GAIN THERAPEUTICS

Corporate Presentation

April 2025

NASDAQ: GANX

Forward-Looking Statements

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These include, but are not limited to, statements about the Company's ability to develop, obtain regulatory approval for and commercialize its product candidates; the timing of future IND submissions, initiation of preclinical studies and clinical trials, and timing of expected clinical results for our product candidates; the Company's success in early preclinical studies, which may not be indicative of results obtained in later studies or clinical trials; the outbreak of the novel strain of coronavirus disease, COVID- 19, which could adversely impact our business, including our preclinical studies and any future clinical trials; the potential benefits of our product candidates; the Company's ability to obtain regulatory approval to commercialize our existing or any future product candidates; the Company's ability to identify patients with the diseases treated by our product candidates, and to enroll patients in clinical trials; the success of our efforts to expand our pipeline of product candidates and develop marketable products through the use of our Magellan platform; the Company's expectations regarding collaborations and other agreements with third parties and their potential benefits; the Company's ability to obtain, maintain and protect our intellectual property; the Company's reliance upon intellectual property licensed from third parties, including the license to use the Company's Magellan platform; the Company's ability to identify, recruit and retain key personnel; the Company's financial performance; developments or projections relating to the Company's competitors or industry; the impact of laws and regulations; the Company's expectations regarding the time during which it will be an emerging growth company under the JOBS Act; and other factors and assumptions described in the Company's public filings.

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GANX Corporate Highlights

Lead Product GT-02287 Advancing into Parkinson's Disease Patients

- **Allosteric modulator** of glucocerebrosidase enzyme (GCase)
- **Disease modifying potential**: slowing/stopping progression of motor and cognitive decline in GBA1 and idiopathic PD
- **Safe and well tolerated in Phase 1 SAD/MAD study and demonstrated target engagement**
- **Biomarker analysis from Phase 1b trial in GBA1 and idiopathic PD patients expected mid-2025**

Multiple assets in discovery and preclinical development

- Assets identified and developed through application of our **Proprietary Magellan™ AI platform**
- Initial disease targets include neurodegenerative diseases, lysosomal storage disorders including Gaucher disease as well as metabolic disease and solid tumors

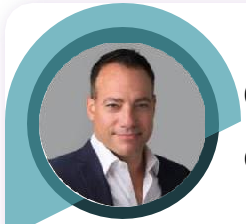
Strong intellectual property estate

- GT-02287 composition of matter patent application with term through 2038 not including Hatch Waxman extension
- Patent applications for 5 NCE families under review

Anticipated Upcoming Milestones

• GT-02287 Phase 1b biomarker analysis	1H25
• GT-02287 Phase 2 planning (US/EU)	2H25

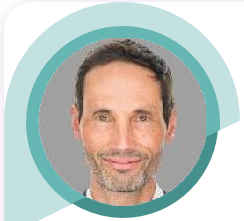
Experienced Leadership:
Extensive Biotech And Pharma Experience



Gene Mack, MBA

Chief Executive Officer

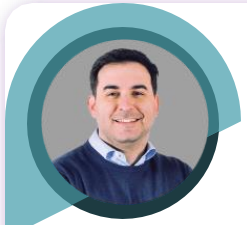
Imcyse · OncoC4 · biom'up · nicox · ΣELLAS · MERCK Oncolmmune · MIZUHO · HSBC · LAZARD



Jonas Hannestad, MD, PhD

Chief Medical Officer

TRANQUIS THERAPEUTICS · ucb · CAPACITY BIO THE MITOPHAGY COMPANY · ALKAHEST · DENALI THERAPEUTICS



Gianluca Fuggetta

Senior Vice President, Finance

pwc

Joanne Taylor, PhD

SVP Research

Prescient · Eisai · ETH zürich

Terenzio Ignoni, PharmD

SVP Technical Operations

Jazz Pharmaceuticals · Vicuron Pharmaceuticals · gentium · Zambon

Experienced Board of Directors:
Extensive Biotech And Pharma Experience (>$30b Transactions)

Khalid Islam, PhD

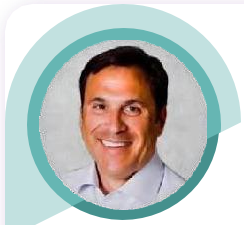
Founder and Chairman

Immunomedics · minoryx therapeutics · ARPIDA · Karolinska Development · MOLMED · gentium · sanofi aventis · FENNEC PHARMA

Claude Nicaise, MD

Independent Member

ALEXION · SAREPTA THERAPEUTICS · ovid THERAPEUTICS · Bristol Myers Squibb



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Hans Peter Hasler

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Dov Goldstein, MD

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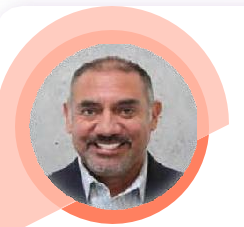
BIOAGE · LOXO ONCOLOGY · indapta · SCHRÖDINGER · ADMA BIOLOGICS



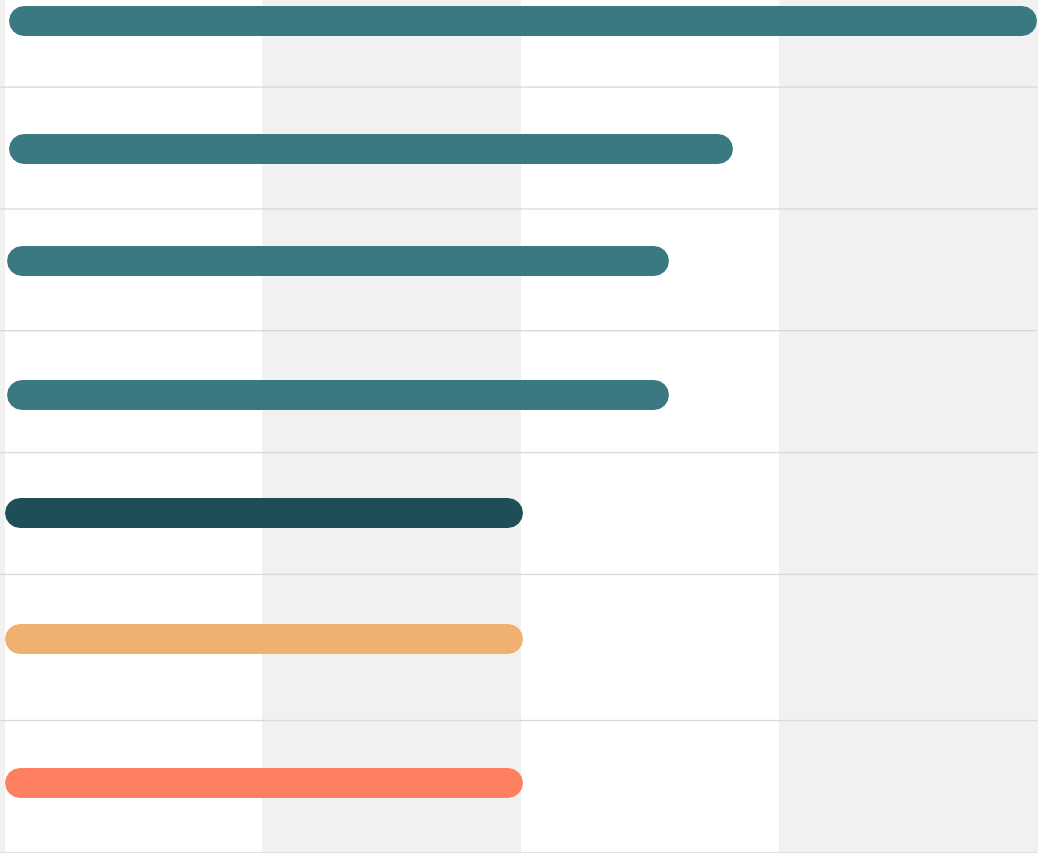
Jeffrey Riley

Independent Member

Pfizer · Synthetic BIOLOGICS · Quest Diagnostics · SmithKline Beecham

Gain Therapeutics Pipeline

ASSET	INDICATION	TARGET	DISCOVERY	RESEARCH	PRECLINICAL	PHASE 1
GT-02287	Parkinson's Disease	GCase				
	Gaucher's Disease	GCase				
	Dementia with Lewy Bodies	GCase				
	Alzheimer's Disease	GCase				
Multiple Undisclosed	Lysosomal Storage Disorders	GALC GLB1				
Undisclosed	Metabolic Diseases	AAT				
Multiple Undisclosed	Oncology: Solid Tumors	DDR2				



Lead Clinical Program

GT-02287
GBA1 Parkinson's Disease

Parkinson’s Disease – Market Opportunity

Parkinson’s Disease

US Market Potential: $4B

Parkinson’s disease is the second most common neurodegenerative disease[1]

Current therapies only treat symptoms and do not prevent disease progression

GBA1-Parkinson’s Disease

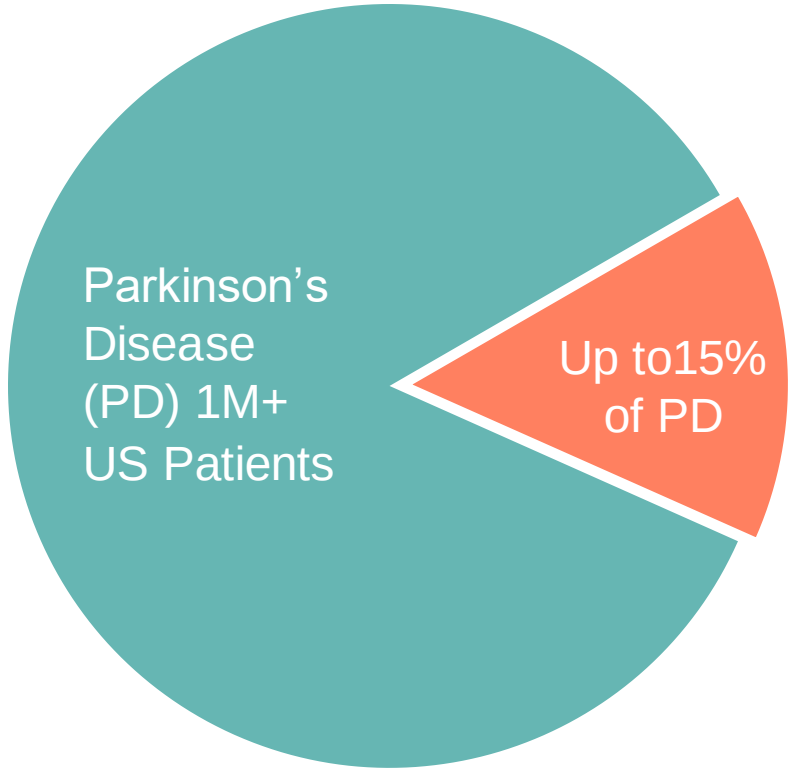
US Market Potential: $3B

Genetically defined subpopulation of Parkinson's disease

Largest genetic risk factor for development of Parkinson’s disease

GBA1 mutations cause misfolding of an important enzyme called GCase

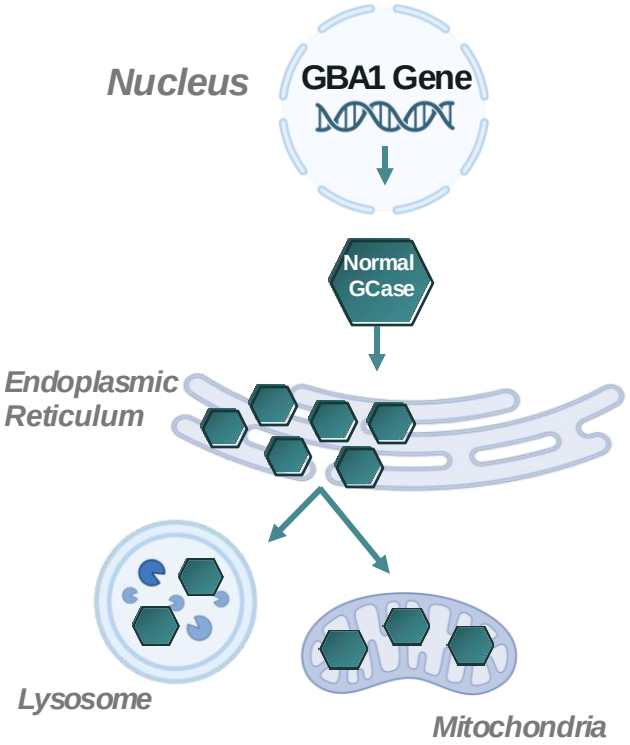
GBA1-PD patients experience earlier disease onset and more severe disease with faster decline in motor and cognition functions



1.“Parkinson’s Disease:Challenges, Progress, and Promise.” National Institute of Neurological Disorders and Stroke, U.S. Department of Health and Human Services, 30 Sept. 2015
2. Smith L and Schapira AHV. GBA Variants and Parkinson Disease: Mechanisms and Treatments. Cells. 2022 Apr 8;11(8):1261. doi: 10.3390/cells11081261

Dysfunctional GCase triggers disease cascade affecting multiple organelle functions and leads to neurodegeneration

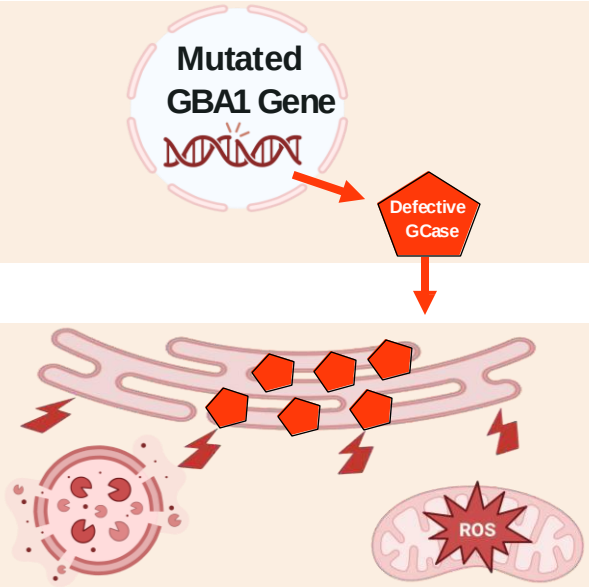
Healthy Dopaminergic Neuron



GCase maintains cell health:

- **Depletes toxic lysosomal substrates**
- **Stabilizes mitochondrial respiratory complex I**

Diseased Dopaminergic Neuron



GCase protein misfolding

↓

- Increased ER stress and ER-associated protein degradation

↓

- Lysosomal and mitochondrial dysfunction
- Accumulation of toxic lysosomal lipid substrates resulting from reduced GCase activity

↓

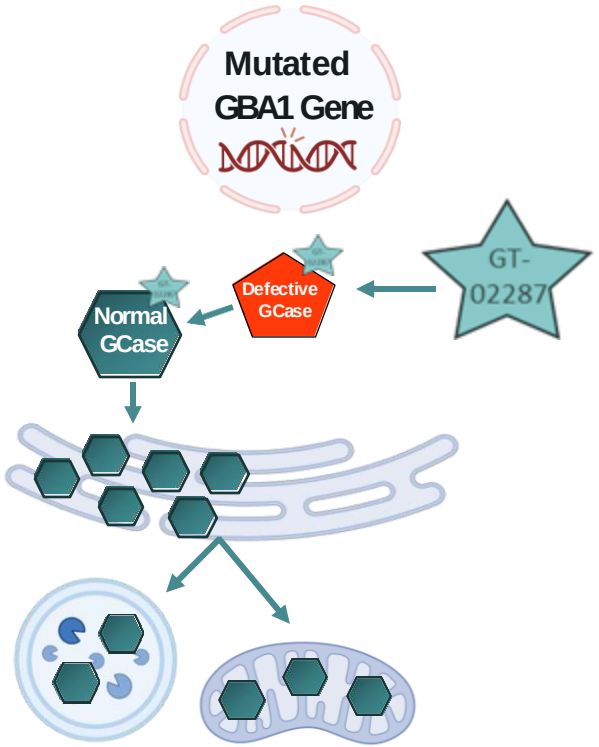
Alpha synuclein aggregation

↓

Increased Risk of PD: Core motor dysfunction, cognitive dysfunction

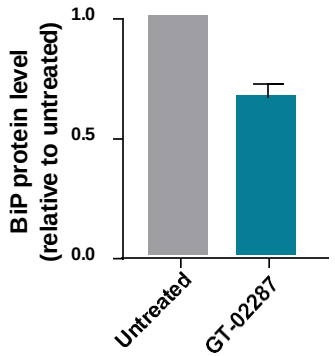
Allosteric modulator GT-02287 restores GCase function, which improves disease cascade and neuronal survival

Dopaminergic Neuron with Restored GCase Function

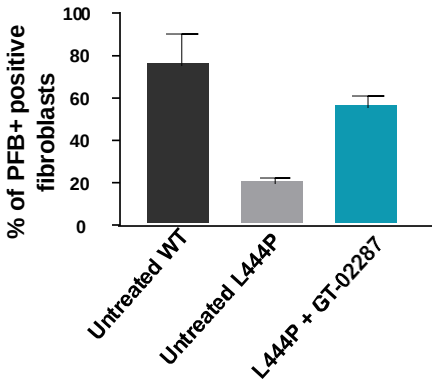


- Corrects protein misfolding
- Restores enzymatic activity

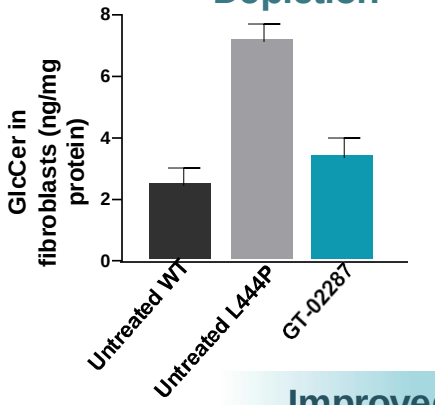
Reduced ER Stress



GCase Activity Restoration

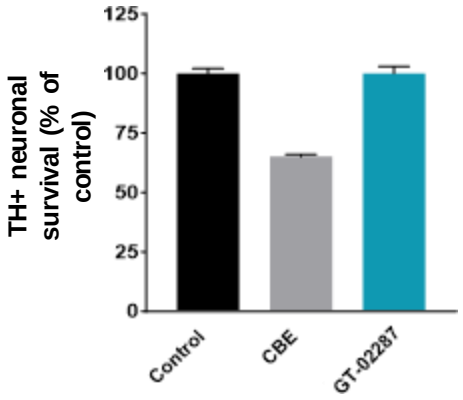


Toxic Substrate Depletion

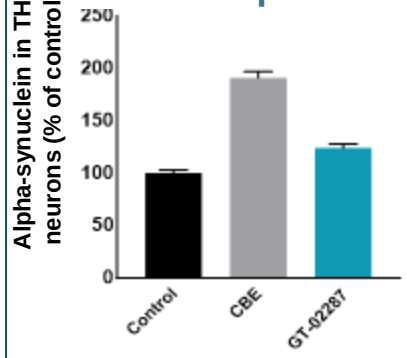


Improved Cellular Health

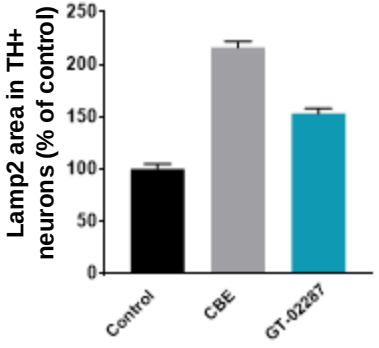
Neuronal Survival



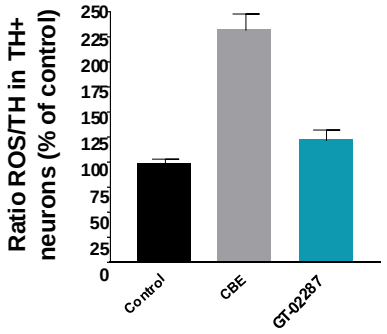
Alpha-Synuclein Depletion



Restored Lysosomal Function



Restored Mitochondrial Function

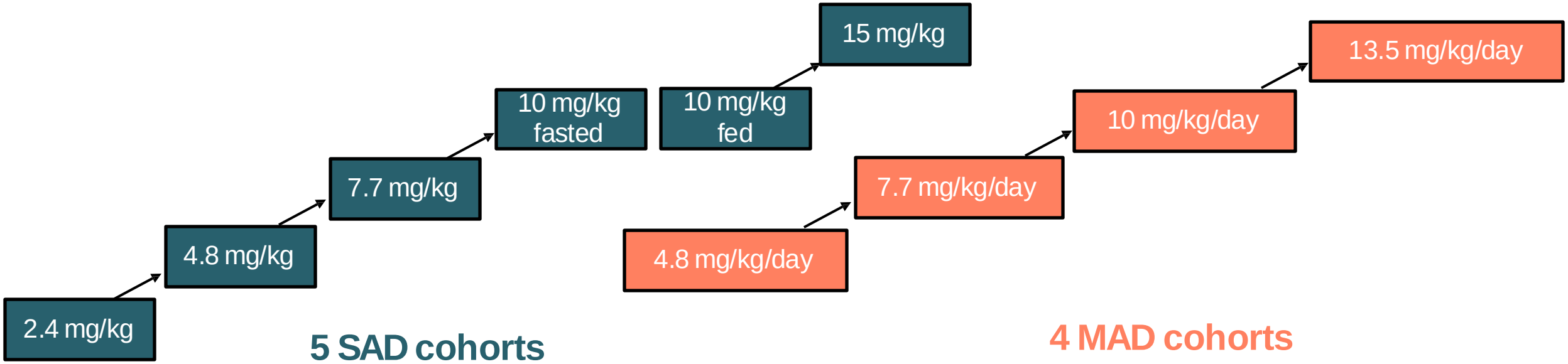


Single- and Multiple-ascending Dose First-in-human Phase 1 Study

Participants:
- Healthy men and women ages 18-65
- 8 subjects per cohort
  - 2 placebo; 6 active

SAD/MAD endpoints:
- Treatment-emergent adverse events
- Clinical labs, vital signs, ECGs, C-SSRS
- Plasma pharmacokinetics

MAD Cohort 4:
- CSF drug levels
- GCase activity in dry blood spots



5 SAD cohorts
Food effect at 10 mg/kg

4 MAD cohorts
Daily dosing for 14 days

GT-02287 was Generally Well-Tolerated, No Serious Adverse Events Observed

- No Serious Adverse Events
- No Severe Adverse Events (CTCAE Grade 3)
- No discontinuations due to AE
- 56.7% (n=17) of active and 40% (n=4) of placebo participants in the SAD had 1 or more TEAE
- 64% (n=16) of active and 50% (n=4) of placebo participants in the MAD had 1 or more TEAE

Adverse Event Profile

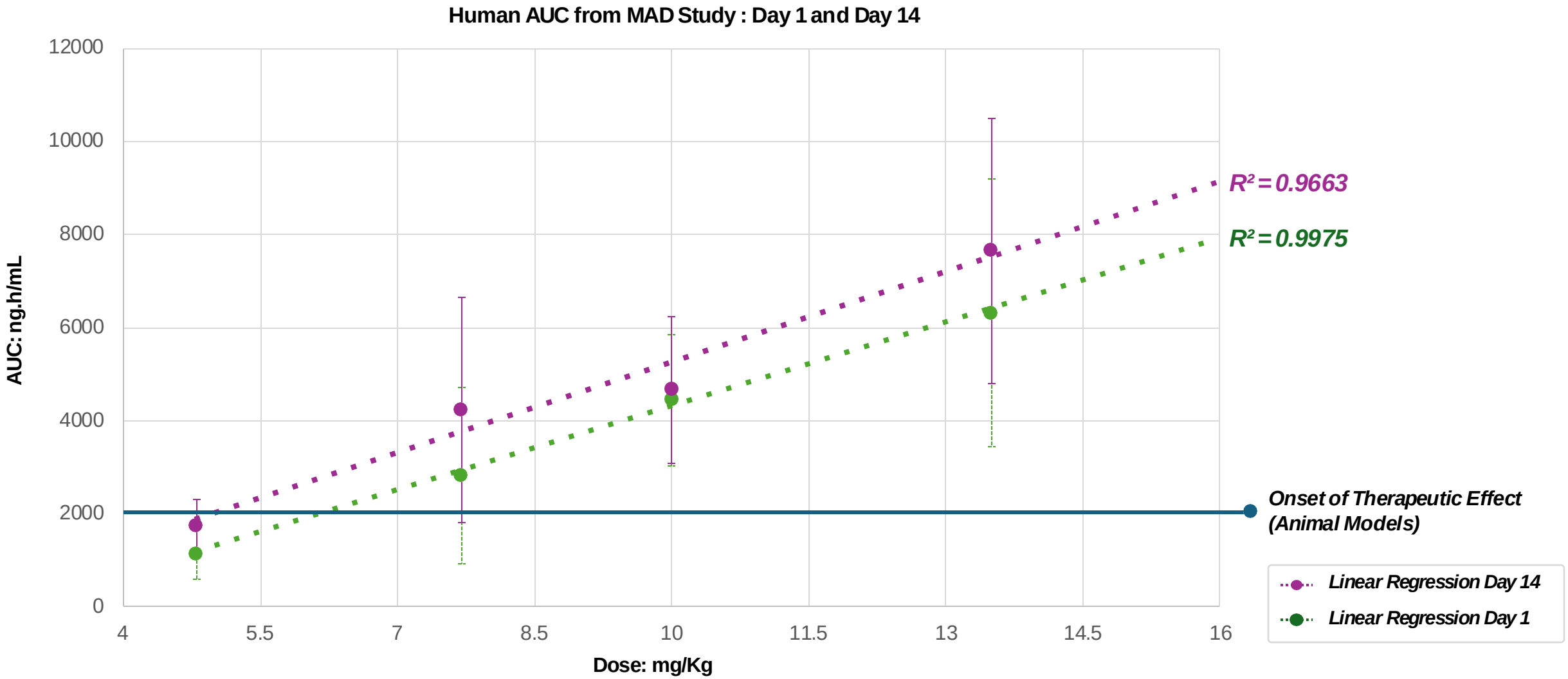
Most common TEAEs in MAD:

- Nausea 32%
- Abdominal pain 8%
- Diarrhea 8%
- Headache 8%

Nausea:

- >90% of events were mild
- >90% of events were <3h in duration
- Incidence increased with dose level
- Incidence decreased with continued dosing

Therapeutic Range: Phase 1 PK Data in Healthy Volunteers



GT-02287 Demonstrates CNS Exposure Comparable to that Observed in Rodents

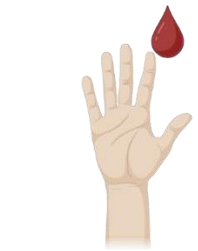
- CSF levels in Humans comparable to those observed at efficacious dose levels in rodents
- CSF levels are low in all species due to low aqueous solubility and high protein binding
- Observed total brain levels in rodents are 2-8 times higher than total plasma levels

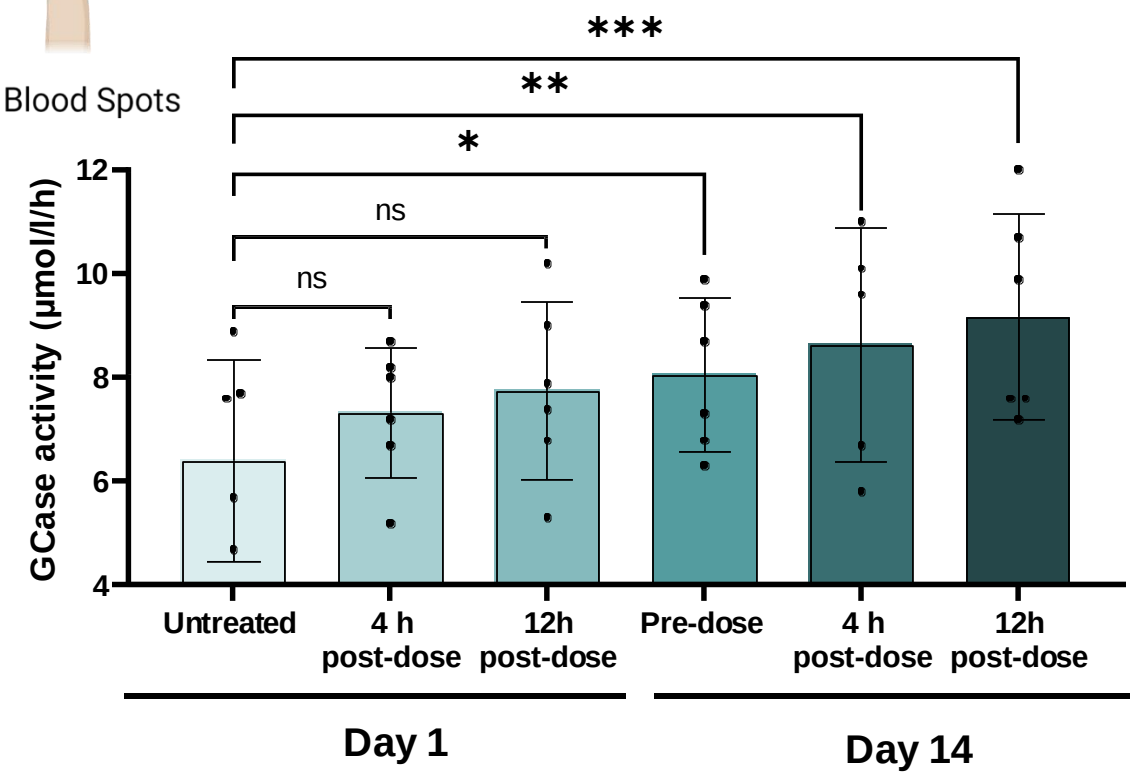
Species	Mean CSF level (ng/mL)	Total brain level (ng/mL)	Mean plasma Cmax (ng/mL) mean Day 14	Timepoint	Dose (mg/kg)
Human (MAD4)	3.1 (1.7-4.9)	Nd	850	Day 13	13.5 PO
Mouse	4	6592	2414	15 min	10 IV
Rat	3	2441	680	1 hour	30 PO

GT-02287 Demonstrates Gcase Target Engagement In Healthy Volunteers

- GCase activity in dry blood spots was measured in MAD Cohort 4
- In GT-02287 subjects, 5 out of 6 had increased GCase activity
- In placebo subjects, no increase was observed (+4% change from baseline)

53% increase in GCase activity observed by Day 14 (p<0.001)





One-way, paired, repeated measures ANOVA.
*p < 0.05; **p < 0.01; ***p < 0.001

Phase 1 Blinded, Placebo Controlled SAD/MAD Trial

Safety

GT-02287 is safe and generally well tolerated in SAD (40 HV) and MAD (32 HV, daily dosing 14 days)

No SAEs, Grade 3 AEs, or clinically-significant changes in ECGs, BP/HR

Plasma Exposure

Plasma exposures in the projected therapeutic range

Adequate safety margins based on toxicology studies

CNS Exposure

GT-02287 is detectable in CSF and in line with rodent levels at effective doses

Target Engagement

GT-02287 modulates GCase activity in blood

Upcoming Anticipated Milestones and Potential Value Inflection Points

1H 2025

Potential clinical POC based on biomarkers of GBA1-Parkinson's disease
(first analysis from Phase 1b clinical trial)

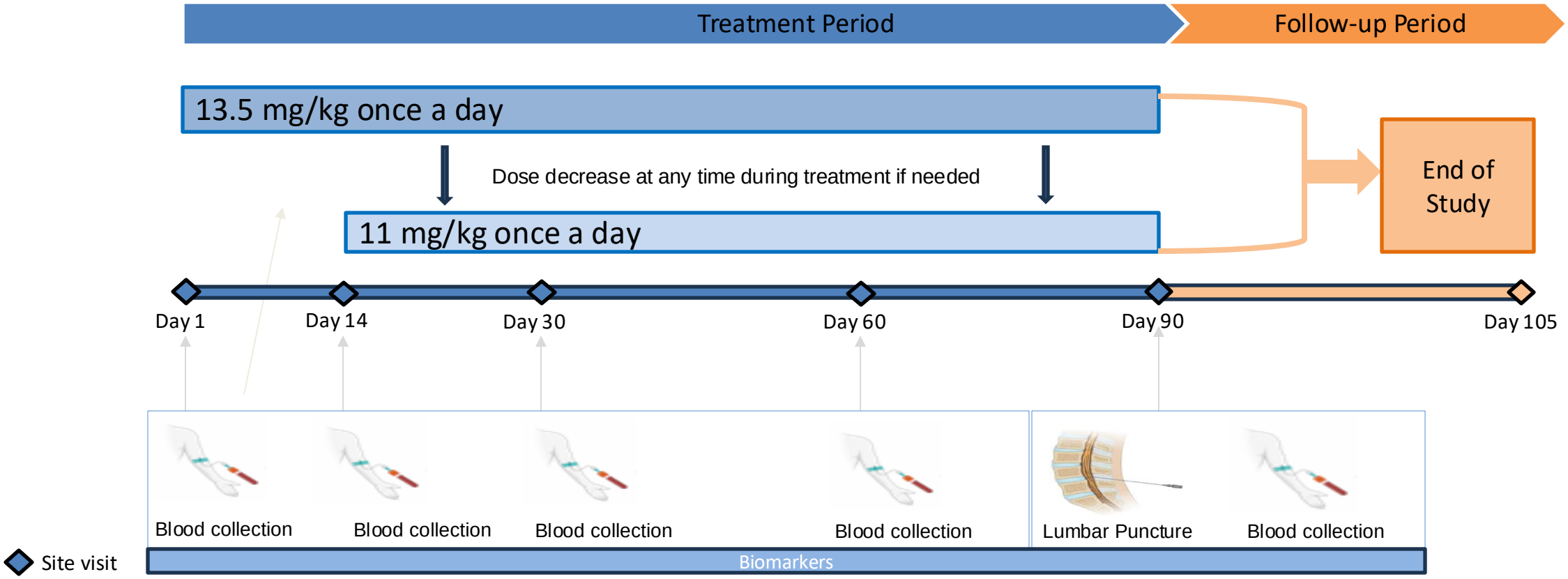
2H 2025

Start of Phase 2 planning

Design of Phase 1b Trial in Parkinson's Disease Patients

An Open-label Study to Assess the Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of GT-02287 in Participants with Parkinson's Disease With or Without a Pathogenic GBA1 Mutation

- Open-Label, single-arm, multicenter study
- Approximately 15-20 patients with or without a GBA1 mutation will be enrolled
- 90-day treatment duration
- 7 sites in Australia with potential to expand to other geographies



Phase 1b Study Objectives

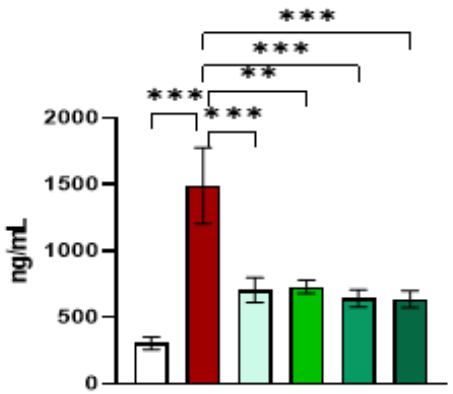
Study Objectives		
		Endpoints
Primary	• To evaluate the safety and tolerability of GT-02287	
Secondary	• To characterize the single-dose and steady state plasma PK profile of GT-02287	
Exploratory	• To assess levels of GT-02287 in CSF after at least 12 weeks of daily administration in participants with PD	Concentration of GT-02287 in CSF at 4 hours post-dose after at least 12 weeks of daily administration of GT-02287
	• Pharmacodynamic response to GT-02287 via biomarkers analysis of plasma, whole blood, blood cells, and CSF samples	• Gcase activity • Sphingolipid levels • Lysosomal and mitochondrial markers • Inflammatory markers
	• To explore the effect of GT-02287 on scores from selected clinical scales and questionnaires over a 90-day treatment	Movement Disorder Society Unified Parkinson's Disease Rating Scale **(MDS-UPDRS, OFF state)** and other standard functional scales including MoCA, ADL, etc.

GT-02287 Prevents GBA1 Disease Cascade in Mouse CBE Model of GBA1-PD

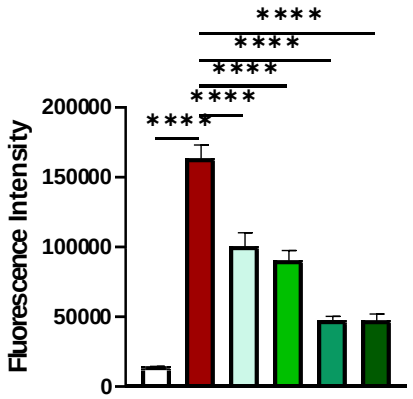
GBA1-PD Model: CBE causes partial knockdown of GCase activity

- **CBE** is an irreversible GCase inhibitor
- Administration of **CBE** models the effects of dysfunctional GCase seen in GBA1-Parkinson's disease

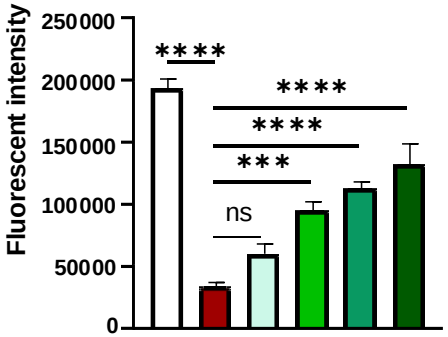
GluCer (Cortex)



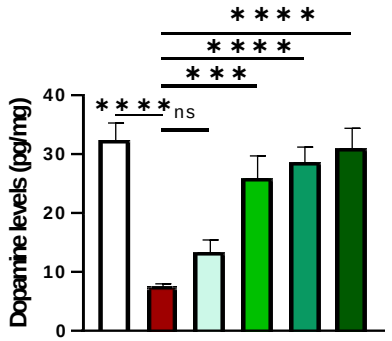
Aggregated α-syn (SN)



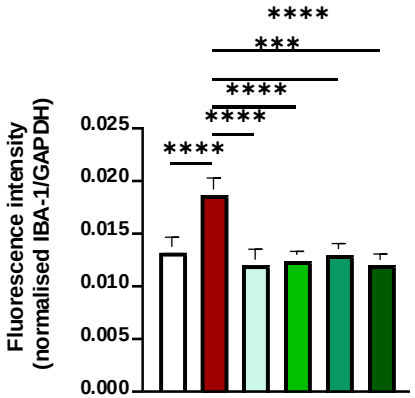
Tyrosine Hydroxylase (SN)



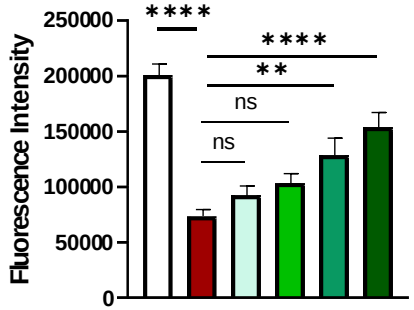
Striatal Dopamine



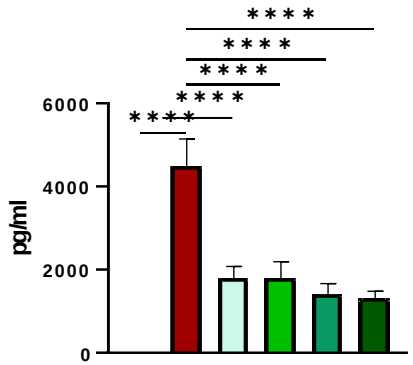
Iba-1 (SN)



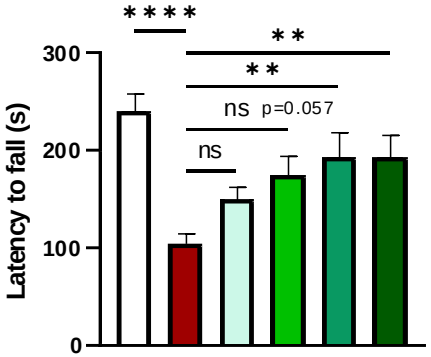
NeuN (Cortex)



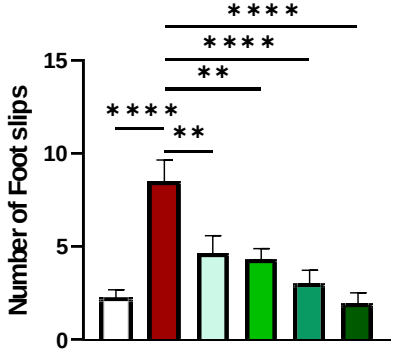
NfL



Wire Hang



Beam Walk



Control | CBE | +GT-02287 (30mg/kg) | +GT-02287 (60mg/kg) | +GT-02287 (90mg/kg) | +GT-02287 (120mg/kg)

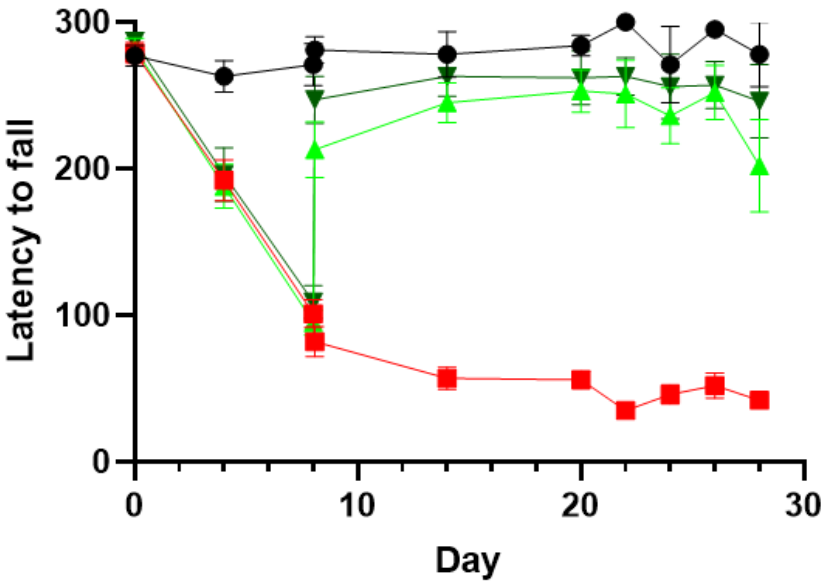
GT-02287 displays a rescue and disease-modifying effect in animal models of GBA1 and iPD

GBA1- PD Model (CBE+PFFs)

α-Syn PFFs

Low Level CBE

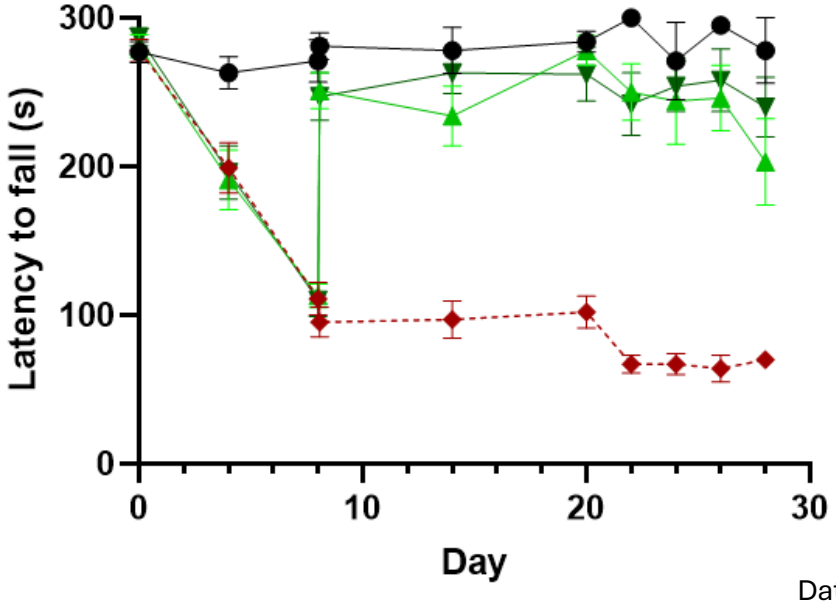
No drug | GT-02287 | Washout



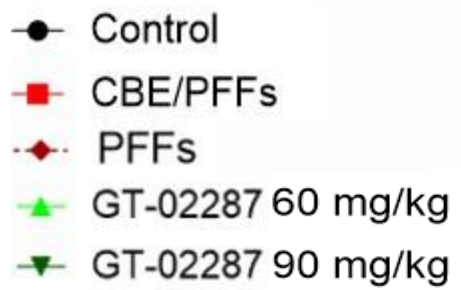
Idiopathic PD Model (PFFs only)

α-Syn PFFs

No drug | GT-02287 | Washout



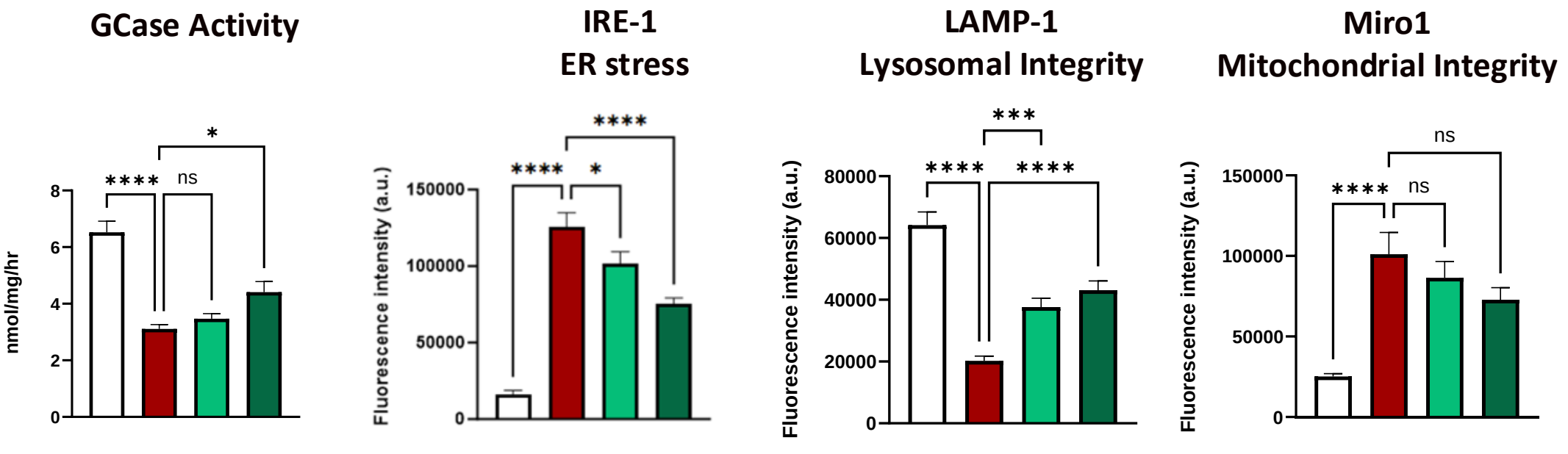
Mouse Wire Hang Rescue & Washout

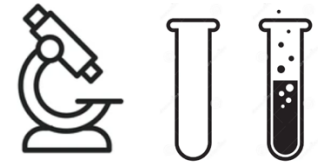


Data is shown as Mean ± S.E.M.(n=14 till day 20, then n=7)

Fast-onset rescue effect of GT-02287 driven by enhanced GCase activity, reduced ER stress and increased lysosomal and mitochondrial integrity

2h post-treatment



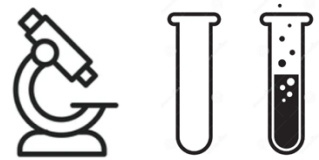


Controls
CBE + PFFs
+ GT-02287 (60 mg/kg,q.d., p.o.)
+ GT-02287 (90 mg/kg,q.d., p.o.)

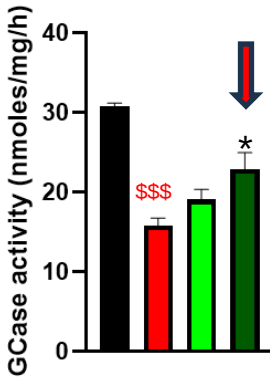
* Significant difference as compared to α-synuclein PFF+CBE.
One-way ANOVA followed by Dunnett's Multiple Comparison Test. *P < 0.05, **P < 0.01 , /***P < 0.001 & ****P < 0.0001.

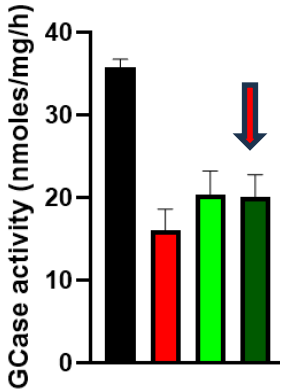
Brain biomarker changes maintained following GT-02287 washout

- *Taken together, data support GT-02287's disease modifying effect*

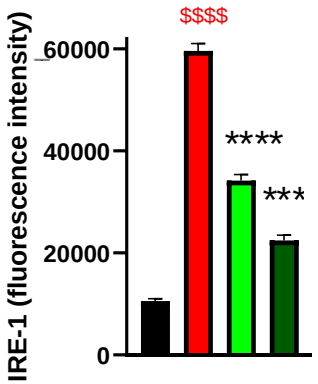


GCase activity

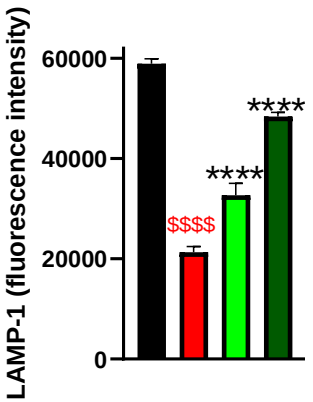




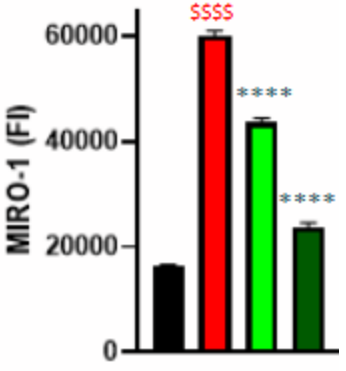
IRE-1 (ER stress)



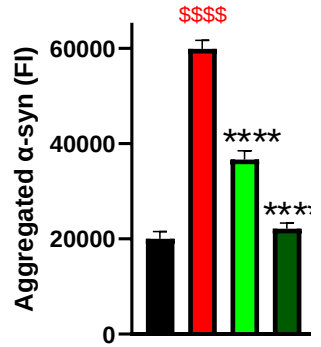
LAMP-1 (lysosomal integrity)



MIRO-1 (mitochondrial health)

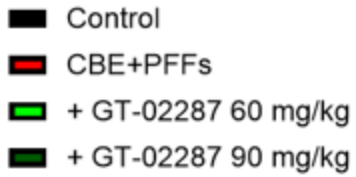


Aggregated α-syn



No washout — **Washout d20-d29**

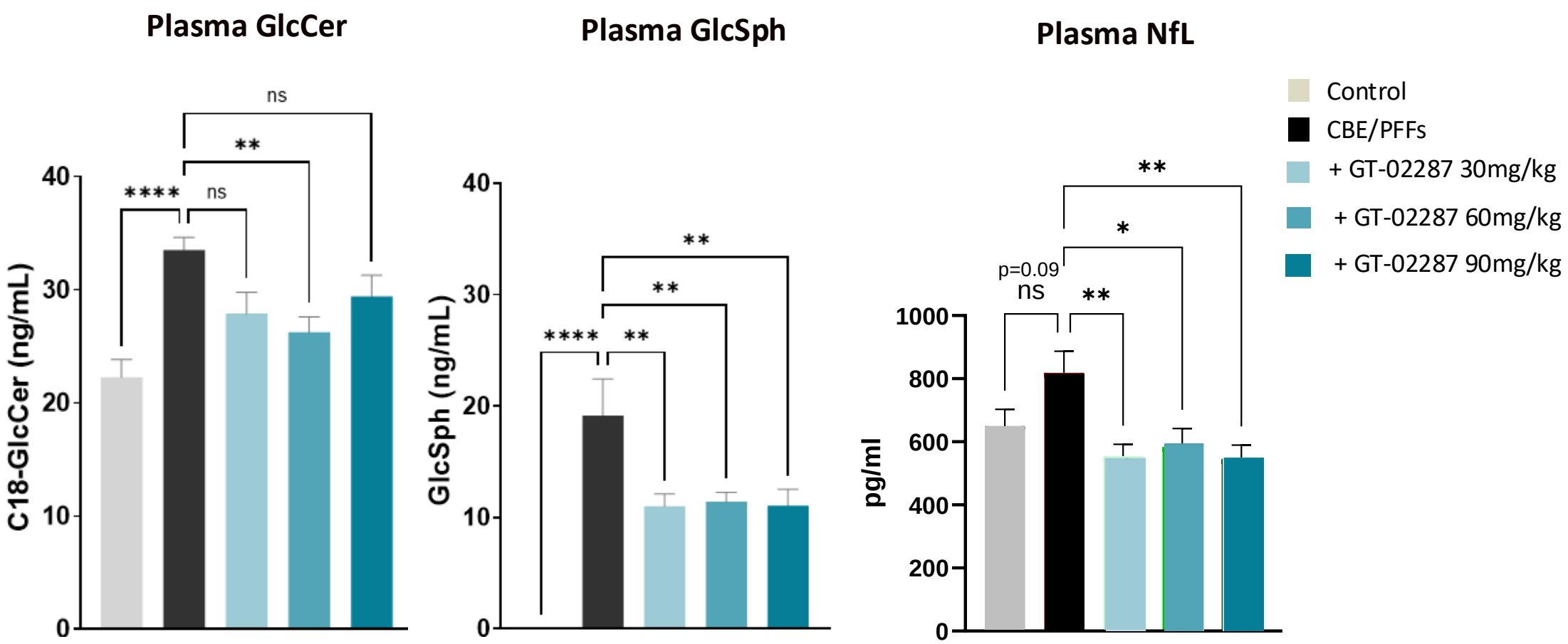
CBE/PFF GBA1-PD model



- Above biomarkers are being measured in blood and CSF in Phase 1b

Data is shown as Mean ± S.E.M. $Significant difference as compared to sham control group * Significant difference as compared to α-synuclein PFF+CBE. One-way ANOVA followed by Dunnett's Multiple Comparison Test. $/*P < 0.05, $$/**P < 0.01 , $$$/***P < 0.001 & $$$$/****P < 0.0001.

Translational plasma-based biomarkers of GT-02287 rescue effect

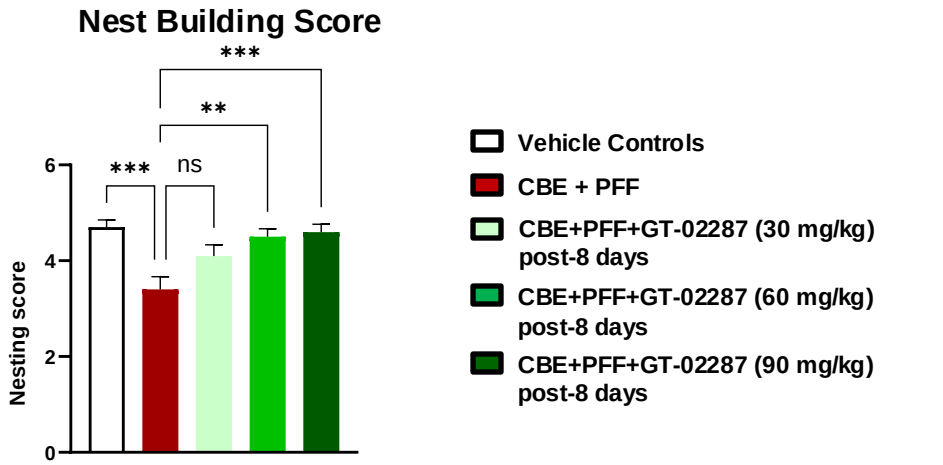


Data shown as Mean ± S.E.M. (n=10). Significant difference as compared to PFFs or PFFs + CBE. One-way ANOVA followed by Dunnett's Multiple Comparison test. ns (non significant). * < P 0.05, ** < P 0.01, **** < 0.0001.

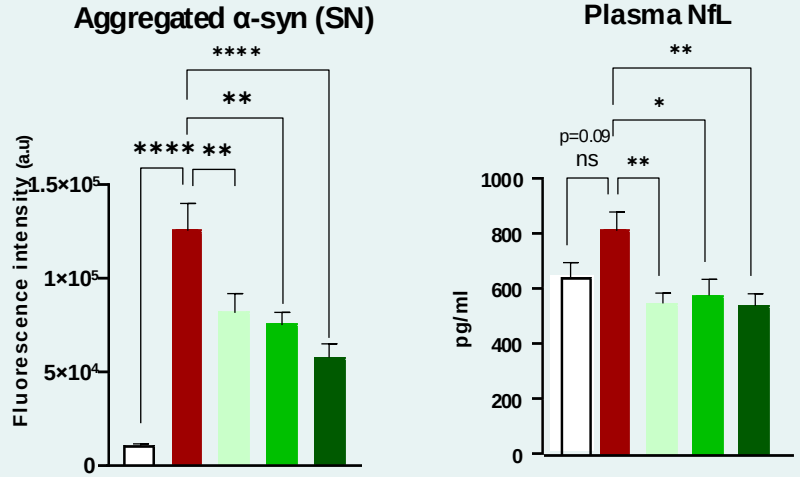
GT-02287 Improves Nest Building Performance in Therapeutic Model of GBA1-PD

Improvements in Nest-building Performance

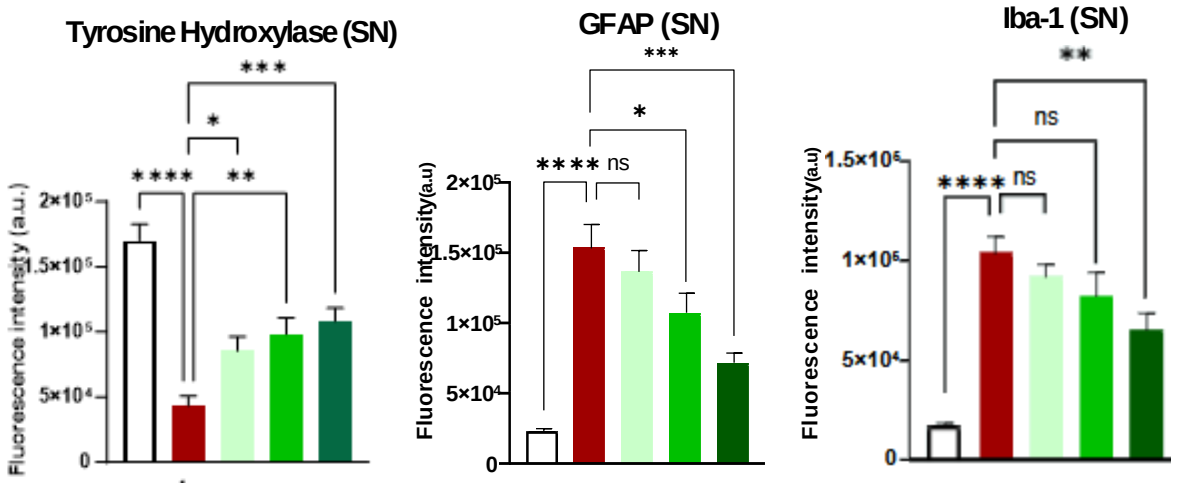
Nest building is a non- invasive test to study activities of daily living and cognitive performance in rodent models



Improvements in Relevant Biomarkers



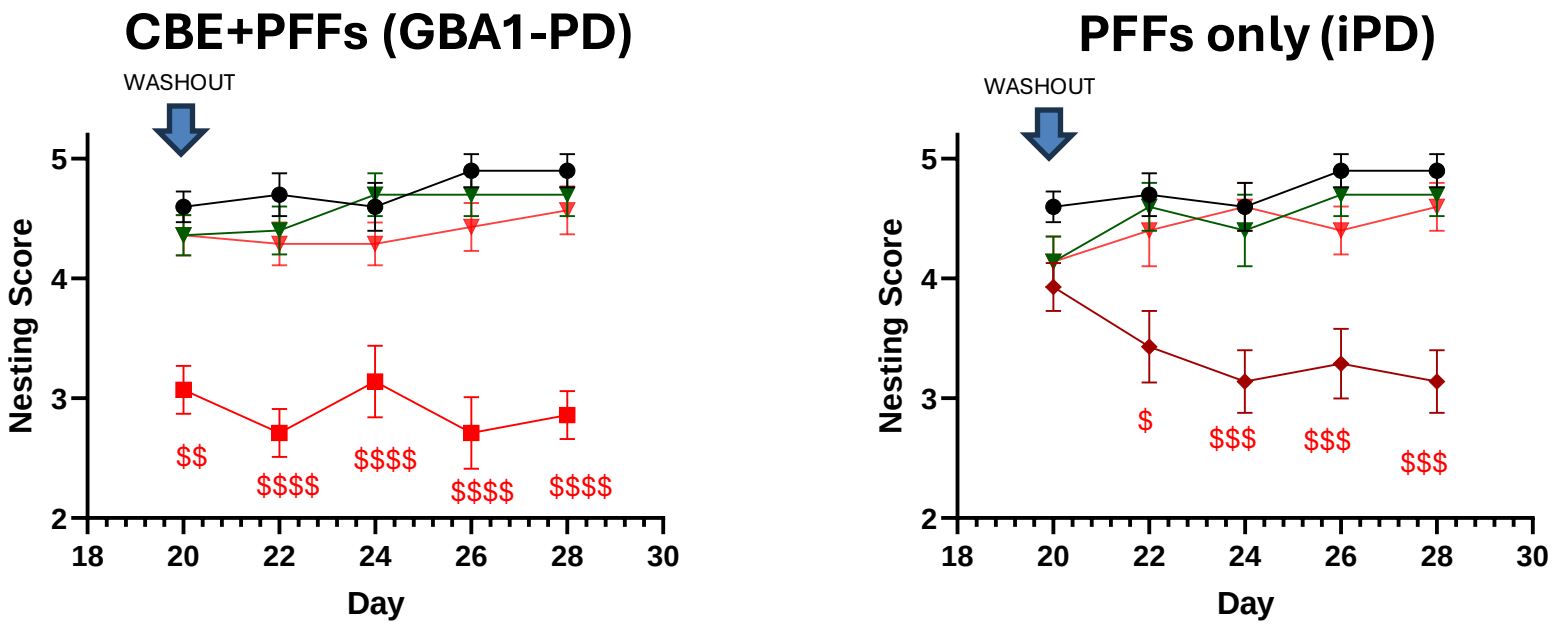
Biomarkers being assessed in ongoing Phase 1b study



Data is shown as Mean ± S.E.M.(n= 7). $Significant difference as compared to sham control group. One-way ANOVA followed by Dunnett's Multiple Comparison Test. $P < 0.05, $$P < 0.01 , $$$P < 0.001 & $$$$P < 0.0001.

Nesting score unaffected by drug washout: evidence of disease modifying effect on complex behaviors

Mouse Nesting Building Washout



Control
CBE+PFFs
PFFs
GT-02287 90mg/Kg
GT-02287 90mg/Kg + washout

Data is shown as Mean ± S.E.M.(n= 7). $Significant difference as compared to sham control group

One-way ANOVA followed by Dunnett's Multiple Comparison Test. $P < 0.05, $$P < 0.01 , $$$P < 0.001 & $$$$P < 0.0001.

GT-02287 has Best-in-Class Profile for GBA1-Parkinson's Disease

	Effect on Disease Cascade	GAIN THERAPEUTICS GT-02287	Bial BIA 28-6156	VANQUA BIO VQ-101
GCase Mechanism of Action	Increases Lysosomal GCase Activity	✓	?	✓
	Reduces ER Stress	✓	?	?
	Reduces Toxic Lipid Substrates	✓	✓ ✗	✓
	Reduces Aggregated α-Synuclein	✓	?	✓
	Improves Lysosomal Function	✓	✓	✓
	Improves Mitochondrial Function	✓	?	?
	Reduces Neuroinflammation	✓	?	?
Disease-Modifying Effect	Provides Neuroprotection	✓	?	?
	Increases Dopamine Levels	✓	?	?
	Restores Motor Function	✓	?	?
	Improves Cognitive Function	✓	?	?

Large Market Potential for GT-02287 for Various Neurodegenerative Diseases

Indication	Rationale	Number of Patients (US)
GBA1-Parkinson's Disease	Patients have dysfunctional GCase due to heterozygous GBA1 mutation	150,000
Idiopathic Parkinson's Disease (IPD)	Increase in GCase activity and target activation in healthy volunteers suggests potential activity in iPD	1,000,000
Gaucher Disease	DysfunctionalGCase due to homozygous GBA1 mutation	6,000
Dementia with Lewy Bodies	GT-02287 reduces aggregated alpha-synuclein,a componentof Lewy bodies	1,000,000
Alzheimer's Disease	GT-02287 has shown positive effects in preclinical models of Alzheimer's disease	5,800,000

Company Background

CORPORATE BACKGROUND

Established in 2017

27 employees in three locations: HQ in Bethesda, Maryland, Lugano, Switzerland, Barcelona, Spain

Founder and Executive Chairman: Dr. Khalid Islam

ANALYST COVERAGE

BTIG	Tom Shrader, Ph.D., CFA
Oppenheimer & Co	Jay Olson, CFA
HC Wainwright	Ram Selvaraju, Ph.D.
Chardan	Keay Nakae, CFA
Maxim	Jason McCarthy, Ph.D.
ROTH	Boobalan Pachaiyappan, Ph.D.
Scotiabank	Louise Chen, MBA

FINANCIAL AND STOCK DATA

IPO (NASDAQ: GANX)

- March 2021
- Led by BTIG and Oppenheimer & Co.

CAPITAL STRUCTURE

- 26.5 million shares outstanding
- No debt*

CASH POSITION

- $10.4 million as of December 31, 2024

GRANT SUPPORT

- Michael J. Fox Foundation for Parkinson's Research
- The Silverstein Foundation for Parkinson's with GBA
- Innosuisse (Swiss Innovation Agency)

THE MICHAEL J. FOX FOUNDATION FOR PARKINSON'S RESEARCH

The Silverstein Foundation for Parkinson's with GBA

Schweizerische Eidgenossenschaft
Confédération suisse
Confederazione Svizzera
Confederaziun svizra
Swiss Confederation
Innosuisse – Swiss Innovation Agency

*Except a 9-year interest-free Swiss government loan ~$0.5 million outstanding at September 30, 2023

Company Contacts

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gmack@gaintherapeutics.com

Apaar Jammu
Manager, Investor Relations and Public Relations
ajammu@gaintherapeutics.com

GAIN THERAPEUTICS

Appendix