Disclosure Slide

Financial Disclosure for:

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Employee of and stockholder in
Applied Therapeutics Inc.

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Positive Biomarker Efficacy Results from the ACTION-Galactosemia Study

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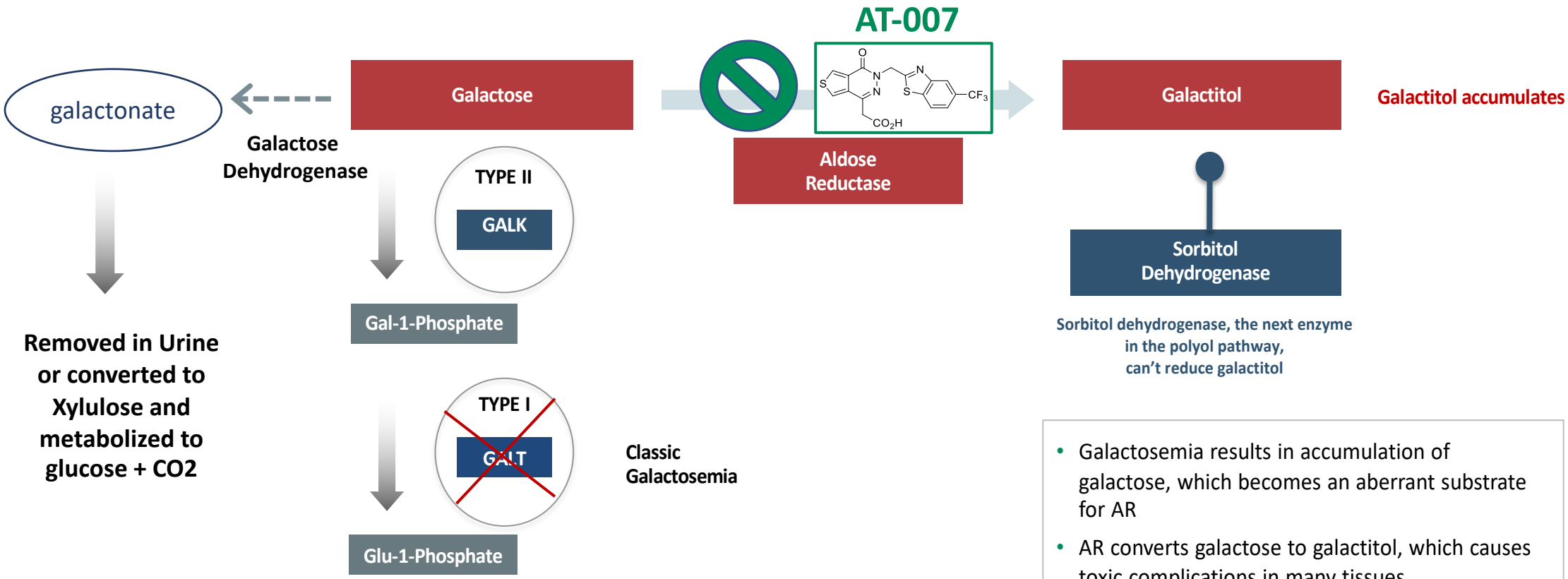
Background

- Galactosemia is an inherited rare metabolic disease, estimated to impact ~3,000 individuals in the US
- Life threatening if not identified and managed immediately at birth
- Long-term consequences of disease include: significant motor, speech, cognitive, and psychiatric impairments, tremor, seizers, frequent pre-senile cataracts, and ovarian insufficiency
- Even with strict dietary restriction of galactose-containing food, endogenous galactose production by the body leads to toxic build-up of galactitol and consequent tissue damage and long-term complications
- No pharmacologic treatments for Galactosemia are currently approved. Standard of care is strict dietary restriction of galactose, which does not prevent long term consequences of disease.

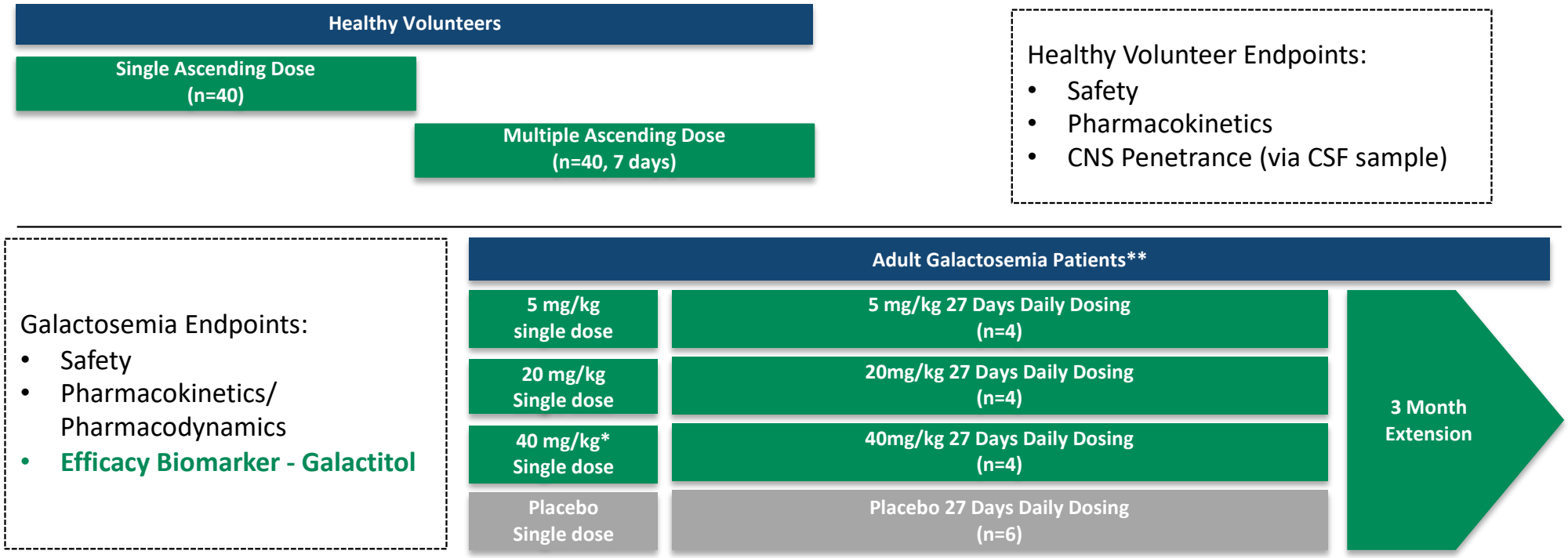
AT-007, a Novel CNS Penetrant Aldose Reductase Inhibitor, Blocks the Production of Galactitol, a Toxic Metabolite of Galactose



- Galactosemia results in accumulation of galactose, which becomes an aberrant substrate for AR
- AR converts galactose to galactitol, which causes toxic complications in many tissues

ACTION-Galactosemia Adult Study

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

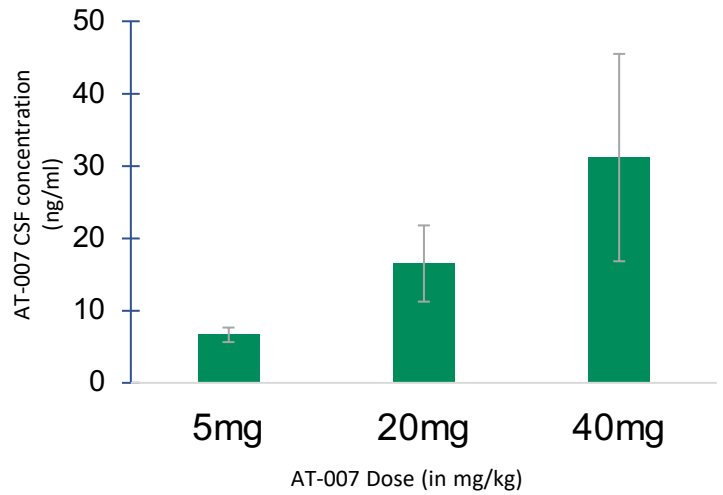


*Based on initial topline data from Jan 2020, the study was expanded to include a 40mg/kg dose in healthy volunteers and then Galactosemia patients. This cohort also included 2 additional placebo patients

**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

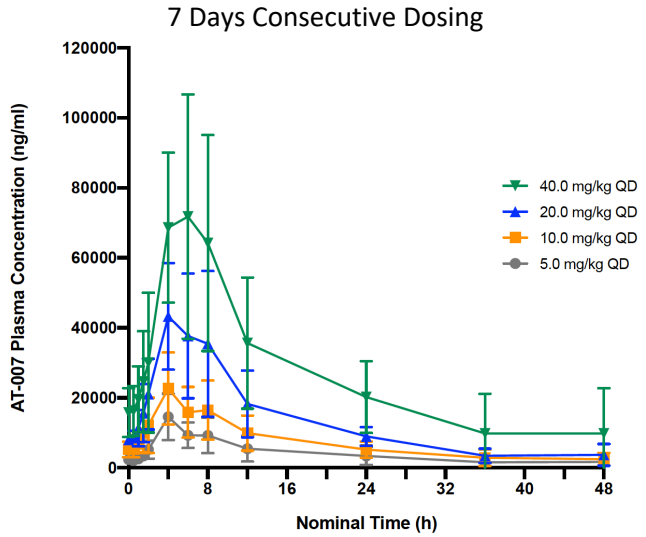
Healthy Volunteers (n=80)

Brain Penetrance



Drug crosses into brain when dosed orally (CNS penetrant)

Pharmacokinetics



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

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

Baseline Characteristics (1/2)

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).

Baseline Characteristics (2/2)

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)	

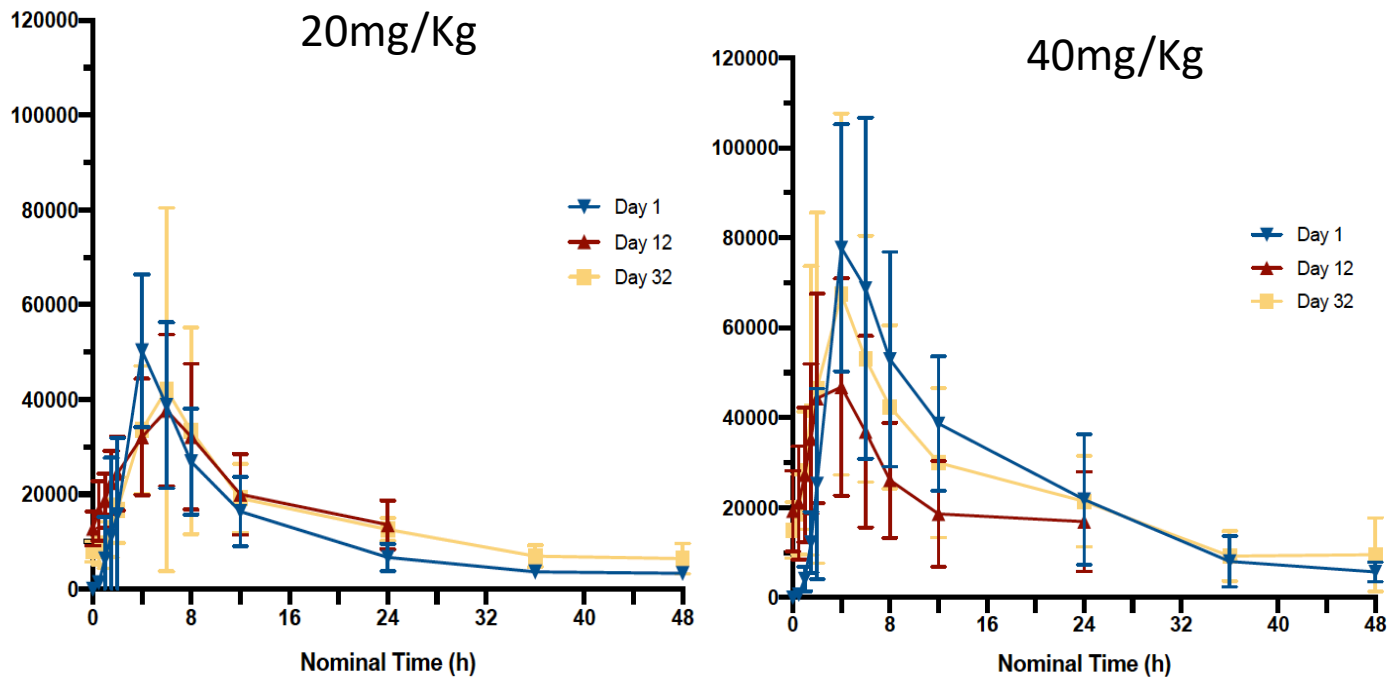
Descriptive Characteristics

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.

Pharmacokinetic Results Support Once Daily Dosing in Galactosemia Patients

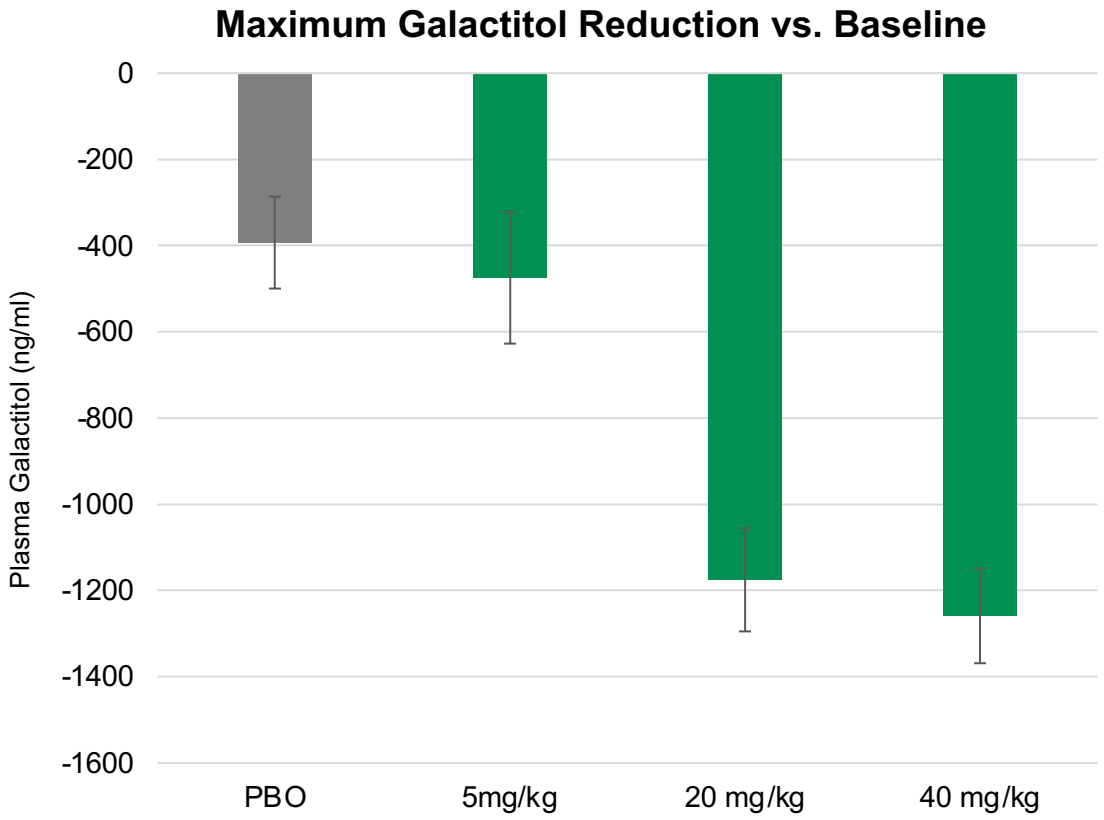
- Plasma PK parameters of AT-007 support once daily oral dosing
- PK profile in Galactosemia patients was similar to healthy volunteers, suggesting similar drug metabolism and clearance
- PK profile suggests no first pass clearance or other PK effects (de-sensitization or induction)



Safety Findings

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



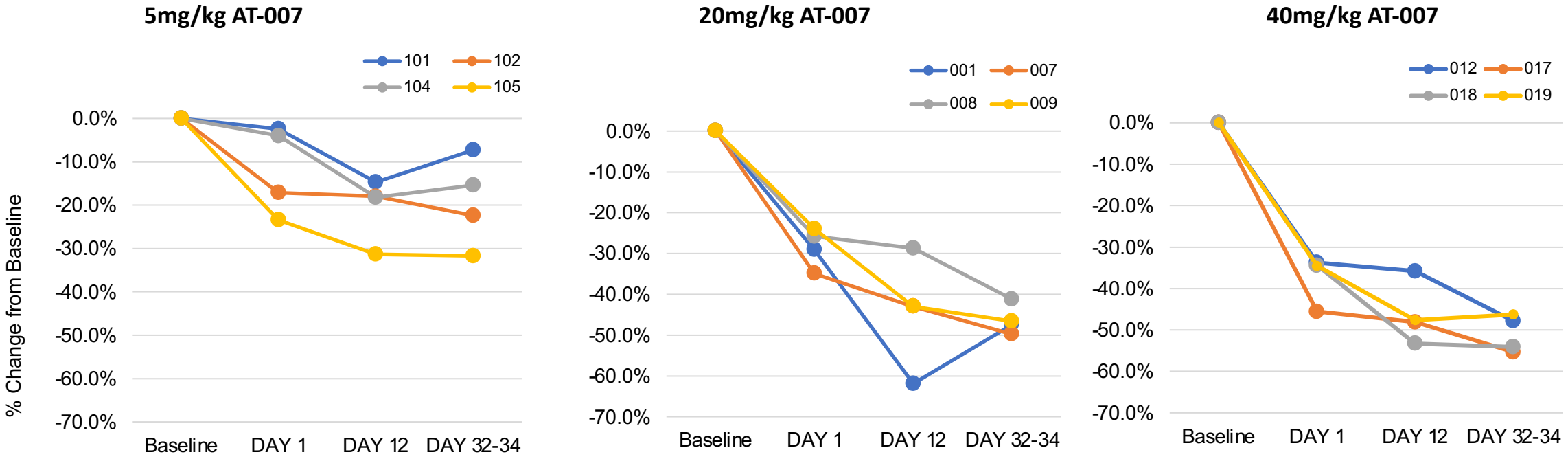
- Significant reduction in galactitol at 20 and 40mg/kg ($p<.01$)
- No significant difference between 20 and 40mg doses
- No significant impact on galactose or Gal-1p levels

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)

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

Conclusions

- AT-007 was safe and well tolerated in adult healthy volunteers and patients with Galactosemia
- AT-007 was shown to be CNS penetrant
- Plasma PK parameters of AT-007 support once daily oral dosing
- In patients with Galactosemia, AT-007 induced rapid and sustained reduction in plasma galactitol
- 20mg/kg and 40mg/kg dosing resulted in significant reduction in plasma galactitol ($p<0.01$ vs. placebo)