UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): **August 6, 2019**

APPLIED THERAPEUTICS, INC.
(Exact name of registrant as specified in charter)

Delaware	**001-38898**	**81-3405262**
(State or Other Jurisdiction of Incorporation)	(Commission File Number)	(I.R.S. Employer Identification No.)
340 Madison Avenue, 19th Fl. **New York, NY 10173**		**10173**
(Address of Principal Executive Offices)		(Zip Code)

Registrant's telephone number, including area code: **(212) 220-9319**

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

o Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

o Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

o Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

o Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company x

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. x

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	**Trading Symbol(s)**	**Name of each exchange on which registered**
Common stock	APLT	The Nasdaq Stock Market LLC

Item 7.01 Regulation FD Disclosure.

On August 6, 2019, Applied Therapeutics, Inc. released a presentation that contains company information to be used by members of management from time to time in a series of meetings with analysts, investors and other third parties. The presentation is attached to this Current Report on Form 8-K as Exhibit 99.1 and is incorporated herein by reference.

The information included in this Current Report on Form 8-K, including Exhibit 99.1 incorporated by reference herein, shall not be deemed "filed" for purposes of Section 18 of the Securities and Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that Section, or incorporated by reference into any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as shall be expressly set forth by specific reference in such filing.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	Description
99.1	August 2019 Corporate Overview Presentation

SIGNATURE

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

APPLIED THERAPEUTICS, INC.

Dated: August 6, 2019

By: /s/ Mark Vignola
Name: Mark Vignola, Ph.D.
Title: Chief Financial Officer

Exhibit 99.1

CORPORATE OVERVIEW AUGUST 2019

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Disclaimer

This presentation is made by Applied Therapeutics, Inc. (the "Company"). Nothing contained in this presentation is, or should be construed as, a recommendation, promise or representation by the presenter or the Company or any director, employee, agent, or adviser of the Company. This presentation does not purport to be all-inclusive or to contain all of the information you may desire. This presentation shall not constitute an offer to sell or the solicitation of an offer to buy the Company's securities, nor shall there be any sale of the Company's securities in any state or jurisdiction in which such offer, solicitation or sale would be unlawful prior to registration or qualification under the securities laws of any such state or jurisdiction.

Various statements in this presentation concerning the Company's future expectations, plans and prospects, including without limitation, the Company's current expectations regarding its strategy, its product candidate selection and development timing, its management team capabilities, and the ability of the Company's product candidates to have a clinically meaningful effect on the target patient populations, constitute forward-looking statements. The use of words such as "may," "might," "will," "should," "expect," "plan," "anticipate," "believe," "estimate," "project," "intend," "future," "potential," or "continue," the negative of these and other similar expressions are intended to identify such forward looking statements. Such statements, based as they are on the current analysis and expectations of management, inherently involve numerous risks and uncertainties, known and unknown, many of which are beyond the Company's control. Such risks include, but are not limited to: the impact of general economic conditions, general conditions in the biopharmaceutical industries, changes in the global and regional regulatory environments in the jurisdictions in which the Company does or plans to do business, market volatility, fluctuations in costs and changes to the competitive environment. Consequently, actual future results may differ materially from the anticipated results expressed in the forward-looking statements. In the case of forward-looking statements regarding investigational product candidates and continuing further development efforts, specific risks which could cause actual results to differ materially from the Company's current analysis and expectations include: failure to demonstrate the safety, tolerability and efficacy of our product candidates; final and quality controlled verification of data and the related analyses; the expense and uncertainty of obtaining regulatory approval, including from the U.S. Food and Drug Administration and European Medicines Agency; the possibility of having to conduct additional clinical trials and our reliance on third parties such as our licensors and collaboration partners regarding our suite of technologies and product candidates. Further, even if regulatory approval is obtained, biopharmaceutical products are generally subject to stringent on-going governmental regulation, challenges in gaining market acceptance and competition.

These risks and uncertainties are described more fully under the caption "Risk Factors" in the Company's filings with the Securities and Exchange Commission. Other risks and uncertainties of which the Company is not currently aware may also affect Company's forward-looking statements. The reader should not place undue reliance on any forward-looking statements included in this presentation. These statements speak only as of the date made and the Company is under no obligation and disavows any obligation to update or revise such statements as a result of any event, circumstances or otherwise, unless required by applicable legislation or regulation.

Corporate Vision & Strategy

A New Way to Develop Drugs

Novel product candidates against previously validated and well known molecular targets, leveraging abbreviated regulatory pathways & recent technological advances to design improved drugs

Expedited development, delivering drugs to patients more quickly

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Investment Highlights

- **Novel pipeline based on unlocking the potential of Aldose Reductase (AR) inhibition**
  - Broad applications for high unmet need in AR-mediated indications
  - AT-001: Large Ph 1/2 SAD/MAD trial in diabetic patients demonstrated POC, no SAEs; Ph 3 registrational program expected to start in Q3 2019
  - AT-007: Proof-of-mechanism in Galactosemia (rare pediatric metabolic disease); Ph 1/2 registrational trial in healthy volunteers and adults with Galactosemia ongoing; Orphan status designation granted in May, 2019 by FDA
  - AT-003: Proof-of-concept in models of retinopathy
- **High operational efficiency**
  - Reduced cost and timeline for development expected based on abbreviated development regulatory framework
    - High unmet need indications
    - Potential to use biomarkers and other non-outcomes-based endpoints
- **Strong IP portfolio covering composition of matter and method of use in target indications, with coverage through 2030's for each patent family**
- **Pipeline expansion into other high unmet need indications under same development strategy**
  - Dual selective PI3K inhibitors for orphan oncology indications (e.g. T-ALL)

Pipeline

Compound	Preclinical	Phase 1	Phase 2	Phase 3*	Dosing Route	Target Tissue	Anticipated Milestones
Aldose Reductase Franchise							
AT-001	Diabetic Cardiomyopathy				Oral	Systemic	Initiate Ph 3 in H2 2019
AT-001	Diabetic Peripheral Neuropathy				Oral	Peripheral Nerve	
AT-001	Acute Myocardial Infarction				SC**	Systemic / Peripheral Nerve	
AT-007	Galactosemia				Oral	CNS	Biomarker data in H2 2019
AT-003	Diabetic Retinopathy				Oral	Retina	Preclinical data 2019; Initiate Ph1 2020
PI3 Kinase Franchise							
AT-104	PTCL, CTCL, TALL***				SC / Oral	Selective δ/γ inhibitor	Initiate Ph 1 2020

* We plan to initiate a pivotal Phase 2/3 clinical trial of this product candidate as the basis for applying for marketing approval with the FDA
** Subcutaneous
*** Peripheral T-cell lymphoma, cutaneous T-cell lymphoma and T-cell acute lymphoblastic leukemia

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Unlocking the Potential of Aldose Reductase Inhibition

Validated Target Resistant to Therapeutic Development	• AR known to play a key role in diabetic complications and heart disease • Past efforts failed to produce sufficiently potent, selective and tolerable drugs
Recent Advances Enable Improved ARI's	• New understanding of structural changes within the active site of AR following enzymatic activation – Utilized advanced crystallography techniques and in situ structural design • Increased potency and selectivity compared to prior compounds with none of the prior off-target safety issues to date
R&D and Regulatory Opportunities	• High unmet need in numerous AR-mediated diseases • Leverage prior ARI programs for streamlined, abbreviated development of our novel compounds • Potential to utilize regulatory pathways designed for accelerated drug development

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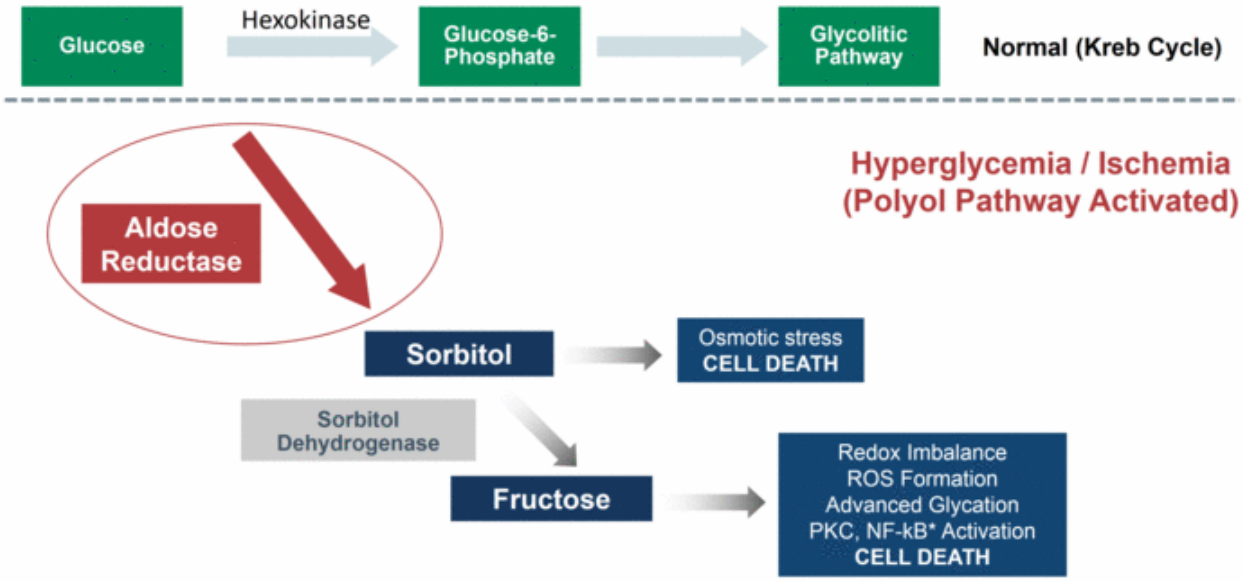
Aldose Reductase Causes Damage to Tissues Under Conditions of Oxidative Stress



*Nf-kB is a protein complex that controls transcription of DNA, cytokine production and cell survival

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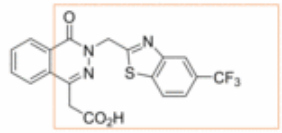
Novel Chemistry For Better Drugs

Backbone



zopolrestat

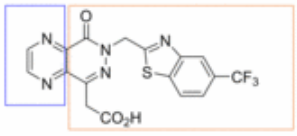
Similar backbone to zopolrestat (prior best in class efficacy, but liver tox issues)

Technological Advancements

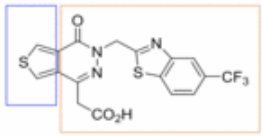
- Advanced crystallography provided novel understanding of structural changes within AR active site
- Many prior ARIs were unable to inhibit redox-activated AR

Impact of Modified Structure

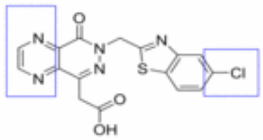
- Functional modifications improve compound's binding affinity and specificity
- Novel dimeric binding within the catalytic core
- Higher enzymatic inhibitory activity
- Increased selectivity leads to less off-target activity and potentially better safety



AT-001



AT-007



AT-003

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Compound Differentiation

Compound	IC_{50}[1]	Maximum Tolerated Dose in Animals	LogD[2]	Tissue Penetration (in rats)		
				Systemic/ Nerve	Retina	CNS
AT-001	30pM	>2,000mg/kg	-1.00	✓	✓	X
AT-007	100pM	>1,000mg/kg	-0.09	✓	✓	✓
AT-003	54pM	>1,000mg/kg	-1.53	✓	✓	X
Zopolrestat (prior Pfizer compound)	10nM	100mg/kg	+0.06	✓	X	X

- High potency (>1,000x more potent than prior best-in-class ARI)
- Targeted penetration into specific tissues

(1) IC_{50} is the amount of a compound required to inhibit 50% of enzyme activity
(2) LogD is a log of partition of a chemical compound between the lipid and aqueous phases. LogD often predicts retinal permeability, with compounds with negative LogD passing through the back of the eye

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Addressing Large Indications in Areas of High Unmet Medical Need – Opportunities for Abbreviated Clinical Development

Indication	Prevalence	Market	Unmet Need	Development Strategy
Diabetic Cardiomyopathy	17-24% Diabetics	~77M patients worldwide	• No therapies approved • No known drugs in development • Entresto approved in stage 4 disease	Independent; Abbreviated Development
Retinopathy	35% Diabetics	~158M patients worldwide	• 2 therapies approved (intravitrial injection) • Anti-VEGFs only for late stage disease	Independent; Abbreviated Development
Diabetic Peripheral Neuropathy	50% Diabetics	~226M patients worldwide	• No disease-modifying therapies approved • Only symptomatic treatments available (Lyrica) • Epalrestat, an off-patent ARI, approved in Japan, China, India	Strategic Partner; Standard Development
Galactosemia	1/50k to 1/90k	~2,800 patients in the US	• No therapies approved; lactose dietary restriction not sufficient • No known drugs in development	Independent; Abbreviated Development (includes PRV)

AT-001 for Diabetic Cardiomyopathy

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Diabetic Cardiomyopathy (DbCM)

Burden of Disease

- Early disease asymptomatic; structural changes to the heart limit contractility and decrease plasticity (fibrosis) (1-2 yrs)
- Decrease in heart function causes symptoms – shortness of breath and limitations in daily activities
- Progresses to overt heart failure and death in many cases within 9 years

Standard of Care

- Diagnosis by echocardiogram & exclusion of other types of heart disease
- Counseling on diabetic glucose control to limit hyperglycemia (insufficient)
- No treatments available; no drugs used off label to slow disease progression

	Stage 1	Stage 2	Stage 3	Stage 4
Symptoms	Asymptomatic; no limitations at rest or on exercise	Mild symptoms; shortness of breath on exercise and ordinary activities	Marked limitation in activity; comfortable at rest	Severe limitations; experience symptoms even at rest
Imaging/ functional features	Decreased tissue velocities			
	Increased LV mass	Increased LV mass & wall thickness		
	Diastolic dysfunction	Diastolic & systolic dysfunction		Severe dysfunction
	Normal EF	Normal EF	EF <50%	
	No cavity dilation	Mild cavity dilation	Marked dilatation	Severe dilation

Initially targeting patients in stage 2 and 3 (~50% of all DbCM patients likely to be most responsive to treatment) with incremental opportunity to target patients in stage 1 and 4

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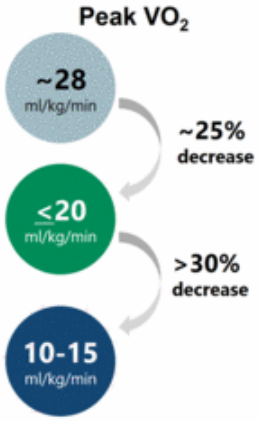
Understanding Diabetic Cardiomyopathy as a Form of Heart Failure

Diabetes **Stage A Heart Failure**	• Metabolic derangement of the myocardium due to diabetes
DbCM **Stage B Heart Failure**	• Cardiac structural abnormalities • Diastolic dysfunction; LVH • Early symptoms of DbCM; noticeable impact on activities • Decreased exercise capacity
Stage C Heart Failure	• Overt Heart Failure • HFpEF or HFrEF • Significant impact on daily activities
Stage D Heart Failure	• Refractory Heart Failure requiring specialized interventions (e.g. LV Assist Device) • Inability to complete daily activities



- ~24% of DbCM patients progress to overt heart failure or death within 1.5 years
- 37% within 5 years

References: Kosmala et al, JACC V O L . 6 5 , NO . 3 , 20 1 5; Swank et al. Circ HF 2012; Wang et al. JACC: Cardiovasc Imaging 2018; From et al. JACC 2010

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Strong Rationale for AT-001 Development in Diabetic Cardiomyopathy: First-in-Class Potential

Building on Prior Body of Evidence

- The role of AR in DbCM is well supported by preclinical and clinical evidence
- Proof of mechanism: Pfizer's zopolrestat achieved proof-of-concept on LVEF in Phase 2 Diabetic Cardiomyopathy trial
- Literature: Effects on heart function (LVEF) leads to effects on exercise tolerance (peak VO_2)

AT-001's Robust Pre-Clinical Profile

- 1,000X more potent than prior best-in-class ARI (zopolrestat), in vitro and in vivo
- Broad exposure: Cardiac and nerve tissue
- Highly favorable preclinical profile: MTD>2,000mg/kg

AT-001's Robust Clinical Profile (Ph 1/2 trial)

- Clinical proof-of-concept via sorbitol biomarker observed in T2D patients
- No drug related AEs observed at any dose; well tolerated
- Heart inflammatory biomarkers in 28 day arm in DbCM patients inform dose selection for pivotal study

AT-001 Phase 1/2 Trial in Type 2 Diabetic Patients

Parts A & B

Design

- 80 Type 2 Diabetic Patients
- All patients remained on concomitant meds
- 40 patients in SAD – (5, 10, 20, 40mg/kg)
- 40 patients in MAD – (5, 20, 40mg/kg; 20mg/kg BID)
- 8 drug treated & 2 placebo in each cohort

Results

- No drug-related AEs in entire study (up to 7 days treatment)
- No abnormal labs
- Normalization of sorbitol (PD biomarker)

Part C

Design

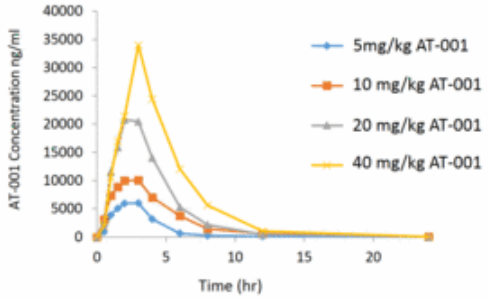
- 30 DbCM patients
- 10 patients per cohort (8 drug treated, 2 placebo)
- 3,000mg/day
  - ER tablet once daily
  - 1,500mg BID (rapid release capsule)
  - 1,000mg TID (rapid release capsule)

Results

- No drug-related AEs in entire study (up to 28 days treatment)
- No drug-related lab abnormalities
- Effect on cardiac biomarker NTproBNP

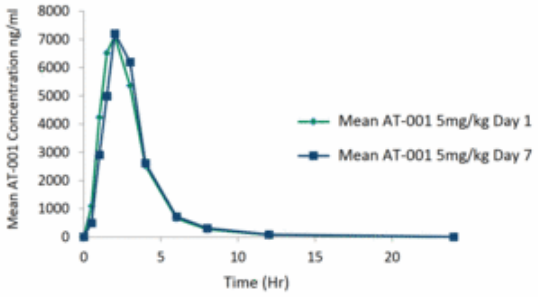
AT-001 Pharmacokinetics

Mean PK Timeframe for Phase 1 SAD Cohorts (each curve represents mean of eight patients)



- Linear dose dependence on C_{max} and AUC confirms clean absorption in the gut and good bioavailability

Multiple Dose PK Profile – No First Pass Clearance or Drug Accumulation



- Half-life of the drug in rapid release capsule is 3-6 hours at higher doses
- Effects on enzyme inhibition for 10-12 hours per dose

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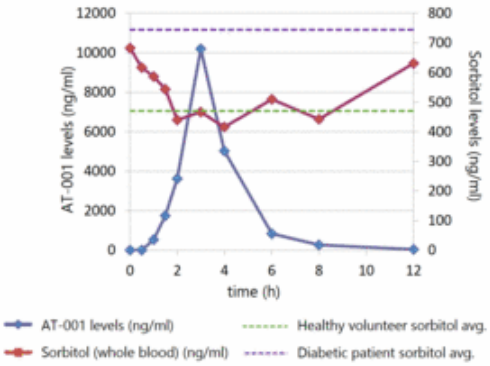
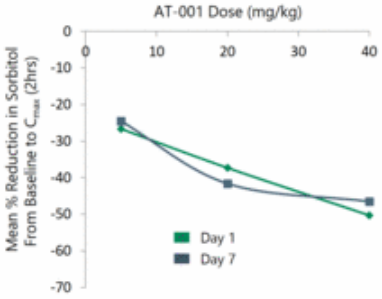
AT-001 Normalizes Sorbitol in Diabetic Patients

Proof of Biological Activity



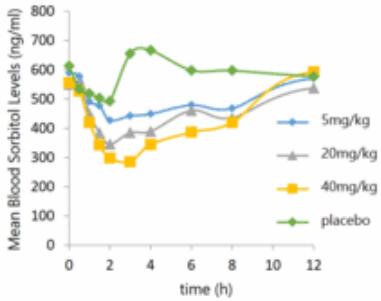
- Drug treatment with AT-001 normalized sorbitol to healthy volunteer levels

Sorbitol Reduction by Dose



- Mean reduction in sorbitol at Day 1 and Day 7: Results are persistent over 1 week of treatment
- At 40mg/kg patients were normalized to healthy volunteer sorbitol levels, demonstrating complete AR inhibition

Sorbitol Normalization Over Time



- Rapid release capsule provides sorbitol normalization effects (PD biomarker) through 10-12hrs post-dose at >10mg/kg
- Includes protection from food-related sorbitol spikes during times of post-prandial hyperglycemia

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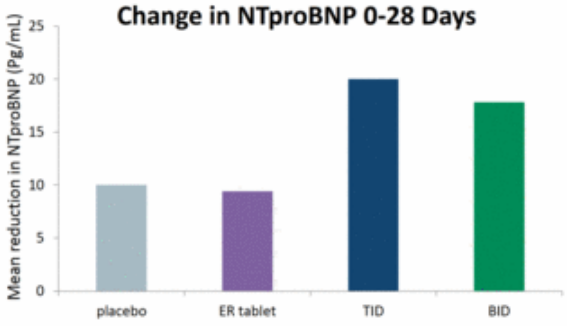
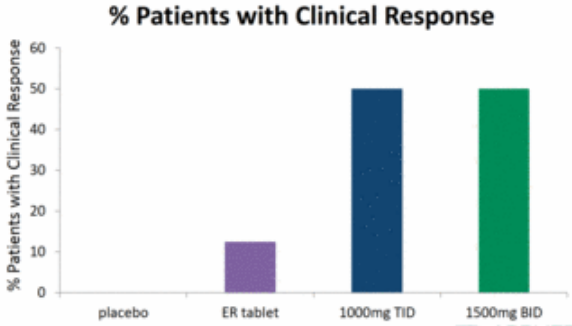
AT-001 Treatment for 28 Days Decreases NT proBNP in Early Stage DbCM Patients

- NTproBNP: Prohormone released in response to changes in left ventricular pressure
  - Used to diagnose overt heart failure and Acute MI
  - Higher levels of in diabetics correlates with higher risk of heart failure and worse outcomes
- Mean change in NTproBNP from baseline to 28 days was greater in patients that received AT-001 BID or TID vs. placebo or ER tablet

- In a responder analysis, 50% of BID/TID treated patients showed a clinically meaningful reduction in NTproBNP at 28 days
  - Defined as >25 pg/mL reduction from baseline
  - Baseline range was 30-235pg/ml
  - Mean at baseline was 65pg/ml





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AT-001 Phase 2/3 Pivotal Study Design

Study Population and Objectives	• Study population: Patients with Type 2 diabetes (T2D) and DbCM at high risk of progression to overt HF • Primary objective: To demonstrate that AT-001 improves or prevents the decline of functional capacity in patients with Diabetic Cardiomyopathy (DbCM) at high risk of progression to overt heart failure • Secondary objective: to demonstrate that AT-001 decreases progression from Stage B HF to Stage C HF

Study Endpoints	• Primary: Peak VO2 at Month 15 (change from baseline)
	  • Repeated at a later time point if necessary as determined by firewalled DMC
	• Secondary:
	  • Progression to overt HF
	  • Changes in NT-proBNP from baseline
	  • Changes in KCCQ
	  • Changes in GLS, LVH, LAVI, DD and RVSP
	• Exploratory: biomarkers (sorbitol, inflammatory biomarkers); renal outcomes (GFR, AUCR); DPN

Design and Dosing	• 675 patients total (225 per arm) • 3 arms: high dose (1500mg BID); low dose (1000mg BID); placebo • 12 month placebo controlled extension study to follow; endpoint CV death/ hospitalization

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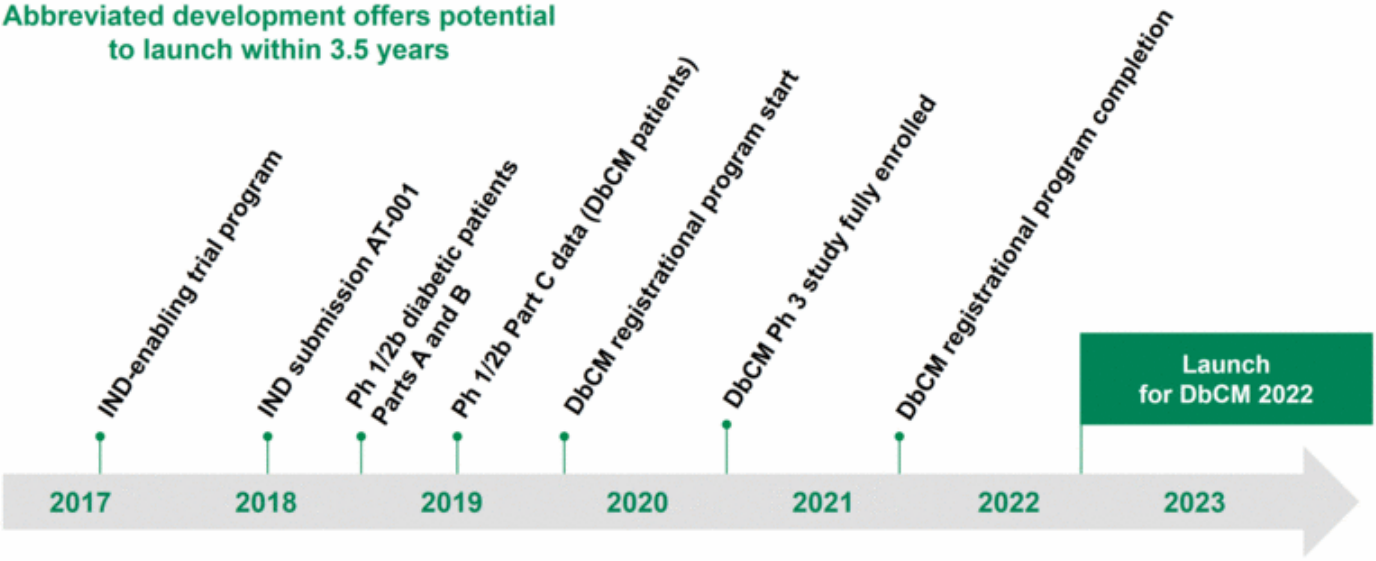
Anticipated Development Timeline
Diabetic Cardiomyopathy

Abbreviated development offers potential to launch within 3.5 years



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AT-001 for Diabetic Peripheral Neuropathy

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Diabetic Peripheral Neuropathy

Burden of Disease

- Aldose Reductase activity in neurons causes osmotic dysregulation and cell death/neuronal dysfunction
- Tingling/burning/stinging sensation and loss of feeling in peripheral tissues
- Significant impact on quality of life and pharmacoeconomic metrics (ability to work)

Standard of Care

- No disease modifying therapies approved
- Epalrestat (ARI) approved for 20+ years in Japan: dosed 3-5x/day; numerous side effects
- Standard of care outside of Japan/China is analgesic (pain) management, primarily Lyrica

Building on Prior Body of Evidence

- Epalrestat is understood to be safe and moderately effective, but unfavorable PK profile (5X daily dosing)
- Never approved in US/EU; now generic in Japan/China
- Phase 4 trials in Japan demonstrated statistical effects on MNCV and symptomatic pain (Hotta et al)

Current Phase 1 SAD/MAD Trial

- Current AT-001 Phase 1 results show favorable PK vs. Epalrestat
- DPN metrics (MNCV) will be captured in Phase 2/3 pivotal Diabetic Cardiomyopathy trial
- Demonstrate POC for AT-001 in DPN and inform on dose selection for registrational DPN trials

Future Path to Registration

- Will require "typical" path to registration
  - 2 large Phase 3 trials
- Design will follow Epalrestat Phase 4 trials– careful selection of patient population and performance of endpoint testing
- Likely to pursue strategic partnership with large pharmaceutical company

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AT-003 for Diabetic Retinopathy

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AT-003 for Diabetic Retinopathy

Burden of Disease

- One of the major causes of blindness worldwide
- Current therapies (anti-VEGFs) are high cost biologics that require intravitreal administration by an ophthalmologist
- Limited access for patients and high economic burden
- AR is an upstream target vs. VEGF – opportunity to blunt damage to the eye at the earliest stages

Standard of Care

- Current treatments (anti-VEGF therapies) target downstream consequences of diabetic complications in the eye
- Lucentis & Eylea are leading approved therapies for DME; limited to treating later stage / more severe stages of disease

Building on Prior Body of Evidence

- Clear proof of mechanism: AR activation / increased sorbitol as the initial pathogenesis of retinopathy is well supported
- Sorbitol build up in the lens causes osmotic dysregulation
- AR knock-out mice do not develop diabetic retinopathy; AR over-expressing mice develop retinopathy earlier than WT
- 2 prior ARIs met endpoints in Phase 2 trials, but were toxic

AT-003 in Preclinical Development

- Proof-of-concept in animal models of retinopathy
- AT-003 displays a similar PK to AT-001, but has greater retinal penetrance
- IND-enabling studies and manufacturing scale up are under way

AT-007 for Galactosemia

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AT-007 for Galactosemia

Burden of Disease

- Rare genetic metabolic disease caused by inability to break down galactose
  - Metabolite of lactose
  - Produced de novo by cells
- Even with strict dietary restriction of external lactose, endogenous galactose is produced within the body, leading to toxic build-up of galactitol
- Long-term consequences of disease include: Frequent pre-senile cataracts, significant motor, speech, cognitive, and psychiatric impairments, and ovarian insufficiency

Standard of Care

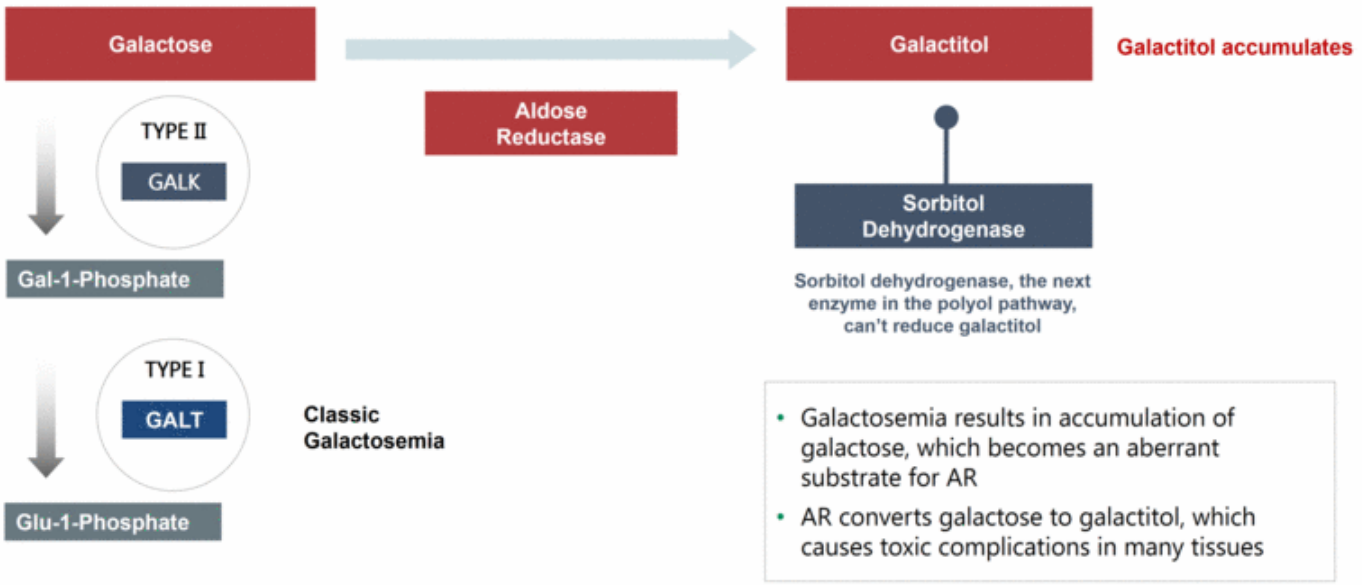
- Mandatory newborn screening in the US/EU; potentially fatal if undetected in first weeks of life and infant is exposed to lactose in breast milk or formula
- No approved therapies
- Standard of care is strict dietary restriction of lactose and galactose, which prevents fatalities, but **does not prevent long term consequences of disease**
- Greatly impacts children's development potential and quality of life (causes severe and permanent cognitive, intellectual and speech deficiencies)
- In adults, frequent cataracts due to galactitol build up in the eye; many develop persistent tremors

Galactosemia Market & Regulatory Environment

- Incidence **1:50,000-1:90,000**
- However, actual number of live patients is much lower than projected; prior to newborn screening, nearly all infants with Galactosemia died
- **~2,800** US patients
- Births per year are estimated at **~80** in the US
- Majority of patients are under the age of 40
- Is a "low prevalence" disease as defined by the FDA

Regulatory Guidelines: Because Galactosemia is a "slowly progressing" rare metabolic disease, under new FDA guidance, surrogate metabolic biomarkers may be acceptable for demonstration of therapeutic activity = low burden of clinical development

Aldose Reductase Activity Causes Toxic Accumulation of Galactitol in Galactosemia



- 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

APPLIED THERAPEUTICS

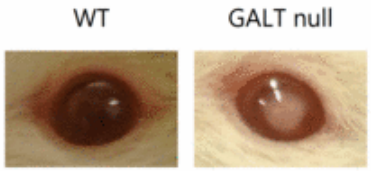
AT-007: Oral CNS Penetrant Aldose Reductase Inhibitor – Summary of Preclinical Data

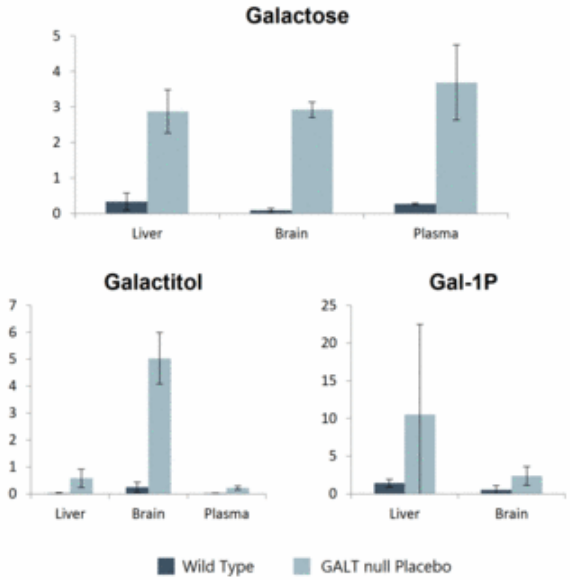
Drug Profile	• Structurally distinct molecule with potent AR inhibition and unique PK profile • Exposure to all Galactosemia target tissues – CNS, nerve and retina penetrant • Oral once-daily dosing (half life 12-18 hrs)
Safety	• No drug-related safety or tolerability issues in Phase 1 healthy volunteer study (SAD) • No safety issues in newborn rat treatment studies, supporting eventual infant/pediatric use
Preclinical Disease Model Takeaways	• Prevented complications of disease in a newborn Galactosemia rat model • Prevented galactosemic cataract formation and prevented CNS abnormalities (rotarod) • Clear biochemical effects correlate with clinical endpoints • Reduced galactitol levels in serum and affected tissues • Did not increase galactose levels or levels of other galactose metabolites (Gal1P)

APPLIED THERAPEUTICS

Galactosemia Animal Model: GALT Deficiency (Classic Galactosemia) Rat

- GALT deficient rats closely mirror human disease:
  - Bilateral cataracts
  - Biochemical effects on galactitol, galactose and Gal1P similar to those seen in humans
  - CNS deficiencies indicative of cognitive, intellectual, memory and motor abnormalities
- To date, no evidence of tremor or ovarian insufficiency





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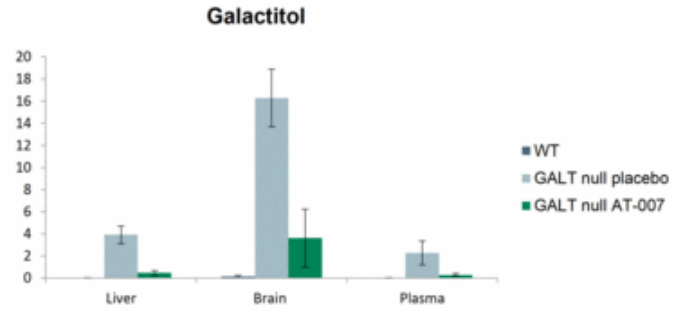
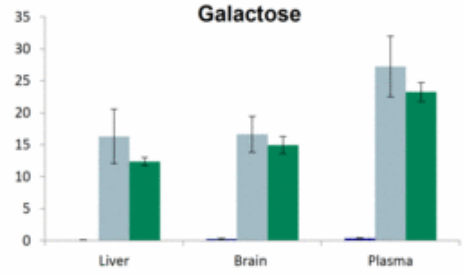
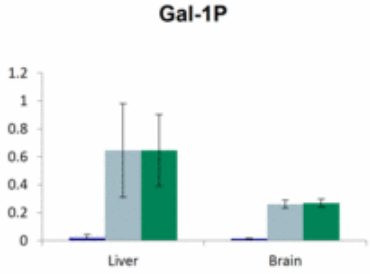
AT-007 Significantly Reduces Galactitol Levels in GALT Null Rats in all Target Tissues



- AT-007 treatment from neonatal Day 1 to Day 10 significantly reduced galactitol in liver, brain and plasma
- Treatment did not increase galactose or Gal1P levels; similar results seen at Day 22 and age 5 months





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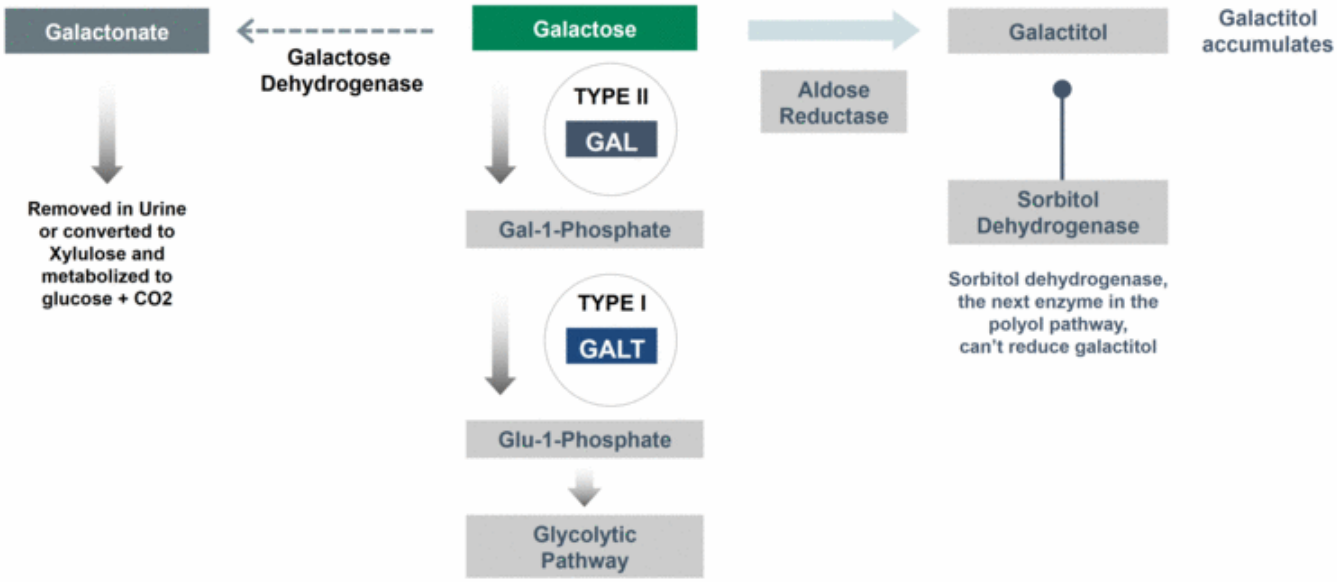
If Blocking AR Doesn't Increase Galactose or Gal-1P…..
Where Does the Extra Substrate Go?

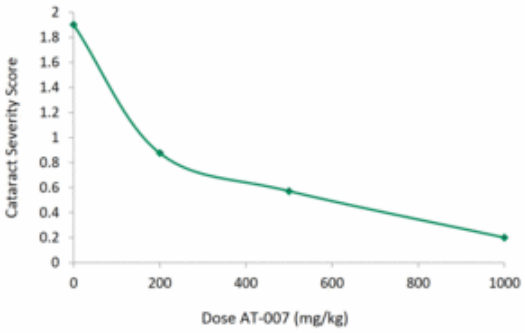


APPLIED THERAPEUTICS

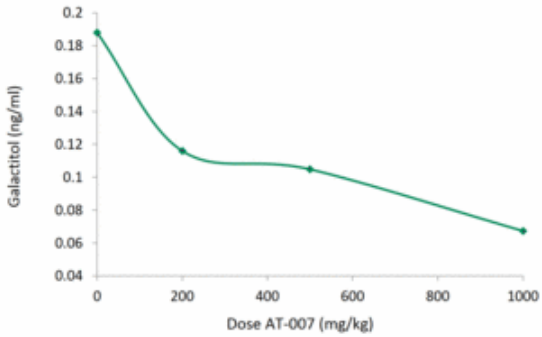
AT-007 Cataract Prevention Dose Response

Greater doses of AT-007 reduced galactitol levels and the severity of cataracts

AT-007 Dose Dependent Reduction of Cataracts



AT-007 Dose Dependent Reduction of Plasma Galactitol



No cataracts in WT or AT-007 treated GALT null rats, but visible cataracts in all GALT null placebo rats at Neonatal Day 22

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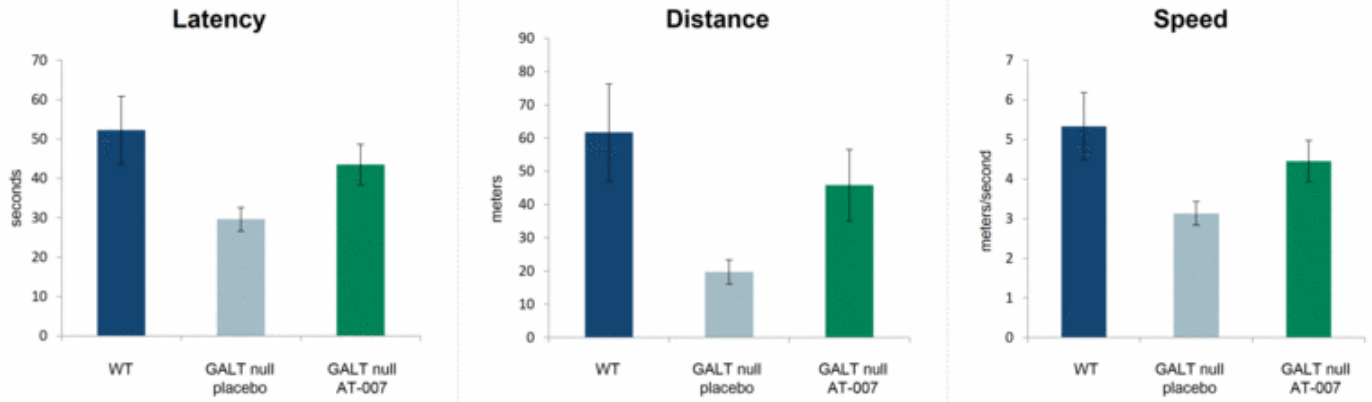
AT-007 Treatment Prevents CNS Deficits in Galactosemia Rat Model



While galactosemic rates showed deficits in learning and motor coordination versus WT rats, treatment with AT-007 was able to prevent these deficiencies and normalize cognitive and motor function

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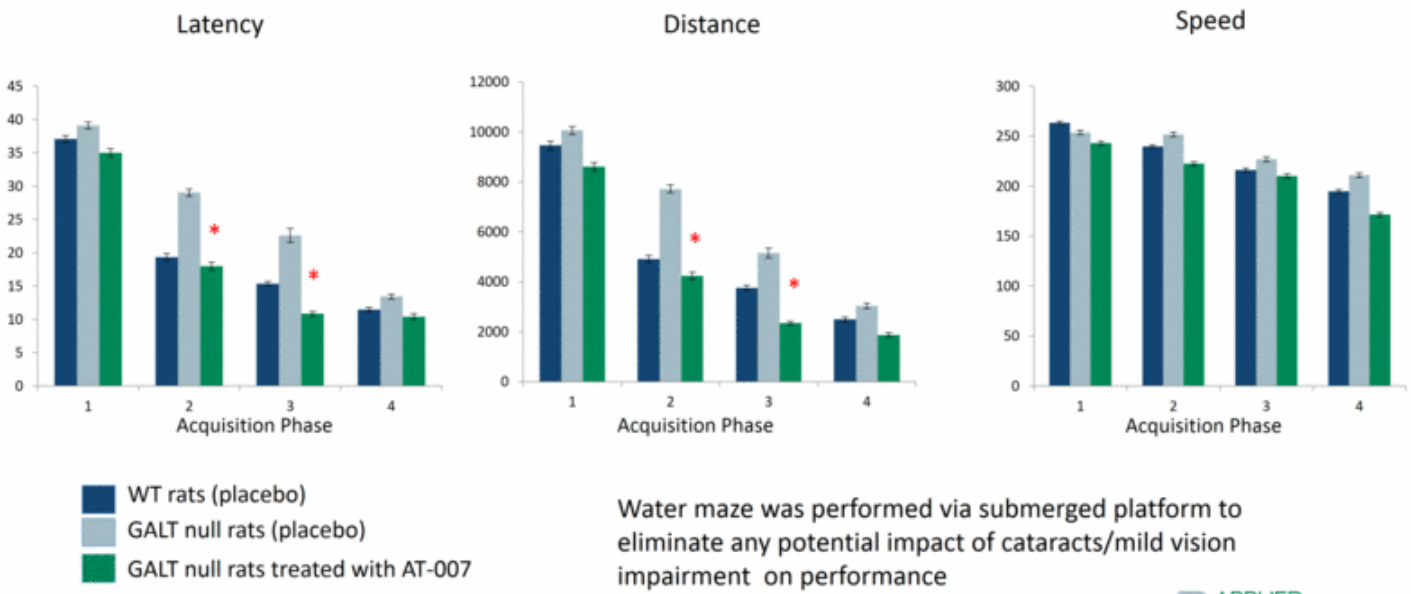
AT-007 Treatment Prevents Learning Deficits in Galactosemia Rat Model (Water Maze)



WT rats (placebo)
GALT null rats (placebo)
GALT null rats treated with AT-007

Water maze was performed via submerged platform to eliminate any potential impact of cataracts/mild vision impairment on performance

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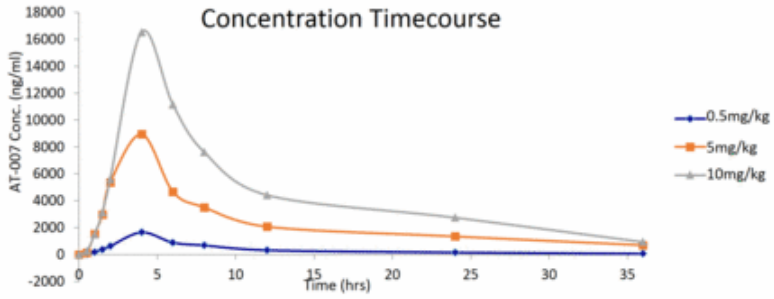
Galactosemia Phase 1/2 Registrational Trial Overview

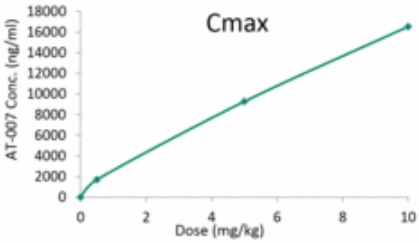
- **Healthy volunteer SAD/MAD**
  - Safety and drug PK
  - 8 subjects per cohort (up to 64 total)
  - Multiple dose for up to 7 consecutive days of treatment
  - Single site in San Antonio

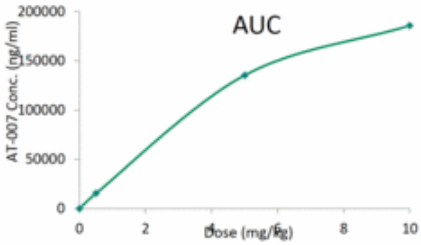
- **Galactosemia SAD/MAD**
  - Safety, drug PK, biomarker assessments
  - 4 subjects per cohort (16 total)
  - Placebo-controlled
  - Allows SAD to MAD transition in same patients
  - Multiple dose for 27 consecutive days of treatment
  - Core study is Classic Galactosemia patients; additional cohort will allow GALKD patients
  - Multicenter (Boston, Atlanta, Minneapolis, California)
- Safety extension to follow

Galactosemia Clinical Trial SAD Data in Healthy Volunteers (Part 1)

- No drug-related safety issues at any dose tested
- Dosing: 0.5, 5.0, 10, 20mg/kg
- PK consistent with once daily dosing (half-life ~12 hours)
- Consistent exposure across patients
- Linear dose response







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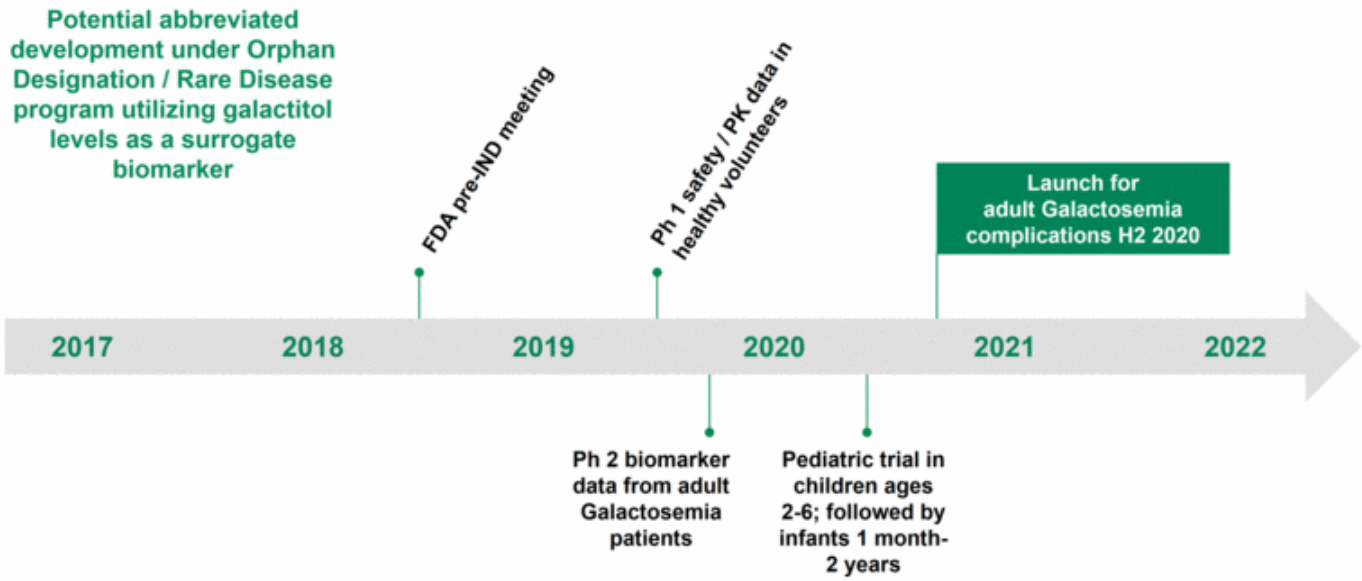
Anticipated Development Timeline: AT-007 for Galactosemia Complications



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Key Anticipated Milestones

Q2 2019 (June 2019)	Start AT-007 Phase 1/2 adult Galactosemia trial
Q3 2019	Readout of AT-007 healthy volunteer data
Q3 2019	Start of AT-001 Diabetic Cardiomyopathy Phase 3 registrational program
Q4 2019	AT-007 Phase 2 adult Galactosemia biomarker data
H1 2020	AT-001 DbCM Phase 2/3 registrational trial fully enrolled
H1 2020	AT-007 Galactosemia pediatric trial start
H2 2020	Additional pipeline programs move into Phase 1 (e.g. PI3k selective inhibitors)

Intellectual Property Summary

- Dominant IP and Freedom to Operate on all compounds & all target indications
- Expected IP runway of at least 10 years post-launch in key indications
- Composition of matter patents that cover AT-001 and related compounds obtained US, EP, JP, CA and AU
  - Patent protection through 2031, regulatory extension of term possible
  - Method claims obtained or currently being pursued
- Composition of matter patent that covers AT-007 and related compounds obtained in US
  - Pending on fast track in Europe, pending in other countries
- Company-owned international applications (PCT) cover methods for treating Galactosemia and additional compound derivatives

Appendix / Backup Slides

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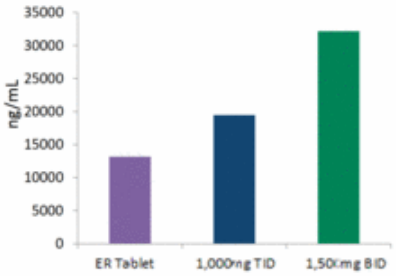
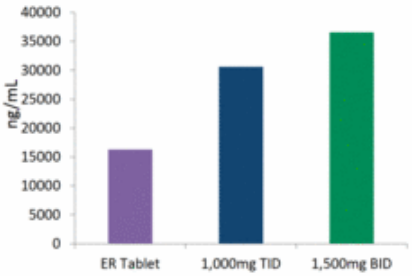
AT-001 Phase 1/2 Part C Dosing Posology and Pharmacokinetics

- BID and TID rapid release capsule dosing provided sustained drug levels over 24 hours
  - ER tablet did not release drug as predicted, providing low overall exposure; defines minimally efficacious dose

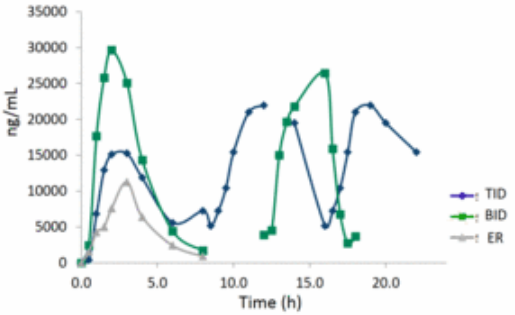
AT-001 C_{max} (mean)



AT-001 AUC (mean)



AT-001 PK profile



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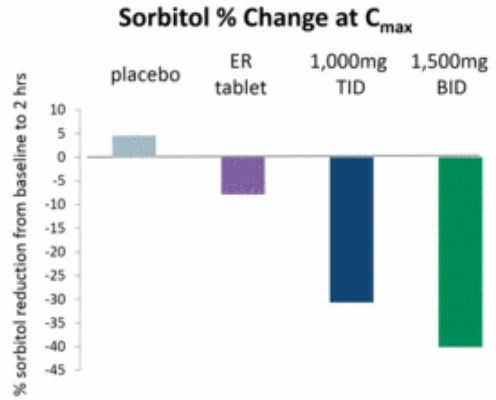
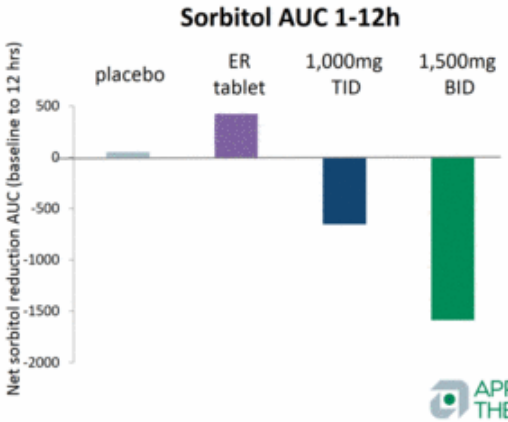
Sorbitol Reduction in Part C of AT-001 Phase 1/2 Study

- Higher C_{max} at first dose achieved with 1500mg BID provided greater sorbitol reduction at 2 hours post-dose

- Sorbitol reduction over 12 hours as measured by AUC is greatest for 1000mg TID
- Significant AUC sorbitol reduction AUC achieved by both 1500mg BID and 1000mg TID AT-001





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AT-001 Phase 3 Study Leadership & Committees

Steering Committee

- **Chair:** James Januzzi, MGH, Boston, MA, USA
- **Cardiologists**:
  - Javed Butler, U Mississippi, MS, USA
  - Justin Ezekowitz, U. Alberta, Canada
  - Nasrien Ibrahim, MGH, Boston, MA, USA
  - Carolyn Lam, NHC, Singapore
  - Thomas Marwick, U. Melbourne, Melbourne, Australia
  - Fayez Zannad, Inserm-CHU, Nancy, France
- **Endocrinologists:**
  - Stefano Del Prato, University of Pisa, Italy
  - Julio Rosenstock, Diabetes Center, Dallas TX, USA

Operational Committee

- **CPET Core Lab:** Greg Lewis, MGH, Boston, MA, USA
- **Echo Core Imaging Center:** Scott Solomon, BWH, Boston, MA, USA
- **Cardiovascular Event Adjudication**: ACI
- **National Coordinators**:
  - **Canada:** Alice Cheng, U. of Toronto, Toronto, Canada
  - **France**: Paul Valensi, Paris-Nord University, Paris, France
  - **UK:** Kamlesh Khunti, U, of Leicester, Leicester, UK
  - **Czech Republic**: Martin Haluzik
  - **USA**: Yehuda Handelsman, Metabolic Institute of America, Tarzana, CA; Luigi Meneghini, UT South Western, Dallas, TX;

Data Monitoring Committee

- **Chair:** Chris Cannon, BWH, Boston, MA, USA
- **Cardiologists**:
  - Mikhail Kosiborod, U. of Missouri, Kansas City, MO, USA
  - Church, VA, USA
- **Endocrinologists:**
  - Larry Leiter, U. of Toronto, Toronto, Canada
- **Biostatistician:**
  - Joe Massaro, Boston University, Boston, MA, USA

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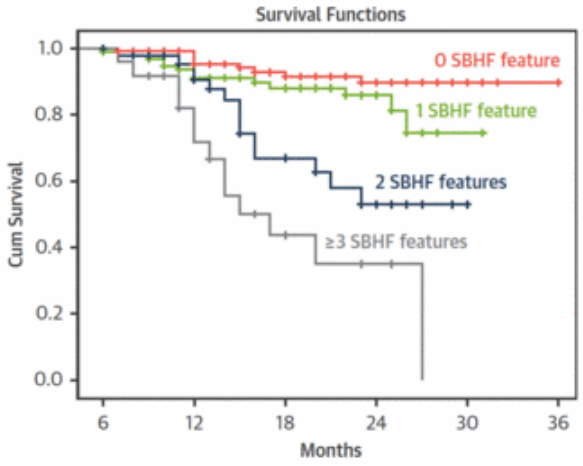
Anticipated Changes in Functional Capacity and Progression to Overt Heart Failure in Study Population

Anticipated mean baseline peak VO2<6 METS (21ml/kg/min) represents a steep slope of decline and strong relationship between changes exercise capacity and ability to perform every day tasks

No. METs	Metabolic "cost" of activity
1	Rest
2-3	Walking 2 mph, eating, dressing
4-5	Walking 4 mph, household tasks
6-7	Walking up stairs Stage 2 Bruce 2.5mph, 12%
8-9	Swimming, tennis
10-11	Jogging 10min/miles Stage 3 Bruce: 3.4mph, 14%
12-14	Intense aerobic sports: squash Stage 4 Bruce: 4.2mph, 16%
>20	Professional athletes/ olympians

MET=3.5ml/kg/min O2; AMA Guides to the Evaluation of Permanent Impairment, Sixth Edition. Author: Robert D. Rondinelli, MD, PhD

Progression to Overt Heart Failure



Wang Y, Marwick TH. JACC: CV Imaging 2018

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