



# HANSA

BIOPHARMA

Investor Road Show  
Presentation Q3 2022

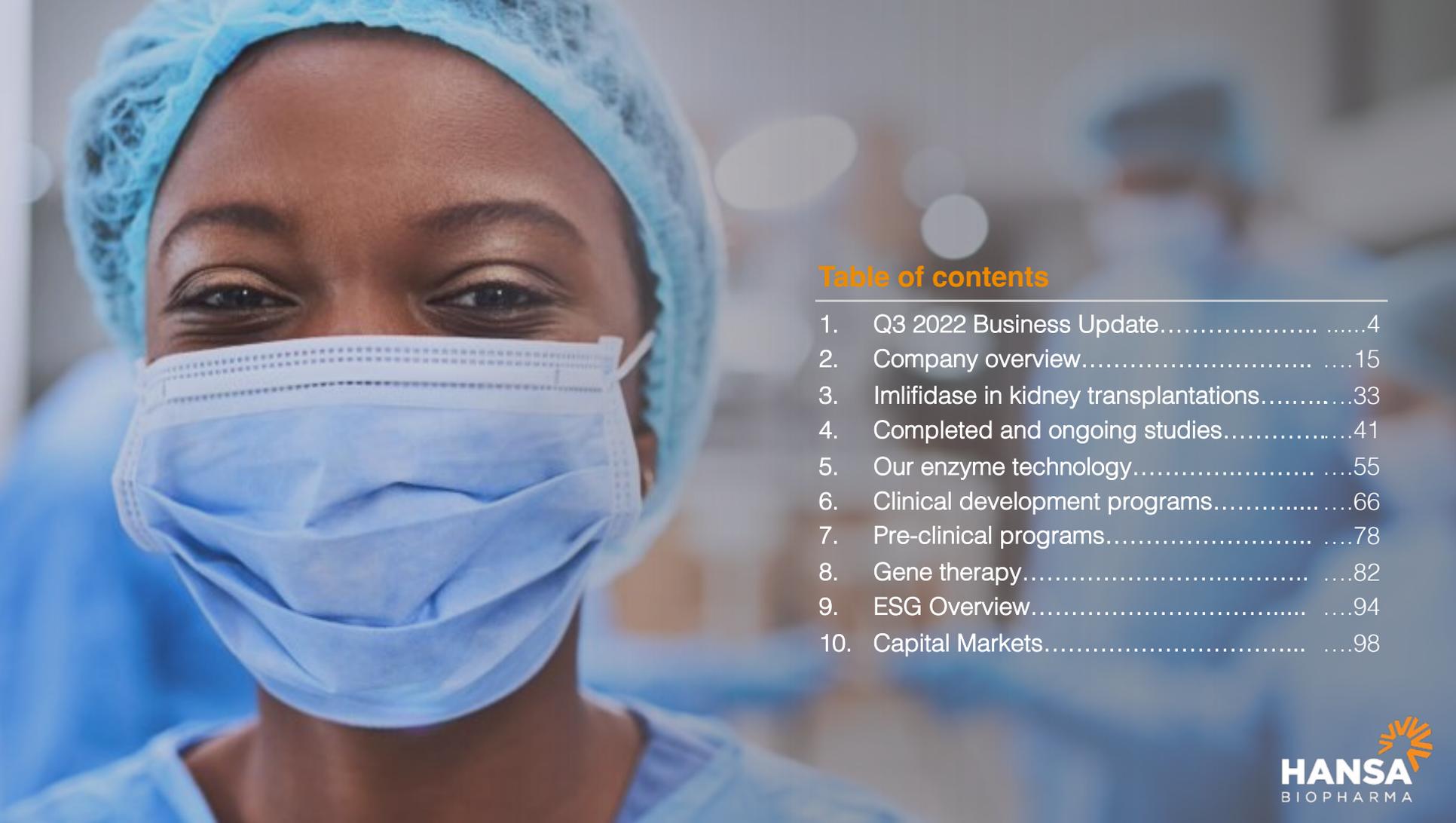
*Lund, October 20, 2022*

# Forward-looking statements

This presentation may contain certain forward-looking statements and forecasts based on our current expectations and beliefs regarding future events and are subject to significant uncertainties and risks since they relate to events and depend on circumstances that will occur in the future. Some of these forward-looking statements, by their nature, could have an impact on Hansa Biopharma's business, financial condition and results of operations [or that of its parent, affiliate, or subsidiary companies]. Terms such as "anticipates", "assumes", "believes", "can", "could", "estimates", "expects", "forecasts", "intends", "may", "might", "plans", "should", "projects", "will", "would" or, in each case, their negative, or other variations or comparable terminology are used to identify forward-looking statements. There are a number of factors that could cause actual results and developments to differ materially from those projected, whether expressly or impliedly, in a forward-looking statement or affect the extent to which a particular projection is realized. Such factors may include, but are not limited to, changes in implementation of Hansa Biopharma's strategy and its ability to further grow; risks and uncertainties associated with the development and/or approval of Hansa Biopharma's product candidates; ongoing clinical trials and expected trial results; the ability to commercialize imlifidase if approved; changes in legal or regulatory frameworks, requirements, or standards; technology changes and new products in Hansa Biopharma's potential market and industry; the ability to develop new products and enhance existing products; the impact of competition, changes in general economy and industry conditions and legislative, regulatory and political factors.

The factors set forth above are not exhaustive and additional factors could adversely affect our business and financial performance. We operate in a very competitive and rapidly changing environment, and it is not possible to predict all factors, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements. Given these risks and uncertainties, investors should not place undue reliance on forward-looking statements as a prediction of actual results.

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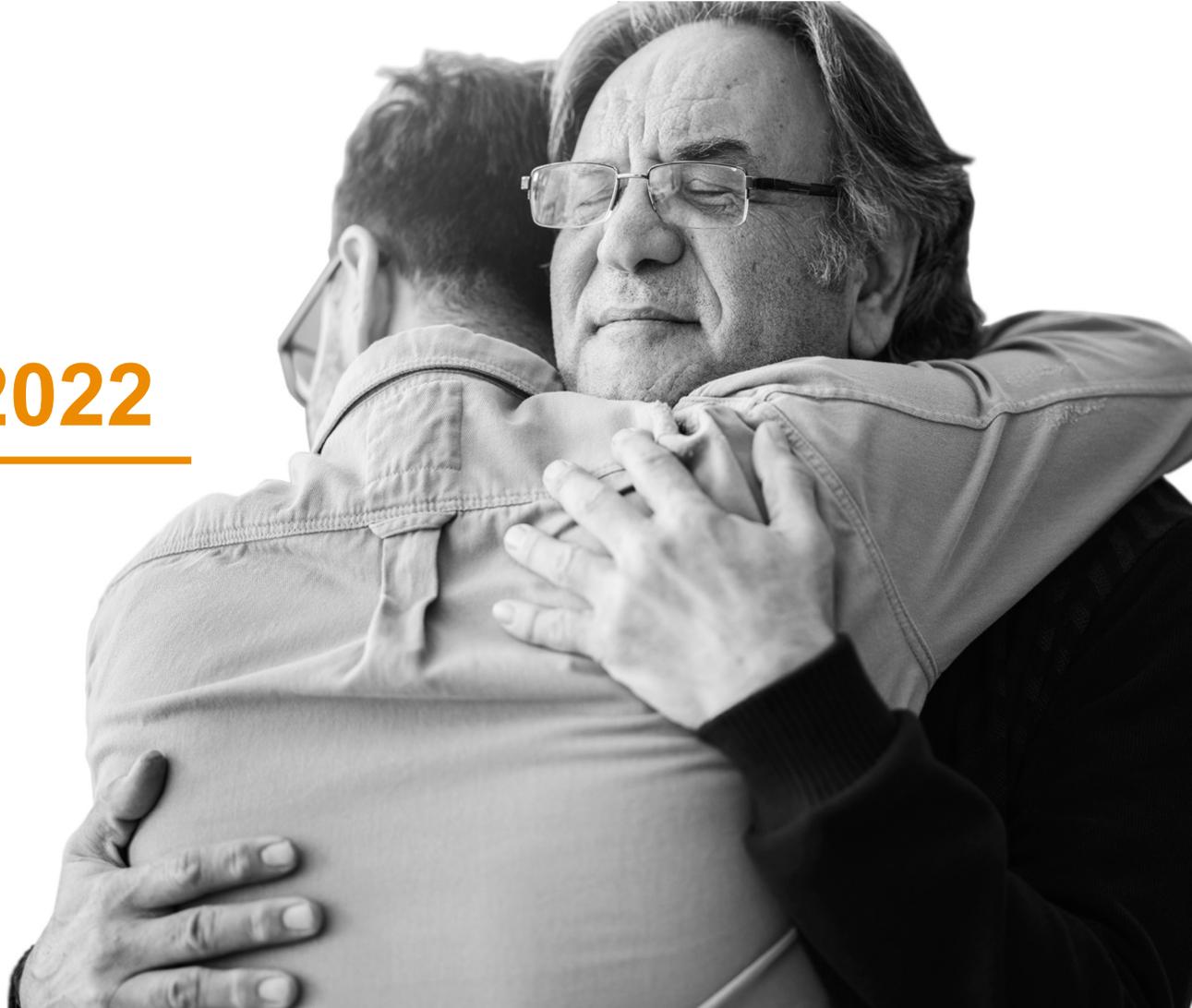
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# Business update Q3'2022

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## Positive reimbursement decisions received in Poland and Scotland; \$70 million raised in non-dilutive financing; ESOT guidelines published in *Transplant International*

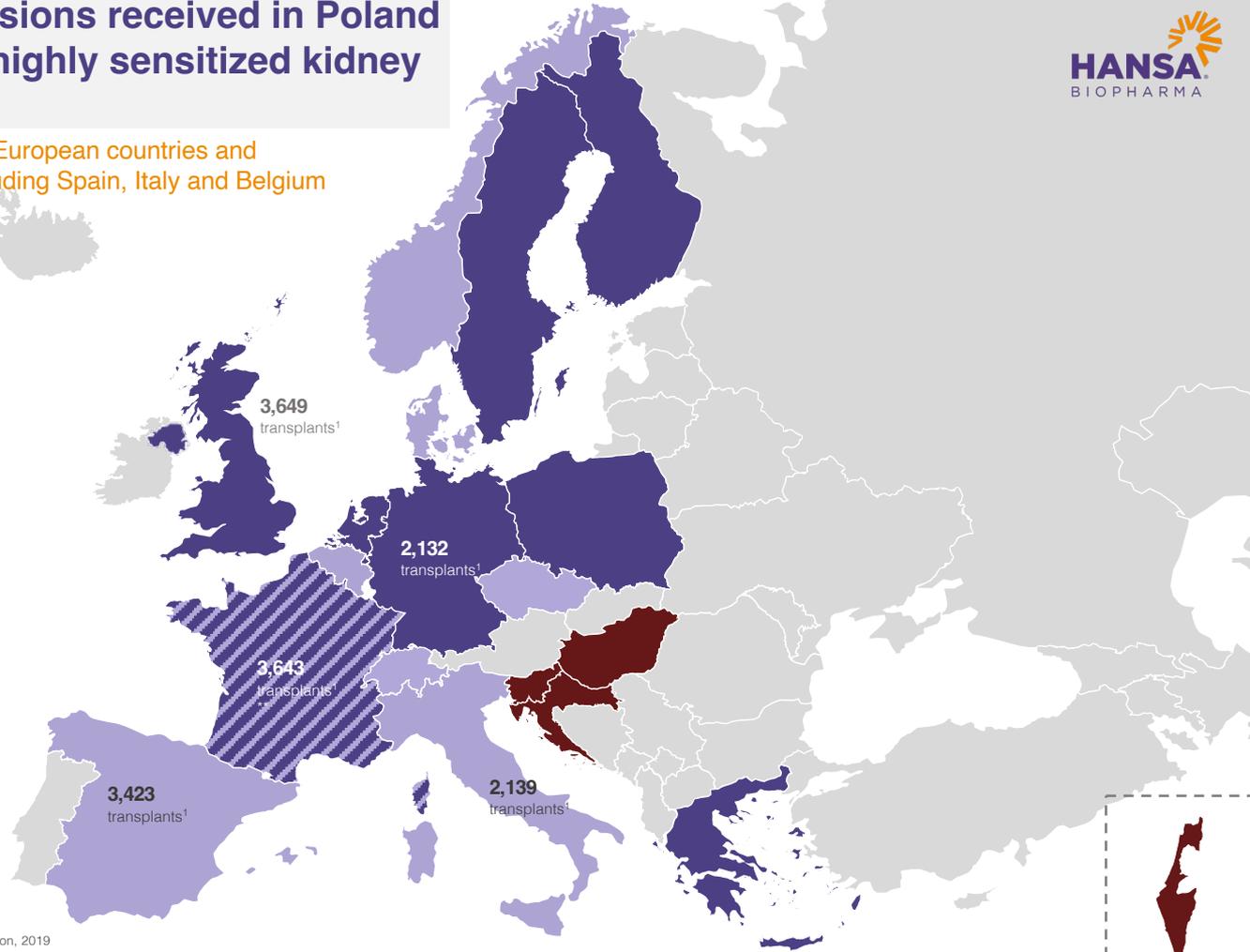
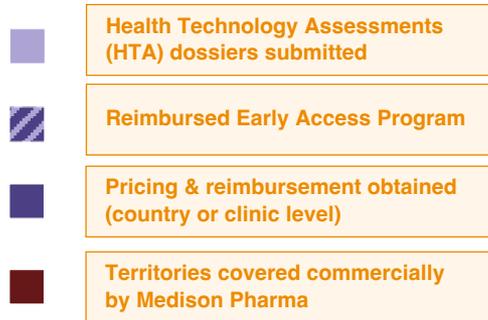
### Highlights for the third quarter of 2022

- ✓ Launch activities and market access efforts in EU progressing as planned
  - Total Q3 revenue of SEK 67m including SEK 23m in product sales and SEK 44m under our agreements with Sarepta and AskBio
  - Positive reimbursement decisions received in Poland and Scotland for Idefix®
  - Market access has now been secured in nine European countries and procedures are ongoing in eight countries including Spain, Italy and Belgium
  - The European Society for Organ Transplantation's (ESOT) guidelines for desensitization treatment of highly sensitized kidney transplant patients published in *Transplant International*.
  - First patient treated in the post-authorization efficacy study (PAES) of imlifidase in highly sensitized kidney transplant patients, at Vall d'Hebron Hospital, Barcelona.
- ✓ Clinical pipeline
  - U.S. ConfldeS Study in kidney transplantation: 39/64 patients enrolled
  - Anti-GBM: Expect to commence Phase 3 study later this year, as previously guided
  - AMR: Patient enrollment completed; First data read-out expected in H2'22
  - GBS: 20/30 patients enrolled in the GBS phase 2 study; Higher infection rates are expected as the winter season approaches as well as additional measures will be implemented to accelerate recruitment in the coming months. Completion of enrollment in the GBS trail is anticipated H2 2022/H1 2023
- ✓ Great Place to Work® certification for the 3<sup>rd</sup> consecutive year
- ✓ \$70 million raised in non-dilutive financing
  - Transaction supports the continued development of Hansa's antibody-cleaving enzyme technology platform while extending the cash runway through 2024



# Positive reimbursement decisions received in Poland and Scotland for Idefirix® in highly sensitized kidney transplant patients

Market access has now been secured in nine European countries and procedures are ongoing in eight countries including Spain, Italy and Belgium



<sup>1</sup>Annual kidney transplantations 2019 (pre-Corona)

\*Transplantation data is from Global Observatory on Donation and Transplantation, 2019

\*\*Pricing & reimbursement obtained in France on an early access basis

# The European Society for Organ Transplantation's (ESOT) guidelines for desensitization treatment of highly sensitized patients published in *Transplant International* in August 2022

## Guidelines represent first international consensus on a management pathway for highly sensitized patients

- The European guidelines document is a result of an expert working group, led by Professor Nizam Mamode M.D. Professor of Transplant Surgery, previously at Guys and St Thomas Hospital, London, and supported by other leading experts in the transplantation field.<sup>1</sup>
- Guidelines include imlifidase and provide a new clinical practice tool for healthcare professionals and represent the first international consensus on a management pathway for highly sensitized patients.
- Guidelines articulate the variability in definitions, approaches, outcomes as well as the perceived success of HLA-related transplantations
- Hansa Biopharma sponsors desensitization workstream as part of ESOT's educational programs, via an educational grant

## *Transplant International*

<https://www.frontierspartnerships.org/articles/10.3389/ti.2022.10511/full>



<sup>1</sup>Mamode N, Bestard O, Claas F, Furian L, Griffin S, Legendre C, Pengel L and Naesens M (2022) European Guideline for the Management of Kidney Transplant Patients With HLA Antibodies: By the European Society for Organ Transplantation Working Group. *Transpl Int* 35:10511. doi: 10.3389/ti.2022.10511

# Continuous progress in our ongoing clinical programs

Enrollment status  
Oct 19, 2022

## Antibody Mediated Rejection Phase 2 study

- 30/30 patients enrolled in the AMR phase 2 study
- Enrollment completed May 2022
- First data read out expected toward the end of 2022\*
- Data from the Phase 2 program will determine the path forward for imlifidase in patients with active AMR episodes



- Patients enrolled
- Patients remaining

## Guillain-Barré Syndrome Phase 2 study

- 20/30 patients enrolled in the GBS program
- Ten centers are active and open for recruitment; Additional measures will be implemented to accelerate recruitment in the coming months.
- Aim to complete enrollment of GBS patients H2'22/H1'23
- Enrollment expected to be boosted from higher infection rates during winter season, while increased capacity at the enrollment sites is also expected to support a faster enrollment
- Aim to communicate first high-level data read out in H2 2023

Enrollment status  
Oct 19, 2022

## Anti-GBM Phase 3 study

- FDA has accepted Hansa's Investigational New Drug (IND) application to proceed with a pivotal global Phase 3 study
- Aim to commence the planned anti-GBM study later this year, as previously guided. Study will target 50 patients\*



- Patients enrolled
- Patients remaining

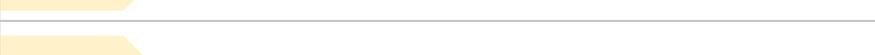


- Patients enrolled
- Patients remaining

## U.S. ConfIdeS Phase 3 study

- Randomized, controlled trial in highly sensitized kidney transplant patients across up to 15 centers
- 39/64 patients enrolled for randomization
  - Aim to complete of enrollment expected toward end of 2022
  - Aim to complete randomization n the first half 2023
  - BLA submission is expected in 2024 under the accelerated approval path

# Broad clinical pipeline in transplantation and auto-immune diseases

Candidate/Project	Indication	Research/Preclinical	Phase 1	Potentially Pivotal/Phase 2	Phase 3	Marketing Authorization	Marketed	Next Anticipated Milestone
Imlifidase	EU: Kidney transplantation in highly sensitized patients <sup>1,2</sup>						EU: Additional agreements around reimbursement from H2'21	
	US: Kidney transplantation in highly sensitized patients <sup>1,2</sup>						Completion of enrollment (64 patients) H2'22	
	Anti-GBM antibody disease <sup>3</sup>						Pivotal Phase 3 study expected to commence in 2022 (50 patients)	
	Antibody mediated kidney transplant rejection (AMR)						First data read-out H2 2022	
	Guillain-Barré syndrome (GBS)						Completion of enrollment (30 patients) H2'22/H1'23	
	Pre-treatment ahead of gene therapy in Limb-Girdle (Partnered with Sarepta)						Preclinical research	
	Pre-treatment ahead of gene therapy in Duchenne (Partnered with Sarepta)						Preclinical research	
	Pre-treatment ahead of gene therapy in Pompe disease (Partnered with AskBio)						Preclinical research	
NiceR	Recurring treatment in autoimmune disease, transplantation and oncology						Completion of GLP toxicology studies in 2022	
EnzE	Cancer immunotherapy						Research	

<sup>1</sup> Results from the Phase 1 study have been published, Winstedt et al. (2015) PLOS ONE 10(7)

<sup>2</sup> Lorant et al American Journal of Transplantation and 03+04 studies (Jordan et al New England Journal of Medicine)

<sup>3</sup> Investigator-initiated study by Mårten Segelmark, Professor at the universities in Linköping and Lund

 Completed

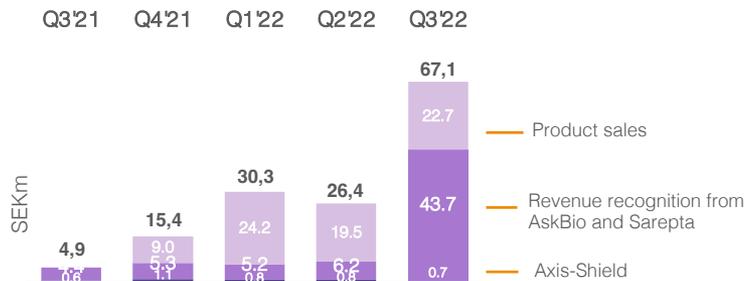
 Planned

 Ongoing

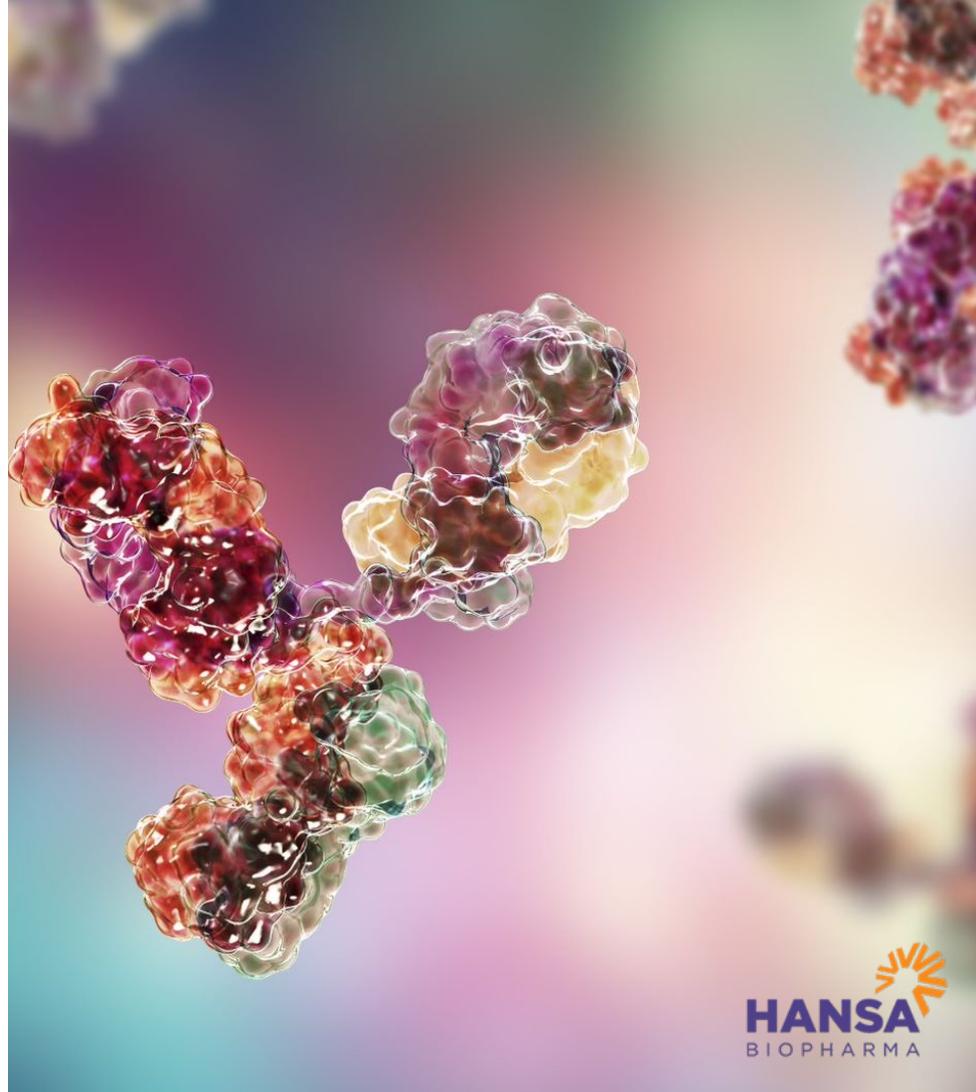
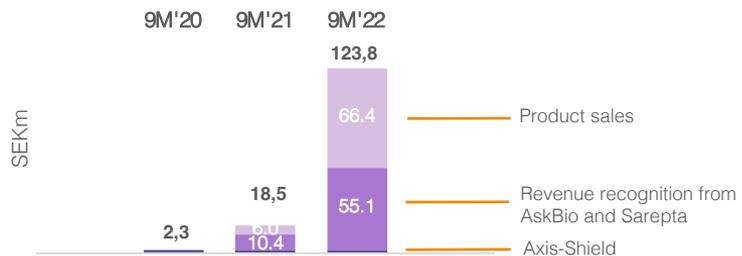
 Post approval study running in parallel with commercial launch

## Total Revenue amounted to SEK 67m in the third quarter including SEK 23m in product sales

### Revenue (Q/Q)

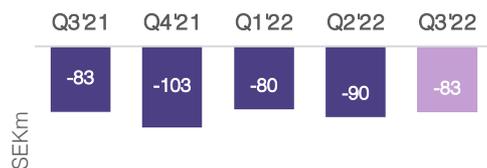


### Revenue (9M/9M)

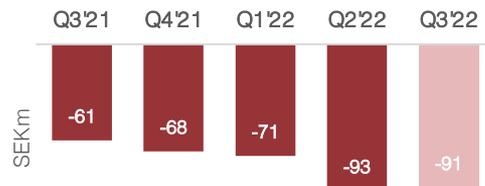


# Continued investments in commercialization and our pipeline

## SG&A expenses (Q/Q)



## R&D expenses (Q/Q)



## Net loss (Q/Q)



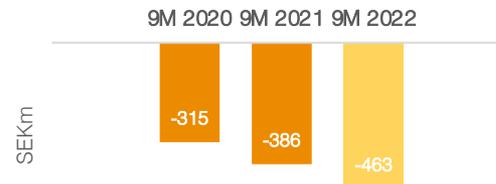
## SG&A expenses (9M/9M)



## R&D expenses (9M/9M)

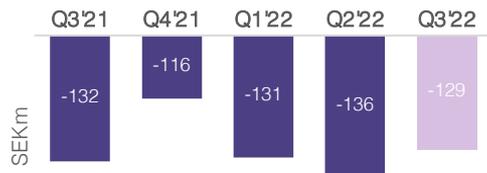


## Net loss (9M/9M)



## With recent financing transaction secured Hansa's cash runway has extended through 2024

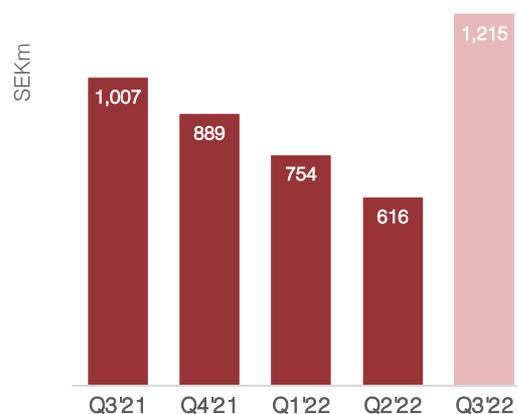
### Operating cash flow (Q/Q)



### Operating cash flow (9M/9M)



### Cash & short-term investments (Q/Q)

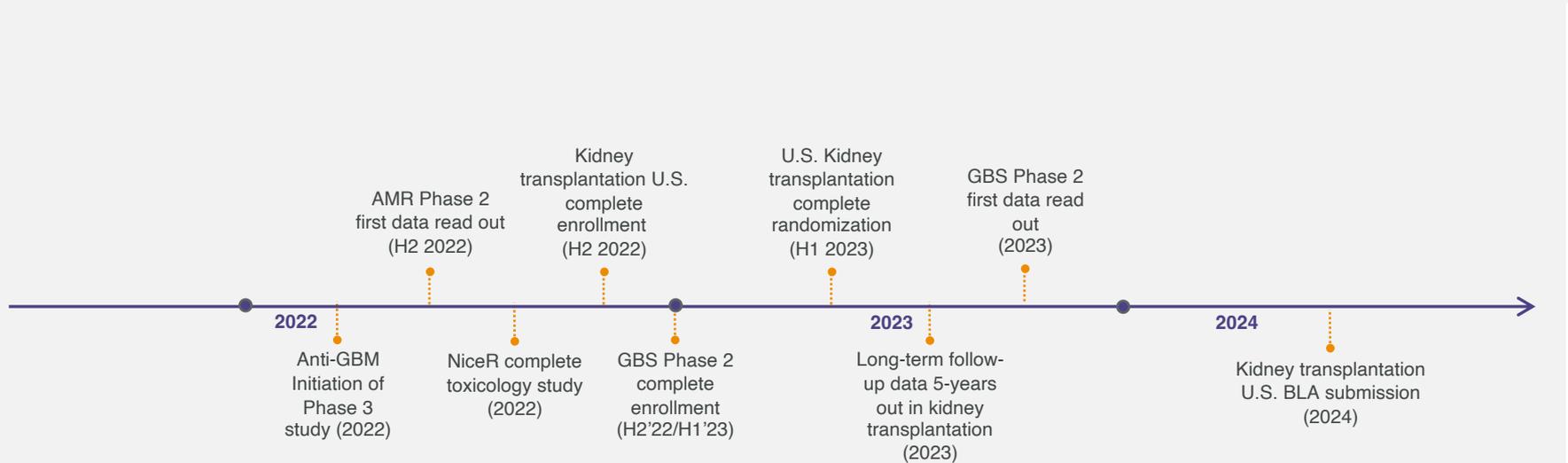


### Number of employees (Q/Q)



# Upcoming milestones

Milestones subject to potential COVID-19 impact



*Guidance assumes no persistent impact or further escalation of the COVID-19 pandemic potentially forcing trial centers to reprioritize patient recruitment or even shut down again.*

# Company overview

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Successful track record...  
Strong momentum...  
Promising future...

## A validated technology

### VALIDATION ACROSS THREE AREAS

- ✓ Approval in kidney transplantations
- ✓ Proof of concept in autoimmune diseases
- ✓ Partnerships to explore gene therapy

## Idefirix® is our first approved drug in Europe\* EUROPE KIDNEY TRANSPLANTS

For highly sensitized patients in Europe

## Broad pipeline in transplantation and autoimmunity

### PROGRAMS IN CLINICAL DEVELOPMENT

US kidney transplants  
Anti-GBM  
Guillain-Barré syndrome (GBS)  
Antibody mediated kidney transplant rejection (AMR)

## Established a high-performance organization

### NEW COMPETENCIES ADDED

145 employees June 2022 (~3x in 3 years)  
Highly qualified team with 20 years on average in life science  
Purpose driven culture

## With current cash position Hansa is financed through 2024 FINANCIALS

SEKm 1,215 in Cash and short term investments (USD ~108m) September 2022

## Created shareholder value and diversified our ownership base

### MARKET CAPITALISATION (USD): ~240m

Listed on Nasdaq Stockholm  
18,000 shareholders  
Foreign ownership make up ~40% through leading international life science specialist funds



\*Idefirix approved in EEA under conditional approval for kidney transplantation

\*\*Actual patient has given consent to provide images

# We are building a global leader in rare diseases

Today

We are launching our first commercially approved product for enablement of kidney transplantation in Europe\*



Tomorrow

We envision a world where patients with rare immunologic diseases can lead long and healthy lives



# Our mission

We leverage our unique enzyme technology platform to develop innovative, lifesaving and life altering immunomodulating therapies, bring these to the patients with rare diseases who need them, and generate value to society at large.



## Develop new therapies



## Extend and improve human lives

Transplantation leads to **dramatically better quality of life and life expectancy than dialysis**

77% of transplanted patients are alive after 8 years vs 44% of patients on dialysis<sup>1</sup>



## Deliver value to society

Transplantation is a **cost-effective intervention vs. dialysis**

Idefixir was named in EMA report as **Outstanding contribution to public health**<sup>3</sup>

USD 115bn, equivalent to 20% of the US Medicare budget, relates to kidney diseases<sup>2</sup>



Desensitization in **kidney transplant patients\***



Exploring treatment options in **anti-GBM\*\***



Exploring treatment options in **GBS\*\***



Exploring treatment options in **AMR\*\***

\* Idefixir approved in EEA under conditional approval for kidney transplantation

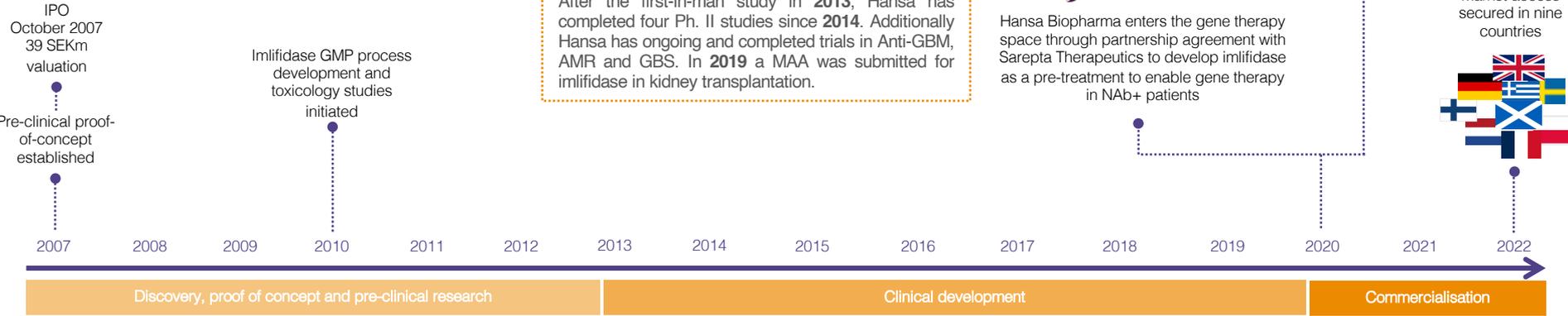
\*\* Imifidase under investigation

<sup>1</sup> Orandi et al. N Engl J Med 2016;374:940-50

<sup>2</sup> <https://www.hhs.gov/about/news/2019/07/10>

<sup>3</sup> [https://www.ema.europa.eu/en/documents/report/human-medicines-highlights-2020\\_en.pdf](https://www.ema.europa.eu/en/documents/report/human-medicines-highlights-2020_en.pdf)

# Hansa Biopharma's history



## 2. Clinical development

After the first-in-man study in **2013**, Hansa has completed four Ph. II studies since **2014**. Additionally Hansa has ongoing and completed trials in Anti-GBM, AMR and GBS. In **2019** a MAA was submitted for imlifidase in kidney transplantation.



Hansa Biopharma enters the gene therapy space through partnership agreement with Sarepta Therapeutics to develop imlifidase as a pre-treatment to enable gene therapy in NAb+ patients



The EU Commission grants conditional approval for Idefirix® in highly sensitized kidney transplant patients in Europe



## 1. Turning foe into friend

The therapeutic potential in using a bacterial enzyme with specificity for IgG-antibodies, to neutralize pathogenic antibodies was discovered around **2006**. The original enzyme, IdeS, has been developed by *Streptococcus pyogenes* over thousands of years and by transferring a majority of the IdeS coding nucleotide into harmless *E. coli*-bacteria, the IgG-cleaving part of the IdeS molecule can be expressed and purified, resulting in the Hansa Biopharma drug imlifidase, i.e. turning a former foe to a friend.

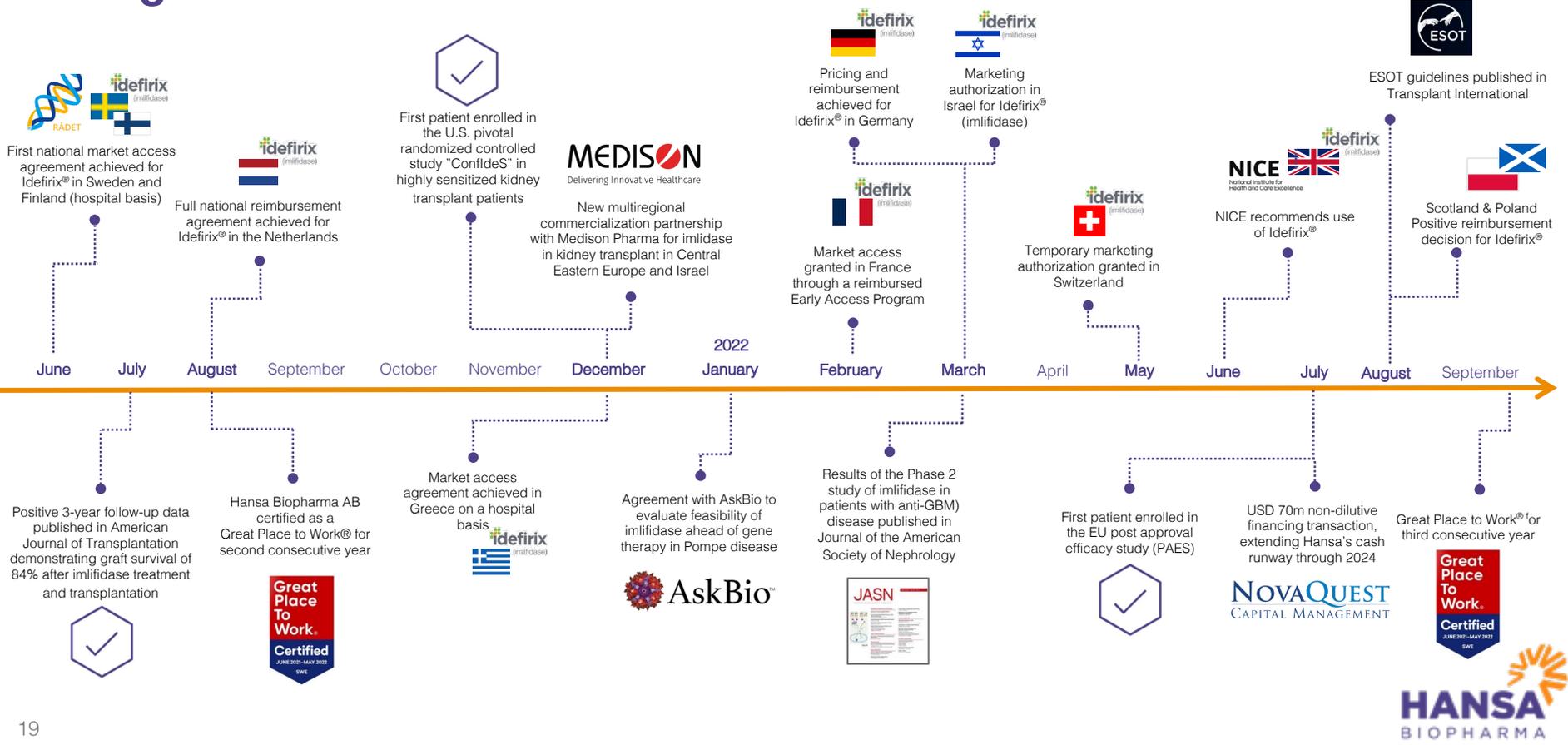
## 3. Commercialization

In August **2020**, Hansa received conditional approval for Idefirix (imlifidase) in kidney transplantation. Additionally, Hansa entered into the gene therapy field through a commercial partnership with Sarepta Therapeutics. Thus far, Hansa achieved market access in the first 7 European markets incl. UK, Germany and France (early access). Market Access procedures are ongoing in 11 additional countries

Hansa Biopharma enters into three collaborations with argenx (combination therapies); Medison (commercial) and AskBio (gene therapy)



# Many milestones achieved during the last 15 months



# Imlifidase

a novel approach to eliminate pathogenic IgG

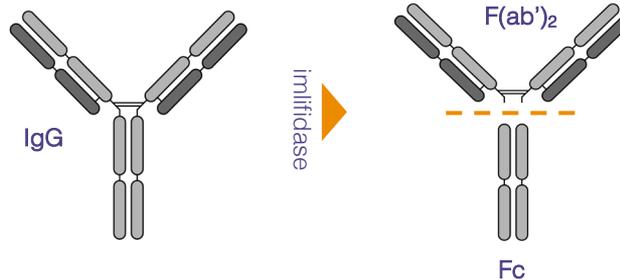
## Origins from a bacteria *Streptococcus pyogenes*

- Species of Gram-positive, spherical bacteria in the genus *Streptococcus*
- Usually known from causing a strep throat infection



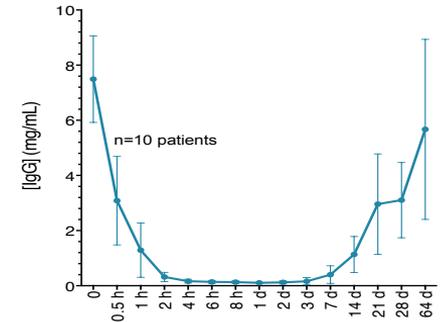
## A unique IgG antibody-cleaving enzyme

- Interacts with Fc-part of IgG with extremely high specificity
- Cleaves IgG at the hinge region, generating one F(ab')<sub>2</sub> fragment and one homo-dimeric Fc-fragment



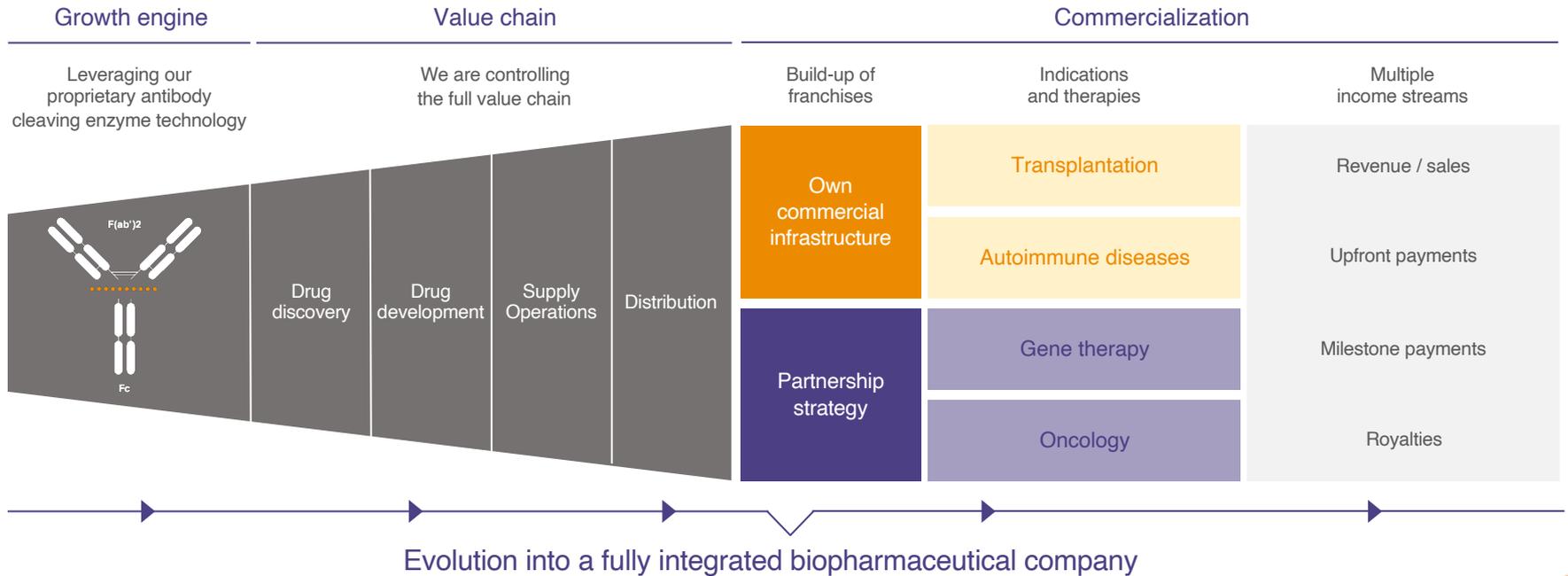
## Inactivates IgG in 2-6 hours

- Rapid onset of action that inactivates IgG below detectable level in 2-6 hours
- IgG antibody-free window for approximately one week

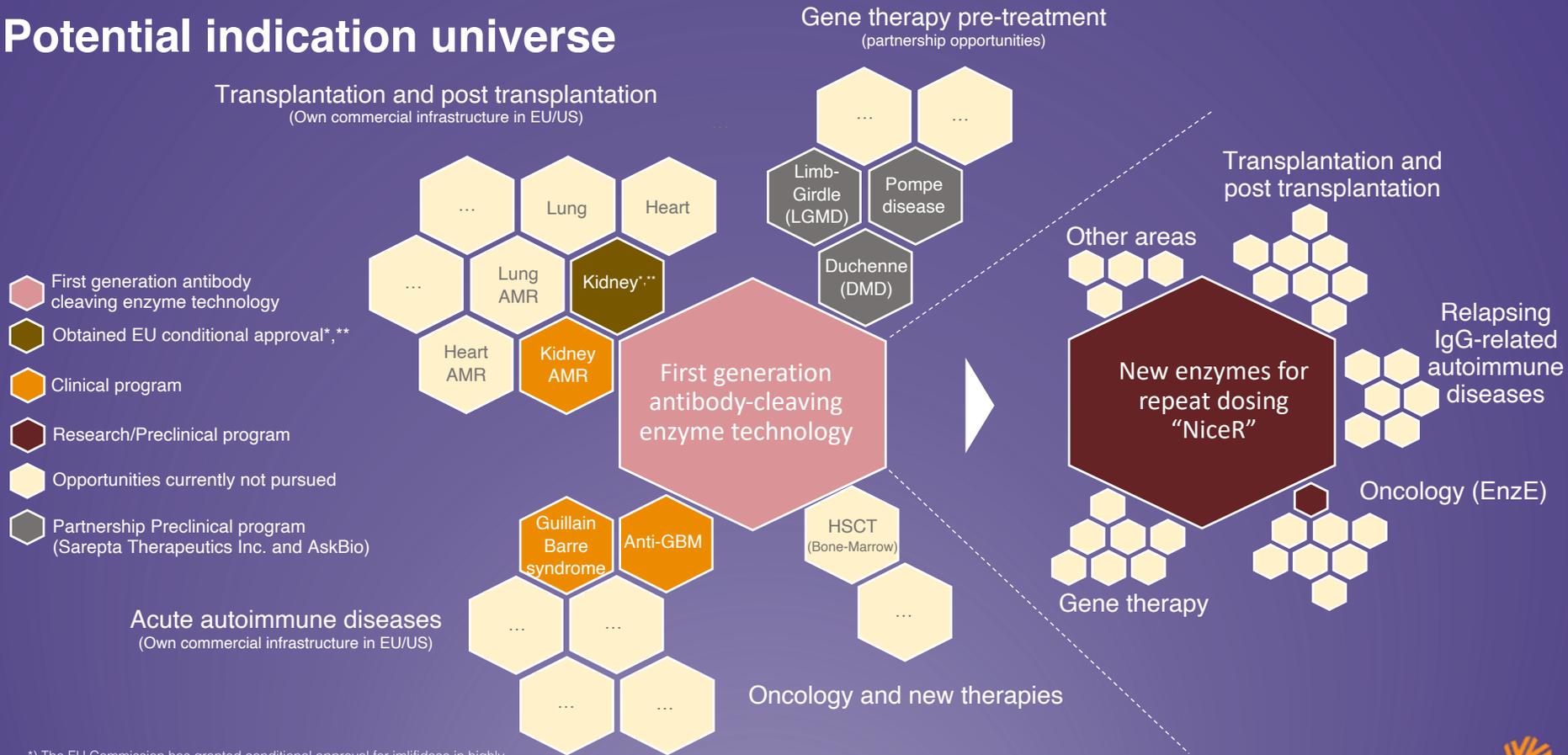


# Our Business model

Leveraging our technology platform to develop new therapies targeting rare diseases with unmet medical need across a range of indications



# Potential indication universe



\*) The EU Commission has granted conditional approval for imlifidase in highly sensitized kidney transplant patients.

\*\*) In the US a new study has commenced targeting a BLA filing by H1 2024

# Our strategic priorities

Our mission is to become a global leader in rare diseases



- 1** Successfully commercialize Idefirix® in kidney transplantation in Europe, the U.S. and selected international markets
- 2** Advance our ongoing clinical programs in AMR and rare autoimmune diseases to regulatory approval
- 3** Develop imlifidase as pre-treatment to gene therapy, starting with our collaborations with Sarepta and AskBio
- 4** Develop our next generation IgG-cleaving enzymes to allow for recurring treatment
- 5** Successfully develop and market our products by pursuing a hybrid partnering model

# Becoming a fully integrated commercial stage biopharmaceutical company

while expanding our technology and global footprint



Pre-clinical

Early-stage clinic

Late-stage clinic

Commercial stage

1

Creating a scientific platform

- Advanced imlifidase from preclinical models through to approval
- Initiated clinical studies in transplantation in EU and the US
- Built the R&D organization
- Validated through peer-reviewed publications (e.g. NEJM and AJT)

2

Preparing the company for commercial success

- Completion of four phase 2 studies in transplantation
- Development of GMP process
- Expanded the pipeline to post-transplantation and autoimmunity
- Established corporate and medical functions
- Expanding the footprint in EU and US

3

Building and capturing value in new indications and markets

- First drug approval in kidney transplantation in EU\*
- Commercialisation
- Market Access secured in the U.K incl. Scotland, Germany, France (early access), Poland, Sweden, Netherlands as well as Finland and Greece on individual hospital basis
- Expanding commercial teams and adding territory management
- Securing supply chain management
- Progressing pipeline and advancing our technology footprint

\* Idefirix approved in EEA under conditional approval for kidney transplantation

# Our culture is driven by people passionate about making changes



## Purpose driven culture

Helping patients with rare diseases serves as a **strong purpose** for our colleagues to **go the extra mile**



## Diverse and international

**~45%**

Internationals across ~30 nationalities

**55/45**

Male/female gender split in the leadership team



## Skilled and experienced team

**>50%**

With relevant PhD in R&D

**~20 years\***

of life science experience on average from Big Pharma, Biotech and Academia

*\*covers Management, R&D, and Commercial functions*



## Motivated workforce

For second consecutive year Hansa is certified as a “Great Place to Work” with **100%** participation rate in the survey



# Experienced Board and Executive Committee

Extensive experience from the global healthcare industry

## Executive Committee



### Sören Tulstrup

**President & CEO (2018)**  
*+30 years in the Healthcare sector*  
*Ex-CEO at Vifor Pharma*  
*Ex-SVP at Shire Pharmaceuticals*  
*Ex-CEO at Santaris Pharma*  
Shareholding: 26,541



### Christian Kjellman

**SVP & CSO/COO (2008)**  
*+20 years in the Healthcare sector*  
*Ex-Head of Research at Cartela*  
*Ex-Senior Scientist at Biolvent,*  
*MSc Chemical Biology, PhD in Tumour Immunology from Lund University*  
Shareholding: 6,213



### Donato Spota

**SVP & CFO (2019)**  
*+20 years in the Healthcare sector*  
*Ex-CFO Basilea Pharmaceutica*  
*Senior Finance roles at Roche*  
Shareholding: 5,673



### Achim Kaufhold

**SVP & CMO (2020)**  
*+40 years in the Healthcare sector*  
*Ex-CMO Basilea Pharmaceutica*  
*Ex-CEO Affitech (merged with Pharmexa A/S)*  
*Ex-CMO Chiron (acquired by Novartis)*  
Shareholding: 0



### Henk D. van Troostwijk

**SVP & CCO (2016)**  
*+20 years in the Healthcare sector*  
*Ex-GM at Raptor Pharmaceuticals*  
*Ex-BU Director at Genzyme Europe*  
Shareholding: 2,564



### Anne Säfström Lanner

**SVP & CHRO (2019)**  
*Ex-Head of HR European Spallation Source*  
*Ex-Head of HR Cellavision*  
Shareholding: 3,565



### Peter Nicklin

**Chairman (2022)**  
*+30 years in the Healthcare sector*  
*Chairman of Tunstall Healthcare, Sciensus & Versantis*  
*Held senior executive roles at Baxter, Bayer, Novartis & Bristol-Myers Squibb*  
Shareholding: 14,500



### Hilary Malone

**Board Member (2021)**  
*COO at Valo Health (US)*  
*Chief Regulatory Officer & Head of Global Regulatory Affairs at Sanofi (2013-2019)*  
*SVP & Head of Worldwide Regulatory Strategy at Pfizer (2009-2011)*  
Shareholding: 0



### Anders Gersel Pedersen

**Board Member (2018)**  
*+30 years in the Healthcare sector*  
*Ex-EVP R&D H.Lundbeck*  
*Chairman of Hansa Biopharma's Scientific Committee*  
Shareholding: 2,500



### Eva Nilsagård

**Board Member (2019)**  
*Board member of several companies, e.g. Adolife, Bufab, Itras, Abirane*  
*Ex-CFO of Vitrolife and Plasta*  
*Chairman of Hansa Biopharma's Audit Committee*  
Shareholding: 3,000



### Mats Blom

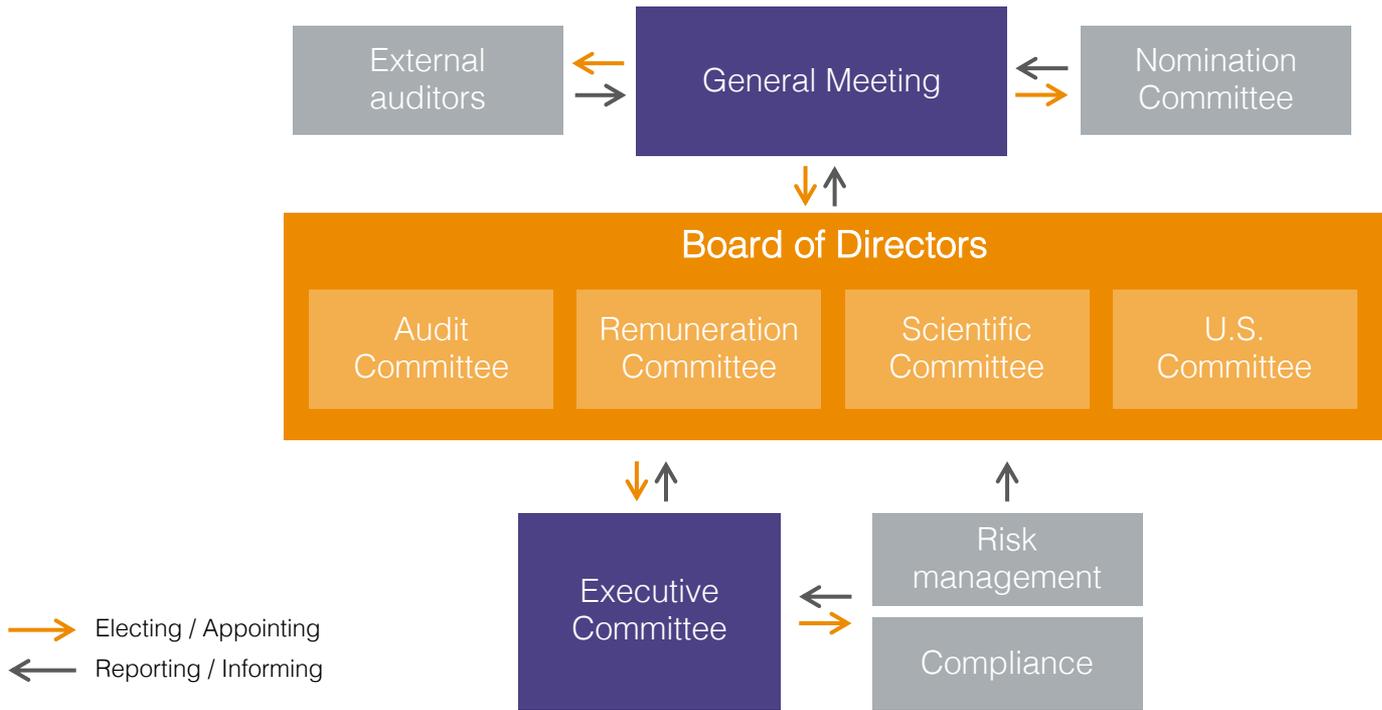
**Board Member (2019)**  
*CFO of NorthSea Therapeutics*  
*Ex-CFO Zealand Pharma*  
*Member of Hansa Biopharma's Audit Committee*  
Shareholding: 1,000



### Andreas Eggert

**Board Member ( 2018)**  
*Ex- SVP at H. Lundbeck A/S*  
*Ex-VP Wyeth/Pfizer in the U.S.*  
*Member of Hansa Biopharma's Audit Committee and Remuneration Committee*  
Shareholding: 5,500

# Hansa Biopharma's Governance Structure



# Strong technology protection

through patents and orphan drug designations

## Patent coverage out to 2035 in key markets

- Our lead product, imlifidase, is protected by six patent families including both granted patents and pending applications and cover the use of isolated imlifidase
- Patents cover use of isolated imlifidase at least in:

Medical use in IgG mediated medical conditions

Dosing in combination therapies incl. transplantation & oncology

Autoimmune diseases

Treatment of transplant rejection

## Orphan drug designation

- Orphan drug designation is granted to drugs intended for rare diseases (affecting max 5 patients in 10,000 persons in EU or affecting less than 200,000 patients in the US)
- The designation provides development and commercial incentives, including ten years of market exclusivity in the EU and seven years in the U.S., protocol assistance on the development of the drug, including clinical studies and certain exemptions from or reductions in regulatory fees

### EMA

#### Marketing Approval with orphan drug designation

- Conditional marketing approval for imlifidase, for the prevention of graft rejection following solid organ transplantation, was achieved in 2020

#### Orphan drug designation

- Imlifidase for the treatment of the rare and acute disease anti-GBM (2018)

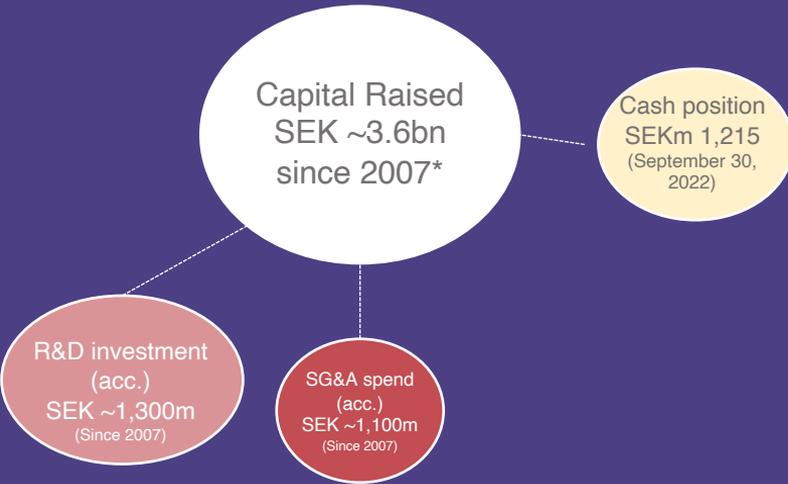
### FDA

#### Orphan drug designations

- Imlifidase for the prevention of antibody-mediated organ rejection in solid organ transplantation (2015)
- Imlifidase for the treatment of Guillain-Barré Syndrome (2018)
- Imlifidase for the treatment of the rare and acute disease anti-GBM (2018)

# Hansa Biopharma is financed through 2024

\$70 million non-dilutive financing transaction announced in July 2022 to support the continued development of Hansa's antibody-cleaving enzyme technology platform



\*Including SEK ~750m from NovaQuest financing agreement & SEK ~100m upfront payments from Sarepta

# Mid-term financial priorities

Our key financial priorities over the coming years will be focused on ensuring a successful European launch of Idefirix<sup>®</sup>, while targeting mid-term product profitability

Hansa is fully financed through 2024 and we expect to use our current cash position to:

**SEK ~1.2bn**

**(USD ~108m)**

in cash and short-term investments  
post recent financing



Fund the launch and commercial expansion of Idefirix<sup>®</sup>  
in kidney transplantation across Europe

Complete our EU post-approval commitments and patient enrollment in our ConfldeS study as well as advance our our long-term follow-up study to the five-year data readout in 2023

Advance our ongoing phase 2 programs in AMR and GBS and initiate a phase 3 clinical program in anti-GBM

Complete the preclinical program for our lead molecule from our next generation enzymes for repeat dosing (“NiceR”) and advance our initiatives in our other indications such as gene therapy and oncology

Fund working capital and general corporate purposes

# An exciting journey ahead!

## ✔ This is just the beginning!

- ✔ Clinical validation
- ✔ External validation
- ✔ Regulatory validation
- ✔ Validated manufacturing
- ✔ Strong IPR
- ✔ Exciting pipeline
- ✔ Strong team

## Key milestones to be achieved

- Expand Idefix<sup>®</sup> label in transplantation and in other solid organs
- Obtain regulatory approval in anti-GBM, GBS and AMR
- Demonstrate PoC in our next gen enzymes (NiceR)
- Expand partnerships in gene therapy and oncology
- Advance clinical studies with imlifidase as pre-treatment in Limb-Girdle, Duchenne and Pompe Disease therapies with Sarepta and AskBio
- Show PoC in new indications such as oncology
- Advance combination treatment into the clinic with argenx to potentially enable new therapeutics in transplantation and autoimmune diseases

## Our future

Hansa Biopharma is a recognized global leader in rare diseases across multiple broad therapeutic areas with several market leading products and a highly valuable pipeline of late stage drug candidates



Stock images

# Imlifidase in kidney transplantation

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# Idefirix® (imlifidase) has received conditional approval in the European Union

Low complexity transplants ← → Higher complexity transplants

~70% of patients<sup>1,2</sup>

15-20% of patients<sup>1,2</sup>

10-15% of patients<sup>1,2</sup>



Highly sensitized patients that are likely to be transplanted with a compatible donor

Highly sensitized patients unlikely to be transplanted under available KAS, including prioritization programs

## Idefirix® is indicated for

*desensitization treatment of highly sensitized adult kidney transplant patients with positive crossmatch against an available deceased donor.*

*The use of Idefirix® should be reserved for patients unlikely to be transplanted under the available kidney allocation system including prioritization programs for highly sensitized patients*

Potential patients

**idefirix®**  
imlifidase

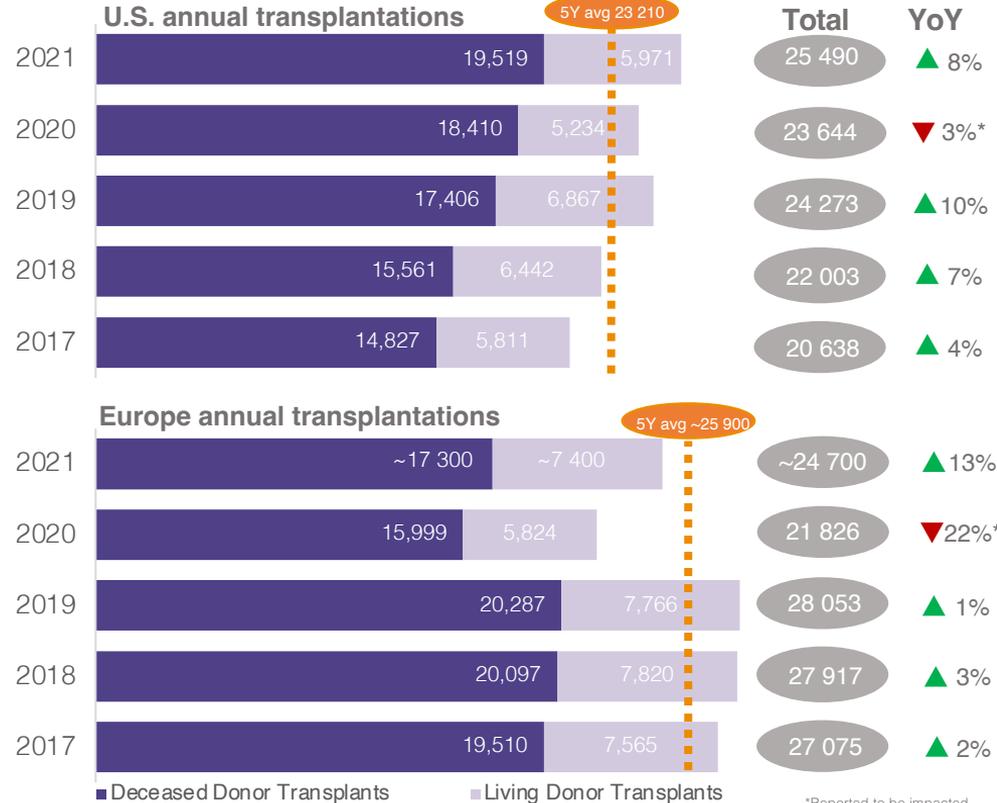
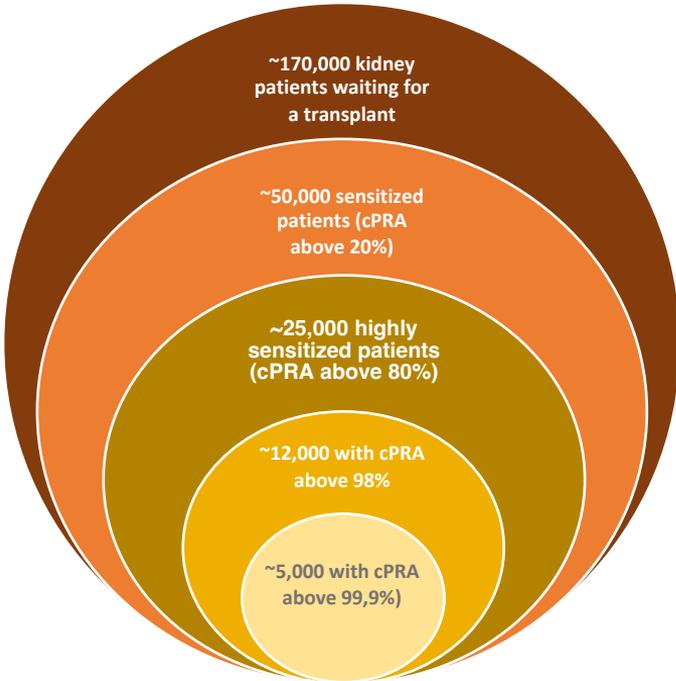


# The kidney transplantation landscape in Europe and the U.S.

Up to 15% of patients waiting for a new kidney are highly sensitized

~50,000 transplants done annually in the U.S. and Europe

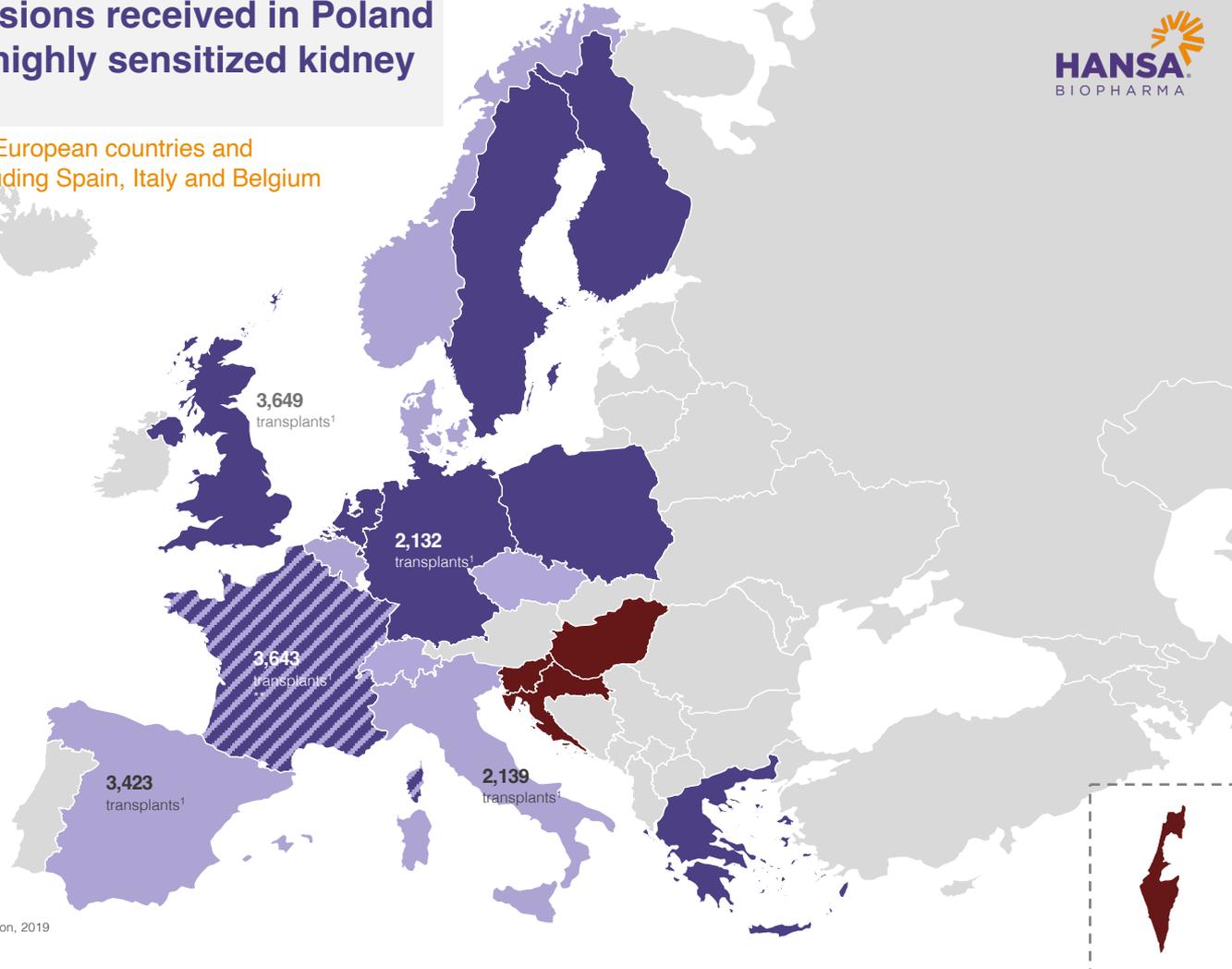
Breakdown of the kidney transplant waitlist in U.S. and EU



\*Reported to be impacted by the COVID-19 pandemic

# Positive reimbursement decisions received in Poland and Scotland for Idefirix® in highly sensitized kidney transplant patients

Market access has now been secured in nine European countries and procedures are ongoing in eight countries including Spain, Italy and Belgium



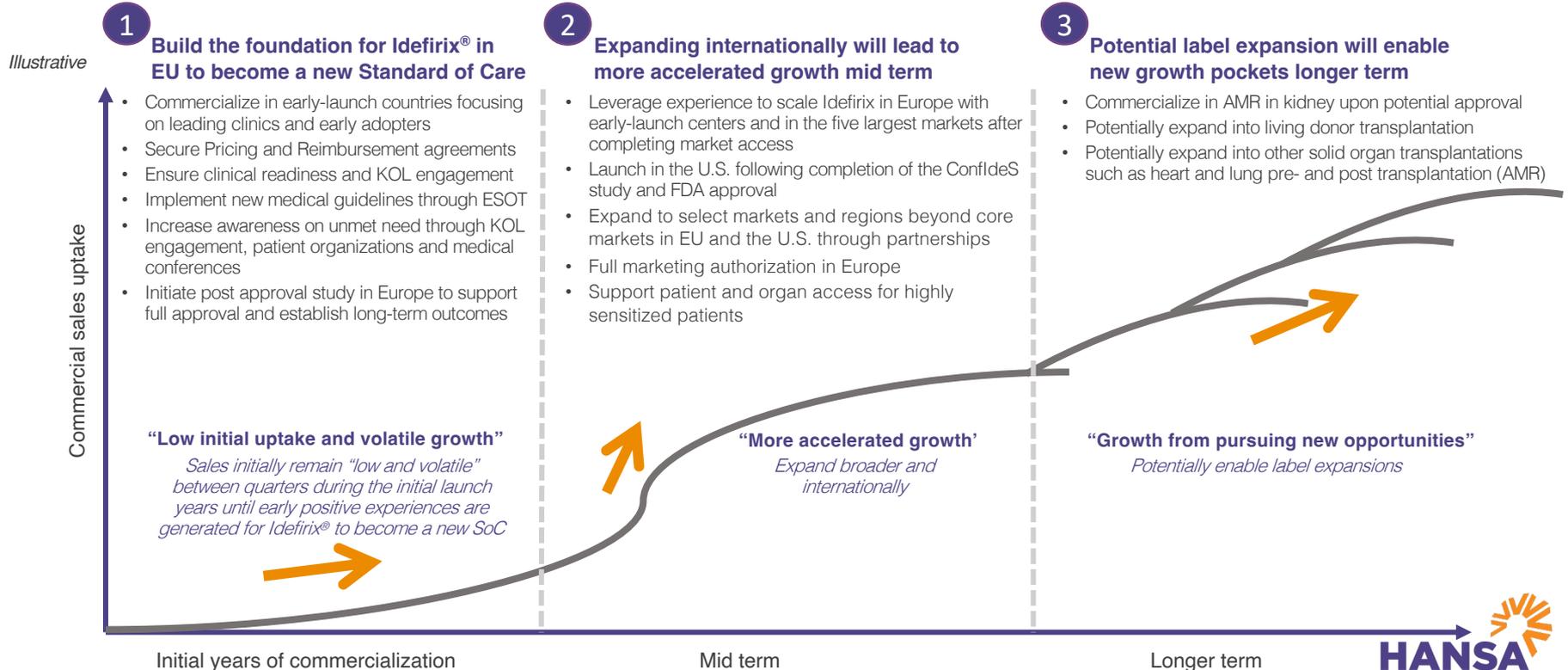
<sup>1</sup>Annual kidney transplantations 2019 (pre-Corona)

<sup>\*</sup>Transplantation data is from Global Observatory on Donation and Transplantation, 2019

<sup>\*\*</sup>Pricing & reimbursement obtained in France on an early access basis

# Our center focused and sequenced launch process will help build the foundation for Idefix<sup>®</sup> to become a new Standard of Care in transplantation

Idefix<sup>®</sup> is the first and only approved treatment in Europe for desensitization treatment of highly sensitized kidney transplant patients. The long-term market uptake is highly dependent on successful early experiences in key early adopter centers



# Approximately 10-15% of patients on wait list are highly sensitized

Highly sensitized patients are difficult to match with an available kidney

## Causes of sensitization include



Pregnancy



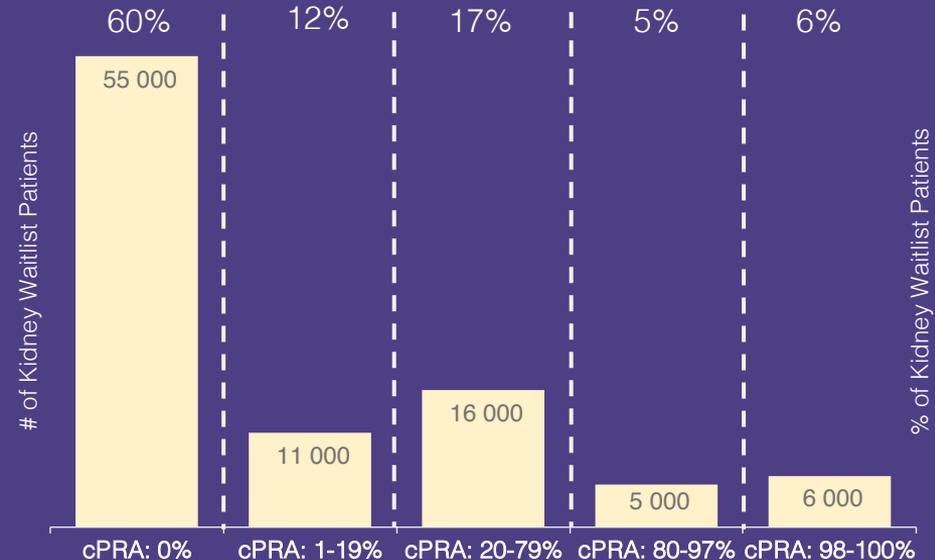
Blood transfusion



Previous transplantations

- Calculated Panel Reactive Antibodies (cPRA) is a measure for HLA-sensitization
- Inability to match or effectively desensitize patients remains a barrier for transplantation in highly sensitized patients
- Allocation Systems such as KAS and Eurotransplant rely on cPRA score to characterize patients for transplant

## US Kidney Waitlist Patients by cPRA



Source: Organ Procurement and Transplant Network

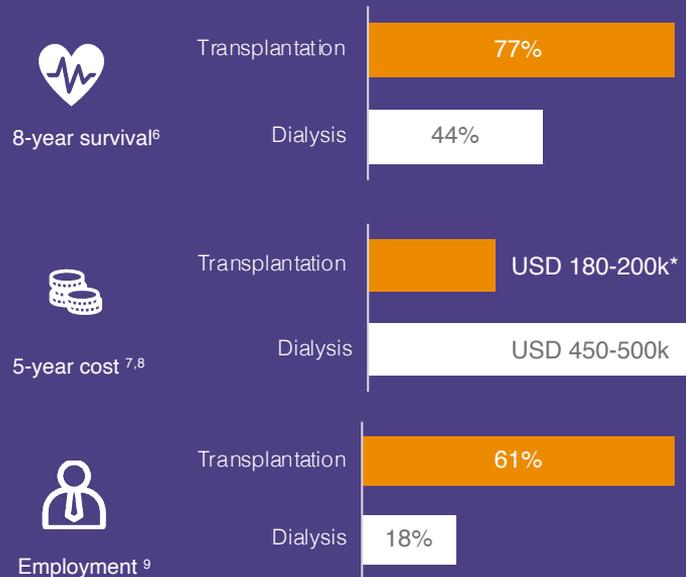
# Transplantation leads to better outcomes

Saves lives, reduce costs and increase quality of life, incl. gains for the society

## Several complications and risks with dialysis

- Undergoing dialysis treatment is associated with many complications and side effects incl. cardiovascular diseases<sup>1</sup>. In the long term, patients may also eventually lose access to dialysis as a result of failed ports, bad veins, and other factors<sup>2</sup>
- In general, patients on the kidney transplant waiting list and who are on dialysis have a lower quality of life than non-dialysed patients or patients who have been transplanted<sup>3</sup>
- First study in Europe on labor market outcomes demonstrates societal gains of enabling transplantation with three times as many transplant patients employed compared to dialysis patients.
- Lastly, extended dialysis is also a high-risk factor for removal from the transplant wait list<sup>6</sup>

## Better outcomes for transplantation patients



<sup>1</sup> Cozzolino et al., 2018

<sup>2</sup> Sinnakirouchenan and Holley, 2011 Shenoy, 2017

<sup>3</sup> Wyld et al., 2012

<sup>4</sup> Jarl et al. Transplantation, 2018, 102:1375-1381

<sup>5</sup> NHS blood and transplant, 2018.

<sup>6</sup> Orandi et al. N Engl J Med 2016;374:940-50

<sup>7</sup> www.usrds.org

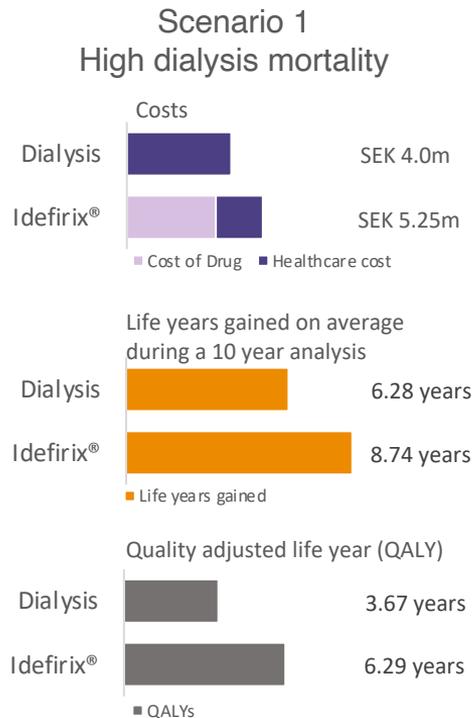
<sup>8</sup> Shehata et al, Transfus Med Rev 201, 24 Suppl 1: S7-S27

<sup>9</sup> Jarl et al. Transplantation, 2018, 102:1375-1381

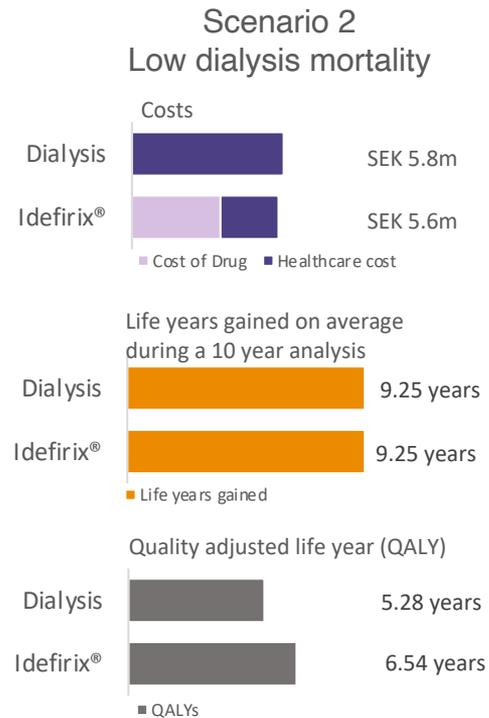
\*Cost of kidney transplantation and 5 years of immuno-suppression treatment<sup>6,7</sup>

# First HTA report (TLV) published in Sweden favourable to the use of Idefirix® in highly sensitized patients incompatible to a deceased donor

Two cost-effectiveness scenarios presented – both within the accepted threshold for costs related to new drugs  
 One scenario even concluding Idefirix treatment would lead to an overall cost saving – rare for orphan drugs



Costs per quality adjusted life year (QALY)  
 SEK 460k (EUR 45k)



Costs per quality adjusted life year (QALY)  
 SEK -170k (EUR -17k)

Scenario 2 supports Idefirix® as a cost saving drug

# First patient experiences with Idefirix (imlifidase) in highly sensitized kidney transplant patients post approval published

## 29-year-old woman transplanted with Idefirix at Erasmus Medical Center, Rotterdam

The woman has had kidney disease since childhood and has been dialysis dependent since 2016, after previously having had two transplantations where the organs were rejected.

Due to high levels of antibodies, it was virtually impossible for her to find a match through Eurotransplant but in March 2022, the 29-year-old was transplanted using Idefirix and is since doing well.

*“She gained new perspective on a good life through transplantation” says nephrologist Annelies de Weerd*

[Link article in Amazing Erasmus from July 7, 2022](#)

## 54-year-old man successfully transplanted at Vall d’Hebron, Barcelona after being on dialysis since 1984

The first patient transplanted in the post-approval study was a 54-year-old man who had been on dialysis since 1984. After two failed transplantation attempts in the 90s, the patient’s immune system became sensitized, with very high antibody levels.

In May 2022, the patient received imlifidase treatment followed by a kidney transplant. After three months, he continues to be followed up on and does not require dialysis.

*“This drug may open the door to transplantation for a group of highly sensitized individuals with virtually no option for a compatible transplant.” says Dr. Francesc Moreso*

[Link article from Vall d’Hebron news forum August 25, 2022](#)

# Completed and ongoing studies in kidney transplantation

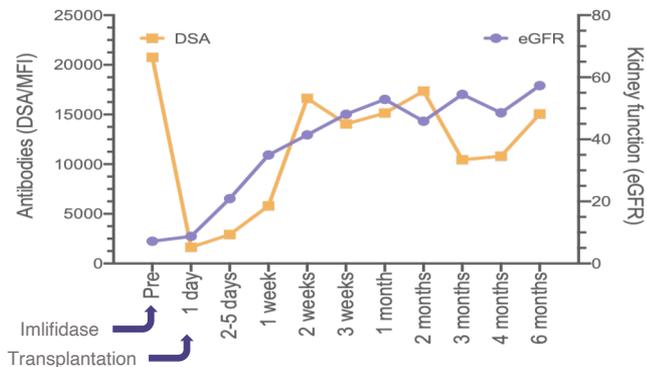
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# Imlifidase enabled kidney transplantation in 46 highly sensitized patients during clinical trials

## Pooled analysis from four Phase 2 trials

- Analysis included 46 patients
  - 50% had a cPRA of 100% (Average 99%)
  - 85% were crossmatch positive
  - 70% were retransplanted
- Donor Specific Antibody (DSA) levels rapidly decreased and all crossmatches were converted to negative, thus enabling transplantation in all patients
- At study completion, all patients alive and graft survival at 94% six months post transplantation
- 5 year follow-up data expected in 2023



## Study design of our four Phase 2 trials

- |                     |                       |   |
|---------------------|-----------------------|---|
| Study 02<br>Phase 2 | <b>Subjects</b>       | 8 patients  |
|                     | <b>Design</b>         | Single-center, single-arm, open-label   |
|                     | <b>Main objective</b> | Efficacy defined as Imlifidase dosing scheme resulting in HLA antibody levels acceptable for transplantation, within 24 hours |
| Study 03<br>Phase 2 | <b>Subjects</b>       | 10 patients   |
|                     | <b>Design</b>         | Single-center, single-arm, open-label, no prior desensitization   |
|                     | <b>Main objective</b> | Safety in the transplantation setting and efficacy defined as HLA antibody levels acceptable for transplantation              |
| Study 04<br>Phase 2 | <b>Subjects</b>       | 17 patients   |
|                     | <b>Design</b>         | Investigator initiated, single-center, single-arm, open-label. All patients had prior desensitization with IVIG and/or PLEX   |
|                     | <b>Main objective</b> | Safety in combination with Cedars Sinai's "standard protocol" for desensitization of highly sensitized patient                |
| Study 06<br>Phase 2 | <b>Subjects</b>       | 18 patients   |
|                     | <b>Design</b>         | Multicenter, multinational, single-arm, open-label  |
|                     | <b>Main objective</b> | Efficacy in creating a negative crossmatch test   |

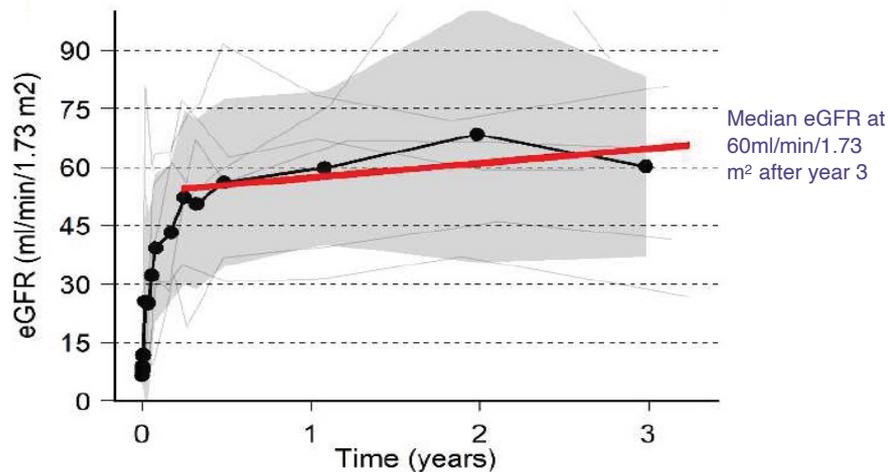
# 3-year follow up demonstrate graft survival of 84% after imlifidase treatment and transplantation

Data accepted for publication in the American Journal of Transplantation<sup>1</sup> [Link AJT article](#)  
30 patients participating in follow-up study at year three

## AMR frequency in line with other desensitization protocols

- Three-year follow-up data shows graft survival of 84% after imlifidase treatment and transplantation and a mean eGFR of 55 mL/min/1.73 m<sup>2</sup> (61 ml/min/m<sup>2</sup> for those without AMR)
- For a subgroup of patients (n=13) with cPRA of  $\geq 99.9\%$  graft survival was 92% and improved kidney function for patients with a mean eGFR at 60ml/min/1.73 m<sup>2</sup> after year three
- 38% of the patients experienced active antibody mediated rejection episodes (AMR) within the first six months, which compares with 25-60% of patients in the literature for highly sensitized patients<sup>2</sup>
- Only two AMR episodes were reported beyond the first 6 months. All AMRs were treated with standard therapies and no graft losses were attributed to AMR
- Patient survival 90% (three deaths unrelated to imlifidase)
- Long-term safety profile indicates no increase in the rates of infection or malignancy
- Next milestone expected in 2023 on the 5-year follow-up data

## Improved kidney function for patients with cPRA $\geq 99.9\%$



# U.S. ConfideS study: Completion of enrollment expected H2 2022; BLA submission expected 2024

## U.S. trial design

64 highly sensitized kidney patients with the highest unmet medical need

- Patients with a cPRA score of  $\geq 99.9\%$  will be enrolled
- First patients enrolled at Columbia University, NYC
- 39 patients enrolled across ten sites October 19, 2022

## 1:1 Randomization

- When a donor organ becomes available and a positive crossmatch with the intended recipient indicates that the organ is not compatible, the patient will be randomized to either imlifidase or to a control arm, where patients either remain waitlisted for a match or receive experimental desensitization treatment\*

## Primary endpoint

- Mean estimated glomerular filtration rate (eGFR) "kidney function" at 12 months.
- For randomized patients who do not undergo transplantation, lose their graft or die before 12 months, eGFR will be set to zero, consistent with kidney failure

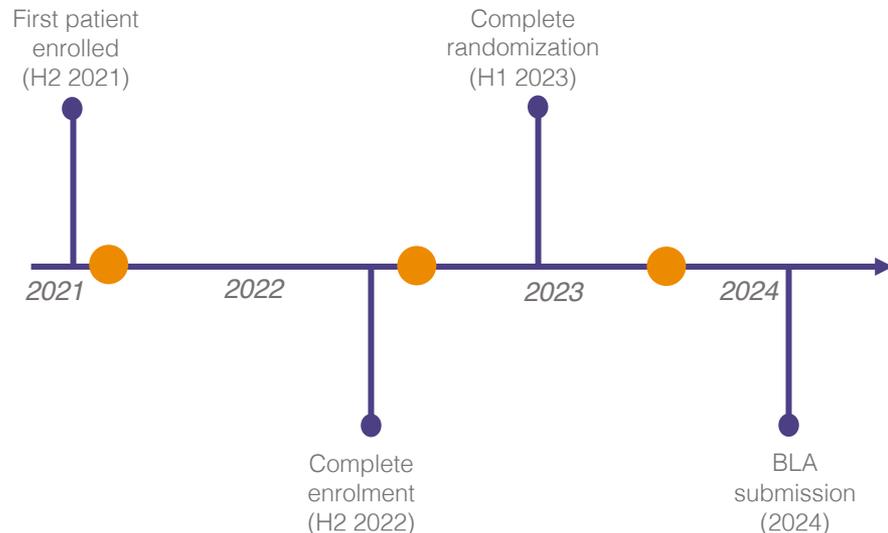
## Secondary endpoint

- Patient survival at 12 months

Up to 15 leading transplantation centers in the U.S. will be engaged in the study

- Robert A. Montgomery, M.D. Professor of Surgery and Director, NYU Langone Transplant Institute, NYC is appointed to be the principal investigator

## Timeline



\*Experimental desensitization treatment can include any combination of plasma exchange (PLEX), intravenous IVIg, anti-CD20 antibody, and eculizumab. Link to the full protocol at [ClinicalTrials.gov](https://clinicaltrials.gov)

# U.S. kidney transplantation landscape

Our ConfideS study is currently enrolling patients across ten leading transplantation centers across seven states covering ~10% of annual kidney transplants in the U.S.; Aim to have up to 15 centers recruiting patients

>23,000<sup>1</sup> annual kidney transplantations

~71%<sup>1</sup> deceased donor

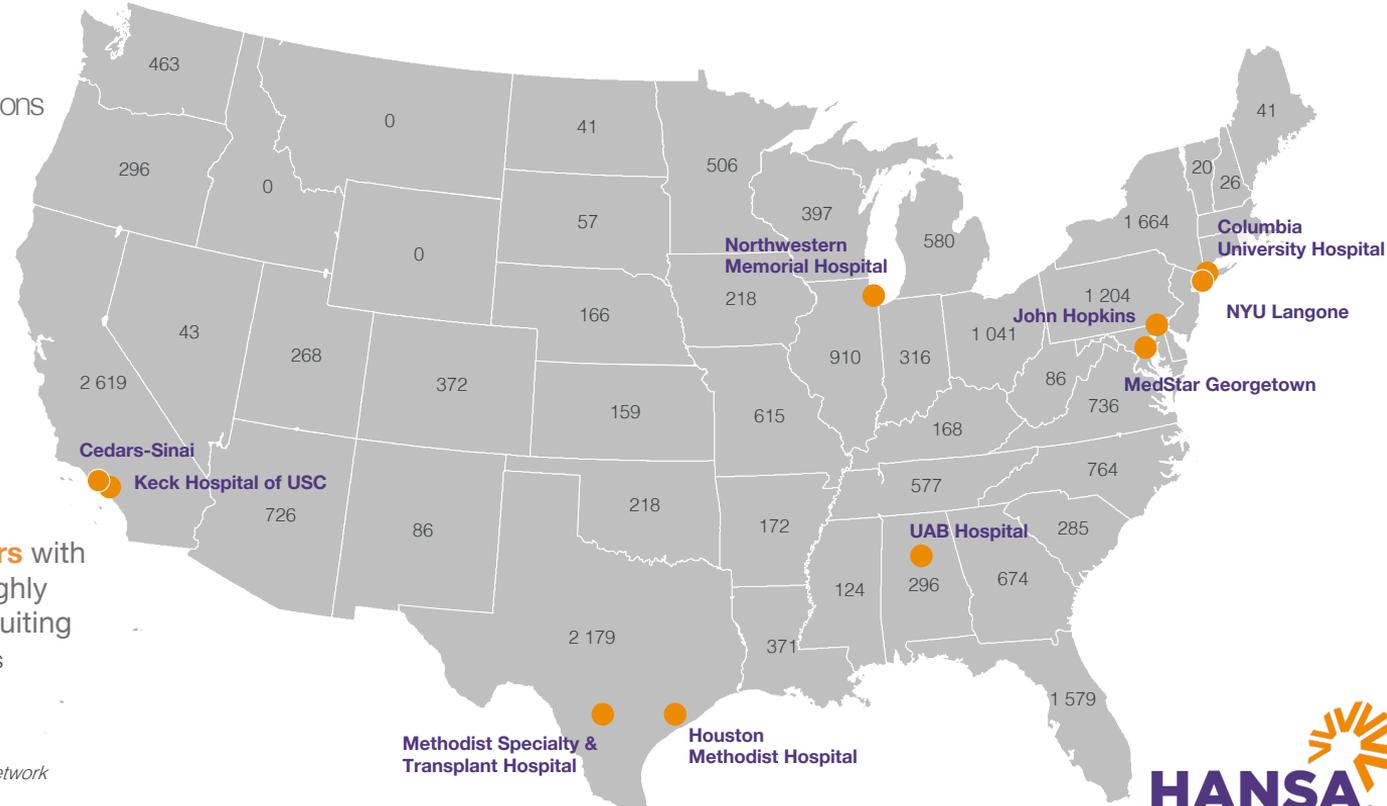
~90,000<sup>2</sup> waiting for a kidney transplant

10-15%<sup>3</sup> of waitlisted patients are highly sensitized

Ten leading transplantation centers with experience in desensitization and highly sensitized patients are currently recruiting

2,542<sup>1</sup> combined annual kidney transplants

334<sup>1</sup> highly sensitized (>80% cPRA)



<sup>1</sup>2019 data from Organ Procurement & Transplantation Network

<sup>2</sup>United Network for Organ Sharing

<sup>3</sup>EDQM. (2020). International figures on donation and Transplantation 2019 and SRTT Database and individual assessments of allocation systems

## First patient treated in post-authorization efficacy study (PAES) of Idefirix® (imlifidase) in highly sensitized kidney transplant patients

The study will provide further important insights regarding Idefirix® desensitization treatment of highly sensitized kidney transplant patients

### An open-label Phase 3 study in 50 patients

- First patient was treated by Dr. Oriol Bestard, Chair of Nephrology and Kidney Transplantation at Vall d'Hebron University Hospital in Barcelona
- Study will enroll 50 highly sensitized patients with positive crossmatch against an available deceased donor across multiple countries and centers in Europe
- The study is an obligation under the conditional marketing authorization for Idefirix® granted by EMA in August 2020, in order to complete a full marketing authorization in the EU
- The aim will be to confirm the long-term efficacy and safety of Idefirix® with the primary objective to determine the one-year graft failure-free survival of the Idefirix® treated and transplanted patients.
- In addition, a total of 50-100 patients undergoing compatible kidney transplantation at the participating centers will be included and serve as a non-comparative concurrent reference cohort, with no formal comparison, to contextualize the one-year graft failure-free survival of the Idefirix® treated patients



# Study to assess imlifidase in combination to optimize patient outcome

in highly sensitized patients with donor specific antibodies (DSA) rebound and antibody mediated kidney transplant rejection

## Trial design (ClinicalTrials.gov ID: NCT05049850)

The study is designed to assess if imlifidase in combination with bortezomib<sup>1</sup>, belatacept<sup>2</sup>, rituximab<sup>3</sup> and IVIg<sup>4</sup> can suppress donor specific antibodies (DSA) and the occurrence of antibody-mediated rejection (AMR) in transplant patients with a positive crossmatch towards their living donor.

### Open label, single arm study

- Imlifidase is administered within the 24-hour prior to a living donor transplantation

### Primary endpoint

- Proportion of patients with DSA rebound (up to 3 months after transplantation)
- Rebound of DSA may cause AMR and is thus a risk for graft loss

### Secondary endpoint

- Proportion of patients with AMR (up to 6 months after transplantation)

The study will be run at the NYU Langone Transplant Institute and is expected to commence in 2022

<sup>1</sup> bortezomib, a proteasome inhibitor which has activity against mature plasma cells, the source of DSA

<sup>2</sup> belatacept, a fusion protein which is crucial in blocking T-cell co-stimulation and which is effective in reducing de novo DSA generation in humans

<sup>3</sup> rituximab, an anti-CD20 monoclonal antibody that targets B-cells and which is an immunomodulatory agent

<sup>4</sup> intravenous immunoglobulin (IVIg) which is commonly used in desensitization regimens and for the treatment of AMR

Link to the full protocol at [ClinicalTrials.gov](https://clinicaltrials.gov)



## Study 01 Phase 1

# The 01 study results

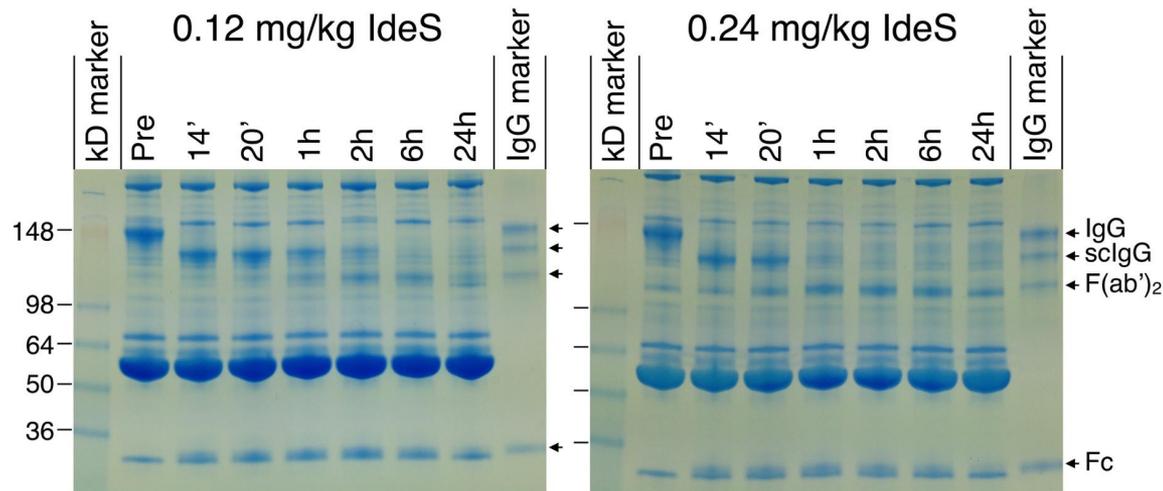
Data showed complete removal of IgG and a good tolerability profile

### Efficacy

- ✓ Rapid degradation of IgG in serum in subjects dosed with 0.12 and 0.24 mg/kg imlifidase. Imlifidase had full effect within 6 hours. The entire IgG pool was converted into F(ab')<sub>2</sub> and Fc-fragments. Maximal effect was accomplished 2-6 hours after dosing.

### Safety

- ✓ Newly synthesized intact IgG was clearly detectable in all subjects after 1-2 weeks after dosing. After 3 weeks the level of intact IgG constituted the main IgG fraction in serum



### CLINICALTRIALS.GOV ID

NCT01802697 (2013/2014)

### SUBJECTS

29 (20 active plus 9 placebo) healthy subjects (Sweden)

### DOSES/FOLLOW UP TIME

The starting dose was 0.01 mg/kg BW and the highest dose group received 0.24 mg/kg BW

### MAIN OBJECTIVES

- The objectives were to assess safety, efficacy in IgG cleavage, pharmacokinetics and immunogenicity of imlifidase following intravenous administration

### STUDY DESIGN

- Randomized placebo-controlled dose-escalation study with 29 (20 active plus 9 placebo) healthy subjects

### STATUS

Completed

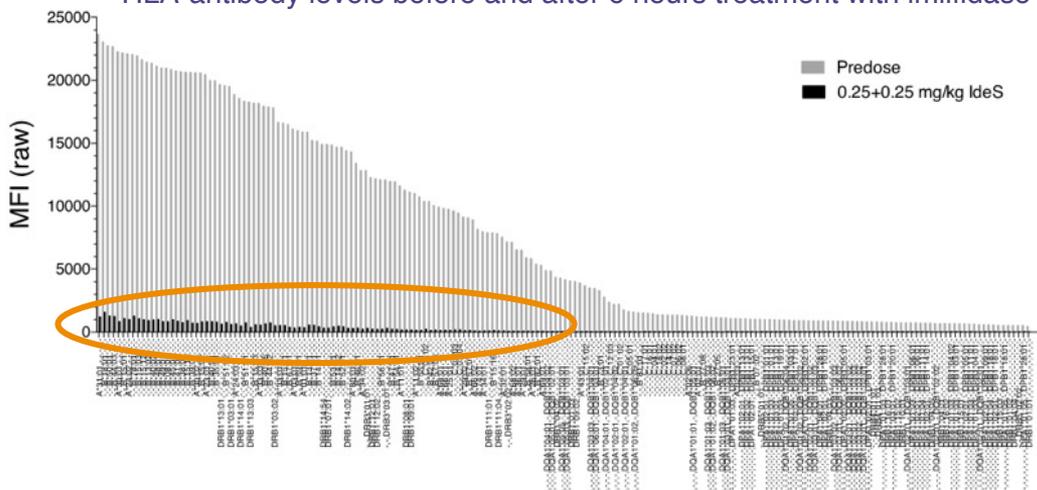
- The 01 study showed that Imlifidase was considered safe to use  
48

## The 02 study results

Data showed that 1-2 doses of imlifidase at 0.25 mg/kg BW resulted in HLA antibody levels acceptable for transplantation<sup>1</sup>

- ✓ Imlifidase is well tolerated in patients with chronic kidney disease
- ✓ Efficacy results strongly support further development in the patient population
- ✓ The first HLA-incompatible transplantation ever after desensitization with imlifidase was performed in one of these patients (2014)

HLA-antibody levels before and after 6 hours treatment with imlifidase



<sup>1</sup> Lorant et al (2018) American Journal of Transplantation (2018)

## Study 03 Phase 2

# The 03 study proved safety and efficacy

HLA antibodies at acceptable levels; enabling transplantation in all patients

CLINICALTRIALS.GOV ID

NCT02475551

SUBJECTS

10 Patients (Sweden)

DOSES/FOLLOW UP TIME

0.25 and 0.50 mg/kg during 180 days

MAIN OBJECTIVES

- Safety in the transplantation setting
- Efficacy defined as HLA antibody levels acceptable for transplantation

STUDY DESIGN

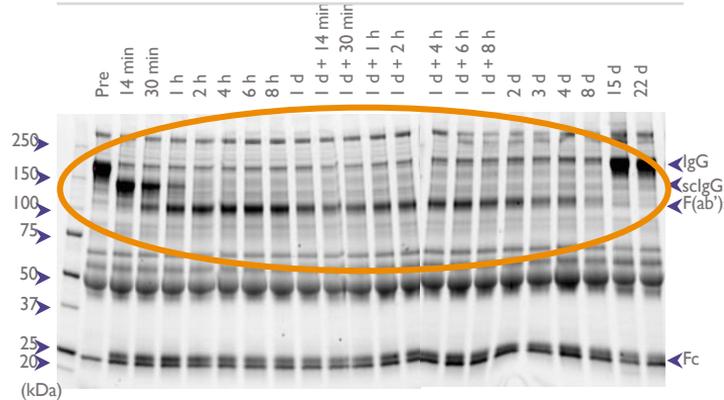
- Single-center, single-arm, open-label, no prior desensitization
- Similar design as 13-HMedIdeS-02 but transplantation part of protocol
- In deceased and living donors

STATUS

Completed

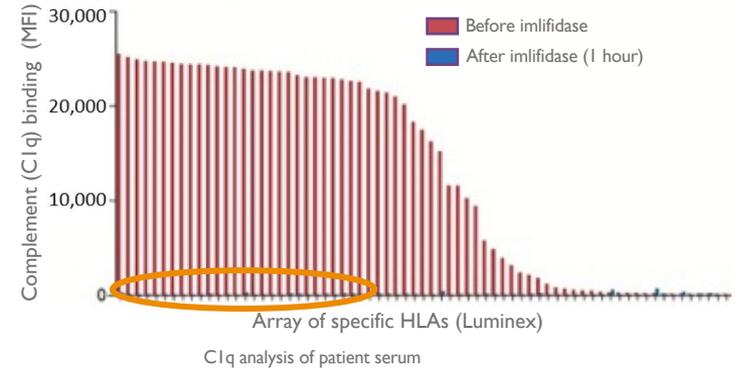
- Proved safety and efficacy with HLA antibodies at acceptable levels; enabling transplantation in all patients

## Analysis of IgG in patient serum before and after imlifidase treatment



SDS-PAGE analysis of patient serum

## Analysis of complement binding HLA antibodies before and after imlifidase



CIq analysis of patient serum

## Protocol

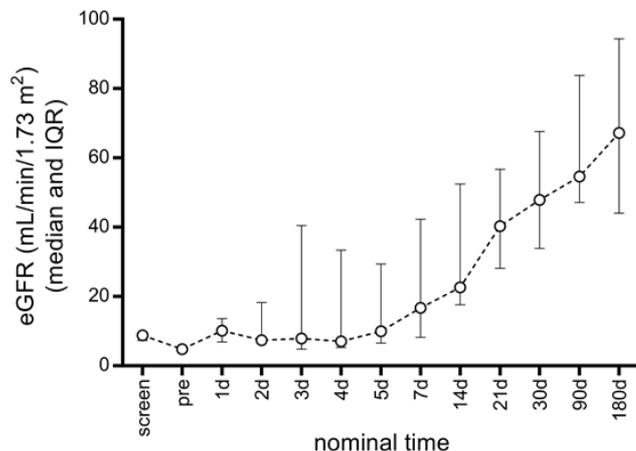


## Study 04 Phase 2

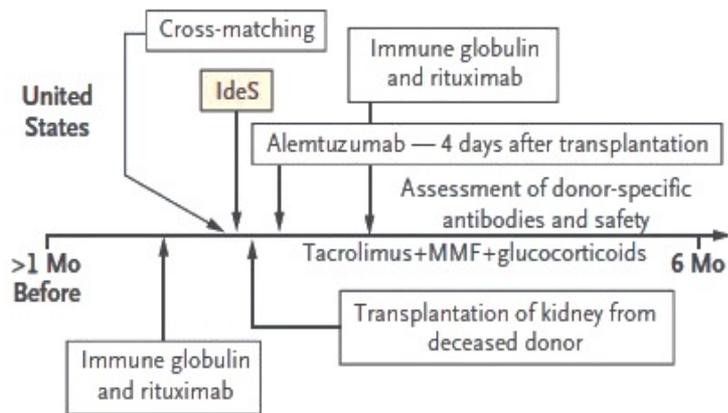
# The 04 study results

Study proved safety and efficacy with Cedar Sinai's standard protocol (rituximab and IVIg)

## Graft function (eGFR) post six months



## Cedar's desensitization protocol in combination with imlifidase



### CLINICALTRIALS.GOV ID

NCT024226684

### SUBJECTS

17 Patients (US)

### DOSES/FOLLOW UP TIME

0.24 mg/kg 180 days

### MAIN OBJECTIVES

- Safety in combination with Cedars Sinai's "standard protocol" for desensitization of highly sensitized patients
- Efficacy in preventing AMR

### STUDY DESIGN

- Investigator initiated study
- Investigator sponsored IND
- Imlifidase to desensitize patients previously treated with rituximab and IVIg
- Deceased donors only

### STATUS

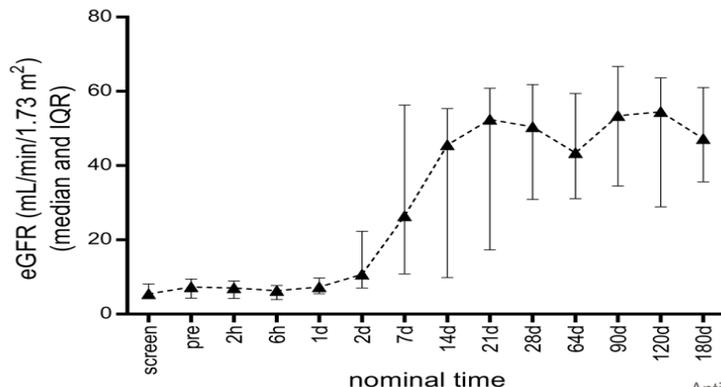
Completed

## Study 06 Phase 2

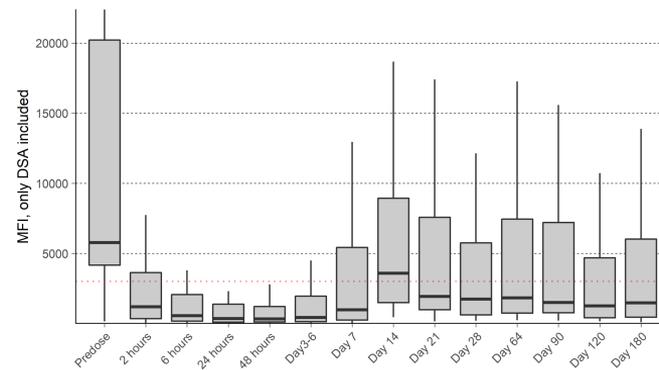
# The 06 study results

Study showed proved safety and efficacy in making highly sensitized patients eligible for kidney transplantation

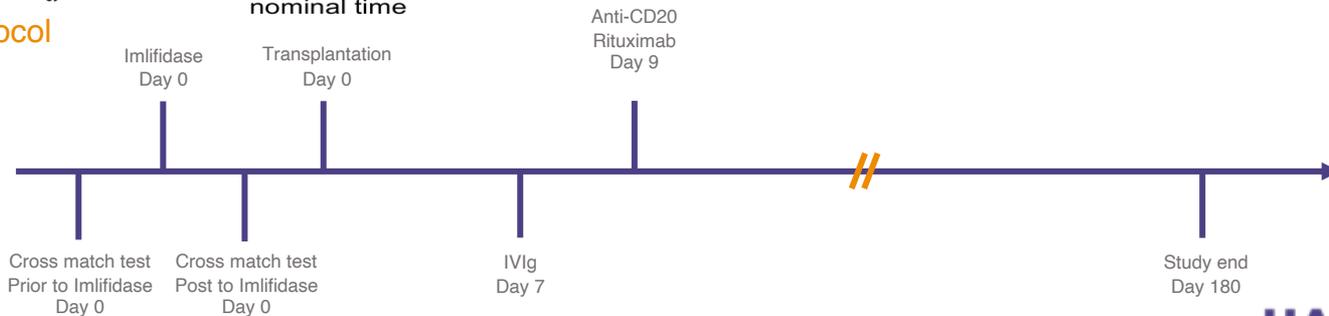
## Graft function (eGFR) post imlifidase



## DSA level pre-dose and post imlifidase



## Protocol



CLINICALTRIALS.GOV ID

NCT02790437

### SUBJECTS

18 Patients (US+Sweden+France)  
19 safety set, 18 efficacy set

### DOSES/FOLLOW UP TIME

0.25 mg/kg 180 days

### MAIN OBJECTIVES

- Efficacy in creating a negative crossmatch test

### STUDY DESIGN

- Multicenter, multinational, single-arm, open-label Included patients who may have had prior unsuccessful desensitization or patients in whom it was unlikely to be effective

### STATUS

Completed

# Completed studies with imlifidase in transplantation

STUDY	SUBJECTS/ COUNTRY	STUDY DESIGN	PRIMARY ENDPOINT	SECONDARY ENDPOINTS	STATUS/ PUBLICATION
Study 01 Phase 1	29 subjects 	<ul style="list-style-type: none"> <li>Randomized placebo-controlled dose-escalation study with 29 (20 active plus 9 placebo) healthy subjects</li> </ul>	<ul style="list-style-type: none"> <li>Safety and tolerability</li> </ul>	<ul style="list-style-type: none"> <li>Efficacy in IgG cleavage, the pharmacokinetics (PK) and immunogenicity of imlifidase</li> </ul>	Complete PLOS ONE (2015) <sup>1</sup>
Study 02 Phase 2	8 subjects 	<ul style="list-style-type: none"> <li>Single-center, single-arm, open-label</li> </ul>	<ul style="list-style-type: none"> <li>Dosing resulting in HLA-antibody reduction (MFI&lt;1100)</li> </ul>	<ul style="list-style-type: none"> <li>Efficacy: HLA antibody reduction acceptable for transplantation (MFI &lt;1100 as measured in SAB assay)</li> </ul>	Complete Lorant et al (2018) American Journal of Transplantation <sup>2</sup>
Study 03 Phase 2	10 subjects 	<ul style="list-style-type: none"> <li>Single-center, single-arm, open-label</li> <li>No prior desensitization</li> </ul>	<ul style="list-style-type: none"> <li>Safety: AEs, clinical laboratory tests, vital signs, ECGs</li> </ul>	<ul style="list-style-type: none"> <li>Efficacy: HLA antibody reduction acceptable for transplantation (MFI &lt;1100 as measured in SAB assay)</li> </ul>	Complete The New England Journal of Medicine (2017) <sup>3</sup>
Study 04 Phase 2	17 subjects 	<ul style="list-style-type: none"> <li>Investigator initiated study, Single-center, single-arm, open-label</li> <li>All patients had prior desensitization with IVIG and/or plasmapheresis</li> </ul>	<ul style="list-style-type: none"> <li>Assessment of efficacy in eliminating DSAs in DSA and flow cytometry positive, highly sensitized patients</li> <li>Assessment of safety</li> <li>Assessment of efficacy/kidney function</li> </ul>	<ul style="list-style-type: none"> <li>Serum creatinine (0-6 months)</li> <li>Proteinuria (0-6 months)</li> <li>DSA at multiple timepoints posttransplant (day 0, D30, D90, D180)</li> </ul>	Complete The New England Journal of Medicine (2017) <sup>3</sup>
Study 06 "Highdes" Phase 2	18 subjects 	<ul style="list-style-type: none"> <li>Multicenter, multinational, single-arm, open-label Included pts who may have had prior unsuccessful desensitization or pts in whom it was unlikely to be effective</li> </ul>	<ul style="list-style-type: none"> <li>Crossmatch conversion in DSA+ patients who have a positive XM test to their available LD or DD</li> </ul>	<ul style="list-style-type: none"> <li>DSA reduction at multiple timepoints (2, 6, 24, 48 h after imlifidase)</li> <li>Time to create negative CDC XM test and/or flow cytometry (FACS) XM test</li> <li>Safety</li> </ul>	Complete Annals of Surgery (Lonze et al, only New York patients) Montgomery et al ATC abstract (2019) <sup>4</sup>
Long-term follow-up study	Up to 46 subjects 	<ul style="list-style-type: none"> <li>A prospective, observational long-term follow-up study of patients treated with imlifidase prior to kidney transplantation</li> </ul>	<ul style="list-style-type: none"> <li>Long-term graft survival in patients who have undergone kidney transplantation after imlifidase administration</li> </ul>	<ul style="list-style-type: none"> <li>Patient survival, kidney function, comorbidity, treatments and QoL</li> <li>Safety</li> <li>DSA</li> <li>Immunogenicity</li> </ul>	Ongoing

<sup>1</sup> Winstedt et al., "Complete Removal of Extracellular IgG Antibodies in a Randomized Dose Escalation Phase I Study with the Bacterial Enzyme IdeS – A Novel Therapeutic Opportunity", PLOS ONE 2015, 10(7)

<sup>2</sup> Lorant et al., "Safety, immunogenicity, pharmacokinetics and efficacy of degradation of anti-HLA antibodies by IdeS (imlifidase) in chronic kidney disease patients" Am J Transplant. 2018 Nov;18(11):2752-2762

<sup>3</sup> Jordan et al., "IgG Endopeptidase in Highly Sensitized Patients Undergoing Transplantation", N Engl J Med 2017;377:442-53.

<sup>4</sup> Montgomery et al., "Safety And Efficacy Of Imlifidase In Highly-sensitized Kidney Transplant Patients: Results From A Phase 2 Study" ATC Abstract, 2019

# Medical Advisory Board in kidney transplantation



## Professor Stanley Jordan

(Chairman) M.D., Ph.D., Director of Kidney Transplantation and Transplant Immunology, Kidney and Pancreas Transplant Center and Director of Division of Pediatric and Adult Nephrology, Cedars-Sinai Medical Center, Los Angeles, California



## Professor Robert Montgomery

M.D., Ph.D., FACS, Director at NYU Langone Transplant Institute, New York, NY, USA



## Professor Christophe Legendre

M.D., Ph.D. Professor at Paris Descartes University and Head of the Adult Nephrology and Transplantation unit at Necker Hospital in Paris.



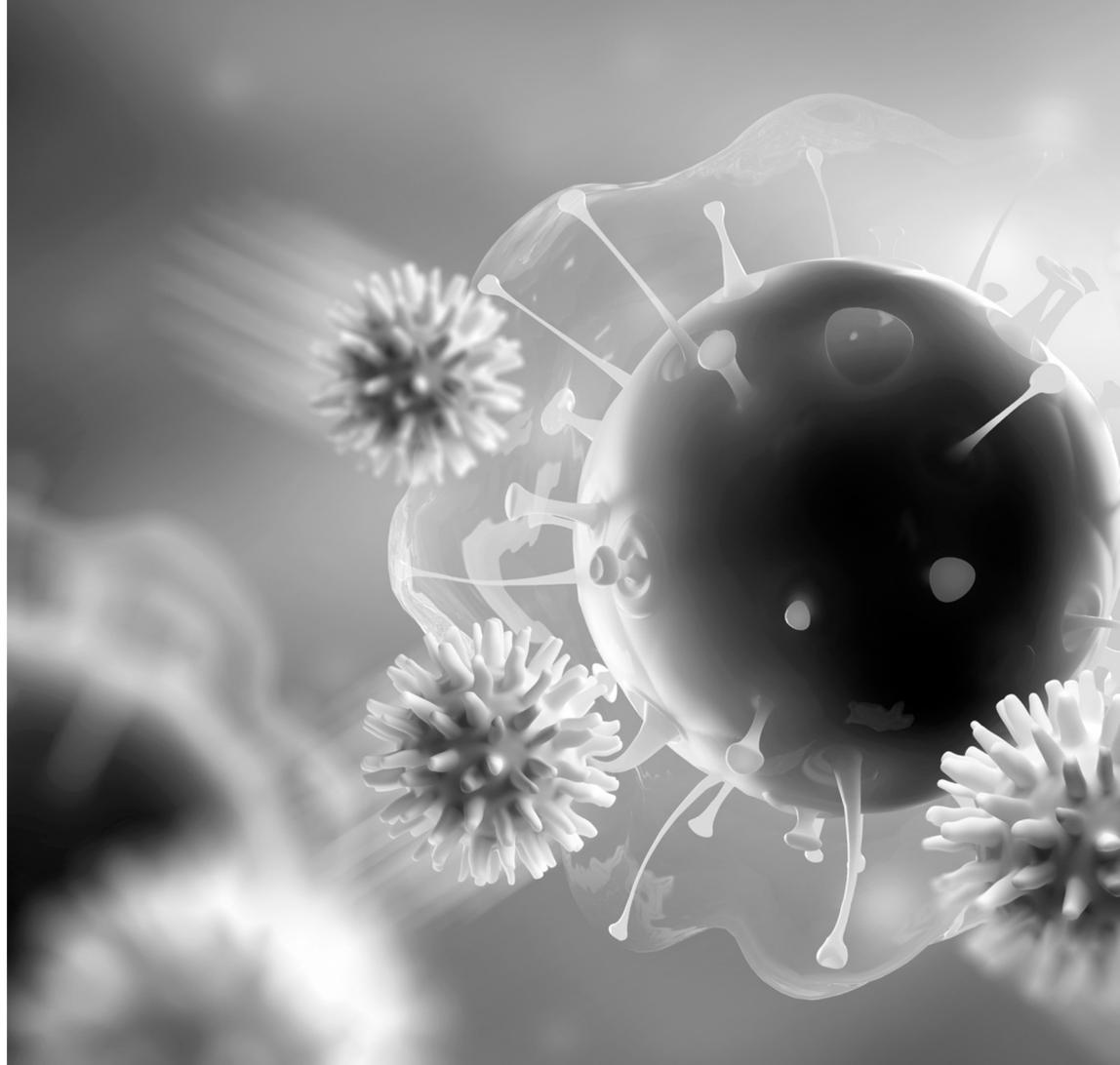
## Professor Kathryn Wood

Ph.D. Fellow of the Academy of Medical Sciences, Professor of Immunology in the Nuffield Department of Surgical Sciences, University of Oxford, England, runs the Transplantation Research Immunology Group



# Our antibody cleaving enzyme technology

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# Broad clinical pipeline in transplantation and auto-immune diseases

Candidate/Project	Indication	Research/Preclinical	Phase 1	Potentially Pivotal/Phase 2	Phase 3	Marketing Authorization	Marketed	Next Anticipated Milestone
Imlifidase	EU: Kidney transplantation in highly sensitized patients <sup>1,2</sup>						EU: Additional agreements around reimbursement from H2'21	
	US: Kidney transplantation in highly sensitized patients <sup>1,2</sup>						Completion of enrollment (64 patients) H2'22	
	Anti-GBM antibody disease <sup>3</sup>						Pivotal Phase 3 study expected to commence in 2022 (50 patients)	
	Antibody mediated kidney transplant rejection (AMR)						First data read-out H2 2022	
	Guillain-Barré syndrome (GBS)						Completion of enrollment (30 patients) H2'22/H1'23	
	Pre-treatment ahead of gene therapy in Limb-Girdle (Partnered with Sarepta)						Preclinical research	
	Pre-treatment ahead of gene therapy in Duchenne (Partnered with Sarepta)						Preclinical research	
	Pre-treatment ahead of gene therapy in Pompe disease (Partnered with AskBio)						Preclinical research	
NiceR	Recurring treatment in autoimmune disease, transplantation and oncology						Completion of GLP toxicology studies in 2022	
EnzE	Cancer immunotherapy						Research	

<sup>1</sup> Results from the Phase 1 study have been published, Winstedt et al. (2015) PLOS ONE 10(7)

<sup>2</sup> Lorant et al American Journal of Transplantation and 03+04 studies (Jordan et al New England Journal of Medicine)

<sup>3</sup> Investigator-initiated study by Mårten Segelmark, Professor at the universities in Linköping and Lund

 Completed

 Planned

 Ongoing

 Post approval study running in parallel with commercial launch

# Continuous progress in our ongoing clinical programs

Enrollment status  
Oct 19, 2022

## Antibody Mediated Rejection Phase 2 study

- 30/30 patients enrolled in the AMR phase 2 study
- Enrollment completed May 2022
- First data read out expected toward the end of 2022\*
- Data from the Phase 2 program will determine the path forward for imlifidase in patients with active AMR episodes



- Patients enrolled
- Patients remaining

## Guillain-Barré Syndrome Phase 2 study

- 20/30 patients enrolled in the GBS program
- Ten centers are active and open for recruitment; Additional measures will be implemented to accelerate recruitment in the coming months.
- Aim to complete enrollment of GBS patients H2'22/H1'23
- Enrollment expected to be boosted from higher infection rates during winter season, while increased capacity at the enrollment sites is also expected to support a faster enrollment
- Aim to communicate first high-level data read out in H2 2023

Enrollment status  
Oct 19, 2022

## Anti-GBM Phase 3 study

- FDA has accepted Hansa's Investigational New Drug (IND) application to proceed with a pivotal global Phase 3 study
- Aim to commence the planned anti-GBM study later this year, as previously guided. Study will target 50 patients\*



- Patients enrolled
- Patients remaining



- Patients enrolled
- Patients remaining

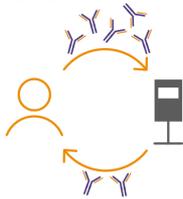
## U.S. ConfldeS Phase 3 study

- Randomized, controlled trial in highly sensitized kidney transplant patients across up to 15 centers
- 39/64 patients enrolled for randomization
  - Aim to complete of enrollment expected toward end of 2022
  - Aim to complete randomization n the first half 2023
  - BLA submission is expected in 2024 under the accelerated approval path

# Development of IgG-modulating technologies

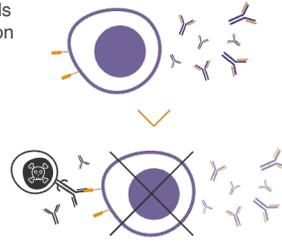
Mechanisms can be both complementary and competing

**PLEX, plasmapheresis, immunoadsorption**  
Mechanically removes antibodies from circulation



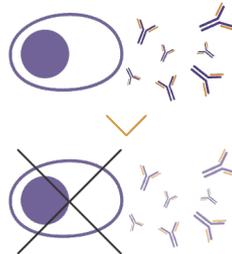
1950s

**B-cell depleting mAbs**  
Lowering antibody levels through B-cell elimination



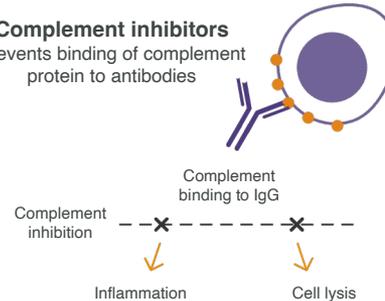
1990s

**Proteasome inhibitors**  
Depletes antibody producing long-lived plasma cells and lowers overall immunoglobulin levels



2000s

**Complement inhibitors**  
Prevents binding of complement protein to antibodies

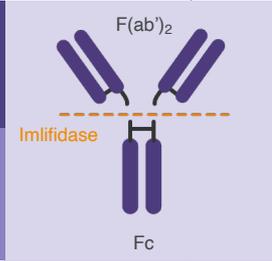


2010s

**Imlifidase – IgG-cleaving enzyme**

Deactivates IgG within 2-6 hours through enzymatic cleavage. IgG-free window for approximately one week

Unique mechanism-of-action is the basis for competitive advantage vs other IgG-modulating therapies

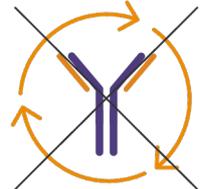


2020s

**IV/SC immunoglobulins**  
IVIg/SCIg contains healthy antibodies that replaces pathogenic antibodies



**FcRn-inhibitors**  
Lowering IgG through blocking of antibody recycling

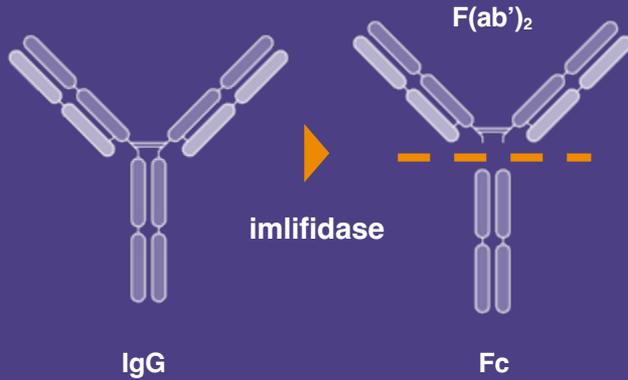


# Imlifidase mode of action

Novel approach to effectively eliminate pathogenic IgG

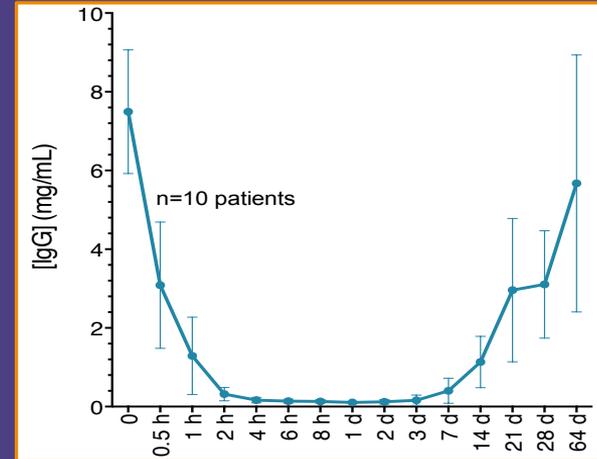
## Proven mechanism of action

- Interacts with Fc-part of IgG with extremely high specificity
- Cleaves IgG at the hinge region, generating one F(ab')<sub>2</sub> fragment and one homo-dimeric Fc-fragment



## Inactivation of IgG in human serum

- Rapid onset of action that takes down IgG below detectable level in 2-6 hours post 15 min infusion
- IgG antibody-free window for approximately one week



# Our unique antibody cleaving enzyme technology may have relevance across a range of indications

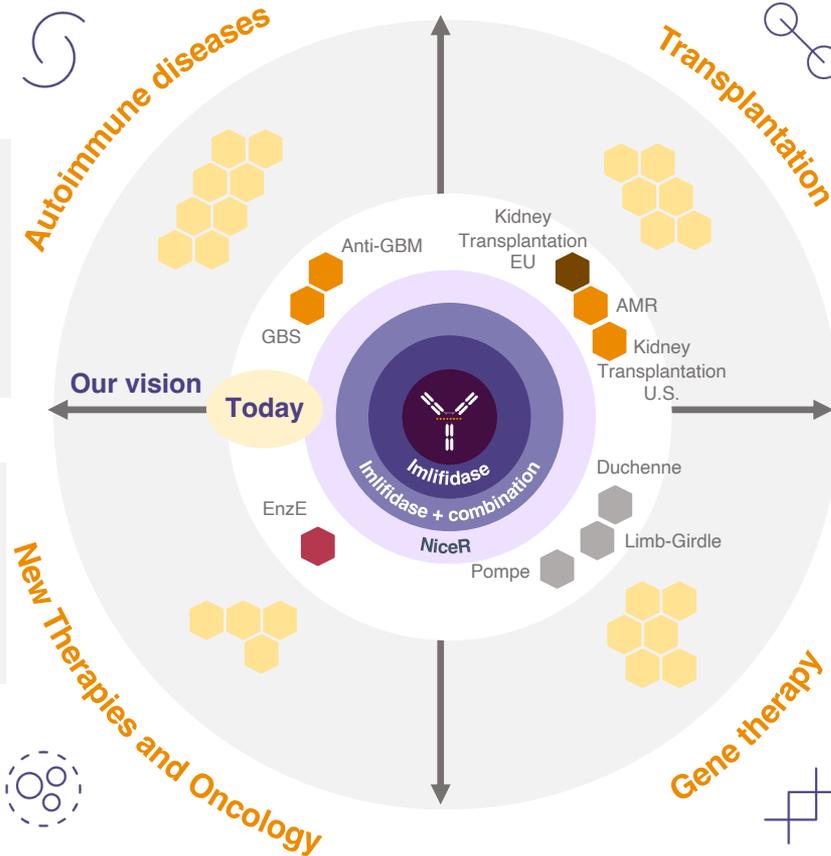
Targeting rare IgG mediated diseases

## Anti-GBM paves the way for development in other autoimmune diseases

- Rapidly progressive glomerulonephritis
- Neurological disorders
- Skin and blood disorders

## IgG-cleaving enzymes to enable or even potentiate cancer therapy

- Allogenic stem cell (bone marrow) transplantation (HSCT)
- Enzyme-based antibody Enhancement (EnzE)



## Expanding our commercial franchises

- Regulatory approval (conditional)
- Clinical development
- Partnership (preclinical development)
- Preclinical development
- Potential indications (currently not pursued)

## Shaping a new standard for desensitization will help enable new indications in transplantations

- Antibody mediated rejection (AMR) in kidney transplantation
- Other transplantation types

## Exploring opportunities in gene therapy

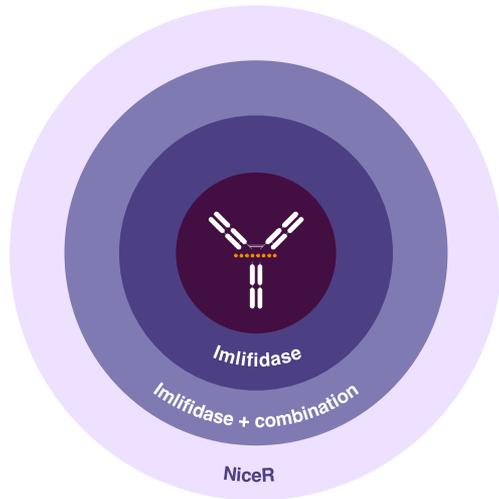
- Encouraging preclinical data published in Nature
- Validation through collaborations with Sarepta and AskBio
- Wide indication landscape beyond

# The technology platform is the primary basis for achieving our vision

Targeting rare IgG mediated diseases and conditions

## Key opportunities:

- Expanding into **new indications**
- Reduce immune response to IgG-cleaving enzyme, i.e. allow **repeated treatment**
- **Combination therapy**, i.e. induction and maintenance therapy



IgG levels after imlifidase treatment in highly sensitized patients  
to the first 30 days



IgG levels after imlifidase treatment in highly sensitized patients – 1 year and beyond

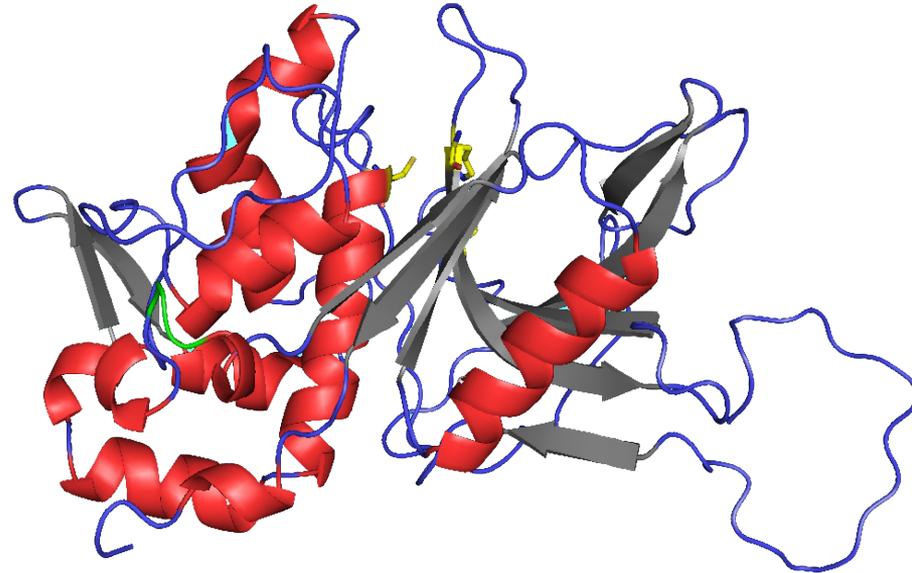


# Our IgG antibody-cleaving enzyme, imlifidase

## Origins from *Streptococcus pyogenes*

- Cysteine protease derived from an Immunoglobulin G (IgG)-degrading enzyme of *Streptococcus pyogenes*
- Contains only one cysteine - no disulfide bridges
- Monomeric protein with a molecular mass of 35 Kilo Dalton
- Isoelectric point of 6.1
- The coding gene for imlifidase is cloned and expressed in *Escherichia coli*

## Imlifidase consists of 311 amino acids



# Imlifidase is a lyophilized product formulation

Shelf life of 18 months at 2-8° Celsius storage

## Imlifidase will be infused in 15 minutes

- The product for commercial supply will be a lyophilized (cold chain) powder concentrate (11 mg solution) for infusion currently with a claimed shelf life of 18 months at 2-8°C storage. Ongoing stability studies indicate a shelf life of at least 24 months.
- Each vial is filled with 1.2 mL of a 10 mg/mL solution before freeze drying (=12 mg). Extractable volume after reconstitution with 1.2 mL sterile water is 1.1 mL of 10 mg/mL solution - resulting in 11 mg product
- The protein concentration, 10 mg/mL, has desirable characteristics with respect to not form aggregates
- Continuous stability programs ongoing to study changes in protein characteristics and performance.
- Imlifidase dose is clinically set to 0.25 mg/kg bodyweight (11 mg / 0.25 mg/kg = 44 kg (BW) / vial content) 2R vial size is suitable for the content



# Supply Chain

## Imlifidase in kidney transplantation



Drug Development



Drug substance  
Manufacturer (API)



Logistics of bulk product  
- handling of drug substance product



Final product  
(packaging and labelling)



Distribution



Clinics and hospitals



Patients



Drug product manufacturer  
(upscaling)



# Manufacturing process

Hansa has close collaborations with highly experienced European based third party CMOs

## Drug substance production process (API)

### Northway Biotech



#### Fermentation/ harvesting

- Working Cell Bank
- Pre-Cultivation
- Main Cultivation
- Cell Harvest

#### Protein purification

- Cell Disruption
- Protein Release

#### Protein purification cont.

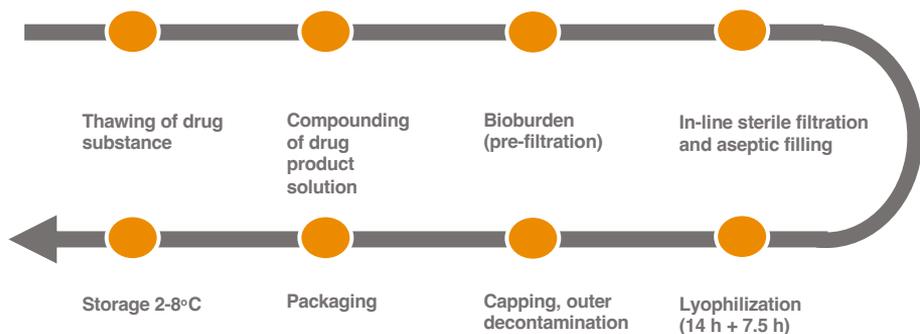
- Ion Exchange Chromatography
- Ceramic Hydroxy Apatite Chromatography
- Hydrophobic Interaction Chromatography
- Ultrafiltration/ Diafiltration

#### Filling

- Formulation, filtration, filling and storage (-80°C)

## Drug product production process (upscaling)

### Baxter



#### Thawing of drug substance

#### Compounding of drug product solution

#### Bioburden (pre-filtration)

#### In-line sterile filtration and aseptic filling

#### Storage 2-8°C

#### Packaging

#### Capping, outer decontamination

#### Lyophilization (14 h + 7.5 h)



#### Facts

- Based in Vilnius, Lithuania
- Start-up Year: 2004
- Capacity: 300 L fermentor (1000 L fermentor in 2020)
- Certifications: GMP compliance, Manufacturing authorization license
- Inspections: National regulatory agency (EU), EU/US customer inspections, FDA mock inspection



#### Facts

- Based in Halle/Westfalen Germany
- Start-up Year: 2001 (contract manufacturing)
- Capacity: 6-35 L drug product solution per batch (5,000-30,000 vials)
- Certifications: GMP compliance, Manufacturing authorization license
- Inspections: National regulatory agency (EU), FDA, EU/US customer inspections



# Clinical development programs

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# Hansa's antibody cleaving enzyme technology

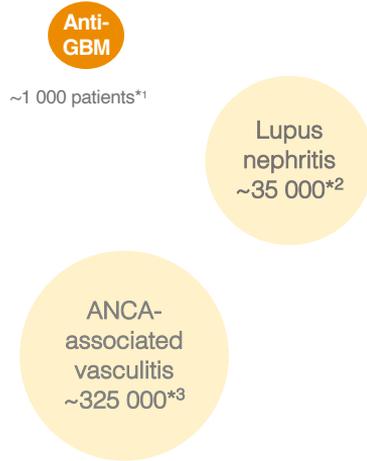
may have relevance in several autoimmune diseases where IgG plays an important role in the pathogenesis

- Clinical programs
- Potential autoimmune indications (currently not pursued)

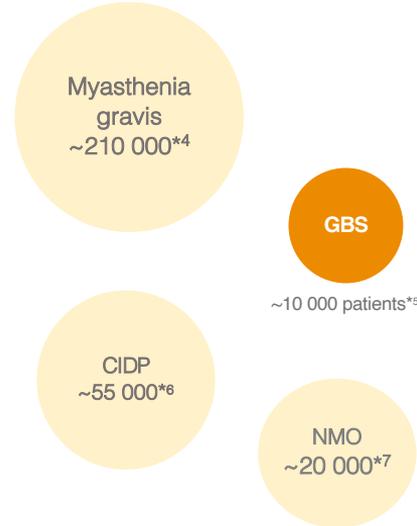


\*Total disease populations in EU & US, based on prevalence and population data

## Rapidly progressive glomerulonephritis



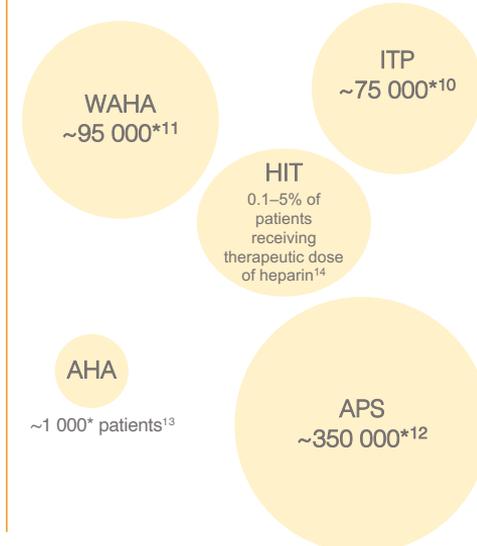
## Neurological disorders



## Skin disorders



## Blood disorders



**CIDP:** Chronic inflammatory demyelinating polyradiculoneuropathy  
**NMO:** Neuromyelitis optica  
**EBA:** Epidermolysis bullosa acquisita  
**ITP:** Immune thrombocytopenia  
**WAHA:** Warm antibody hemolytic anemia  
**APS:** Antiphospholipid syndrome  
**AHA:** acquired hemophilia A  
**HIT:** Heparin-induced thrombocytopenia

<sup>1</sup>DeVrieze, B.W. and Hurley, J.A. *Goodpasture Syndrome*. StatPearls Publishing, Jan 2021.

<sup>2</sup><https://www.ncbi.nlm.nih.gov/books/NBK459291/> [accessed 2021-03-29]

<sup>3</sup>Patel, M et al. *The Prevalence and Incidence of Biopsy-Proven Lupus Nephritis in the UK*. Arthritis & Rheumatism, 2006.

<sup>4</sup>Berti A, Cornec D, Crowson CS, Specks U, Matteson EL. *The Epidemiology of ANCA Associated Vasculitis in the U.S.: A 20 Year Population Based Study*. Arthritis Rheumatol. 2017;69.

<sup>5</sup>*Myasthenia Gravis*. National Organization for Rare Disorders. <https://rarediseases.org/rare-diseases/myasthenia-gravis/> [accessed 2021-03-29]

<sup>6</sup>*Guillain-Barré syndrome*. Orpha.net. [https://www.orpha.net/consor/cgi-bin/OC\\_Exp.php?id=GBSExpert-2103](https://www.orpha.net/consor/cgi-bin/OC_Exp.php?id=GBSExpert-2103) [accessed 2021-03-29]

<sup>7</sup>*Chronic Inflammatory Demyelinating Polyneuropathy: Considerations for Diagnosis, Management, and Population Health*. The American Journal of Managed Care. <https://www.ajmc.com/view/chronic-inflammatory-demyelinating-polyneuropathy-considerations-for-diagnosis-management-and-population-health> [accessed 2021-03-29]

<sup>8</sup>Marrie, R.A. *The Incidence and Prevalence of Neuromyelitis Optica*. International Journal of MS Care. 2013 Fall: 113-118

<sup>9</sup>Mehren, C.R. and Gniadecki, R. *Epidermolysis bullosa acquisita: current diagnosis and therapy*. Dermatol Reports, 2011-10-05

<sup>10</sup>Wentzell, S. et al. *Prevalence Estimates for Pemphigus in the United States*. JAMA Dermatol, May 2019: 627-629.

<sup>11</sup>*Immune Thrombocytopenia*. National Organization for Rare Disorders. <https://rarediseases.org/rare-diseases/immune-thrombocytopenia/> [accessed 2021-03-29]

<sup>12</sup>*Warm Autoimmune Hemolytic Anemia*. National Organization for Rare Disorders. <https://rarediseases.org/rare-diseases/warm-autoimmune-hemolytic-anemia/> [accessed 2021-03-29]

<sup>13</sup>Ilvinoova, E. et al. *Prevalence and Significance of Non-conventional Antiphospholipid Antibodies in Patients With Clinical APS Criteria*. Frontiers in Immunology, 2018-12-14.

<sup>14</sup>NORD. *Acquired Hemophilia* [accessed 2022-10-17], available at <https://rarediseases.org/rare-diseases/acquired-hemophilia/>

<sup>15</sup>Hogan M, Berger JS. *Heparin-induced thrombocytopenia (HIT): Review of incidence, diagnosis, and management*. Vascular Medicine. 2020;25(2):160-173. doi:10.1177/1358863X19898253

# Anti-GBM, a rare acute autoimmune disease

Positive read-out from phase 2 study with 2/3 of anti-GBM patients achieving dialysis independence six months after treatment

## Anti-GBM

- Indication: Antibodies are directed against an antigen intrinsic to the glomerular basement membrane (GBM) causing acute injury of kidney and/or lung
- Anti-GBM affects 1.6 in a million people annually with majority of patients losing their kidney function<sup>1,2</sup>, requiring chronic dialysis and kidney transplantation
- Phase 2 study concluded that imlifidase leads to rapid clearance of anti-GBM antibodies, with two-thirds of patients achieving dialysis independence six months after treatment
- U.S. FDA has accepted Hansa's Investigational New Drug (IND) application to proceed with a Phase 3 study of imlifidase in 50 anti-GBM patients across U.S. and EU.
- The new global phase 3 study is expected to commence in 2022
- Our Anti-GBM program obtained Orphan Drug designation from both FDA and European Commission in 2018



## Anti-GBM Phase 2

# Imlifidase in Anti-GBM

The idea is that imlifidase in anti-GBM patients may cleave IgG bound to the GBM within a few hours and prevent further renal damage

Today only a fraction of the total IgG antibodies are removed with plasma exchange and IgG in the interstitial tissue and bound to the GBM remains

### CLINICALTRIALS.GOV ID

NCT03157037 (Since March 2017)

### SUBJECTS

15 patients targeted. Patients will be monitored for six months  
Recruitment at 15 clinics

### DOSES/FOLLOW UP TIME

Dosage 0.25mg/kg 180 days follow up

### MAIN OBJECTIVES

- Primary objective is to evaluate the safety and tolerability of imlifidase on background of standard of care, and assess efficacy based on renal function at six months after treatment

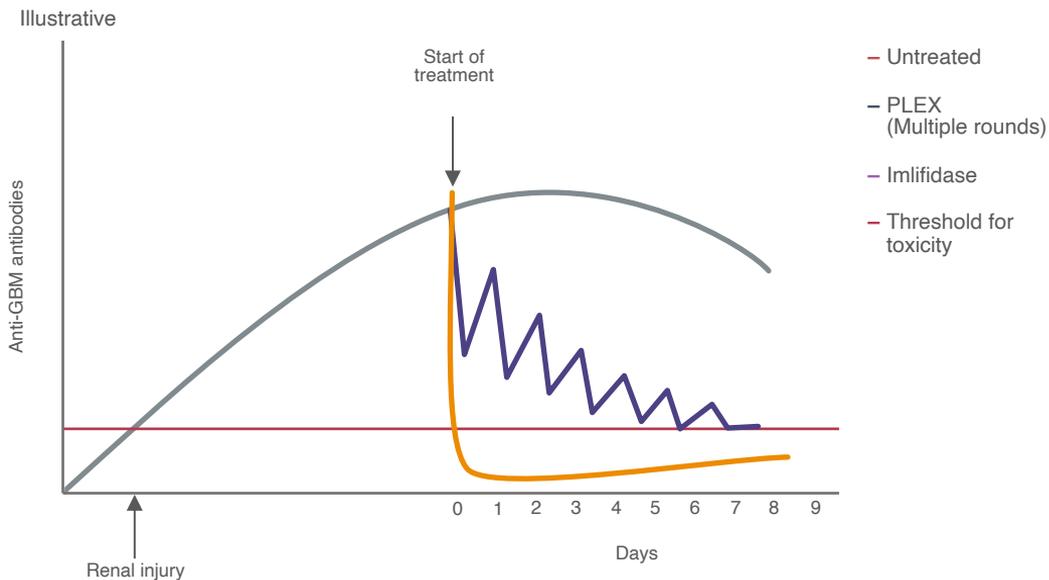
### STUDY DESIGN

- Open label, multicenter, single arm Phase 2 study with adverse renal prognosis
- Investigator initiated study

### STATUS

Plans to initiate a Phase 3 study of imlifidase to treat 50 anti-GBM patients

## Potential of using imlifidase vs. PLEX in anti-GBM







# Phase 2 study to evaluate safety, tolerability and efficacy of imlifidase

in patients with Guillain-Barré syndrome (GBS)

## Design of the GBS trial

- Open-label, single-arm trial in combination with SoC treatment given within 10 days of onset of GBS
- Infusion of 0.25mg/kg imlifidase at Day 1, followed by IVIg (400 mg/kg) at Days 3-7, and follow-up of PK/PD for 14 days, safety and efficacy parameters at 6 months and 12 months
- 30 patients targeted and matched to controls based on geographical location, age, presence of diarrhea, severity of condition
- Outcome compared to matched controls (up to 4 controls per patients) from the IGOS<sup>1</sup> database

## Main objective

- To evaluate safety, tolerability, PK/PD, and efficacy of imlifidase in GBS patients in combination with SoC intravenous immunoglobulin

## Status

- 20/30 patients enrolled end of Q2 2022
- 10/10 sites are recruiting patients
- Recruitment will be done across France, UK and The Netherlands
- Enrollment is expected to be completed in H2 2022 (temporary halted during 2019 due to Covid-19)
- First data readout H2 2023

**In 2018, the FDA granted Orphan Drug Designation to imlifidase for the treatment of GBS**

# Guillain-Barré syndrome

GBS is an acute autoimmune attack on the peripheral nervous system

## GBS can affect anyone at any age

- GBS is an acute autoimmune attack on the peripheral nervous system, which rapidly and progressively weakens extremities.
- Only parts of the patients fully recover from GBS, thus a high unmet medical need for new treatments; 40% lose strength and have pain while mortality is 3-7%
- Addressable population of ~10,000<sup>1</sup> per year in 7MM<sup>2</sup>
- Current Standard of Care is treatment with IVIG or PLEX
- The Phase 2 study is an open-label, single arm, multi-center study evaluating the safety, tolerability and efficacy of imlifidase in GBS patients in combination with standard of care intravenous immunoglobulin (IVIg)
- 20/30 patients enrolled end of Q2 2022. Ongoing recruitment of patients at 10 centers across France, UK and the Netherlands.
- Initiatives implemented to support the completion of enrollment incl. simplification of the protocol and increased capacity; Up to six new sites to be added in the coming months
- Completion of enrollment expected in H2 2022/H1 2023 with a first data read-out in H2 2023
- In 2018, the FDA granted Orphan Drug Designation to imlifidase for the treatment of GBS

<sup>1</sup> McGrogan et al. Neuroepidemiology 2009;32(2):150-63.

<sup>2</sup> 7MM = Seven major markets – US, Germany, UK, France, Spain, Italy, and Japan



## GBS Phase 2

# New Phase 2 study initiated in GBS to evaluate safety, tolerability and efficacy of imlifidase in GBS patients

### CLINICALTRIALS.GOV ID

NCT03943589 (2019)

### SUBJECTS

30 patients targeted  
Recruitment at ten clinics in Europe  
(France, U.K. and the Netherlands)

### DOSES/FOLLOW UP TIME

Dosage 0.25mg/kg follow up 180 days  
and 12 months

### MAIN OBJECTIVES

- safety and effectiveness of imlifidase in patients diagnosed with GBS

### STUDY DESIGN

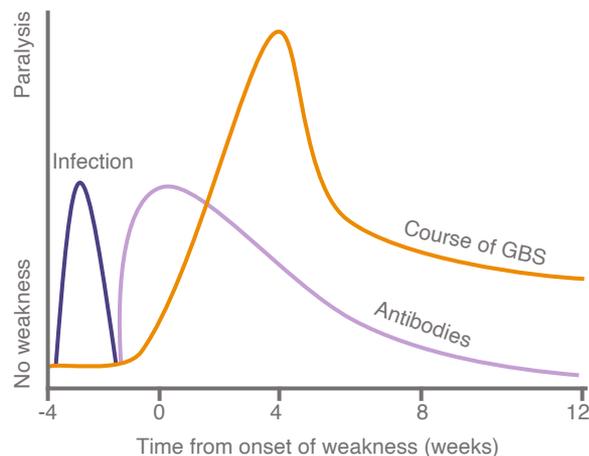
- Study is an open-label, single arm, multi-center trial evaluating safety, tolerability and efficacy of imlifidase, in combination with standard of care, IVIg, to treat GBS

### STATUS

Ongoing recruitment

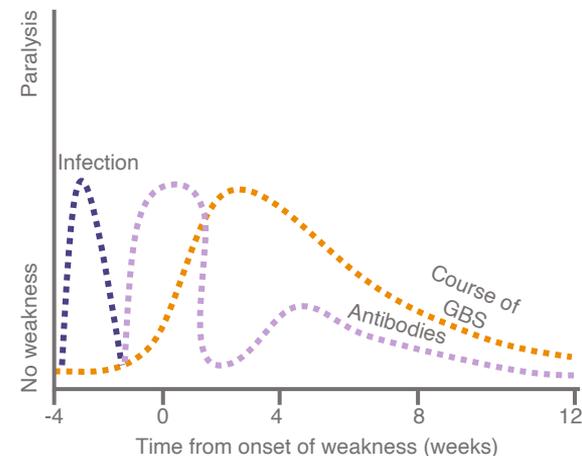
## Today's Standard of Care IVIg or PLEX

*Illustrative*



## Potential with imlifidase

*Illustrative*



# Enrollment in Phase 2 program in Antibody Mediated Rejection (AMR) post kidney transplantation completed

Long term graft survival is challenged by AMR episodes post transplantation

## Indication

- Acute antibody mediated rejection episodes post transplantation occurs in 5-7% of kidney transplants<sup>1</sup> annually and is a significant challenge to long term graft survival
- Today's standard of care include plasma exchange, steroids and IVIg.
- There is no approved treatment for AMR

## Phase 2 Study

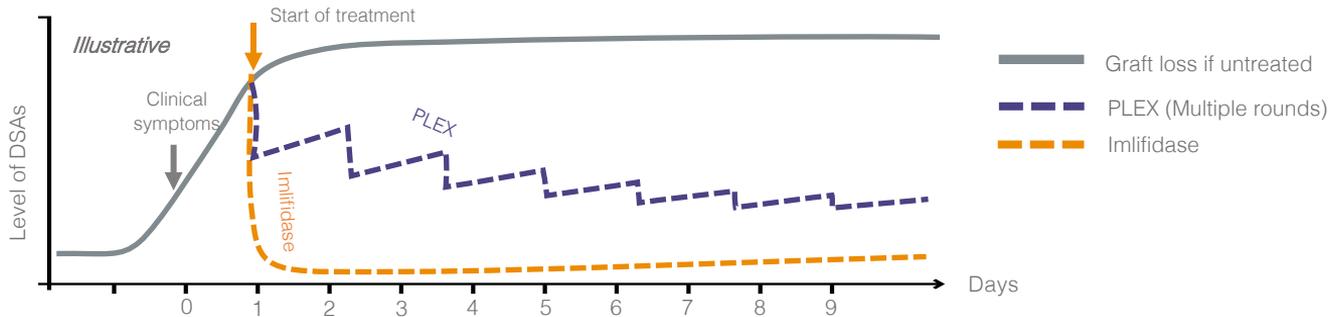
- 30 patients with active or chronic active AMR episodes post kidney transplantation have been enrolled and randomized 2:1 to imlifidase vs. SoC
- The AMR phase 2 program is a randomized, open-label, multi-center and controlled study
- 20 individuals have been randomized to receive imlifidase treatment comprised of one intravenous dose of 0.25mg/kg, while 10 individuals in the active control arm received 5-10 sessions of plasma exchange (PLEX)
- Efficacy and safety is monitored over a six-month period post treatment.

## Path forward

- ✓ **H1'22:** Completion of enrollment
- **H2'22:** Phase 2 data read-out
- ▼ **Decision on a regulatory path forward**

<sup>1</sup> Puttarajappa et al., Journal of Transplantation, 2012, Article ID 193724.

Potential of using imlifidase vs. PLEX in AMR



# Antibody Mediated Rejection

Long term graft survival is challenged by AMR post transplantation

## There is no approved treatment for AMR

- Active antibody mediated rejection after transplantation occurs in 5-7% of kidney transplants<sup>1</sup> annually<sup>4</sup> and is a significant challenge to long term graft survival
- Today's standard of care include plasma exchange, and treatment with steroid and IVIg. AMR patients not treated successfully risk graft failure, dialysis and return to the waitlist
- The AMR Phase 2 study is a randomized, open-label, multi-center, active control study designed to evaluate the safety and efficacy of imlifidase in eliminating donor specific antibodies (DSAs) in the treatment of active episodes of acute and chronic acute AMR in kidney transplant patients
- Completion of enrollment in 30 patient at 14 centers across the US, Europe and Australia was done May 2022
- First data read out expected in H2 2022

<sup>1</sup> Puttarajappa et al., Journal of Transplantation, 2012, Article ID 193724.

<sup>2</sup> Seven major markets – US, Germany, UK, France, Spain, Italy, and Japan



## AMR Phase 2

# AMR Phase 2 study

Aim of the study is test imlifidase ability to reduce the amount of donor specific antibodies in AMR patients post transplantation

### CLINICALTRIALS.GOV ID

NCT03897205 (2019)

### SUBJECTS

30 patients targeted (20 patients will be treated with imlifidase and 10 with Plasma exchange). Recruitment from 11 sites in the U.S., EU and Australia.

### DOSES/FOLLOW UP TIME

1 dose of imlifidase (0.25 mg/kg) or 5-10 sessions of plasma exchange

### MAIN OBJECTIVES

- Imlifidase ability to reduce the amount of DSA in comparison with plasma exchange in patients who have an active AMR post transplantation
- Ensure safety for patients

### STUDY DESIGN

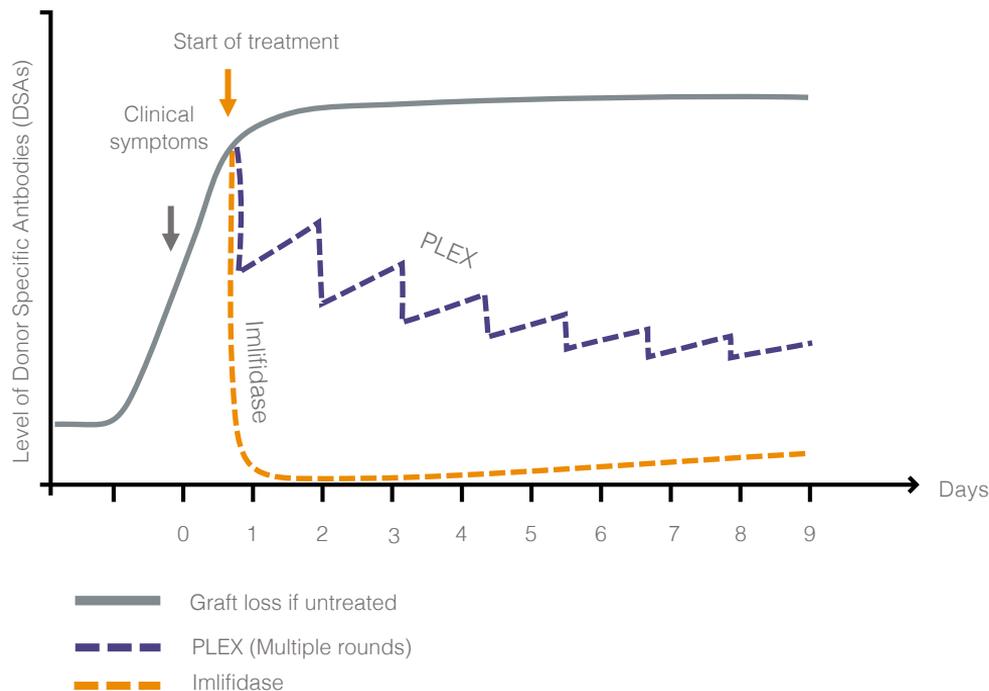
- Randomized, open-label multi-center active control study, designed to evaluate the safety and efficacy of imlifidase in eliminating DSA in active AMR

### STATUS

Completed enrollment awaiting first data read out H2 2022

## Potential of using imlifidase vs. PLEX in AMR

*Illustrative*



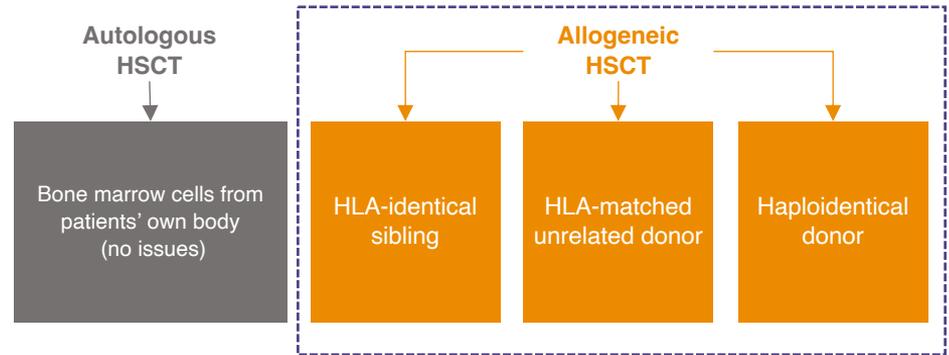
# Exploring potential use of imlifidase in allogeneic hematopoietic stem cell transplantation (HSCT)

Desensitization treatment of patients with high levels of donor specific antibodies (DSA) prior to allogeneic HSCT transplant is a challenge; Imlifidase may have the potential to inactivate DSAs prior to transplantation

## Transplantations are often acutely needed, which reduces the time available to find an adequately matched donor

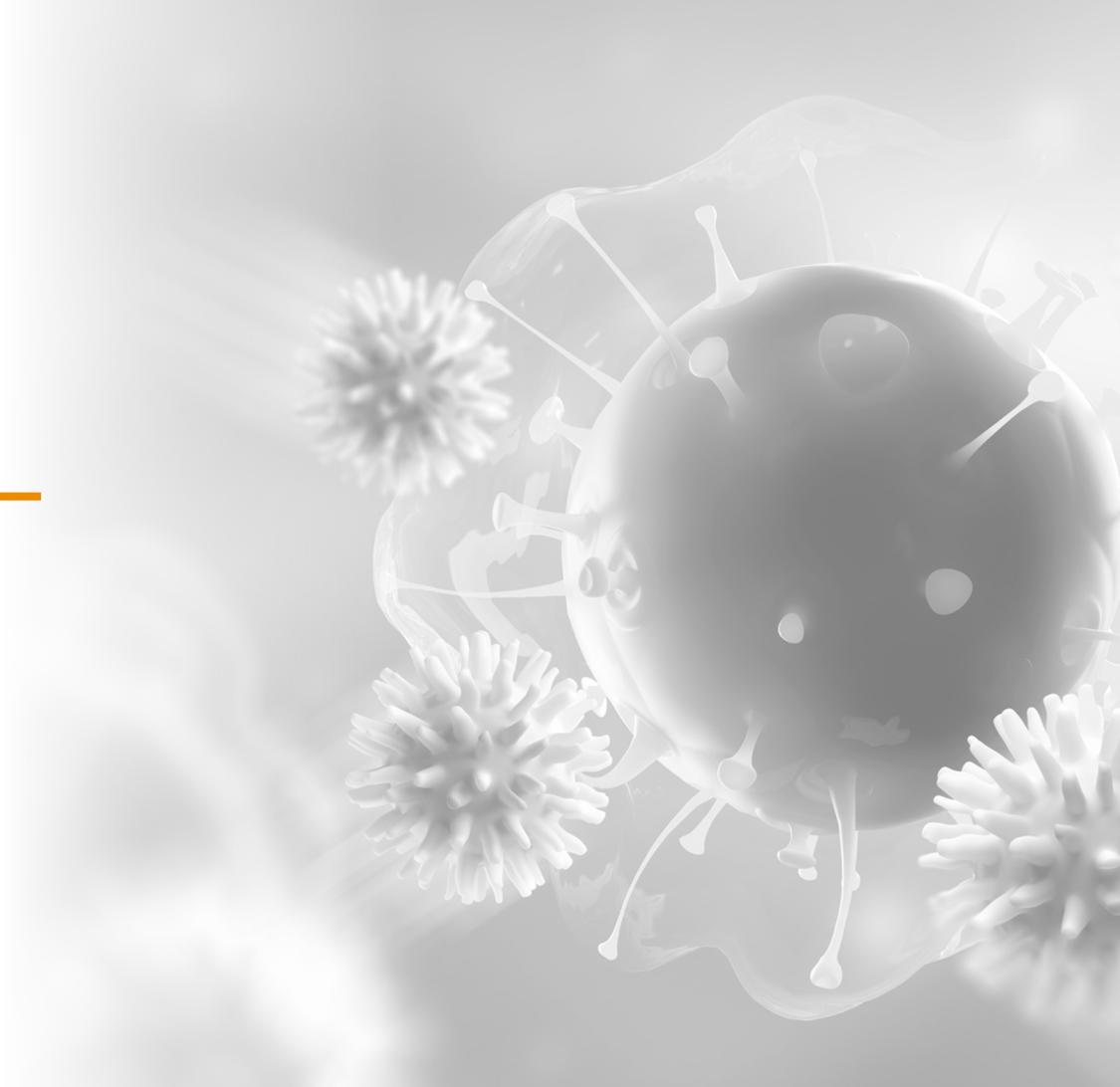
- Haploidentical donors (e.g. parents, children) are often available and transplant outcome is good (e.g. engraftment, graft survival, survival)
- However, presence of donor specific antibodies (DSAs) have a negative impact on transplant outcome<sup>2</sup> (e.g. graft failure and survival) Prevalence of DSAs in allogeneic HSCT is typically between 10-21%<sup>1</sup>.
- There are currently no approved drugs to manage patients with high levels of DSAs and current desensitization methods are inadequate, thus preventing patients from having a potentially life-saving HSCT
- Consensus recommendations published<sup>1</sup> by the EBMT<sup>3</sup> on testing, monitoring and treatment of patients with donor specific antibodies recommend to desensitize all patients with DSAs
- Imlifidase may have the potential to transform the standard of care by enabling clinicians to inactivate DSAs prior to transplantation

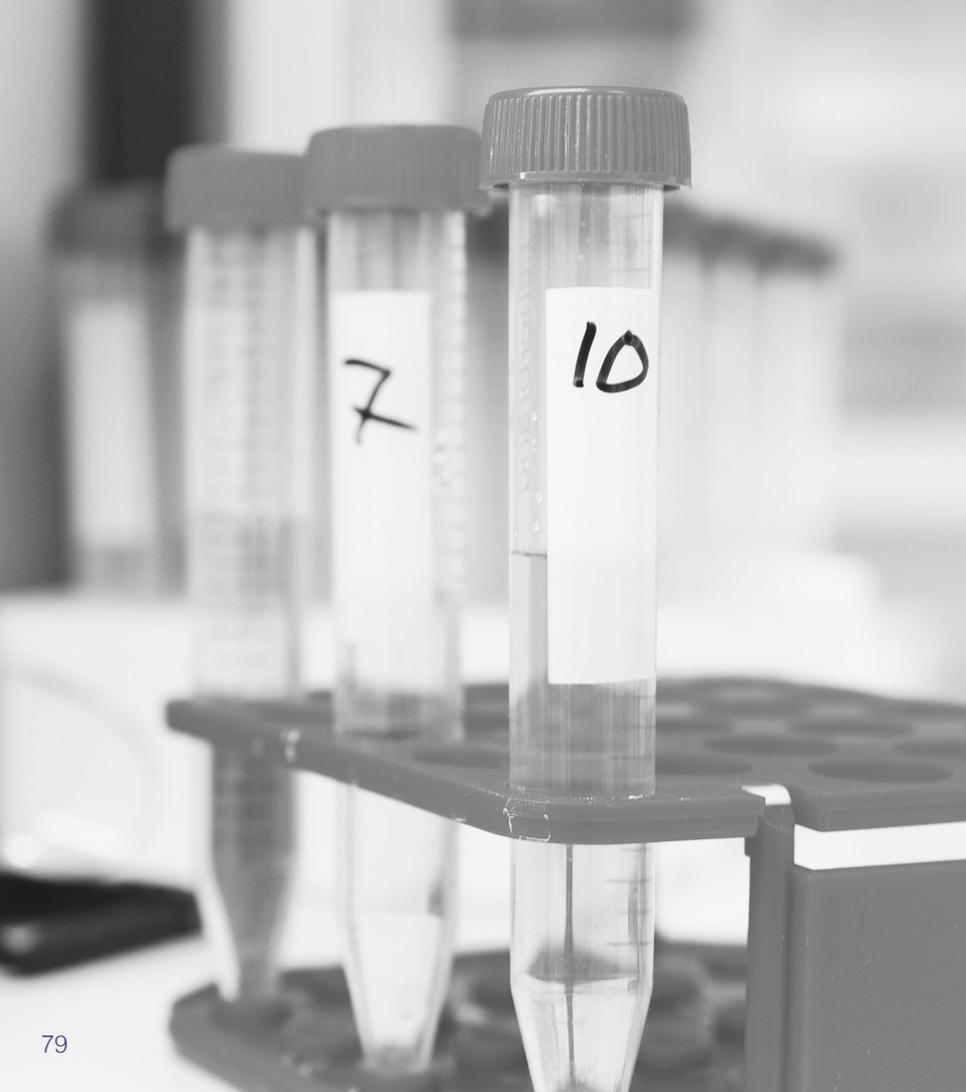
## Pre-existing DSAs may result in primary graft failure and poor survival after allogeneic hematopoietic stem cell transplantations



# Pre-clinical programs

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## Preclinical collaboration with argenx BV

Collaboration to evaluate the potential combination of companies' IgG-modulating approaches

- A combination of Hansa's IgG antibody-cleaving enzyme, and efgartigimod, argenx's FcRn antagonist could potentially be used in both the acute and chronic setting of autoimmune diseases and transplantation to potentially unlock additional therapeutic value
- Under the agreement, both parties will contribute equally in terms of resource allocation and will share all IP and data developed through the collaboration
- Both parties will maintain exclusive rights to their respective technologies and products.

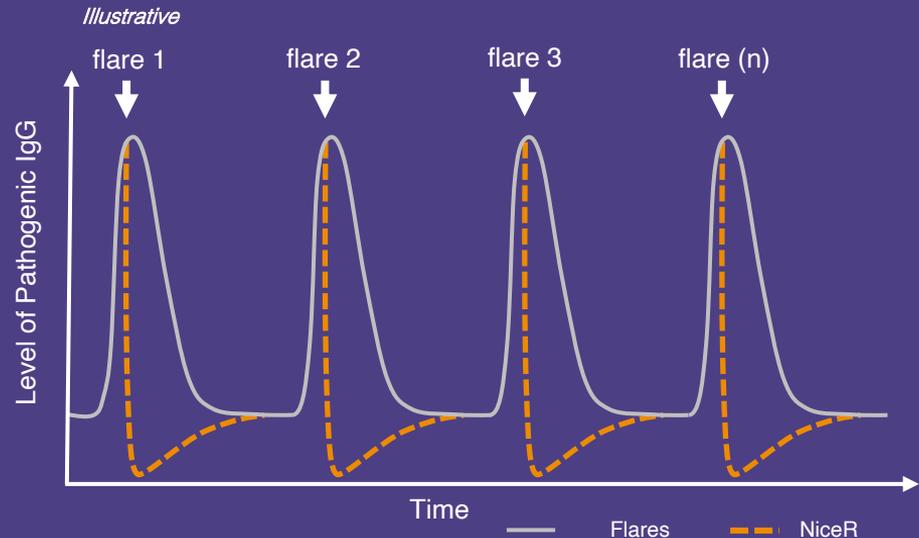
# “NiceR” for repeat dosing

a new set of enzymes for repeat dosing for potential inactivation of flares in relapsing diseases

## NiceR - Novel Immunoglobulin Cleaving Enzymes for Repeat dosing with lower immunogenicity

- Potential application for a broad array of indications, including reoccurring AMR, relapsing autoimmune diseases and oncology
- The first selected promising new drug candidate from the NiceR program is an IgG-cleaving enzyme (cysteine peptidase) with characteristics based on a homolog to imlifidase, but with lowered immunogenicity
- IND-enabling tox studies initiated in H1'21. Completion of GLP tox studies in 2022

## NiceR can potentially inactivate flares



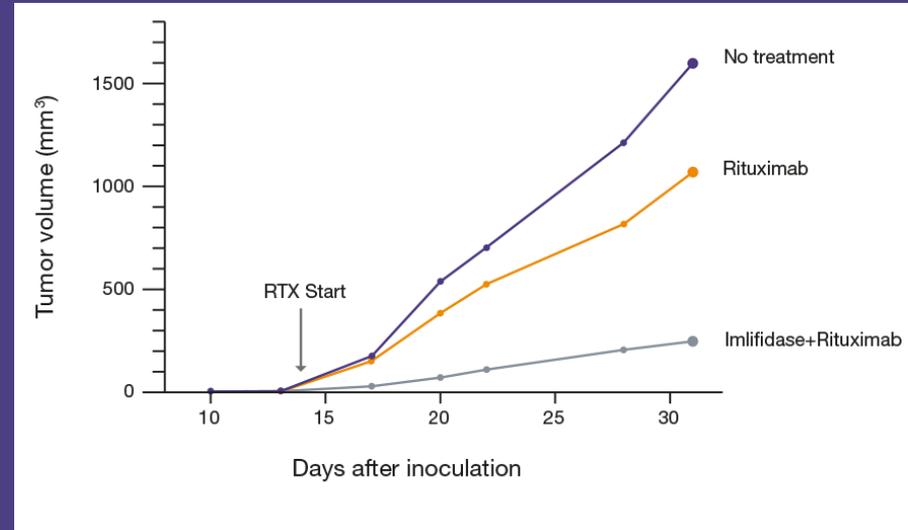
# Our antibody cleaving enzymes

may potentially improve the therapeutic effect of immunotherapy in oncology (EnzE)

## Proof of concept demonstrated in vivo for mice

- Enzyme based antibody enhancement through pre-treatment
- The abundance of normal IgG in blood interferes with therapeutic monoclonal antibodies
- Pre-treatment with imlifidase / NiceR has potential to significantly potentiate antibody-based cancer therapies
- Suppressive effect of IVIg on effector cell function abrogated by imlifidase
- Imlifidase can significantly improve the therapeutic effect of rituximab

## Mice with human IgG (~9mg/mL)



<sup>1</sup> Järnum et al. Mol Cancer Ther 2017;16:1887-1897

# Gene Therapy

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# Exploring opportunities in gene therapy

Exploring the opportunities in systemic administration of gene therapy for our unique antibody cleaving enzyme platform to potentially enable gene therapy treatment in NAb+ patients

A  
revolutionary  
approach

Significant  
unmet need

Encouraging  
pre-clinical  
data

Partnership  
strategy

# Tropism and target tissue

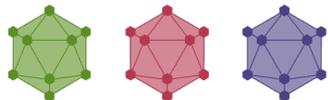
AAV subtypes targets different tissues



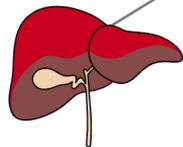
AAV 1, 2 & 5



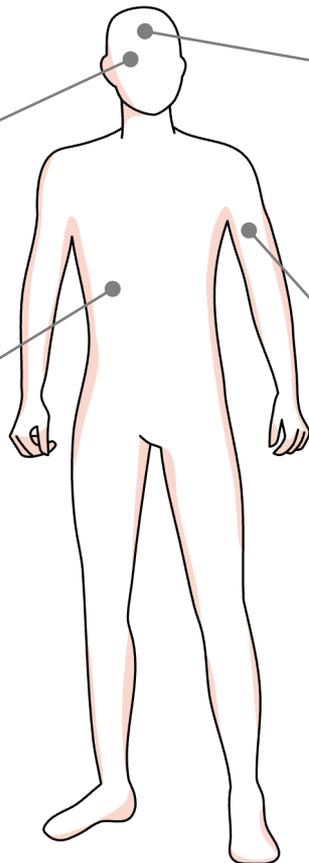
**Eye (local target)**  
 $\sim 1 \times 10^{11}$  vg



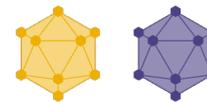
AAV 3, 7 & 8



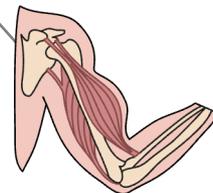
**Liver (systemic)**  
 $\sim 1 \times 10^{14}$  vg



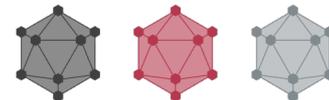
**Brain (local target)**  
 $\sim 1 \times 10^{12}$  vg



AAV 4 & 8



**Muscle (systemic)**  
 $\sim 1 \times 10^{15}$  vg



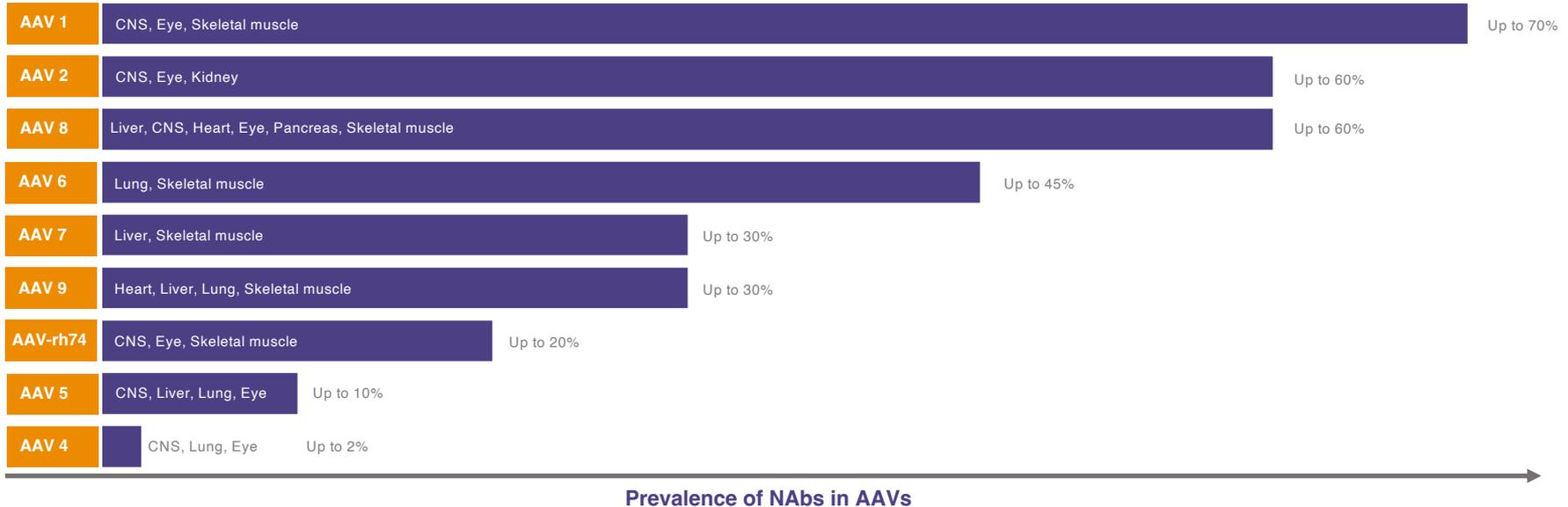
AAV 6, 7, rh74

## Target tissues

Dose of gene therapy (vg)

# Neutralizing antibodies are a barrier that precludes gene therapies

from working in a large group of patients. The prevalence of NABs varies significantly across the different vectors

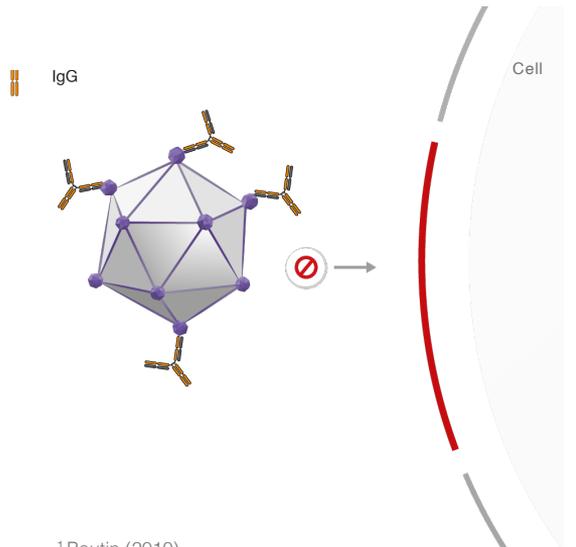


Source: Boutin et al (2010), Griffin et al (2019), Wang et al (2018), Calcedo & Wilson (2013), Falese et al (2017), Haiyan et al (2017), Ellsworth et al (2018), Greig et al (2017)

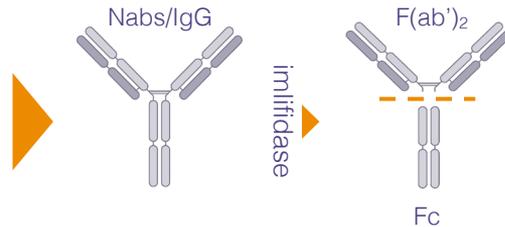
# Neutralizing antibodies (Nabs) are immunological barriers in gene therapy; imlifidase may potentially eliminate Nabs

Between approximately 5% and 70%<sup>1,2</sup> of patients considered for gene therapy treatment carry neutralizing anti-AAV antibodies forming a barrier for treatment eligibility

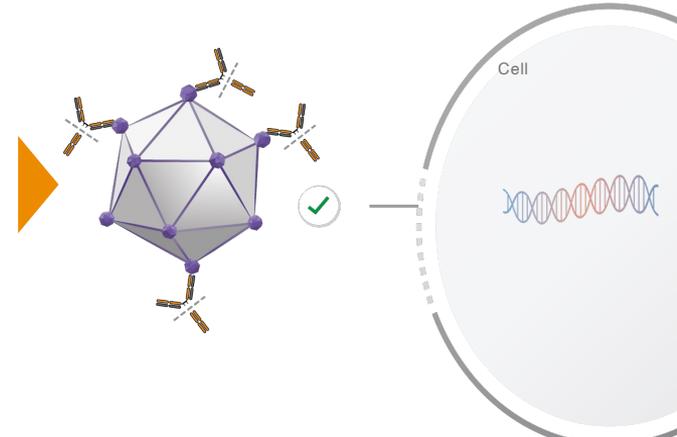
1 Antibodies prevent effective transfer of healthy gene sequence and can be a safety concern



2 Imlifidase is a unique IgG antibody-cleaving enzyme that cleaves IgG at the hinge region with extremely high specificity



3 The idea is to eliminate the neutralizing antibodies as a pre-treatment to enable gene therapy

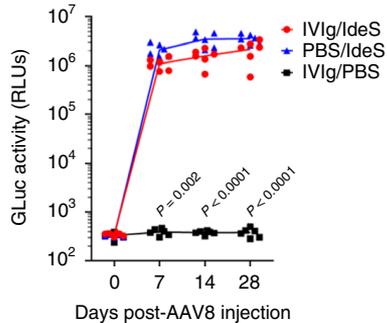


# Imlifidase (IdeS) was highlighted in Nature Medicine<sup>1</sup>

with encouraging outcome demonstrating imlifidase as a potential solution to overcome pre-existing antibodies to AAV-based gene therapy

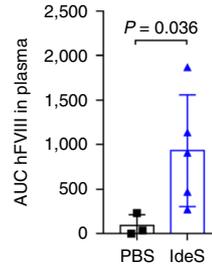
## Imlifidase tested in a animal model

- Imlifidase decreased anti-AAV antibodies and enabled efficient gene transfer



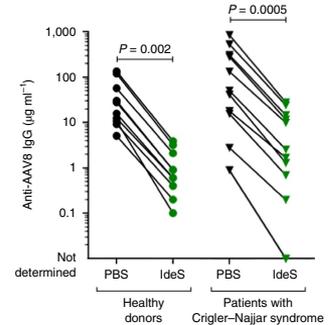
## Imlifidase tested in NHP ahead of AAV vector infusion

- Pre-treatment with imlifidase in anti-AAV positive nonhuman primates (NHP) ahead of AAV vector infusion was safe and resulted in enhanced liver transduction and hFVIII plasma levels

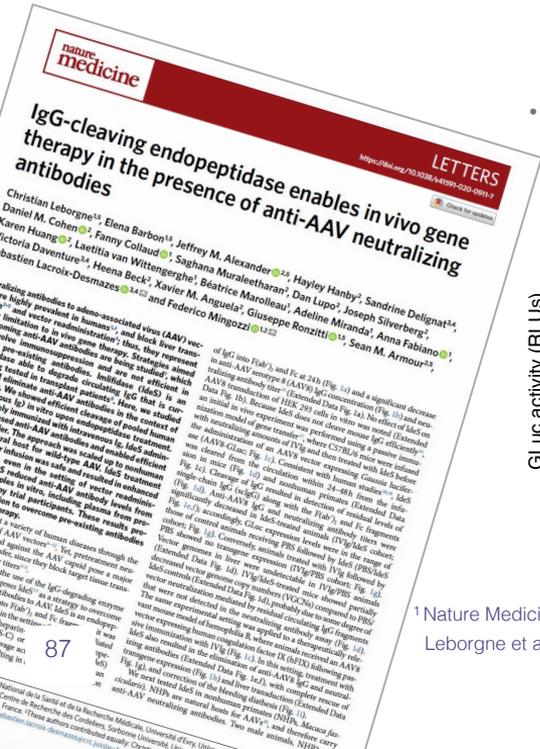


## Imlifidase tested in human plasma samples (GT patients)

- Imlifidase reduced anti-AAV antibody levels from human plasma samples in vitro, incl. plasma from prospective gene therapy trial participants



<sup>1</sup> Nature Medicine <https://doi.org/10.1038/s41591-020-0911-7>  
 Leborgne et al. Nat Med (2020)



# Global and exclusive agreement with Sarepta Therapeutics

to develop and promote imlifidase as pre-treatment ahead of gene therapy in select indications



## Indication exclusivity:

- Duchenne Muscular Dystrophy (DMD)
- Limb-Girdle Muscular Dystrophy (LGMD)

## Hansa's key resources

- Imlifidase validated with positive clinical efficacy and safety data as well as European approval
- Positive preclinical data published in *Nature*
- Clear path to U.S. approval (kidney transplant)



## Sarepta's key resources

- World leader within gene therapy targeted at muscular dystrophies
- Pre-clinical plan: PoC and IND-tox
- Clinical / Regulatory
- Promotion

## Collaborative research, development and commercialization – working together at every stage



# Collaboration with AskBio to evaluate imlifidase in gene therapy targeting Pompe disease

Feasibility program to evaluate imlifidase as pre-treatment ahead of gene therapy in Pompe disease for patients with pre-existing neutralizing antibodies (NAbs) to adeno-associated virus (AAV)



## Hansa's key resources and deliverables

- Imlifidase validated with positive clinical efficacy and safety data as well as European approval
- Significant know-how around antibody cleaving enzymes
- Clear path to U.S. approval (kidney transplant)
- Hansa supplies material and provides additional support

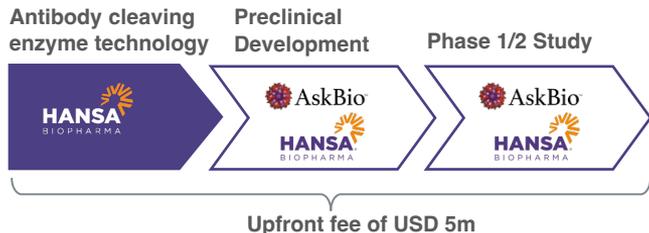


Fully owned subsidiary of Bayer AG

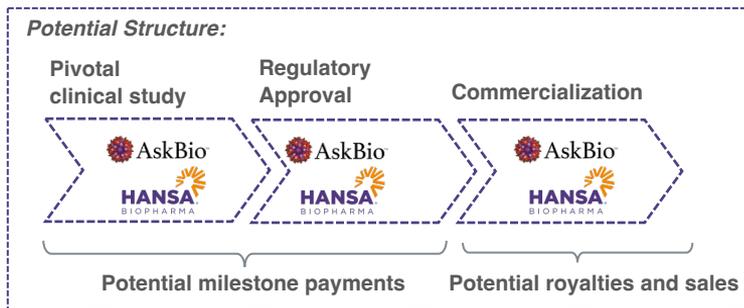
## AskBio's key resources and deliverables

- Early innovator in the Gene Therapy space with AAV platform and ongoing clinical stage Pompe disease program
- Conducts pre-clinical and clinical trials according to agreed plan

Current agreement scoped around a feasibility program which covers preclinical work and a Phase 1/2 study



Exclusive option for AskBio to negotiate a potential full development and commercialization agreement



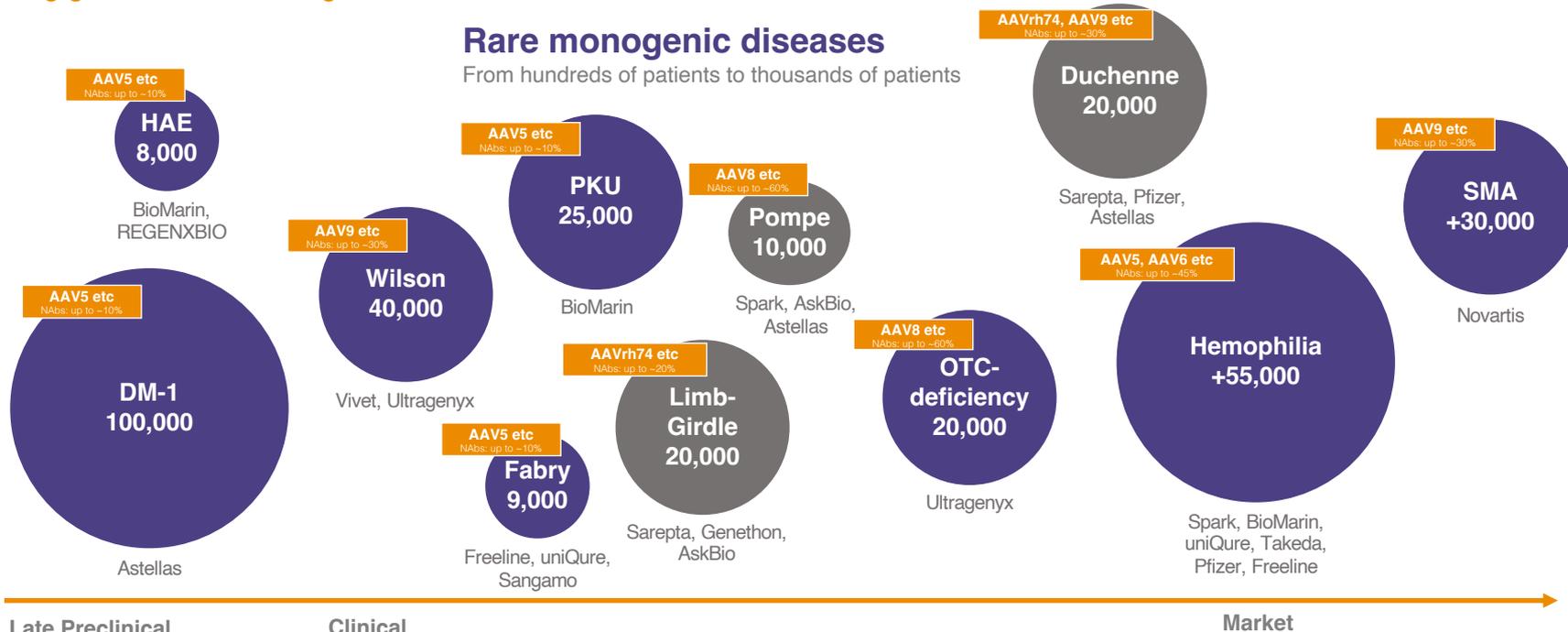
# Systemic gene therapy is an emerging opportunity

with a focus on the potential to correct issues causing genes in rare monogenic diseases

- Preclinical programs with Sarepta and AskBio
- Potential gene therapy indications (currently not pursued)

## Rare monogenic diseases

From hundreds of patients to thousands of patients



Late Preclinical

Clinical

Market

● Size of indication (US & EU)

# Duchenne Muscular Dystrophy (DMD) SRP-9001

## About Duchenne Muscular Dystrophy (DMD)<sup>1</sup>

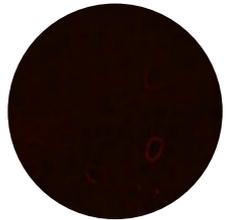
- Rare, fatal neuromuscular genetic disease
- Muscle weakness noticeable by age 3 to 5, and most patients use a wheelchair by the time they are 11
- Cardiac and respiratory muscle deterioration becomes life-threatening
- 1/3,500 to 5,000 male births (worldwide)
- Approximately 15% of patients have pre-existing IgG antibodies to rh74

## SRP-9001 micro-dystrophin gene therapy for treatment of DMD

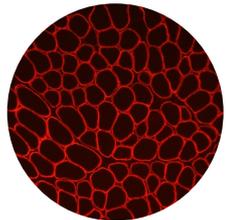
- AAVrh74 vector with micro-dystrophin transgene
- Broad patient experience
- 4 ongoing clinical trials – including recently initiated pivotal study
- Robust micro-dystrophin protein expression with commercially representative process material
- Functional benefits sustained up to 3 years after administration
- Observed safety profile is consistent
- On September 29, 2022, Sarepta announced that it had submitted a Biologics License Application (BLA) to the U.S. FDA for the accelerated approval of SRP-9001 to treat ambulant patients with DMD.

For further information regarding Sarepta's gene therapy programs, please refer to [www.sarepta.com](http://www.sarepta.com)

Pre-treatment



Post-treatment



Source:

<sup>1</sup> Sarepta Therapeutics <https://investorrelations.sarepta.com/static-files/e9393c38-646f-45ee-9f56-955f3bfad71>

<sup>2</sup> National Institutes of Health. Genetics Home Reference. Duchenne and Becker muscular dystrophy. <https://ghr.nlm.nih.gov/condition/duchenne-and-becker-muscular-dystrophy>. Accessed Jan 2020.

<sup>3</sup> Sarepta Therapeutics <https://investorrelations.sarepta.com/static-files/e9393c38-646f-45ee-9f56-955f3bfad71>

# Limb-Girdle muscular dystrophy (LGMD) SRP-9003

## About limb-girdle muscular dystrophy

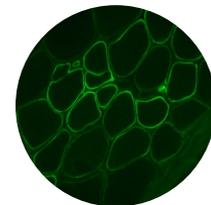
Limb-girdle muscular dystrophy is a group of diseases that cause weakness and wasting of the muscles

- Caused by defects in genes encoding for proteins residing within the sarcolemma, cytosol or nucleus of the muscle cell
- LGMD subtypes are often grouped according to which protein is affected
- Approximate global prevalence of 1.63 per 100,000 individuals; over 30 subtypes exist
- Approximately 15% of patients have pre-existing IgG antibodies to rh74

## SRP-9003 $\beta$ -sarcoglycan (SGCB) gene therapy for treatment of LGMD2E

- AAVrh74 vector with transgene  $\beta$ -sarcoglycan
- Open label study ongoing (N=6)
- Interim analysis disclosed in May 2021<sup>2</sup>:
  - Two dosing cohorts
    - Cohort 1 (n=3) -  $1.85 \times 10^{13}$  vg/kg; 2-year follow-up
    - Cohort 2 (n=3) -  $7.41 \times 10^{13}$  vg/kg; 1-year follow-up
  - No new safety signals, and treatment-related AEs occurred early and were transient and manageable
  - Robust, dose-dependent SGCB protein expression in all patients at Day 60, resulting in reconstitution of the sarcoglycan complex; SGCB expression sustained up to 2 years in cohort 1
  - Demonstrated functional improvements, including both NSAD and timed function tests, compared to baseline that were sustained for 2 years in cohort 1 and 1 year in cohort 2

$\beta$ -sarcoglycan



For further information regarding Sarepta's gene therapy programs, please refer to [www.sarepta.com](http://www.sarepta.com)

\*Doses are based on titer method using supercoiled plasmid standard

Source:

- 1) National Institutes of Health. Genetics Home Reference. Duchenne and Becker muscular dystrophy. <https://ghr.nlm.nih.gov/condition/duchenne-and-becker-muscular-dystrophy>. Accessed Jan 2020
- 2) Rodino-Klapac et al. Presented at the annual meeting of the American Society of Cell and Gene Therapy May 11-14, 2021

# Pompe Disease (PD) AAV2/8-LSPHGAA

## About Pompe Disease

- Defect in a gene making an enzyme called acid alpha-glucosidase (GAA), which is used to break down glycogen
- Accumulation of glycogen result in severe impact on the normal organ and muscle function
- Current standard of care is enzyme replacement therapy (ERT)
- Approximate incidence is 1 per 40,000<sup>1</sup> births, or ~200 per year in the US + EU
- Prevalence is estimated to be around 10,000 in the US and Europe combined<sup>2</sup>
- Approximately 40-60%<sup>3,4</sup> of patients have pre-existing IgG antibodies to AAV8

## AskBio's AAV2/8-LSPHGAA gene therapy

- AAV2 vector genome cross-packaged as AAV8
- Liver-specific promoter to express GAA enzyme
- Open label Phase I/II study ongoing
- Study in 8 Late-Onset Pompe Disease patients
- ClinicalTrials.gov: [NCT03533673](https://clinicaltrials.gov/ct2/show/study/NCT03533673)

For further information regarding AskBio's gene therapy program, please refer to [www.askbio.com](http://www.askbio.com)

Sources:

<sup>1</sup>Pompe Disease, <https://rarediseases.org/rare-diseases/nompe-disease/> [accessed 2022-02-08]

<sup>2</sup>Calculated by Hansa on the basis of incidence numbers from <https://rarediseases.org/rare-diseases/nompe-disease/> and life expectancy estimates from <https://nompediseaseaware.com/late-onset-nompe-disease/> as well as population statistics for the United States and European Union/Europe.

<sup>3</sup>ESGCT 27th Annual Congress Abstracts, Sensitivity of different AAV serotypes to pre-existing NAbs, [https://www.esgct.eu/home/Barcelona%202019/NEW\\_Abs%20Barcelona%20Abstracts.pdf](https://www.esgct.eu/home/Barcelona%202019/NEW_Abs%20Barcelona%20Abstracts.pdf)

<sup>4</sup>Boutin et al. Prevalence of serum IgG and neutralizing factors against adeno-associated virus (AAV) types 1, 2, 5, 6, 8, and 9 in the healthy population: implications for gene therapy using AAV vectors. Hum Gene Ther. 2010. <https://pubmed.ncbi.nlm.nih.gov/20095819/>

# ESG Overview

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# Formalising our ESG approach

At Hansa, we have always strived to achieve sustainable business practices. We are now formalizing our approach to sustainability and ESG issues, starting with identifying our key material focus areas.



**Our mission:** We leverage our unique enzyme technology platform to develop innovative, lifesaving and life altering immunomodulating therapies, bring these to the patients with rare diseases who need them, and generate value to society at large.

# Our key ESG material aspects

## Environment

### Climate & waste impacts of production and logistics

Hansa's environmental impact is small because our production is limited in volume. However, as we grow, we need to be transparent about, and make efforts to limit, our climate and waste impacts.



## Social

### Unmet needs and equity in health

Patients with rare conditions in general, and highly sensitized patients in particular, have many unmet needs which our therapies help address. These unmet needs can also be reinforced by ethnic or socio-economic status, particularly regarding access to organ transplants. Collaboration with patient groups can help us reach even more patients who can benefit from our treatments.



### Putting patients first

In the biopharma industry, there is a risk that patient access to innovative treatment is delayed. Hansa can therefore provide bridge financing on a case-by-case basis to benefit patients who have limited treatment options.



### Employee wellbeing, diversity and inclusion

Ensuring employee wellbeing, diversity and inclusion is a fundamental commitment at Hansa. It is also essential for attracting talent in a fast-growing organization and delivering on our strategy.



### Third-party risks

We diligently select new business partners, as well as monitor our existing partners and require them to comply with all laws and regulations and our Code of Conduct.



### Pricing

In Europe, value-based pricing and universal health coverage is common, but in other countries access is a pressing issue. We can expand access to unfunded patients through collaboration with patient groups.



## Governance

### Safety, efficacy and ethics

To build a successful company and achieve our mission to extend and enhance the lives of the patients we serve, we must hold ourselves to the very highest standards. Trust is at the core of everything we do.



### Return to investors

Biopharma companies need to remain economically attractive as an investment, so as to continue to secure capital and develop new treatments.



# UN Sustainable Development Goals

The Sustainable Development Goals (SDGs) were adopted by all UN Member States in 2015 as a universal call to action to end poverty, protect the planet and ensure that all people enjoy peace and prosperity by 2030. They have since become a gold standard for sustainability across businesses, and each of our recommended factors have been developed to align with relevant goals.



# Capital Markets

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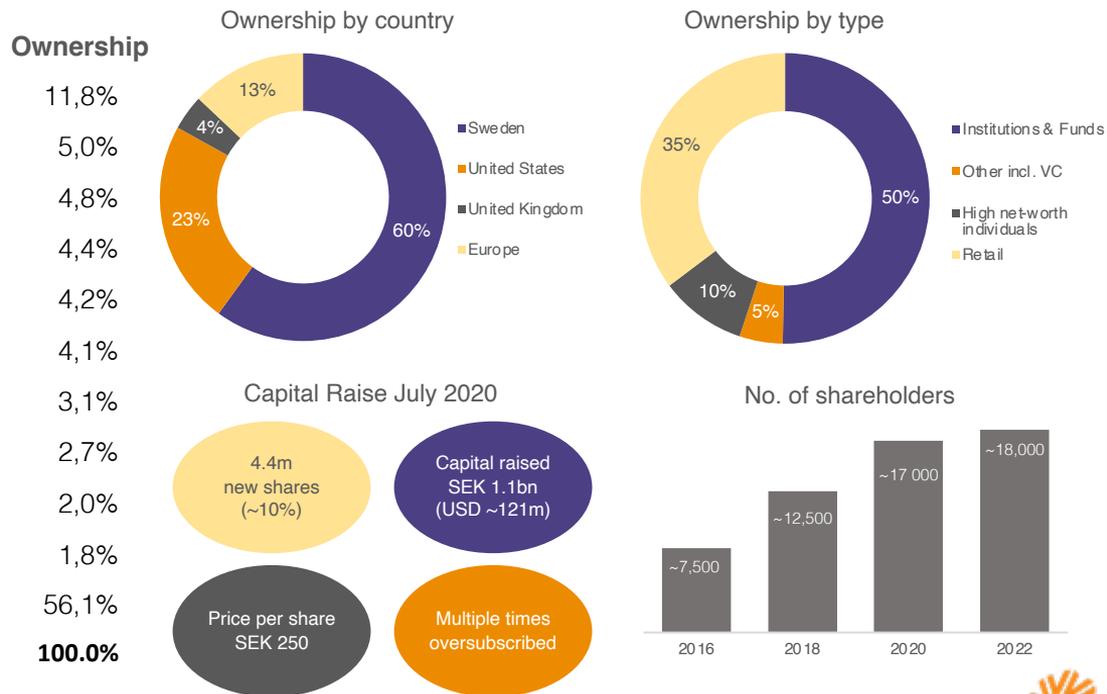


# Ownership in Hansa Biopharma

## Top 10 ownership as per September 30, 2022

Name	No. of shares	Ownership
Redmile Group, LLC	5 252 057	11,8%
Fjärde AP-Fonden (AP 4)	2 207 397	5,0%
Nexttobe AB	2 155 379	4,8%
Invesco Advisers, Inc.	1 973 931	4,4%
Försäkrings AB Avanza Pension	1 894 818	4,2%
Olausson, Thomas	1 820 500	4,1%
Tredje AP-Fonden (AP 3)	1 389 650	3,1%
The Vanguard Group, Inc.	1 223 839	2,7%
Schroder Investment Management	888 132	2,0%
C WorldWide Asset Management	799 749	1,8%
Other	24 982 666	56,1%
<b>Total</b>	<b>44,588,118</b>	<b>100.0%</b>

## Classification of ownership as per Dec 31, 2021



# Company collected consensus

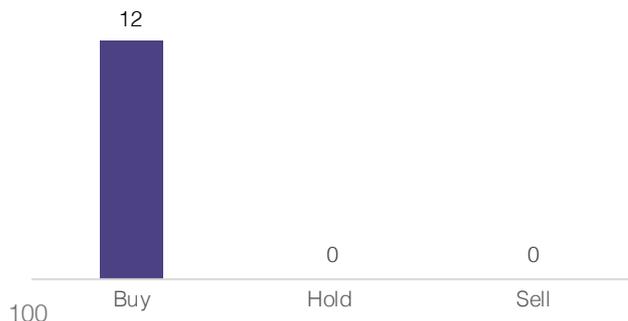
Consensus is based on a collection of analyst estimates pre our Q3 2022 report (October 14, 2022)



	Price Target, SEK	WACC	Patient uptake, EU			Revenue, SEKm		
			FY'22e	FY'23e	FY'24e	FY'22e	FY'23e	FY'24e
Average	238	11,1%	28	59	107	106	205	358
Median	228	11,5%	28	59	103	115	197	330
High	410	15,0%	42	114	282	129	347	746
Low	121	7,6%	16	22	30	53	72	96
<i>Number of contributions</i>	12	12	12	12	12	12	12	12

	EBIT, SEKm			Operating Cash Flow, SEKm			Cash position, SEKm		
	FY'22e	FY'23e	FY'24e	FY'22e	FY'23e	FY'24e	FY'22e	FY'23e	FY'24e
Average	-629	-623	-498	-599	-618	-600	1 056	717	497
Median	-646	-617	-507	-598	-618	-535	1 035	523	559
High	-455	-462	779	-454	-424	-332	1 646	1 887	1 658
Low	-743	-792	-1 126	-727	-870	-1 010	645	164	-443
<i>Number of contributions</i>	12	12	12	11	11	11	9	9	8

## Analyst recommendations



Bank/Research Institution	Analyst	Location	E-mail
SEB	Christopher Uhde, PhD	Stockholm	<a href="mailto:christopher.uhde@seb.se">christopher.uhde@seb.se</a>
ABG Sundal Collier	Adam Karlsson	Stockholm	<a href="mailto:adam.karlsson@abgsc.se">adam.karlsson@abgsc.se</a>
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Redeye	Johan Unnerus	Stockholm	<a href="mailto:johan.unnerus@redeye.se">johan.unnerus@redeye.se</a>
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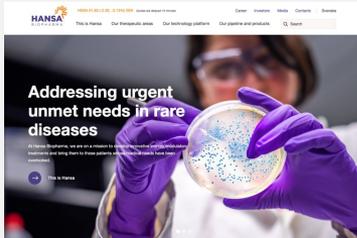


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## Calendar and events

Oct 20, 2022	Redeye After Work presentation, Gothenburg
Oct 21, 2022	Redeye Lunch presentation, Stockholm
Oct 26, 2022	Økonomisk Ugebrev Life Science Conference, Copenhagen
Oct 27, 2022	HCA Capital Expert call on the commercial progress/launch strategy
Nov 10-11, 2022	Bryan, Garnier & Co NDRS Paris & London
Nov 22, 2022	Bryan Garnier KOL Expert call on kidney transplantation (virtual)
Nov 23, 2022	SEB Healthcare Seminar 2022, Stockholm
Nov 24, 2022	Redeye Life Science Day, Stockholm
Dec 1, 2022	Erik Penser Banks Temadag - Health Care, Stockholm
Dec 2, 2022	Geneva Corporate Access Midcap Event, Geneva
Dec 15, 2022	DNB Nordic Healthcare Conference, Oslo
Jan 9, 2023	JPM Week, San Francisco
Feb 2, 2023	Interim Report for January-December 2022
Mar 14, 2023	Carnegie Nordic Healthcare Seminar 2023
Mar 30, 2023	2022 Annual Report
April 20, 2023	Interim Report for January-March 2023
June 14, 2023	2023 Annual General Meeting
July 20, 2023	Half-year Report for January-June 2023
Oct 19, 2023	Interim Report for January-September 2023



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