Top-Line Phase 3 Results
DTX401 for Glycogen Storage Disease Type Ia (GSDIa)

May 30, 2024

Forward Looking Statements

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Disclaimer

DTX401 is an investigational drug and is currently not approved by any regulatory authority

DTX401 for Glycogen Storage Disease Type Ia (GSDIa)

GSDIa disease: Defect in liver's ability to release glucose due to G6Pase deficiency

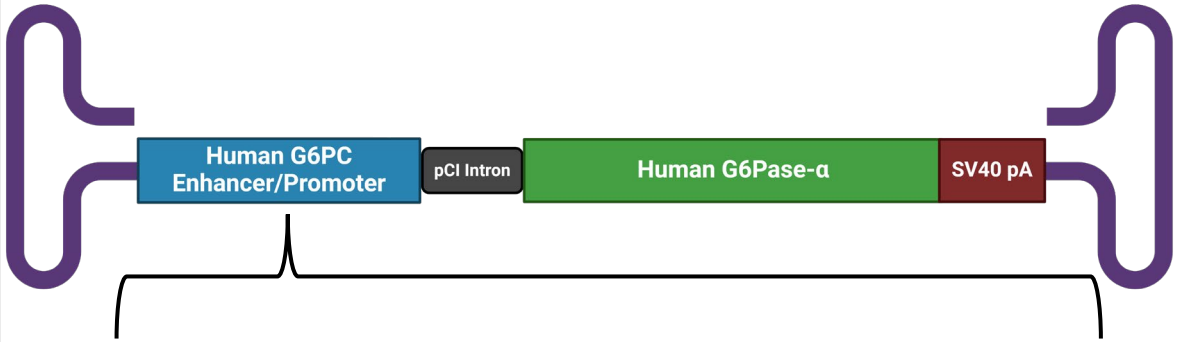
- Life-threatening hypoglycemia
- Severe metabolic liver disease with long-term complications in 70-80% patients

Current treatment: Diet and uncooked cornstarch (CS)

- Adults ± 300 to 350 grams per 24-hour period
- CS doses typically every 3-4 hours, including overnight
- Overnight tube feeds (pediatric patients)
- Only curative approach is liver transplantation

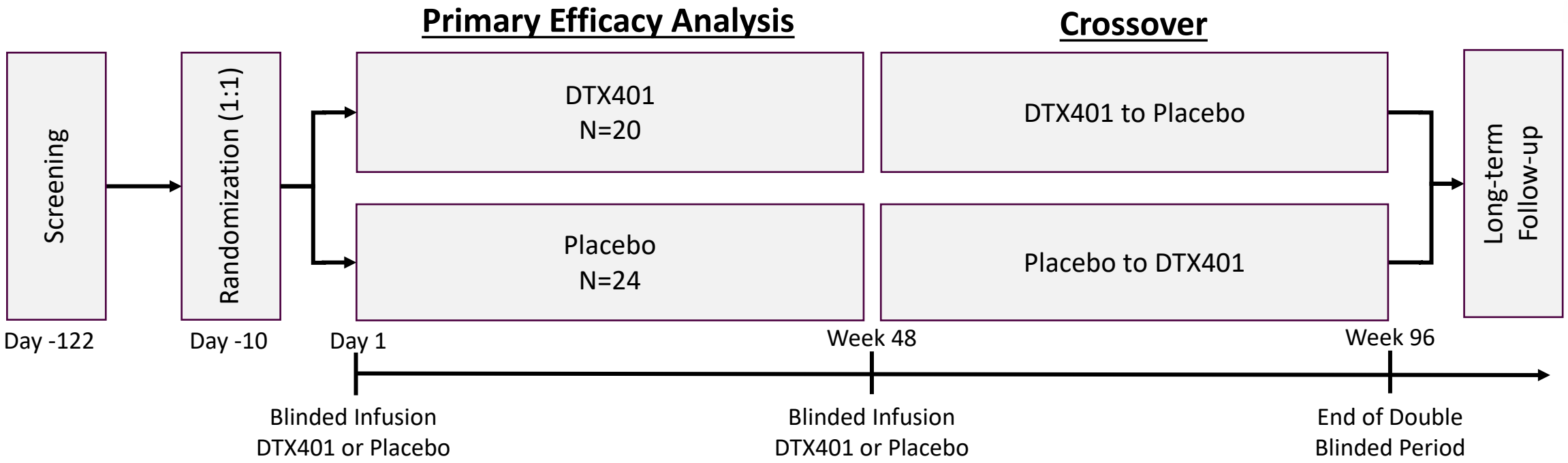
Daily cornstarch consumption

DTX401: single stranded AAV8 vector encoding codon optimized G6PC sequence with native G6PC promoter & enhancer



Insulin Response	Glucocorticoid Response
Eating	Fasting / Exercise / Stress
↓	↓
Glucose up	Glucose down
↓	↓
Insulin	Glucagon
↓	↓
Suppresses gene	Induces gene

Phase 3 *GlucoGene* Study Design



Phase 1/2 – Open Label

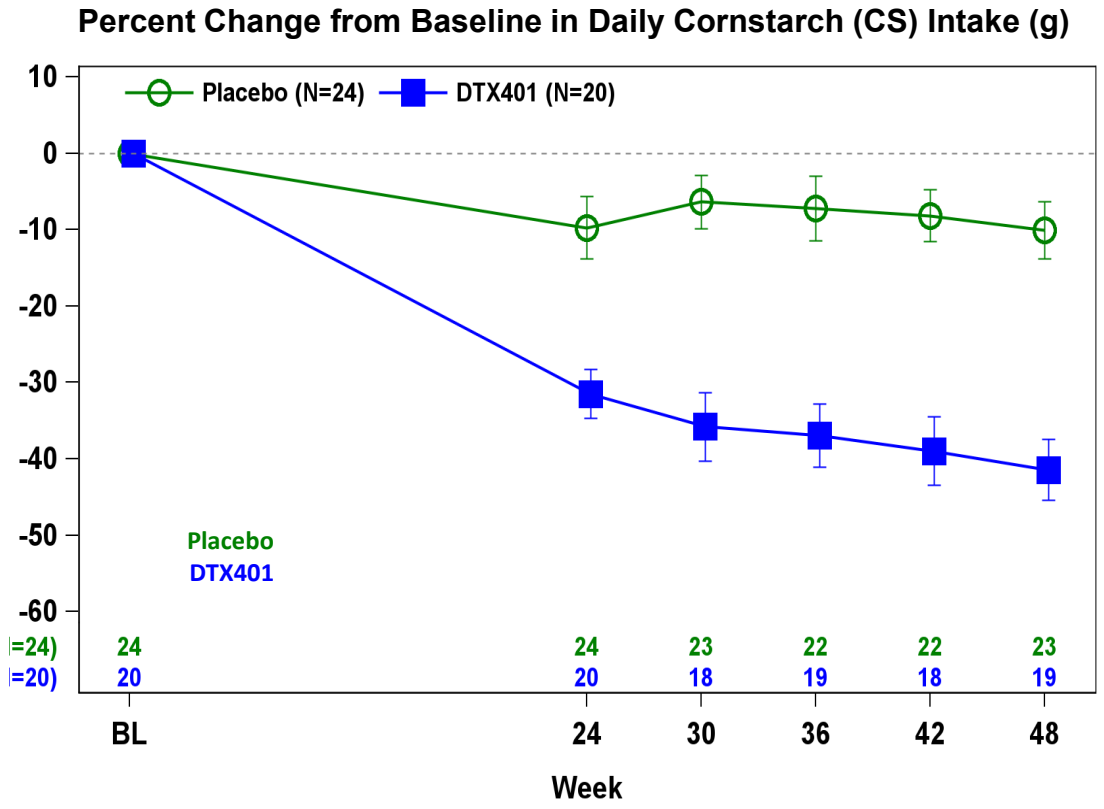
- Open and label, single arm (DTX401 only)
- Direct access to continuous glucose monitor (CGM) data for investigators to manage cornstarch titration
- Established safety and dose for phase 3

Phase 3 *GlucoGene* – Double Blind

- 1:1 randomization to DTX401 or Placebo
- Investigators blinded to real time glucose data
  - Unblinded 3rd party physician guided titration of cornstarch
- Registrational design

Primary Endpoint Achieved: Statistically Significant Reduction (41%) in Daily Cornstarch Intake at Week 48 ($p < 0.0001$) with Maintenance of Glucose Control

Persuasive statistically significant cornstarch reduction continuing through Week 48



-10.1 value skewed by one spurious patient (note Std Dev=18.0)

% Change BL to W48	Placebo N=24	DTX401 N=20	p-value
Mean (SD)	-10.1# (18.0)	-41.4 (17.5)	
Median	-2.9	-36.9	
LS Mean (SE)	-10.3 (4.1)	-41.3 (4.5)	<0.0001

Mean Baseline CS (g): Placebo was 269g and DTX401 was 296g

Responder Analysis at Week 48

≥ 30% reduction in cornstarch

- 13/19 (68%) in DTX401 arm compared to 3/23 (13%) in placebo ($p = 0.0003$)

≥ 50% reduction in cornstarch

- 7/19 (37%) in DTX401 compared to 1/23 (4%) in placebo ($p= 0.0038$)

Patients Treated with DTX401 Showed Significant Reduction in **Frequency and Quantity** of Day and Nighttime Cornstarch vs Placebo

Total Daily Cornstarch (CS) Doses

Total Daily CS Doses (n)	Placebo N=24	DTX401 N=20	p-value
Baseline Mean (SD)	5.1 (1.4)	5.8 (1.4)	
Δ BL to W48 Mean (SD)	-0.1 (0.6)	-1.1 (0.9)	
Δ BL to W48 LS Mean (SE)	**-0.2 (0.2)**	**-1.1 (0.2)**	**0.0011**

"With these Phase 3 results, the significant reduction in cornstarch intake with continued management of glucose control has the potential to offer meaningful benefit to patients while improving quality of life on a daily basis."

Rebecca Riba-Wolman, M.D.
Director of the Glycogen Storage Disease Program & Disorders of Hypoglycemia at Connecticut Children's Medical Center and investigator on the study

Nighttime Cornstarch (CS) Doses and Grams

Nighttime CS Doses (n)	Placebo N=17	DTX401 N=17	p-value
Baseline Mean (SD)	1.8 (1.1)	1.7 (0.7)	
Δ BL to W48 Mean (SD)	+0.3 (1.4)	-0.4 (0.6)	
Δ BL to W48 LS Mean (SE)	**+0.4 (0.3)**	**-0.4 (0.3)**	**0.0410**

Changes from baseline for patients who required nighttime CS at baseline

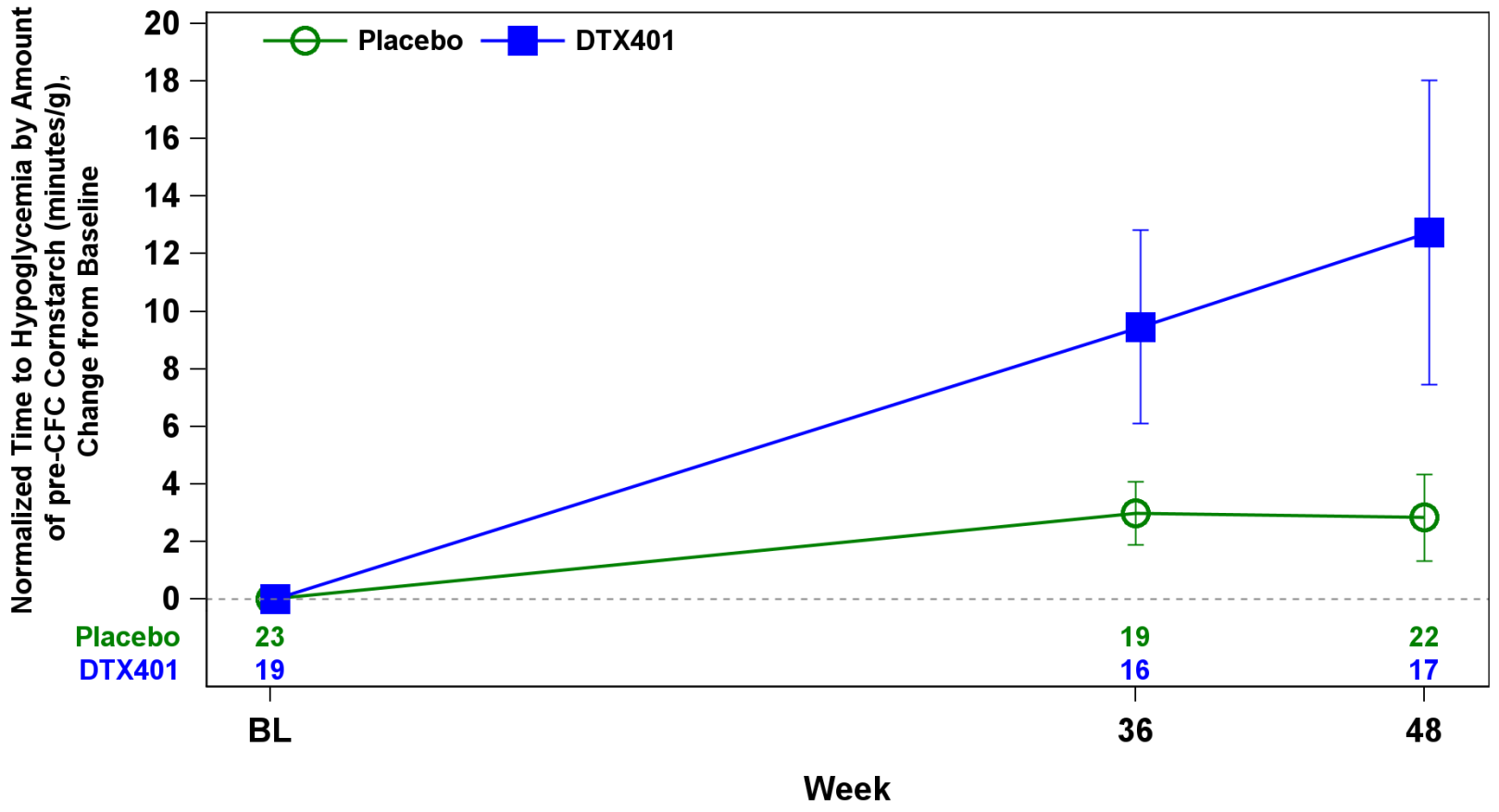
Nighttime CS Intake (g)	Placebo N=17	DTX401 N=17	**p-value**
Baseline Mean (SD)	100 (74.4)	87.4 (37.0)	
%Δ BL to W48 Mean (SD)	+8.5 (69.3)	-42.4 (29.3)	
%Δ BL to W48 LS Mean (SE)	**+6.9 (14.5)**	**-44.1 (15.0)**	**0.0091**

Changes from baseline for patients who required nighttime CS at baseline

DTX401 Showed ~5x More Improvement in TTH per Gram of Cornstarch

Providing greater protection from severe hypoglycemia versus placebo (p-value=0.0269)

Change from Baseline in time (minutes) to hypoglycemia (< 54 mg/dL) per gram of cornstarch in a controlled fasting challenge (CFC)



DTX401 Patients Maintained Glucose Control, with Significant CS Reductions
Avoiding severe episodes of hypoglycemia

Analysis	Statistic	Placebo (N = 24)	DTX401 (N = 20)	LS Mean Difference	p-value
Hypoglycemic Range < 70 mg/dL Change from Baseline to Week 48 in % of Glucose Values in Range					
All continuous glucose monitor (CGM) data	LS Mean (SE) Median (SD)	0.08 (0.86) 0.60 (2.59)	3.13 (0.96) 1.2 (5.24)	3.05 (1.21)	Non-inf: <0.0001
All self-monitoring blood glucose (SMBG) data	LS Mean (SE) Median (SD)	1.17 (2.40) 2.60 (10.91)	3.43 (2.58) 2.10 (10.31)	2.25 (3.43)	Non-inf: 0.0253
Severe Hypoglycemic Range < 54 mg/dL Change from Baseline to Week 48 in % of Glucose Values in Range					
All CGM data	LS Mean (SE) Median (SD)	0.23 (0.23) 0.10 (0.71)	0.74 (0.26) 0.30 (1.19)	0.51 (0.33)	Non-inf: <0.0001
All SMBG data	LS Mean (SE) Median (SD)	0.94 (1.69) 0.00 (2.69)	1.19 (1.82) 0.00 (4.30)	0.24 (2.43)	Non-inf: <0.0001

Patients Treated with DTX401 Reported Moderate to Much Improved PGIC Scores and Support 30% Reduction in Cornstarch as Clinically Meaningful

PGIC at Week 48	Placebo (N=23)	DTX401 (N=19)	p-value
Median Patients Global Impression of Change (PGIC) Score#	+1.0 Minimally Improved	+2.0 Moderately Improved	0.132*
Much Improved (+3.0)	9%	26%	
Worsening to No Change (-3.0 to 0.0)	48%	21%	

PGIC is a 7-point scale ranging from -3 = Much Worse to 3 = Much Improved
* Trial was not designed to have 80% power for this endpoint.

Emerging themes from interviews provide further insight to changes while in the study

- Better glycemic stability
- Improved physical appearance / physical function (ability to play sports/exercise)
- Less restrictive, easier to plan diet
- Improved emotional health (less worry)
- Less fatigue
- Some report blinded CGM made it hard to manage GSDIa (leading to over-compensation on SMBG, worsening control)

Acceptable and Expected Safety Profile

- Consistent and acceptable safety profile with no new safety signals identified
- Vector-induced hepatic effects were expected and managed with corticosteroids
  - 76% of DTX401 patients with liver enzyme elevations vs 12% of Placebo patients
  - All in DTX401 arm were non-serious and were mild to moderate in severity, except one Grade 3 event
  - Majority of events were transient and managed with corticosteroids
- Infusion related reactions (IRR), including hypersensitivity occurred in both treatment arms
  - Two serious IRR were reported in two DTX401-treated patients at baseline
  - Two non-serious IRRs were reported in the Placebo group
  - No IRRs occurred after implementation of risk minimization measures including slow staged ramp of infusion
- No AAV8 class effects of DRG toxicity or thrombotic microangiopathy were observed
- Long term safety profile of DTX401, including AAV class effects and risks, will continue to be monitored

Phase 3 Successful Across Primary and Key Secondary Endpoints

		p-value
Primary Endpoint	%Δ daily cornstarch intake	<0.0001
Key Secondary Endpoints	# of total daily doses of cornstarch	0.0011
	%Δ glucose values in hypoglycemic range (<70 mg/dL), assessed for non-inferiority	<0.0001
	Patient Global Impression of Change score at Week 48 (median)	0.132

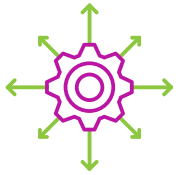
Key Takeaways

- GSDIa is a severe, life-threatening metabolic disease, with long term complications due to inability to control glucose
- Phase 3 data demonstrate DTX401 significantly reduces patients dependance on cornstarch, while maintaining glucose control
- Substantial unmet need and we have best-in-class experience commercializing rare disease medicines

Next Steps

Regulatory: Pre-BLA discussion with FDA in 2H-2024
CMC: Complete tech transfer to internal facility and execute PPQ lots

Additional data to be presented at a future scientific conference



BLA submission expected in 2025

Thank You

IR@ultragenyx.com