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# *Transforming the lives of people with rare diseases*

Analyst and Media event June 11, 2019
Cord, Stockholm

# Today's agenda and presenters

12:05 Welcome and short introduction

12:10 Business & Pipeline update by Sören Tulstrup, CEO & President

12:30 Q&A

12:40 Focus presentation by Dr. Tomas Lorant, Senior Medical, Director

***'Making the impossible possible' kidney transplantation in highly sensitized patients***

13:20 Q&A

13:30 End of event

# Forward-looking statements

This presentation may contain certain forward-looking statements and forecasts based on uncertainty, since they relate to events and depend on circumstances that will occur in the future and which, by their nature, will have an impact on Hansa Biopharma's business, financial condition and results of operations. The terms "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 statement. There are a number of factors that could cause actual results and developments to differ materially from those expressed or implied in a forward-looking statement or affect the extent to which a particular projection is realized. Factors that could cause these differences include, but are not limited to, implementation of Hansa Biopharma's strategy and its ability to further grow, risks associated with the development and/or approval of Hansa Biopharma's products candidates, ongoing clinical studies and expected study results, the ability to commercialize imlifidase, 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.

No assurance can be given that such expectations will prove to have been correct. Hansa Biopharma disclaims any obligation to update or revise any forward-looking statements, whether as a result of new information, future events or otherwise.



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# Business & Pipeline update

Sören Tulstrup,
CEO Hansa Biopharma

# Lead product on cusp of potential commercialisation

## Lead, late-stage clinical program: IDEFIRIX (imlifidase) in kidney transplantation

- MAA under review by the EMA
- Decision to conduct complementary analyses with respect to transplantability of the highly sensitized patients in our successfully completed Phase 2 studies and of matched controls of highly sensitized patients from the U.S. transplant registry with a view to further illustrate the value of IDEFIRIX in the U.S. healthcare system.
- Hansa to request FDA-meeting upon completion of analyses - expected 2H 2019. Meeting to determine U.S. regulatory path forward for filing and approval of IDEFIRIX in the U.S.
- Long-term, observational follow-up study in up to 46 highly sensitized patients is ongoing

## Earlier clinical pipeline progresses: Imlifidase in other indications

- Acute AMR in kidney transplantation: received CTA and Ethics Committee approval for Phase 2 study
- Anti-GBM antibody disease: 8/15 patients treated in Phase 2 study.
- GBS: received CTA and Ethics Committee approval for Phase 2 study

## Next generation immunomodulatory enzymes

- NiceR - lead candidate selected for clinical development



**IDEFIRIX is the brand name under which the MAA for imlifidase was submitted for regulatory approval for treatment to enable kidney transplantation in highly sensitized patients.*

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# Conclusions from the ATC conference in Boston June 1-5th

***Three-year Outcomes of Highly-sensitized Kidney Transplant Recipients Desensitized with IgG Endopeptidase."*** **by Dr. Huang, MD, Ass. Prof. and Transplant Nephrologist at Cedars-Sinai**

- Dr. Huang reported a statistically significant reduction in time on the waitlist for transplantation among imlifidase treated patients compared to similarly sensitized matched controls.
- The matched control analysis showed statistically significant shorter time to transplant in both the current and previous U.S. Kidney Allocation System (KAS). Believe Imlifidase will complement the new KAS system and will facilitate reduced time to kidney transplantation in highly sensitized patients
- Follow up data from the U.S. investigator-initiated Phase 2 study of imlifidase for kidney transplantation in highly sensitized patients. Results show excellent graft survival out to three years with graft survival in line with deceased donor transplantation of non-sensitized patients.

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# Conclusions from the ATC conference in Boston June 1-5th

***"Safety and Efficacy of Imlifidase in Highly-Sensitized Kidney Transplant Patients: Results from a Phase 2 Study."* by Robert A. Montgomery, M.D., Director, NYU Langone Transplant Institute, NYC**

- The safety and efficacy data on imlifidase provide hope to highly sensitized patients, who today are very difficult or impossible to transplant, and face an extremely poor prognosis.

- Six months follow up results continue to show that imlifidase has enabled all patients to undergo transplantation resulting in good kidney function and graft survival,"

***"A Prognostic Drug Development Tool to Assess the Transplantability at the Time of Listing for Kidney Transplant Candidates."* by Dr. Everly, Director of the Terasaki Research Institute in LA**

- Dr. Everly reported on the results of simulations done in highly sensitized patients, which demonstrated that transplant rates could be increased by 25% if there were a therapy to address the HLA antibody barrier.

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# Imlifidase in kidney transplantation

Melissia B.
On dialysis

# Addressing a significant unmet need

Human leukocyte antigen (HLA) sensitization is a major immunological barrier to kidney transplantation and desensitization is a critical step in optimizing outcomes

HLA sensitization occurs in patients with anti-HLA antibodies to potential donors (DSAs), resulting in significantly lower likelihood of donor matching

Highly sensitized patients are more likely to remain on long-term dialysis

- Debilitating disease state
- Poor QOL
- Increased mortality
- High cost

~ 9,000 patients die every year on kidney transplant waitlists in the U.S. and Europe[1]

[1] Organ Procurement and Transplantation Network (OPTN); EDQM Council of Europe



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# Addressable patients in kidney transplantation in Europe and the U.S.

## Pre-transplant treatment

- 15% of kidney waitlist patients are highly sensitized (~ 30K patients)[1,2]
- 15% of kidney waitlist patients are moderately sensitized (~ 30K patients)[1,2]
- Adjusted for current rate of organ donation, ~ 12K sensitized patients annually could benefit from imlifidase
- More than 3K donated kidneys are discarded in the U.S. alone[3]

## Treatment of antibody mediated rejection (AMR)

- ~10% of all transplanted patients experience AMR[4]
  - ~ 4K of the 40K patients transplanted annually
  - ~ 40K of the 400K patients currently living with a kidney transplant

[1] Jordan et al. British Medical Bulletin, 2015, 114:113–125
[2] Orandi et al. N Engl J Med 2016;374:940-50
[3] Organ Procurement and Transplantation Network (OPTN)
[4] Jordan et al. British Medical Bulletin, 2015, 114:113-125



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# Phase 2 studies demonstrated potential to significantly improve transplantation outcomes for highly sensitized patients

## Imlifidase enabled kidney transplantation for all 35 highly sensitized patients

- Following imlifidase treatment, patients had a rapid cross-match conversion and a clinically significant reduction in donor specific antibodies

## Study patient population extremely unlikely to receive a compatible kidney transplant

- Median calculated Panel Reactive Antibody (cPRA) >99.5%, with more than half at 100%
- Mean time on dialysis prior to imlifidase-enabled transplantation >7 years
- Majority of patients had experienced previous failed kidney transplants

## Graft survival at study completion, six months post-transplantation, was 91%

- 32 patients were off dialysis with good kidney function with estimated glomerular filtration rate (eGFR) within the expected range



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# Completed and ongoing studies with imlifidase in kidney transplantation

| Study | Subjects | Status | Publication |
|---|---|---|---|
| Phase 1 (Sweden) | 29 healthy subjects | • Completed 2014 | PLOS ONE (2015)[1] |
| Phase 2 (Sweden) | 8 sensitized patients | • Completed 2015 | American Journal of Transplantation (2018)[2] |
| Phase 2 (Sweden) | 10 sensitized patients | • Completed 2016 | The New England Journal of Medicine (2017)[3] |
| Phase 2 (US) | 17 highly sensitized patients | • Completed 2018 | |
| Highdes Phase 2 (US, France, Sweden) | 18 highly sensitized patients | • Completed 2018 | |
| Observational follow-up study (US, France, Sweden) | Up to 46 previously treated and transplanted patients | • Enrolling. Transplanted patients to be followed up to five years | |

1 Winstedt et al. (2015) PLoS ONE 10(7): e0132011
2 Lorant et al. Am J Transplant. 2018;1–11
3 Jordan et al. N Engl J Med 2017;377:442-53



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# Positive interaction with regulatory agencies regarding imlifidase in kidney transplantation

## European Medicines Agency

- Submitted Marketing Authorisation Application for IDEFIRIX (INN: imlifidase) to EMA on February 5, 2019
- EMA accepted MAA submission on February 28, 2019
- An opinion of from the EMA Committee for Medicinal Products for Human Use (CMPH) is expected within 210 days plus potential clock stops for applicant responses

## U.S. Food and Drug Administration

- Overall positive End of Phase 2 Meeting with the FDA
  - Agency acknowledged high unmet medical need
  - Dialogue to continue in subsequent meeting
- Hansa is currently conducting complementary analyses on transplantability
  - The analyses include data from matched controls of highly sensitized patients from the U.S. transplant registry and from the successfully completed Phase 2 studies of imlifidase.
- Once completed, Hansa will request next meeting with FDA to determine U.S. regulatory path forward



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# Preparing for commercialization

## Well positioned to bring IDEFIRIX to market

- Highly concentrated transplant market reachable by small commercial team
- In EU5, 70-80% of all kidney transplantations are performed at 15-20 centers in each EU5 country
- In the U.S., 50 transplant centers represent more than half of all kidney transplants
- Reimbursement Strategy based on cost of dialysis as benchmark
- Expanding commercial infrastructure: Medical Affairs, Market Access and Patient Advocacy



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# Imlifidase in other indications

# Current enzyme technology pipeline opportunities

| Candidate / Project | Indication | Research/ Preclinical | Phase 1 [1] | Phase 1/2 | Phase 2 | Reg. interact. | Registration | Next Anticipated Milestone |
|---|---|---|---|---|---|---|---|---|
| **Imlifidase** | Kidney transplantation in highly sensitized patients | | | | | | | MAA review by EMA |
| | Anti-GBM antibody disease | | | | | | | Finalize enrollment of 15 patients |
| | Antibody mediated kidney transplant rejection (AMR) | | | | | | | Recruitment of patients over the coming 12 months |
| | Guillain-Barré syndrome | | | | | | | Recruitment of patients over the coming 18 months |
| **NiceR** | Recurring treatment in autoimmune disease, transplantation and oncology | | | | | | | Development of CMC process / Tox studies |
| **EnzE** | Cancer immunotherapy | | | | | | | Research phase |

Planned Ongoing Completed

[1] Present and future imlifidase Phase 2 studies to be based on the same Phase 1 study. Results from the Phase 1 study have been published, Winstedt el al. (2015) PLOS ONE 10(7).



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# Imlifidase in anti-GBM antibody disease

## Anti-GBM (Goodpasture's disease): rare, acute autoimmune disease affecting the kidneys and lungs

- Orphan Drug designation from FDA and European Commission
- Affects 1 in 1MM per year[1]
- 2/3 of patients lose kidneys[2], requiring chronic dialysis and kidney transplantation

## Investigator initiated Phase 2 study

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

- Eight of ~15 patients currently enrolled
- Up to 15 clinics in Europe
- Patients will be monitored for six months

Limited follow-up data currently available

- Data generated from the first seven patients indicate favorable response and that imlifidase appears to be well tolerated



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

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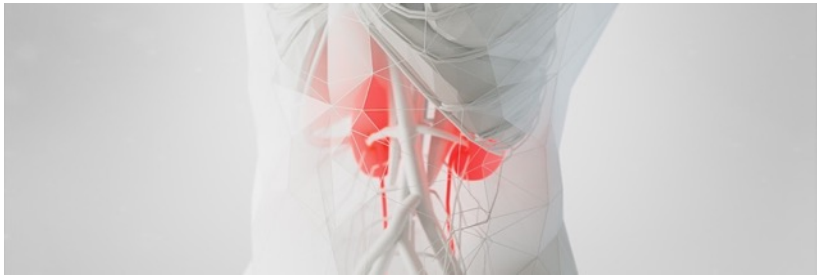
# Acute kidney antibody mediated rejection (AMR)

## Indication overview

- Acute AMR after transplantation is a significant challenge to long term graft survival
- Occurring in ~10% of kidney transplants[1]
- ~ 4K of the 40K yearly US+EU transplants
- ~ 40K of the 400K patients currently living with a kidney transplant in US+EU



## Treatment options

- There are no approved drugs for treatment of AMR; PE and steroids are primarily used today
- AMR patients not treated successfully risk graft failure, dialysis and return to transplantation waitlist

## Imlifidase opportunity

- Imlifidase treatment of AMR is a quick and effective method to inactivate donor specific antibodies

[1] Puttarajappa et al., Journal of Transplantation, 2012, Article ID 193724
[2] Jordan et al., British Medical Bulletin, 2015, 114:113-125
[3] http://www.irodat.org



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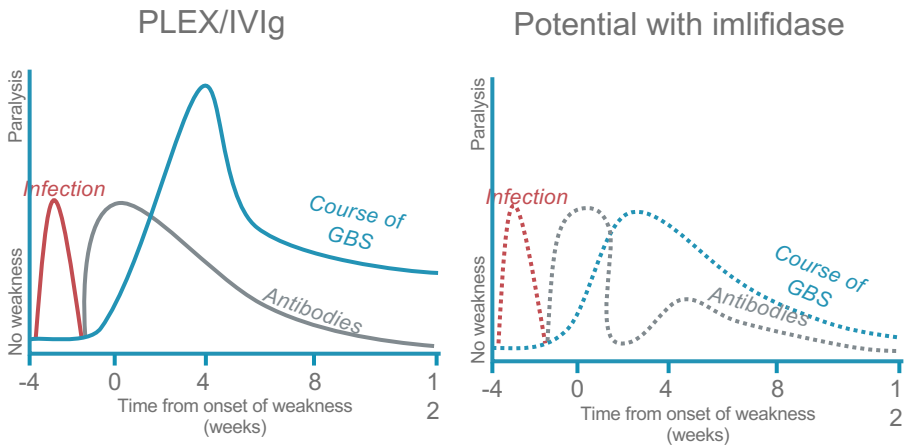
# Guillain-Barré syndrome

## Indication overview

- GBS is a rare, acute autoimmune attack on the peripheral nervous system
  - Rapidly and progressively weakens extremities
  - 3-7% mortality; 40% lose strength and have pain
- Can affect anyone, at any age
- Addressable population of ~ 11,000[1] per year in 7MM[2]
- FDA Orphan Drug designation for imlifidase in GBS

## Treatment options

- Current SOC is treatment with IVIg or PE
- Only parts of the patients fully recover from GBS, thus a high unmet need for new treatments




[1] McGrogan et al. Neuroepidemiology 2009;32(2):150-63
[2] 7MM=Seven major markets – US, Germany, UK, France, Spain, Italy, and Japan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# Next generation enzymology

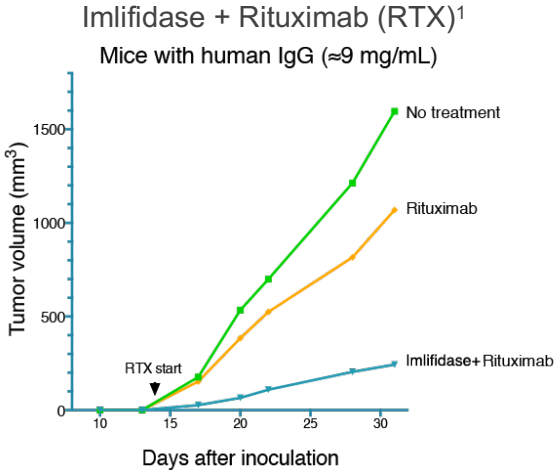
# Next generation enzyme technology: NiceR

NiceR: IgG cleaving enzymes candidates with lower immunogenicity and with the potential for repeat dosing

- Potential application for a broad array of indications, including relapsing autoimmune diseases and oncology
- Lead candidate selected
- Development of a GMP-manufacturing process and toxicology studies

# EnzE – imlifidase in oncology

PoC demonstrated *in vivo* for mice




- Suppressive effect of IVIg on effector cell function abrogated by imlifidase
- Imlifidase can significantly improve the therapeutic effect of rituximab

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 potentiate antibody based cancer therapies

[1] Järnum et al. Mol Cancer Ther 2017;16:1887-1897



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# Corporate

Ron S.
Donor kidney recipient

Stephanie vR.
Caregiver

# Financials

- Listed on Nasdaq Stockholm (ticker: HNSA)
- Cash position:  SEK 759m / USD 80m (March 31, 2019)
- Net loss: Q1’19: SEK 72m / USD 8m – FY’18: SEK -248m / USD -27m
- Q4 2018 Offering: 50 MM USD placed with top international funds
- Cash runway throughout 2020
- Approx. 70 employees in Lund, Sweden and the U.S.



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# Near-term milestones

- ✓ Hansa to request FDA-meeting upon completion of complementary analysis of transplantability data in order to determine regulatory path forward. Meeting expected 2H 2019
- ✓ IDEFIRIX (imlifidase) MAA review process 210 days plus potential clock stops
- ✓ Patient recruitment in AMR and GBS Phase 2 study over the next 12-18 months
- ✓ Finalize enrollment to Phase 2 in anti-GBM study; 8 of 15 patients enrolled
- ✓ Development of GMP process and toxicology studies for our lead NiceR candidate



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