Imlifidase treatment for overcoming pre-formed immunity

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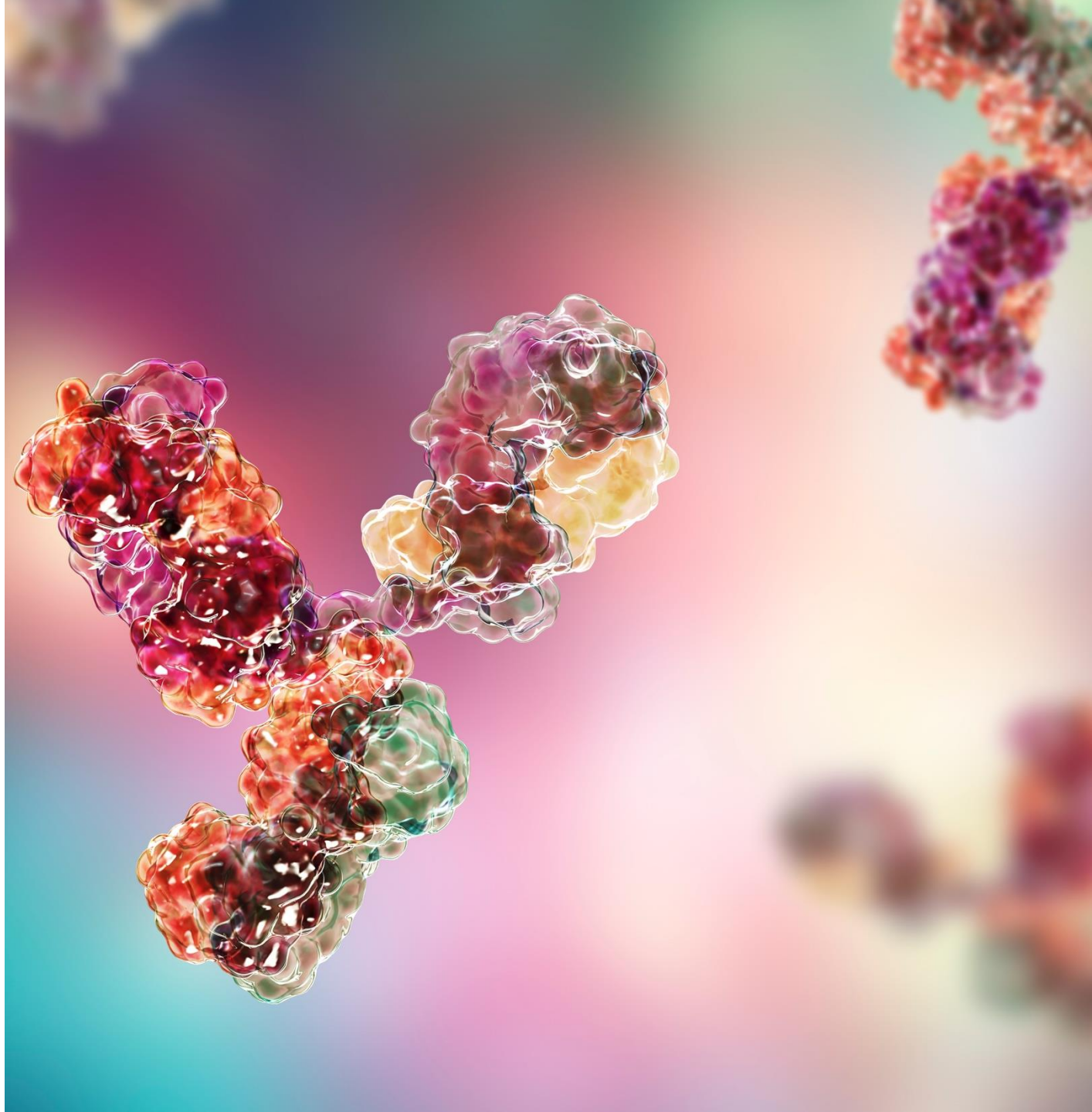
17th Open Scientific EIP Symposium on Immunogenicity of Biopharmaceuticals

16-19 March 2026
Lisbon, Portugal

HANSA BIOPHARMA

Job Code: HANS-MA.EU.26.004-001 Date of Creation: February 2026



Disclaimer

Hitto Kaufmann is employed by Hansa Biopharma AB and is a shareholder of the company.

Addressing orphan / rare indications

THERAPEUTIC FOCUS

- **Desensitization**
  - **Enabling Transplantation**
    Paradigm shift for highly sensitized kidney transplant patients
  - **Enabling Gene Therapy**
    Partnerships for pre-treatment to enable AAV gene therapy treatments
- **Rare autoimmune disease**
  - **GBS**
    Following successful POC Phase 2 trial

IMLIFIDASE

- **Imlifidase conditionally approved in the EU[1]**
  - For desensitization prior to kidney transplantation
- **BLA submitted to FDA (Dec 19 2025)**
  - Based on positive US Phase 3 trial in kidney transplantation ($p<0.0001$)
- **BLA application accepted February 2026**

[1]Imlifidase SmPC EN- June 2025

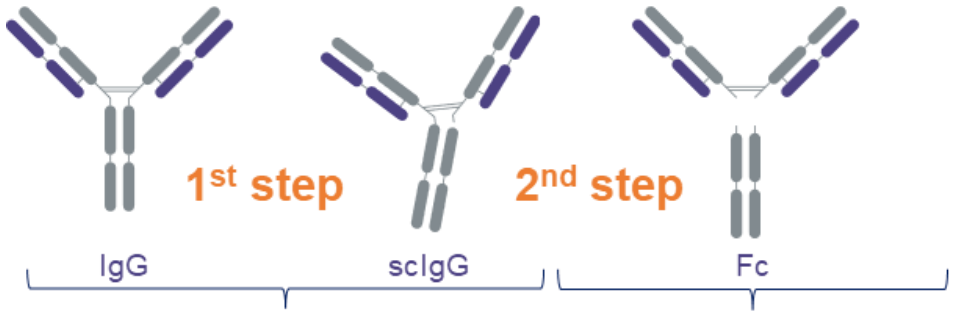
Imlifidase – an innovative approach to eliminate pathogenic IgG

Derived from a bacteria *Streptococcus pyogenes*

- Identified as IdeS: IgG-degrading enzyme of *S. pyogenes*[1]
- INN: imlifidase[2]
- 35 kDa cysteine protease
- Cleaves **all forms of IgG** (free, antigen-bound and membrane-bound)
- Strict substrate specificity, does not cleave IgA, IgD, IgE and IgM
- Effectively neutralizes Fc-dependent effector functions, including ADCC, ADCP, and CDC

A unique IgG antibody-cleaving enzyme

IgG is cleaved in a two-step process[3,4]

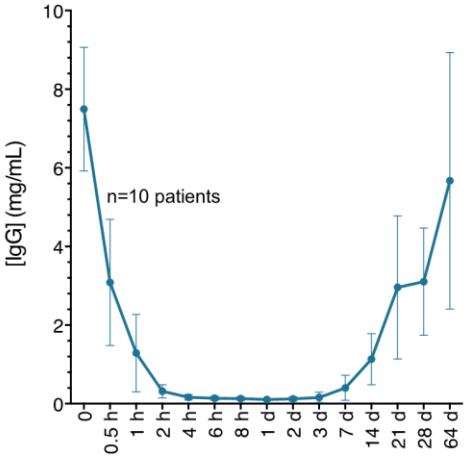


STEP 1: Single-cleaved IgG molecule (scIgG) with one intact heavy chain is generated

STEP 2: One F(ab')$_2$ fragment and one Fc fragment are generated

Inactivates IgG in 2-6 hours

- Administered *iv* over 15-30 minutes
- Rapid onset of action that inactivates IgG in 2-6 hours[5,6]
- IgG antibody-low window for approximately one week



[1] von Pawel-Rammingen et al., EMBO, 2002; 21:1607-1615
[2] Imlifidase SmPC EN- June 2025
[3] Winstedt L et al. PLoS One 2015;10:e0132011
[4] Ryan MF et al. Mol Immunol 2008;45:1837–46
[5] Jordan S et al., NEJM 2017; 377:442-53
[6] Lorant T et al., 2018; 18:2752-2762

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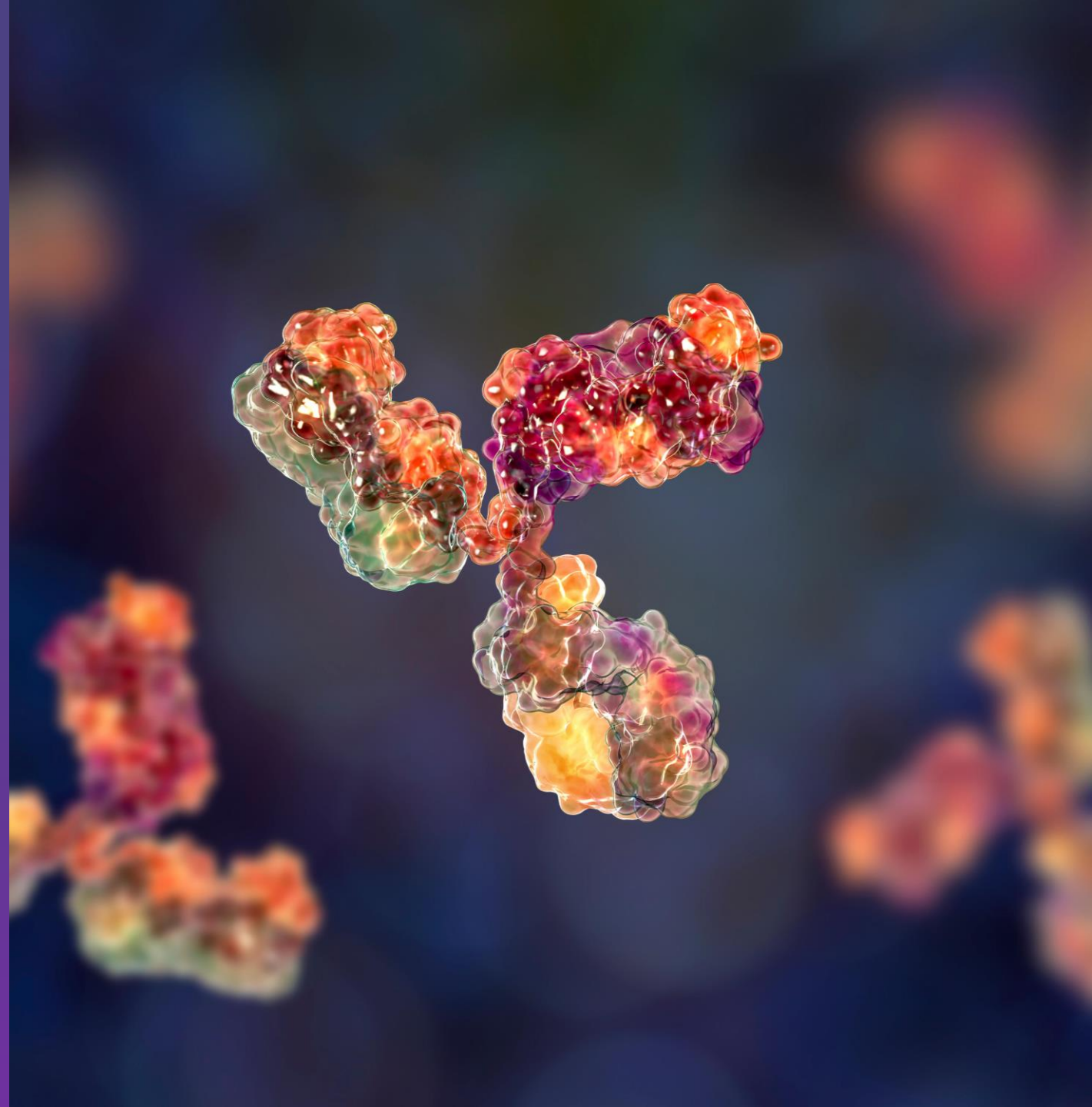
DESENSITIZATION

Transplantation

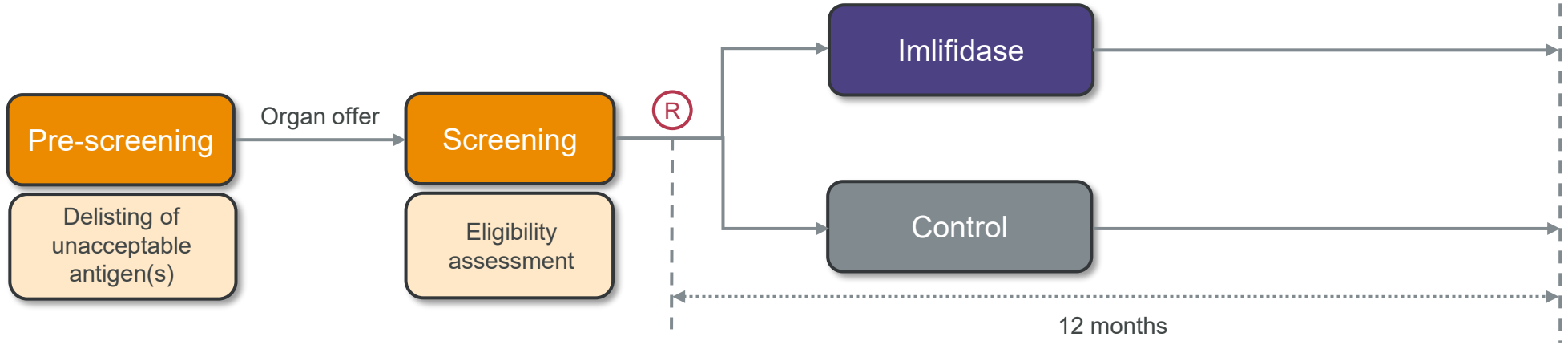


Hansa Biopharma's Phase 3 pivotal ConfIdeS trial

Study Overview

- Open-label, controlled, randomized trial evaluating 12-month kidney function in highly sensitized kidney transplant patients with positive crossmatch against a deceased donor, comparing desensitization using imlifidase with standard of care.

- **Primary Endpoint:** Estimated glomerular filtration rate (eGFR)
- **Secondary Endpoint:** Graft and patient survival parameters, antibody mediated rejection parameters, anti-drug antibody measures, imlifidase PK



ClinicalTrials.gov ID: NCT04935177

R = Randomized

Press Release - ConfIdeS Results

- At 12 months, mean eGFR was 51.5 mL/min/1.73m[2] in the imlifidase arm versus 19.3 mL/min/1.73m[2] in the control arm with a statistically significant and clinically meaningful difference of 32.2 mL/min/1.73m[2] (p<0.0001)
- Imlifidase was generally well tolerated with a safety profile consistent with previous clinical trial experience
- Submission of a Biologic License Application (BLA) under accelerated approval pathway planned for end of 2025

Lund, Sweden, 24 September 2025. Hansa Biopharma AB, ("Hansa" or "the Company"), (Nasdaq Stockholm: HNSA), today announced positive topline results from the US Phase 3 ConfIdeS trial of imlifidase, evaluating 12-month kidney function in highly sensitized (cPRA ≥99.9%) adult kidney transplant patients with positive crossmatch against a deceased donor, versus the control arm. The trial was well conducted, with patient retention in excess of 90%, and met the primary endpoint of kidney function at 12 months as measured by mean estimated Glomerular Filtration Rate (eGFR) with a p-value of <0.0001. The Company plans to submit a BLA under the accelerated approval pathway to the US Food and Drug Administration (FDA) by the end of 2025.

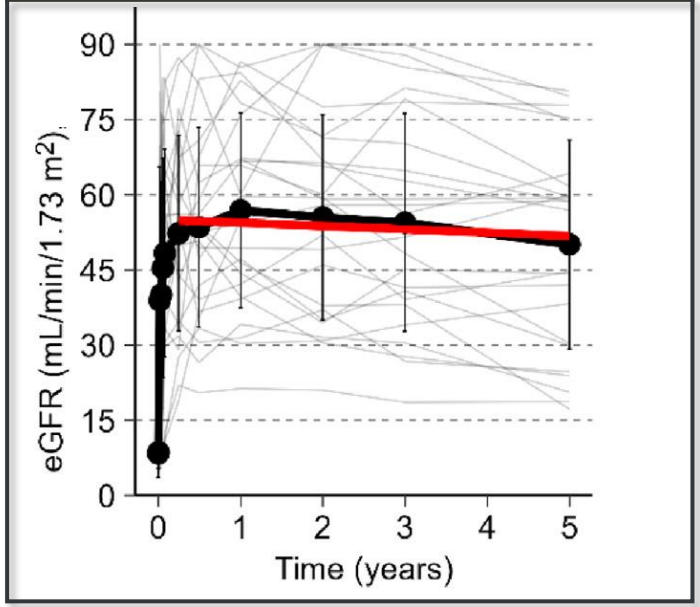
Hansa Biopharma. (24 September 2025). *Imlifidase successfully meets primary endpoint in pivotal US Phase 3 ConfIdeS trial in kidney transplantation* [Press release]

Long-term (5 years) follow-up phase 2 study showed durable graft and patient survival

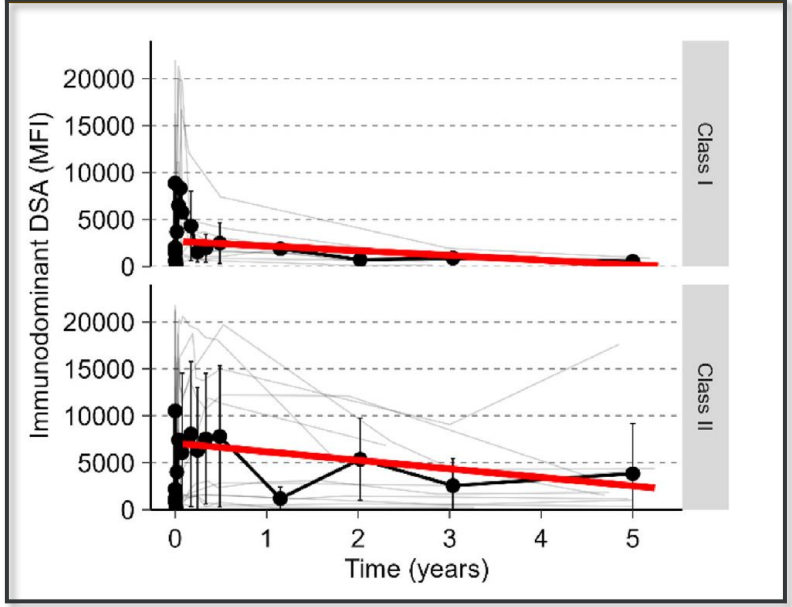
Study Overview

- Extended pooled analysis from four phase 2 studies - 17-HMedIdeS-14 study[1]
- A long-term follow-up phase 2 study of patients who have received a kidney transplant following desensitization with imlifidase

eGFR



DSA



Key Takeaways

- 82% (CI: 70%-96%) five-year graft survival
- 90% (CI: 80%-100%) patient survival
- 50 ml/min/1.73m² eGFR
- DSA rebounded with levels progressively decreasing over time – no increase in DSA between 3 and 5 years.

eGFR - estimated glomerular filtration rate is a measure of how well kidneys are functioning
DSA – Donor Specific Antibodies

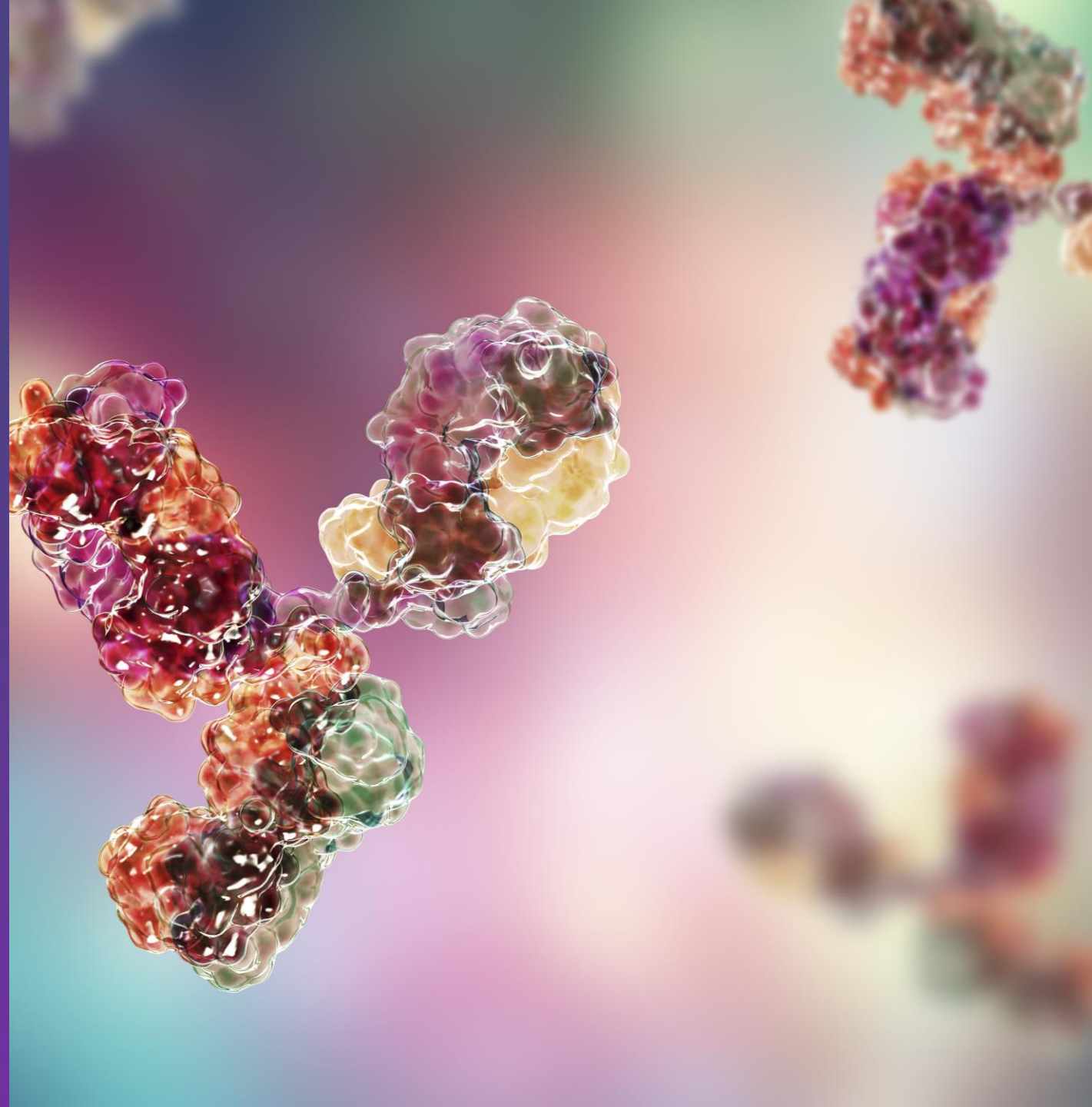
[1] Jordan SC, Maldonado AQ, Lonze BE, et al. Long-term outcomes at 5 years posttransplant in imlifidase-desensitized kidney transplant patients. Am J Transplant. 2025;25(4):878-880.

ClinicalTrials.gov ID: NCT02790437

DESENSITIZATION

Gene Therapy

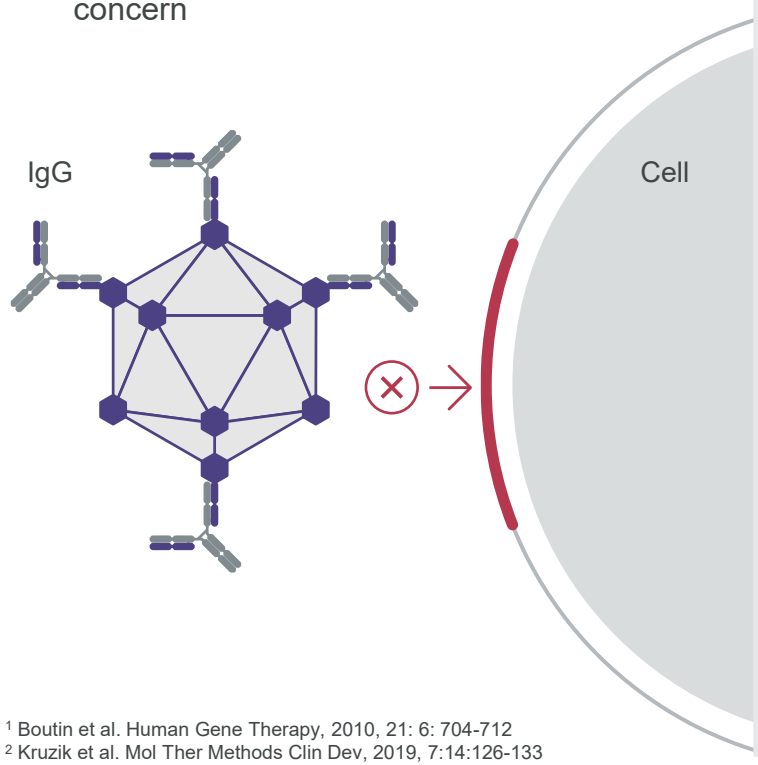
Disclosure - data in this section is from an indication currently in development



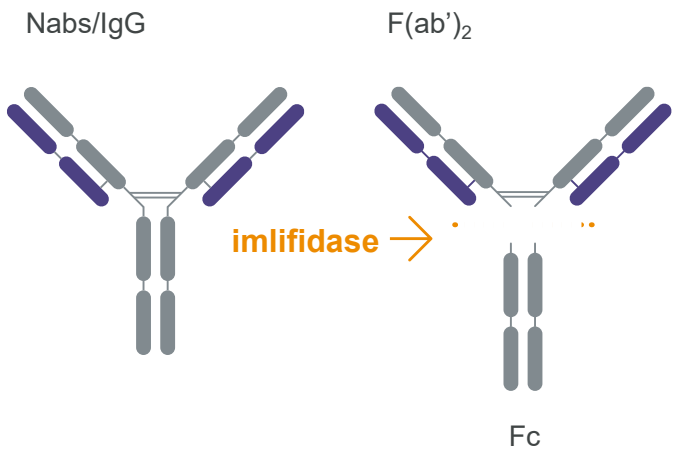
Antibodies are immunological barriers in gene therapy; imlifidase can cleave anti-AAV antibodies

On average, 30%[1,2] of patients considered for gene therapy treatment carry neutralizing anti-AAV antibodies forming a barrier for treatment eligibility

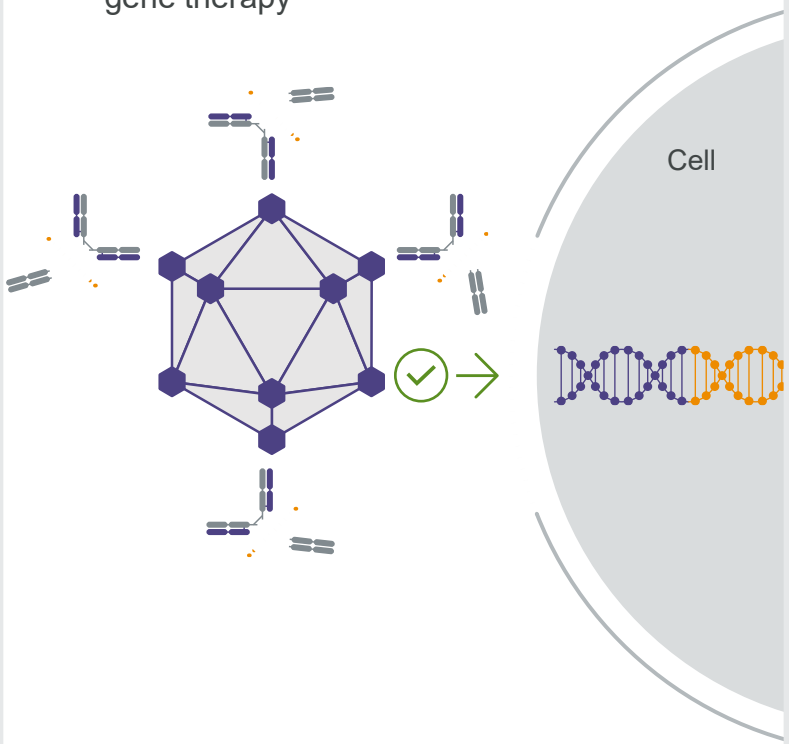
1 Antibodies prevent effective transfer of desired gene product and can be a safety concern



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



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



[1] Boutin et al. Human Gene Therapy, 2010, 21: 6: 704-712
[2] Kruzik et al. Mol Ther Methods Clin Dev, 2019, 7:14:126-133

Desensitization may enable access to gene therapies for rare disease patients with anti-AAV antibodies

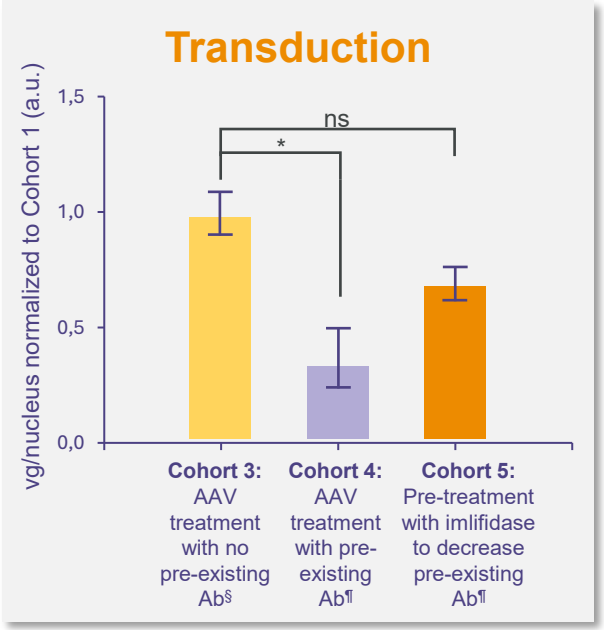
PREVALENCE

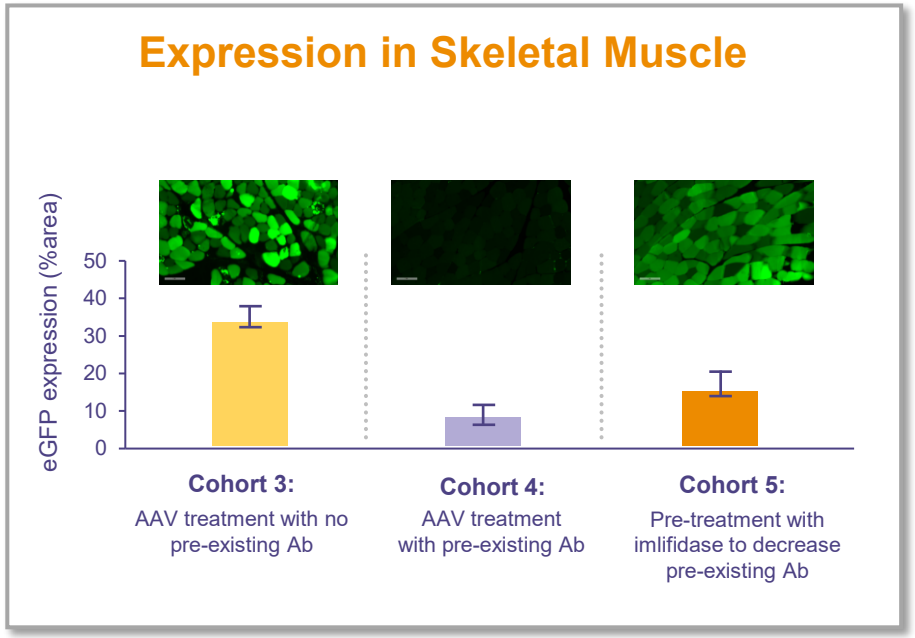
- Over 7,000 known rare monogenic diseases worldwide[1]
- AAVs are used as a delivery system for most gene therapies[2-6]
- 1-3 people cannot benefit from gene therapies due to anti-AAV antibodies[3-6]

PEOPLE WITH ANTI-AAV ANTIBODIES

- AAVs are from common viruses; many people have been exposed and developed antibodies against them[4,5]
- Anti-AAV antibodies excludes rare disease patients from Gene Therapy trials and treatments[3]

Imlifidase pre-treatment decreases pre-existing antibodies and enhances transduction and transgene expression in NHPs





Data from animal models

*P<0.05. †Data are represented as mean ± SEM and analyzed by one-way ANOVA followed by post-hoc analysis with Dunnett's multiple comparison test . ‡Data are represented as the mean ± SEM for the percent area for all of the muscle tissues analyzed at terminal necropsy. §AAVrh74 titer ≤1:400. ¶AAVrh74 titer 1:800–1:1600.

AAV, adeno-associated virus; AAVrh74, adeno-associated virus rhesus isolate serotype 74; Ab, antibody; a.u., arbitrary units; eGFP, enhanced green fluorescent protein; NHP, non-human primate; ns, not significant; vg, viral genome.

[1] The landscape for rare diseases in 2024. The Lancet Global Health, Editorial 2024 Mar 12(3): e341 doi; 10.1016/S2214-109X(24)00056-1
[2] Boycott K.M, et al. Rare-disease genetics in the era of next-generation sequencing: discovery to translation. Nat Rev Genet. 2013 Oct;14(10):681-91. doi: 10.1038/nrg3555. Epub 2013 Sep 3. PMID: 23999272.
[3] Boutin S, 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 Jun;21(6):704-12. doi: 10.1089/hum.2009.182. PMID: 20095819.
[4] Calcedo R, Wilson JM. Humoral Immune Response to AAV. Front Immunol. 2013 Oct 18;4:341. doi: 10.3389/fimmu.2013.00341. PMID: 24151496; PMCID: PMC3799231
[5] Veron P, Leborgne C, Monteilhet V, Boutin S, Martin S, Moullier P, Masurier C. Humoral and cellular capsid-specific immune responses to adeno-associated virus type 1 in randomized healthy donors. J Immunol. 2012 Jun 15;188(12):6418-24. doi: 10.4049/jimmunol.1200620. Epub 2012 May 16. PMID: 22593612.
[6] Kruzik A, et al. Prevalence of Anti-Adeno-Associated Virus Immune Responses in International Cohorts of Healthy Donors. Mol Ther Methods Clin Dev. 2019 Jun 7;14:126-133. doi: 10.1016/j.omtm.2019.05.014. PMID: 31338384; PMCID: PMC6629972.

Hansa Biopharma's imlifidase facilitates access to gene therapies

Current partnerships

SAREPTA THERAPEUTICS

Indication exclusivity

- Duchenne Muscular Dystrophy (DMD) - 1/3,500 to 5,000 male births worldwide
- Limb-Girdle Muscular Dystrophy (LGMD) - global prevalence of ~1.6 per 100K individual

GENETHON
CURE THROUGH INNOVATION

Indication exclusivity

- Crigler-Najjar syndrome – ultra-rare condition with approximate incidence is 0.6-1 case per one million people

Clinical Progress

Reported supportive DMD topline data and safety in three patients treated with imlifidase prior to ELEVIDYS

Reported the first successful treatment of a Crigler–Najjar patient with pre-existing AAV8 antibodies.

Crigler-Najjar (CN) syndrome is an ultra-rare hereditary disorder caused by deficiency in UGT1A1 (liver enzyme)

UGT1A1 - Uridyl-diphosphate-GlycuronosylTranferase 1 polypeptide A1

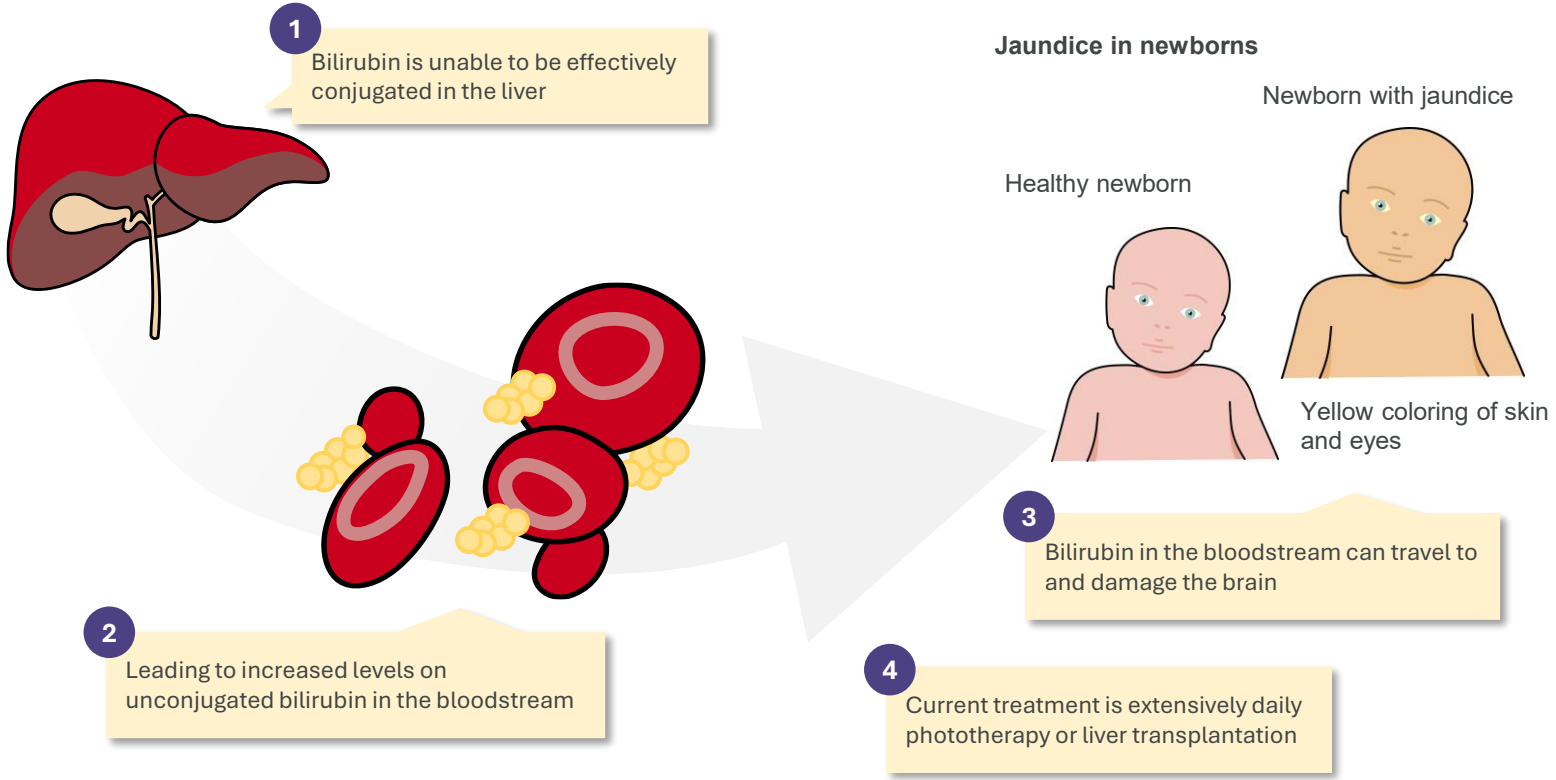
Incudences

- An ultra-rare indication impacting
- 0.6-1 per 1,000,000 newborns around the world[1,2]
- ~30% of patients have pre-existing IgG antibodies to AAV8

Indication

- Build-up of free bilirubin in serum and body tissues, which can become toxic in the brain[3]
- Severity can vary from mild to severe, no medication approved for treatment so far

Build-up of free bilirubin in serum and tissue can become toxic in the brain



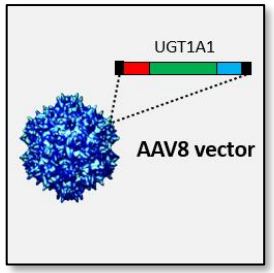
[1] Collaud F, Bortolussi G, Guianvarc'h L, Aronson SJ, Bordet T, Veron P, Charles S, Vidal P, Sola MS, Rundwasser S, Dufour DG, Lacoste F, Luc C, Wittenberghe LV, Martin S, Le Bec C, Bosma PJ, Muro AF, Ronzitti G, Hebben M, Mingozzi F. Preclinical Development of an AAV8-hUGT1A1 Vector for the Treatment of Crigler-Najjar Syndrome. Mol Ther Methods Clin Dev. 2019 Mar 15;12:157-174.
[2] Ebrahimi A, Rahim F. Crigler-Najjar Syndrome: Current Perspectives and the Application of Clinical Genetics. Endocr Metab Immune Disord Drug Targets. 2018;18(3):201-211.
[3] American Liver Foundation, https://liverfoundation.org/liver-diseases/pediatric-liver-information-center/pediatric-liver-disease/crigler-najjar-syndrome/ [Accessed 2023-06-13]

Imlifidase to overcome AAV8 immunity in seropositive Crigler-Najjar patients

To give participants with pre-existing anti-AAV8 antibodies access to gene therapy treatments, this trial aims to demonstrate the safety and efficacy of GNT0003 following imlifidase pre-treatment in adult participants with severe CNS requiring daily phototherapy and presenting with pre-existing anti-AAV8 antibodies.

GNT-018-IDES – Phase 2 trial

- ≥ 16 year (n=3)
- Severe Crigler-Najjar syndrome (>6h daily phototherapy)
- With detectable AAV8 NAb
- Dosed with both imlifidase and GNT0003 (AAV8 viral vector containing UGT1A1 transgene)



Primary objective

- Assess **efficacy** of a single intravenous administration of GNT0003 **following imlifidase pre-treatment** in participants with severe CNS requiring phototherapy and pre-existing AAV8 antibodies

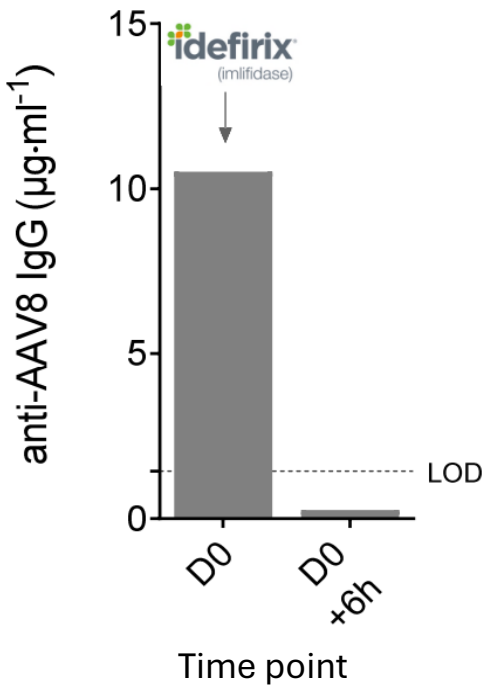
Secondary objective

- **Collect data on safety and tolerability** of GNT0003 and imlifidase, efficacy of imlifidase, pharmacokinetic and pharmacodynamic profile of GNT0003, and Quality of Life

ClinicalTrials.gov ID: NCT06518005

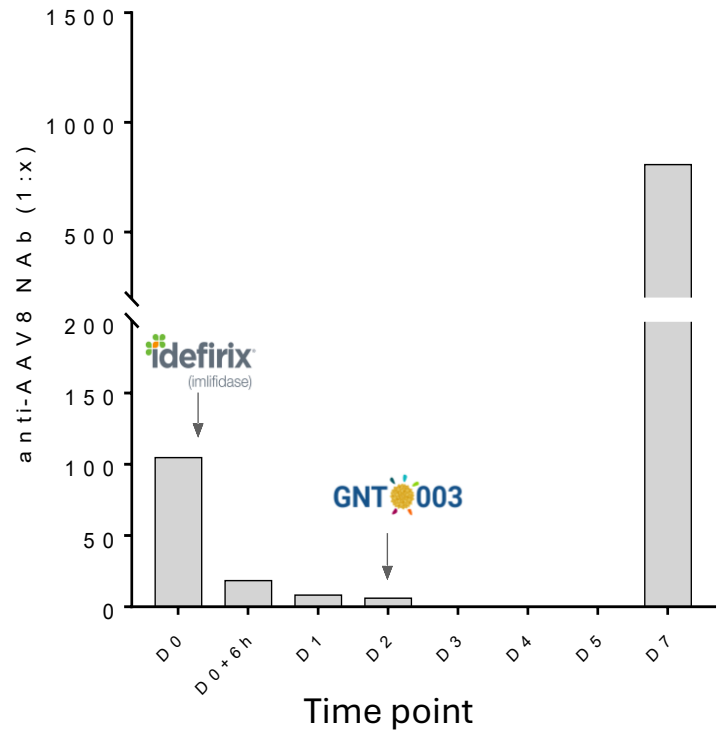
Measurement of anti-AAV8 antibodies in the first treated patient

In vitro assay →
Detection of intact total anti-AAV8 IgG antibodies



Cell-based _in vitro_ assay →
Detection of neutralizing antibodies and fragments

Time point	anti-AAV8 Nab, titer (1:x)
D0	104.8
D0 + 6h	18.4
D1	8.2
D2	6.1
D3	ND
D4	ND
D5	ND
D7	807.3

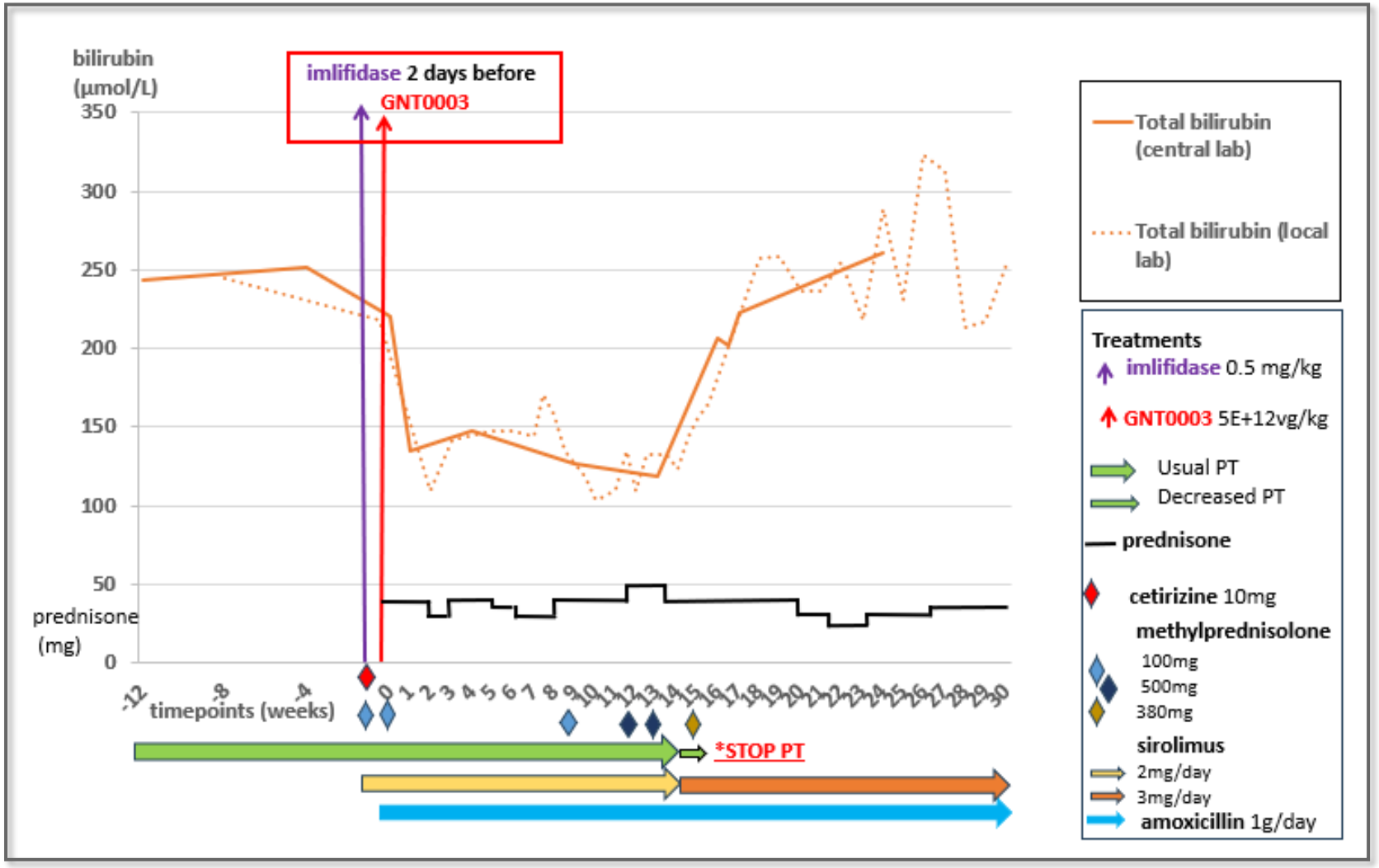


Genethon Data on file; Presented at ESGCT October 2025, Sevilla, Spain

ClinicalTrials.gov ID: NCT06518005

Enabling AAV gene therapy: patient case from ongoing clinical trial in Crigler Najjar

Female
22 YO
CNS Type 1
Fibroscan = 5 Kpa
12H daily phototherapy



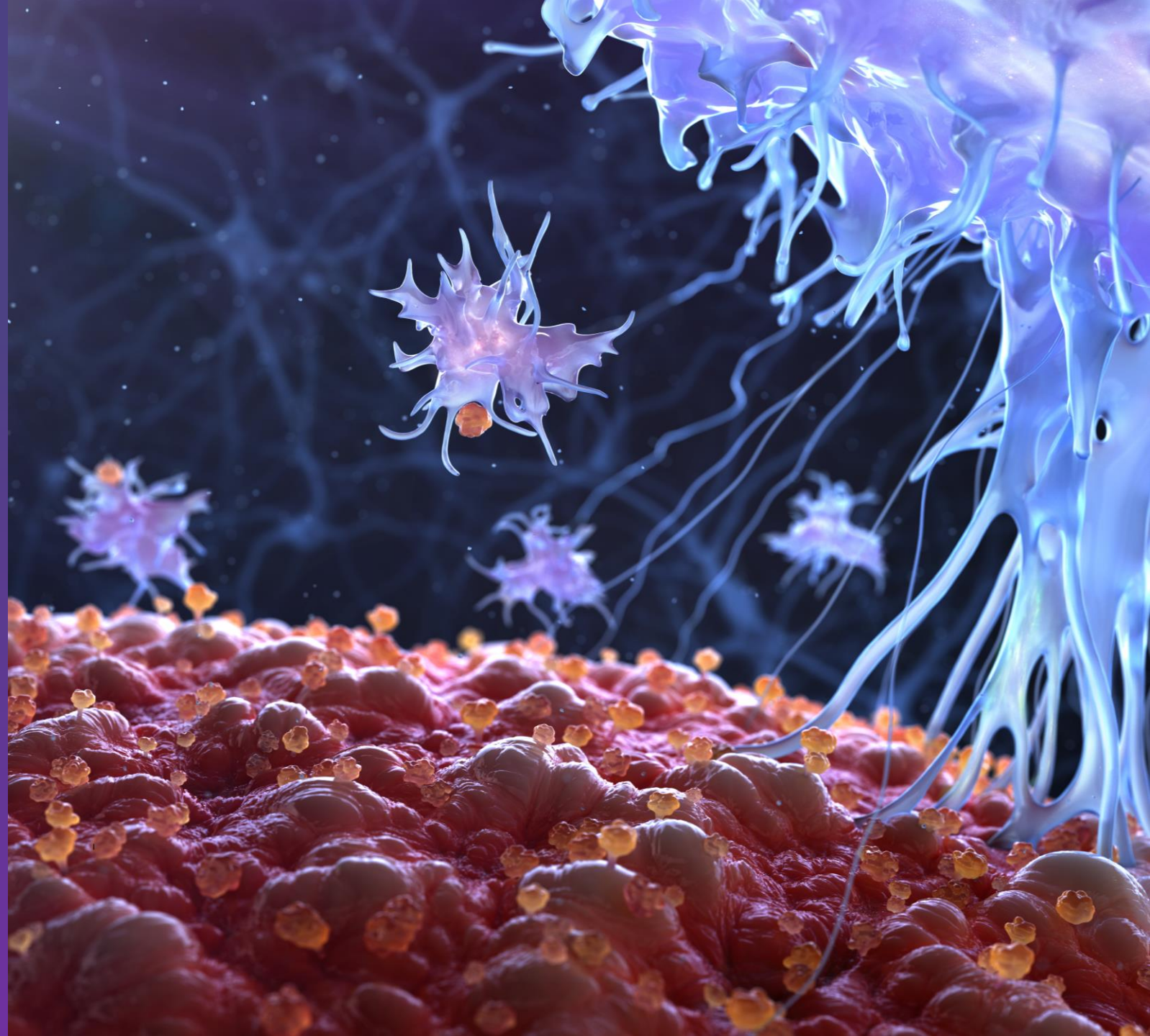
Genethon Data on file; Presented at ESGCT October 2025, Sevilla, Spain

Clinicaltrials.gov identifier: NCT06518005

Next generation Compound – Autoimmune Focus

HNSA-5487

Disclosure - data in this section is from an asset currently in development



Press Release - Phase 1 clinical trial with HNSA-5487

Study Overview

- Double blind, randomized, placebo-controlled trial in 36 healthy volunteers received a single ascending doses of HNSA-5487 administered as a single intravenous (IV) infusion.
- Assessed safety, tolerability, PK and PD, and immunogenicity.

Hansa Biopharma's HNSA-5487 Achieved Rapid and Highly Robust IgG Reduction by More Than 95% and Clear Redosing Potential in First-in-Human Trial

7 Oct 2024, 10:00

Lund, Sweden, 7 October 2024. Hansa Biopharma AB, ("Hansa" or the "Company") (Nasdaq Stockholm: HNSA), today announced positive results from a 12-month follow up analysis from the NICE-01 trial of HNSA-5487, the Company's next generation immunoglobulin G (IgG)-cleaving molecule, assessing IgG recovery, immunogenicity and redosing potential.

In the NICE-01 trial, HNSA-5487 demonstrated rapid and highly robust reduction of IgG levels by more than 95 percent within a few hours post treatment. In a 12-month follow up analysis IgG levels returned to normal range six months after initial dosing. This confirms that HNSA-5487 mirrors the extremely high efficacy of imlifidase, the Company's first-generation IgG-cleaving enzyme, in reducing total IgG levels. No serious adverse events were observed and as previously communicated HNSA-5487 is safe and well tolerated.

Importantly, HNSA-5487 demonstrated lower pre-treatment anti-drug antibody (ADA) levels and significantly reduced ADA responses when compared to imlifidase, confirming an attractive immunogenicity profile with a clear redosing potential. HNSA-5487 also demonstrated highly robust reduction in IgG levels with similar efficacy in nearly 100 percent of serum samples collected in the trial and analyzed at six- and 12-months after the initial dose.

Hansa Biopharma. (7 October 2024). *Hansa Biopharma's HNSA-5487 Achieved Rapid and Highly Robust IgG Reduction by More Than 95% and Clear Redosing Potential in First-in-Human Trial* [Press release]

Phase 2 Study demonstrated the role imlifidase may play in halting the progression of GBS

Guillain-Barré Syndrome

A rare, acute, paralyzing, inflammatory disease of the peripheral nervous system caused by the immune system damaging nerve cells and structures[1].

Symptoms

Rapid onset and progression of muscle weakness leading to severe paralysis of the arms and legs. Most GBS patients also have sensory disturbance (tingling, numbness or ataxia) and pain, and some patients have double vision or problems with swallowing[1].

Treatment

No FDA approved treatments. IVIg/PLEX are considered standard of care. IVIg is approved in the EU[1].

Prevalence

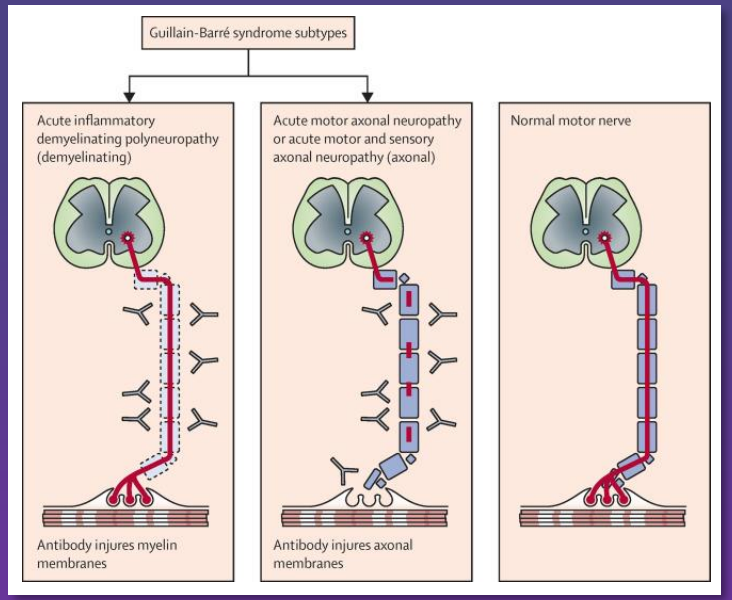
Affects 0.4-3.25 in 100,000 people annually. Approximately 100,000 cases annually in the world[2].

Unmet Need

~25% of patients require mechanical ventilation for days to months following the acute autoimmune attack, and 20% are unable to walk after six months[3].

Phase 2 Study Results[4]

- Rapid overall improvement in functional status including expedited muscle recovery
- 37% of patients able to walk independently at Week 1
- 67% of patients able to walk independently at Week 8
- 63% of patients able to run or had no functional disability (GBS DS<1) at 6 months
- Administration of imlifidase was overall safe and well tolerated

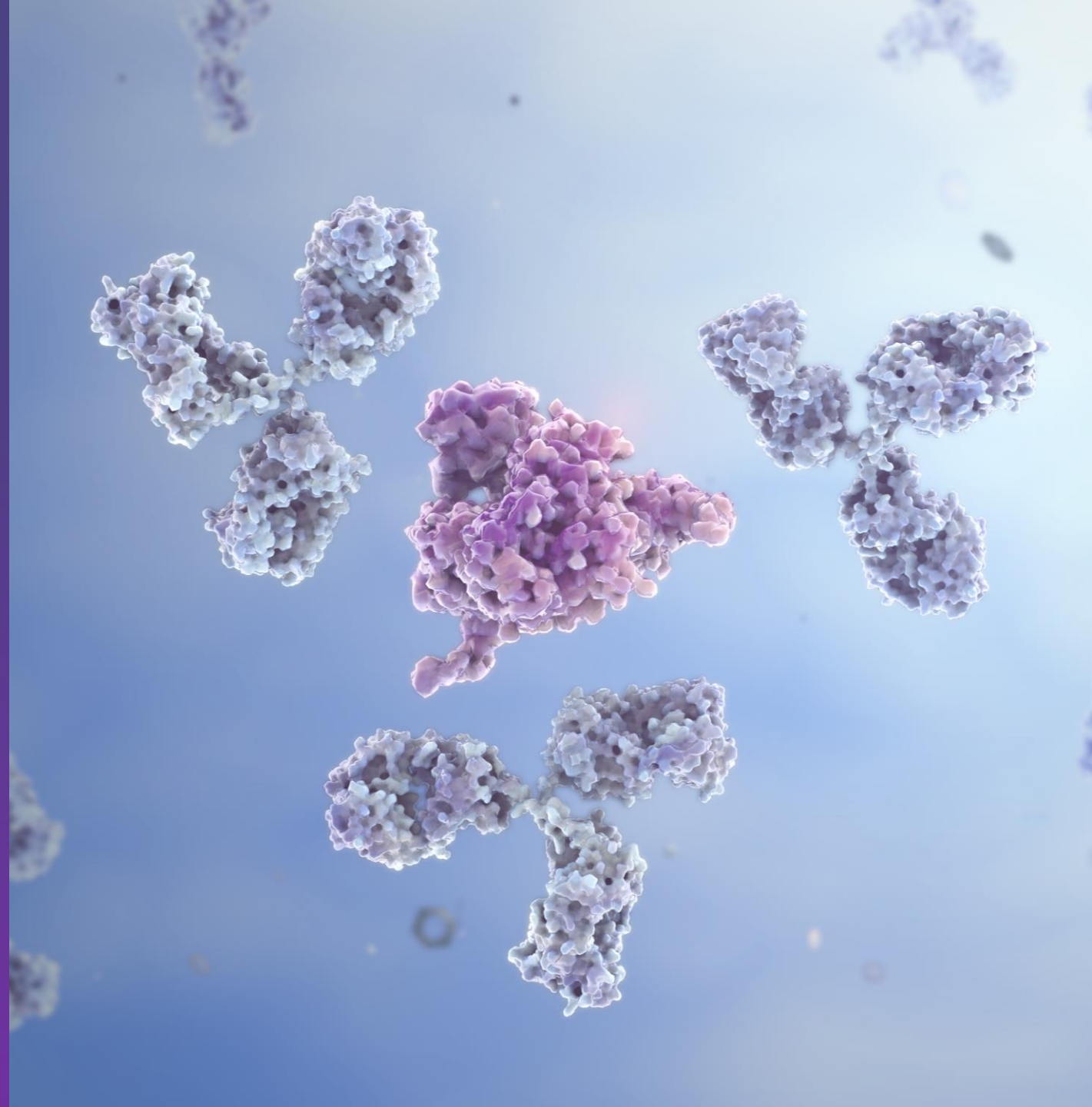


GBS disability score (DS) is defined as: 0 = Healthy; 1 = Minor symptoms and capable of running; 2 = Able to walk independently 10 meters or more but unable to run; 3 = Able to walk more than 10 meters across an open space with help; 4 = Bedridden or chair bound; 5 = Needing mechanical ventilation; 6 = Dead

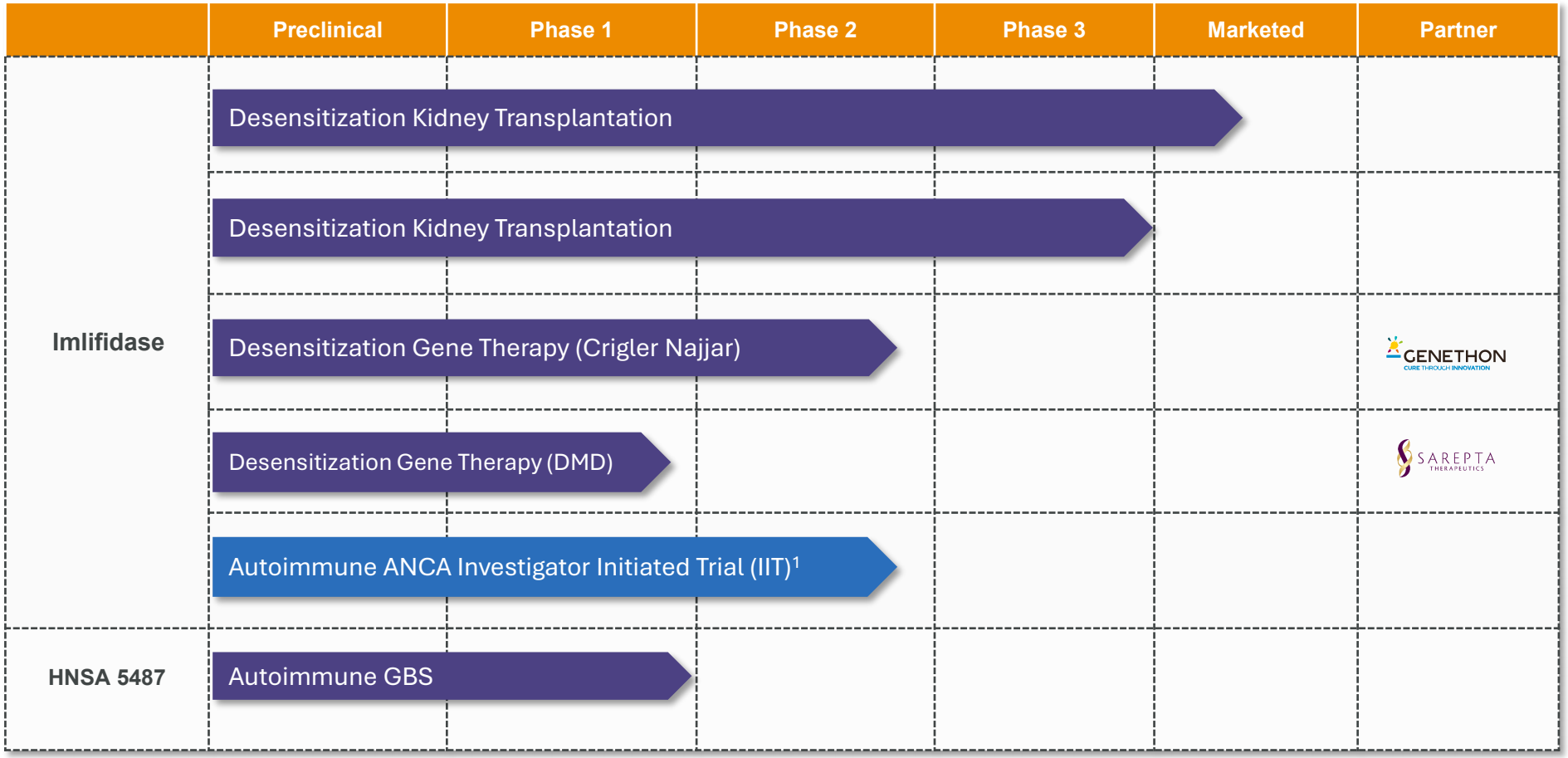
[1] Van Doorn PA. Diagnosis, treatment and prognosis of Guillain-Barré syndrome (GBS). Presse Med. 2013 Jun;42(6 Pt 2):e193-201. doi: 10.1016/j.lpm.2013.02.328
[2] Bellanti R et al. Guillain-Barré syndrome: a comprehensive review. Eur J Neurol. 2024 May 30;31(8):e16365. doi: 10.1111/ene.16365
[3] Fletcher DD et al. Long-term outcome in patients with Guillain-Barré syndrome requiring mechanical ventilation. Neurology. 2000 Jun 27;54(12):2311-5. doi: 10.1212/wnl.54.12.2311
[4] Attarian S et al. Outcomes in Patients with Severe Guillain-Barré Syndrome Treated with Imlifidase and Standard-of-Care Immunoglobulin, PNS Annual meeting in Edinburgh 17-20 May 2025

Clinicaltrials.gov ID: NCT03943589

PIPELINE



Focused Pipeline in Desensitization and Autoimmune Diseases



[1] Investigator-initiated study by Dr. Adrian Schreiber and Dr. Philipp Enghard, at Charité Universitätsmedizin, Berlin, Germany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Thank you