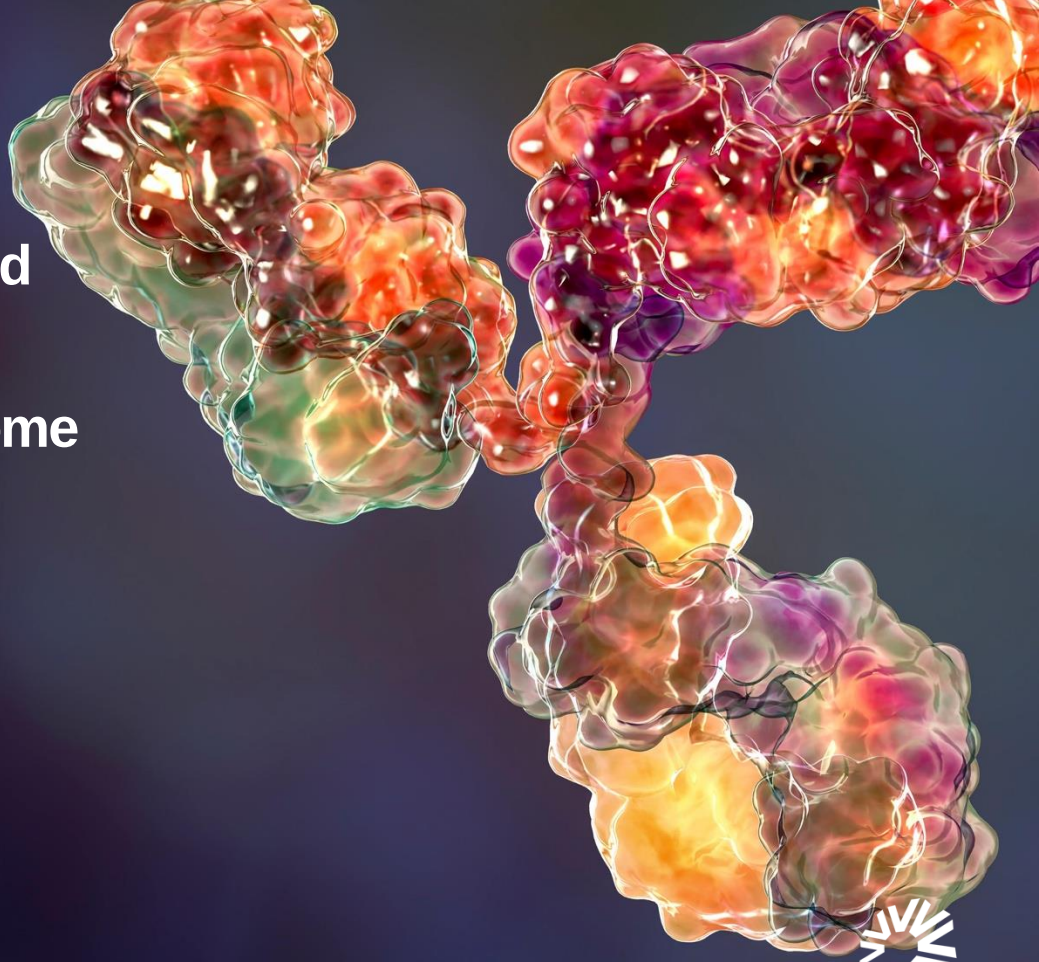
Hansa Biopharma announces positive full results from 15-HMedIdeS-09 Phase 2 study and indirect treatment comparison of imlifidase in Guillain-Barré Syndrome

18 December 2024

Søren Tulstrup, President and CEO
Hitto Kaufmann, CR&DO



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GBS is a rare, acute inflammatory disease driven by IgG

Guillain-Barré Syndrome

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

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 or numbness or ataxia) and pain, and some patients have double vision or problems with swallowing.

Treatment

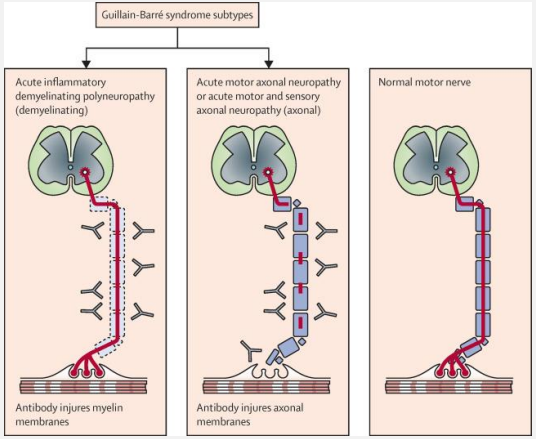
No FDA approved treatments. IVIg/PLEX are considered standard of care. IVIg is approved in the EU.

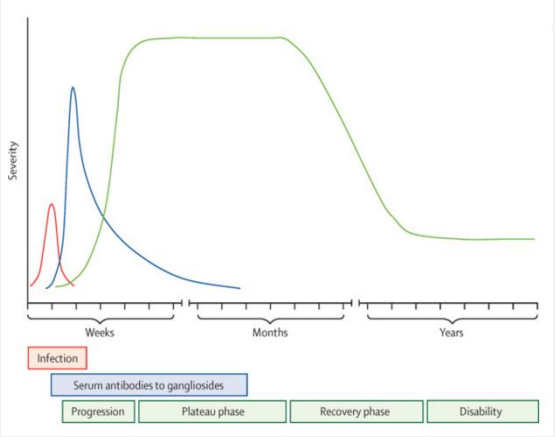
Prevalence

Affects 1-2 in 100,000 people annually.[3] Approximately 3,000 – 6,000 cases annually in the US.

Unmet Need: Approximately 25% of patients require mechanical ventilation for days to months following the acute autoimmune attack, and 20% are unable to walk after six months.[1, 2]

IgG is a key driver of inflammatory attacks on peripheral nerves and has been clinically linked to the severity and progression of the disease.





Willison et al, Lancet, 2016, Vol 388: 10045:717-727

"In the treatment of GBS and subsequent recovery process, early improvement and the ability to walk independently are important clinical milestones as they indicate a return to basic mobility and independence, and to an improved quality of life for patients. This analysis supports the potential role of imlifidase followed by standard of care IVIg as a potentially new treatment option in GBS. These are important results for patients and clinicians in the GBS community."

Professor Shahram Attarian,
Head of Department of Neuromuscular Diseases and ALS,
Hopitaux Universitaires de Marseille (APHM).

1. 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
2. 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
3. McGrogan A, et al. Neuroepidemiology. 2009; 32(2):150-63

IgG cleaving technologies have the potential to transform the autoimmune treatment landscape

80 + types of autoimmune diseases, many of which are chronic, unpredictable, and have debilitating, recurring symptoms. **IgG is a significant factor in many autoimmune diseases.**

In GBS, **IgG is a key driver of inflammatory attacks** on peripheral nerves and has been clinically linked to the severity and progression of the disease.

Current approaches to care in autoimmune diseases have **significant side effects, are time consuming, and may not be effective for all patients**. For many conditions there are no FDA approved treatments.

Rapid reduction of IgG levels has the potential to benefit GBS patients by depleting pathological IgG antibodies, thereby halting disease progression resulting in faster recovery and less severe disease.

Imlifidase – a first in class IgG cleaving enzyme - in combination with standard of care (IVIg) may play a significant role in the treatment of GBS. Unlike other molecules, imlifidase can effectively and very rapidly cleave IgG – potentially halting the progression of nerve damage associated with GBS and stopping the progression of the disease.

"List of Autoimmune Diseases". Autoimmune Registry Inc. https://www.autoimmuneregistry.org/autoimmune-diseases. Accessed June 4, 2024
Pisetsky, D.S. Pathogenesis of autoimmune disease. Nat Rev Nephrol 19, 509–524 (2023). https://doi.org/10.1038/s41581-023-00720-1
Theofilopoulos A N, Dixon F J. Adv Immunol. 1985;37:269–390.
Feldmann M, Brennan F M, Maini R N. Cell. 1996;85:307–310.
Kotzin B L. Cell. 1996;85:303–306.
Hellmich B, Sanchez-Alamo B, Schirmer JH, et al EULAR recommendations for the management of ANCA-associated vasculitis: 2022 update Annals of the Rheumatic Diseases 2024;83:30-47.
Cherin P, Marie I, Michallet M, et al. Management of adverse events in the treatment of patients with immunoglobulin therapy: A review of evidence. Autoimmun Rev. 2016 Jan;15(1):71-81. doi: 10.1016/j.autrev.2015.09.002. Epub 2015
Yuki N, Hartung HP (June 2012). "Guillain-Barré syndrome". The New England Journal of Medicine. 366 (24): 2294–304. doi:10.1056/NEJMra1114525. PMID 22694000

Hansa has conducted a Phase 2 single arm study and comparative analysis to assess the potential of imlifidase in GBS

15-HMedIdeS-09 Phase 2 single arm study to evaluate single dose imlifidase (0.25 mg/kg) in combination with IVIg

Indirect treatment comparison with IGOS real-world comparator group treated with IVIg to evaluate efficacy of imlifidase in combination with IVIg versus IVIg alone

15-HMedIdeS-09 Phase 2 Study Results

The 15-HMedIdeS-09 Phase 2 Study demonstrated the role imlifidase may play in halting the progression of GBS

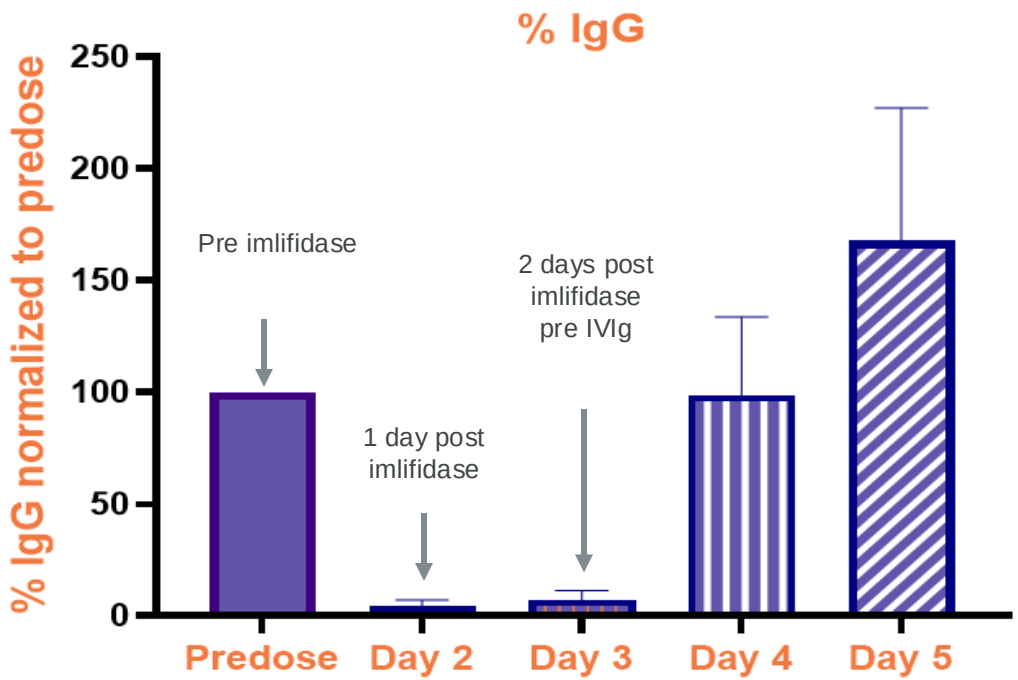
15-HMedIdeS-09

- Open-label, single arm, multi-center study across the UK, France, and the Netherlands
- Patients with severe GBS were included (GBS DS ≥ 3)
- Evaluated the safety, tolerability, and efficacy of single dose of imlifidase (0.25 mg/kg) in combination with IVIg in 27 adult GBS patients

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
IGOS – International GBS Outcome Study
OR - odds ratio

Rapid overall improvement in functional status	• Expedited muscle recovery • Fast return to independently walking • Improvement by at least one grade on GBS disability score at median time of six days • Median time to independently walk was 16 days
Improvement at week 1	• 37% of patients were able to walk independently • Mean improvement in muscle strength was 10.7 points (MRC sum score)
Improvement at week 8	• 67% of patients were able to walk independently (GBS DS 2) • 41% of patients regained the ability to run (GBS DS 1) • 37% had improved by at least 3 points on the GBS DS
Durability and tolerability	• 63% of patients were able to run or had no functional disability (GBS DS ≤1) at six months • Administration of imlifidase was overall safe and well tolerated

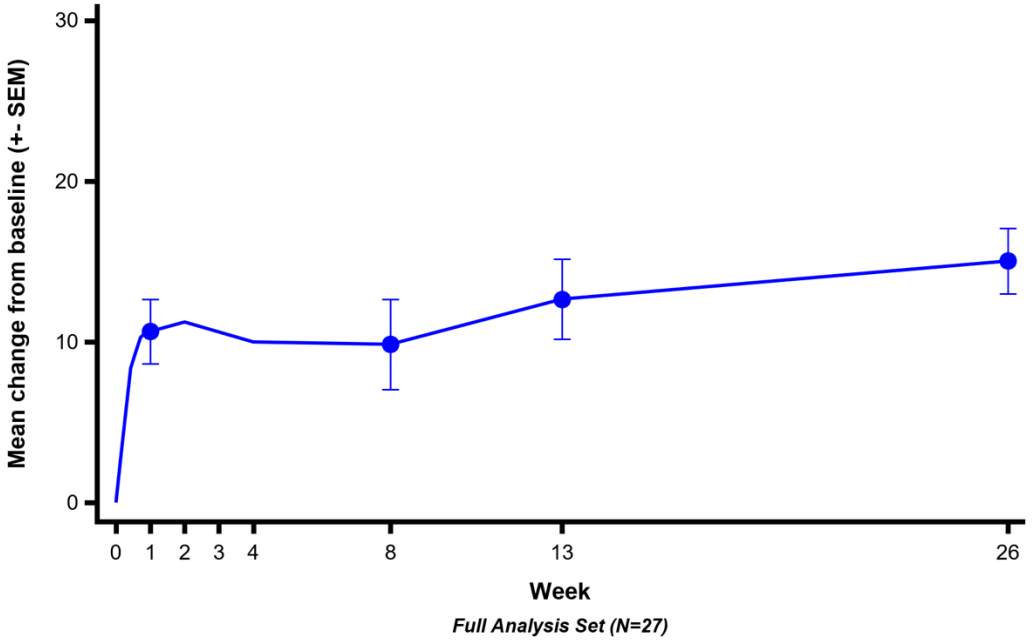
Data underscore imlifidase ability to very rapidly and robustly reduce IgG



KEY TAKEAWAYS

- ✓ Imlifidase rapidly reduces total IgG including pathological antibodies that causes GBS
- ✓ Standard of care IVIg is initiated 48 h after imlifidase
- ✓ IgG levels return to normal

Recovery of muscle strength is seen as early as week 1 in patients treated with imlifidase in combination with IVIg



KEY TAKEAWAYS

- ✓ Muscle weakness is a primary symptom of GBS and can lead to paralysis
- ✓ Regaining muscle strength is a key factor in recovery and returning to daily activities
- ✓ Mean improvement in muscle strength was 10.7 points (MRC sum score)

Ko KJ, Ha GC, Kang SJ. Effects of daily living occupational therapy and resistance exercise on the activities of daily living and muscular fitness in Guillain-Barré syndrome: a case study. J Phys Ther Sci. 2017 May;29(5):950-953. doi: 10.1589/jpts.29.950. Epub 2017 May 16. PMID: 28603379; PMCID: PMC5462706.

Phase 2 demonstrates imlifidase followed by IVIg lead to improvement in GBS DS at week 1 and 2 and continued improvement at later timepoints

	PERCENTAGE (number) ≤ 1 GBS DS	PERCENTAGE (number) ≤ 2 GBS DS	PERCENTAGE (number) ≤ 3 GBS DS
Week 1	56% (15/27)	33 (9/27)	7% (2/27)
Week 2	67% (18/27)	44% (12/27)	7% (2/27)
Week 4	74% (20/27)	52% (14/27)	22% (6/27)
Week 8	78% (21/27)	63% (17/27)	37% (10/27)
Month 6	89% (24/27)	85% (23/27)	52% (14/27)

KEY TAKEAWAYS

- ✓ Rapid improvement in GBS DS at week 1 and 2
- ✓ Continued improvement in GBS DS at later timepoints

Improvement in GBS DS is key to shortening recovery time and increasing the chance of a full recovery

Increasing proportion of patients able to walk and run over time

	Able to walk independently (GBS DS ≤ 2)	Able to run (GBS DS ≤ 1)
Week 1	37% (10/27)	15% (4/27)
Week 2	48% (13/27)	19% (5/27)
Week 4	52% (14/27)	33% (9/27)
Week 8	67% (18/27)	41% (11/27)
Week 26	85% (23/27)	63% (17/27)

KEY TAKEAWAYS

- ✓ Rapid progression to independently walking
- ✓ Continuous improvement over time
- ✓ Additional improvement resulting in ability to run

Early improvement and regaining the ability to walk independently faster are important clinical milestones in GBS as they indicate a return to basic mobility and independence, and to an improved quality of life for patients

Comparison of imlifidase data to historical published data illustrates benefit of imlifidase and IVIg in GBS patients

Patients treated with imlifidase + IVIg had faster time to improvement and were able to walk sooner than patients on IVIg

	Admission	Median Time to walking *(reaching GBS DS2)*	Median Time to Improvement *(1 GBS DS grade or more)*
imlifidase + IVIg		16 days	6.0 days
IVIg		49-55 days	22-30 days

"The early improvements observed by imlifidase in severe GBS patients are remarkable."

Professor David Cornblath, M.D. Professor Emeritus, Neurology
Johns Hopkins University School of Medicine

JET-GBS study Lancet Neurol 2018;17:519-29, Lancet 1997 Vol 349, January 25, NEJM 1992 Apr 23;326(17), Lancet 1997 Vol 349, January 25 NEJM 1992 Apr 23;326(17)

15-HMedIdeS-09 indirect analysis to IGOS real-world comparator group treated with IVIg

15-HMedIdeS-09 patient data and IGOS real-world comparator data are similar

		15-HMedIdeS-09 imlifidase, N=27 n (%)	IGOS IVIg, N=754 n (%)
Media Age		60	60
Female Gender		13 (48)	319 (42)
Baseline GBS DS	3	6 (22)	218 (29)
	4	20 (74)	478 (63)
	5	1 (4)	58 (8)
Baseline MRC sum score	N	27	747
	Median	42	45
	Mean (SD)	39 (14)	41 (15)
Mean days from onset of weakness to start of treatment (SD)		4.5 (1.8)	5.6 (3.1)
Cranial Involvement at baseline		12 (44)	329 (44)
Presence of diarrhea (<4 wks prior to screening)		15 (56)	211/752 (28)

KEY TAKEAWAYS

- ✓ Propensity score weighting used all available patients (IGOS - IVIg treated)
- ✓ Active treatment arm patients (15-HMedIdeS-09) weighted to match external control prognostic variables
- ✓ Valid approach to contextualize data when a direct comparison is not available

Indirect treatment comparison demonstrates the robust, consistent benefit of imlifidase in combination with IVIg in GBS

15-HMedIdeS-09 data compared to IGOS

- Indirect comparison of 15-HMedIdeS-09 Phase 2 single arm trial data (n=27) to IGOS real-world IVIg comparator group with severe GBS patients (n=754)
- Unanchored matched-adjusted indirect comparison[1] method

Weighted Prognostic Variables

Time from weakness onset to treatment initiation and baseline values for:

● Age ● GBS DS ● Cranial Nerve Involvement ● MRC sum score ● Diarrhea

Clinically Meaningful Endpoints

Identified four clinically meaningful endpoints related to disease recovery including GBS DS and MRC sum score

Median time to return to independently walking **6 weeks sooner** than IVIg comparator group (*p=0.03*)	
Median time to improvement by at least one grade on GBS DS **3 weeks sooner** (*p=0.002*)	
Week 1	**6.4 times** more likely to walk independently *(odds ratio 95% CI: 2.3-17.5, p<0.001)*
Week 4	**4.2 times** more likely to walk independently *(odds ratio 95% CI: 1.6-11.5, p=0.005)*

Phillippo DM, et al. NICE DSU Technical Support Document 18. 2016.

Imlifidase in combination with IVIg delivers clinically meaningful benefit to patients with severe GBS

Substantial early improvement in functional status in Phase 2 study

well tolerated/consistent safety profile

Patients treated with imlifidase plus IVIg in Phase 2 study had rapid overall improvement in functional status

Rapid overall improvement in functional status	**37%** returned to walking independently
	Median time to independently walking (**16 days**)
	Median time to improve **by at least one** grade on GBS DS (6 days)
	MRC sum score of **10.7 points**
4 WEEKS	**33%** regained the ability to run
8 WEEKS	**67%** able to walk independently
	41% regained the ability to run
	37% improved by at least 3 points in GBS DS
6 MONTHS	**63%** able to run or had no functional disability

Significantly faster improvement in clinically meaningful measures vs standard of care IVIg

In comparison to IGOS-IVIg group (n=754), patients experienced significantly faster improvement across clinically relevant measures

Median time to return to independently walking **6 weeks sooner** than IVIg comparator group (p=0.03)

Median time to improvement by at least one grade on GBS DS **3 weeks sooner** (p=0.002)

1 WEEK	**6.4 times** more likely to walk independently (OR 95% CI: 2.3-17.5, p<0.001)
4 WEEKS	**4.2 times** more likely to walk independently (OR 95% CI: 1.6-11.5, p=0.005)

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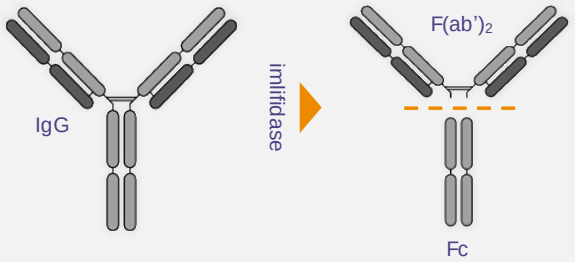
IGOS – International GBS Outcome Study
OR - odds ratio

Hansa is addressing unmet medical need in IgG driven immune mediated diseases

Two IgG- cleaving compounds

IMLIFIDASE

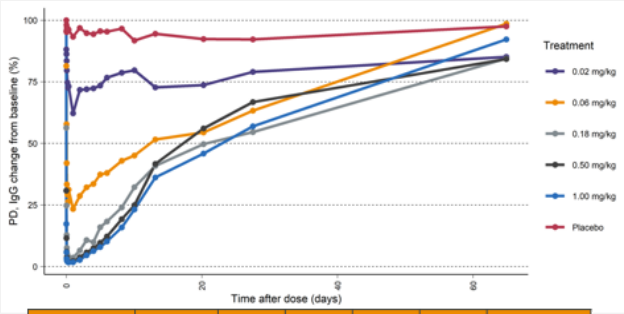
first generation, first in class, single dose therapy with proven efficacy and safety



- ❑ Conditionally approved in the EU for desensitization in kidney transplantation
- ❑ Seven clinical trials in 9 indications across key therapy areas

HNSA-5487

second generation molecule with redosing potential



	0.02 mg/kg n=4	0.06 mg/kg n=4	0.18 mg/kg n=6	0.50 mg/kg n=6	1.00 mg/kg n=6	Imlifidase** 0.25 mg/kg n=23
Responders*	0%	25%	83%	100%	100%	88%

*A subject with IgG level <5% of baseline 24 hours post dosing
** Data from 18-HMedAdas-15 and 2**-HMedStd-29

- ❑ Demonstrated rapid and robust reduction in IgG with confirmed redosing potential
- ❑ Clinical development path focused on acute exacerbations in neuro-autoimmune diseases

Q&A

HANSA BIOPHARMA LEADERSHIP

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President & CEO

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Chief R&D Officer