



## Investor Presentation

*Lund, Sweden  
December 8-9 2020*



*...at Hansa Biopharma we envision a world where all patients with rare immunologic diseases can lead long and healthy lives...*

# Forward-looking statement

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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# Business update Q3



# Hansa advances into commercial stage following conditional EU approval; Gene therapy partnership with Sarepta

## Highlights for the third quarter 2020

- Imlifidase in kidney transplantation
  - The EU Commission granted conditional approval for Idefix® (imlifidase) in highly sensitized kidney transplant patients in the European Union
  - New US study: Recruitment of first patient expected in H1 2021, given the continued impact of the COVID-19 pandemic in the US and the timeline to finalize the study protocol. BLA expected in 2023
- Partnership with Sarepta Therapeutics to develop imlifidase as pre-treatment ahead of gene therapy in select indications
- Clinical pipeline
  - Anti-GBM: Positive high-level data read out in September with 2/3 of patients achieving dialysis independence six months after treatment
  - Enrollment in AMR/GBS temporarily halted due to COVID-19 pandemic. Reinitiation of enrollment expected in Q4 2020 under a risk-based site-by-site approach
- SEK 1.1bn / USD 121m direct placing of new ordinary shares to fund R&D programs and commercial build-up
- Hansa Biopharma AB certified as a Great Place to Work®
  - Max Sakajja VP, Corporate Development, appointed to a new role as VP, Int. Markets to prepare expansion strategy outside EU



# Imlifidase has received conditional approval in the European Union

## Imlifidase in kidney transplantation

### EMA (Europe)

- imlifidase received conditional approval for “*desensitization treatment of highly sensitized adult kidney transplant patients with a positive crossmatch against an available deceased donor*”
- The MAA for imlifidase in kidney transplant was accepted for review by EMA back in 2019 based on data from four completed phase 2 studies across Sweden, France and the US

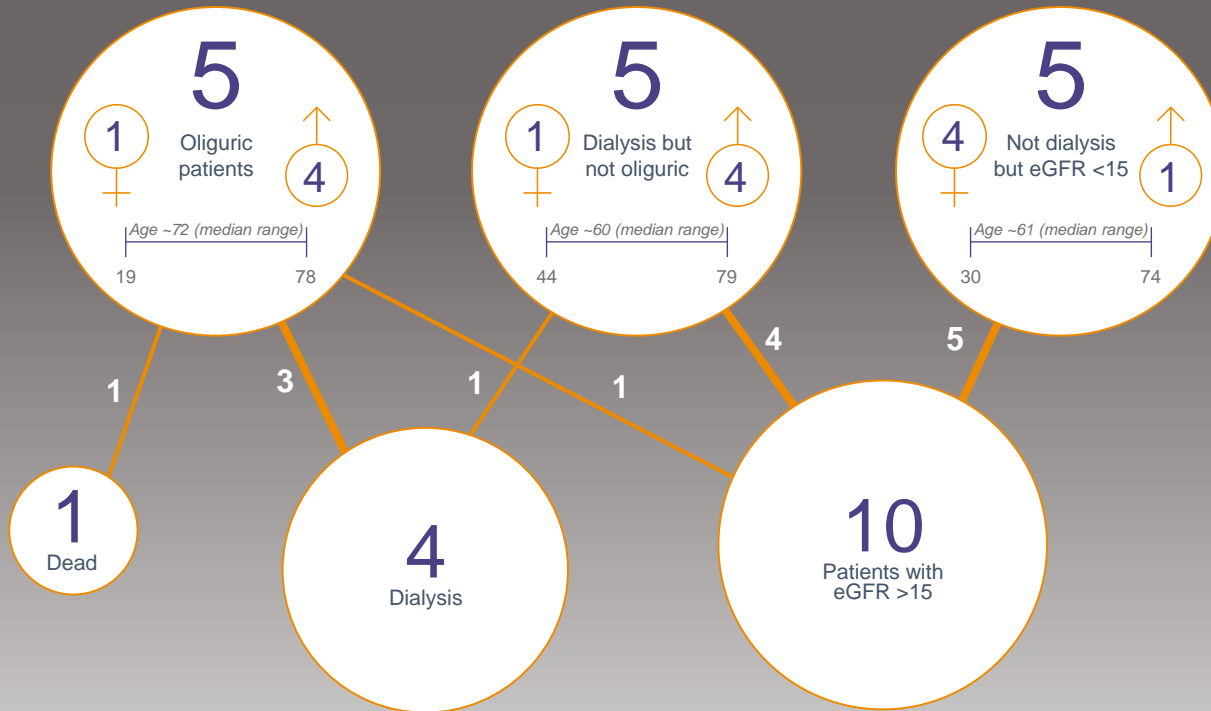
### FDA (US)

- Given the existence of the US Kidney Allocation System (KAS), FDA has requested a Randomized Controlled Trial to be completed prior to potential submission of a BLA (Exp. 2023)
- Proposed study protocol submitted June 2020 and discussions are currently ongoing with the FDA. Once the final protocol has been agreed upon, Hansa Biopharma will proceed to set up centers in the US and start to enroll patients
- Given the continued impact of the COVID-19 pandemic in the US affecting patient enrollment and the timeline for the finalization of the study protocol Hansa expects recruitment of the first patient to be in H1 2021



# Positive high-level data from Phase 2 study anti-GBM disease marks an important milestone for expansion of imlifidase outside transplantation

2/3 of patients achieving dialysis independence six months after treatment



## High-level data read out

- Study concludes that imlifidase leads to rapid clearance of anti-GBM antibodies, with two-thirds of patients achieving dialysis independence six months after treatment
- Normally 2/3 of patients will lose kidney function and end up in dialysis after six months
- Next step is to engage with regulators and agree on a path forward toward BLA/MAA in anti-GBM



# Positive high-level data read-out in the Anti-GBM study. Reinitiation of recruitment in AMR & GBS in Q4'20

## Ongoing Phase 2 programs

Enrollment status  
end Q3'2020



### Anti-GBM (investigator-initiated study)

- Phase 2 study completed with positive high-level data read-out from 15 patients
- Next step is to engage with regulators and agree on a path forward toward BLA/MAA in anti-GBM



### Antibody Mediated Rejection

- 4/30 patients enrolled in AMR study
- Recruitment is expected to be reinitiated in Q4 2020
- Enrollment is expected to be completed H2 2021



### Guillain-Barré Syndrome

- 4/30 patients enrolled in GBS study
- Recruitment is expected to be reinitiated in Q4 2020
- Enrollment is expected to be completed in H2 2021

■ Patients enrolled  
■ Patients left





# Broad 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: Commercial launch Q4 2020
	US: Kidney transplantation in highly sensitized patients <sup>1,2</sup>				**) )			First patient dosed H1 2021
	Anti-GBM antibody disease <sup>3</sup>							Next step is to engage with regulators and agree on a path forward toward BLA/MAA
	Antibody mediated kidney transplant rejection (AMR)							Complete enrolment of 30 patients H2'21
	Guillain-Barré syndrome (GBS)							Complete enrolment of 30 patients H2'21
	Limb-Girdle (LGMD) & Duchenne (DMD) (Pre-treatment ahead of gene therapy with Sarepta)							Research phase
NiceR	Recurring treatment in autoimmune disease, transplantation and oncology							Development of CMC process / Tox studies
EnzE	Cancer immunotherapy							Research phase

Completed Ongoing

<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)

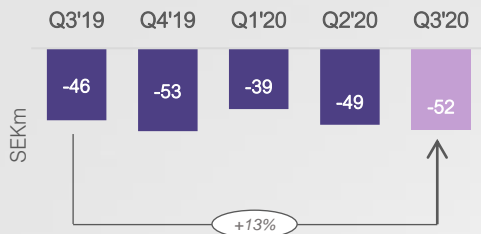
<sup>3</sup> Investigator-initiated study by Märten Segelmark, Professor at the universities in Linköping and Lund

\*) The EU Commission has granted conditional approval for imlifidase in highly sensitized kidney transplant patients. A post-approval study will commence in parallel with the launch

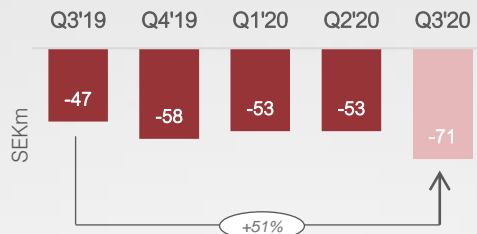
\*\*) FDA: Proposed study protocol submitted June 2020. Discussions are currently ongoing with the FDA. Once the final protocol has been agreed upon, Hansa Biopharma will proceed to set up centers in the US and start to enroll patients. Given the continued impact of the COVID-19 pandemic and the timeline for the finalization of the study protocol Hansa expect recruitment of the first patient to be in H1 2021

# Hansa Biopharma continues to invest in the R&D pipeline and the commercial preparation towards the expected launch in Q4 2020

SG&A expenses (Q/Q)



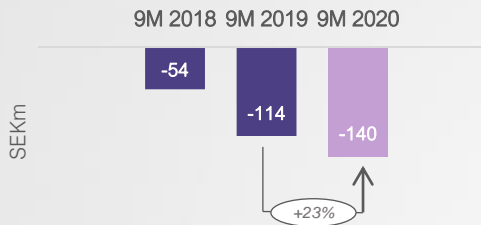
R&D expenses (Q/Q)



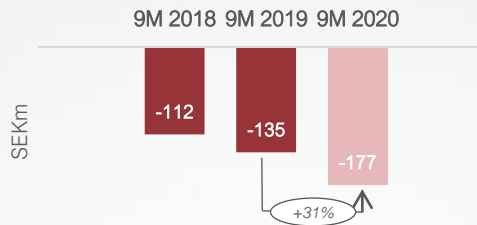
Net loss (Q/Q)



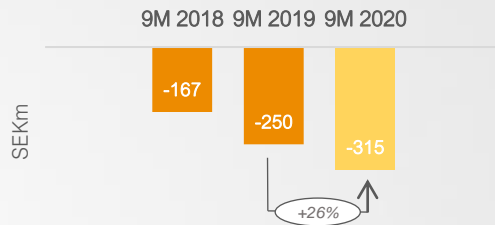
SG&A expenses (9M/9M)



R&D expenses (9M/9M)

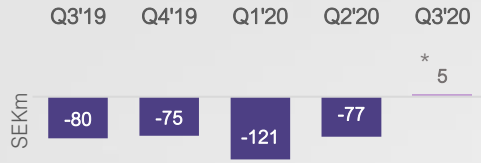


Net loss (9M/9M)

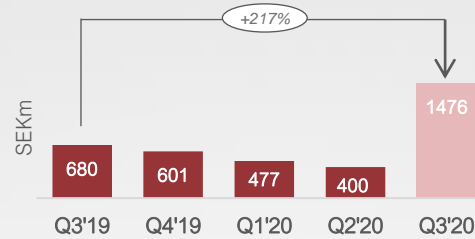


# Cash position stood at SEK 1.5bn (~USD 150m) end of Q3 2020; Hansa Biopharma is financed through 2023

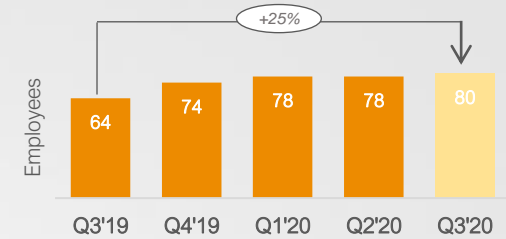
Operating cash flow (Q/Q)



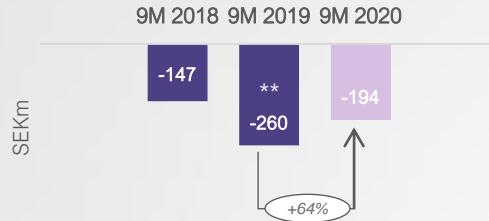
Cash & short term investments (Q/Q)



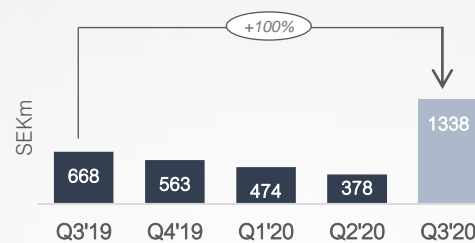
Number of employees (Q/Q)



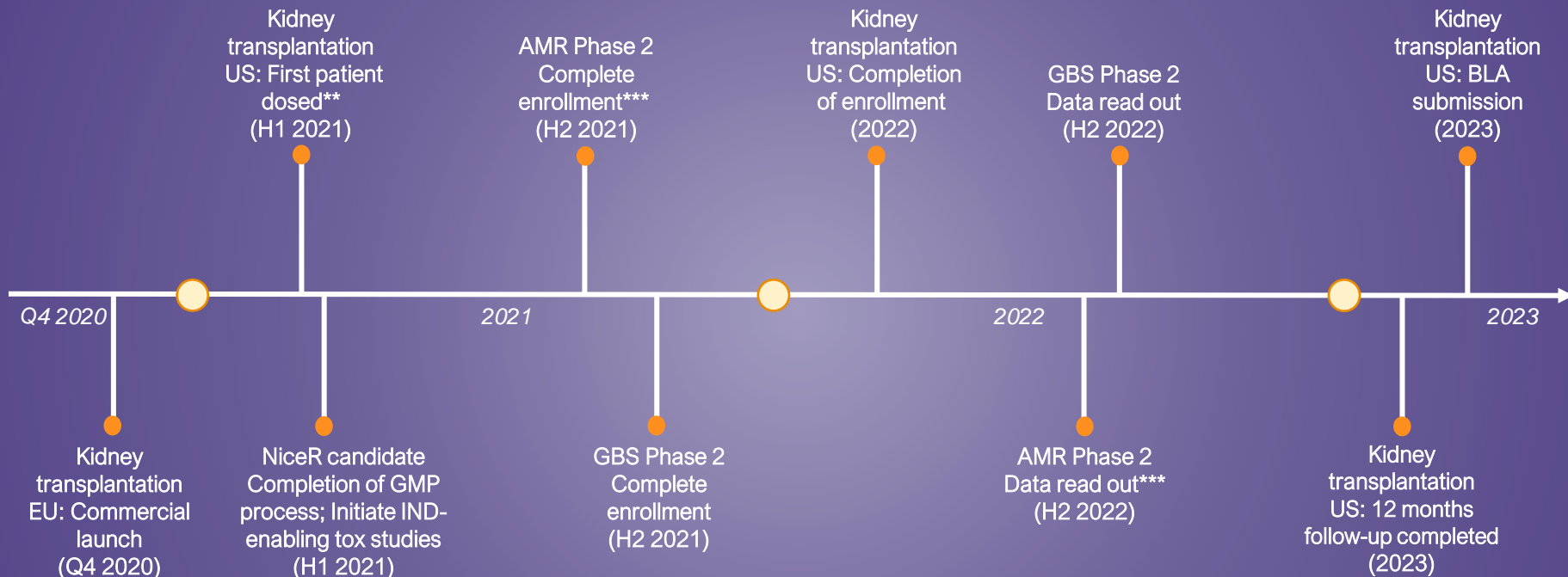
Operating cash flow (9M/9M)



Shareholders equity (Q/Q)



# Upcoming milestones



\*\*) FDA: Proposed study protocol submitted June 2020. Discussions are currently ongoing with the FDA. Once the final protocol has been agreed upon, Hansa Biopharma will proceed to set up centers in the US and start to enroll patients. Given the continued impact of the COVID-19 pandemic and the timeline for the finalization of the study protocol Hansa expect recruitment of the first patient to be in H1 2021

\*\*\*) AMR/GBS Due to the impact from the COVID-19 pandemic, the enrollment in GBS and AMR were temporarily halted for the past six months. Hansa Biopharma expects to reinstate enrollment of these studies in Q4 2020 under a risk-based, site-by-site approach. Enrollment of patients in the AMR study is now expected to be completed in the second half of 2021, while completion of patient enrollment in the GBS study is still expected in the second half of 2021. High-level data readout for both studies are expected in the second half of 2022.

# Company Overview



# Hansa Biopharma at a glance



## Company background

- Founded 2007 with HQ in Lund, Sweden
- Søren Tulstrup, CEO – Ulf Wiinberg, Chairman
- ~80 employees (~2/3 in R&D) end of Q3 2020
- Operations in Sweden, US & across Europe
- Market cap: SEK ~11bn (~1.25 bn USD) end of September 2020
- Listed on Nasdaq OMX Stockholm (HNSA)



## Leader in immunomodulatory enzymes for rare IgG-mediated diseases

- Imlifidase is a unique IgG antibody-cleaving enzyme. If approved, imlifidase may have the potential to meet a large unmet need and preserve and transform the lives of people with rare diseases
- Imlifidase has been studied in five clinical studies in kidney transplantation
- Imlifidase has been published in peer-reviewed journals (e.g. New England Journal of Medicine and the American Journal of Transplantation)



## Broad pipeline in transplantation and autoimmune diseases

- Lead indication in kidney transplantation in highly sensitized patients
  - The European commission has granted conditional approval for Idefix™ (imlifidase) in highly sensitized kidney transplant patients in the European Union
  - US: Study protocol for RCT submitted June 2020, discussions with FDA ongoing
- Anti-GBM antibody disease (Phase 2)
- Antibody mediated kidney transplant rejection (AMR) (Phase 2)
- Guillain-Barré syndrome (GBS) (Phase 2)
- NiceR - Recurring treatment in autoimmune disease, transplantation and oncology (Preclinical)
- EnzE – Cancer immunotherapy (Preclinical)



## Key financials\*

• Cash & short-term inv.	9M'20* SEK 1.5bn (9M'19 SEK 680m)	FY'19 SEK 601m
• Operating Profits/Loss	9M'20* SEK -317m (9M'19 SEK -250m)	FY'19 SEK -360m
• Operating cash flow	9M'20* SEK -194m (9M'19 SEK -260)	FY'19 SEK -335m

\* Unaudited

*...at Hansa Biopharma we envision a world where all patients with rare immunologic diseases can lead long and healthy lives...*



# Imlifidase – a novel approach to eliminate pathogenic IgG



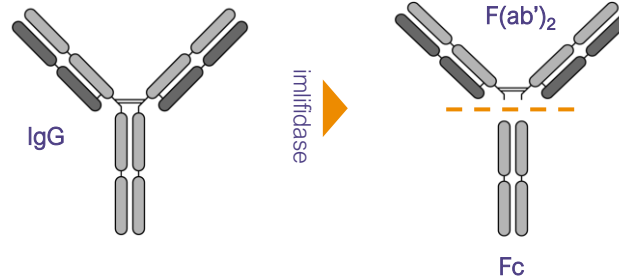
## Origins from *Streptococcus pyogenes*

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



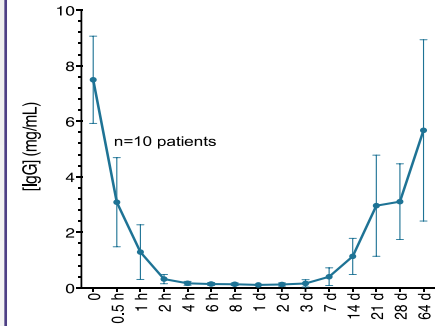
## Imlifidase, a unique IgG antibody-cleaving enzyme

- Interacts with Fc-part of IgG with extremely high specificity
- Cleaves IgG at the hinge region, generating one  $F(ab')_2$  fragment and one homo-dimeric Fc-fragment



## Imlifidase inactivates IgG in 2 hours

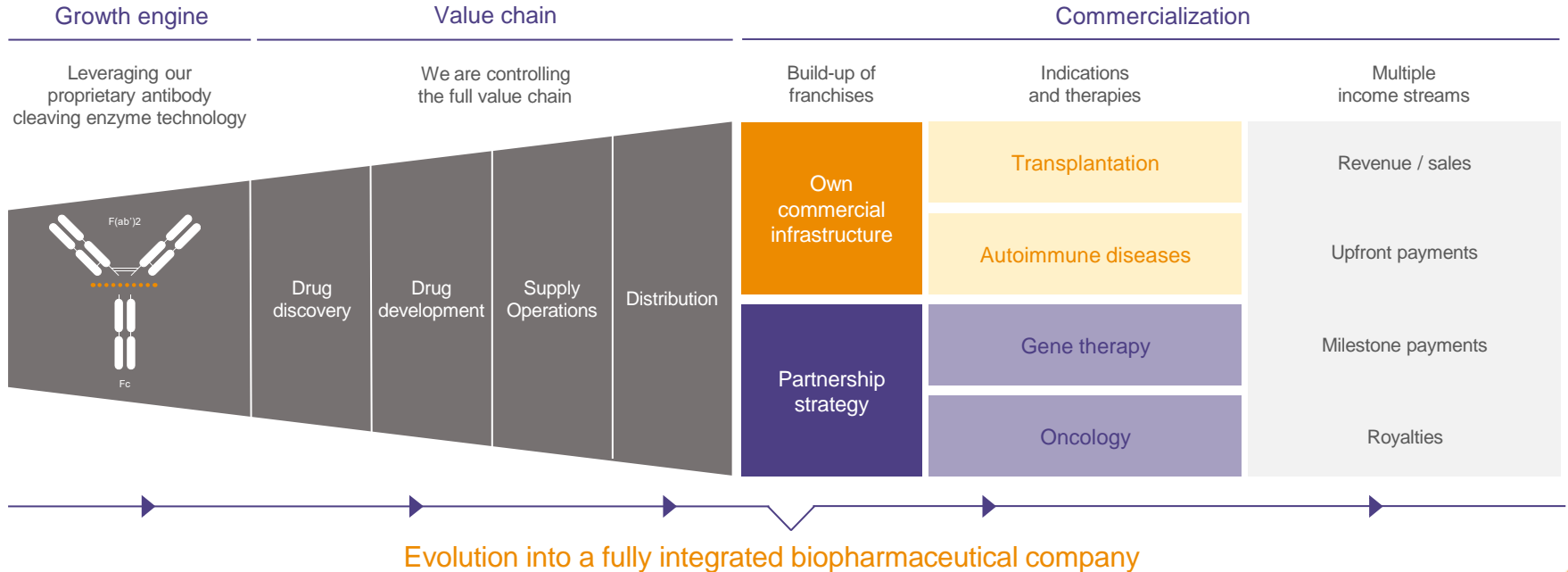
- Rapid onset of action that inactivates IgG below detectable level in 2 hours
- IgG antibody-free window for approximately one week



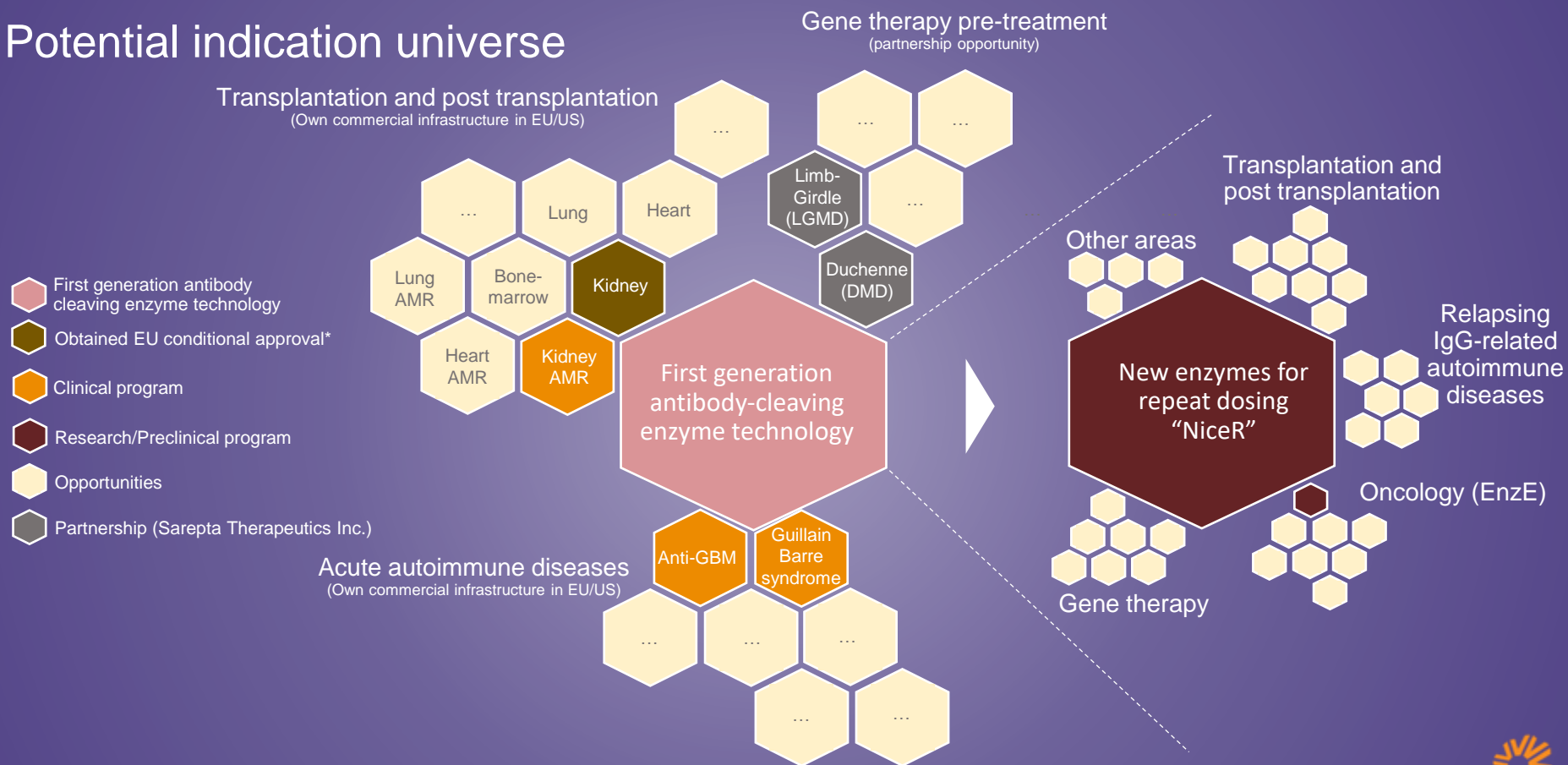


# Leveraging our technology platform

Developing new therapies targeting rare diseases with unmet medical need across a range of indications



# Potential indication universe



\* US: Study protocol submitted June 2020, study expected to be initiated H1 2021. The new clinical study could support BLA submission by 2023

# Our unique enzyme technology platform offers significant potential for growth and expansion

## Our strategic priorities



Establish a commercial and medical infrastructure in Europe ahead of commercial launch



Marketing authorization obtained in Europe for imlifidase as a treatment for highly sensitized patients to enable kidney transplantation. Conduct a new randomized, controlled study in the US in the context of KAS to support a BLA filing by 2023



Investigate the potential of imlifidase in autoimmune indications and post transplantation

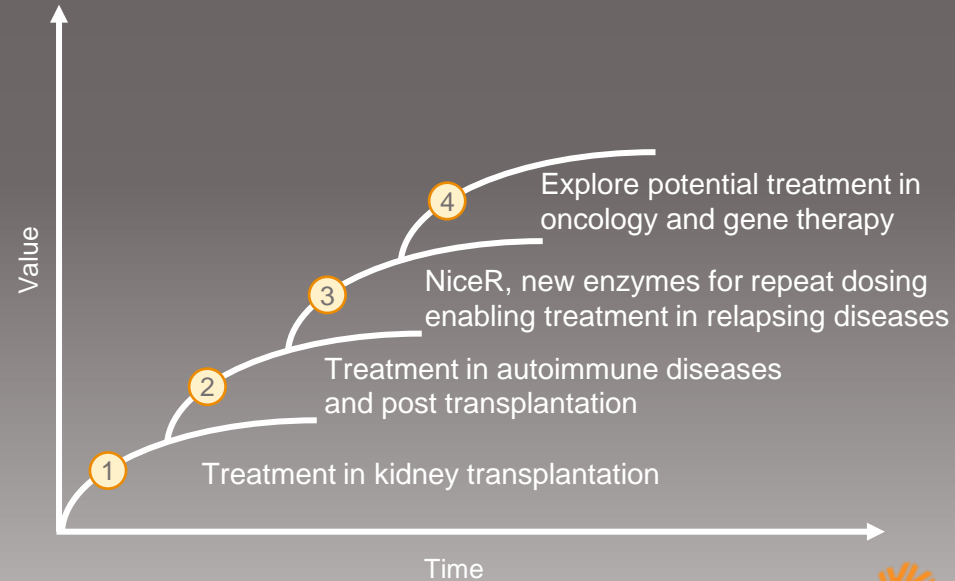


Advance a new set of immunomodulatory enzymes designed for repeat dosing in relapsing diseases (NiceR) into clinical development



Explore potential combination therapies with imlifidase in oncology and in gene therapy

## Our road map for growth and expansion



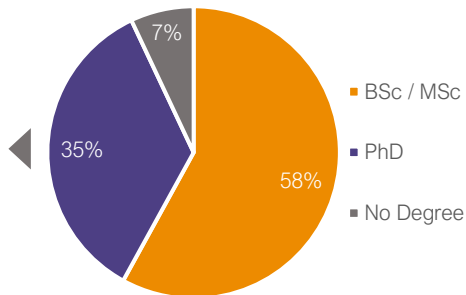
# The Hansa team has extensive experience from international life science industry and academia

Highly educated team with more than 1,100 “man years” in the life science industry and academia

More than 1/3 of the team holds a relevant life science PhD

PhD specializations include

- Applied Microbiology
- Biotechnology
- Cell and Molecular Biology
- Clinical Infection Medicine
- Engineering
- Experimental Clinical Chemistry
- Experimental Medicine
- Immune Technology
- Medical Microbiology
- Medical Science
- Physiological Chemistry



Vast experience from life science; +50% has worked in Big Pharma

Biotech

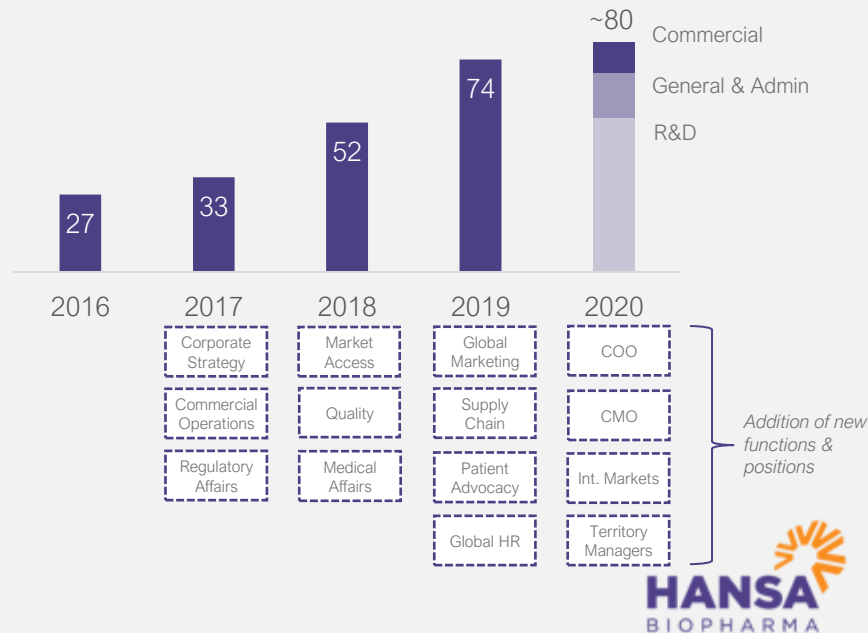


Commercial-stage/Big pharma



We are building an organization in preparation to become a commercial-stage biopharma company

Staff has tripled in 5 years as new competences are being added



# Experienced Board and Executive Committee with many years in 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



**Christian Kjellman**

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



**Donato Spota**

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



**Achim Kaufhold**

**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)



**Henk D. van Troostwijk**

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



**Anne Säfström Lanner**

**CHRO (2019)**  
Ex-Head of HR European  
Spallation Source  
Ex-Head of HR Cellavision



**Ulf Wiinberg**

**Chairman (2016)**  
+30 years in the Healthcare sector  
Ex-CEO at Lundbeck (2008-14)  
Ex-President at Wyeth of the global  
consumer health care and European  
Pharma business



**Birgit Stattin Norinder**

**Board Member (2012)**  
Ex-CEO and Chairman at Prolifix Ltd.  
Ex- SVP, Pharmacia & Upjohn  
Member of Hansa Biopharma Scientific  
Committee and Remuneration Committee



**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



**Eva Nilsagård**

**Board Member (2019)**  
interim CFO at OptiGroup AB  
CEO of Nilsagård Consulting AB  
Ex-CFO of Vitrolife and Plasta  
Chairman of Hansa Biopharma's Audit  
Committee



**Mats Blom**

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



**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

# From technology development to commercialisation in 13 years



Hansa Medical founded  
IdeS (imlifidase) discovered  
and patented by Prof. Lars  
Björk, M.D. Lund University



Partnship with  
Axis-Shield  
for HBP-test



Imlifidase  
first-in-man study



Start imlifidase  
Phase 2 at  
Cedars Sinai and  
UUh



Imlifidase NEJM-  
publication;  
Anti-GBM initiated



Imlifidase MAA submitted  
to EMA;  
AMR & GBS Phase 2  
initiated



Partnship with  
Sarepta for gene  
therapy

2007

Project IdeS (imlifidase)  
initiated



2013

Imlifidase GMP process  
development and  
toxicology studies initiated



2014

Imlifidase 1<sup>st</sup> Phase 2



2015

Initiation of imlifidase  
HighdeS study



2016

2017

Imlifidase: 46  
transplants enabled



2019

Imlifidase: EU  
commission approval



2020

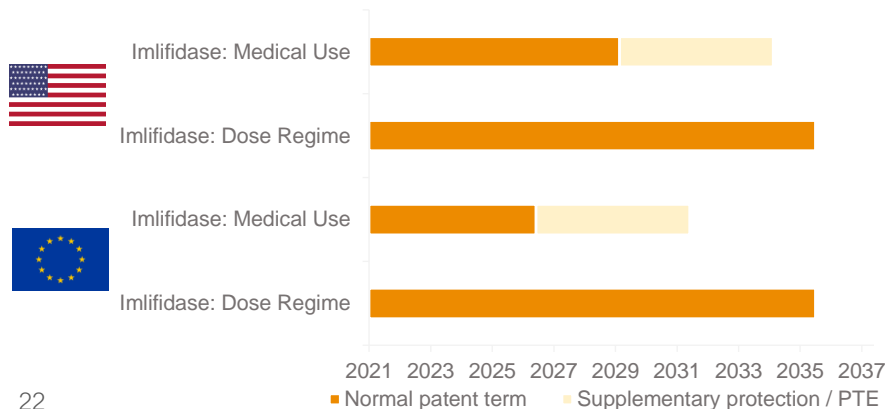
Positive anti-  
GBM Phase 2  
Data



# Strong technology protection through patents and orphan drug designation

## Patent coverage out to 2035 in key markets

- Hansa Biopharma's portfolio consist of 11 separate patent families incl. 7 patent families in relations to the use of imlifidase (granted/pending)
- Patents cover use of isolated imlifidase in:



## 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).
- Designation provides development and commercial incentives incl. 10 years market exclusivity in EU and 7 years in the US

**EMA**  
Orphan drug designation

- Imlifidase for the prevention of graft rejection following solid organ transplantation (2017)
- Imlifidase for the treatment of the rare and acute disease anti-GBM (2018)

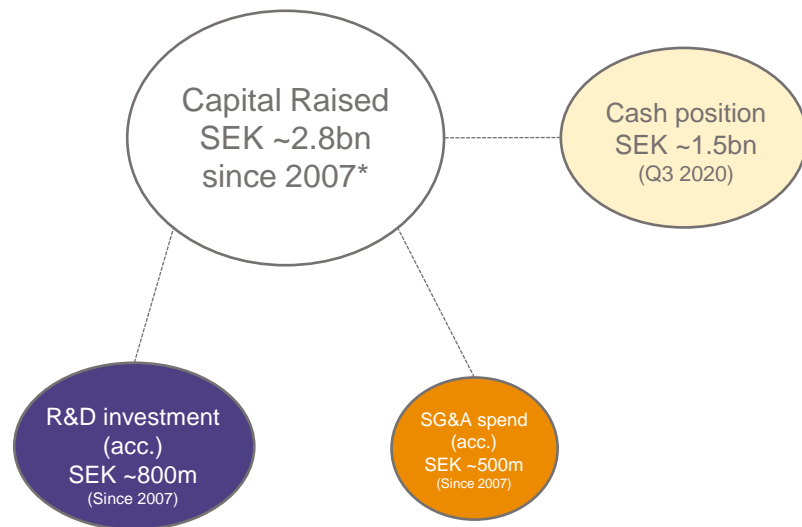
**FDA**  
Orphan drug designation

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



## With the recent capital injection Hansa Biopharma is financed into 2023

Since 2007 Hansa has mainly been backed by VCs funding the development of our enzyme platform



Capital injection from new shares (SEK 1.1bn) and Sarepta (SEK 100m) will finance Hansa into 2023



# Imlifidase in kidney transplantation



# Kidney transplantation 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>

<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.

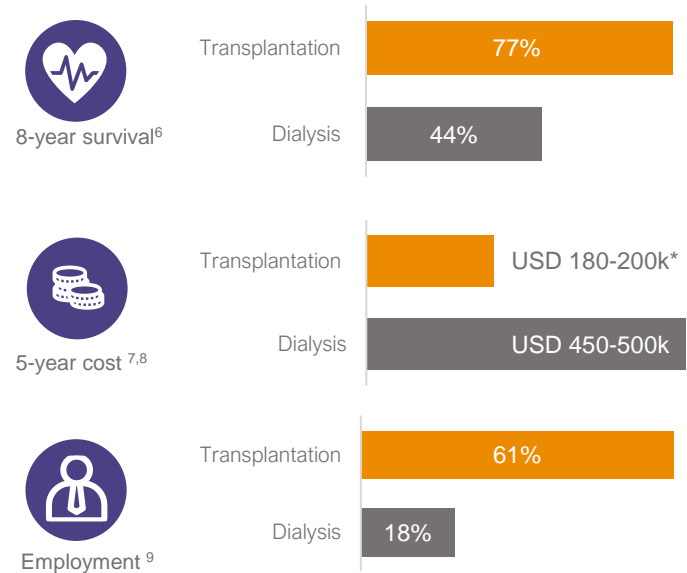
<sup>6</sup> Orandi et al. N Engl J Med 2016;374:940-50

<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

## Transplantation leads to better outcomes



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

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

## Highly sensitized patients are difficult to match

- Causes of sensitization include



Pregnancy



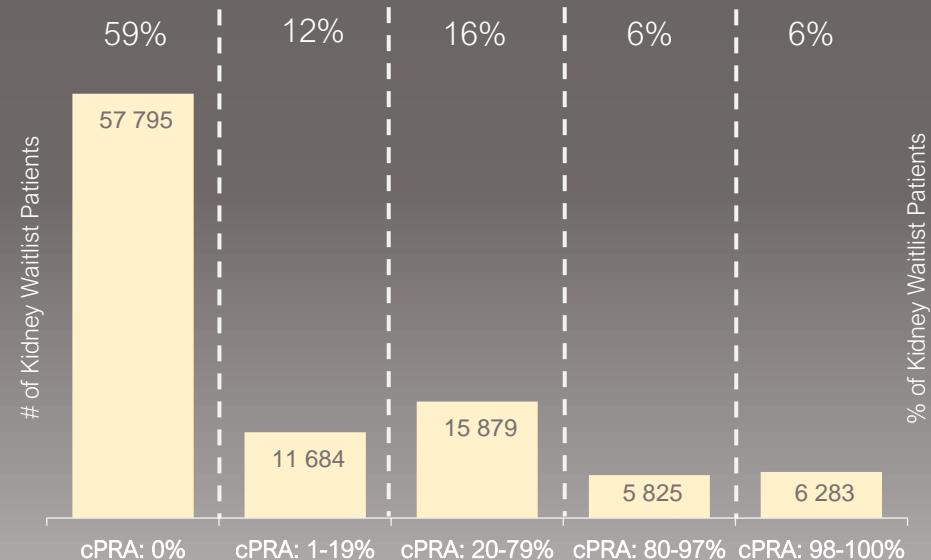
Blood transfusion



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 in 2018



Source: Organ Procurement and Transplant Network,  
Advanced Report. Analysis as of September 25, 2018

# Imlifidase may enable transplantation in highly sensitized kidney patients

## Creating equity for highly sensitized patients

- Allocation systems increase transplantation rates, however the rates for highly sensitized patients are still very low compared with average or non-sensitized patients
- If approved, imlifidase may potentially:
  - Complement allocation systems (e.g. KAS, Euro-transplant) to reduce time to transplant in highly sensitized patients
  - Reduce the need for antibody matching and give sensitized patients access to a larger pool of organs
  - Reduce the risk for co-morbidities and mortality associated with dialysis and waiting time
  - Increase transplant rates in highly sensitized patients
  - Help reduce the number of discarded kidneys (1,000 donated kidneys are discarded in the U.S. alone every year<sup>3</sup>)

<sup>1</sup> Jordan et al. British Medical Bulletin, 2015, 114:113–125

<sup>2</sup> Orandi et al. N Engl J Med 2016;374:940-50

<sup>3</sup> Organ Procurement and Transplantation Network (OPTN)

<sup>4</sup> Jordan et al. British Medical Bulletin, 2015, 114:113-125

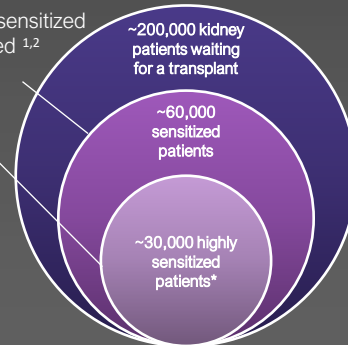


*Delilah, a 23 years old highly sensitized kidney transplant patient from California*

### U.S. + EU Kidney Transplant Waitlist Breakdown

>30% of waitlist patients are sensitized

- 15% moderately sensitized<sup>1,2</sup>
- 15% highly sensitized<sup>1,2 \*</sup>



~40,000 transplants done annually in the US and EU.

\*Patients with sensitivity above cPRA 80%

Source: The U.S. Department of Health and Human Services and .irodat.org

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

Low complexity transplants ← → Higher complexity transplants

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

Non or less sensitized  
(cPRA < 20%)

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

Moderately sensitized  
(20% > cPRA < 80%)

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

Highly sensitized  
(cPRA > 80%)

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



Actual patient have given consent to provide images

<sup>1</sup> EDQM. (2020). International figures on donation and Transplantation 2019

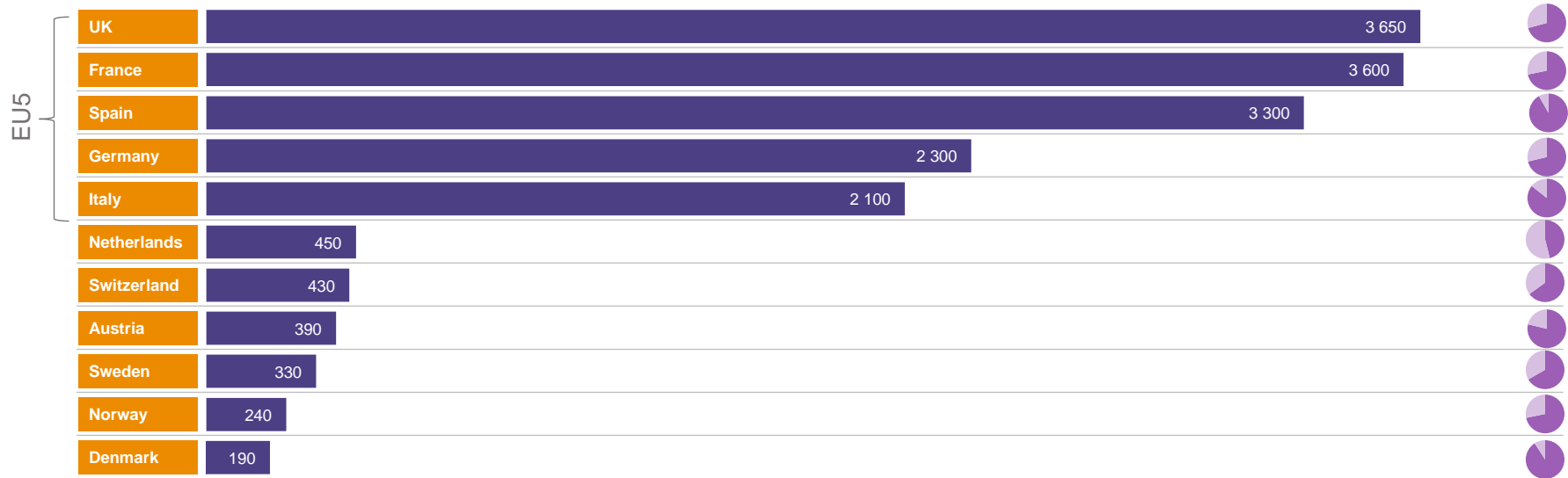
<sup>2</sup> SRTR Database and individual assessments of allocation systems

# European kidney transplantation landscape

Approximately 15,000 annual kidney transplants in EU5 +2,000 annual kidney transplants in Netherlands, Sweden, Norway, Denmark, Austria and Switzerland<sup>1</sup>

- Transplants annual
- Living donor transplants
- Deceased donor transplants

## Patients



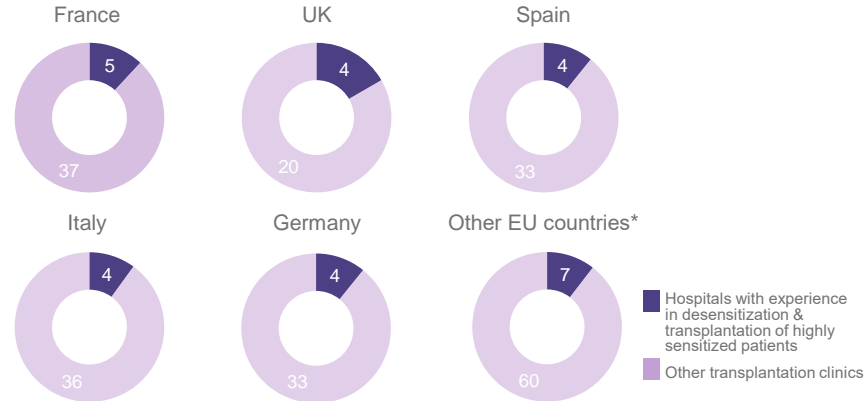


# Early launch in centres of excellence

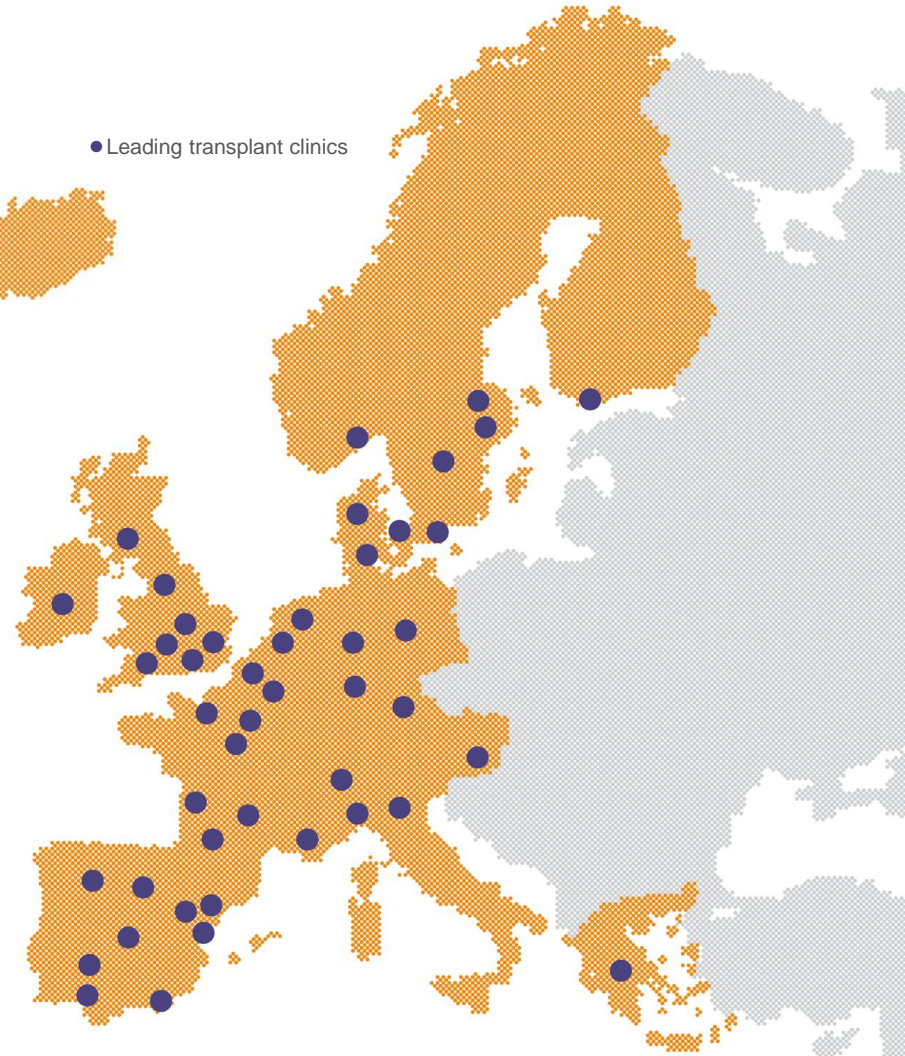
## First launch wave defined

1. Launch Idefix® with kidney transplant specialists who have experience in desensitization
2. Create positive momentum with Idefix as the new Gold Standard in desensitization protocols
3. Prepare post approval study to confirm filing data

## Leading transplantation centres perform the majority of all transplantations in EU

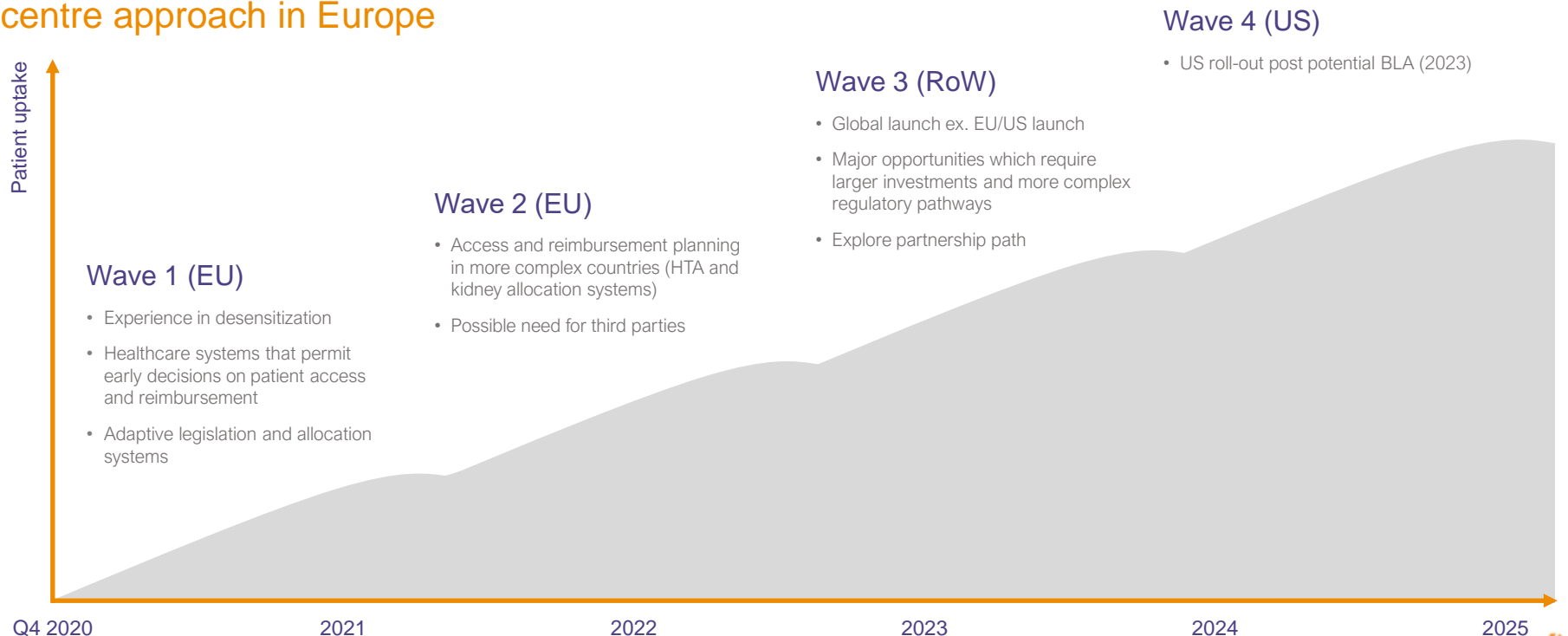


● Leading transplant clinics



# Plans for global expansion

Launching in waves with centre-by-centre approach in Europe



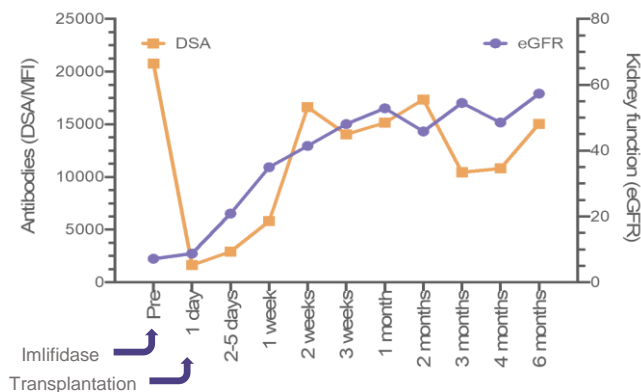
Completed and  
ongoing studies in  
kidney transplantation









# Imlifidase has enabled kidney transplantation in 46 highly sensitized patients

## 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



## Study design of our four Phase 2 trials

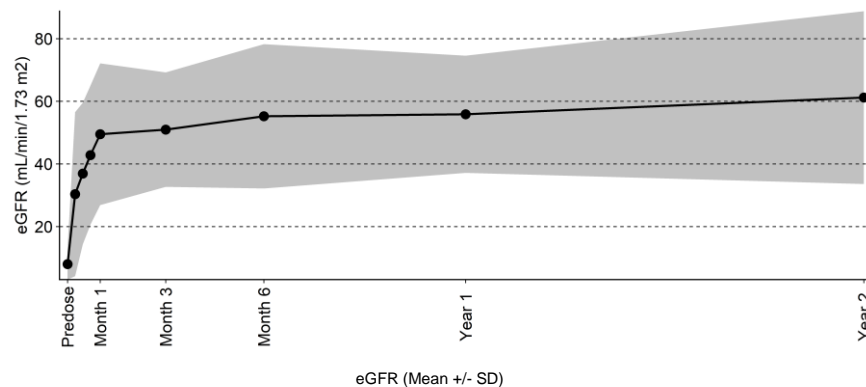
Study 02 Phase 2	Subjects	8 patients 
	Design	Single-center, single-arm, open-label
	Main objective	Efficacy defined as Imlifidase dosing scheme resulting in HLA antibody levels acceptable for transplantation, within 24 hours
Study 03 Phase 2	Subjects	10 patients 
	Design	Single-center, single-arm, open-label,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

## Two year follow-up data show graft survival of 90% and well functioning kidneys in 92% of these patients

### AMR frequency in line with less sensitized patients

- Two-year follow-up data post imlifidase treatment and transplantation show 90% graft survival for 31 patients
- Of the patients with data at two years, 92% had a well functioning kidney with median eGFR of 61ml/min/1.73 m<sup>2</sup>
- 33% of the patients experienced active antibody mediated rejections (AMR) within the first six months, which compares with 25-60% of patients in the literature for this group of highly sensitized patients<sup>1</sup>
- Only one patient experienced an AMR episode later than six months after transplantation
- The analysis concludes that the AMR frequency was comparable with other studies with less sensitized patients in crossmatch positive patients

### Median eGFR at 61ml/min/1.73 m<sup>2</sup> after year 2



## Study 01 Phase 1

# The 01 study 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  $F(ab')_2$  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

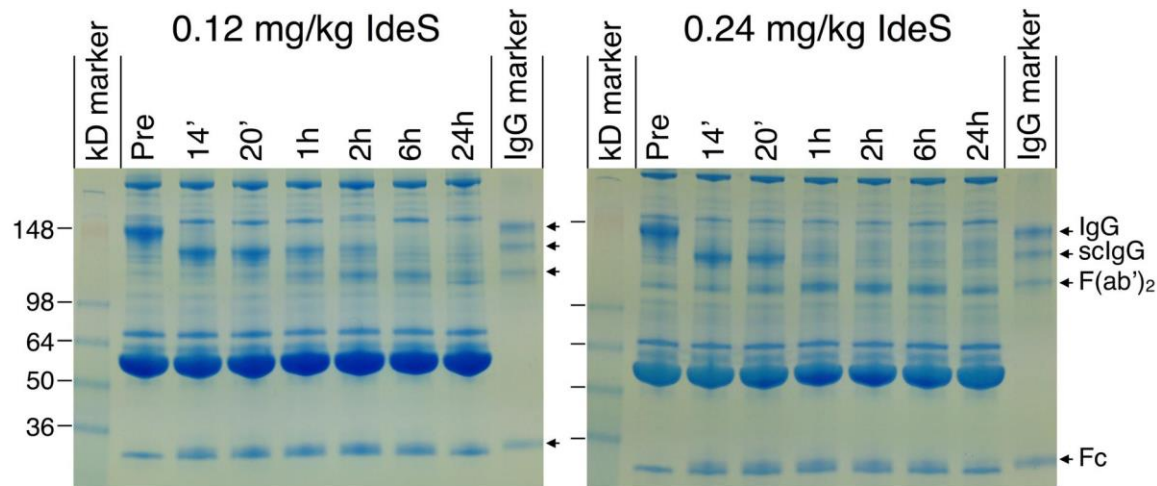
## STUDY DESIGN

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

## STATUS

Completed

- The 01 study showed complete removal of IgG and that Imlifidase was considered safe to use





## Study 02 Phase 2

The 02 study 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)

CLINICALTRIALS.GOV ID

NCT02224820

### SUBJECTS

8 Patients with chronic kidney disease (Sweden)

### DOSES/FOLLOW UP TIME

0.12 & 0.25 mg/kg BW given once or twice within 48 hours

### MAIN OBJECTIVES

- Efficacy defined as Imlifidase dosing scheme resulting in HLA antibody levels acceptable for transplantation, within 24 hours from dosing
- Safety

### STUDY DESIGN

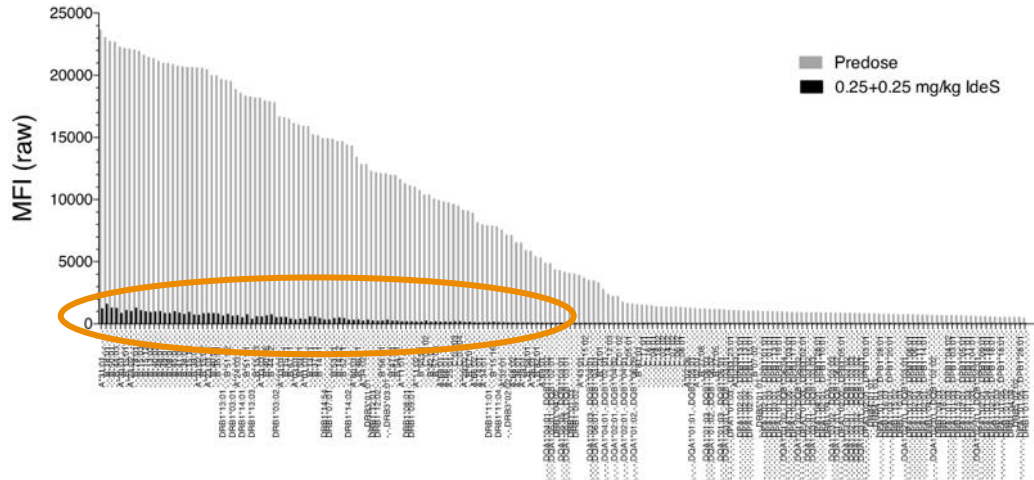
- Single-center, Single arm with ascending doses, open-label
- Transplantation not part of protocol

### STATUS

Completed

- Primary efficacy endpoint reached
- Safe and well tolerated

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



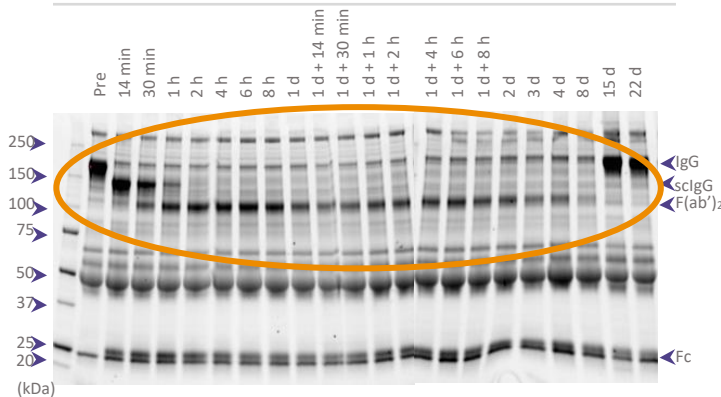
<sup>1</sup> Lorant et al (2018) American Journal of Transplantation (2018)



## Study 03 Phase 2

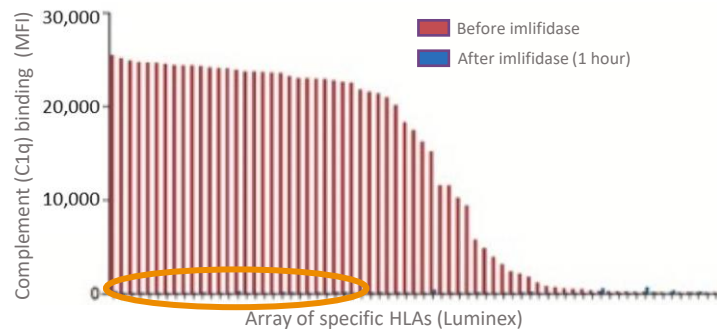
The 03 study proved safety and efficacy with HLA antibodies at acceptable levels; enabling transplantation in all patients

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



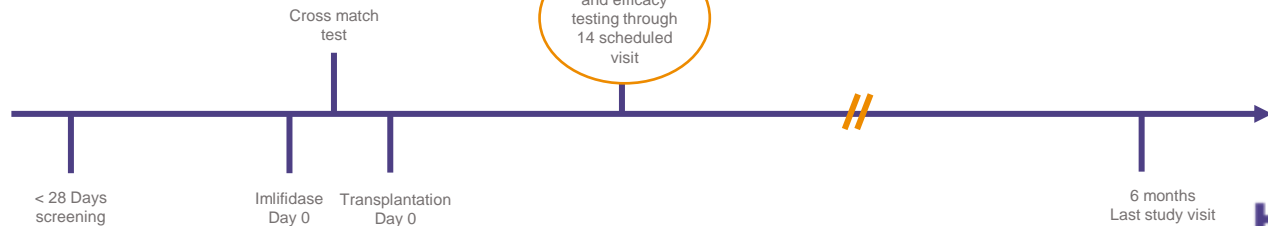
SDS-PAGE analysis of patient serum

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



C1q analysis of patient serum

### Protocol



The 04 study proved safety and efficacy with Cedar Sinai's standard protocol (rituximab and IVIg)

CLINICALTRIALS.GOV ID

NCT024226684

## SUBJECTS

17 Patients (US)

### DOSES/FOLLOW UP TIME

## MAIN OBJECTIVES

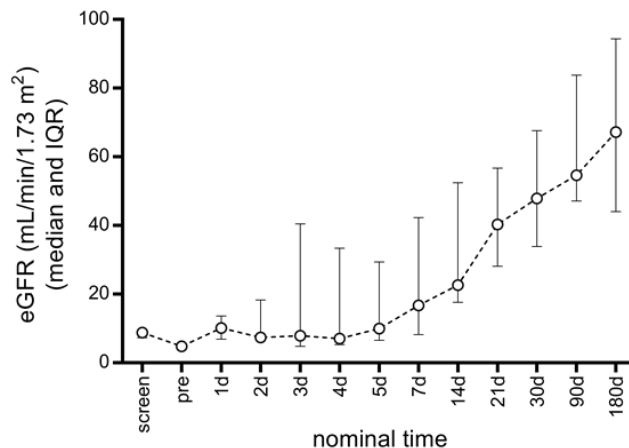
## STUDY DESIGN

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

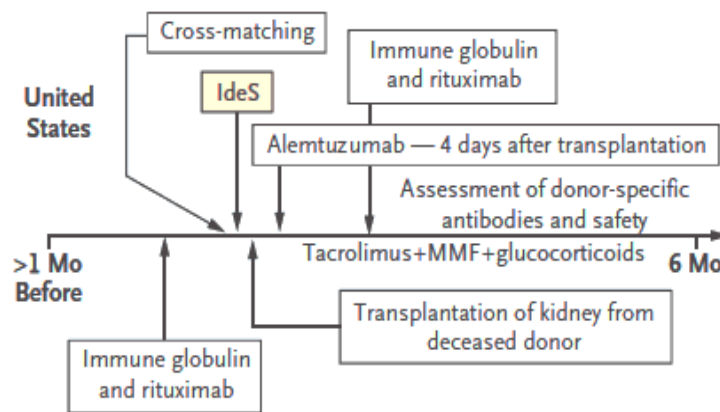
## STATUS

Completed

## Graft function (eGFR) post six months



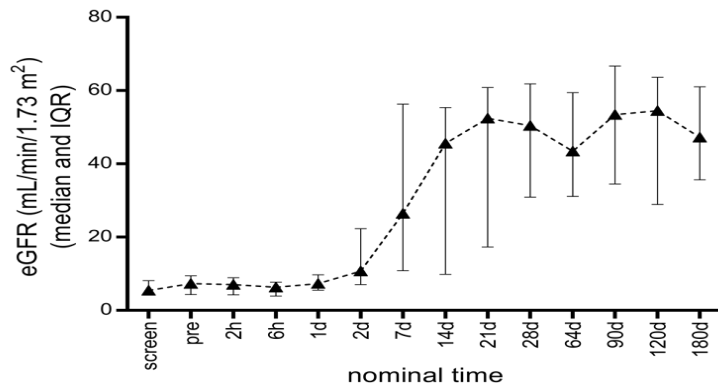
## Cedar's desensitization protocol in combination with imlifidase



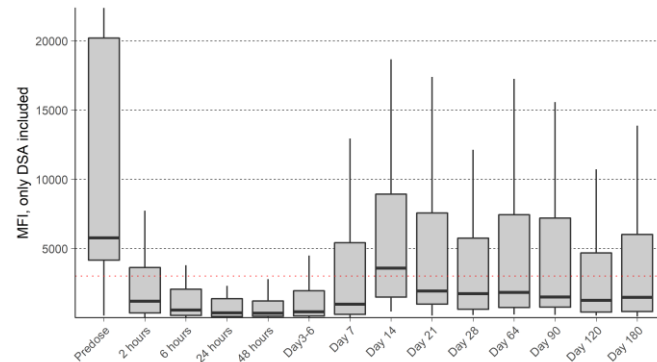
## Study 06 Phase 2

# The 06 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



Jordan SC, et al. (2019). Results from the international phase II study on the safety and efficacy of imlifidase in highly-sensitized kidney transplant patients. Abstract presented at ATC.

# Overview of all 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 "Highdoses" 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



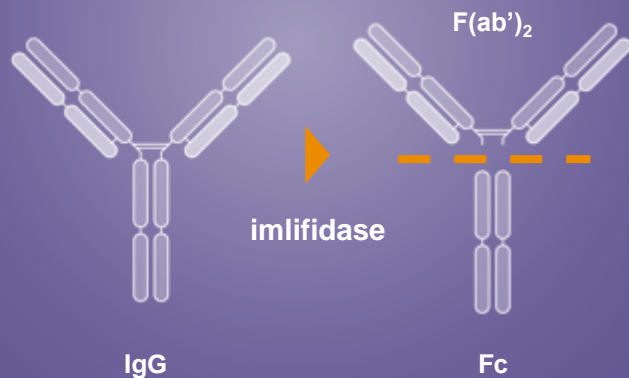
# CMC - Imlifidase



# Imlifidase, a novel approach to effectively eliminate pathogenic IgG

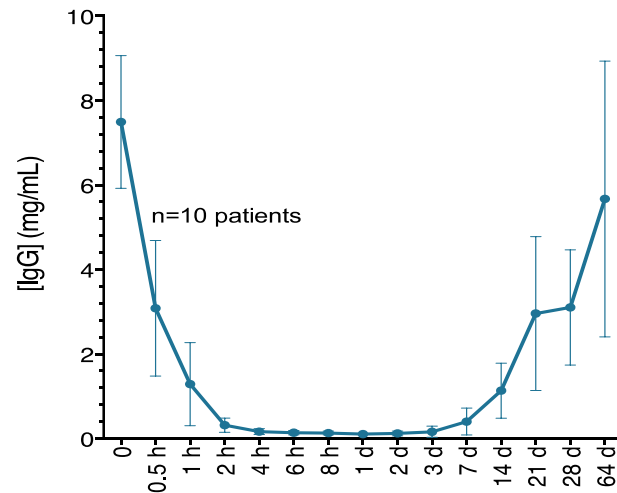
## Proven mechanism of action

- Interacts with Fc-part of IgG with extremely high specificity
- Cleaves IgG at the hinge region, generating one  $F(ab')_2$  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 hours post 15 min infusion
- IgG antibody-free window for approximately one week

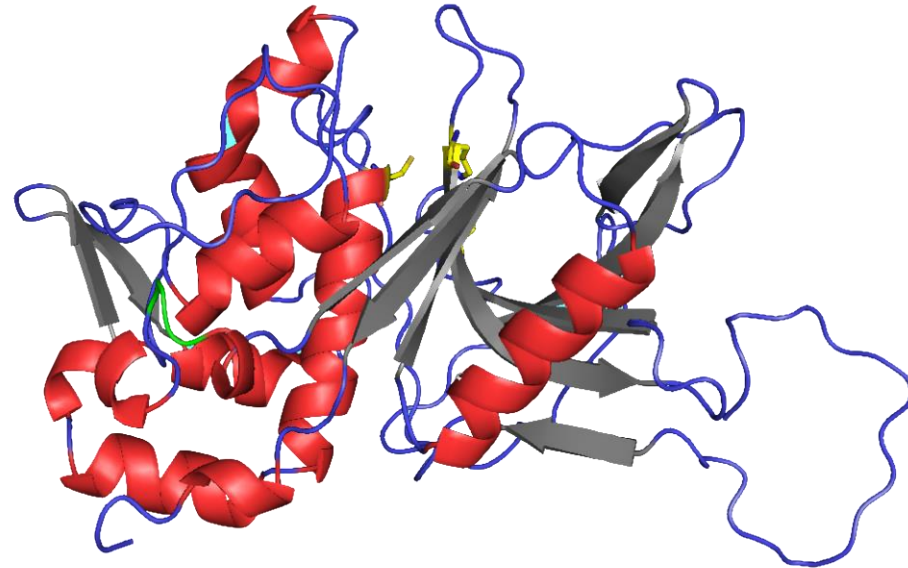


# Our IgG antibody-cleaving enzyme

## 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 with a shelf life of 12 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 12 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



### Drug product composition

- Imlifidase protein
- Mannitol
- Tween
- EDTA
- Tris-HCl

# Supply Chain for imlifidase in kidney transplantation



# Manufacturing will be done in close collaboration with highly experienced European based third party CMOs

## Drug substance production process (API)

### Biotechpharma



#### Fermentation/ harvesting

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

#### Protein purification

- Cell Disruption
- Protein Release

#### Protein purification cont.

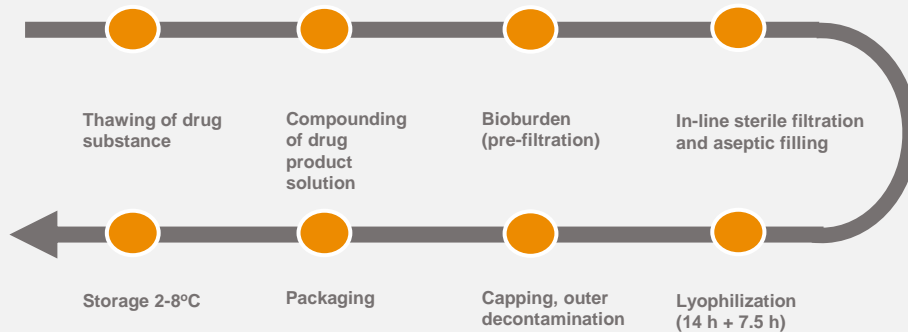
- Ion Exchange Chromatography
- Ceramic Hydroxy Apatite Chromatography
- Hydrophobic Interaction Chromatography
- Ultrafiltration/ Diafiltration

#### 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)

**biotechpharma**

#### 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

**Baxter**

#### 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

**HANSA**  
BIOPHARMA

# Clinical development programs



# Broad 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: Commercial launch Q4 2020
	US: Kidney transplantation in highly sensitized patients <sup>1,2</sup>				**			First patient dosed H1 2021
	Anti-GBM antibody disease <sup>3</sup>							Next step is to engage with regulators and agree on a path forward toward BLA/MAA
	Antibody mediated kidney transplant rejection (AMR)							Complete enrolment of 30 patients H2'21
	Guillain-Barré syndrome (GBS)							Complete enrolment of 30 patients H2'21
	Limb-Girdle (LGMD) & Duchenne (DMD) (Pre-treatment ahead of gene therapy with Sarepta)							Research phase
NiceR	Recurring treatment in autoimmune disease, transplantation and oncology							Development of CMC process / Tox studies
EnzE	Cancer immunotherapy							Research phase

Completed Ongoing

<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

\*) The EU Commission has granted conditional approval for imlifidase in highly sensitized kidney transplant patients. A post-approval study will commence in parallel with the launch

\*\*) FDA: Proposed study protocol submitted June 2020. Discussions are currently ongoing with the FDA. Once the final protocol has been agreed upon, Hansa Biopharma will proceed to set up centers in the US and start to enroll patients. Given the continued impact of the COVID-19 pandemic and the timeline for the finalization of the study protocol Hansa expect recruitment of the first patient to be in H1 2021

# Positive high-level data read-out in the Anti-GBM study. Reinitiation of recruitment in AMR & GBS in Q4'20

## Ongoing Phase 2 programs

Enrollment status  
end Q3'2020



### Anti-GBM (investigator-initiated study)

- Phase 2 study completed with positive high-level data read-out from 15 patients
- Next step is to engage with regulators and agree on a path forward toward BLA/MAA in anti-GBM



### Antibody Mediated Rejection

- 4/30 patients enrolled in AMR study
- Recruitment is expected to be reinitiated in Q4 2020
- Enrollment is expected to be completed H2 2021



### Guillain-Barré Syndrome

- 4/30 patients enrolled in GBS study
- Recruitment is expected to be reinitiated in Q4 2020
- Enrollment is expected to be completed in H2 2021

■ Patients enrolled  
■ Patients left





# Anti-GBM, a rare acute autoimmune disease affecting kidneys and lungs; Positive data read-out in Q3 2020

## 2/3 of Anti-GBM patients lose kidney function<sup>2</sup>

- 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
- Study concludes that imlifidase leads to rapid clearance of anti-GBM antibodies, with two-thirds of patients achieving dialysis independence six months after treatment
- Positive data demonstrates potential to increase renal survival in anti-GBM antibody disease and marks an important milestone for expansion of imlifidase outside transplantation
- Next step is to engage with regulators and agree on a path forward toward BLA/MAA in anti-GBM
- Our Anti-GBM program obtained Orphan Drug designation from both FDA and European Commission in 2018

1 Kluth et al. J Am Soc Nephrol. 1999 Nov;10(11):2446-53

2 Hellmark et al. J Autoimmun. 2014 Feb-Mar;48-49:108-12



# Favourable pre-clinical studies show that imlifidase degrades IgG bound to the GBM in vivo; preventing renal damage in animals

## 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

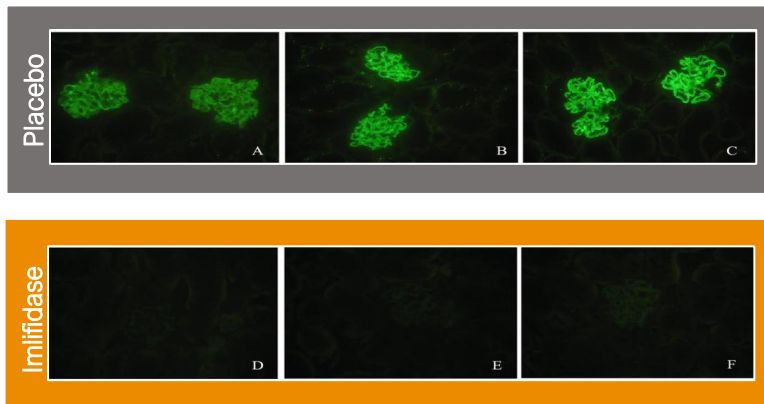
## STUDY DESIGN

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

## STATUS

Ongoing

## Mouse anti-rabbit IgG (Fc specific)



## Inclusion criteria

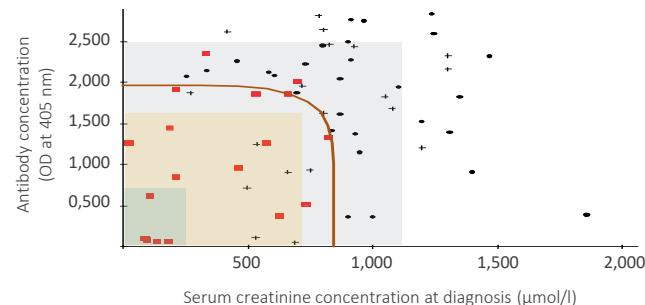
**Inclusion:** Toxic anti-GBM antibodies level as considered by the investigator. eGFR < 15 ml/min/1.73 m<sup>2</sup> or if the patient is non-responsive to standard treatment, and has lost >15 ml/min/1.73 m<sup>2</sup> after start of treatment

**Exclusion:** Anuria for more than 2 days (less than 200 ml during last 48 hours); Dialysis dependency for more than 5 days

Yang et al. Favorable pre-clinical studies: "Imlifidase degrades IgG bound to the GBM in vivo, thereby preventing renal damage in this animal model. Nephrology Dialysis Transplantation, 2010;25(8): 2479-86.

## Anti-GBM creatinine and antibody concentration

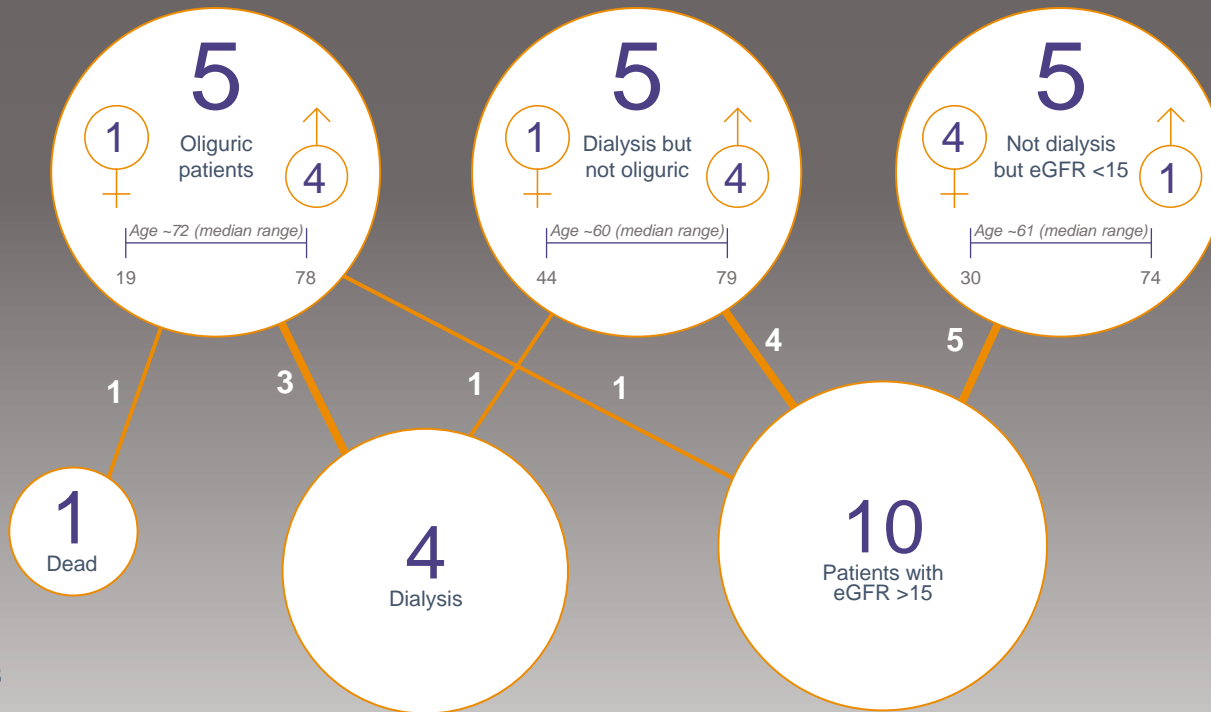
- Both creatinine and levels of antibodies predict outcome and we expect that imlifidase can treat the disease by degrading IgG bound to the GBM





# Positive high-level data from Phase 2 study anti-GBM disease marks an important milestone for expansion of imlifidase outside transplantation

2/3 of patients achieving dialysis independence six months after treatment



## High-level data read out

- Study concludes that imlifidase leads to rapid clearance of anti-GBM antibodies, with two-thirds of patients achieving dialysis independence six months after treatment
- Normally 2/3 of patients will lose kidney function and end up in dialysis after six months
- Next step is to engage with regulators and agree on a path forward toward BLA/MAA in anti-GBM

# Long term graft survival is challenged by antibody mediated rejection post transplantation

## There is no approved treatment for AMR

- Active antibody mediated rejection after transplantation occurs in 10-15% of kidney transplants<sup>1</sup> or ~ 3,200<sup>2,3</sup> new patients 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 AMR in kidney transplant patients.
- 4/30 patient treated with imlifidase in AMR. 6/8 sites have been initiated to recruit patients in the US, Europe and Australia.
- Enrollment is expected to be completed H2 2021

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

<sup>2</sup> Jordan et al., British Medical Bulletin, 2015, 114:113-125.

<sup>3</sup> <http://www.irodat.org>.

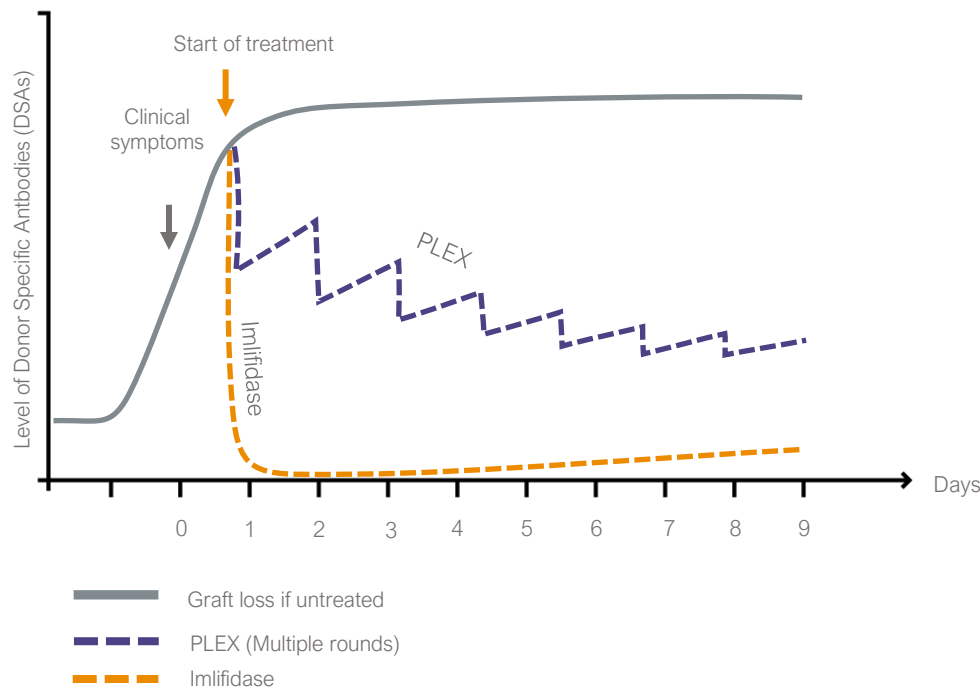
<sup>4</sup> Seven major markets – US, Germany, UK, France, Spain, Italy, and Japan

## AMR Phase 2

# New AMR Phase 2 study initiated to test imlifidase ability to reduce the amount of DSA in AMR patients post transplantation

## Potential of using imlifidase vs. PLEX in AMR

*Illustrative*



CLINICALTRIALS.GOV ID

NCT03897205 (2019)

### SUBJECTS

30 patients targeted (20 patients will be treated with imlifidase and 10 with Plasma exchange). Recruitment from 8 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

Ongoing

# Guillain-Barré syndrome 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 ~ 11,000<sup>1</sup> per year in 7MM<sup>2</sup>
- Current Standard of Care is treatment with IVIG or PLEX
- The new 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)
- 4/30 patients enrolled. 6/10 sites are recruiting patients across France, UK and the Netherlands. Enrollment is expected to be completed in H2 2021
- 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

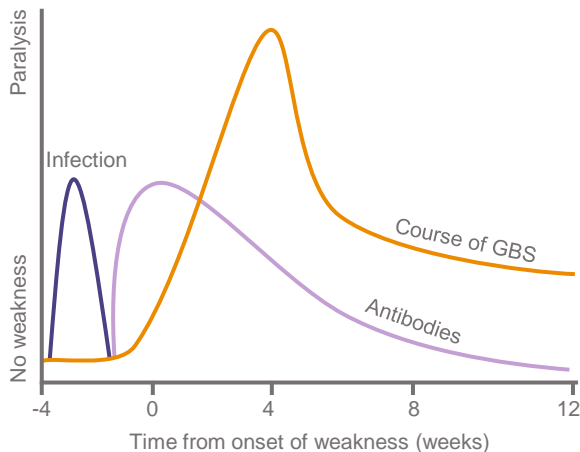
- Study is an open-label, single arm, multi-center trial evaluating safety, tolerability and efficacy of imlifidase, in combination with standard of care, IVIg, to treat GBS

### STATUS

Ongoing

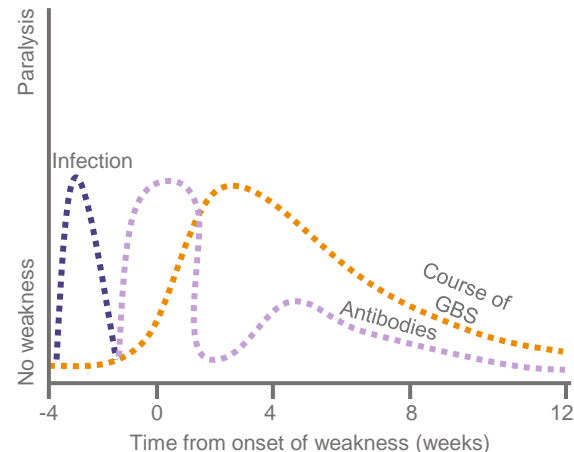
## Today's Standard of Care IVIg or PLEX

*Illustrative*



## Potential with imlifidase

*Illustrative*



# Pre-clinical programs

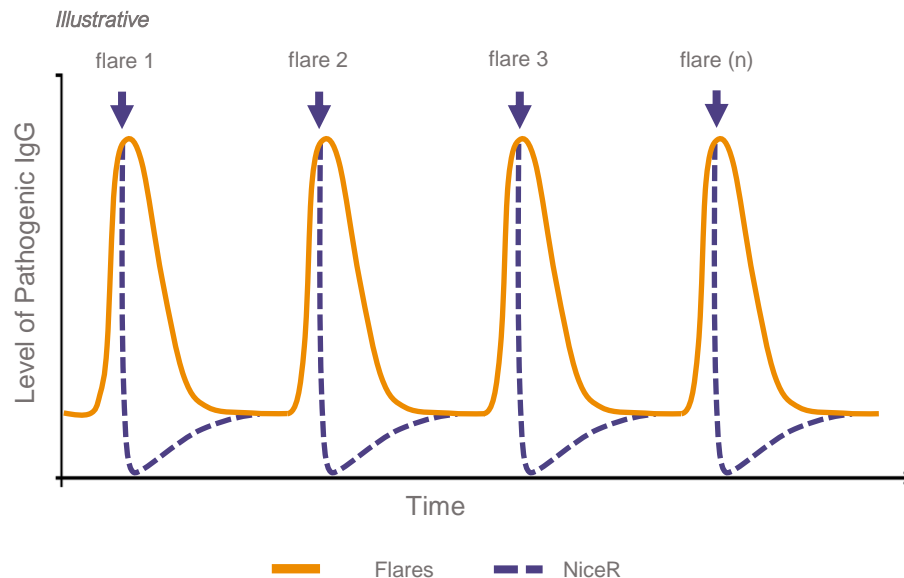


# “NiceR” – new set of enzymes for repeat dosing; potentially enabling treatment of relapsing diseases

## IgG-cleaving enzyme 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.
- Completion of GMP-manufacturing process in the first half of 2021
- Initiate IND-enabling tox studies in the first half of 2021

## NiceR can potentially inactivate flares

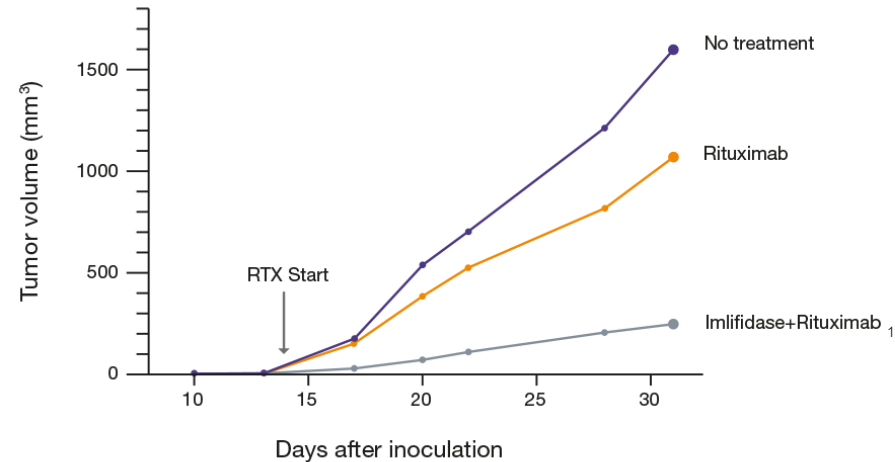


# Imlifidase / NiceR can potentially improve the therapeutic effect in oncology (EnzE)

## 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

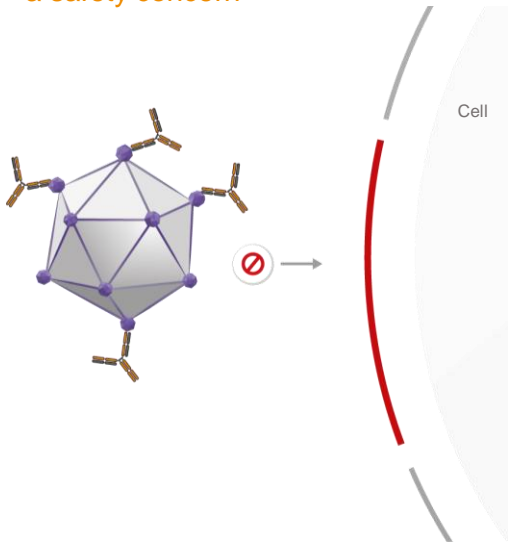


# Neutralizing antibodies (Nabs) are immunological barriers in gene therapy

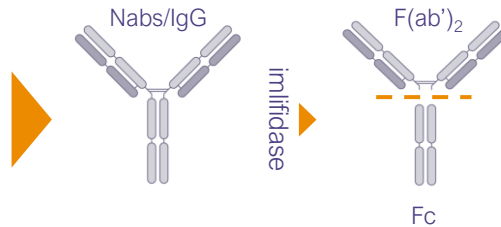
*Between approximately 5% and 70%<sup>1,2</sup> of patients considered for gene therapy treatment carry neutralizing anti-AAV antibodies forming a barrier for treatment eligibility*

*Our hypothesis is that imlifidase has the potential to eliminate neutralizing antibodies as a pre-treatment, prior to the introduction of gene therapy*

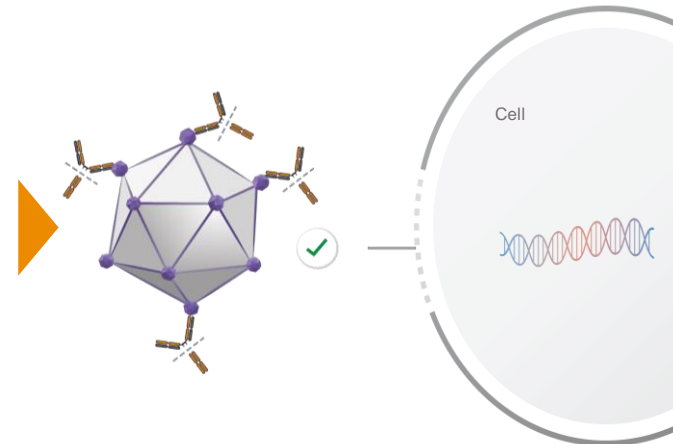
- 1 Antibodies prevent effective transfer of healthy gene sequence and can be a safety concern



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

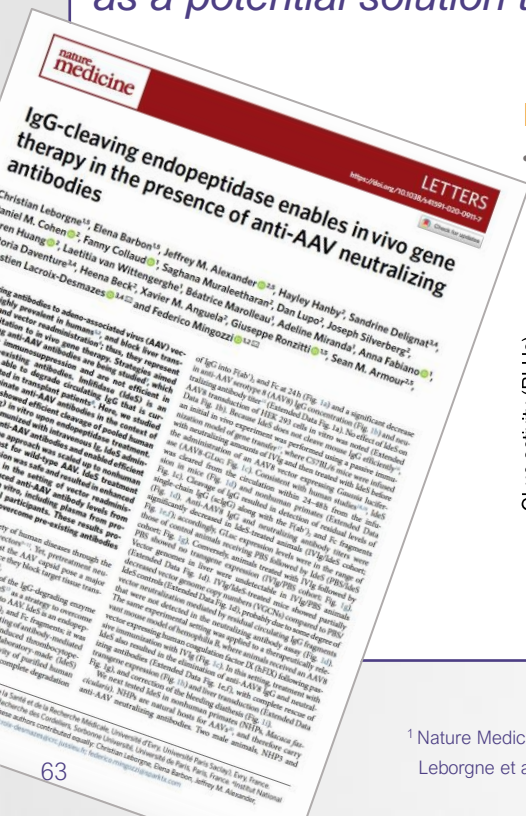


- 3 The idea is to eliminate the neutralizing antibodies as a pre-treatment to enable gene therapy



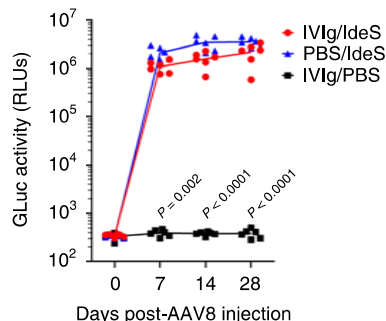
# Imlifidase (IdeS) was highlighted in Nature Medicine<sup>1</sup> with encouraging outcome

## Results from preclinical studies with imlifidase (ideS) in gene therapy demonstrate imlifidase as a potential solution to overcome pre-existing antibodies to AAV-based gene therapy



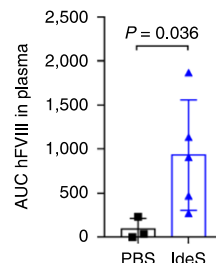
### Imlifidase tested in a hemophilia mouse model

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



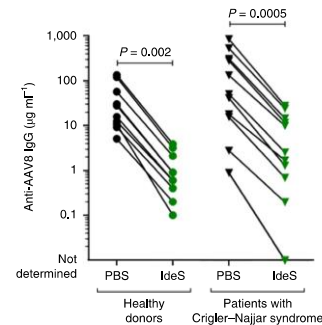
### Imlifidase tested in NHP ahead of AAV vector infusion

- 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)

# Exclusive agreement with Sarepta Therapeutics to develop and promote imlifidase as pre-treatment ahead of gene therapy in select indications

## A unique opportunity to combine efforts...

...and to use the unique features of imlifidase to potentially enable gene therapy treatment in patients who today aren't eligible for these breakthrough therapies due to pre-existing neutralizing antibodies in two indications with a very high unmet medical need

## Structure of the partnership

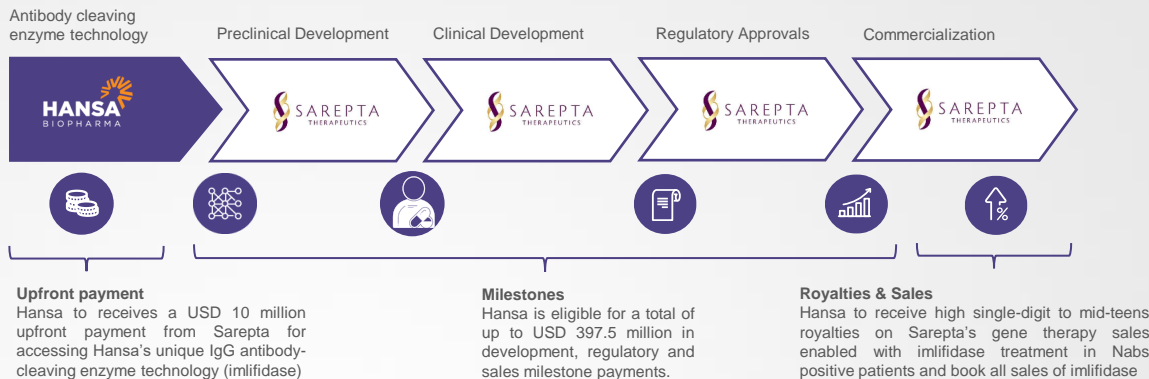
Sarepta will be responsible for conducting

- Pre-clinical/clinical studies with imlifidase
- Regulatory approvals
- Promotion of imlifidase as a pre-treatment to Sarepta's gene therapies following potential approval

Hansa will supply product, support with know-how and involve in the regulatory approval process

## Hansa's financial participation

Potential total deal value for Hansa amounts to up to USD ~400m plus royalties and incremental imlifidase sales

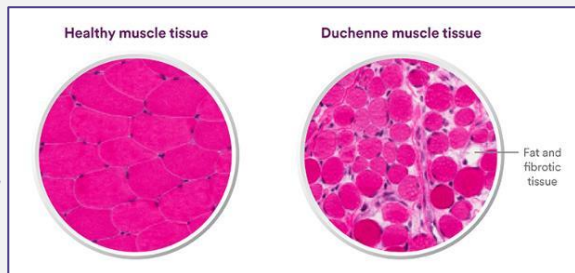


# Sarepta obtains a global and exclusive license to imlifidase in DMD and LGMD in gene therapy

## About Duchenne muscular dystrophy (DMD)

- Duchenne muscular dystrophy is a rare genetic disease caused by mutation in the DMD gene, encoding for the protein dystrophin
- Muscles in the body become weak and most patients use wheelchair by the age of 12
- Affects one in 3,500 to 5,000 males born worldwide (approximately 400-500 annual male cases in the US) of which approximately 15-20% are estimated to have pre-existing antibodies to AAV-based gene therapy which prevents the patients from being treated with gene therapy

*"On average, every day DMD takes the life of a child in the United States..."*

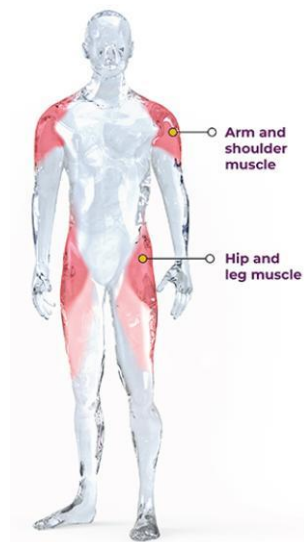


Source: Sarepta Therapeutics

<https://investorrelations.sarepta.com/static-files/0c4aca61-9419-45a5-afb1-f2092644627>

## About Limb-girdle muscular dystrophy (LGMD)

- Limb-girdle muscular dystrophy is a group of diseases that cause weakness and wasting of the muscles
- May be caused by a single gene defect affecting specific proteins within muscle cells
- Global prevalence of 1.63 per 100,000 individuals (of which approximately 15-20% are estimated to have pre-existing antibodies to AAV-based gene therapy which prevents patients from being treated with gene therapy)



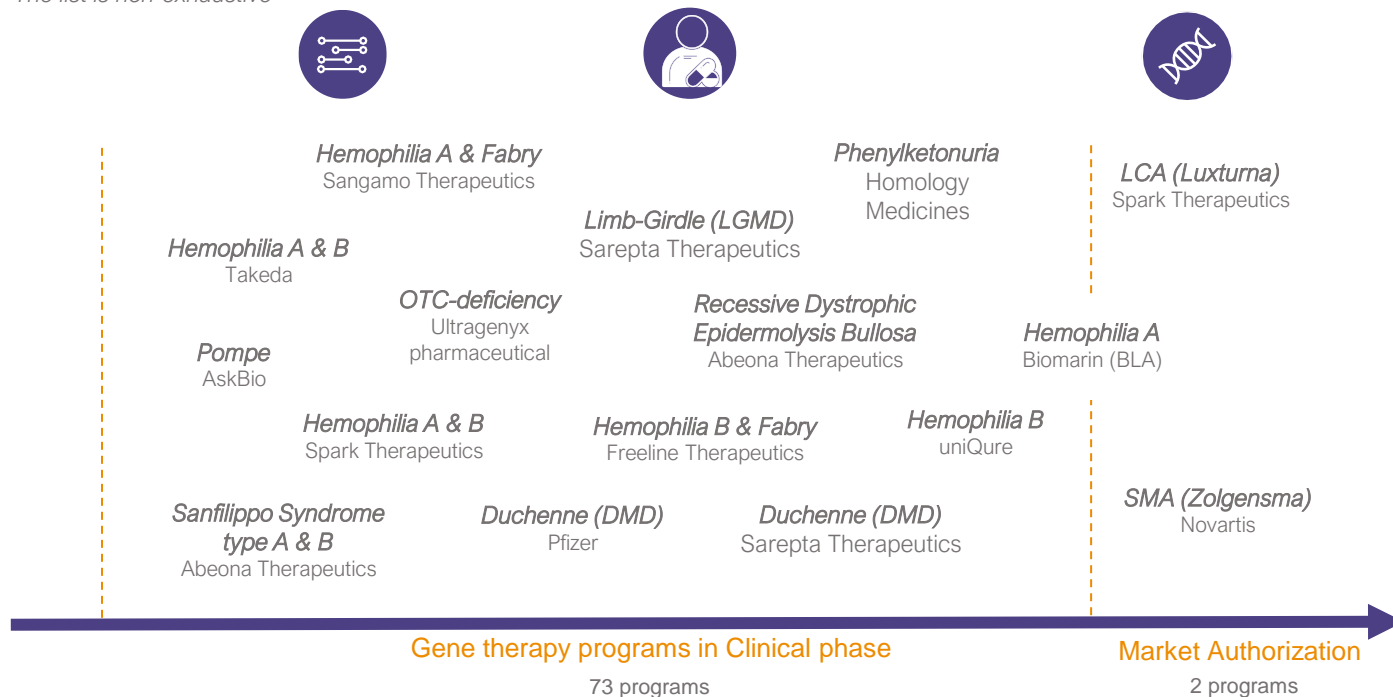
Source: Sarepta Therapeutics

<https://investorrelations.sarepta.com/static-files/0c4aca61-9419-45a5-afb1-f2092644627>

# Emerging landscape in gene therapy

## Examples of big pharma and specialized players targeting rare diseases in gene therapy

The list is non-exhaustive



Today experimental protocols are used based on plasmapheresis, or with immunosuppressants; however these protocols have not demonstrated sufficient efficacy and safety

187 *in vivo* programs are ongoing in gene therapy including 73 clinical stage programs<sup>1</sup>

Two *in vivo* gene therapy products have been approved by FDA: **Luxturna** from Sparks/Roche and **Zolgensma** from Novartis

<sup>1</sup> Alacrita Consulting 2019 estimate based on publicly available data

# Capital Markets



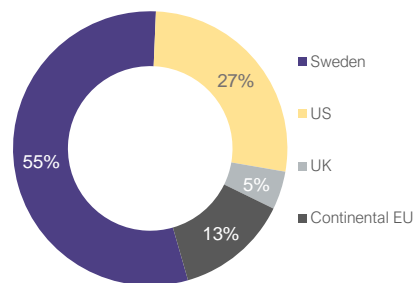
# Ownership in Hansa Biopharma

## Top 10 ownership as per September 30, 2020

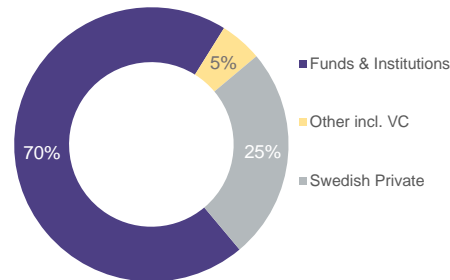
Name	No. of shares	Ownership in pct.
Consonance Capital Management	2 655 009	6.0
Redmile Group	2 323 708	5.2
NXT2B	2 155 379	4.8
Invesco	1 938 841	4.4
Thomas Olausson	1 750 474	3.9
Fourth Swedish National Pension Fund	1 536 624	3.5
Avanza Fonder AB	1 387 380	3.1
Handelsbanken Fonder AB	1 329 744	3.0
Gladiator	1 025 000	2.3
ClearBridge, LLC	1 012 786	2.3
Other	27 358 507	61.5
Outstanding A shares in total	44 473 452	100.0

## Classification of ownership

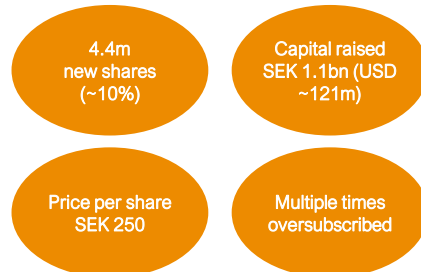
Ownership by country



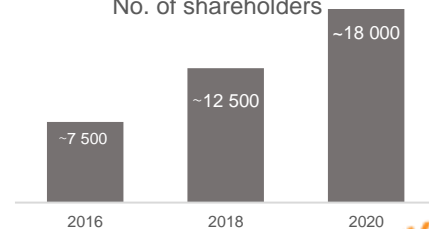
Ownership by type



Capital Raise July 2020



No. of shareholders





# Hansa Biopharma - Market data and share price development

## Market data (Sep 2020)

Stock Exchange: Nasdaq, Stockholm since Nov 2015  
(First North Oct 2007- Nov 2015)

Ticker HNSA

Market Cap: SEK ~10bn (USD ~1.15 bn)

52-week range: SEK 59-288 per share

Avg. Daily Turnover: vol ~565k shares

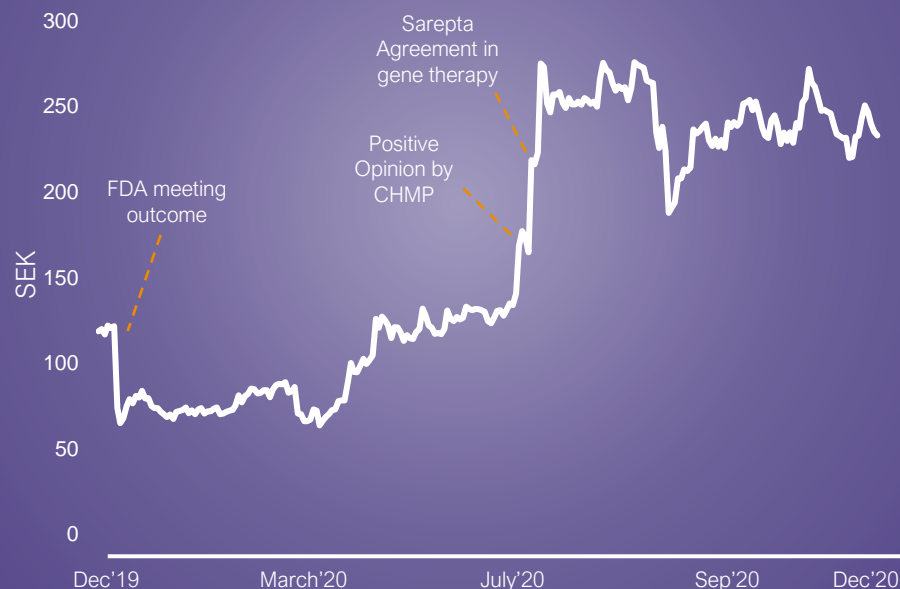
Shares outstanding: 44 473 452

Shareholders ~18,000

Top 5 Shareholders:	Consonance Capman	6.0%
As per September 2020	Redmile Group*	5.2%
	NXT2B	4.8%
	Invesco	4.4%
	Thomas Olausson	3.9%

\*Redmile Group has increased ownership to above 10% as per 25 November 2020

## 12 months Share price development (Dec 2020)



# Analysts covering Hansa Biopharma (ticker: HNSA, NASDAQ Stockholm)

Analyst	Bank / Research institution (year of initiation)	Location	Email	Phone
Christopher Uhde	SEB (2016)	Stockholm	<a href="mailto:christopher.uhde@seb.se">christopher.uhde@seb.se</a>	+46 (0) 876-385 53
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Charles Weston	RBC (2017)	London	<a href="mailto:Charles.Weston@rbccm.com">Charles.Weston@rbccm.com</a>	+44 7935 202349
Ingrid Gafanhão	Kempen (2019)	Amsterdam	<a href="mailto:ingrid@gafanhao@kempen.com">ingrid@gafanhao@kempen.com</a>	+31 689 937 525
Naresh Chouhan	Intron Health Research (2020)	London	<a href="mailto:naresh@intronhealthresearch.com">naresh@intronhealthresearch.com</a>	+44 7939 224 322
Maneka Mirchandaney	Evercore (2018)	New York City	<a href="mailto:maneka.mirchandaney@evercoreisi.com">maneka.mirchandaney@evercoreisi.com</a>	+1 646 740 1482
Erik Hultgård	Carnegie (2019)	Stockholm	<a href="mailto:erik.hultgard@carnegie.com">erik.hultgard@carnegie.com</a>	+46 (0) 858-869 237
Ludvig Svensson	Redeye (2008)	Stockholm	<a href="mailto:ludvig.svensson@redeye.se">ludvig.svensson@redeye.se</a>	+46 (0) 704-962 535
Joseph Hedden	RX Securities (2016)	London	<a href="mailto:joseph@rxsecurities.com">joseph@rxsecurities.com</a>	+44 773 061 8803
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[www.hansabiopharma.com](http://www.hansabiopharma.com)



## Calendar

Dec 8-9, 2020	Jefferies Road Show (virtual)
Dec 10, 2020	ABG Road Show (virtual)
Jan 11-14, 2021	J.P. Morgan Healthcare Conference (virtual)
Jan 14, 2021	H.C. Wainwright BioConnect Conference (virtual)
Jan 18, 2021	SEB Nordic Healthcare seminar (virtual)
Feb 2, 2021	Interim report Jan-Dec 2020
Feb 10, 2021	Vator Swiss Nordic Conference (virtual)
Mar 9, 2021	Carnegie Nordic Healthcare seminar (virtual)
April 8, 2021	Annual Report 2020
April 22, 2021	Interim report for Jan-Mar 2021
May 5, 2021	Kempen Life Sciences Conference (virtual)
May 19, 2021	RBC Capital Markets Global Healthcare Conference (virtual)
July 15, 2021	Interim report for Jan-Jun 2021
Oct 21, 2021	Interim report for Jan-Sep 2021

