high-dose monthly IVIG with rituximab administered between to lower the levels of anti-HLA antibodies and to prevent rebound of antibodies after HLA incompatible transplantation. The patients are kept in the programme for many months waiting for an organ offer from a deceased donor. However, the protocol is still slow (one complete cycle takes one month) and leaves much room for improvement of subsequent acute rejection (8–50% reported) and AMR rates (8–41% reported).

Highly HLA sensitised patients poorly served by current desensitisation methods
There is a significant unmet medical need for new methods of desensitising patients awaiting a kidney transplant who are highly sensitised to HLA (>80% cPRA). While current approaches such as PLEX/IVIG and IVIG/rituximab can be effective in desensitising patients who are mild to moderately HLA sensitised, it is rare to transplant patients with high HLA sensitivity with these protocols.

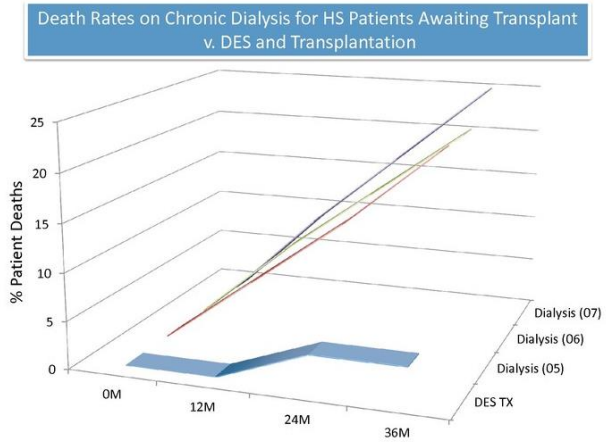
A major study demonstrated the survival benefit of HLA desensitisation…
A major study published in the New England Journal of Medicine (NEJM) by Orandi *et al.* (2016) demonstrated a survival benefit in kidney transplants from HLA-incompatible living donors who underwent current methods of HLA desensitisation. The study estimated the survival benefit for 1,025 kidney transplant recipients from HLA-incompatible living donors versus matched control patients who remained on the waiting list (waiting list only group), or who remained on the waiting list or received a transplant from a deceased donor (waiting list-or-transplant control group). The study showed that patients who received HLA-incompatible kidney transplantation had statistically significantly higher survival rates than transplant control or waiting list groups at one, three, five and eight years post-transplant (see Table 6). We note separate research published by Vo *et al.* (Transplantation, 2013, 95 (6): 852-858) has demonstrated the benefit of HLA desensitisation plus transplantation versus remaining on dialysis (see Figure 6). However, a study conducted in the UK determined that survival was comparable between HLA-incompatible living donor kidney transplanted patients and those remaining on dialysis (Manook *et al.*, 2017. Lancet, 389 (10070) 727–734).

Table 6: Survival rates of HLA-incompatible kidney transplant patients versus controls

	One year	Three years	Five years	Eight years
HLA-incompatible LD transplant	95.0%	91.7%	86.0%	76.5%
Waiting list / DD transplant control	94.0%	83.6%	74.4%	62.9%
Waiting list only control	89.6%	72.7%	59.2%	43.9%

Source: New England Journal of Medicine (2016), 374: 940-950

Figure 6: Transplant patients have an improved survival versus those on dialysis



Source: Vo *et al.*, (2013) Transplantation, 95 (6): 852-858

…and cost proves highly favourable compared to dialysis

There is also a significant economic argument for performing HLA-incompatible transplants over long-term dialysis. The accrued costs of IVIG desensitisation, kidney transplant and five years of immunosuppression in the US are estimated to be around $206,000 vs over $420,000 for five years of dialysis. Cost data are available in certain European markets, and these show that transplantation is also favourable from a cost perspective to five years of transplantation – in France ~$195,000 vs ~$490,000; in Italy ~$105,000 vs ~$190,000; in Spain ~$73,000 vs ~$210,000; in the UK ~$90,000 vs ~$230,000; and in Sweden ~$85,000 vs ~$420,000.

Imlifidase offers the potential of faster and more effective desensitisation…

The functional significance of a faster acting desensitisation treatment is the potential for reduced planning required for a kidney transplant, which greatly facilitates the ability to perform *deceased*-donor transplants. Also, current desensitisation protocols have limited efficacy for highly sensitised patients. There remains a high unmet medical need in this group for novel desensitising strategies. Hansa's imlifidase specifically degrades IgG in a rapid and highly efficient manner, offering the potential of a faster, more effective desensitisation than existing processes/products.

…and has generated strong results from multiple clinical studies

Hansa has conducted one Phase I and four Phase II trials of imlifidase in HLA sensitised kidney transplantation, all with positive outcomes. See Table 7 for a summary of the clinical trials of imlifidase completed to date and their key results. The Phase I trial demonstrated that imlifidase has a relatively benign safety profile (no serious adverse events) with rapid and near-complete degradation of IgG (see Figure 7). Phase II trials have also shown favourable drug safety and demonstrated that imlifidase could remove DSAs and enable kidney transplantation in highly HLA sensitised patients, many of who would have been unlikely to receive a transplant

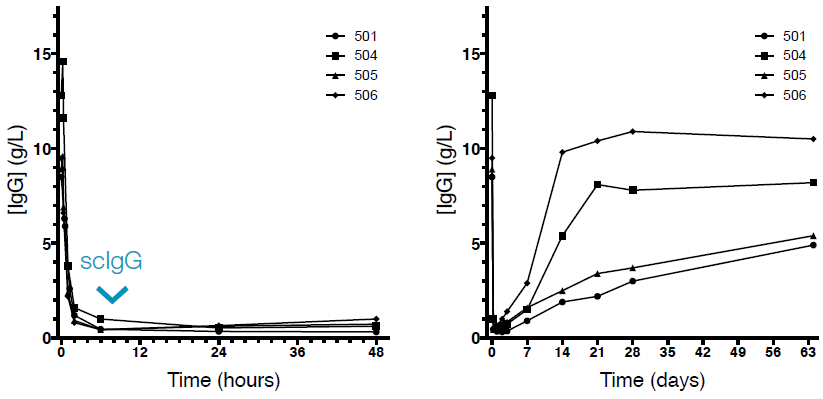
otherwise. To date, a total of 46 HLA sensitised patients (most highly HLA sensitised) have received kidney transplants following imlifidase desensitisation. Results from a Phase II investigator-initiated trial led by Stanley Jordan at Cedars-Sinai Medical Center (Los Angeles, US) and a Phase II trial in Sweden (NCT02475551) have been published in The New England Journal of Medicine (2017, 377: 422–53) and results from some patients from the Phase II "Highdes" trial have been published in Annals of Surgery (2018, 268 (3):488-496).

Table 7: Summary of imlifidase clinical trials

Trial	Design	Regimen	Key results
Phase I (NCT01802697)	Single centre; randomised; double blind; placebo controlled; 29 healthy volunteers	Single IV imlifidase doses of 0.01, 0.04, 0.12 or 0.24mg/kg, or placebo	Rapid, near complete removal of IgG in all subjects receiving 0.12 and 0.24mg/kg doses, favourable safety/tolerability profile*
Phase II – Sweden (NCT02224820)	Single centre; open-label; 8 patients with ESRD on the transplant waitlist; median cPRA 93%	IV imlifidase 0.12 or 0.25mg/kg given once or twice (second dose within 48 hours)	HLA levels acceptable for transplantation in all patients, one patient successfully received a subsequent transplant post imlifidase treatment with stable graft reported at >36 months follow-up**
Phase II – Sweden (NCT02475551)	Single centre; open-label; 10 patients with ESRD on the transplant waitlist; median cPRA 81%	IV imlifidase 0.25mg/kg + transplant, horse ATG induction immunosuppression	Imlifidase enabled transplantation in all ten patients, graft survival at six months 100%***
Phase II – US, investigator-initiated (NCT02426684)	Single centre; open-label; 17 patients with ESRD on the transplant waitlist; median cPRA 96% for 14 patients in NEJM publication	IVIG + rituximab pre-transplant, IV imlifidase 0.24mg/kg + transplant, alemtuzumab induction immunosuppression, IVIG + rituximab post-transplant	Imlifidase enabled transplantation in all 17 patients, graft survival at six months was 94% with one loss due to non-HLA-antibody mediated hyperacute rejection.*** At three years two further graft losses have occurred and one death, with mean eGFR 60.8 ml/min/1.73m^2 at one year and 47.5ml/min/1.73 m^2 at three years. AMR occurred in 41% of patients and cell-mediated rejection in 47%
Phase II – "Highdes" (NCT02790437)	Multi-centre; open-label; 18 patients with ESRD on transplant waiting lists; median cPRA 99.6%	IV imlifidase 0.25mg/kg + transplant, alemtuzumab induction immunosuppression, IVIG + rituximab post-transplant	Met primary objective of imlifidase treatment, turning positive crossmatch test to negative to enable transplantation in all 18 patients. At six months, graft survival was 89% (two graft losses due to primary non-function), patient survival 100%, and median eGFR was 50 ml/min/1.73m^2. 25% of patients experienced AMR

Source: Rx Securities; *results published in *PLOS ONE* (2015) https://doi.org/10.1371/journal.pone.0132011; **published in American Journal of Transplantation (2018), 18: 2752–2762; ***results published in the New England Journal of Medicine (2017), 377: 442-53

Figure 7: Phase I data showing rapid IgG depletion by imlifidase with IgG rebound from ~day 7

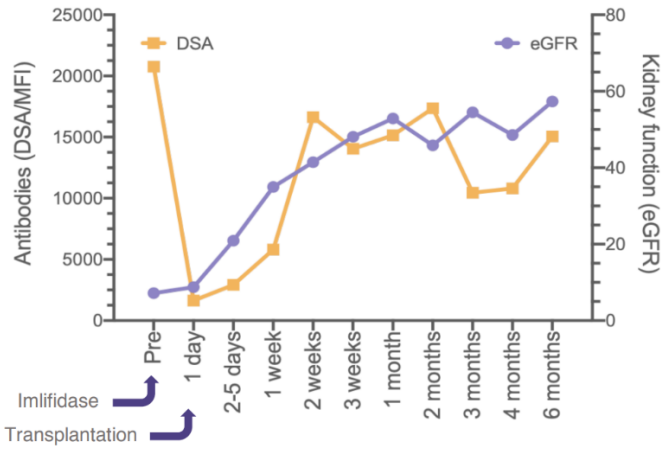


Source: PLOS ONE (2015) https://doi.org/10.1371/journal.pone.0132011; data shown from four subjects who received 0.24mg/kg dose

Pooled six-month results from 46 transplantees were presented at ESOT 2019

In September 2019, pooled six-month results for all 46 imlifidase-enabled transplants across Phase II clinical trials were presented at the European Society for Organ Transplantation (ESOT) annual conference. The key demographics of the population overall were: median age 43 years; 54% male; 70% re-transplants; 93% DSA-positive; 85% crossmatch-positive pre-imlifidase treatment; mean cPRA 99% (50% had 100% cPRA). Following imlifidase treatment utilising the different regimens listed in Table 7, 39 patients received a deceased donor transplant, and seven received a graft from a living donor. Imlifidase treatment led to a rapid decrease in DSA levels and conversion of positive crossmatches to negative in all patients (see Figure 8), enabling transplantation of all 46 patients. The majority of patients who were DSA positive before imlifidase had DSA rebound to levels at or below the pre-dose level. AMR episodes occurred in 33% of patients, within the historical expected range reported with transplantation of highly HLA-sensitised patients (indeed, rates of 20–60% after PLEX desensitisation). All episodes of AMR resolved with standard of care treatments. Patients' estimated mean glomerular filtration rate (eGFR), a marker of kidney function, was stable at around 60 ml/min/1.73m^2 (see Figure 8), which is comparable with historical reports of eGFR post-kidney transplantation in adults. After the studies, all patients were alive, and graft survival was 94% (43/46).

Figure 8: Imlifidase removes DSAs enabling kidney transplants with good six-month graft function



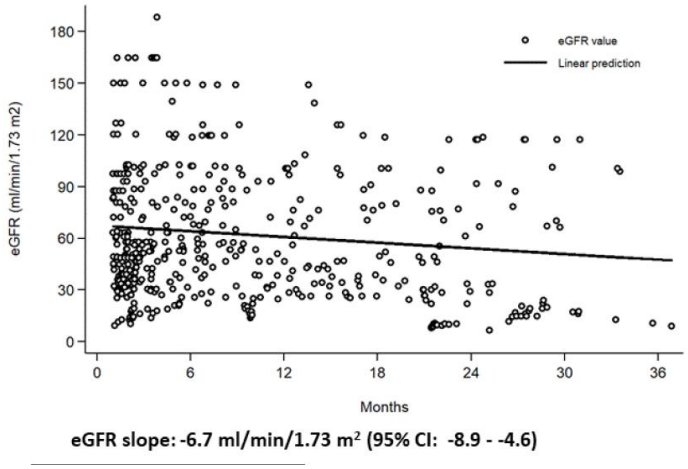
Source: Hansa Biopharma

Longer-term follow up data reported so far have been encouraging

The US investigator-initiated trial reported three-year patient outcomes at ATC 2019. From the 16 patients (one not included in the analysis due to hyperacute rejection causing graft loss), DSA rebound following imlifidase treatment and transplantation was generally mild out to 30 months. There were seven episodes of AMR and eight episodes of cell-mediated rejection. There were two graft losses unrelated to imlifidase, at 2.6 and 3.2 years post-transplantation. One death occurred ten months post-transplant. Mean eGFR was 60.8 ml/min/1.73m^2 at one year, falling to 47.5 ml/min/1.73m^2 at three years (see Figure 9). We believe these longer-term data are encouraging as, critically, graft survival and mean eGFR at three years post-transplant are in line with historical rates for deceased donor transplantation of non-sensitised patients. In addition to these three-year outcomes reported from the US investigator-initiated trial, pooled results out to two years from all patients from the imlifidase Phase II studies who were crossmatch positive at study entry were presented at the Cutting Edge of Transplantation summit in March 2020. This group comprised 39 of the 46

imlifidase-treated transplant patients (32 of the 39 received a deceased donor graft). Three graft losses occurred within a year, leaving 36 patients with a functioning graft at six months. Two-year death-censored survival was 24/27 patients (89%), and two-year overall graft survival was 24/30 patients (80%). There were three deaths, all in the crossmatch positive population and occurring in the period seven to 12 months after transplantation, resulting in a 1-year survival rate of 29 (91%) of the 32 patients with available data. Deaths were deemed unrelated to imlifidase or kidney function. Kidney function assessments showed that 28 (87%) of the 32 patients with data, and 23 (88%) of the 26 crossmatch positive patients with data, had a functioning kidney at six months. AMR was documented in 15 of the 39 crossmatch positive patients during the first six months after transplantation, and one additional case of AMR occurred between six months and one year after transplantation. No additional AMR was identified in any patient in the period one to two years after transplantation.

Figure 9: Kidney function at three years post-imlifidase-enabled transplantation



Source: Huang *et al*., presented at ATC 2019 (19-A-1966-ATC)

Long-term follow-up study following all transplanted patients, more data to come

Hansa is conducting a long-term follow-up study encompassing all of the patients who received a kidney transplant following desensitisation with imlifidase. This study's (NCT03611621) primary outcome is graft survival over five years, and secondary outcomes are overall survival, kidney function (eGFR, creatinine levels and proteinuria) and to record comorbidities and quality-of-life-related outcomes. We expect data generated from this study will help build a strong healthcare economic argument for imlifidase desensitisation in discussions with payers and prescribers.

Imlifidase's potential validated by awards of PRIME and Fast Track in our view

The FDA and EMA have granted imlifidase key regulatory designations, and we believe these provide critical validation of the drug's potential for enabling kidney transplantation in severely HLA sensitised patients. The EMA granted imlifidase access to its Priority Medicines (PRIME) scheme in May 2017, and the FDA awarded the drug Fast Track designation in October 2018. Both of these designations facilitate enhanced interactions with regulators, which we believe should raise the likelihood of approvals. They also provide opportunities for accelerated regulatory reviews following the filing of marketing applications. Imlifidase has also been granted ODD by the FDA and EMA for the prevention of AMR in solid organ transplant patients.

Hansa has filed for approval in Europe with a CHMP opinion due in Q2 2020

In March 2019, the European Medicines Agency (EMA) accepted for review a Marketing Authorisation Application (MAA) for imlifidase as a treatment to enable kidney transplantation in highly sensitised patients. Hansa responded to Day 180 questions from the EMA's Committee for Medicinal Products for Human Use (CHMP) in late March 2020. We anticipate an opinion from the CHMP on the MAA following either of the Committee's meetings in May (25–28) or June (22–25). If positive, we would expect formal conditional approval by the European Commission approximately two months later, with full approval subject to a post-authorisation study running in parallel with the drug's initial commercial launch.

In the US, the FDA requested additional information in light of KAS...

In January 2019, Hansa announced that the FDA had requested additional information regarding imlifidase treatment in the context of KAS (see Appendix, page 33) which has led to an increase in the transplantation rate in the cPRA 98–100% bracket since its introduction in December 2014. However, having analysed the transplant trend data since KAS, we conclude that access to transplantation for severely sensitised patients (cPRA ≥99.9%) remains poor and that imlifidase could potentially address this.

…leading to matched control analyses showing benefit with imlifidase

Following initial discussions with the FDA, Hansa conducted analyses comparing imlifidase-treated patients to similarly sensitised "matched control" patients. The results were presented at the ATC 2019 by Dr Edmund Huang of Cedars-Sinai Medical Center, and have been discussed with the FDA. While the presentation is not publically available, Dr Huang summarised that there was a statistically significant reduction in time on the waitlist for transplantation among imlifidase-treated patients compared to similarly sensitised matched controls. The analysis also demonstrated a significantly shorter time to transplant under both the new and previous KAS. The presentation won ATC's People's Choice Award for the most impactful presentation. As shorter time on the waitlist translates to improved outcomes for patients, we believe this finding represents further evidence of imlifidase's value to highly sensitised patients.

Hansa is now planning a further clinical trial targeting a BLA filing in 2023

In December 2019, Hansa announced that it had agreed with the FDA a regulatory path forward for imlifidase in kidney transplantation, which requires the Company to conduct a further clinical trial. Hansa is currently planning a randomised, controlled clinical trial of imlifidase in approximately 50 very highly sensitised (cPRA ≥99.9%) kidney transplant candidates. In the treatment group, patients will be treated with imlifidase and receive an HLA-mismatched deceased donor kidney transplant. In the control group, patients remain on the waitlist and will only be transplanted if an HLA compatible graft becomes available (highly unlikely in the cPRA ≥99.9% population in our view). The primary endpoint, as requested by the FDA, is to be a surrogate marker of kidney function, the eGFR at six and 12 months. We understand that patients will be assigned a score depending on their eGFR, with patients in the non-transplant group remaining on dialysis assigned a score of zero (if imlifidase treated and transplanted patients later experience graft loss, this would also result in a score of zero). We anticipate a positive outcome on this surrogate marker would lead to Hansa filing a BLA under the accelerated approval pathway in 2023. There will be a longer-term follow-up of patients in this new trial of graft and patient survival, with the data generated potentially supporting full approval in the future. We anticipate Hansa submitting the protocol for the trial to the FDA during Q2 and its initiation in Q4 2020, though acknowledge the ongoing COVID-19 pandemic could delay this timeline.

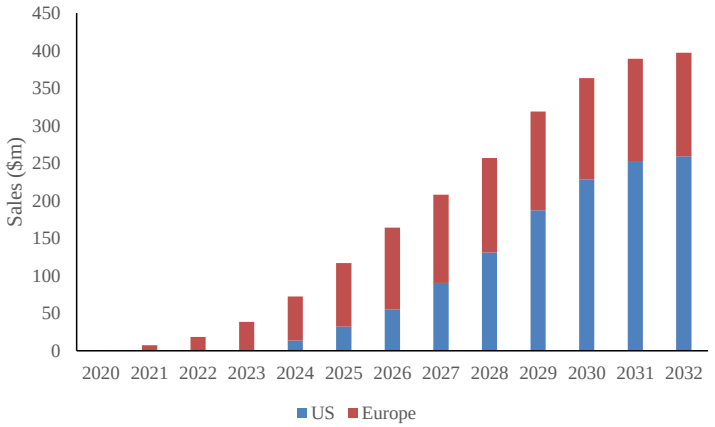
Hansa aims to self-market imlifidase in Europe and the US capturing its full value

Hansa's stated strategy is to self-commercialise imlifidase in Europe and the US (while looking to partner in other regions), an approach which we endorse as it will enable the Company to capture the full value of the drug. In most countries, kidney transplants occur in a relatively small number of specialised centres. Hansa's European launch strategy is to initially focus on the leading transplantation centres and clinicians in the field in a sequenced manner, to ensure that they gain knowledge around desensitisation with imlifidase and become early adopters having had a positive experience. For example, in the UK there are 20 kidney transplant centres (vs 1,257 hospitals overall) but some transplant much higher numbers of patients than others (and we expect Hansa would initially target one or more of these). The Company aims to harness the post-approval efficacy study of imlifidase to further physician education with the drug and increase adoption. We believe Hansa can effectively market and sell imlifidase with a relatively compact sales team. Management has guided towards double-digit sales personnel numbers in key geographies (we assume approximately 10–15 in Europe and 20 in the US, where there are 260 kidney transplant centres). In the US, we understand Hansa will initially target the top 50 kidney transplant centres.

We project imlifidase launches in 2020 and forecast peak sales of $400 million

Our product model for imlifidase conservatively assumes use to facilitate deceased donor kidney transplantation in the most severely HLA sensitised patients. Transplantation statistics and simulations show that patients with cPRA of 99.9% to 100% (we estimate ~2,200 patients in the US and ~1,900 in Europe with "active" waitlist status) are highly unlikely to find an acceptable donor match. Hence, their chance of transplantation is remote without desensitisation to facilitate an HLA mismatched transplant. Our model assumes substantial penetration rates in this population and prices in line with those of other orphan drugs capable of transforming patient outcomes – at launch an average of $250,000 in European countries and $375,000 in the US. We note that Hansa has also discussed the possibility of exploring value-based payment models, which are becoming a common method of supporting orphan drug pricing. We project first launches of imlifidase in Europe in H2 2020, though we caveat that the ongoing COVID-19 pandemic could result in a delay to this timeline. We anticipate US launch of imlifidase in 2024. We forecast peak sales of ~$400 million in 2032 for imlifidase in kidney transplantation (see Figure 10).

Figure 10: Imlifidase sales forecast for use in desensitisation for kidney transplantation



Source: R_X Securities estimates

Imlifidase – potential beyond transplantation

Potent IgG inactivation opens doors to other indications for imlifidase

Clinical trials of imlifidase to date have shown it to be a potent and rapid inactivator of IgG antibodies. In addition to its lead indication of HLA desensitisation for kidney transplantation, we believe it could prove an effective treatment in numerous acute care indications related to obstructive/pathogenic IgG (see Figure 11). Indeed, an investigator-initiated Phase II trial in anti-glomerular basement membrane disease (anti-GBM) is fully recruited with results slated for Q3 2020, while Phase II trials in acute AMR associated with kidney transplantation and in Guillain-Barré syndrome (GBS) are ongoing. PLEX or other slow-acting immunodepletion strategies are the main options for all of these diseases/syndromes, and there remains an opportunity for a more rapid and effective method of IgG depletion, such as imlifidase.

Figure 11: Imlifidase has broad application in several IgG-related disorders

Transplantation	Neurology	Hematology	Nephrology	Other
› Sensitized kidney transplantation patients	› Guillain-Barré syndrome	› Thrombotic thrombocytopenic purpura (TTP)	› Anti-GBM disease	› Flares in Systemic Lupus Erthematosus (Rheumatology)
› Highly sensitized kidney transplantation patients	› Anti-NMDA receptor encephalitis	› Catastrophic Anti-Phospholipid Syndrome (CAPS)	› ANCA associated vasculitis	› Flares in Pemphigus (Dermatology)
› Kidney transplant AMR	› Myastenic crisis	› Life threatening ITP	› Lupus nephritis	› Life threatening Anti Drug Antibodies (ADA)
› Sensitized heart transplant patients	› Relapsing Neuromyelitis optica	› Hemolytic disease of newborn		
› Heart transplant AMR	› Steroid refractory multiple sclerosis relapse	› Neonatal alloimmune thrombocytopenia		
› ABOi kidney transplantation	› Acute CIDP	› Refractory autoimmune hemolytic anemia		
	› Lambert-Eaton myastenic syndrome			

Source: Hansa Biopharma AB

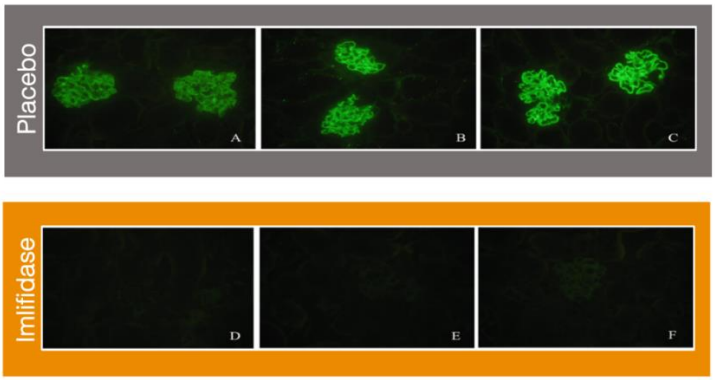
Anti-GBM is a rare disease where IgG attacks the kidneys and lungs

Anti-GBM, also known as Goodpasture's syndrome, is a rare autoimmune disease where IgG antibodies attack the basement membranes of the kidneys and lungs causing loss of renal function, high blood pressure and pulmonary haemorrhage. It affects approximately 1.6 in a million people globally annually, causing loss of kidney function in around two-thirds of patients and is fatal in some. The inciting events that lead to anti-GBM are unclear, but smoking, hair dye use, exposure to hydrocarbon fumes, metallic dust, and certain drugs, have been associated with increased risk. Genetics may also play a part, with reports of a small number of cases in more than one family member. There are no drug therapies specifically approved to treat anti-GBM. The current treatment options are PLEX, steroids and cyclophosphamide. Early intervention is critical for the best chance of kidney and patient survival.

Imlifidase has generated positive preclinical data in anti-GBM…

A publication in Nephrology Dialysis Transplantation (Yang *et al*., 2010, 25 (8): 2479–2486) highlights positive preclinical results demonstrating the efficacy of imlifidase and a related endopeptidase in a mouse model of anti-GBM. Mice injected with anti-GBM antibodies developed severe albuminuria (a marker for kidney disease), though the administration of imlifidase could entirely prevent this. Immunofluorescence studies showed that imlifidase treatment effectively removed the anti-GBM antibodies (see Figure 12). There was also a significant reduction of the deposition of the complement components C3 and C1q (protein complexes that promote inflammation) and this diminished the recruitment of leukocytes (immune cells) to glomeruli of the kidneys.

Figure 12: Imlifidase degraded anti-GBM antibodies (fluorescent green) in a mouse model



Source: Yang *et al*., 2010. Nephrology Diagnosis Transplantation, 25 (8): 2479–2486.

…and a Phase II trial is now fully recruited with results due in Q3 2020

Hansa is collaborating with Professor Mårten Segelmark at Linköping University and Lund University Hospitals (Sweden) to investigate imlifidase for the treatment of anti-GBM. Professor Segelmark is leading an open-label Phase II trial (initiated in March 2017) to test whether a single dose of imlifidase 0.25mg/kg can improve outcomes for patients with severe anti-GBM (patients with eGFR <15ml/min/1.73m^2 or if the patient is non-responsive to standard treatment, and has lost >15 ml/min/1.73 m^2 after the start of treatment) when added to current treatments (steroids, immunosuppressants and PLEX). The primary objectives are to evaluate the safety and tolerability of imlifidase and the proportion of patients who do not need dialysis six months post-treatment. In January 2020, recruitment into the trial finalised with 15 patients across centres in five European countries. We anticipate first results in Q3 2020 from the trial. We believe the bar for success depends on the severity of disease in the patients recruited. We note in those in renal failure requiring dialysis at presentation, the one-year kidney survival rate is 8% and patient survival rate is 65%.

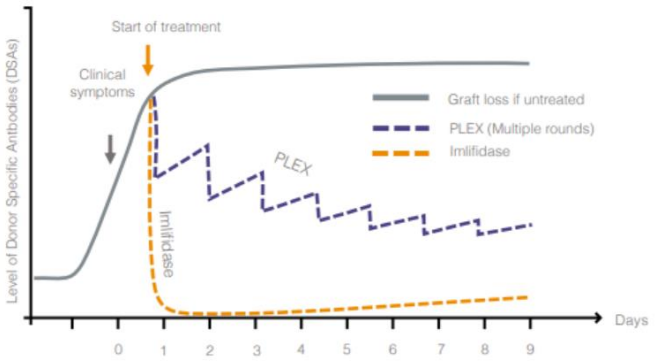
We estimate an ~$250 million annual market opportunity in anti-GBM

There are no drugs specifically approved to treat anti-GBM, and the current treatment approaches centred on PLEX are slow to remove the offending antibodies leaving much room for improvement in efficacy in our view. As imlifidase rapidly and near-completely degrades IgG antibodies, we believe it could be an effective treatment for people with severe anti-GBM. We estimate the addressable population for imlifidase in anti-GBM is ~900 patients per year in the US, Europe and Japan and accordingly calculate a market opportunity of ~$250 million per annum. Hansa has received ODDs from the FDA and EMA for imlifidase for the treatment of anti-GBM.

Imlifidase could address the problem of acute AMR with kidney transplantation

The definition of acute AMR is the rejection of a solid organ graft caused by antibodies directed against HLA, blood group antigens or endothelial cell antigens. AMR injures graft organs, mainly via activation of the complement system. Acute AMR is characterised by graft dysfunction manifesting over days and is a result of DSAs that may either be pre-formed or develop *de novo* after transplantation. It occurs in 10–15% of solid organ transplant recipients and remains a significant issue associated with loss of graft function. There are no approved drugs for acute AMR, the mainstay of treatment is currently PLEX, steroids and IVIG, all of which have limited efficacy. PLEX is not efficient enough to cope with the high antibody titres in severe acute AMR (see Figure 13), and while IVIG is more effective, symptom improvement takes on average 2–5 days.

Figure 13: Imlifidase could improve treatment of AMR vs PLEX



Source: Hansa Biopharma AB

Phase II kidney transplant acute AMR trial recruitment slated to close in H1 2021

Hansa initiated a randomised, open-label, multi-centre, Phase II trial of imlifidase for the treatment of acute AMR associated with kidney transplantation in 2019. This trial aims to recruit up to 30 patients with active AMR (four treated to date) at eight centres in the US, EU and Australia. Patients are randomised 2:1 to receive a single dose of imlifidase 0.25mg/kg or 5–10 sessions of PLEX. The primary endpoint is maximum DSA reduction within five days from the start of treatment and secondary outcomes look at efficacy measures six-months post-treatment (DSA levels, eGFR levels, serum creatinine/albumin levels and graft loss). We anticipate finalisation of recruitment into the trial in H1 2021 and results in H1 2022.

Kidney transplant acute AMR could be a $500 million market in our view

Hansa has already demonstrated the efficacy of imlifidase in eliminating DSAs and enabling kidney transplantation. We therefore believe it is reasonable to assume the drug is likely also to be an effective treatment for rapidly degrading antibodies responsible for AMR. While current treatments are often successful, they are slow to act and are often not efficient enough to treat severe AMR, meaning there is a high unmet need for a drug such as imlifidase in our view. We estimate that there are ~3,200 new kidney transplant patients in the US, Europe and Japan experiencing acute AMR every year and consequently believe that the market opportunity approaches $500 million per annum. We have identified one other candidate that could potentially be competitive with imlifidase in acute AMR in kidney transplantation – CSL Behring is assessing a human plasma-derived C1 esterase inhibitor (CSL842) as an add-on to IVIG therapy in a Phase III trial in refractory AMR (readout expected in 2026).

Hansa is also developing imlifidase for Guillain-Barré syndrome…

Hansa is also developing imlifidase for the treatment of GBS, a rare and potentially fatal autoimmune disease characterised by rapid-onset muscle weakness to the extremities. GBS results from the generation of IgG antibodies and inflammatory cells that cross-react with epitopes on peripheral nerves and roots, which leads to damage of nerve cells. 20–30% of patients require mechanical ventilation. The prevalence of GBS is estimated to be in the range of 1–2 per 100,000 people annually. The exact cause of GBS is unknown. It is thought that, at least in some cases, an immune response is initiated to fight an infection and that some chemicals on infecting bacteria and viruses resemble those on nerve cells, which, in turn, also become targets of attack. Most cases usually start a few days or weeks following a respiratory or gastrointestinal viral infection, and occasionally surgery will trigger the syndrome. Recently, some countries worldwide reported an increased incidence of GBS following infection with the Zika

virus. There are no drug therapies specifically approved to treat GBS. The current standard treatments are PLEX and IVIG, though up to 40% of patients do not respond to treatment resulting in disability, pain and potentially death in 3–7% of cases.

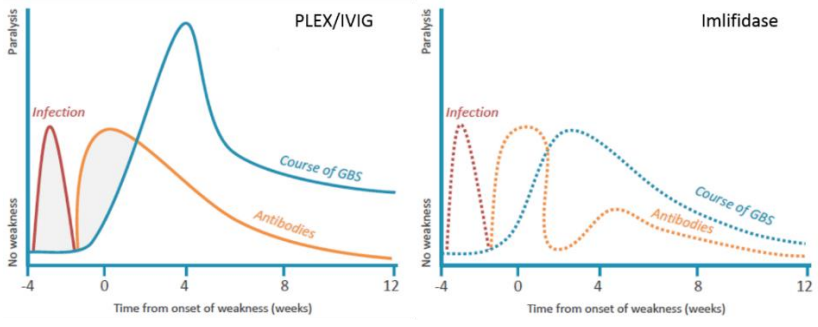
…with a Phase II trial currently recruiting patients

In 2019 Hansa initiated an open-label, single-arm, multi-centre Phase II trial of imlifidase in patients with GBS. This trial aims to recruit up to 30 patients (four treated to date) at up to ten sites in the UK, France and the Netherlands to receive a single dose of imlifidase 0.25mg/kg on day 1 of treatment followed by standard IVIG 0.4g/kg for five consecutive days from day 3. The primary endpoints of the trial are safety measures and improved functional outcome at four weeks as assessed by the 6-point GBS Disability Score. In this scoring system, 0= healthy; 1= minor symptoms and capable of running; 2= able to walk independently ≥10 metres but unable to run; 3= able to walk ≥10 metres across an open space with help; 4= bedridden or chair-bound; 5= needing mechanical ventilation; and 6= dead. A range of secondary endpoints are further testing functional capabilities from four weeks to one year after therapy, as well as healthcare economic outcomes and biochemical measures. We anticipate the completion of recruitment into the trial in H2 2021 and results in H2 2022.

Competitors in the pipeline also pursuing >$1billion market opportunity in GBS

We believe there is a significant unmet need in the treatment of GBS. There are no specifically approved drugs, and the current standard treatments PLEX and IVIG are slow to act, meaning permanent nerve damage could result before significant levels of the pathogenic IgG antibodies are removed (see Figure 14). Furthermore, 40% of patients do not respond to these treatments at all. We estimate that the addressable patient population for imlifidase in GBS is approximately 11,000 patients per year in the US, Europe and Japan and believes this equates to a market opportunity of over $1 billion annually. Hansa has received ODD from the FDA for imlifidase for the treatment of GBS. Other companies have also identified the attractive commercial potential of this market. Annexon Inc. is conducting an open-label, single-arm, Phase I/II trial of ANX005, an anti-C1q antibody, combined with IVIG. We anticipate results from this trial in H1 2021. In September 2019, Annexon reported outcomes from a Phase Ib dose-escalation trial of ANX005 in 31 GBS patients, without disclosing specific data. ANX005 treatment resulted in full and prolonged C1q engagement and classical cascade inhibition, measured in the blood and cerebrospinal fluid. Patients showed significantly reduced levels of neurofilament light chain (a biomarker of nerve damage) and consistent trends for improvements on GBS outcome measures, including an early impact on muscle strength. Cellenkos is conducting a Phase I dose-escalation trial of CK0801, a cord blood-derived T regulatory cell therapy, in up to 18 patients with treatment-resistant GBS, with results from this trial likely in 2021.

Figure 14: Imlifidase could improve treatment of GBS vs current therapies PLEX and IVIG



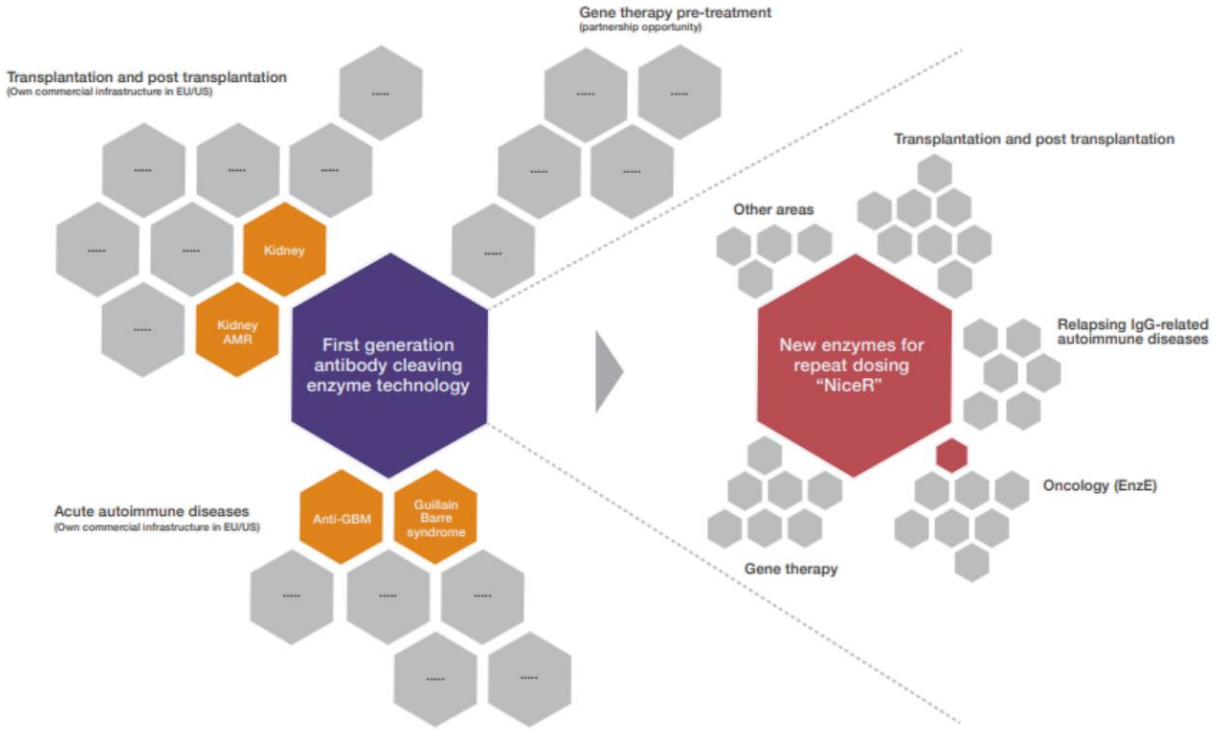
Source: Hansa Biopharma AB

Future growth prospects from Hansa's platform

Hansa's technology could reach beyond acute autoimmune indications

We believe Hansa's endopeptidase technology platform could have applications reaching beyond the acute autoimmune indications discussed in the previous sections (see Figure 15). The Company is exploring the possibility of applying its technology to enable broader access to gene therapies and potentially enable re-dosing. Hansa is also developing endopeptidases with lower immunogenicity for repeat dosing, the "NiceR" programme, with a lead candidate selected. A drug that can be repeat-dosed could have therapeutic potential in treating regular symptom "flares" that are associated with some chronic autoimmune diseases, or as a treatment to enhance the efficacy of therapeutic antibodies (the "EnzE" project in the oncology field).

Figure 15: Potential indication universe for Hansa's endopeptidase technology platform



Source: Hansa Biopharma AB

Gene therapy uses viral vectors to replace faulty genes…

There are approximately 5,000–8,000 human diseases arising from mutations in a single gene (monogenic diseases) that collectively affect about 6% of the global population. Gene therapy is a rapidly growing treatment modality to address these disorders whereby replacement of the defective gene with its functional copy occurs. For monogenic disorders, delivery of the genetic information encoding the "healthy gene" into human cells (transduction) is usually accomplished within the body ("*in vivo*") by a viral "vector" (a modified virus), though there has also been testing of non-viral methods. Several different types of virus have been developed as gene therapy vectors, though adeno-associated virus (AAV) vectors are by far the most common. Gene therapies are also being developed to treat non-monogenic disorders (where multiple gene mutations cause disease or where the cause of the disease is non-genetic, examples include cancer, HIV/AIDs, Parkinson's disease and congestive heart failure).

…and is a rapidly growing area of medicine…

The gene therapy field has grown considerably over the last few years, with over 180 *in vivo* gene therapy programmes now in development, including over 70 in clinical trials. The first gene therapy to be approved for a monogenic disorder was uniQure's Glybera® (alipogene tiparvovec) for the treatment of lipoprotein lipase deficiency in 2012 (by the EMA, though withdrawn in 2017 for commercial reasons), which was based on AAV Serotype 1 (AAV1). More recent approvals include Novartis' Luxturna® (voretigene neparvovec-rzyl, based on AAV2) for the treatment of biallelic RPE65 mutation-associated retinal dystrophy (by the FDA in December 2017 and EMA in November 2018) and Zolgensma® (onasemnogene abeparvovec-xioi, based on AAV9) for spinal muscular atrophy with bi-allelic mutations in the survival motor neuron 1 gene (by the FDA in June 2019, positive CHMP opinion in March 2020). Also, BioMarin filed for approvals of its haemophilia A gene therapy valoctocogene roxaparvovec (based on AAV5) in November 2019 and December 2019 respectively.

…but sensitisation against viral vectors remains a barrier to effective treatment

The main issue with the use of AAV vectors is that an estimated 50–90% of the human population has been exposed to AAV infection, and around 50% of cases lead to the development of neutralising antibodies (NAbs) against AAV capsid proteins. Pre-formed NAbs can bind to and prevent gene therapies from entering the target cell, thereby reducing the transgene expression in the desired tissues and, ultimately, the gene therapy efficiency. Several studies have attempted to characterise this phenomenon further. Some have suggested that pre-formed antibodies have little or no effect, while others have reported that a NAb titre as low as 1:5 in the blood can fully prevent AAV transduction *in vivo*. Pre-screening for the presence of NAbs against specific AAV serotypes has been a common feature in clinical trials. Regardless of whether a patient has pre-formed AAV NAbs, the administration of an AAV-based gene therapy almost always provokes an immune response generating long-lasting NAbs. This prevents the ability to re-dose therapies in the future, which is desirable as transgene expression is likely to reduce over time with the natural turnover of initially transduced cells.

Hansa is seeking partners to assess its enzyme technology in gene therapy

Historically, PLEX and immunosuppressants reduced NAbs and broadened access to gene therapies, though there are no standard protocols with proven efficacy. We believe Hansa could use its endopeptidase technology platform to address the limitations of NAbs on gene therapy. Degradation of the IgG NAbs with an endopeptidase drug such as imlifidase could create a window in which to administer or re-dose a gene therapy and maximise the chances of efficient transduction and efficacy. We understand Hansa is currently in discussions for a collaboration to test its endopeptidase technology in gene therapy and expect further details on a potential programme during 2020.

The NiceR programme is developing IgG cleaving enzymes for repeat dosing…

While imlifidase has proven extremely effective at eliminating IgG, it is a bacterial enzyme that provokes an immune response. Indeed, in clinical trials, patients develop anti-imlifidase antibodies over the two weeks following treatment with levels decreasing slowly over the subsequent months. This prevents the re-treatment of patients with imlifidase, at least in the short term. To overcome this issue, Hansa is developing NiceR – a programme to develop novel IgG cleaving enzymes with lowered immunogenicity for repeat dosing. We believe this programme has the potential to extend beyond imlifidase's reach and target indications which are characterised by re-occurring acute exacerbations of symptoms caused by IgG antibodies (see Figure 15).

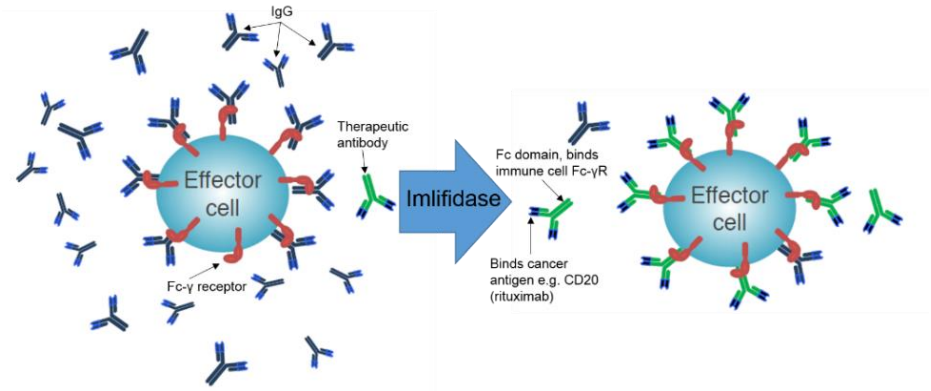
…a lead candidate has been selected and could enter the clinic in H2 2021

In March 2019, Hansa selected a first drug candidate from the NiceR programme. This candidate is an IgG-cleaving enzyme (a cysteine peptidase) with characteristics based on a homologue to imlifidase, but with less immunogenicity. Hansa is currently establishing a GMP manufacturing process for the candidate and aims to complete this and IND-enabling toxicology studies during H1 2021. We believe a first-in-human clinical trial could start in H2 2021.

Hansa's EnzE programme is for cancer antibody enhancement…

Many antibody-based cancer therapies rely on activation of the immune system via antibody-dependent cell-mediated cytotoxicity (ADCC). The antibodies bind to antigens on cancer cells and once attached, the antibody attracts immune cells to destroy the cancer cells through the binding of the Fc part of the antibody to Fc-γ receptors on the surface of the immune cells (see Figure 16). However, IgG is abundant in the blood and can bind to and effectively block the Fc-γ receptors on immune cells, which can consequently reduce the efficacy of the antibody. A treatment which removes IgG, such as imlifidase or NiceR, could enhance the efficacy of cancer antibody therapeutics. With global sales of cancer antibody therapies forecast to exceed $90 billion by 2024 (EvaluatePharma®), we believe there could be a substantial opportunity for effective antibody enhancement drugs.

Figure 16: Principle of EnzE in cancer therapy



Source: Hansa Biopharma AB

…and has achieved preclinical proof-of-concept

The EnzE programme has generated promising *in vitro* results (published in Journal of Molecular Biology, 2012, 420 (1-2):1-7) and demonstrated *in vivo* proof-of-concept (POC) in a mouse model of cancer (published in Molecular Cancer Therapeutics, 2017, 16 (9): 1887–97). In a mouse model of lymphoma, infusion of mice with human IgG significantly impaired the efficacy of the anti-CD20 monoclonal antibody rituximab (Roche's Rituxan®/MabThera®). However, pre-treatment of mice with imlifidase after IgG dosing significantly rescued the therapeutic effect of rituximab. We understand that having demonstrated preclinical POC with imlifidase, current and future work on the EnzE programme will use NiceR repeat dosing technology (necessary as antibody therapies for cancer are typically dosed multiple times over weeks to months).

Valuation – our fair value is SEK 190/share

We use discounted cash flow analysis to value Hansa's lead drug imlifidase
A generally accepted method for estimating the value of development-stage drug candidates in the pharmaceutical industry is to model the cash flows from potential sales of drugs launched in the future and then discount back to determine a present-day value. Discount rates for publicly quoted companies in the biotechnology sector usually range from 10–16% in our experience, and this range can be supported using sector betas and the Capital Asset Pricing Model. The actual rate which we consider appropriate varies from company to company according to the financial strength and the requirement for additional capital. When valuing development stage programmes, we also apply specific risk adjustments, using both industry-standard success probabilities, including specific therapeutic area considerations and our technical judgement.

Focusing on imlifidase in HLA desensitisation for kidney transplantation…
Our valuation of Hansa Biopharma focuses on imlifidase in its lead indication of HLA desensitisation for kidney transplantation. We would highlight three key points that underpin our enthusiasm for imlifidase in this indication: (1) a significant number of patients with ESRD on dialysis are so severely HLA sensitised that their chances of finding a compatible donor are very remote, yet; (2) transplantation is proven to have favourable outcomes over remaining on long-term dialysis and; (3) results from clinical trials have been compelling and suggest imlifidase can facilitate HLA-mismatched transplants in these severely sensitised patients and potentially improve long-term outcomes in our view.

…with Hansa set to capture full value by self-commercialising
Many of the biotechnology companies we analyse have assets in their pipeline that are either already partnered or in all likelihood will be partnered, with the biotech company benefiting from milestone payments and royalties. While this varies based on the stage of development, it is not unusual for a biotechnology company to retain less than a third of the value of the drug following a partnership deal. Hansa's stated strategy and one we endorse is to sell imlifidase directly. In most countries, kidney transplants occur in a relatively small number of specialised centres. For example, in the UK, there are 20 kidney transplant centres vs 1,257 hospitals overall, and in the US, there are 260 hospitals with kidney transplant programmes vs over 6,100 hospitals. We believe Hansa can effectively market and sell the drug with relatively compact sales teams. By selling imlifidase directly, Hansa will be able to retain 100% of the economic value of the drug. While a significant investment will be required to establish the sales and marketing infrastructure (this effort is ramping in Europe in anticipation of potential first launches later this year), we believe it could be highly profitable (operating margins of around 70% in the medium term) with the opportunity to leverage this infrastructure by in-licensing additional products.

We value imlifidase at SEK 155/share based on peak sales of $400 million…
With compelling clinical results generated, Hansa has filed an MAA with the EMA for imlifidase in kidney transplantation, and we anticipate a decision in Q2 2020. The Company is also finalising plans for a randomised, controlled trial in the US to support a BLA via the accelerated approval pathway, which we expect in 2023. Our sales forecast for imlifidase assumes first launches in Europe in H2 2020 and US launch in 2024 (we conservatively exclude other markets at this time). We assume a territory price range of $250,000–$375,000 per patient, which is consistent with other drugs for orphan diseases that can transform treatment outcomes. Based on use exclusively in patients with severe levels of HLA sensitisation (PRA ≥99.9%), we forecast peak sales

of imlifidase of $400 million in 2032. Applying a 70% probability of success at this time (reflecting our belief that while the clinical data generated to date are strong, the FDA's request for a further trial has led to new clinical risk and elevated regulatory risk) our rNPV for imlifidase is SEK 155/share.

…with significant upside in transplantation, anti-GBM, GBS and AMR

As a rapid inactivator of IgG antibodies, imlifidase could prove an effective treatment in numerous indications related to obstructive/pathogenic IgG. In this note, we have highlighted that the collective commercial opportunity from Hansa's three initial target indications past kidney transplantation – anti-GBM, acute AMR and GBS (Phase II trials ongoing) – exceeds $1 billion. We conservatively have not included these indications in our imlifidase sales forecast at this time. Still, we may look to include them following the generation of proof-of-concept data and feedback from regulatory agencies. With results from the anti-GBM trial anticipated in Q3 2020, if positive, Hansa is likely to discuss the data with the FDA and EMA to determine what further studies may be required to support filings. These potential label expansions represent significant upside to our SEK 155/share valuation of imlifidase in our view. We have undertaken a sensitivity analysis to assess the impact of modelled peak sales for imlifidase on the derived rNPV per share (see Table 8).

Table 8: Derived risk-adjusted fair value (SEK/share) for imlifidase based on 2032 sales

	Annual peak sales				
Discount Rate	**$100m**	**$250m**	**$400m**	**$550m**	**$700m**
8%	33	116	199	282	365
10%	25	91	155	225	292
12%	18	72	127	181	236

Source: R_X Securities

We assign SEK 35/share for the broader endopeptidase platform at this time

While our key valuation focus for Hansa is on imlifidase in kidney transplantation, we view the Company as a platform business that has other commercially attractive facets. The gene therapy space is a "hot" area of drug development at this time, and we are particularly enthused about the potential for Hansa's endopeptidase technology to broaden patient access to treatment here, and also to possibly facilitate re-dosing. Hansa is currently engaged in discussions with development partners in this field and we anticipate an update this year. While at an early stage of development, we are excited about the next-generation endopeptidase programme, NiceR, noting that this repeat-dosing technology could be used in chronic autoimmune indications and also potentially to enhance the efficacy of therapeutic antibodies in cancer therapy (EnzE). Based on market values attributed to comparative technology and factoring in the endopeptidase platform's stage of development, we attribute a value of SEK 35/share in our sum-of-the-parts analysis.

Our fair value for Hansa Biopharma is SEK 190/share

Based on our rNPV for imlifidase and adding in our estimated value of the broader endopeptidase platform, we derive a fair value for Hansa Biopharma of SEK 190/share at this time, an approximate 57% upside to the current share price. As confidence grows in the outlook for imlifidase and initial data in additional indications are generated, we believe there is significant scope for upward revision of our valuation based on an increased peak sales outlook for the drug.

Appendix – the US Kidney Allocation System

What changed with the introduction of KAS?

In December 2014, a new kidney allocation system (KAS) started for deceased donor transplantation in the US. A primary goal of KAS was to eliminate or reduce extreme longevity mismatches, where either the transplanted kidney is expected to long outlive the recipient or not last long enough to avoid the recipient returning to the waiting list. A second goal was to broaden patient access by increasing transplant opportunities for candidates with cPRA scores at or near 100%. KAS also aimed to broaden patient access for historically disadvantaged candidates, often African Americans and other minorities, who may spend years on dialysis before being referred for transplantation. Awarding points for time spent on chronic, maintenance dialysis before being wait-listed was intended to compensate for such inequities in access. Also, the new system expanded transplant opportunities by allowing medically suitable blood type B candidates, who historically have had low transplant rates, to receive blood subtype A2 or A2B kidneys. Another aim was to increase the recovery and utilisation of high KDPI kidneys. KDPI 86–100% kidneys, whose discard rates exceed 40%, but may still benefit some patients, are now distributed to a combined local/regional list of candidates. The intent was to incentivise organ procurement organisations, whose local centres do not utilise these kidneys, to recover them for acceptance in adjacent donor service areas that will transplant them into suitable recipients. Other KAS goals included maintaining elevated access for paediatrics and prior living donors, and preserving waiting time as a core component. Figure 17 illustrates how KAS changed the way that kidneys are allocated in the US.

Figure 17: Approximate ordering of candidates under the old scheme and KAS

Old Deceased Donor Kidney Allocation System[1] (pre 12/4/2014)

SCD or DCD (Age<35)	SCD or DCD (Age 35+)	ECD[2]	DCD & ECD[2]
0 ABDR mismatch*	0 ABDR mismatch*	0 ABDR mismatch*	Local 0 ABDR mismatches
Local prior living donors	Local prior living donors	Local candidates	Local candidates
Local high CPRA**	Local candidates	Regional candidates	Regional candidates
Local pediatrics	Regional Candidates	National candidates	National candidates
Local adults	National Candidates		
Regional high CPRA**			
Regional pediatrics			
Regional adults			
National high CPRA**			
National pediatrics			
National high CPRA**			

** Included local, regional, and national distribution. (SCD=standard criteria donor; ECD=expanded criteria donor; DCD=donation after circulatory death)*
*** Classification included candidates with CPRA at least 80% with a total score higher than the highest scoring candidate with CPRA<80%*
[1] Candidates sorted within each classification by total points. Points awarded for waiting time, CPRA ≥ 80%, pediatric, prior living donor, HLA-DR matching.
[2] Candidates sorted by waiting time only.

New Kidney Allocation System (KAS)[3,4] (12/4/2014-present)

KDPI 0-20%	KDPI 21-34%	KDPI 35-85%	KDPI 86-100%
CPRA 98-100%*	CPRA 98-100%*	CPRA 98-100%*	CPRA 98-100%*
0 ABDR mismatch (EPTS 0-20%)	0 ABDR mismatch	0 ABDR mismatch	0 ABDR mismatch
Local prior living donors	Local prior living donors	Local prior living donors	Local + regional A2/A2B-->B
Local pediatrics	Local pediatrics	Local A2/A2B-->B	Local + regional candidates
Local A2/A2B-->B (EPTS 0-20%)	Local A2/A2B-->B	Local candidates	National A2/A2B-->B
Local EPTS 0-20%	Local candidates	Regional A2/A2B-->B	National candidates
0 ABDR mismatch (EPTS 21-100%)	Regional pediatrics	Regional candidates	
Local A2/A2B-->B (EPTS 21-100%)	Regional A2/A2B-->B	National A2/A2B-->B	
Local EPTS 21-100%	Regional candidates	National candidates	
Regional pediatrics	National pediatrics		
Regional A2/A2B-->B (EPTS 0-20%)	National A2/A2B-->B		
Regional A2/A2B-->B (EPTS 21-100%)	National candidates		
Regional EPTS 21-100%			
National pediatrics			
National A2/A2B-->B (EPTS Top 20%)			
National EPTS 0-20%			
National EPTS 21-100%			

** Includes eligible national 100% candidates, eligible regional 99-100% candidates, and local 98-100% candidates.*
[3] Broad classification groups are shown to illustrate the approximate order of candidates in KAS. For the full, detailed list of classifications, see OPTN Policy 8.
[4] Candidates are ordered by allocation points within each classification. Points are awarded for waiting time (back-dated to start of dialysis), CPRA sliding scale, pediatric, prior living donor, HLA-DR match. Only waiting time points are used for KDPI 86-100%.

Source: Stewart *et al*., American Journal of Transplantation (2016) 16 (6): p1834–1847

What goes into a KDPI score?

Kidneys from deceased donors are classified according to the Kidney Donor Profile Index (KDPI). The KDPI score is derived directly from the Kidney Donor Risk Index (KDRI) score. The KDPI is the percentage of donors in the reference population that have a KDRI less than or equal to the donor's KDRI. Ten components make up the KDRI score: age, ethnicity, creatinine levels, history of hypertension, history of diabetes, cause of death, height, weight, donor type and HCV status.

What goes into an EPTS score?

Each candidate on the kidney waiting list, after turning 18 years of age, receives an Estimated Post Transplant Survival (EPTS) score. A candidate's EPTS score represents the percentage of kidney candidates in the nation with a longer expected post-transplant survival time. The following determine the EPTS: (1) time on dialysis; (2) whether or not the candidate has diabetes; (3) whether or not the candidate has had any prior solid organ transplant; and (4) age. Calculation of the EPTS score occurs when the candidate is registered on the waiting list and is updated daily, and any time a transplant hospital reports changes to any EPTS factors for a candidate.

Kidney allocation points determine the position on the waiting list

Within each KDPI classification, candidates are sorted according to the total number of kidney allocation points they have accrued, then by the date and time of the candidate's registration (oldest to most recent). Candidates receive points according to Table 9.

Table 9: Kidney allocation points

If a candidate is:	and following allocation sequence used:	Then points received =
Registered for transplant	KDPI ≤20%; 21–34%; 35–85% or >85%	1/365 points for each day since qualifying criteria met
Aged 0 -10 at time of match and a 0-ABDR mismatch with the donor	KDPI ≤20%; 21–34%; 35–85%	4
Aged 11-17 at the time of match and a 0-ABDR mismatch with the donor	KDPI ≤20%; 21–34%; 35–85%	3
Aged 0 -10 at time of match and donor has a KDPI score<35%	KDPI ≤20%; 21–34%	1
A prior living donor	KDPI ≤20%; 21–34%; 35–85%	4
HLA sensitised (cPRA at least 20%)	KDPI ≤20%; 21–34%; 35–85%	See Figure 3 (page 14)
A single HLA-DR mismatch with the donor	KDPI ≤20%; 21–34%; 35–85%	1
A zero HLA-DR mismatch with the donor	KDPI ≤20%; 21–34%; 35–85%	2

Source: Organ Procurement and Transplant Network, Policy 8 – Allocation of Kidneys

US kidney transplant and waiting list statistics

In 2019 there were 23,401 kidney transplants conducted in the US, including 16,534 deceased donor transplants. Approximately 43% of deceased donor transplants were in HLA sensitised patients, 8.0% in highly sensitised (cPRA 98–100%) patients (see Table 10). As of March 2020, approximately 40% of the ~94,300 patients on the kidney transplant waiting list in the US (including 40% with "inactive" status) are HLA sensitised. An estimated 6,000 candidates on the kidney waiting list have a willing incompatible living donor that they are unable to utilise. ~6% of waiting list patients are highly sensitised (see Table 11).

Table 10: cPRA status of kidney transplants in the US in 2019

	Deceased		Living		All	
cPRA	*N*	*%*	*N*	*%*	*N*	*%*
0%	9,402	57	4,814	70	14,216	61
1–19%	1,791	11	819	12	2,610	11
20–79%	2,735	17	942	14	3,677	16
80–97%	1,277	7	200	3	1,477	6
98–100%	1,325	8	68	1	1,393	6
Unknown	4	<1	24	<1	28	<1
Total	**16,534**		**6,867**		**23,401**	

Source: Organ Procurement and Transplant Network, Advanced Report. Analysis as of 3 March 2020

Table 11: cPRA status of US kidney transplant waiting list candidates as of March 2020

cPRA	*N*	*%*
0%	57,802	60
1–19%	11,433	11
20–79%	15,963	17
80–97%	5,598	6
98–100%	5,805	6
All cPRA*	**94,315**	

Source: Organ Procurement and Transplant Network, Advanced Report. Analysis as of 3 March 2020; *total less than the sum of categories due to some patients included in multiple categories)

In Europe, France performs the most deceased donor kidney transplants

Table 12 shows the number of kidney transplants performed in 2018 in the five major markets in Europe – France, Germany, Italy, Spain and the UK. Table 13 shows kidney transplant waiting list numbers in Europe, where recently published.

Table 12: Kidney transplants performed in major European countries in 2018

	France	Germany	Italy	Spain	UK	Total
Deceased	3,026	1,653	1,831	3,020	2,628	**12,158**
Living	541	638	293	290	1019	**2,781**
Total	3,567	2,291	2,124	3,310	3,647	**14,939**

Source: International Registry in Organ Donation and Transplantation

Table 13: Kidney transplant waiting lists in Europe, "active" status (date)

	France	Germany	Italy	Spain	UK	Total
Patients	8,065 (12/2018)	6,850 (01/2020)	6,770 (12/2018)	3,933 (12/2018)	4,730 (02/2020)	**30,348**

Source: Global Observatory on Donation and Transplantation; National registries

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