ATRIUM THERAPEUTICS™

Atrium Therapeutics

12 November 2026

www.atriumtherapeutics.com

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Forward-Looking Statements

FORWARD LOOKING STATEMENTS AND OTHER INFORMATION: Certain statements in this Presentation may constitute "forward-looking statements" for purposes of the federal securities laws. Our forward-looking statements include, but are not limited to, statements regarding our future results of operations and financial position, including our expected cash runway; business strategies and plans; research and development plans, including the anticipated timing of initiating IND-enabling studies and of nominating additional development candidates; the anticipated timing, costs, design, dosing, enrollment, number and location of trial sites and conduct of our ongoing and planned preclinical studies and clinical trials for our product candidates; the timing of the reporting of data from our clinical trials, the timing and likelihood of regulatory filings and approvals for our product candidates, the timing and likelihood of success of our research and development programs, plans and objectives of management for future operations and future results of anticipated product development efforts; the design, capability and scalability of our AOC platform, including its ability to efficiently deliver to cardiac tissue and to directly target pathogenic RNA across multiple genetically defined cardiomyopathies; the therapeutic potential of our product candidates, including their potential to modify disease progression and the potential of ATR 1072 to address PRKAG2 Syndrome; the extent to which results observed in our nonclinical studies, including studies using surrogate molecules in nonclinical models, may be predictive of results in humans; the potential for modulating calcium cycling to improve diastolic function in cardiomyopathies; our ability to expand into additional indications; our estimates of disease prevalence and market opportunity and identification of higher disease prevalence; and the potential receipt of milestone payments under our collaborations. The forward-looking statements contained in this Presentation are based on our current expectations and beliefs concerning future developments and their potential effects on us. There can be no assurance that future developments affecting us will be those that we have anticipated. These forward-looking statements involve a number of risks, uncertainties (some of which are beyond our control) or other assumptions that may cause actual results or performance to be materially different from those expressed or implied by these forward-looking statements including, but not limited to: the initiation, timing, progress, potential registrational quality, and results of our research and development programs, preclinical studies, any clinical trials, Investigational New Drug Application, and other regulatory submissions; our ability to identify and nominate additional development candidates on our anticipated timeline or at all; the beneficial characteristics, including potential safety, efficacy and therapeutic effects of our product candidates and the potential advantages of our product candidates compared to alternative therapies; the potential for clinical trial results to differ from the results of our nonclinical studies, including data from animal models and from studies using surrogate molecules; the limitations of nonclinical models, which may not fully replicate human disease; the success and capabilities of the RNA delivery platform, including its ability to efficiently deliver to cardiac tissue; the prevalence of certain diseases and conditions we intend to treat and our estimates of the potential market opportunity for our product candidates; the number of patients that we will enroll in our clinical trials and the number and location of trial sites; the timing of and costs involved in obtaining and maintaining regulatory approval of our current product candidates and any future product candidates that we may identify or develop; our ability to meet future regulatory standards with respect to our product candidates, if approved; our plans relating to the further development and manufacturing of our product candidates, including for additional indications that we may pursue; the rate and degree of market acceptance and therapeutic benefits of our product candidates, if approved; our ability to develop or partner and progress our current and future product candidates; the implementation of our strategic plans for our business, product candidates, research programs and technologies; the scope of protection we are able to establish and maintain for intellectual property rights covering our product candidates; anticipated developments related to our competitors and our industry; our competitive position and the success of competing therapies that are or may become available; our ability to maintain our current license agreements and collaborations and identify and enter into future license agreements and collaborations; the expected potential benefits of strategic collaborations with third parties and our ability to attract collaborators with development, regulatory, manufacturing or commercialization expertise; our reliance on third parties to conduct preclinical studies and clinical trials of our product candidates; our ability to efficiently and cost-effectively conduct our current and future clinical trials; our reliance on third parties for the manufacture of our product candidates; our plans relating to sales strategy, manufacturing and commercializing our product candidates, if approved; anticipated regulatory developments in the United States and foreign countries in which we may seek regulatory approval for our product candidates in the future; the timing and likelihood of the achievement of milestones pursuant to our existing collaboration agreements; our ability to attract and retain key scientific and management personnel; the costs of operating as a public company; the accuracy of our estimates regarding future expenses, future revenue, capital requirements and the need for additional financing; the period over which we estimate our existing cash and cash equivalents will be sufficient to fund our future operating expenses and capital expenditure requirements; our ability to obtain funding for our operations necessary to complete further development and commercialization of our current and future product candidates; our anticipated use of our existing resources, estimates of our expenses, capital requirements and needs for additional financing; general economic, political and market conditions, including inflationary pressures, interest rates, and changes in trade policy; and other factors specified in the Company's Registration Statement on Form 10, initially publicly filed by the Company with the Securities and Exchange Commission (the "SEC") on December 10, 2025 and in other filings and furnishings made by the Company with the SEC from time to time. Should one or more of these risks or uncertainties materialize, or should any of our assumptions prove incorrect, actual results may vary in material respects from those projected in these forward-looking statements. We undertake no obligation to update or revise any forward-looking statements, whether as a result of new information, future events or otherwise, except as may be required under applicable securities laws.

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Our vision:

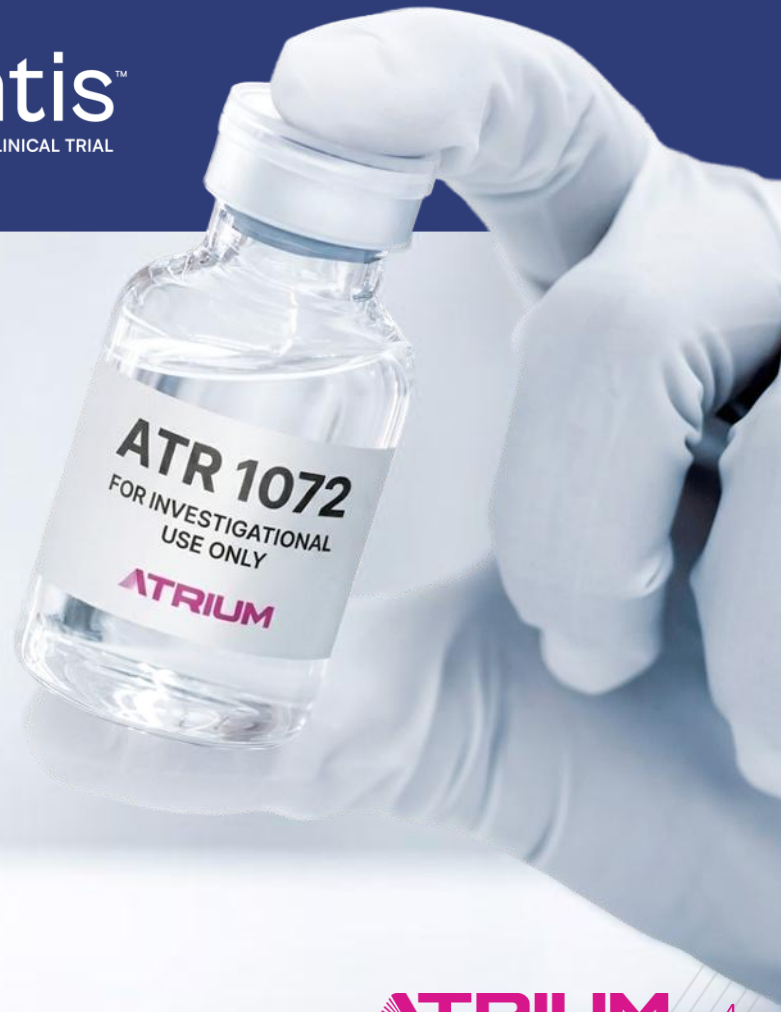
To pioneer precision RNA medicines for the heart and profoundly improve the lives of people impacted by cardiac diseases

Atrium has made solid progress since our launch in February 2026

KEY MILESTONES

- ATR 1072 cleared for trials in the U.S. and Canada
- First patient dosed in Phase 1/2 clinical trial – Corventis™

corventis™
PRKAG2 SYNDROME PHASE 1/2 CLINICAL TRIAL



1. **PRKAG2 syndrome patient identification:**
   Build bottom-up view of full patient population

2. **ATR 1072 & ATR 1086:**
   Expand into additional cardiomyopathies with shared pathways

3. **Next development candidate:**
   Build the pipeline in rare cardiomyopathy

Atrium is at the forefront of genetic cardiomyopathy treatment, and we're moving fast

Patients and physicians are looking for more effective treatment options for genetic cardiomyopathies, and the market is primed for precision therapies

Rare Cardiac Disease with High Unmet Need

Serious, genetically driven cardiomyopathies with significant unmet need - no approved disease-modifying therapies exist today[1]

Proven Ability to Execute with Urgency

Atrium has dosed its first patient in Corventis™, the first interventional clinical trial for people living with PRKAG2 syndrome (Ph 1/2)

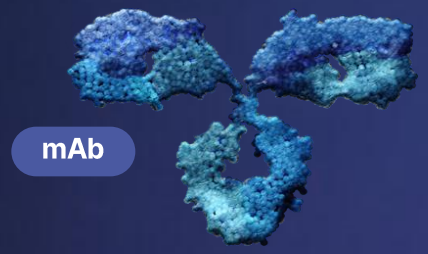
Targeted Platform, Focused Pipeline

A targeted RNA delivery platform powering two lead programs - ATR 1072 (PRKAG2 syndrome) and ATR 1086 (PLN cardiomyopathy) – and two undisclosed precision cardiology targets

[1]Hutt, E, et al, *"Medical Treatment Strategies for Hypertrophic Cardiomyopathy." American Journal of Cardiology vol 212, S33-41*

A precision RNA platform primed for genetic cardiomyopathies

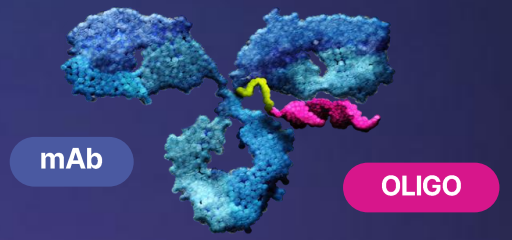
Monoclonal Antibodies



Oligonucleotide Therapies



Antibody Oligonucleotide Conjugate (AOC)



Targeted Delivery

- ✓ RNA delivery technology designed to efficiently reach heart tissue
- ✓ Built on technology developed at Avidity including same antibody and linker

Genetic Precision

- ✓ Designed to directly target pathogenic RNA
- ✓ Potential to modify disease progression

Scalable Platform

- ✓ AOCs applicable across multiple genetically-defined cardiomyopathies
- ✓ Efficient expansion potential to additional indications

Leadership team expertise in rare disease and RNA



Kath Gallagher | Chief Executive Officer and Board Member

20+ years in the biopharmaceutical industry leading portfolio strategy, program management, investor relations and corporate affairs in preclinical to commercial stage companies

AVIDITY, AKCEA, MERRIMACK



Rocio Martin | Chief Strategy Officer

20+ years in various senior strategy, management and commercial roles in clinical and commercial organizations

AVIDITY, KRONOS, AUDENTES, ULTRAGENYX, CELGENE



Steve Hughes, MD | Chief Medical Officer

25+ years in biopharmaceutical industry contributing to 50+ clinical trials and multiple product filings and launches in rare disease, cardiovascular and neurology therapy areas

AVIDITY, IONIS, BIOGEN, CSL BEHRING, SANOFI



Brendan Winslow | Chief Financial Officer

15+ years of financial leadership experience in biotech and diversified healthcare, including global operations, commercialization and strategic transformations

AVIDITY, ACADIA, BAXTER



Stephanie Kenney | Chief Corporate Affairs Officer

25+ years in biopharmaceutical industry leading corporate affairs, investor relations and marketing at preclinical to commercial stage companies in autoimmune, cardiovascular and renal therapy areas

AVIDITY, HANSA, ASTRAZENECA



Husam Younis, PhD, PharmD | Chief Scientific Officer

20+ years in drug discovery and development, including rare disease and SVP of development science at Avidity

AVIDITY, NGM, IONIS, PFIZER

Atrium Board Members

Sarah Boyce (Chair)

AVIDITY BIOSCIENCES · AKCEA THERAPEUTICS · IONIS

Carsten Boess

KINIKSA · ALEXION AstraZeneca Rare Disease

W. Michael Flanagan, Ph.D.

AVIDITY BIOSCIENCES · G · GILEAD

Kath Gallagher

AVIDITY BIOSCIENCES · AKCEA THERAPEUTICS · merrimack

Simona Skerjenac

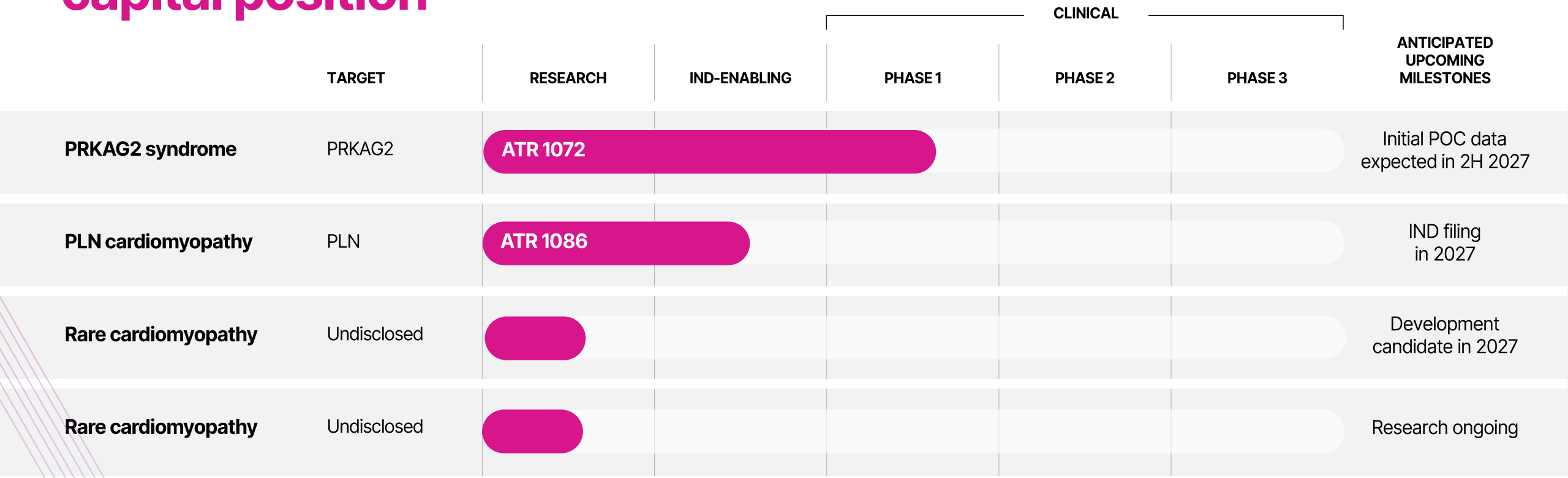
Roche · The Medicines Company · Lilly

Troy Wilson

KURA ONCOLOGY · intellikine · wellspring biosciences

ATRIUM

Robust wholly-owned pipeline supported by strong capital position



$294M
pro-forma cash, cash equivalents, and investments as of Sept 30, 2026[1]

Strong balance sheet
with runway through the end of 2028

$1.5B
potential R&D milestone payments from existing collaborations with BMS and LLY[2]

1 Includes the $15M milestone earned from Bristol Myers Squibb announced on August 13, 2026 and net proceeds from the $50M private placement financing announced on October 8, 2026
2 Receipt of such milestone payments are subject to the terms and conditions of the collaboration agreements with BMS and LLY, respectively, assigned to the Company in connection with the Separation and Distribution from Avidity

About Genetic Cardiomyopathies



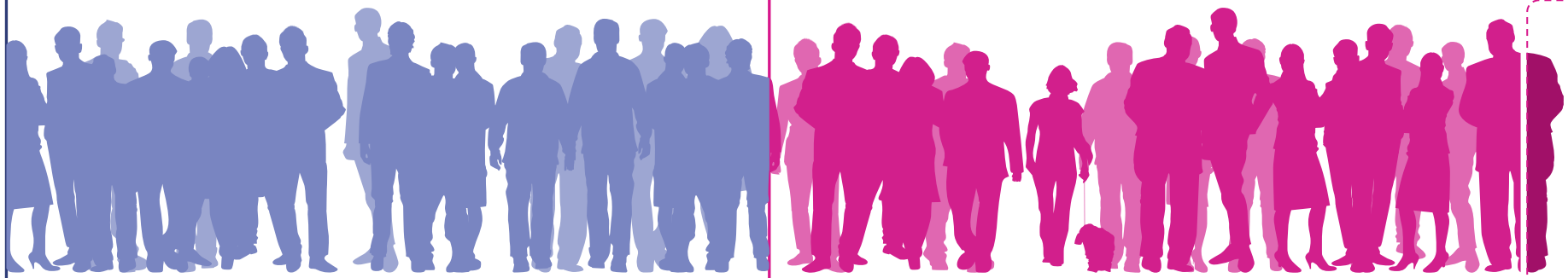
Millions of people with genetic cardiomyopathies lack disease-modifying treatments

Approximately 1% of patients with genetically driven cardiomyopathies are getting genetic testing[1]

~2 Million
diagnosed in the US[2]

50%
have underlying genetic driver of disease[3,4]

Most managed through symptom control[5]



Limited
targeted or etiology-specific therapies today[6]

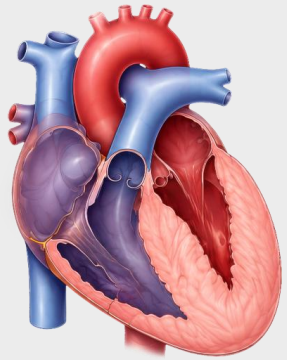
Opportunity for RNA-based precision therapies

[1]*Longoni, M. et al, "Real-world Utilization of Guideline-Directed Genetic Testing in Inherited Cardiovascular Diseases." Front. Cardiovasc. Med 10:1272433 (2023)*
[2]*Kramer,C. Et al, "Hypertrophic Cardiomyopathy Registry: The rationale and design of an international, observational study of hypertrophic cardiomyopathy. Am Heart J. 2015 Aug;170(2):223-30 and Ababio, Yaa et al, "Prevalence and Clinical Burden of Idiopathic Dilated Cardiomyopathy in the United States". Am J of Medicine Open Volume 10, 2023.*
[3]*Ho, CY. "Genotype and lifetime burden of disease in hyptertrophic cardiomyopathy*
[4]Cheng, Z,. et al, "Hypertrophic Cardiomyopathy: From Phenotype and Pathogenesis to Treatment". *Frontiers in Cardiovascular Medicine vol. 8 (2021).* DOI=10.3389/fcvm.2021.722340
[5]*Hutt, E, et al, "Medical Treatment Strategies for Hypertrophic Cardiomyopathy." American Journal of Cardiology vol 212, S33-41*
[6]*Aro, A. et al,* "Population Burden of Sudden Death Associated With Hypertrophic Cardiomyopathy". *Circulation vol 136 (2017)*

Three phenotypes across the genetic cardiomyopathy spectrum

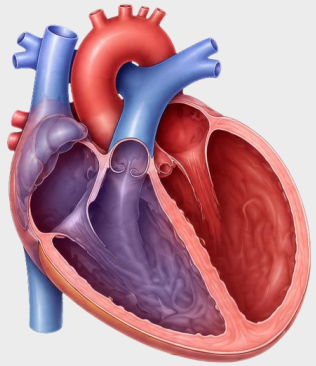
Changes in cardiac structure and function can present independently and in combination

Hypertrophic Cardiomyopathy *(HCM)*



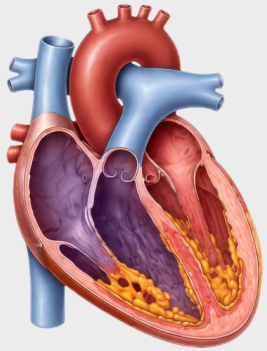
Dyspnea, chest pain, palpitations, syncope

Dilated Cardiomyopathy *(DCM)*



Fatigue, exertional dyspnea, fluid retention, arrhythmias, thromboembolic events

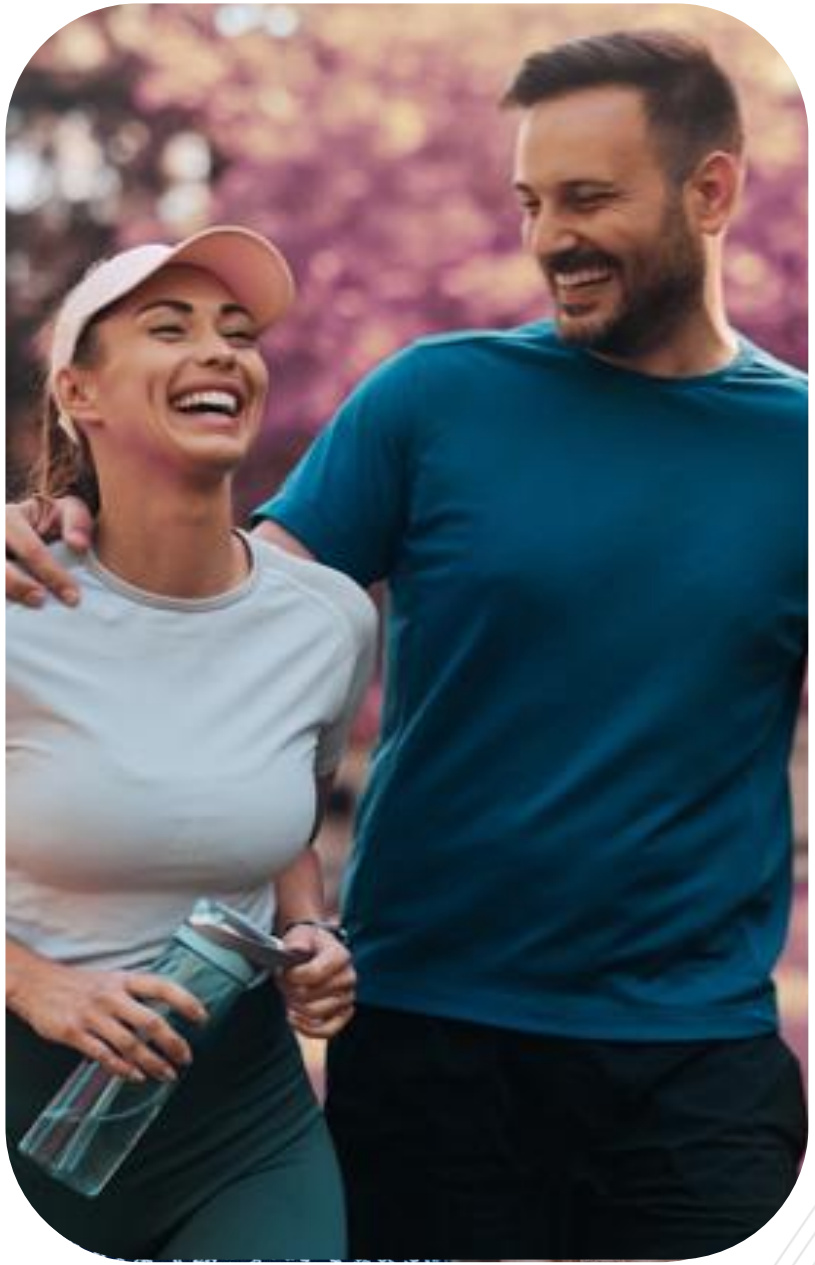
Arrhythmogenic Cardiomyopathy *(ACM)*



Palpitations, syncope, ventricular arrhythmias

ATR 1072

PRKAG2 Syndrome



PRKAG2 syndrome

A rare, progressive disease that can lead to sudden cardiac death

- Autosomal dominant disease caused by gene mutations in PRKAG2 that leads to AMPK overactivity resulting in glycogen accumulation in heart muscle
- Contributes to cardiomyopathy due to thickened heart muscles, electrical conduction problems and arrhythmias
- Causes heart failure and sudden cardiac death
- Current treatment limited to symptom management for arrhythmias and myocardial hypertrophy
- No therapy targeting root cause of disease
- Typically emerges during adolescence and early adulthood[1]

0
Approved therapies

1,000-2,000
People with PRKAG2 in the U.S.[2]

~100%
of people inheriting a pathogenic mutation will develop symptoms[3]

[1] van der Steld, L et al. "PRKAG2 syndrome, a rare hypertrophic cardiomyopathy: a Brazilian long-term follow-up with extracardiac disorders." *Einstein (Sao Paulo, Brazil)* vol. 22 eAO0549. 26 Jul. 2024, doi:10.31744/einstein_journal/2024AO0549
[2] Murphy, R, et al. "Adenosine Monophosphate-Activated Protein Kinase Disease Mimicks Hypertrophic Cardiomyopathy and Wolff-Parkinson-White Syndrome." Journal of the American College of Cardiology vol 45 (2005). doi:10.1016/j.jacc.2004.11.053
[3] Hu, D, et al. "Identification, clinical manifestation and structural mechanisms of mutations in AMPK associated cardiac glycogen storage disease."EBioMedicine 54 (2020) 102723

PRKAG2 syndrome prevalence likely exceeds our initial estimate

This work continues, building towards a confident view of the full population

Patient identification strategy is focused in three areas

1. **Uncover the already-diagnosed**
   Direct, bottom-up engagement with major genetic-testing labs
2. **Engage the patient community**
   Build presence and advocacy where patients already are
3. **Move the field of genetic testing**
   Partner across stakeholders to widen testing and recognition

Early findings to uncover the already diagnosed

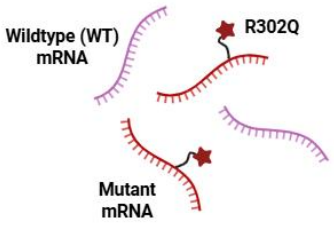
- **Our initial prevalence estimate of 1,000 - 2,000[1] PRKAG2 syndrome patients** was conservative based on published literature
- Early efforts have **already uncovered close to 2,000 individuals with** the PRKAG2 mutation so far from only a subset of engaged labs[2]
- **True population likely larger** - still unmeasured

[1] Murphy, R, et al. "Adenosine Monophosphate-Activated Protein Kinase Disease Mimics Hypertrophic Cardiomyopathy and Wolff-Parkinson-White Syndrome." Journal of the American College of Cardiology vol 45 (2005). doi:10.1016/j.jacc.2004.11.053
[2] Data on file: Internal sources based on discussions with genetic testing providers

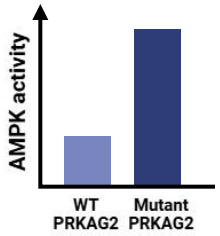
ATR 1072 designed to silence mutant PRKAG2 to normalize AMPK activity

Mechanism of Disease

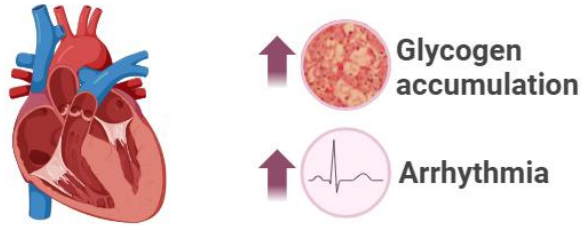
PRKAG2 is the regulatory component of AMPK



Mutant PRKAG2 leads to overactivation of AMPK

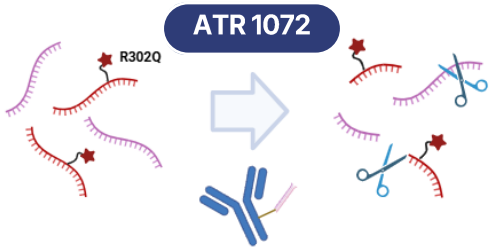


Hypertrophic cardiomyopathy (HCM) characterized by glycogen accumulation and arrhythmia



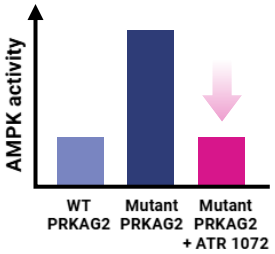
Therapeutic Approach

ATR 1072-mediated degradation of cardiac PRKAG2 mRNA

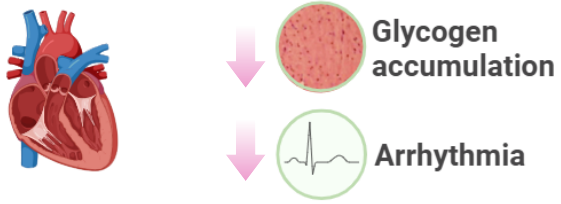


= Targeted siRNA-mediated RNA degradation

Reduced mutant PRKAG2 leads to normalization of AMPK activity

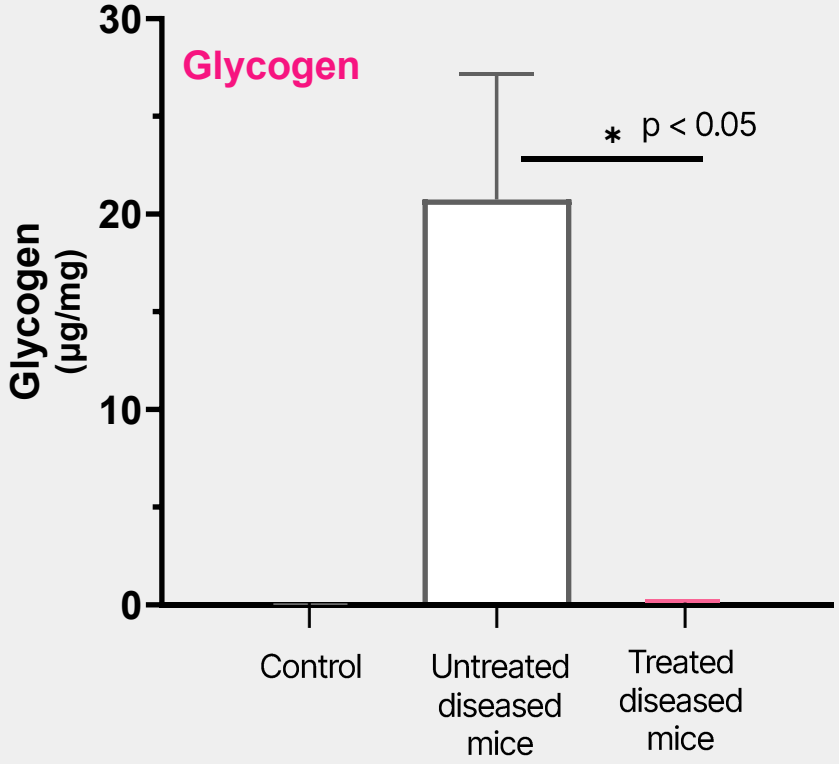


Attenuates HCM disease progression



Targeting PRKAG2 mRNA in the heart led to reversal of glycogen accumulation as well as improvement in other key features of the disease in nonclinical model[1]

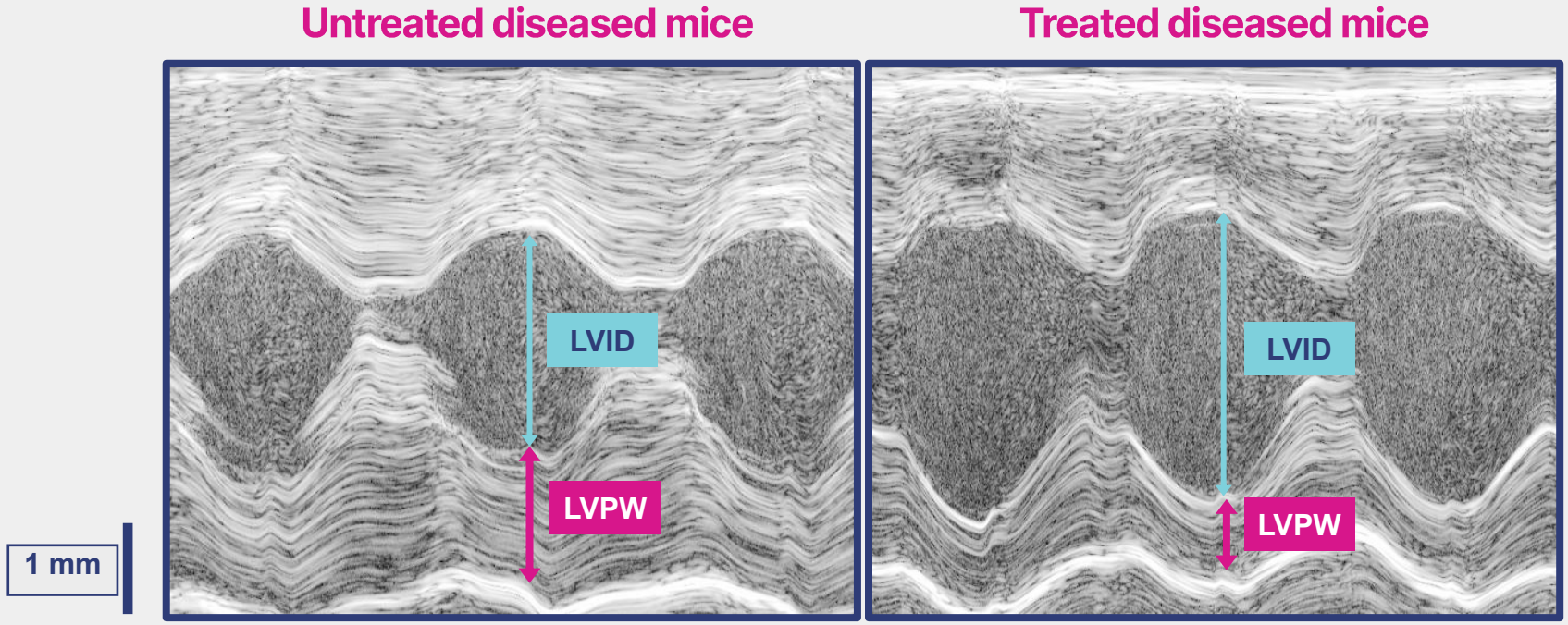
- Encouraging results in measures of hypertrophy include reduction in heart weight and left ventricular wall thickness
- Treatment also led to improvement in ECG parameters measuring electrical conduction including PR interval
- Further reinforces scientific rationale for ATR 1072 targeting the root cause of PRKAG2 syndrome
- Reversibility of downstream parameters consistent with earlier nonclinical data



[1] Data on file: Mice received PRKAG2^{R302Q} AAV for 3 wk followed by mATR 1072 (single dose 3 mg/kg, siRNA component), a mouse-active surrogate of ATR 1072. Data presented at 4 wk post mATR 1072; mean ± SD, n=9-10/grp. *One-Way ANOVA

ATR 1072 improved measure of cardiac hypertrophy in echocardiogram in nonclinical model[1]

Cardiac wall thickness decreased at 4 weeks after treatment

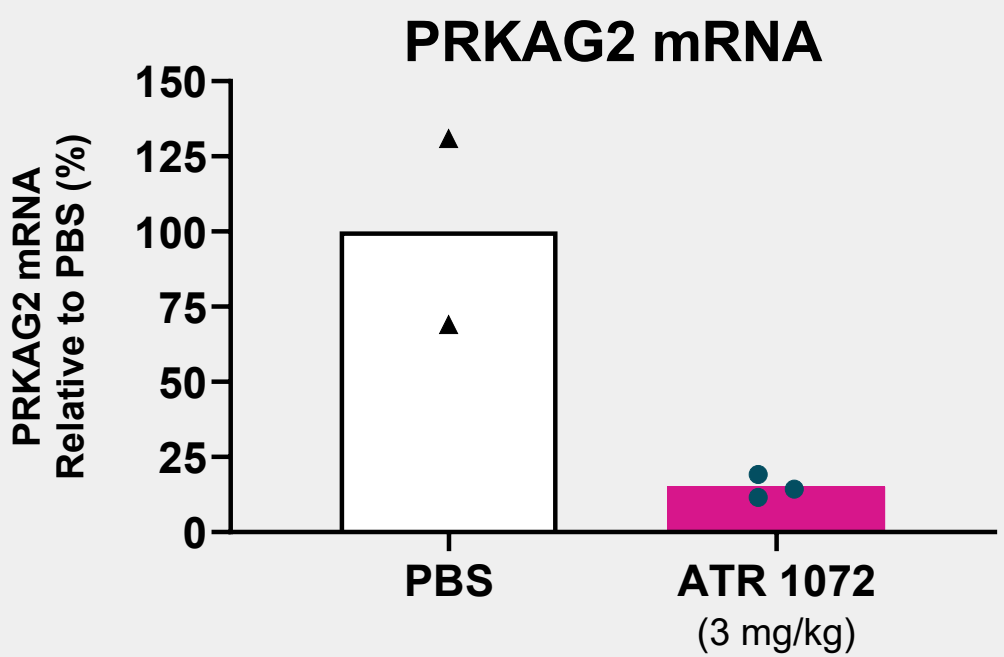


LVID: Left ventricular internal diameter; LVPW: Left ventricular posterior wall thickness

[1] Data on file. This is a representative echocardiogram image.

ATR 1072 has a favorable nonclinical safety profile and robust target knockdown[1]

ATR 1072 activity in monkey heart following a single dose at 28 days of treatment



ATR 1072 was generally well tolerated in 9-month, repeat dose chronic toxicity study in cynomolgus monkey

- No dose limited toxicity in any organ system at the highest dose tested
- No effects on cardiac function associated with PRKAG2 mRNA reduction including assessments of ECG, echocardiogram, histopathology

[1] Data on file: Based on preclinical studies

ATR 1072: First trial targeting PRKAG2 syndrome ongoing

corventis™
PRKAG2 SYNDROME PHASE 1/2 CLINICAL TRIAL

Initial trial data demonstrating proof of concept anticipated in 2H 2027

48-week treatment

PART A - Dose Escalation*

Cohort A1	Cohort A2	Cohort A3
40 mg	80 mg	160 mg
n = 4	n = 4	n = 4

Safety review committee evaluation prior to dose escalation

PART B - Expansion

Cohort B

Recommended Ph 2 dose
n = 25

Long-Term Extension

All participants

Open label adaptive trial design
~37 participants enrolled, **~15** sites globally

Adults (18-65 yrs) w/ confirmed PRKAG2 mutation and cardiac phenotype consistent with PRKAG2 syndrome

Primary endpoint: Incidence of treatment-emergent adverse events (TEAEs)

Secondary endpoints: PRKAG2 mRNA reduction and siRNA tissue concentrations (cardio biopsy in Part A only), plasma PK

Exploratory endpoints: Echocardiogram, ECG and Holter parameters, biomarkers, immunogenicity, clinical outcomes, and optional cardiac MRI findings

* Dose based on siRNA weight; flat dosing IV Q6W Equivalent to 0.5, 1.0, 2.0 mg/kg

ATR 1086

PLN Cardiomyopathy



PLN Cardiomyopathy

A rare progressive disease with frequent family history

- PLN-R14del is the most common disease-relevant PLN mutation
- Mutant PLN-R14del forms aggregates and impairs cardiomyocyte function
- Characterized by dilated, arrhythmogenic or hypertrophic cardiomyopathy
- Notable for frequent family history of premature sudden cardiac death and progressive cardiac failure
- High incidence of sudden cardiac death, ventricular arrhythmias and cardiac transplantation
- Current treatment focuses on symptom management[1]
- No therapy to target root cause of disease

0
Approved therapies

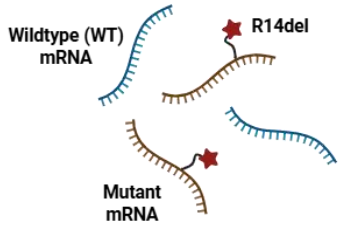
2,000-4,000
People with pathogenic PLN variants in the U.S.[2]

[1] Vafiadaki E, et al. "Phospholamban R14del disease: The past, the present and the future." Frontiers in Cardiovascular Medicine vol 10 (2023). doi:10.3389/fcvm.2023.1162205
[2] Internal sources based on discussions with genetic testing providers

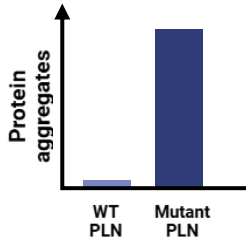
ATR 1086: Designed to silence mutant PLN to prevent protein aggregates and target root cause of disease[1]

Mechanism of Disease

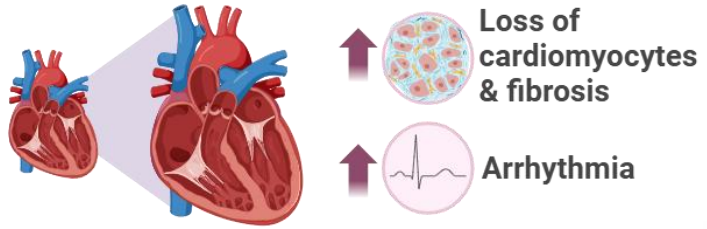
Phospholamban (PLN) regulates Ca2+ handling in cardiomyocytes



R14del mutation on PLN causes PLN to form protein aggregates

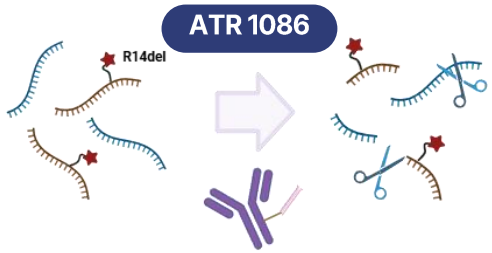


Dilated and Arrhythmogenic cardiomyopathy (DCM & ACM)



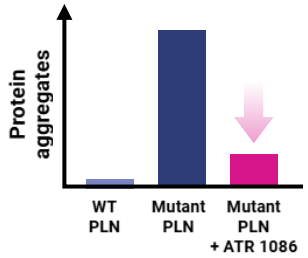
Therapeutic Approach

ATR 1086 mediated degradation of cardiac PLN mRNA

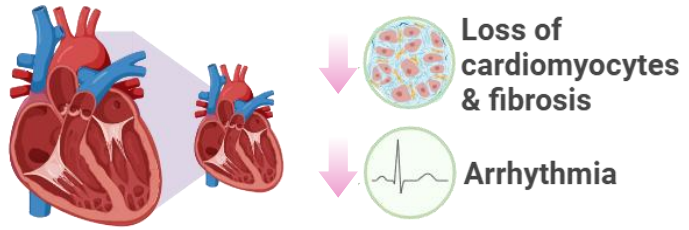


= Targeted siRNA-mediated RNA degradation

Reduced mutant PLN prevents protein aggregate formation



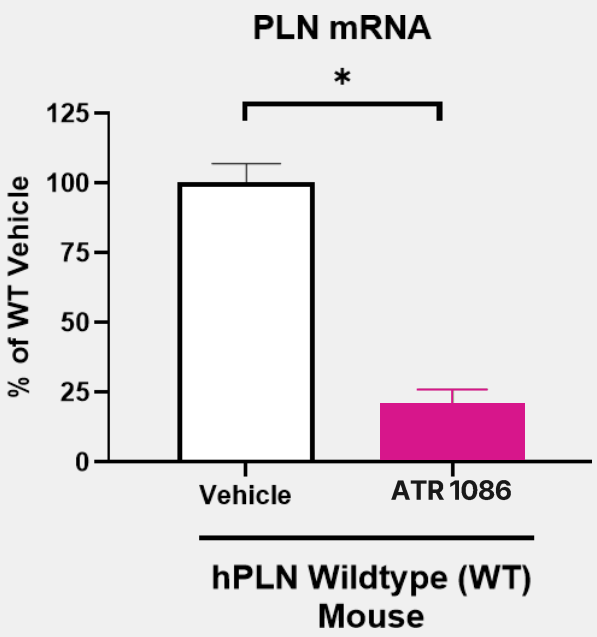
Attenuates DCM & ACM disease progression



[1] Data on file: Based on preclinical studies

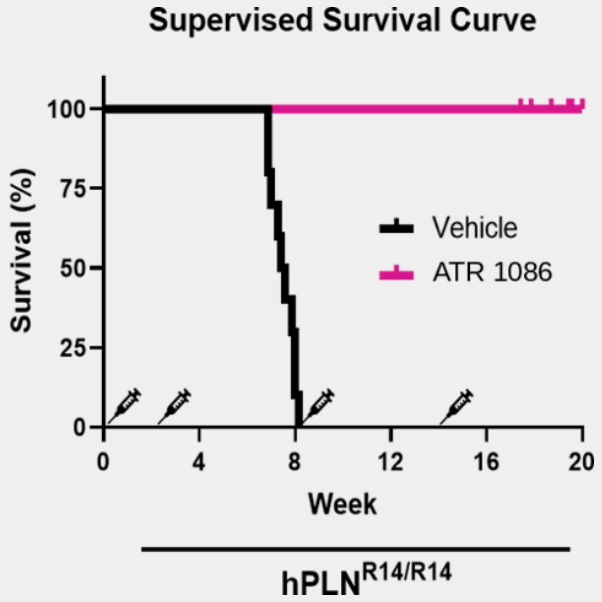
ATR 1086 demonstrates functional improvement and survival in preclinical model of disease[1]

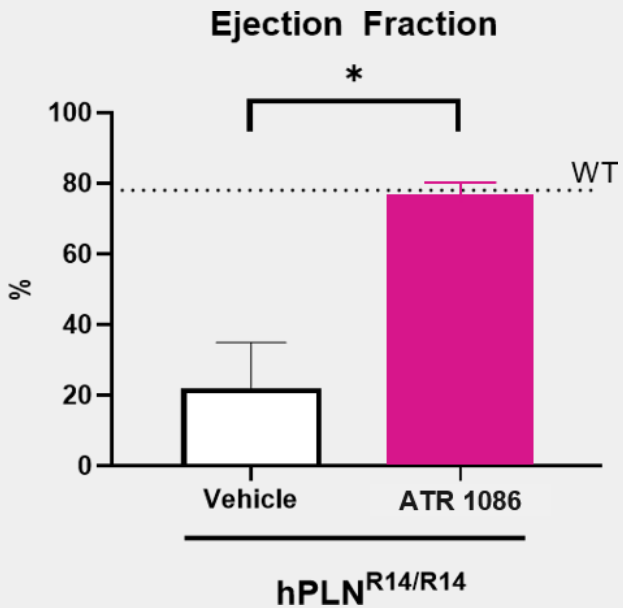
Reduction of human PLN expression in the heart following treatment with ATR 1086 (6 mg/kg)



PLN mRNA levels were measured in cardiac tissue in transgenic mice expressing hPLN WT.

Improved survival (Kaplan-Meier survival curve) and ejection fraction following repeated ATR 1086 treatment (6 mg/kg) in a humanized mouse model of hPLNR14/R14





Ejection fraction measured at 6-weeks of treatment. Dotted lines indicate WT levels. Data are presented as mean ± SEM. Student's t-test, * $p < 0.05$.

[1] Data on file: Based on preclinical studies

Expansion Opportunities for ATR 1072 and ATR 1086

A biology-driven pipeline with multiple indication expansion opportunities



ATR 1072 and ATR 1086 have opportunities for indication expansion beyond a single genetically defined population

Central Pathways in Cardiac Function

AMPK

Energy sensing
PRKAG2 regulates AMPK activity, the key energy sensor in the heart

ATR 1072

Opportunities for Indication Expansion

AMPK dysregulation is implicated across multiple genetic cardiomyopathies beyond PRKAG2 syndrome

Ca^{2+}

Calcium handling
PLN inhibits SERCA2a, an essential mediator of calcium cycling

ATR 1086

Influencing calcium cycling may improve diastolic function in multiple cardiomyopathies beyond PLN cardiomyopathy

Atrium is accelerating momentum post-launch, with strong execution and multiple milestones ahead

	Achievements	Anticipated Upcoming Milestones
ATR 1072	☑ GMP manufacturing ☑ IND clearance and NOL ☑ First patient dosed in Corventis™ Ph 1/2 trial	☐ Initial proof-of-concept data in 2H 2027
ATR 1086	☑ Identified lead candidate ☑ Preclinical proof-of-concept ☑ GMP manufacturing and IND-enabling studies initiated	☐ IND filing in 2027
Rare cardiomyopathies	☑ Identified two promising targets	☐ Third development candidate in 2027

Atrium has the expertise, leadership and focused pipeline to deliver in precision cardiology

Platform

Proprietary RNA delivery platform ideal for precision cardiology

Pipeline

Focused pipeline with indication expansion opportunities

Execution

Strong balance sheet with experienced leadership team

IR Contact

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ATRIUM THERAPEUTICS™