ACTION-Galactosemia:
Clinical Experience with Adult Galactosemia Patients and Path Forward

Galactosemia Foundation Conference, July 17-19, 2020

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AT-007 is an investigational drug being studied in patients with Classic Galactosemia. It has not been approved by the FDA.

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Galactosemia Overview

Rare metabolic disease affecting ~2,800 patients in the US; ~80 new births per year

Caused by enzyme deficiency and inability to metabolize the simple sugar galactose

Galactose is formed by metabolism of external lactose, but **Galactose is also produced naturally by the body** (endogenously)

No approved therapies; mandatory newborn screening and initiation of dairy free diet; Dietary restriction prevents fatalities, but **does not prevent long term consequences of disease**

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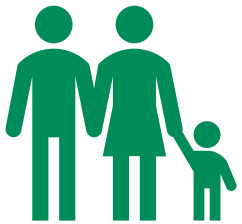
Galactosemia Clinical Presentation

Acute Newborn

Life threatening if not identified and managed immediately:

- **Hepatic and Renal Failure**
- **Brain Swelling** (Edema/ Encephalopathy/ Pseudotumor Cerebri)
- **Sepsis**

Chronic/Long-Term



- **CNS Complications**
  - Low IQ / intellectual deficits
  - Motor skills / coordination
  - Seizures
  - Tremors
  - Speech/ language
  - Learning, behavioral, social impairments
  - Psychiatric problems (anxiety, depression)
- **Primary Ovarian Insufficiency**
- **Cataracts**

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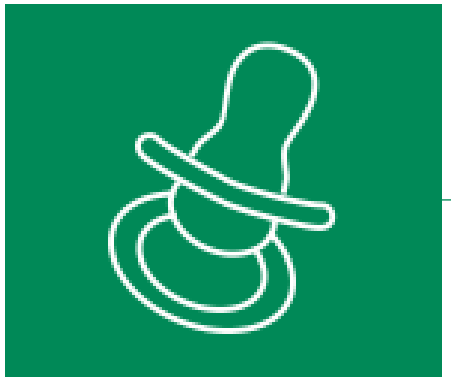
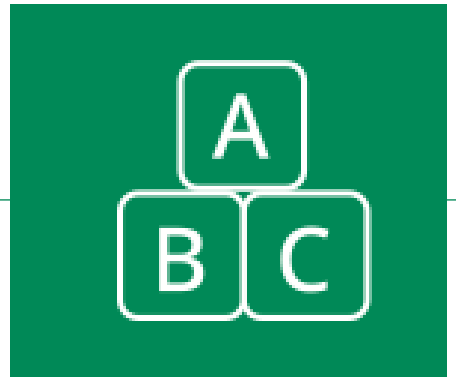
Galactosemia: Disease at Different Stages of Life

Newborns



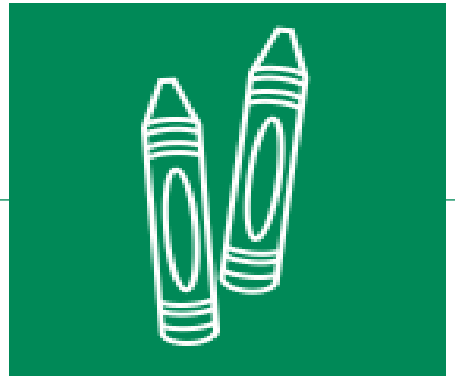
Newborns are screened for Galactosemia, but sometimes symptoms can develop before the results are available; **acute complications may be serious**, requiring intensive care or even causing death

Infants & Toddlers



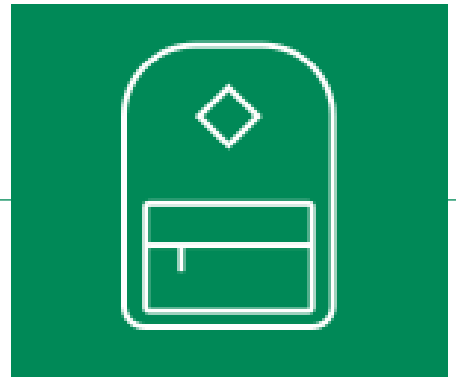
Toddlers may develop early signs of **developmental delays including growth and coordination, as well as speech problems**

Primary School Children



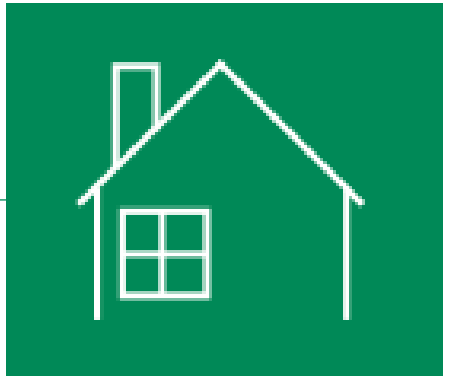
Developmental delays, learning, motor skill, behavioral and emotional problems may become more noticeable during this stage as children go to school

Teens



Teens with Galactosemia can struggle as a result of **behavioral, cognitive, or developmental issues**, including **puberty delays (& fertility issues in females)**

Adults



Because of long-term health issues, including **seizures, tremors or cataract**s, it may be **difficult for adults with Galactosemia to become independent**

Everyone with Galactosemia will experience disease differently, but this slide includes some common health issues that can occur at different stages of life

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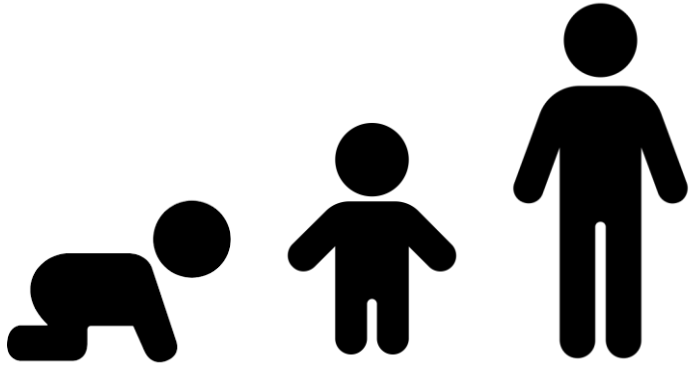
Dietary Restriction and Endogenous Galactose Production

Diet Can Reduce Exposure to Galactose From Lactose-Containing Foods

- Acute complications in the newborn period may be caused by external galactose (breast milk or dairy formula)
- Dietary restriction of lactose is important to prevent acute disease and death in infancy

However, the Body Produces Galactose On Its Own, Even With Diet



- Every cell in the human body makes galactose on its own (“endogenous”)
- Long-term complications of Galactosemia are caused by endogenous production of galactose, not by lack of dietary control

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Galactosemia is a Slowly Progressive Rare Metabolic Disease

- **~2,800 living** US patients ; **~80 new births per year**
- **~3,500 living** EU patients; **~120 new births per year**
- Prevalence estimates 1:40,000-1:90,000 – differs by country/ ethnicity
- Majority of patients are under the age of 40, as newborn screening was adopted in the 1980s and 1990s
- Under new FDA guidance, surrogate metabolic biomarkers may be acceptable for demonstration of therapeutic activity

1. Diseases with less than 5,000 living US patients are termed “low prevalence”; Pyhtila et al. Newborn Screening for Galactosemia. JIMD. 2014.pdf; Decision Resources Group epidemiological assessment data on file

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Role of Galactitol (a toxic metabolite of galactose) in Galactosemia Complications

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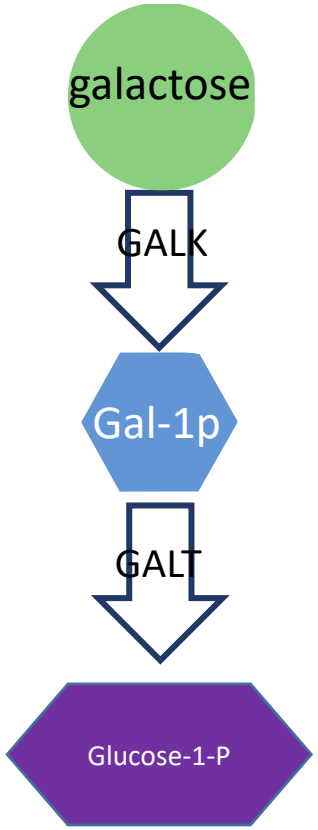
Galactosemia:

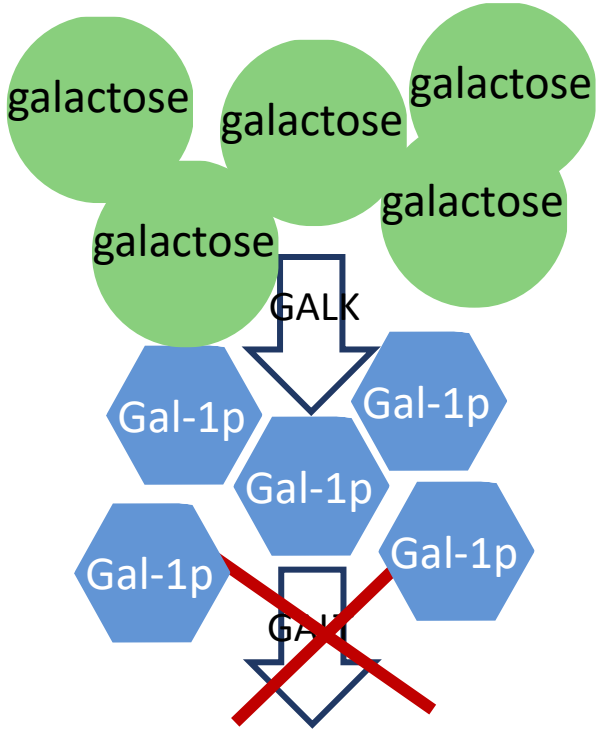
Enzyme Deficiency in GALT or GALK Leads to Inability to Metabolize Galactose

Galactose Metabolism



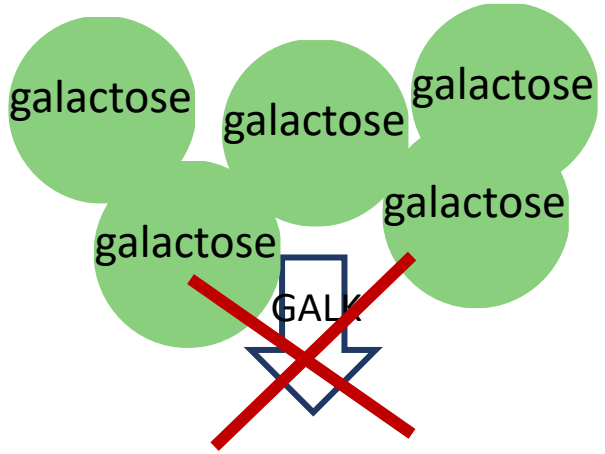
Energy Production

Classic Galactosemia



GALT Enzyme Deficiency

Galactokinase Deficiency



GALK Enzyme Deficiency

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The Role of Aldose Reductase in Galactosemia

- When galactose levels are abnormally high in blood and tissues, the enzyme Aldose Reductase can convert galactose to galactitol
- This does not happen in healthy people, and galactitol is a toxic, abnormal metabolite

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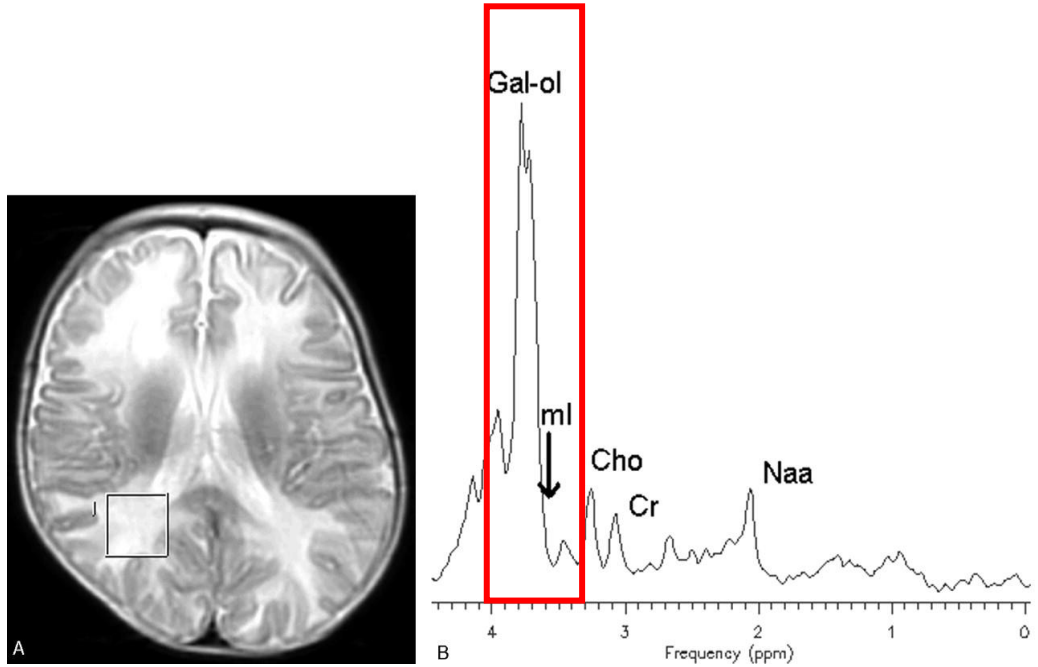
Galactitol Accumulates in Various Tissues Including the CNS

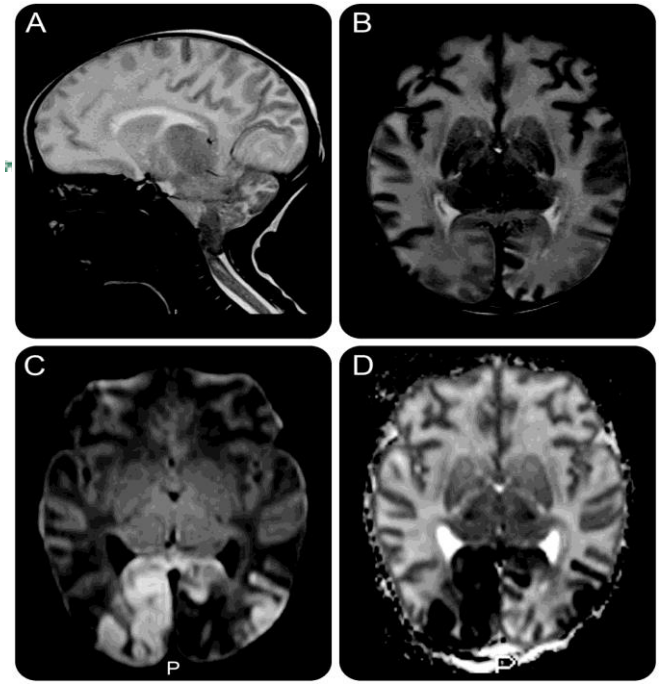
In vivo evidence of brain galactitol accumulation in an infant with Galactosemia and encephalopathy



Berry G et al *J of Pediatrics* 138(2):260-2, 2001

Otaduy MCG, et al American Journal of Neuroradiology 27 (1) 204-207, 2006

Galactitol peak and fatal cerebral edema in Classic Galactosemia



(A) Sagittal and (B) axial turbo-spin-echo T2-weighted images, (C) DWI, and (D) ADC. (A) Massive edema causes cerebellar tonsils to descend into the foramen magnum. (B) Brain and cerebellum appear diffusely swollen with reduced gray/white matter differentiation. (C) DWI and (D) ADC maps show large posterior areas of restricted diffusion consistent with cyto-toxic edema.

Martinelli D et al *Neurology* 86:e32-e33, 2016

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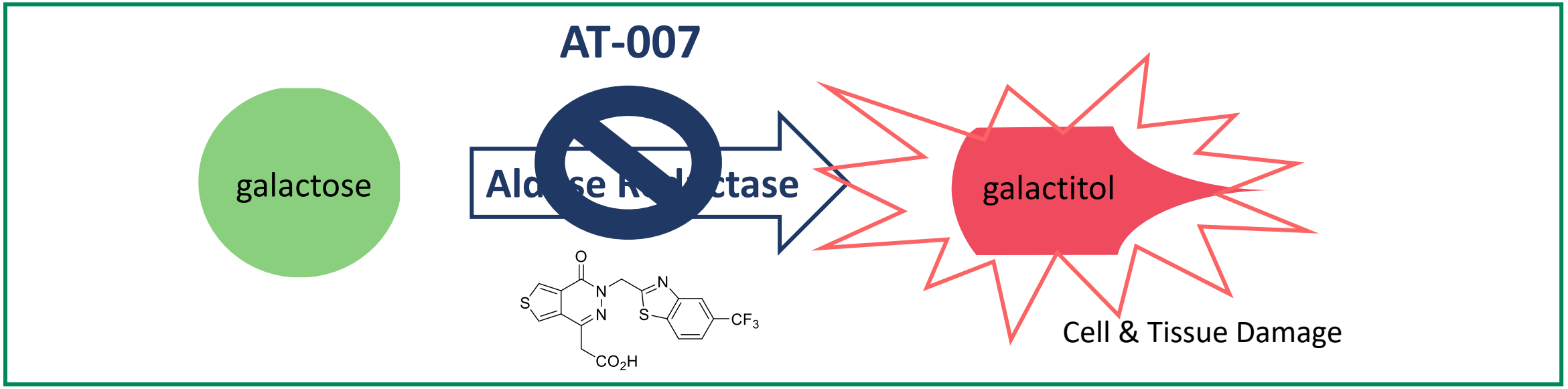
AT-007 is an Investigational Drug That Blocks Aldose Reductase Activity and Stops Conversion of Galactose to Galactitol

- AT-007 was specifically designed to penetrate the Central Nervous System – to cross into the brain and reach neurons
- In clinical trials, AT-007 is dosed orally once daily as a capsule or as a liquid suspension for children



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Aldose Reductase Inhibition as a Therapeutic Target for Galactosemia

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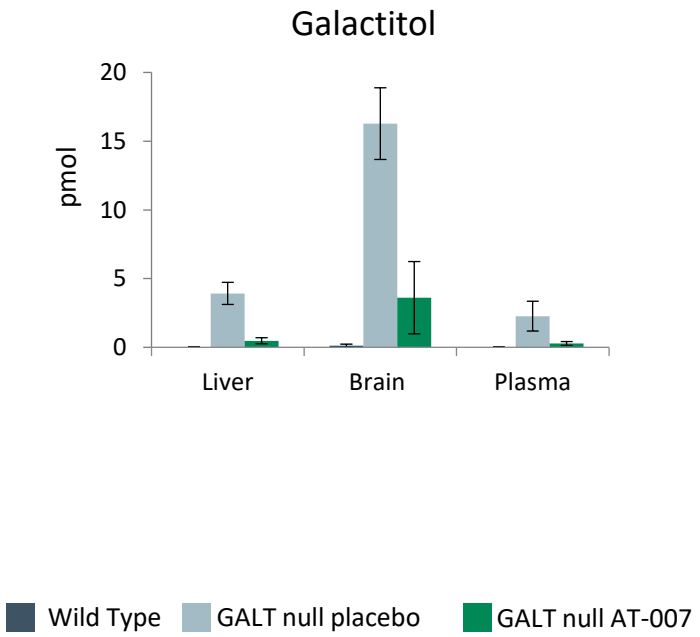
AT-007 Treatment Corrects All 3 Aspects of Disease in the Galactosemia Rat Model

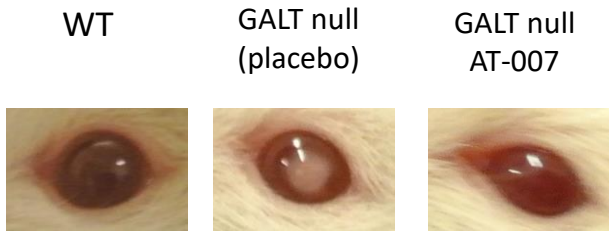
Biochemical Effects

AT-007 treatment significantly reduced galactitol levels in all tissues without increasing galactose or Gal1p



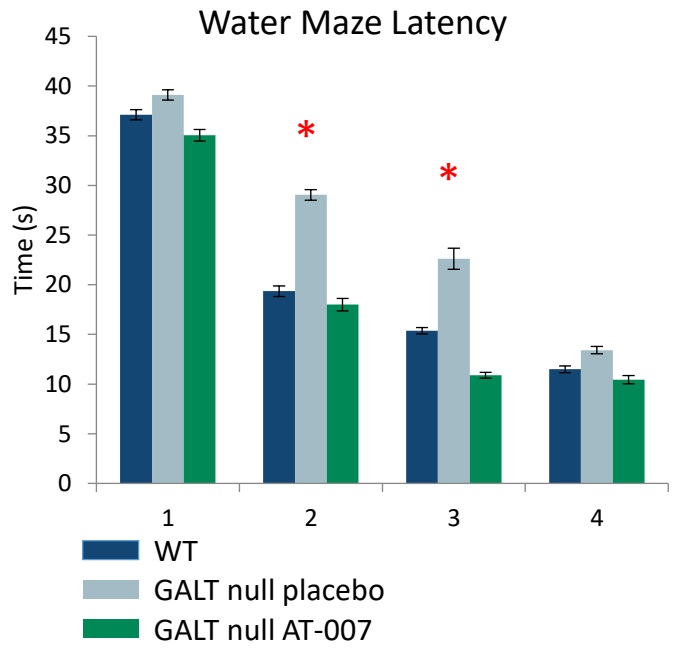
Tissue Deposition of Galactitol

AT-007 treatment prevented galactitol accumulation in tissues, resulting in absence of cataracts



CNS Outcomes

AT-007 treatment normalized CNS outcomes on both water maze and rotarod



* Statistically significant vs. WT & AT-007 treated

Rats were on a lactose-restricted diet similar to humans; rat breast milk contains very low lactose levels; supplemented with soy formula; rat chow has low galactose levels similar to allowed foods such as legumes

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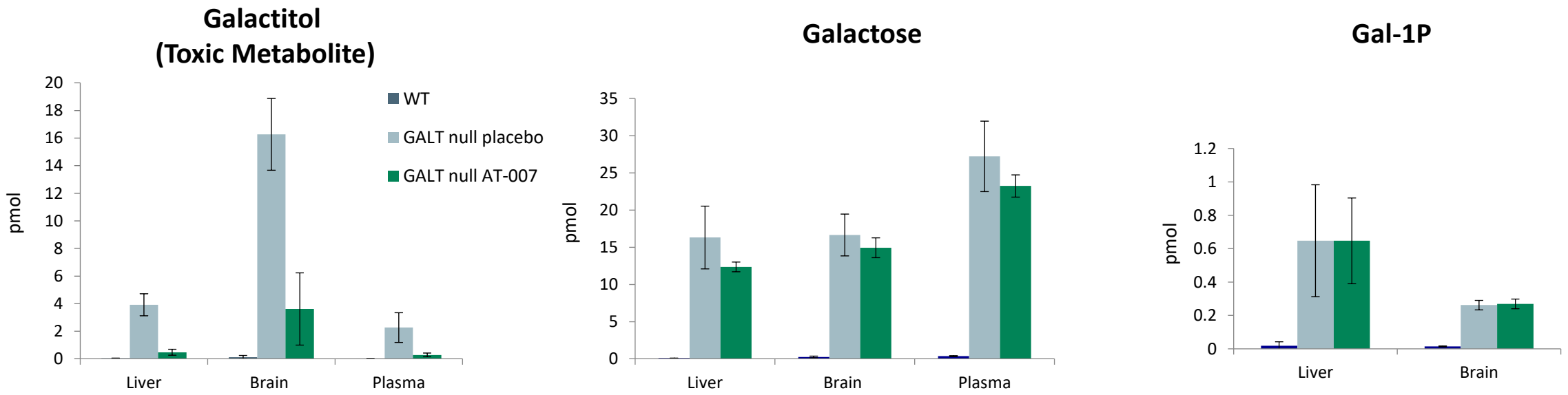
A Closer Look: AT-007 Significantly Reduces Galactitol Levels in all Target Tissues Without Increasing Galactose or Gal-1P



- AT-007 treatment from neonatal Day 1 to Day 10 significantly reduced galactitol in liver, brain and plasma
- AT-007 treatment did not increase galactose or Gal-1P levels; similar results seen at Day 22 and age 5 months

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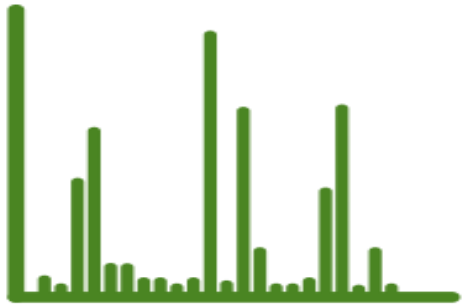
Summary: AT-007 Preclinical (Animal) Studies

Safety & PK/PD

AT-007 was safe and well tolerated in animals, with a broad dosing/ exposure window to humans

Biochemical Manifestations



In an animal model of Galactosemia, AT-007 prevented biochemical manifestations of disease; prevented production of toxic galactitol in blood and tissues, without adversely impacting galactose or Gal-1p

Clinical Manifestations

Prevented clinical manifestations of disease in animals including CNS abnormalities (learning, cognition, motor)

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Clinical Program: ACTION-Galactosemia Trial Design

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Galactosemia Phase 1/2 Registrational Study (ACTION-Galactosemia)

Multi-Center Placebo-Controlled Study in Healthy Volunteers & Adult Galactosemia Patients

Healthy Volunteers

- **Single Ascending Dose (n=40)**
- **Multiple Ascending Dose (n=40, 7 days)**

Healthy Volunteer Endpoints:

- Safety
- Pharmacokinetics
- CNS Penetrance (via CSF sample)

Galactosemia Endpoints:

- Safety
- Pharmacokinetics/ Pharmacodynamics
- **Efficacy Biomarker - Galactitol**

Adult Galactosemia Patients**

5 mg/kg single dose	**5 mg/kg 27 Days Daily Dosing (n=4)**
20 mg/kg Single dose	**20mg/kg 27 Days Daily Dosing (n=4)**
40 mg/kg* Single dose	**40mg/kg 27 Days Daily Dosing (n=4)**
Placebo Single dose	**Placebo 27 Days Daily Dosing (n=6)**

3 Month Extension

*Based on initial topline data from Jan 2020, the study was expanded to include a 40mg/kg dose in healthy volunteers and then Galactosemia patients. This cohort also included 2 additional placebo patients

**Due to the small size of the population and burden of study participation (travel, missed work for caregivers etc), the protocol proactively allowed for patients to participate in more than 1 cohort. If participating in a second cohort, the patient had to remain blinded, washout for ≥ 1 month, and a new baseline was taken. (Crossover design is in line with FDA guidance

Patients were on lactose-restricted diet prior to enrollment and throughout study

Clinical Program: ACTION-Galactosemia Trial Healthy Volunteer Data

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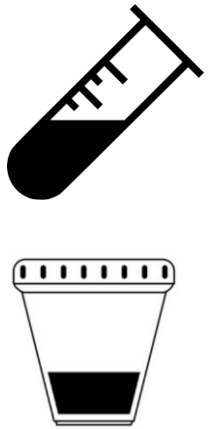
Summary: Healthy Volunteer Data

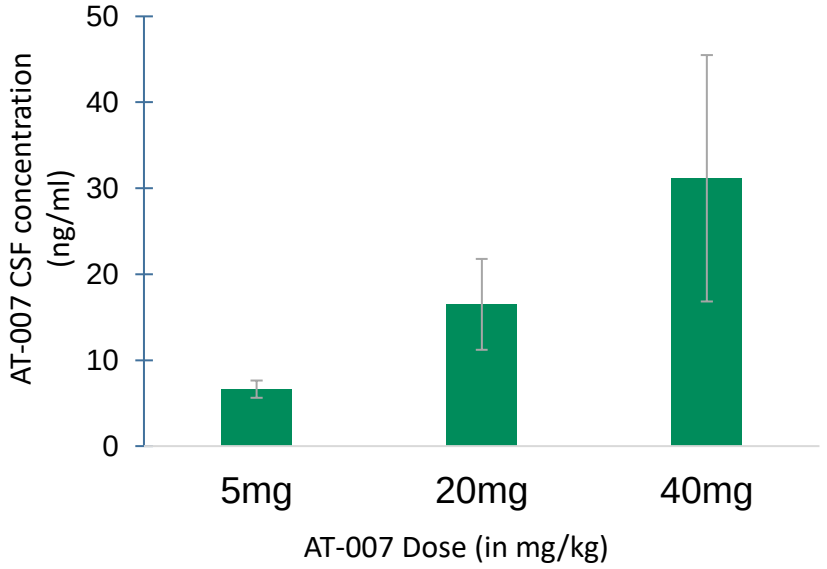
AT-007 Was Safe and Well Tolerated; PK Supportive of Once-Daily Dosing

Safety



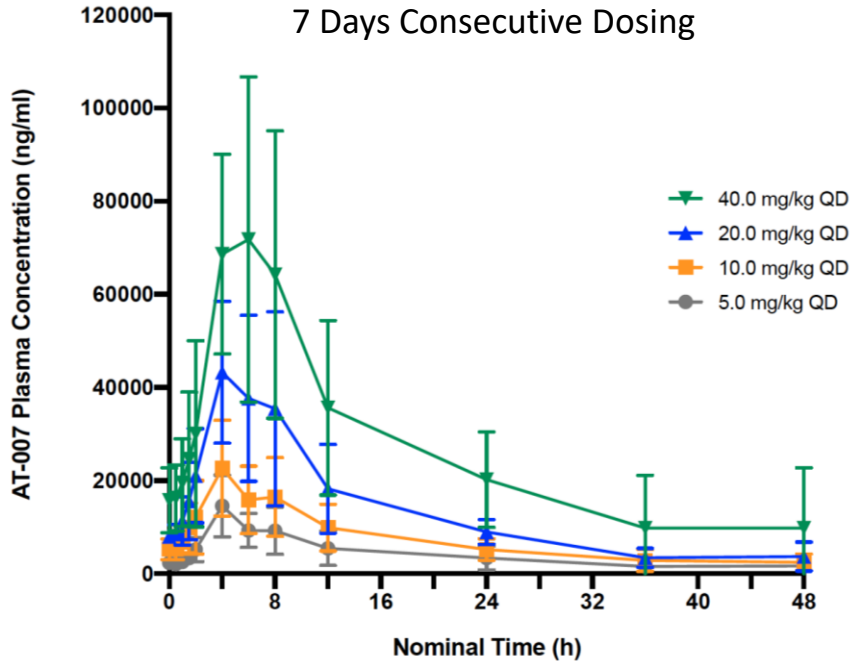
~80 healthy volunteers treated; AT-007 was safe and well tolerated at all doses

Brain Penetrance



Drug crosses into brain when dosed orally (CNS penetrant)

Pharmacokinetics



Dose-dependent increase in exposure; supportive of once daily oral dosing

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Clinical Program: ACTION-Galactosemia Adult Galactosemia Patient Data

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ACTION-Galactosemia Trial Data
Adult Galactosemia Patient Baseline Demographics

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Baseline Demographic and Diagnostic Characteristics (n=14)
Broad Age Range, Multiple Genetic Mutations Represented

Subject	Age	Gender	Ethnicity	BMI	Gene mutation	Urine galactitol (mM/urine creatine mol/L) Screening	Plasma galactitol (ng/ml) Baseline*	GALT enzyme activity (Mmol/h/mg)
2003-101	33	M	Caucasian	24.3	Q188R/Q188R	208	2450	0
2003-102†	51	M	Caucasian	21.7	Q188R/Q188R	123	2280 2215	0
2003-104	19	M	Caucasian	21.6	Q188R/Q188R	137	2115	0
2003-105	22	F	Caucasian	22.7	Q188R/Q188R	255	2795	0
2004-001†	37	M	Caucasian	21.3	Q188R/Q188R	152	2640 3020	0
2004-004	40	M	Caucasian	32.7	N314D/ c119-116 deletion	102	2475	0
2004-005	24	F	Caucasian	23.1	Q188R/Q188R	142	1995	0
2002-002†	19	F	Caucasian	23.9	K285N/c119-116 deletion	139	2395 2775	0
2004-007	19	F	Caucasian	21.4	Q188R/Q188R	133	2490	0
2004-008	22	M	Caucasian	17.4	Q188R/Q188R	130	2075	0
2004-009†	28	M	Caucasian	20.5	Q188R/Q188R	99	2527 2440	0
2004-012	44	M	Caucasian	25.8	D98N/Q188R	104	2415	0
2004-013	24	M	Caucasian	19.8	Q188R/Q188R	112	2485	0
2004-015	45	F	Caucasian	33.7	Q188R/Q188R	196	3420	0
Summary	**30.5 ± 11.04**	**5F and 9M**	**Caucasian**	**23.56 ± 4.57**	**11 Q118R homozygous and 3 compound heterozygous**	**145 ± 45.0**	**2468 ± 350.1**	**0**

† Patients participated in multiple cohorts. >1 month washout was performed between cohorts. Second baseline plasma galactitol noted for these patients.

* Baseline plasma galactitol was calculated as the mean of Day -1 and Day 1 time 0 (prior to dosing).

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Baseline Demographic and Diagnostic Characteristics
Cohorts Well Balanced

Subject	Age	Gender	BMI	Ethnicity	Gene mutation	Urine galactitol (mM/urine creatine mol/L)	Plasma galactitol (ng/ml)	GALT enzyme activity Mmol/h/mg
PLACEBO								
2004-001	37	M	21.3	Caucasian	Q188R/Q188R	**153**	2640	0
2004-004	40	M	32.7	Caucasian	N314D/ c119-116 deletion	**103**	2475	0
2004-005	24	F	23.1	Caucasian	Q188R/Q188R	**142**	1995	0
2002-002	19	F	23.9	Caucasian	K285N/c119-116 deletion	139	2395	0
2004-013	24	M	19.8	Caucasian	Q188R/Q188R	**112**	2485	0
2004-015	45	F	33.7	Caucasian	Q188R/Q188R	**196**	3420	0
MEAN (SD)	**31.5 (10.5)**	**3F/3M**	**25.8 (6)**	**6 Caucasians**	**4 Q188R homozygous and 2 compound heterozygous**	**141 (33.0)**	**2568 (470.1)**	**0**
5mg/kg								
2003-101	33	M	24.3	Caucasian	Q188R/Q188R	**208**	2450	0
2003-102	51	M	21.7	Caucasian	Q188R/Q188R	**123**	2280	0
2003-104	19	M	21.6	Caucasian	Q188R/Q188R	**137**	2115	0
2003-105	22	F	22.7	Caucasian	Q188R/Q188R	**255**	2795	0
MEAN (SD)	**31.3 (14.5)**	**1F/3M**	**22.6 (1.3)**	**4 Caucasians**	**4 Q188R homozygous**	**181 (61.9)**	**2410 (290.8)**	**0**

┼ Patients who participated in a second cohort but were transferred to a different site due to COVID19 received a new subject number

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APPLIED THERAPEUTICS

Baseline Demographic and Diagnostic Characteristics

Cohorts Well Balanced (continued)

Subject	Age	Gender	BMI	Ethnicity	Gene mutation	Urine galactitol (mM/urine creatine mol/L)	Plasma galactitol (ng/ml)	GALT enzyme activity Mmol/h/mg
20mg/kg								
2004-001	37	M	21.3	Caucasian	Q188R/Q188R	153	3020	0
2004-007	19	F	21.4	Caucasian	Q188R/Q188R	133	2490	0
2004-008	22	M	17.4	Caucasian	Q188R/Q188R	130	2075	0
2004-009	28	M	20.5	Caucasian	Q188R/Q188R	99	2527	0
MEAN (SD)	**26.5 (7.9)**	**1F/3M**	**20.2 (1.9)**	**4 Caucasian**	**4 Q188R homozygous**	**129 (22.3)**	**2528 (386.7)**	**0**
40mg/kg								
2004-012	44	M	25.8	Caucasian	D98N/Q188R	104	2415	0
2004-017†	19	F	23.9	Caucasian	K285N/N314D	160	2775	0
2004-018†	29	M	21.3	Caucasian	Q188R/Q188R	113	2440	0
2004-019†	51	M	22.7	Caucasian	Q188R/Q188R	103	2215	0
MEAN (SD)	**35.8 (14.5)**	**1F/3M**	**23.4 (1.9)**	**4 Caucasians**	**2Q188R and 2 compound heterozygous**	**120 (27.0)**	**2461 (232.1)**	**0**
Overall Summary	**31.3 ± 11.3**	**6F and 12M**	**23.3 ± 4.1**	**Caucasian**	**11 Q118R homozygous and 3 compound heterozygous**	**144 (42.4)**	**2486 (342.7)**	**0**

† Patients who participated in a second cohort but were transferred to a different site due to COVID19 received a new subject number for the second cohort

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APPLIED THERAPEUTICS

Galactosemia Patient Baseline Clinical & Descriptive Characteristics (n=14*)

Clinical Characteristics

CNS Disorders	Psychiatric Disorders
Seizures (n=6)	Anxiety (n=5)
Dementia (n=1)	Depression (n=6)
Encephalopathy (n=1)	ADHD (n=3)
Tremor	

Endocrine Disorders	
Primary ovarian insufficiency (All Females)	Short stature (n=1)
Gynecomastia (n=1)	Osteopenia (n=2)
Erectile dysfunction (n=1)	Vitamin D deficiency (n=7)
Hypothyroidism (n=1)	

Descriptive Characteristics

Patient Quality of Life
Living with family members or proximity of caregiver (all, n=14)
Able to travel only with caregiver (n=9)
Unemployed and/or not in school (n=7)
Employed (primarily manual employment, unskilled labor n=7)
Secondary education (n=2)

*A total of fourteen individual patients participated in the study; four of them participated in more than one cohort (2 cohorts); >1 month washout was performed between cohorts.

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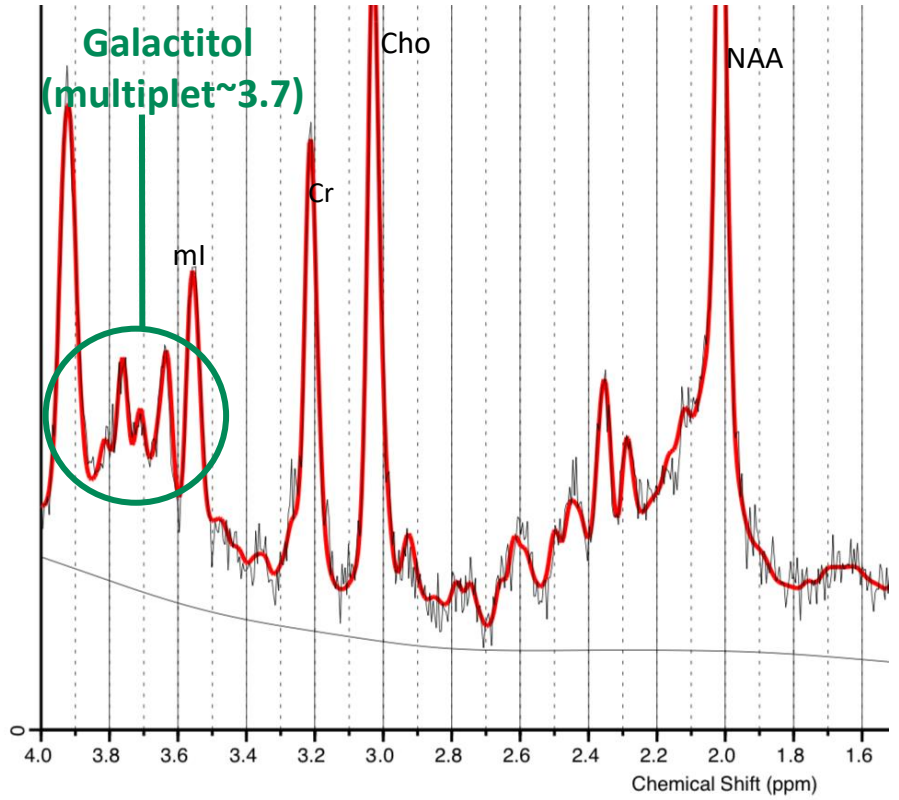
APPLIED THERAPEUTICS

Galactitol Quantitation in the Brain by 3T MR Spectroscopy (Baseline)

- Galactitol can be quantitatively assessed in the brain by MR Spectroscopy
- Galactitol is not present in the brain of healthy volunteers and is only present in Galactosemia patients
- In “old” studies with low power magnets, the abnormal galactitol peak was only visible in patients who were not on a compliant diet
- Higher power 3T MRI/MRS now allows detection and quantitation of galactitol in the brain of patients on a galactose-free diet, representing galactitol in the brain formed by endogenous galactose production



Representative baseline MRS of adult Galactosemia patient from ACTION-Galactosemia study

(on galactose-free diet; 3T MRI)

mI=myoinositol; Cr=creatine; Cho=choline; NAA=N-acetyl aspartate

Effects of AT-007 on brain galactitol will be presented at upcoming conference

APPLIED THERAPEUTICS

ACTION-Galactosemia Trial Data

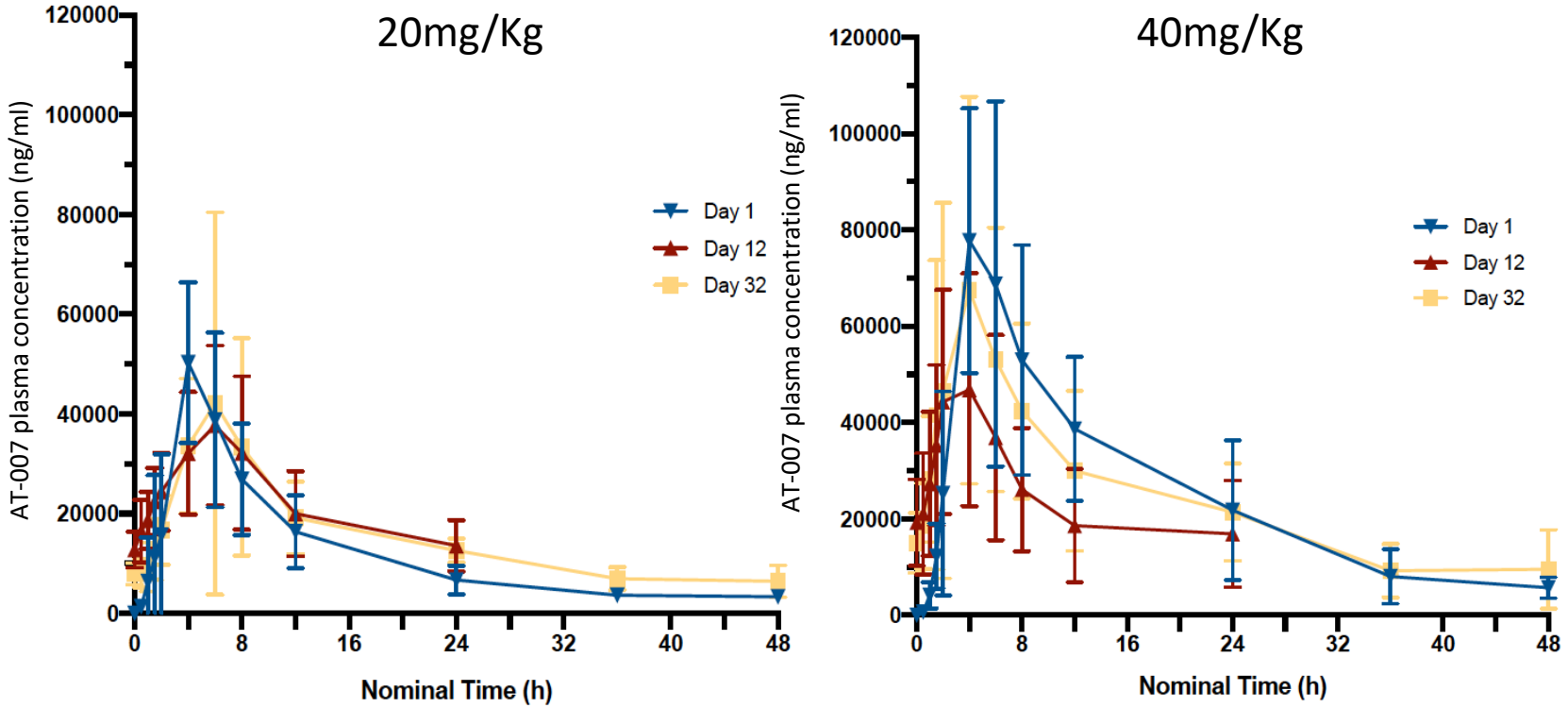
AT-007 Pharmacokinetics and Safety Data in Galactosemia Patients

AT-007 is an investigational drug being studied in patients with Classic Galactosemia. It has not been approved by the FDA.

APPLIED THERAPEUTICS

Pharmacokinetic Results Support Once Daily Dosing in Galactosemia Patients

- Plasma PK parameters of AT-007 support once daily oral dosing
- PK profile in Galactosemia patients was similar to healthy volunteers, suggesting similar drug metabolism and clearance
- PK profile suggests no first pass clearance or other PK effects (de-sensitization or induction)



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APPLIED THERAPEUTICS

Detailed Safety Findings - AT-007 Safe and Well-Tolerated

SYSTEM ORGAN CLASS & PREFERRED TERM	NUMBER (%) OF PATIENTS, NUMBER OF EVENTS			
	Placebo N=6	AT-007 (5 mg/kg) N=4	AT-007 (20 mg/kg) N=4	AT-007 (40 mg/kg) N=4
Any Adverse Event	1 (17.0), 3	3 (75.0), 6	2 (50.0), 2	1 (25.0), 1
Cardiac Disorders	1 (17.0), 1	0 (0.0), 0	0 (0.0), 0	0 (0.0), 0
Tachycardia	1 (17.0), 1	0 (0.0), 0	0 (0.0), 0	0 (0.0), 0
Ear and Labyrinth Disorder	0 (0.0), 0	1 (25.0), 1	0 (0.0), 0	0 (0.0), 0
Ear discomfort	0 (0.0), 0	1 (25.0), 1	0 (0.0), 0	0 (0.0), 0
Gastrointestinal Disorders	1 (17.0), 1	1 (25.0), 1	0 (0.0), 0	0 (0.0), 0
Dyspepsia	1 (17.0), 1	0 (0.0), 0	0 (0.0), 0	0 (0.0), 0
Abdominal Discomfort	0 (0.0), 0	1 (25.0), 1	0 (0.0), 0	0 (0.0), 0
General Disorder and Administration site conditions	1 (17.0), 1	0 (0.0), 0	0 (0.0), 0	0 (0.0), 0
Feeling hot	1 (17.0), 1	0 (0.0), 0	0 (0.0), 0	0 (0.0), 0
Infections	0 (0.0), 0	2 (50.0) 2	0 (0.0), 0	1 (25.0), 1
Upper respiratory tract infection	0 (0.0), 0	2 (50%) 2	0 (0.0), 0	0 (0.0), 0
Urinary tract infection	0 (0.0), 0	0 (0.0), 0	0 (0.0), 0	1 (25.0), 1
Injury/ Procedural Complications	0 (0.0), 0	1 (25.0), 1	0 (0.0), 0	0 (0.0), 0
Contusion	0 (0.0), 0	1 (25.0), 1	0 (0.0), 0	0 (0.0), 0
Musculoskeletal and Connective Tissue Disorders	0 (0.0), 0	0 (0.0), 0	1 (25.0), 1	0 (0.0), 0
Mobility decreased	0 (0.0), 0	0 (0.0), 0	1 (25.0), 1	0 (0.0), 0
Psychiatric Disorder	0 (0.0), 0	0 (0.0), 0	1 (25.0), 1	0 (0.0), 0
Anxiety	0 (0.0), 0	0 (0.0), 0	1 (25.0), 1	0 (0.0), 0
Skin and Subcutaneous Tissue Disorders	0 (0.0), 0	1 (25.0), 1	0 (0.0), 0	0 (0.0), 0
Pruritus	0 (0.0), 0	1 (25.0), 1	0 (0.0), 0	0 (0.0), 0

AT-007 is an investigational drug being studied in patients with Classic Galactosemia. It has not been approved by the FDA.

APPLIED THERAPEUTICS

AT-007 Safety in Adult Galactosemia Patients

AT-007 Was Safe and Well Tolerated at All Doses Tested

Laboratory & clinical assessments demonstrated safety and tolerability

Pharmacokinetics (drug levels over time) supports once-daily dosing

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APPLIED THERAPEUTICS

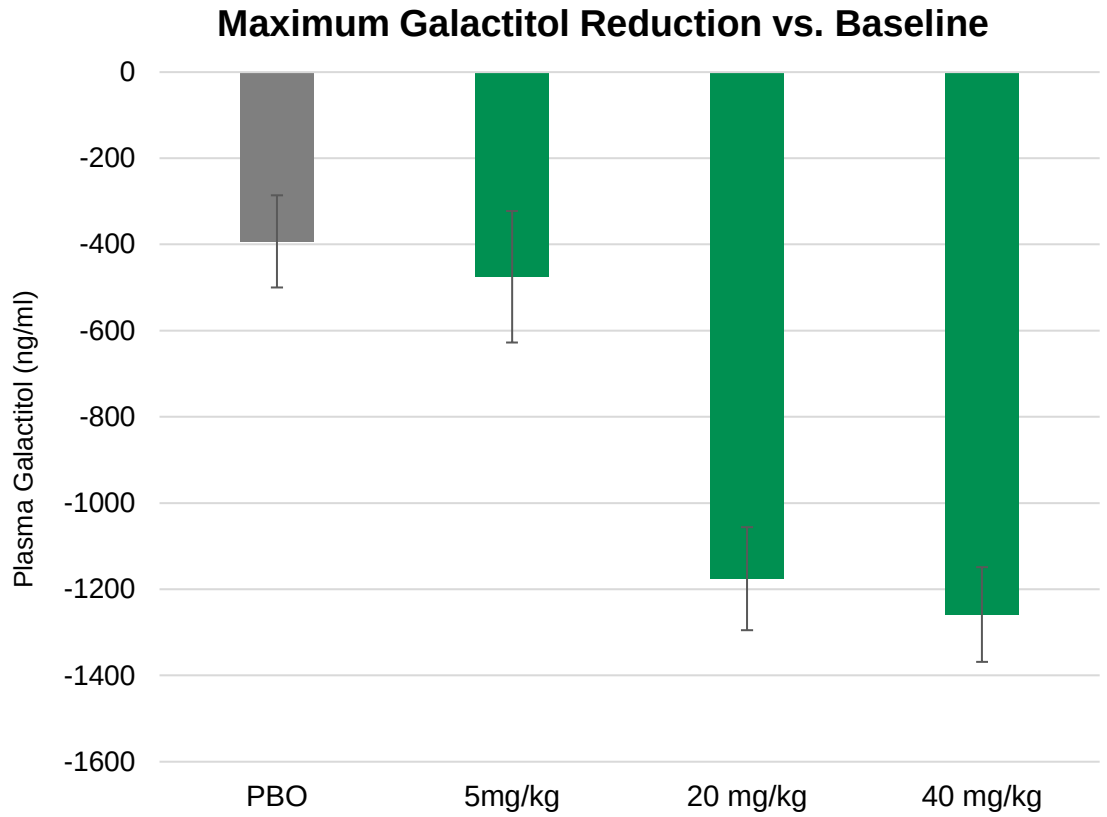
ACTION-Galactosemia Trial Data
AT-007 Efficacy Biomarker Results in Galactosemia Patients

AT-007 is an investigational drug being studied in patients with Classic Galactosemia. It has not been approved by the FDA.

APPLIED THERAPEUTICS

Biomarker Results

AT-007 Significantly Decreased Galactitol Levels in Plasma at 20 and 40mg/kg



P<0.01 for 20mg/kg vs. placebo and 40mg/kg vs. placebo; Placebo group updated to include 2 additional patients who participated in 40mg/kg cohort; Maximal reduction on Day 32
All biomarker assays were developed, validated, and performed by Icon Labs Whitesboro, NY (independent 3rd party lab)

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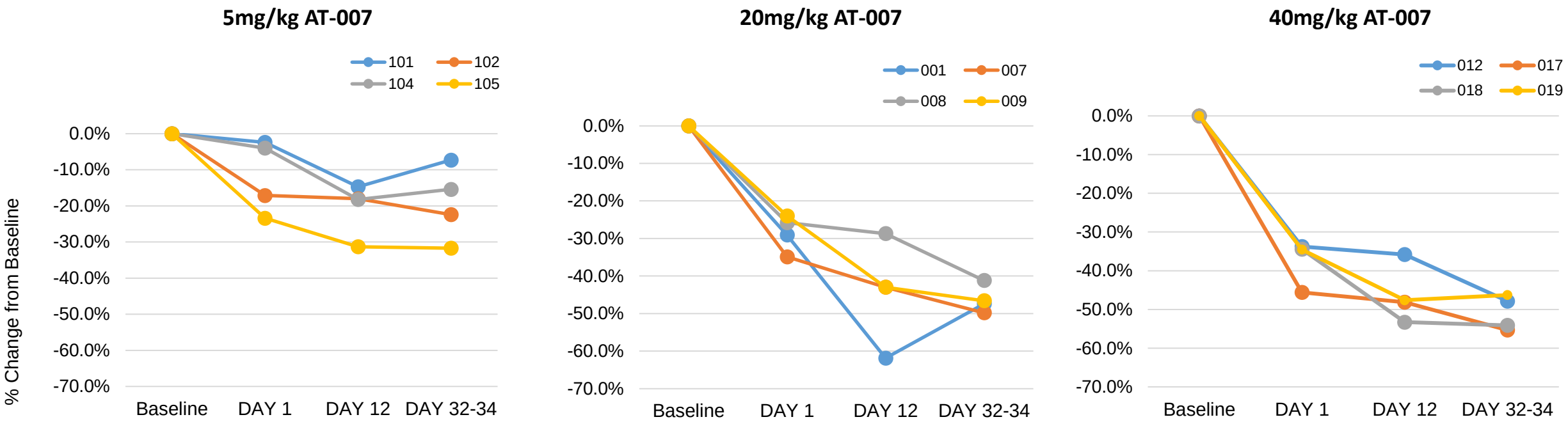
APPLIED THERAPEUTICS

AT-007 Decreased Galactitol Levels in All Treated Patients

Decrease was Dose-Dependent, Rapid and Sustained; Statistically Significant at 20 & 40mg/kg

Individual Maximum Reduction in Galactitol Percent Change From Baseline



Further Characterization of AT-007 in adult Galactosemia patients in ongoing long-term safety study

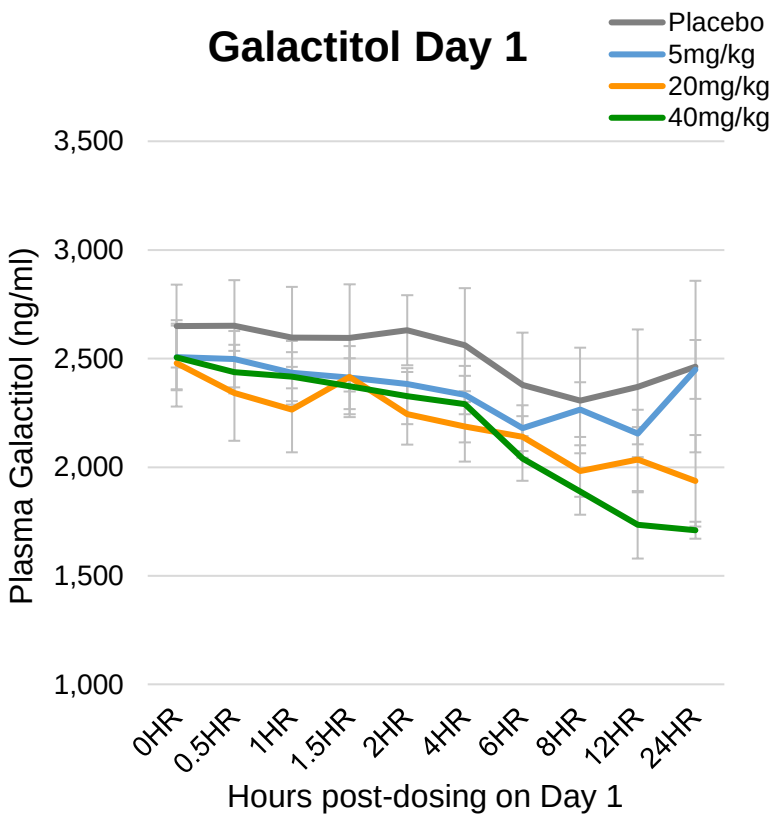
AT-007 is an investigational drug being studied in patients with Classic Galactosemia. It has not been approved by the FDA.

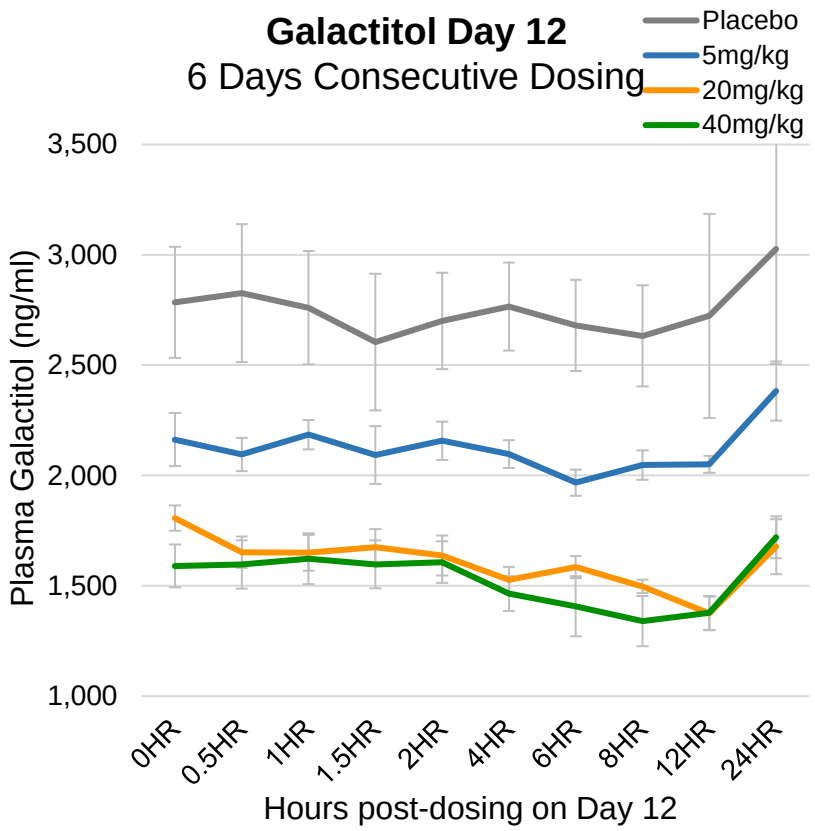
APPLIED THERAPEUTICS

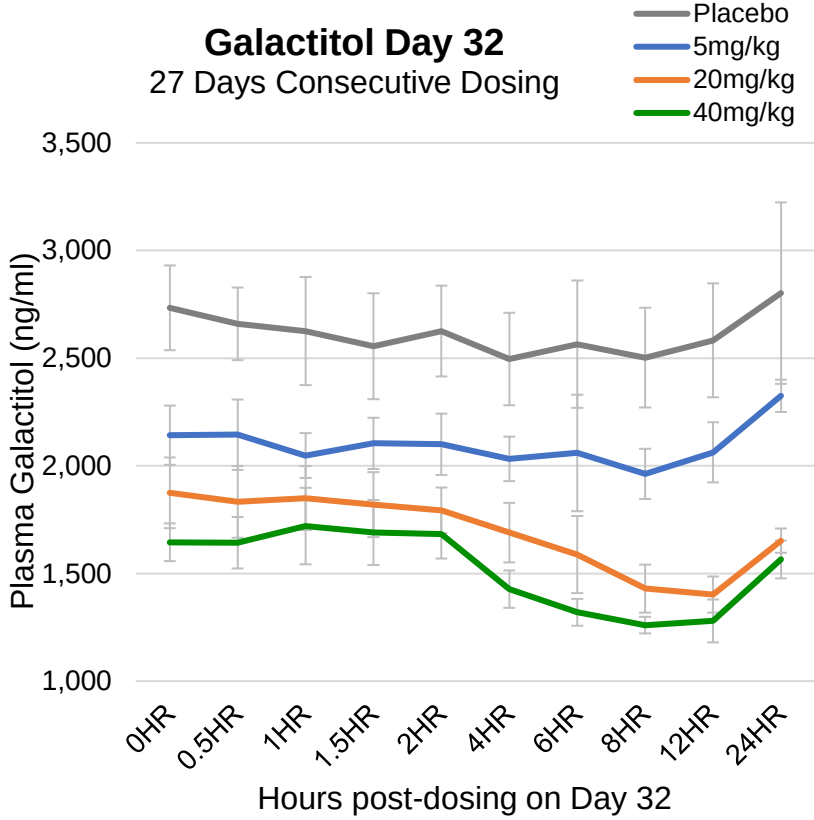
AT-007 Galactitol Reduction is Rapid and Sustained

Reduction Begins on 1st Day of Treatment and is Sustained Over 1 Month of Treatment

Galactitol Reduction is Sustained Over the 24hr Dosing Period at Steady State (Day 12 and Day 32), Supporting Once Daily Oral Dosing







Data for each cohort is shown as mean ±SEM; Baseline mean galactitol was not statistically different between cohorts

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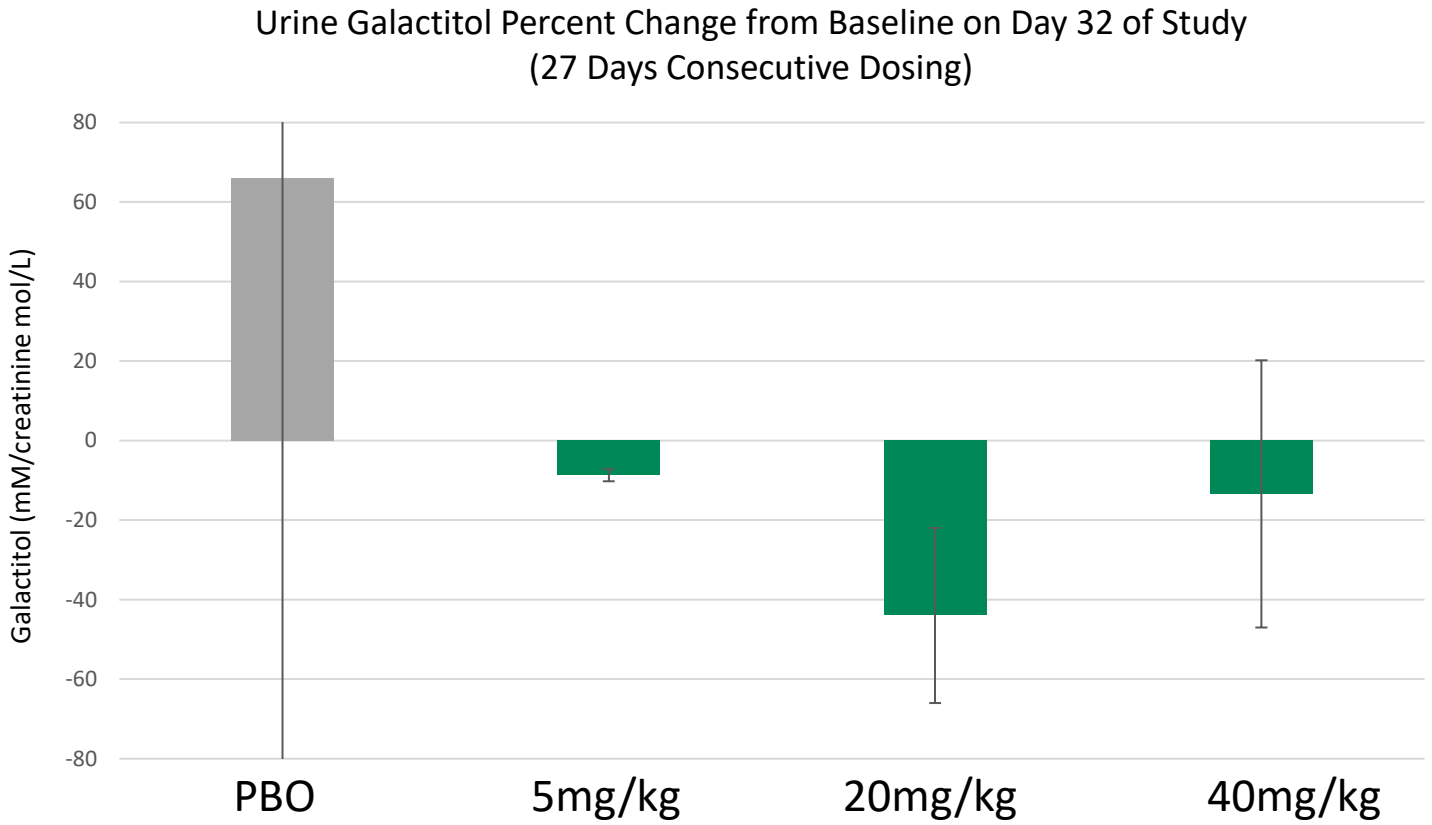
APPLIED THERAPEUTICS

Urine Galactitol Exploratory Analysis:

Data Confirms Plasma Galactitol as More Appropriate Sample for Accuracy, as Urine Concentration and Renal Clearance Change Day to Day



Note: Data is preliminary and may be updated as additional samples may become available. Any data not analyzed was due to creatinine values not available at time of data analysis; if creatinine values can be determined, data will be updated to include additional patients
Current data includes: Placebo n=3; 5mg/kg n=2; 20mg/kg n=3; 40mg/kg n=4

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APPLIED THERAPEUTICS

AT-007 for Treatment of Galactosemia: Future Development Plans

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APPLIED THERAPEUTICS

AT-007 Adult Extension Study – Currently Ongoing

- 90 Day treatment period
- Designed to support long-term safety, pharmacokinetics and biomarker effects
- Open to those who participated in 28-day core study and new patients
- Revised to primarily at-home visits to address burden of travel to sites/ impact on families and COVID-19 concerns
- Transition into long-term open-label extension (extended dosing period)

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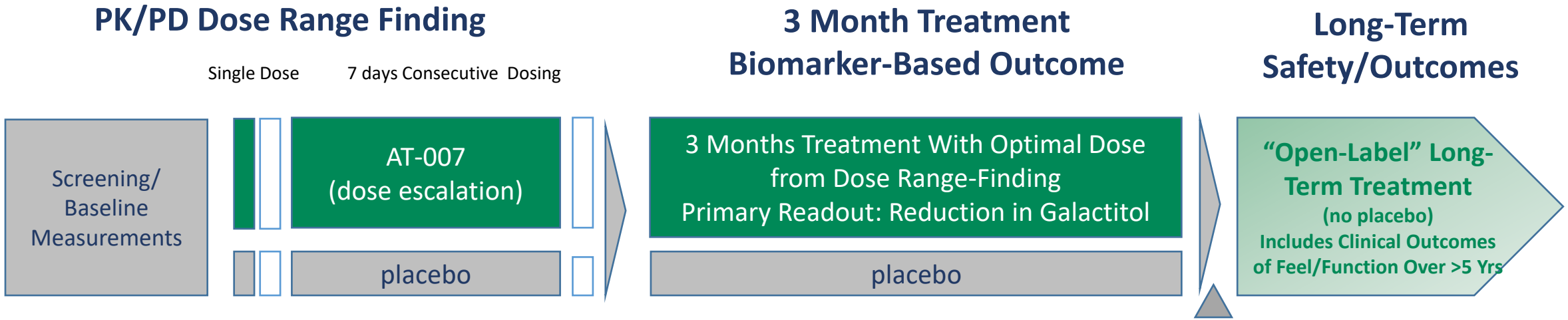
APPLIED THERAPEUTICS

ACTION-Galactosemia Kids Pediatric Registrational Clinical Study Underway



- Dose range finding PK/PD study to determine optimal dose in children, followed by 3-month biomarker-based assessment of galactitol reduction for NDA submission
  - Initial study (pre-NDA) will enroll children ages 2-17
  - Additional cohort will enroll infants age 2 mo-2 yrs (timing TBD)
- A long-term clinical outcomes study (not required for approval) will follow post-NDA submission to assess impact on how patients feel and function and provide long-term data to support long-term market access, adherence and persistence on therapy

▲ Planned NDA submission

For more details please see pediatric study presentation, today at 5:30pm – 6:15pm

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APPLIED THERAPEUTICS

ACTION-Galactosemia Trial Data
Summary & Conclusions

AT-007 is an investigational drug being studied in patients with Classic Galactosemia. It has not been approved by the FDA.

APPLIED THERAPEUTICS

Summary: ACTION-Galactosemia Adult Study Results

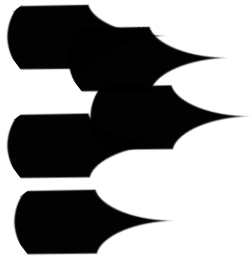
AT-007 was safe & well-tolerated in the ACTION-Galactosemia adult study

- Includes 80 healthy volunteers and 14 Classic Galactosemia patients

AT-007 was shown to be CNS penetrant

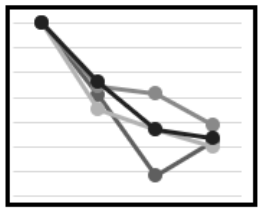
- Important in Galactosemia, which includes significant CNS clinical presentation
- Supports once-daily oral dosing

Galactitol is a toxic metabolite formed in Galactosemia patients



- Not formed in healthy people
- Detectable in blood and tissues, including the brain

AT-007 induced rapid and sustained reduction in plasma galactitol



- 20 and 40mg/kg dosing resulted in significant reduction in plasma galactitol ($p<0.01$ vs. placebo)
- No significant change in galactose or Gal-1p

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APPLIED THERAPEUTICS

Thank You

Thank you to all of the families who participated in the ACTION-Galactosemia study and made this development program possible

APPLIED THERAPEUTICS