ENPP1 Deficiency Program Update Conference Call

July 26, 2023

Callum
Living with
ENPP1 Deficiency

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This presentation and any statements made orally during this presentation contain estimates and other statistical data made by independent parties and by us relating to market size and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such data and estimates. In addition, projections, assumptions and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk. Neither Inozyme Pharma, Inc. nor its affiliates, advisors or representatives make any representations as to the accuracy or completeness of that data or undertakes to update such data after the date of this presentation.

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Statements in this presentation about future expectations, plans, and prospects, as well as any other statements regarding matters that are not historical facts, may constitute forward-looking statements that involve substantial risks and uncertainties. These statements include, but are not limited to, statements relating to the initiation, timing and design of our clinical trials, our research and development programs, the availability of preclinical study and clinical trial data, planned regulatory filings, the timing of planned launch of INZ-701, if approved, and the period over which we believe that our existing cash, cash equivalents and short term investments will be sufficient to fund our operating expenses.

The words “anticipate,” “believe,” “continue,” “could,” “estimate,” “expect,” “intend,” “may,” “might,” “plan,” “potential,” “predict,” “project,” “should,” “target,” “will,” “would” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. We may not actually achieve the plans, intentions or expectations disclosed in these forward-looking statements, and you should not place undue reliance on these forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in these forward-looking statements. For a discussion of risks and uncertainties, and other important factors, any of which could cause our actual results to differ from those contained in the forward-looking statements, see the “Risk Factors” section in our most recent Annual Report on Form 10-K filed with the Securities and Exchange Commission, as well as discussions of potential risks, uncertainties and other important factors, in the Company’s most recent filings with the Securities and Exchange Commission.

In addition, the forward-looking statements included in this presentation represent our views as of the date of this presentation. We anticipate that subsequent events and developments will cause our views to change. However, while we may elect to update these forward-looking statements in the future, we specifically disclaim any obligation to do so. These forward-looking statements should not be relied upon as representing our views as of any date subsequent to the date of this presentation.

Inozyme is at the forefront of developing transformative therapies for rare diseases of pathologic mineralization and intimal proliferation

- ✓ **ENPP1 Deficiency is a serious disease with no approved therapies**
  - Substantial population: 10K+ patients expected in major addressable markets; >550 confirmed or known patients identified, with evidence for >200 additional patients based on medical record screen
  - INZ-701 has demonstrated rapid, significant, and sustained increase in plasma pyrophosphate (PPi) levels and exhibited a favorable safety profile in ongoing clinical trial of adult patients with ENPP1 Deficiency
- ✓ **Defined path to global regulatory approvals with FDA and EMA**
  - Finalized pediatric pivotal trial design with PPi as primary endpoint in US, supported by trends in appropriate secondary endpoints, and co-primary endpoint (RGI-C of $p<0.2$) in EU for pediatric pivotal trial
  - Pediatric pivotal trial planned for Oct. 2023 – Topline data expected mid-2025
  - Launch targeted as early as 2H 2026 in infants and pediatric patients, if approved
- ✓ **In a position of financial strength, with several anticipated upcoming milestones and a pipeline designed for long-term value creation**
  - $140.2M* expected to fund operations into Q1 2025; 46.4M common shares outstanding**
- ✓ **Experienced team with a track record of success in rare disease and a strong focus on execution**

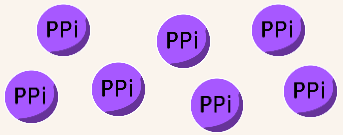
*Represents cash, cash equivalents & short-term investments as of 6/30/23, The estimated cash figure is preliminary and unaudited, represents a management estimate as of the date of this presentation and is subject to completion of our financial closing procedures, **As of 6/30/23

Yves Sabbagh, Ph.D.

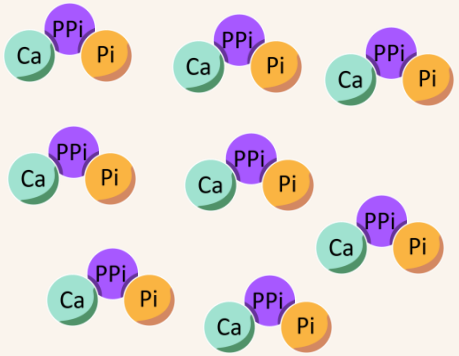
SVP and Chief Scientific Officer

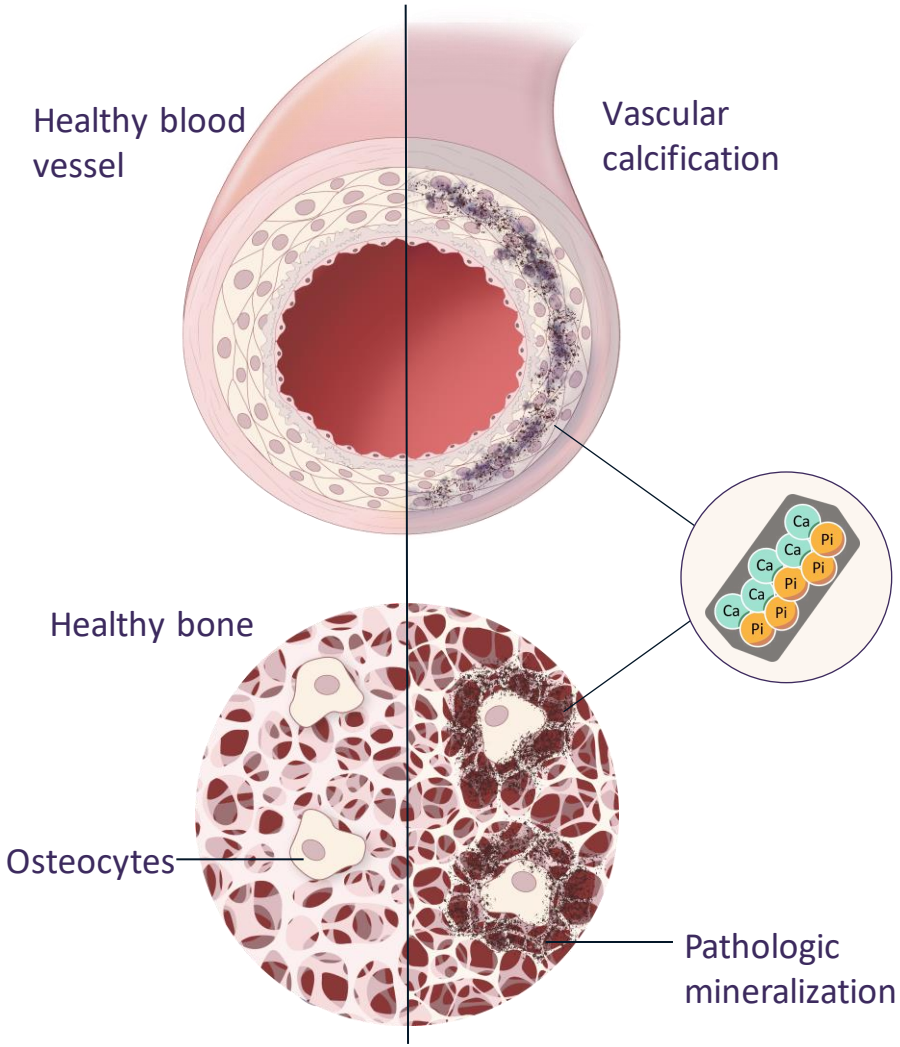
PPi is a master regulator of mineralization

Normal levels of PPi



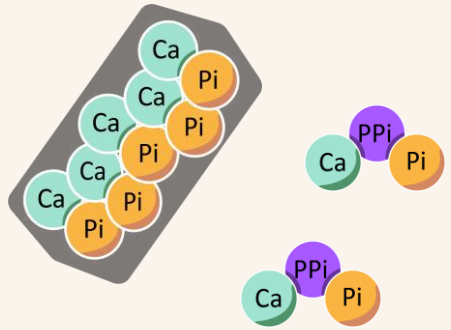
PPi prevents and inhibits Ca-Pi crystal formation





Low levels of PPi

Low PPi leads to Ca-Pi crystal formation

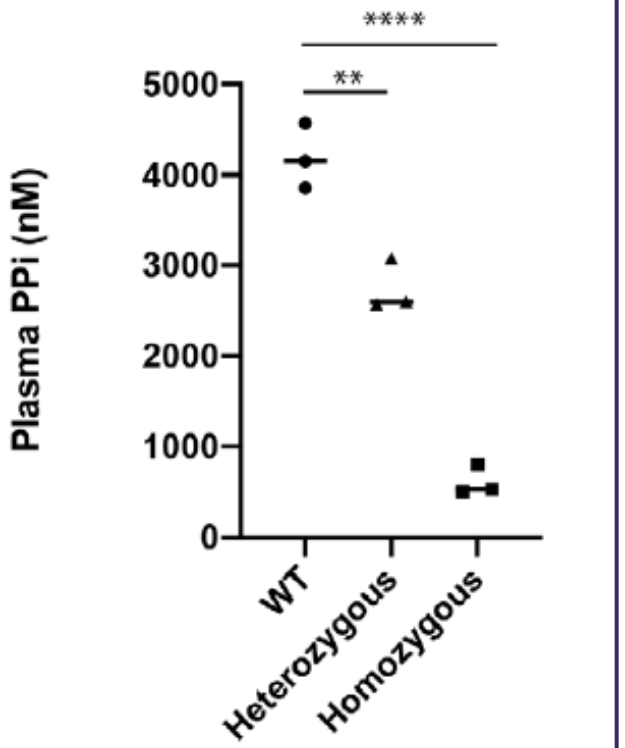


Inorganic pyrophosphate (PPi) PPi Calcium Ca Phosphate Pi

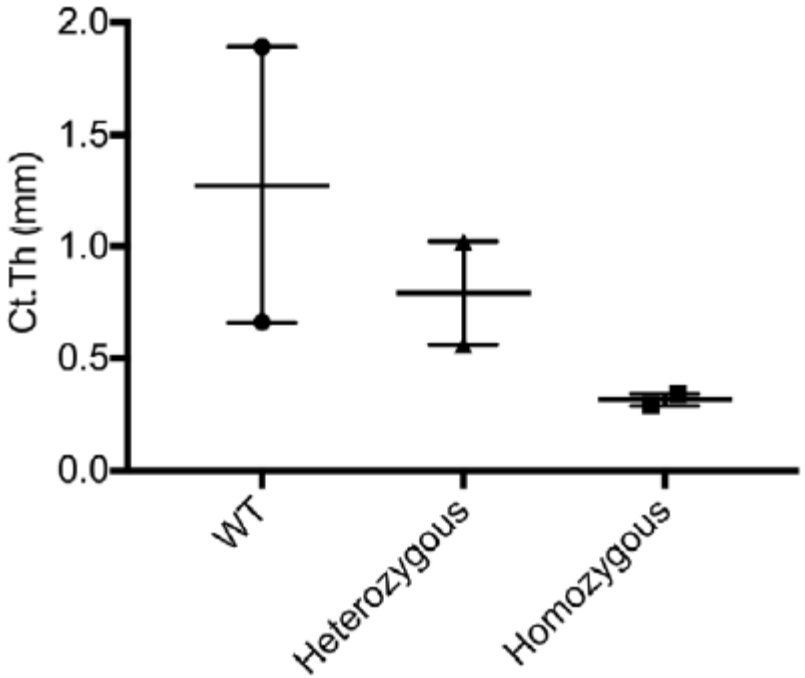
Correlation of PPi levels with skeletal phenotypes in humans

A continuum in skeletal phenotype severity and PPi levels

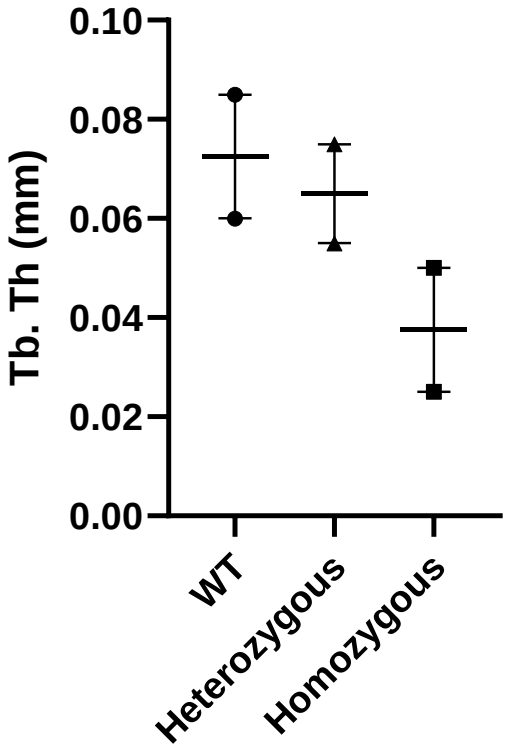
Plasma PPi



Cortical Bone Thickness



Trabecular Bone Thickness



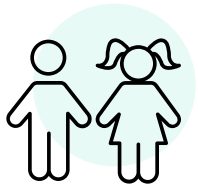
Adapted from Oheim et. Al, JBMR 2019

Burden of ENPP1 Deficiency across age spectrum

GACI/IIAC
0-1 Years

50% mortality within 6 months of birth

Severe cardiovascular complications

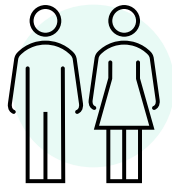


ARHR2 (Rickets)
1-13 years

Impaired growth
Orthopedic surgery

Skeletal defects: Rickets

Hearing loss



ARHR2 (Osteomalacia)
13+ Years

Bone & joint pain and stiffness
Immobility

Skeletal defects: Osteomalacia

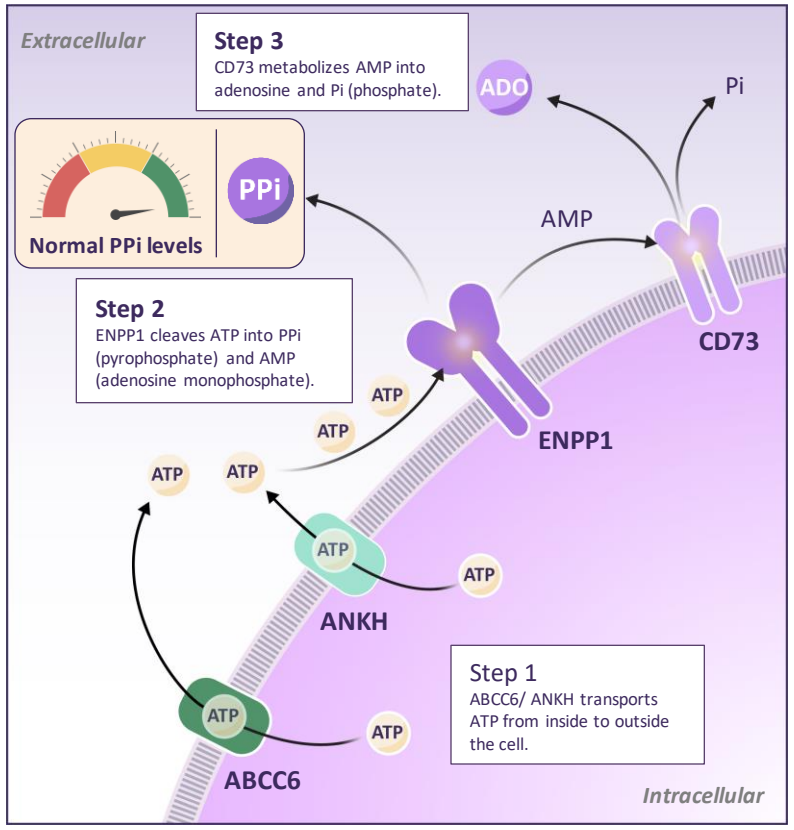
Hearing loss

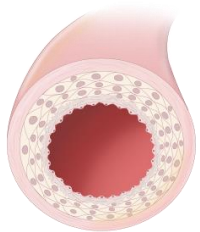
Joint, tendon, and ligament complications

GACI: Generalized Arterial Calcification of Infancy, IIAC : Idiopathic Infantile Arterial Calcification, ARHR2: Autosomal Recessive Hypophosphatemic Rickets Type 2

ENPP1 enzyme is the primary driver of plasma PPi levels

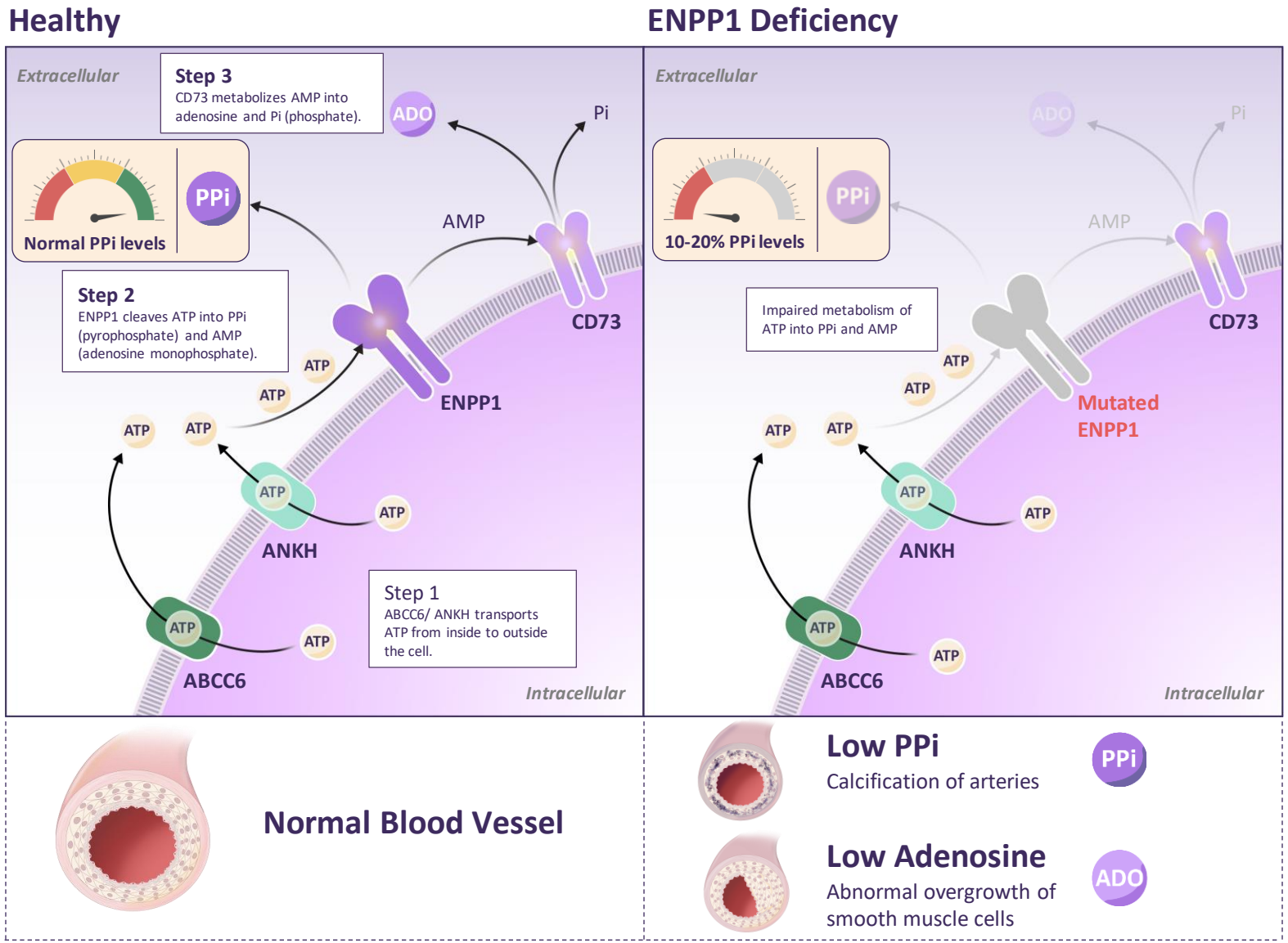
Healthy



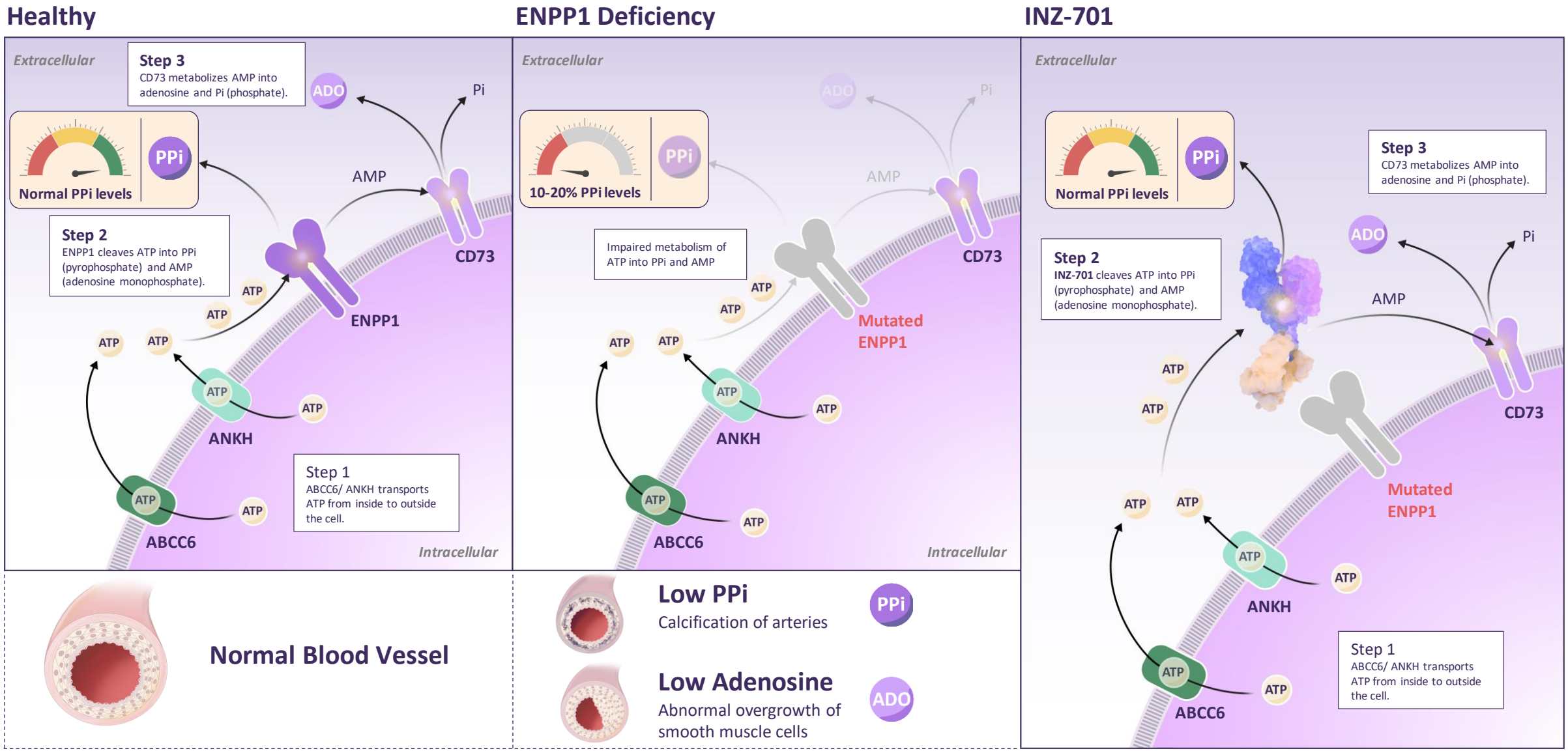


Normal Blood Vessel

Mutated ENPP1 enzyme leads to low plasma PPi levels



INZ-701 is designed to increase PPi levels in ENPP1 Deficiency

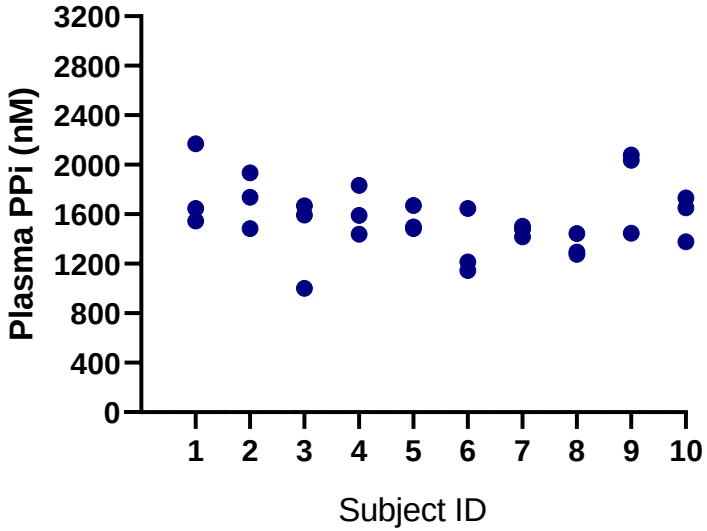


Established a validated, sensitive and reproducible PPi assay

PPi Assay

- Adenosine triphosphate (ATP) sulfurylase/luminescence-based method to measure PPi in human plasma
- Validation was performed following FDA Guidance for Industry: Bioanalytical Method Validation (May 2018) to demonstrate method performance characteristics are fit for their intended use

Healthy Subject PPi levels

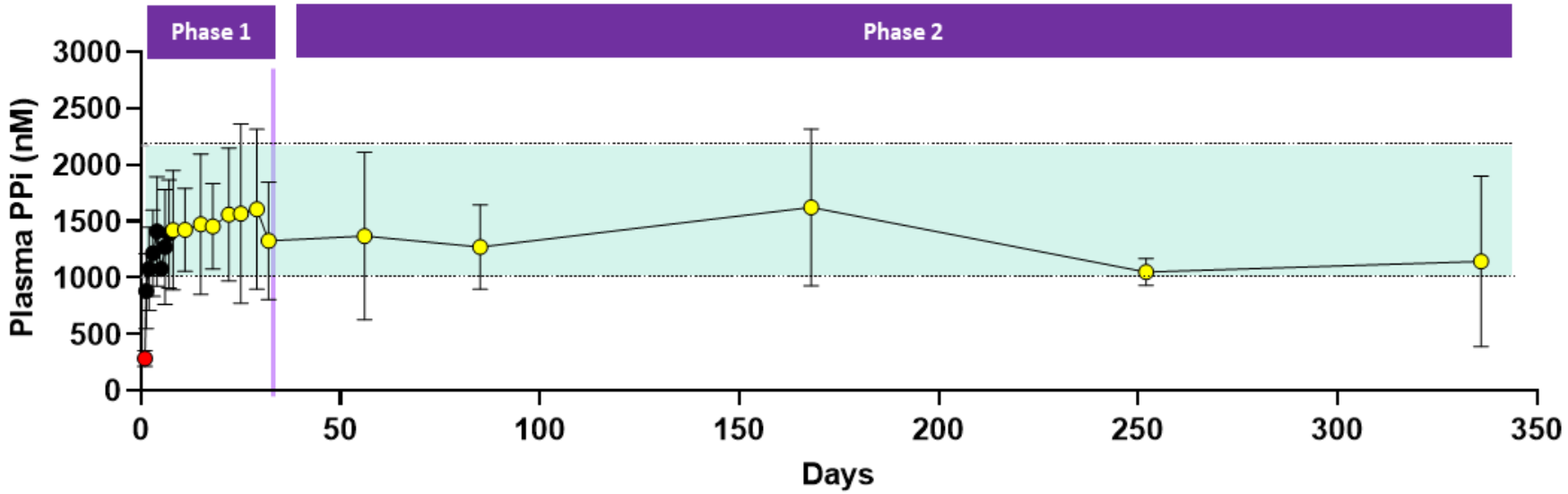


- Subjects aged 18-30 yrs old
- 3 values/subject
- Collected after overnight fast

(Khursigara et al, Bone 2023)

INZ-701 rapidly increased PPi levels within 6hrs of first dose and normalized levels were sustained in ongoing adult ENPP1 trial

Cohort 1 (0.2mg/kg)



- Baseline PPi (pre-dose) + 1st INZ-701 dose
- PPi measurement (post-dose)
- PPi measurement (pre-dose)
- Healthy subject PPi levels (n=10)

Data cut January 25, 2023; Cohort 1: n=2 post week 12. Data presented as mean± SD.

Kurt Gunter, M.D.

SVP and Chief Medical Officer

Key regulatory and clinical milestones for INZ-701 in ENPP1 Deficiency

Regulatory

- ✓ Fast Track Designation in US
- ✓ Orphan Designation in US and EU
- ✓ Rare Pediatric Disease Designation in US (priority review voucher eligibility)
- ✓ Paediatric Investigation Plan (PIP) agreed with EMA
- ✓ Finalized pediatric pivotal trial design
- ❑ Breakthrough Therapy Designation

Clinical

- ✓ Completed enrollment in first 3 cohorts of adult trial; fourth cohort of INZ-701 at 1.2 mg/kg (n=3) added to evaluate once weekly dosing
- ✓ Initiated ENERGY-1 phase 1b trial in infants (1-12 mos.)
- ❑ Interim clinical update from first 3 cohorts in adult trial expected in Sep. 2023
- ❑ On track to initiate ENERGY-3 pivotal trial in pediatric patients (≥1 to <13 yrs.) in Oct. 2023

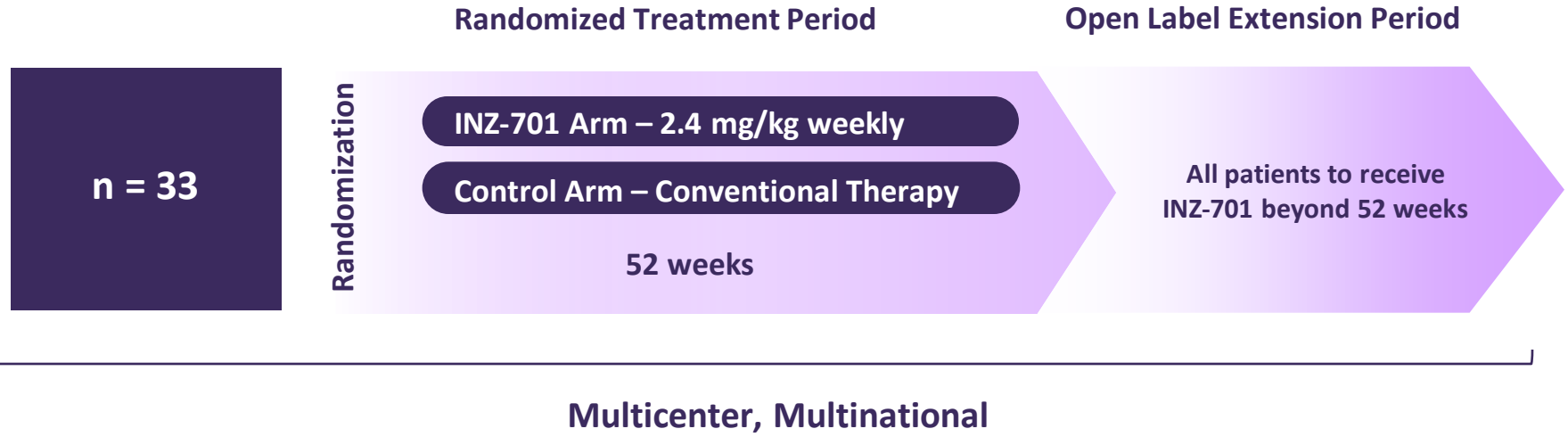
ENERGY-3: ENPP1 Deficiency Pediatric Pivotal Trial (ARHR2)

Initiation planned for October 2023

Population: *Pediatric*

- Confirmed genetic diagnosis
- Radiographic evidence of skeletal abnormalities
- ≥1 year and <13 years
- Low plasma PPi

Design: Randomized (2:1), Open Label



Endpoints

US

- **Primary**: Change in plasma PPi from baseline over time
- **Secondary**: Trends in RGI-C score, RSS, Growth Z-score; PK

EU

- **Co-Primary**:
  - Change in plasma PPi from baseline over time
  - RGI-C score (with $p<0.2$)
- **Secondary**: RSS, Growth Z-score; PK

RGI-C: Radiographic Global Impression of Change, RSS: Rickets Severity Score, PK: Pharmacodynamic, ARHR2: Autosomal Recessive Hypophosphatemic Rickets Type 2

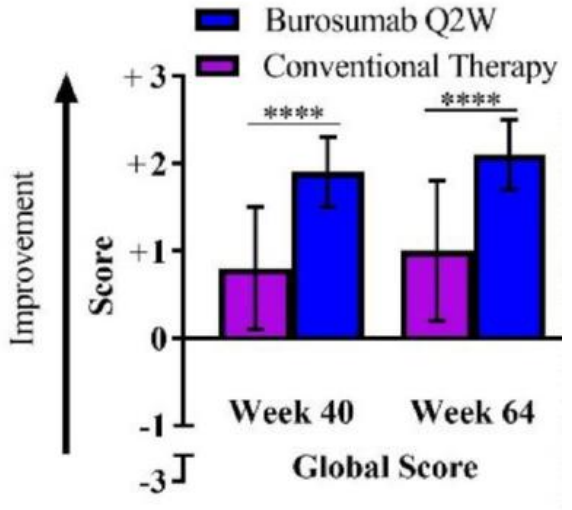
RGI-C (Radiographic Global Impression of Change): An accepted quantitative score for rickets/skeletal abnormalities

- RGI-C has supported the approval of therapies for other genetic forms of rickets

Whyte et al, J Bone Min Res, 33:868, 2018

- Each form of rickets has disease-specific radiographic features
  - We are currently developing an RGI-C specific for ENPP1 Deficiency
  - Scoring system based on extensive natural history x-ray database

Burosumab treatment in XLH resulted in RGI-C of +1.9 vs +0.8 for conventional therapy at week 40



****p<0.0001

Imel et al, Lancet, 393: 2416, 2019

RGI-C: Radiographic Global Impression of Change, XLH: X-Linked Hypophosphatemia

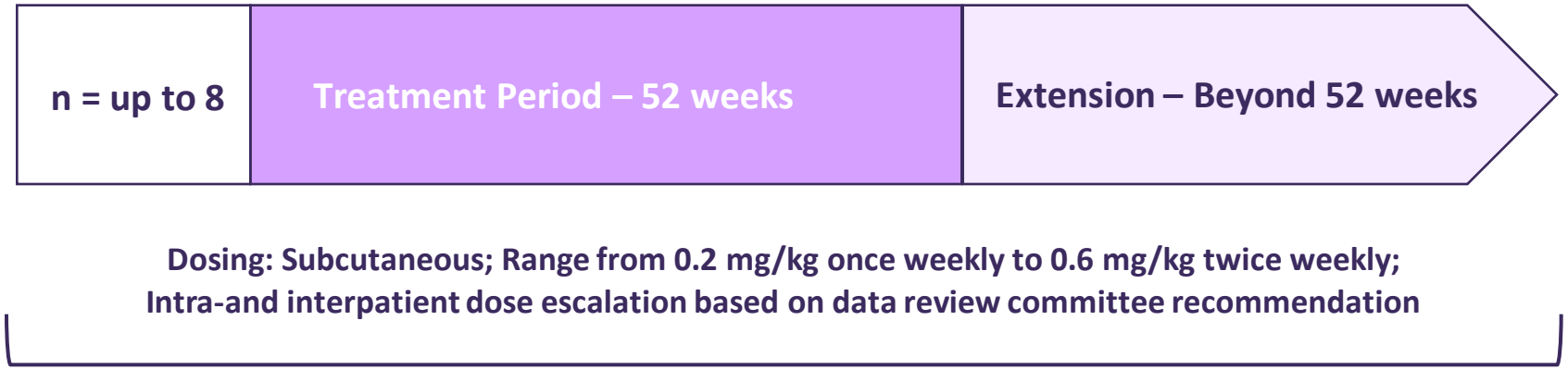
ENERGY-1 Trial: Phase 1b in infants with ENPP1 Deficiency (GACI)

Initiated in Q2 2023

Population: *Infant*

- 1-12 months
- Confirmed genetic diagnosis

Design: Single arm, Open Label



Endpoints:

Primary

- **Safety** and **tolerability** of INZ-701

Additional

- Plasma **PPi**
- **Survival**, **growth**, **development**, **functional performance**, **cardiac function**, **biomarkers** related to **bone** and **mineral metabolism**, healthcare utilization

clinicaltrials.gov: NCT05734196
GACI: Generalized Arterial Calcification of Infancy

Planned Path to Global Approval of INZ-701 in ENPP1 Deficiency

ENERGY-1: Infant (1-12 mos.)
Phase 1b
Single arm (n=8)

Endpoints

Safety** and **tolerability

ENERGY-2: Infant (0-12 mos.)
Pivotal
Single arm per agreed PIP** (n=12)

***PPi + survival** as co-primary*

ENERGY-3: Pediatric (≥1-<13 yrs.)
Pivotal
Randomized – 2:1 (n=33)

***PPi** as sole primary* (US) and co-primary with **RGI-C** (EU)*

ENERGY-4: Adolescent and Adult (13+)
Pivotal
Randomized – 2:1 (n=30)***

***PPi** as sole primary* (US) and co-primary with **BMC/BMD** expected (EU)*

*Supported by trends in appropriate secondary endpoints
**Plan to conduct this trial ex-U.S.. Discussions are ongoing with FDA regarding design of this trial in the U.S.
***Subject to regulatory discussions and appropriate financial resources

Basis for Planned Marketing Applications

1st BLA/MAA

- Adult Phase 1/2 full data
- ENERGY-3 full data
- ENERGY-1 available data
- ENERGY-2 available data
  - Natural history control group; patients matched on covariates associated with mortality

Additional filings

- ENERGY-4 full data (Supplemental BLA/MAA)
- Japan, Brazil, Middle East

RGI-C: Radiographic Global Impression of Change, BMC/BMD: Bone mineral content/density, BLA: Biologics license application, MAA: Marketing authorisation application

Matt Winton, Ph.D.

SVP and Chief Operating Officer

Potential to deliver approved therapy for ENPP1 Deficiency and capitalize on significant commercial opportunity

Sizeable patient population with high unmet need

Connected, collaborative, and motivated patient community

Aligned KOLs/HCPs at well known global centers of excellence

Inozyme Readiness

- 10,000+ patients expected in major addressable markets – North America, Europe, Japan, Brazil, and Middle East
- Advancing understanding of the genetic prevalence – Estimated 1:64,000[1] pregnancies worldwide

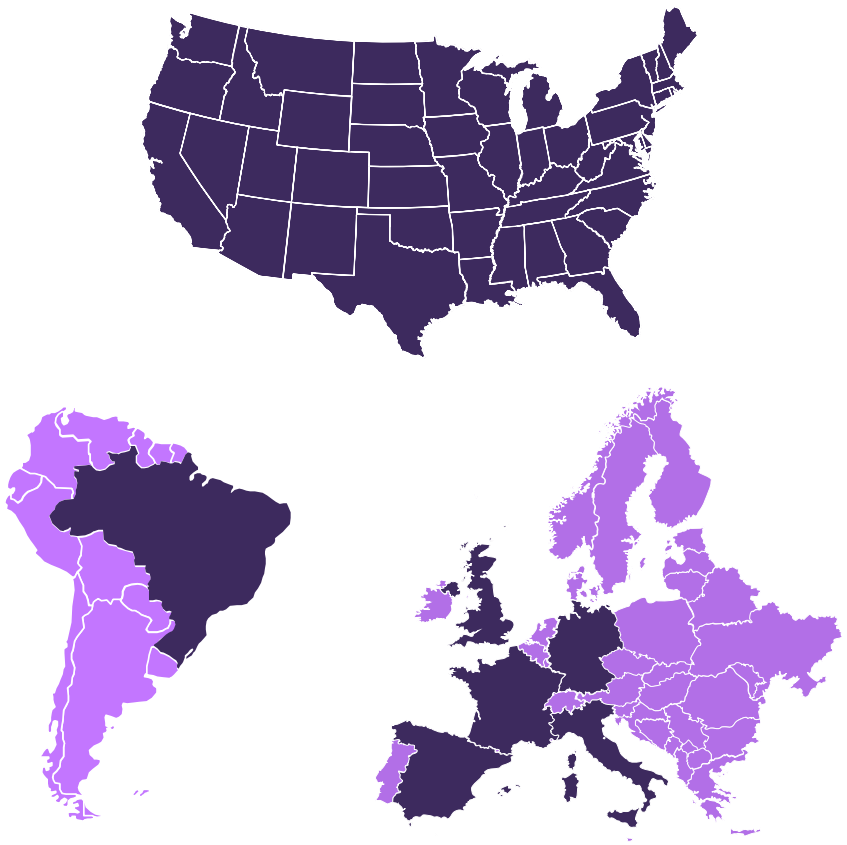
- Building strong relationships with patient and caregiver community
- Supporting programs and research partnerships to further characterize disease burden

- Executing data generation strategy to drive scientific leadership
- Broadening reach to increase awareness of HCPs and improve time to diagnosis

Source: 1. Ferreira et al. Orphanet Journal of Rare Diseases, 2022.

Ongoing efforts to increase disease awareness, educate patient and medical communities, and improve access to genetic testing

Growing Our Global Footprint



Currently evaluating Inozyme presence in Japan and Middle East

Expanding HCP Audience

Infant and Pediatric ENPP1

- Fetal and pediatric cardiology
- Neonatology
- Pediatric endocrinology
- Mamaternal-fetal medicine
- Genetics

Adult ENPP1

- Endocrinology
- Nephrology
- Genetics
- Bone specialists

Increasing Congress Attendance

NeoHeart Cardiovascular Management of the Neonate

Society for Maternal-Fetal Medicine

PES Pediatric Endocrine Society

ASHG American Society of Human Genetics

ASBMR The American Society for Bone and Mineral Research

Human Growth Foundation

ECTS European Calcified Tissue Society

8th World Congress of Pediatric Cardiology and Cardiac Surgery

Partnering to Remove Barriers to Diagnosis

ipm.ai PART OF REAL CHEMISTRY

BeginNGS NEWBORN GENOMIC SEQUENCING to end the diagnostic odyssey

GENOMENON®

PREVENTION GENETICS

INVITAE

BlueDil int'l

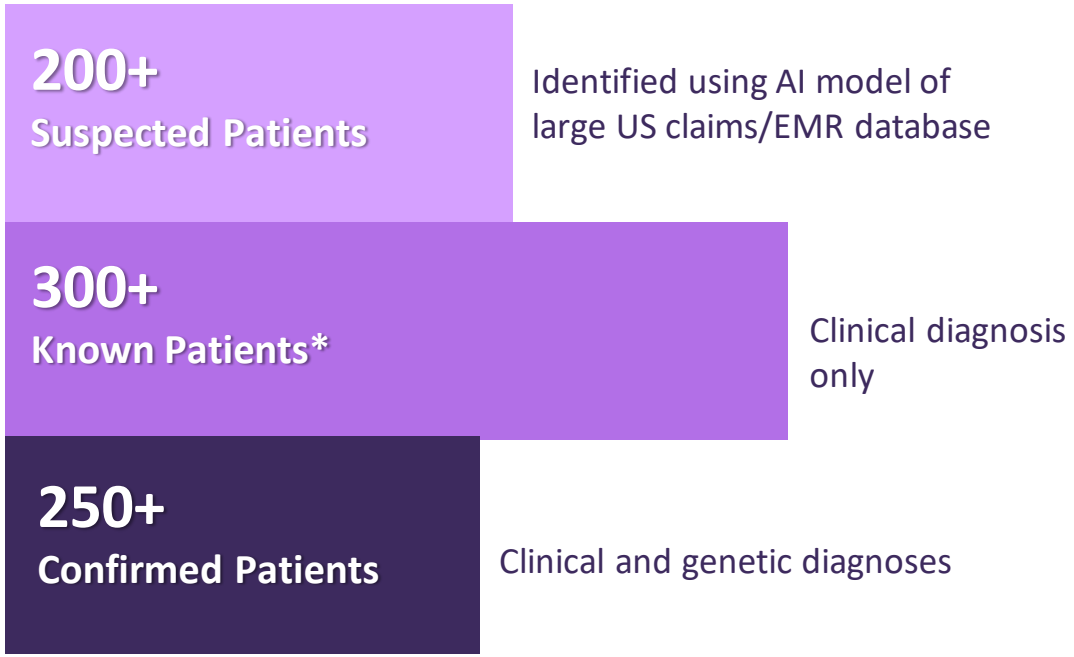
GACI Global circulating hope

CENTOGENE

Rady Children's

Experienced team continues to make strong progress identifying patients

750+ Global patients identified with **confirmed, known, or suspected** ENPP1 Deficiency



Internal data as of 5/31/23

- ~50 patients identified since last update; progress to-date is in line or ahead-of select rare disease analogs**
- Inozyme patient database currently enriched for pediatric patients
  - Plan to leverage consented patients >1 to <13 years of age to support timely trial enrollment of ENERGY-3
  - Global newborn screening and genetic testing partnerships to support ENERGY-1 and will support ENERGY-2 enrollment
- Number of identified patients increasing rapidly with patient/physician education, initiation of clinical trials, and progress towards potential regulatory approval

* Phenotypic findings of disease only. ** Based on internal analysis conducting in H2 2022 using publicly available data sources; analysis available in Inozyme Corporate Deck.

Sanjay Subramanian, M.S., MBA

Chief Financial Officer

Current liquidity projected to fund cash flow requirements into Q1 2025

$140.2M*

Anticipated cash runway extended by two additional quarters to Q1 2025

*Represents cash, cash equivalents & short-term investments as of 6/30/23, The estimated cash figure is preliminary and unaudited, represents a management estimate as of the date of this presentation and is subject to completion of our financial closing procedures.

Anticipated milestones provide robust news flow

Milestone	2023	2024	2025
ENPP1 Deficiency			
Initiate ENERGY-1 – Phase 1b Trial in Infants	✓		
Interim Data - Adult Phase 1/2 Trial – Cohorts 1-3	Sep. 23		
Initiate ENERGY-3 – Pivotal Trial Pediatric Patients	Oct. 23		
Topline Data – Adult Phase 1/2 Trial*		Q1 24	
Initiate ENERGY-2 – Pivotal Trial in Infants – Ex. U.S.		Q2 24	
Interim Data – ENERGY-1 Trial		2H 24	
Topline Data – ENERGY-3 Trial			Mid-Year
ABCC6 Deficiency			
Interim Data - Adult Phase 1/2 Trial	Sep. 23		
Topline Data – Adult Phase 1/2 Trial*		Q1 24	
Initiate Phase 2 Trial**		Q4 24	

*48-week data from Cohorts 1-3, **Pending regulatory discussions and appropriate financial resources

Q&A

inozyme pharma

Thank you to the patient community, physicians and investigators

ENERGY-1 Trial Endpoints: Phase 1b trial in infants with ENPP1 Deficiency

Objective	Endpoint
Primary Objective	**Primary Endpoint**
• Assess the safety and tolerability of INZ-701	• Adverse events • Vital signs and weight • Lab tests including chemistry, hematology, and urine tests • Immunogenicity • Concomitant medications • Electrocardiogram • Left ventricular ejection fraction
Secondary Objectives	**Secondary Endpoints**
• PK/PD activity of INZ-701	• INZ-701 plasma concentration-time profiles and PK parameters • PPi levels • ENPP1 Activity
Exploratory Objectives	**Exploratory Endpoints**
• Assess survival • Assess changes in physical growth: weight and body length • Assess infant development and functional performance • Assess change in biomarkers relates to bone and mineral metabolism • Assess healthcare utilization	• Overall survival • Growth Z-score • Bayley-3 • Phosphate; FGF23; TmP/GFR • Number of days in hospital, in intensive care unit, or using mechanical ventilation

ENERGY-3 Trial Endpoints: Pivotal trial in peds. with ENPP1 Deficiency

Objective	Endpoint
Primary Objective	**Primary Endpoint**
• Determine if INZ-701 increases PPi levels	• Change from baseline over time in plasma PPi concentration through Week 52
Secondary Objectives	**Secondary Endpoints**
• Improvement in skeletal abnormalities • Improvement in growth • PK and INZ-701 activity	• RGI-C global scores, RGI-C regional scores, RSS • Growth Z-score • INZ-701 plasma concentration and specific activity
Tertiary Objectives	**Tertiary Endpoints**
• Motor performance and mobility • Pain • Mobility and fatigue • Physical and psychosocial health • Patient reported outcomes • Metabolism biomarkers • Healthcare utilization • Hearing • Safety	• Peabody Development Motor Scale, Six-minute walk test • PROMIS Pediatric Pain Interference T-scores • PROMIS Pediatric Physical Function Mobility and Fatigue T-cores • Change in Short Form-10 • Change in GIC – Patient, Caregiver, Clinician • Vitamin D3, FGF23, BALP, CTX, P1NP, Serum Phosphate, TmP/GFR • Number of musculoskeletal surgeries, hospitalizations, ER visits • Standard audiometric measures, HEAR-QL • Vital signs, weight, ECG, AEs, ADAs, Concomitant medications