inozyme pharma

OUR MISSION: Fulfill an unmet medical need with therapeutic breakthroughs in diseases of abnormal mineralization

January 2021

Legal Disclaimer

This presentation and any statements made orally during this presentation also 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.

Forward-Looking Statement Disclaimer

This presentation contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this presentation, including statements regarding our strategy, future operations, future financial position, future revenue, projected costs, prospects, plans and objectives of management, are forward-looking statements. 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. 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.

Developing Therapeutic Breakthroughs in Diseases of Abnormal Mineralization

- Strong Scientific Rationale w/ Robust Preclinical Data in Predictive Animal Models
- Lead Candidate (INZ-701) With Opportunities For Multiple Rare Diseases
- Sizeable Markets with High Unmet Medical Need and No Approved Therapies
- H1’21: Ph. 1/2 Clinical Studies in ENPP1 and ABCC6 Deficiencies Expected
- H2’21: Prelim. Safety and Biomarker Clinical Data for Both Indications Expected
- Experienced Management Team with Strong Track Record in Rare Diseases

inozyme pharma

Management Team and Leadership

Extensive Rare Disease Drug Development Expertise

Axel Bolte
Co-founder, President and Chief Executive Officer

HBM Partners · Allena Pharmaceuticals · PTC Therapeutics · iVERIC bio

Steve Basso
Senior Vice President of Finance

Alexion · Pfizer

Pedro Huertas, M.D., Ph.D.
Senior Vice President and Chief Medical Officer

genzyme · Shire · ELO Eloxx Pharmaceuticals · Pfizer

Steven Jungles
Senior Vice President and Chief Technical Operations Officer

brammer bio · BIOMARIN · ultragenyx pharmaceutical · HARVARD MEDICAL SCHOOL

Henric Bjarke
Senior Vice President and Chief Operating Officer

Alexion · Pharmacia · eyetech · iVERIC bio

Kevin Johnson, Ph.D., MBA
Senior Vice President, Regulatory Affairs

magenta · imara · Vtesse · gsk

Yves Sabbagh, Ph.D.
Senior Vice President and Chief Scientific Officer

genzyme · SANOFI

Board of Directors

Sarah Bhagat	Axel Bolte	Reinaldo Diaz	Martin Edwards
Rob Hopfner	Ed Mathers	Lynne Sullivan	Doug Treco (Chair)

inozyme pharma

Rich Pipeline of Indications of Abnormal Mineralization

Initial Focus on Genetic Diseases followed by Expansion into Non-Genetic Diseases

ASSET	PROGRAM	STAGE OF DEVELOPMENT				NEXT ANTICIPATED MILESTONE
		Research	IND Enabling	Phase 1/2	Phase 2/3	
INZ-701 (ENPP1-Fc)	GENETIC DISEASES					
	ENPP1 Deficiency *11–12K patients worldwide*					Initiate Ph. 1/2 H1' 2021
	ABCC6 Deficiency *>67K patients worldwide*					Clear CTAs Early 2021
	NON-GENETIC DISEASES					
	Calciphylaxis					Generate pre-clinical proof of concept
	Diseases of Neointimal Proliferation					Generate pre-clinical proof of concept

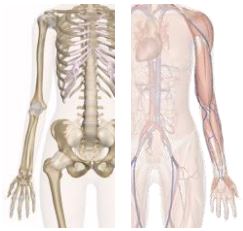
We retain worldwide, exclusive development and commercial rights to INZ-701

inozyme pharma

What do Diseases of Abnormal Mineralization Look Like?

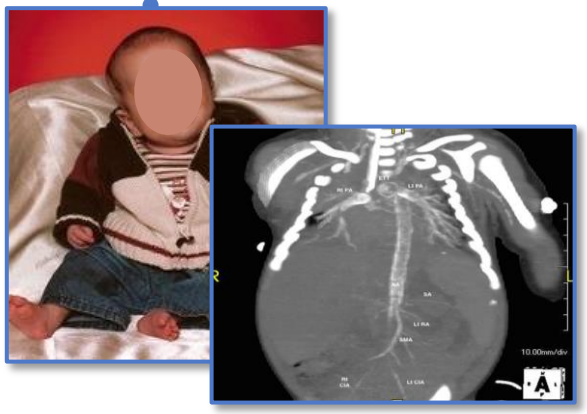
ENPP1 Deficiency Affects Patients of All Ages in Devastating Ways

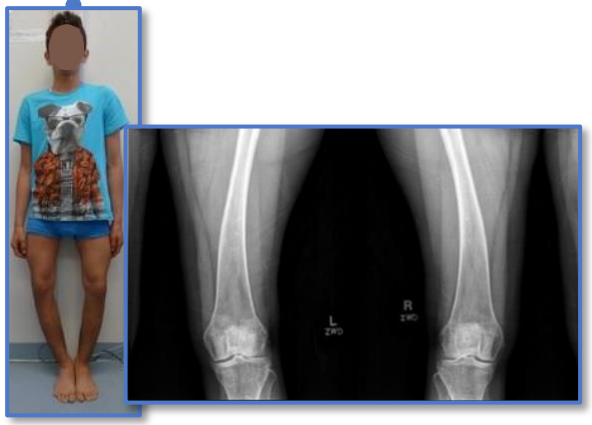
Potential Effects of Pathological Mineralization



- ~45-50% of infants with ENPP1 deficiency die within 12 months of birth*
- Effects are seen outside skeleton (Ex. vascular system)
- Can cause bone softening, clogged arteries, and blindness

INFANCY **ADOLESCENCE** **ADULTHOOD**





For illustrative purposes only. Individual patient experiences may vary.

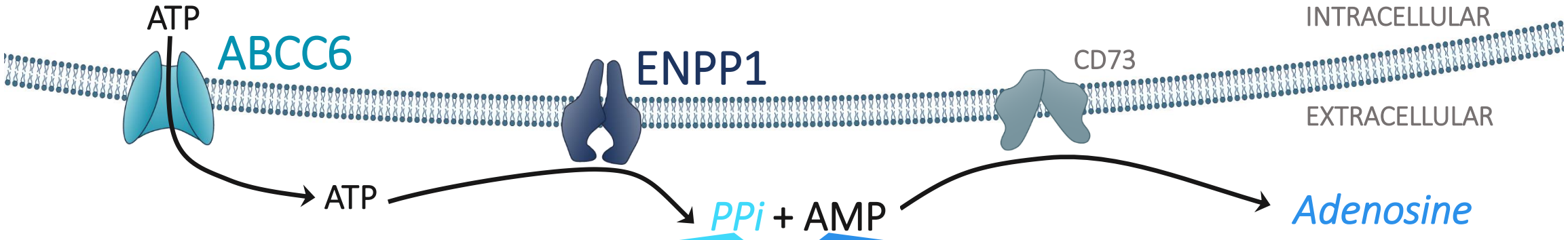
Sources: Rutsch F, et al., *CIRCGENETICS.* 2008; 133-140.

Biology of ENPP1 and ABCC6 Deficiency

inozyme pharma

How ENPP1 and ABCC6 Work

The Biologic Pathway that Regulates Mineralization and Neointimal Proliferation



Maintains Healthy Mineralization

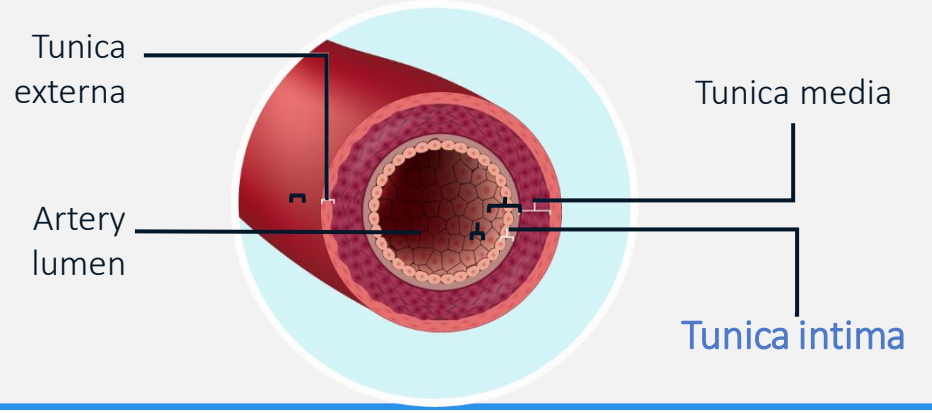
PPi inhibits growth and formation of hydroxyapatite, which results in:

- Maintenance of healthy bones and teeth

- Inhibition of pathological ectopic mineralization (i.e., mineralization of arteries, organs, and joints)

Maintains Healthy Vessel Wall Thickness

Adenosine inhibits neointimal proliferation

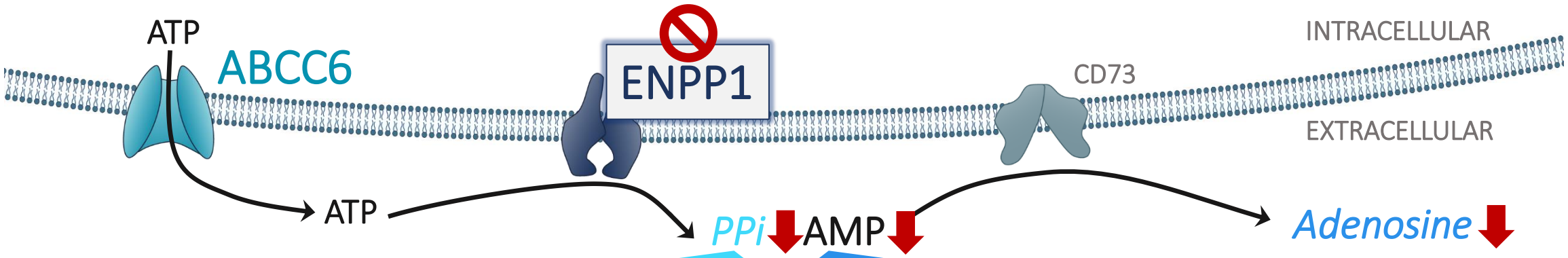


ABCC6 = Adenosine triphosphate binding cassette transporter protein subfamily C member 6; AMP=adenosine monophosphate; ARHR2 = Autosomal recessive hypophosphatemic rickets type 2; ATP=adenosine triphosphate; ENPP1 = ectonucleotide pyrophosphatase/phosphodiesterase 1; PPi = pyrophosphate

Sources: 1. Jansen RS, et al. *Arterioscler Thromb Vasc Biol*. 2014;34(9):1985-1989. **2.** Nitschke Y, et al. *Am J Hum Genet*. 2012;90(1):25-39. **3.** Nitschke Y, et al. *Exp Mol Med*. 2018;50(10):1-12.

ENPP1 Deficiency

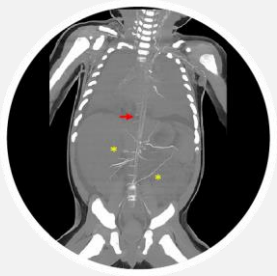
Low Levels of PPi and Adenosine Lead to Pathological Mineralization and Neointimal Proliferation



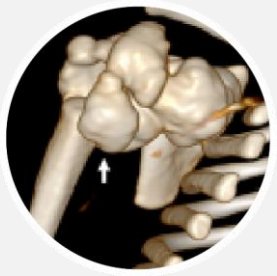
Pathological Mineralization

Ectopic mineralization
(arteries, joints, and organs)

Calcification of descending aorta and arteries

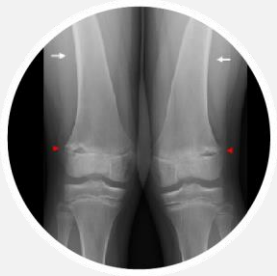


Mineralization of shoulder joint



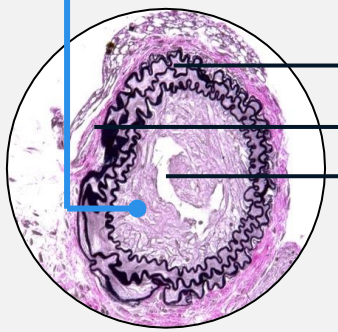
Under-mineralization of bones

Irregularities in the distal femoral metaphyses and rickets



Neointimal Proliferation

Cells within artery wall

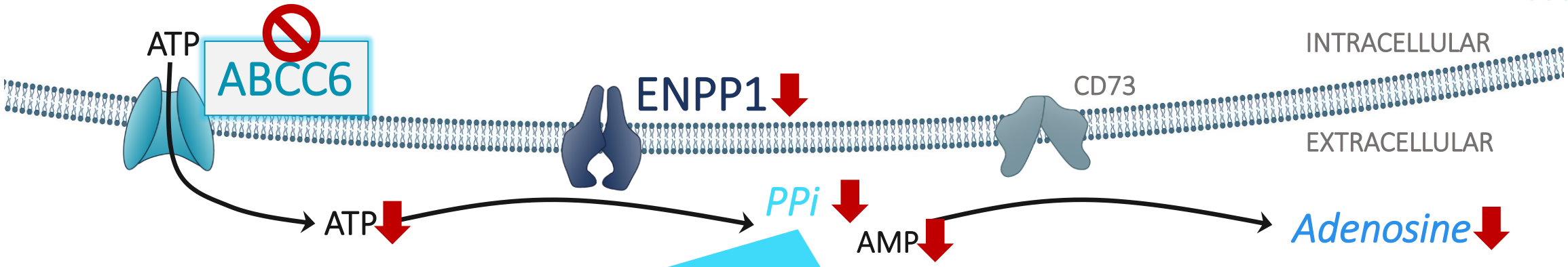


Accumulation of smooth muscle cells in the tunica intima resulting in thickening of arterial walls

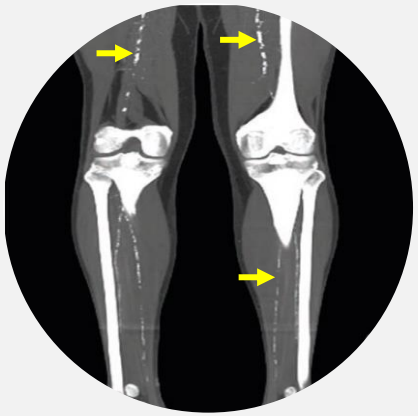
Sources: 1. Jansen RS, et al. *Arterioscler Thromb Vasc Biol*. 2014;34(9):1985-1989. **2.** Nitschke Y, et al. *Am J Hum Genet*. 2012;90(1):25-39. **3.** Nitschke Y, et al. *Exp Mol Med*. 2018;50(10):1-12. **4.** Orriss IR, et al. *Curr Opin Pharmacol*. 2016;28:57-68. **5.** Boyce AM, et al. *Curr Osteoporos Rep*. 2020;18(3):232-241.

ABCC6 Deficiency is a Chronic Disease of high Morbidity

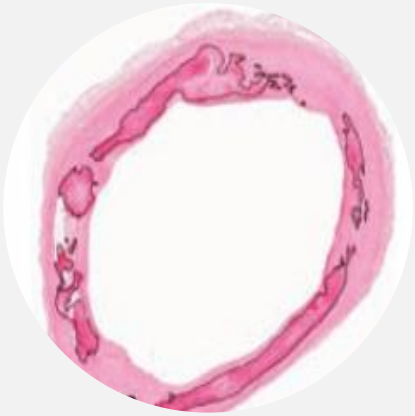
Reduced Levels of PPi and ENPP1 Lead to Pathological Mineralization



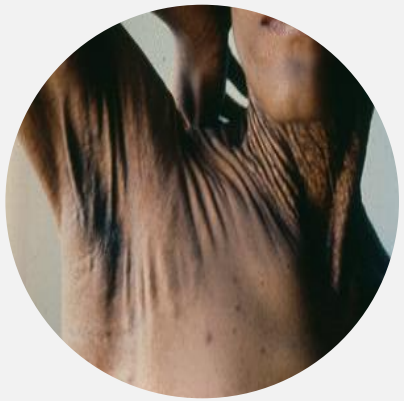
Pathological Mineralization



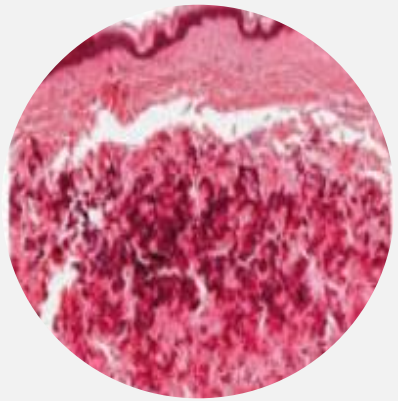
CT Scan of Vascular Calcification



Histology of Vascular Calcification



Skin lesions

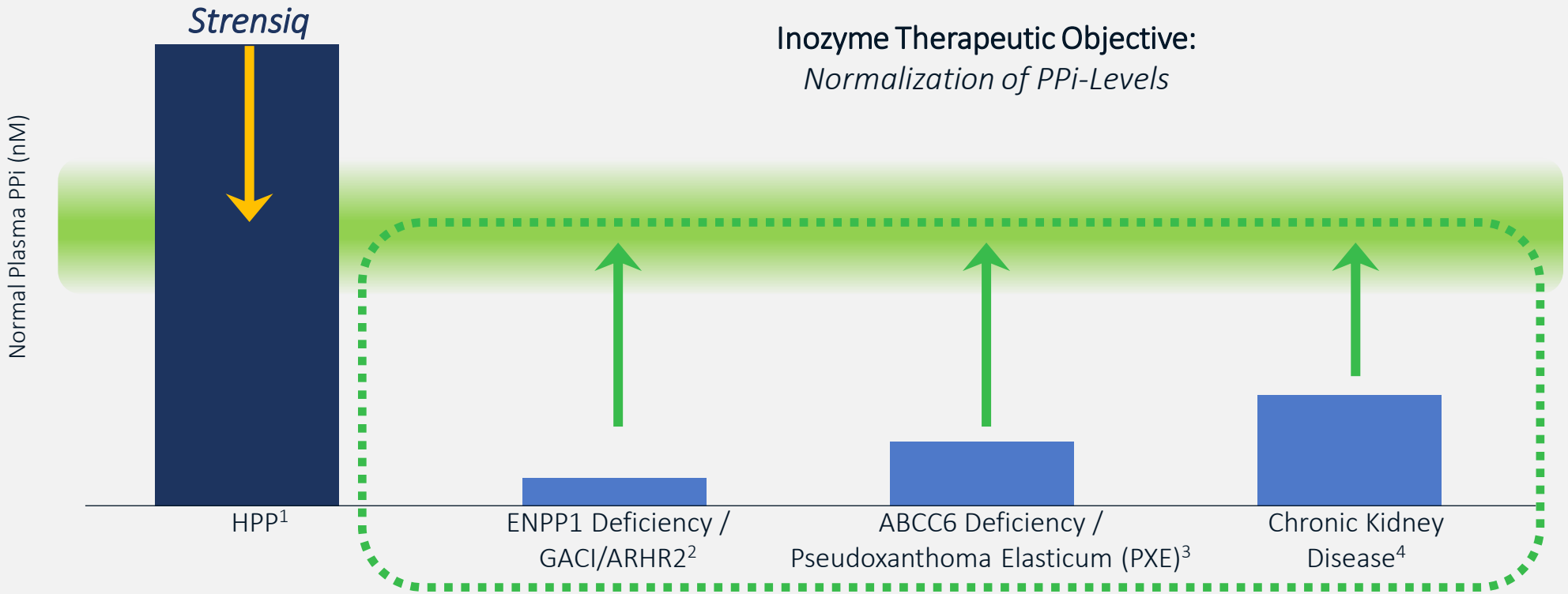


Histology of Skin Alterations

Sources: 1. Jansen RS, et al. *Arterioscler Thromb Vasc Biol*. 2014;34(9):1985-1989. **2.** Nitschke Y, et al. *Am J Hum Genet*. 2012;90(1):25-39. **3.** Nitschke Y, et al. *Exp Mol Med*. 2018;50(10):1-12. **4.** Orriss IR, et al. *Curr Opin Pharmacol*. 2016;28:57-68. **5.** Boyce AM, et al. *Curr Osteoporos Rep*. 2020;18(3):232-241.

Normalization of PPi is the Therapeutic Objective in Several Diseases

Normalization of Excessive PPi Levels Has Been Achieved by Strensiq



Sources: 1. Hypophosphatasia Reported in Whyte et al. JCI Insight. 2016;1(9):e85971. **2.** Nitschke et al., 2018. **3.** Kauffenstein et al., 2018. **4.** O'Neill et al, 2010.

ENPP1 Deficiency is a Disease With High Morbidity and Mortality

Low Levels of PPi Lead to Pathological Mineralization and Neointimal Proliferation

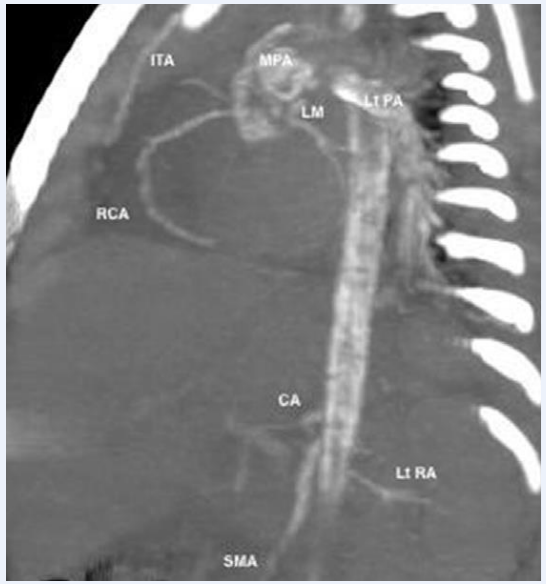
Historical Definition

Generalized Arterial Calcification of Infancy (GACI) — 0 – 3 Years

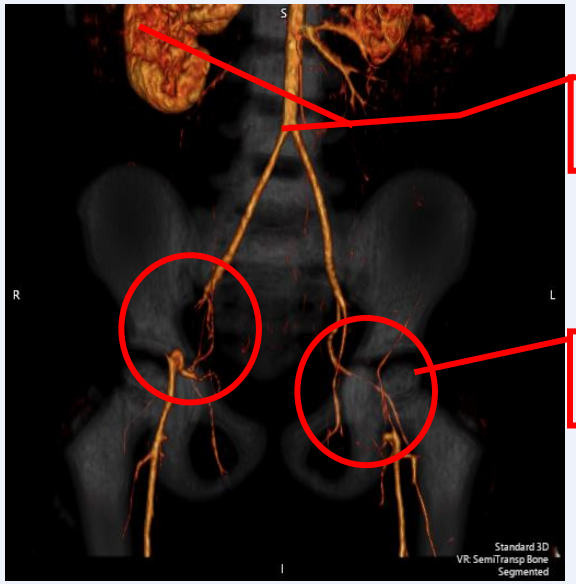
Autosomal Recessive Hypophosphatemic Rickets Type 2 (ARHR2) — 3 – 18 Years; 18+ Years

New Definition

ENPP1 Deficiency



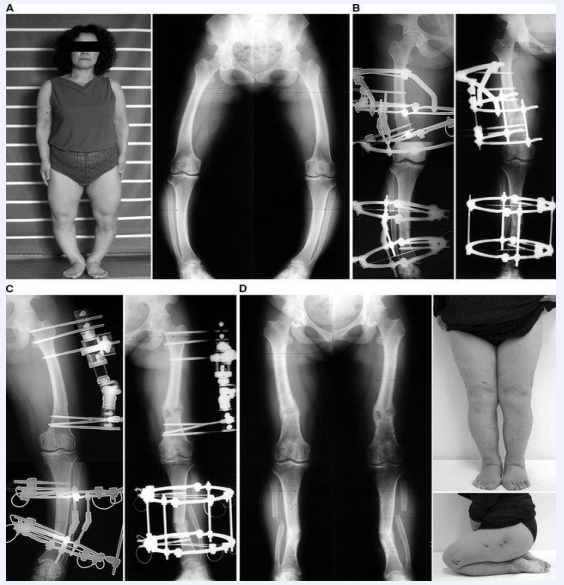
Calcification



Organ and arterial calcification

Obstructive neointimal proliferation

Organ Calcification & Neointimal Proliferation



Skeletal Defects

ABCC6 Deficiency is Commonly Known as Pseudoxanthoma Elasticum

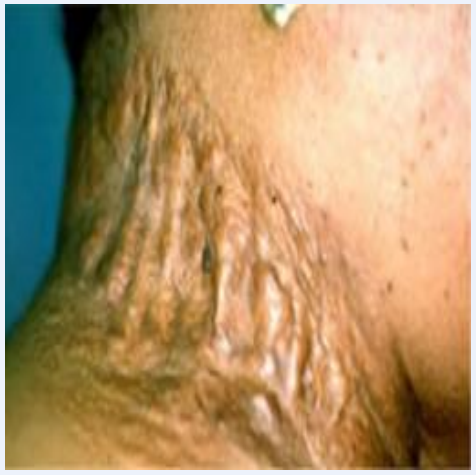
Focus on Patients with Severe Manifestation Leading to High Unmet Medical Need

Historical Definition — Pseudoxanthoma elasticum (PXE)

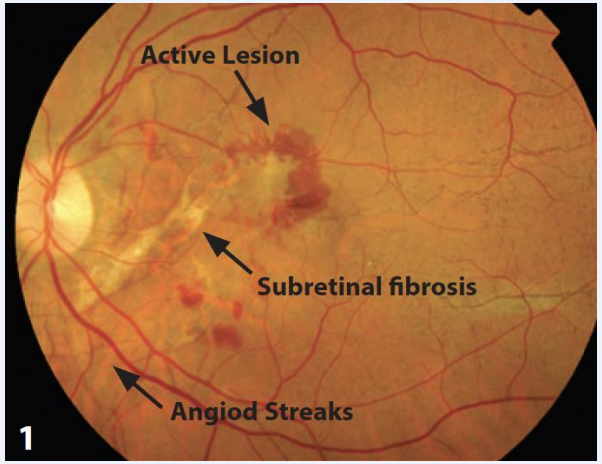
Onset in 20s-30s | Progressively Effects Adult Population

New Definition — ABCC6 Deficiency

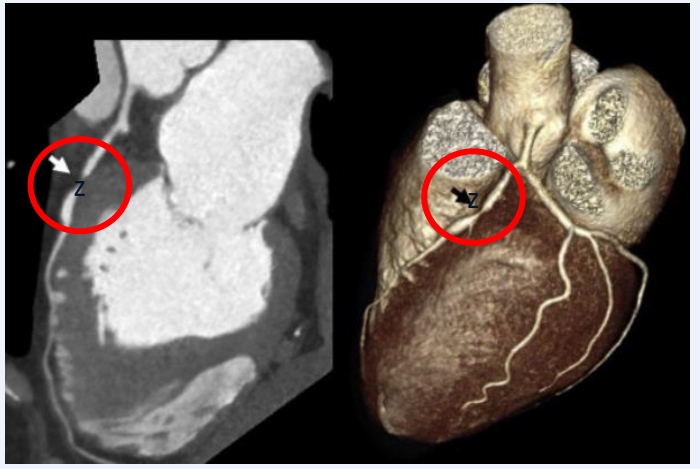
Pseudoxanthoma elasticum (PXE)



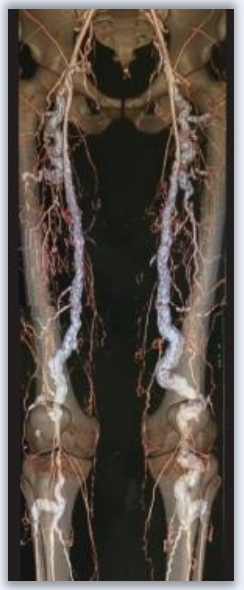
Skin lesions



Retinal abnormalities



Neointimal Proliferation



Vascular Calcification

Our Solution: INZ-701

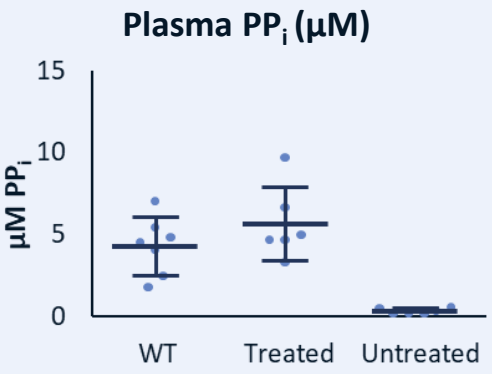
Pre-clinical Development

inozyme pharma

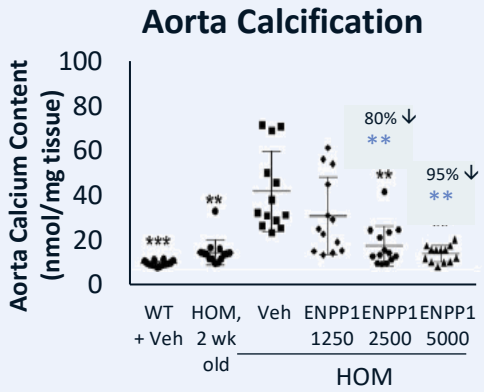
An Earlier Version of INZ-701 (ENPP1-Fc) Prevented Vascular Calcification and Mortality in a Predictive ENPP1-Deficient Mouse Model (*asj*)

1. *Normalized plasma PP_i levels*
2. *Reduced arterial calcification*
3. *Restored weight*
4. *Prevented early mortality*

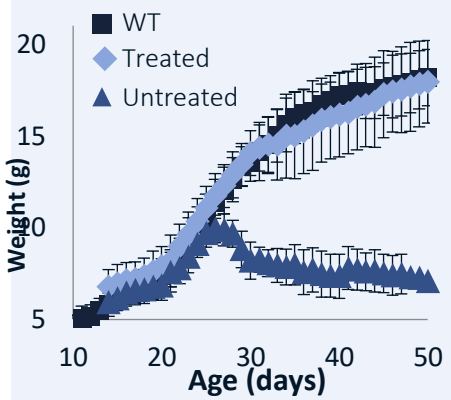
Biochemical



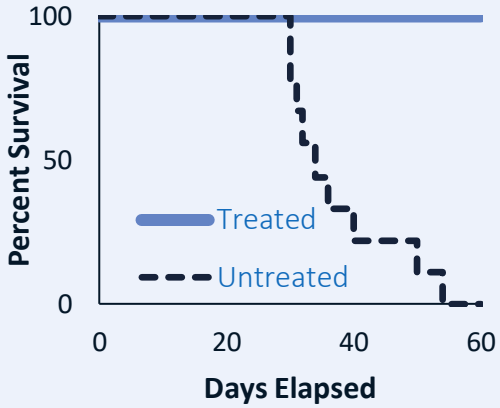
Consequences of Calcification



Results of Tx Restoring Growth



Increased Survival

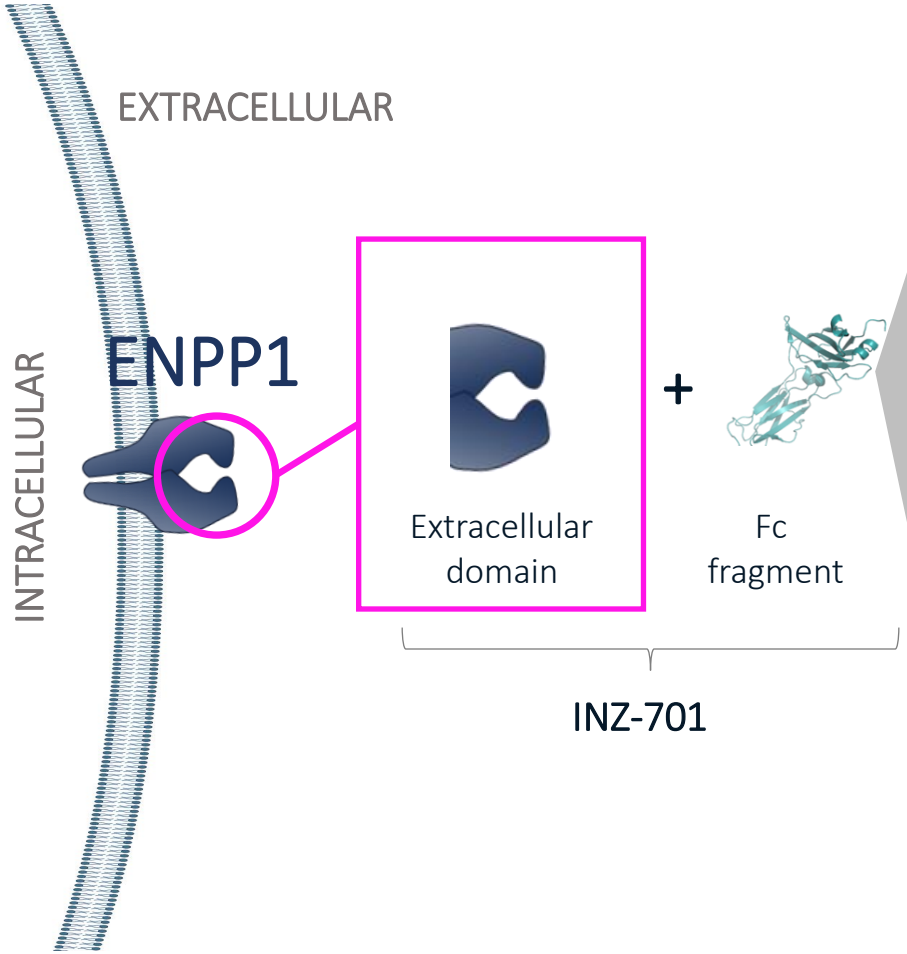


100% survival of treated asj/asj-mice; normalized PP_i levels

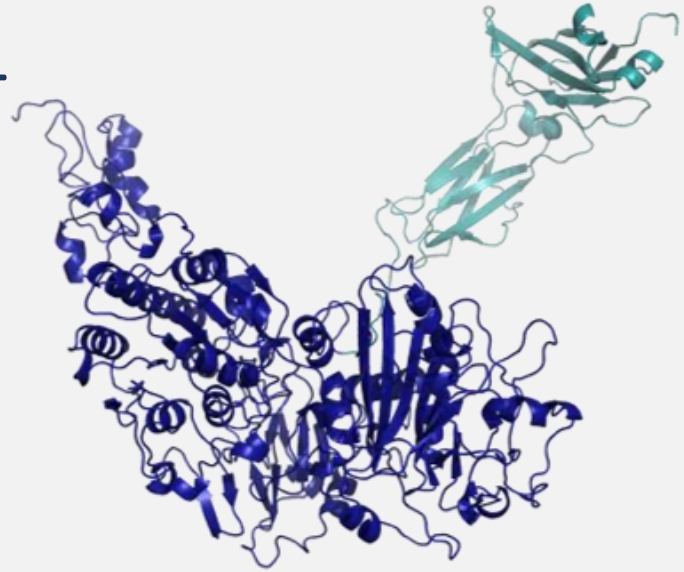
Sources: **1., 3., 4.** Albright RA, et al., 2015. **2.** Khan T, *Dis Model Mech*, 2018 Oct 8; 11 (10)

INZ-701 has been Designed to Replace Lost Enzymatic Function of ENPP1

Pharmacological Properties have been Optimized



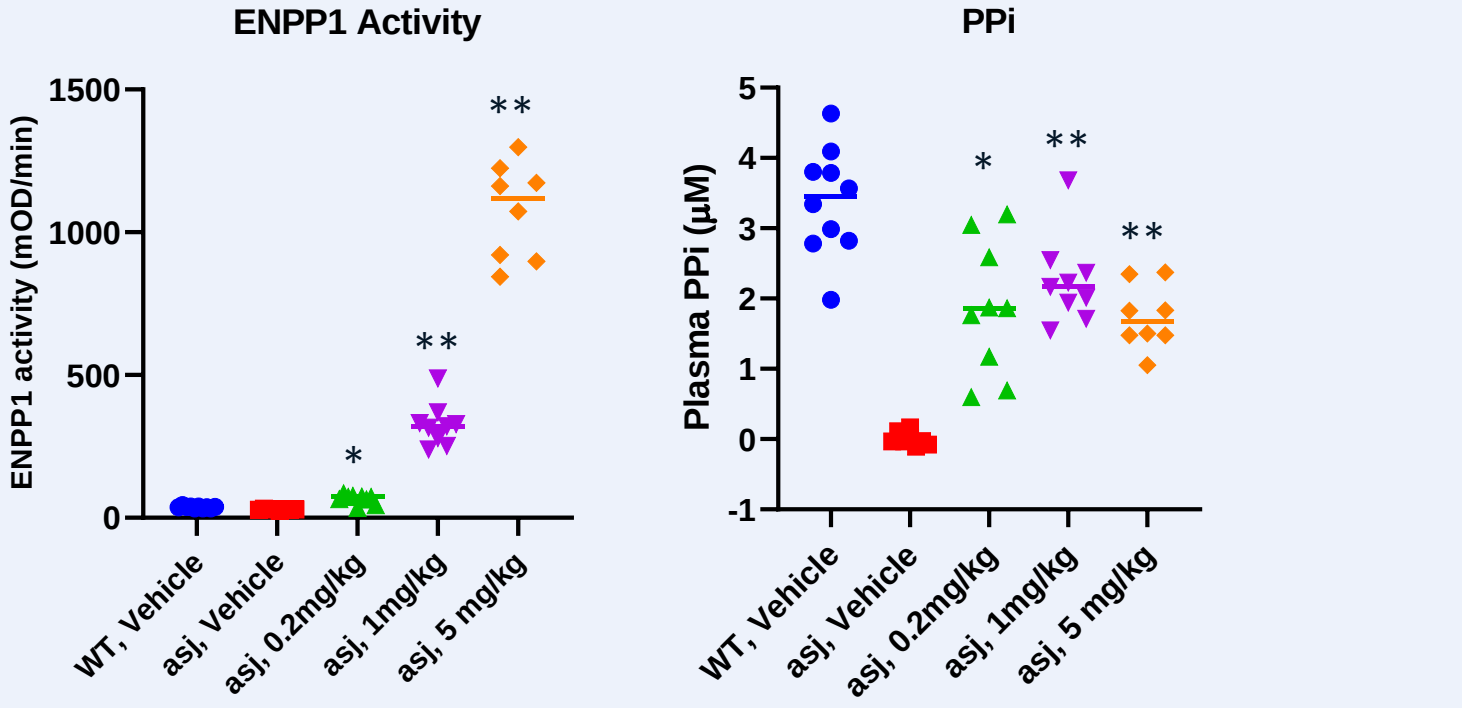
INZ-701



- **Protein:** Recombinant human ENPP1 (Ectonucleotide pyrophosphatase/phosphodiesterase 1)
- **Construct:** Recombinant Fc fusion protein with soluble extracellular domain of ENPP1
- **Dosing:** SC ; 2x/week in Ph. 1/2 for ENPP1 deficiency
- **Enzymatic Properties:** High catalytic efficiency (Kcat/Km)

INZ-701 Restored PPi-Levels in Predictive ENPP1 Deficient Murine Model (asj)

Biomarker Proof of Concept in Animals Achieved with INZ-701



* $P \leq 0.01$; ** $P \leq 0.001$

Asj-Mouse Model:

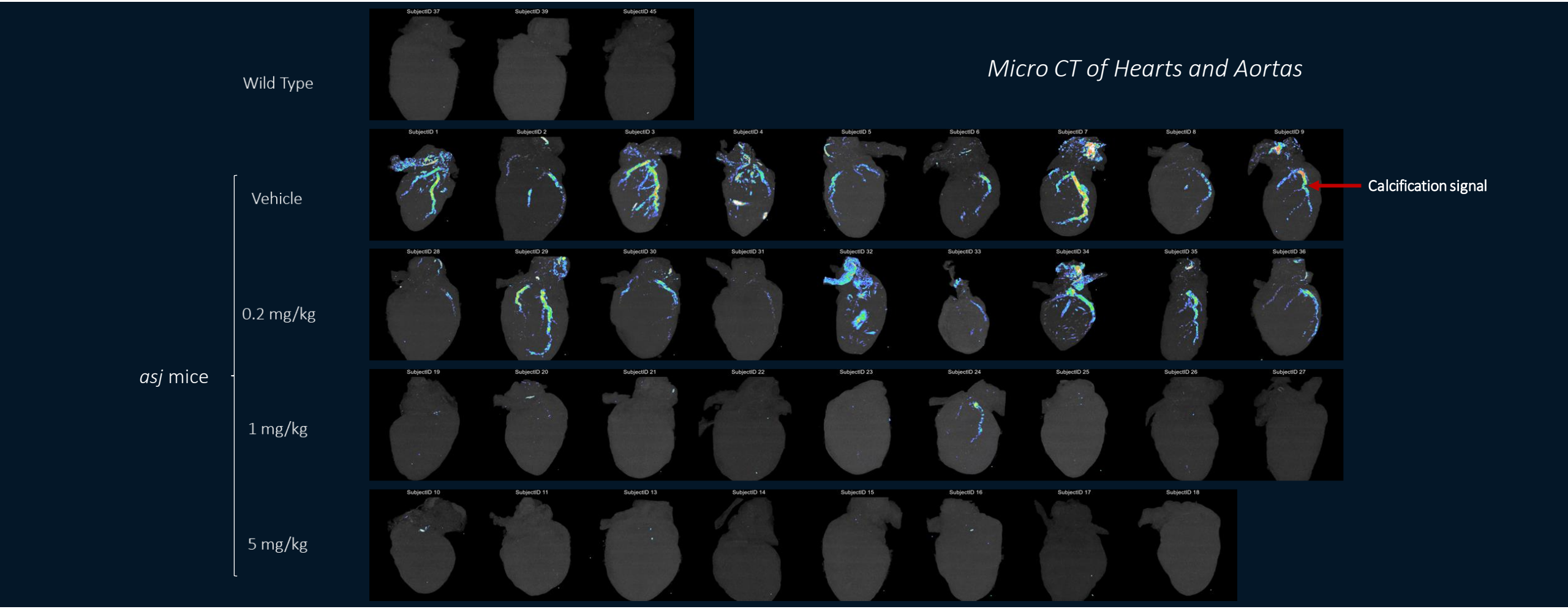
- Failure to thrive and gain weight
- Extensive vascular calcification
- Premature mortality
- Mimics human disease

Therapy start at age of 2 weeks (D1) and end at 10 weeks (D56)

Sources: *Internal, Unpublished Data.*

INZ-701 Prevented Cardiovascular Calcification in ENPP1-Deficient asj Mice

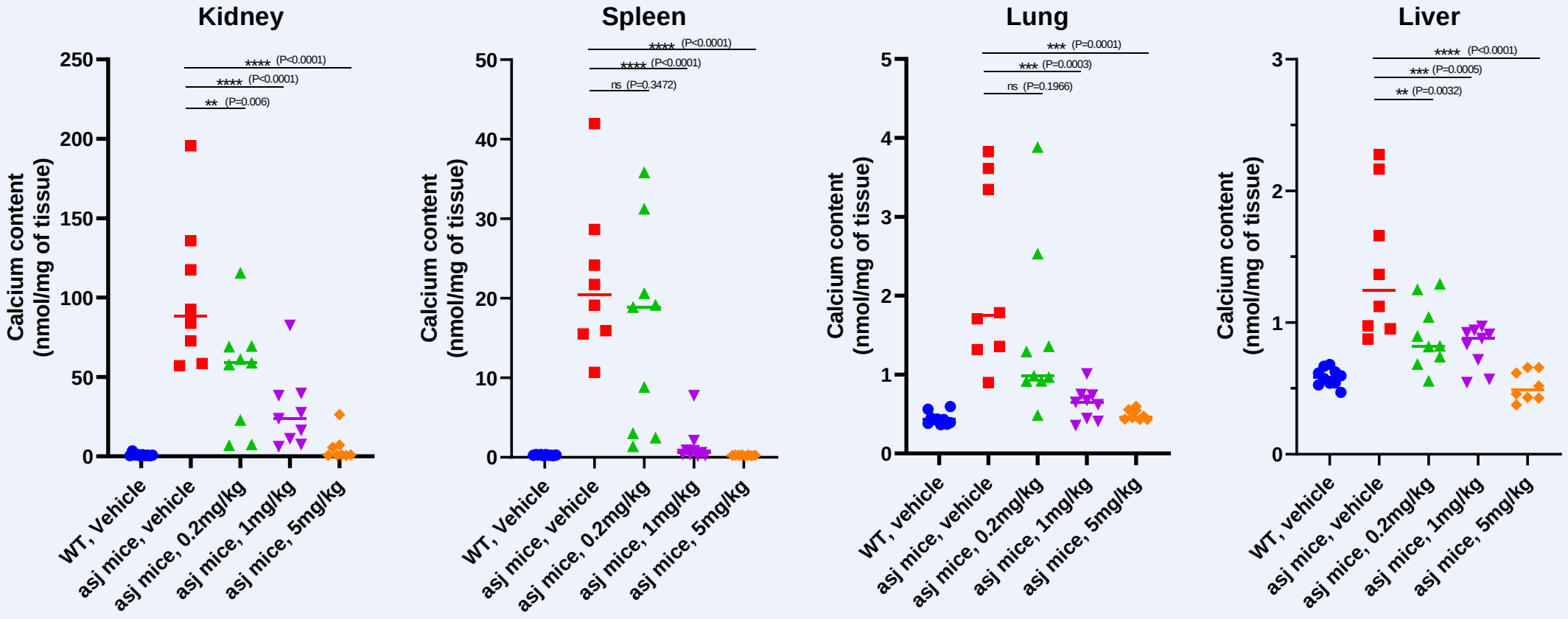
Validation of Pharmacological Effect in Representative Animal Model



Sources: *Internal, Unpublished Data.*

INZ-701 Prevented Calcification in Kidney, Spleen, Lung and Liver in ENPP1-Deficient Mice (asj)

Prevented Calcification in Critical Organs in Representative Animal Model



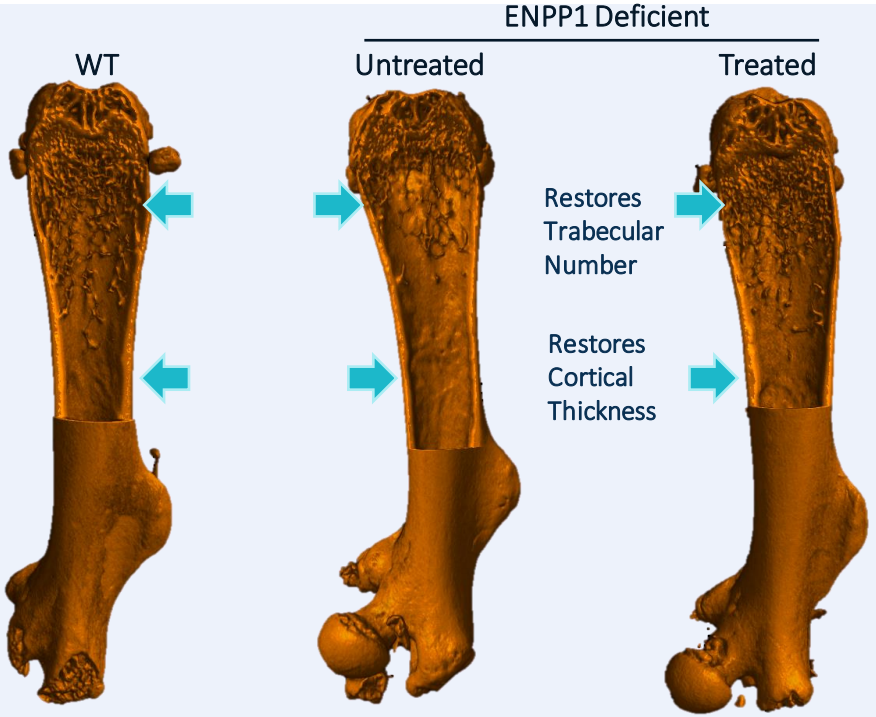
Mice on the acceleration diet, starting at week two, with both INZ-701 and vehicle control every other day for eight weeks.

Sources: *Internal, Unpublished Data.*

INZ-701 Prevented Bone Loss and Restored Growth in ENPP1-Deficient Mice (asj)

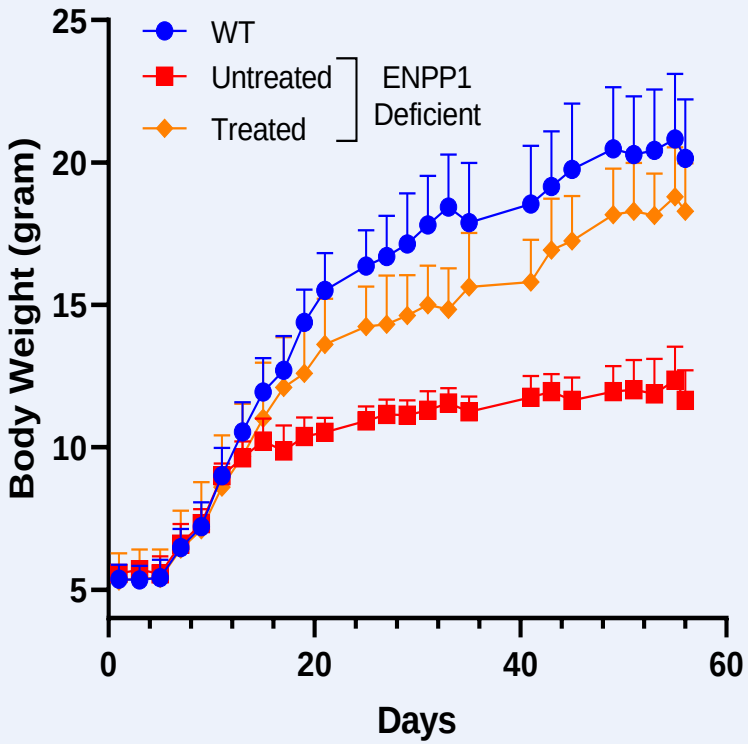
Corresponding Effects seen in Bones in Representative Animal Model, Restoring Growth

1 *Corrected bone defects*



	WT	Untreated	Treated
Average Trabecular Number (1/mm)	2.601	1.407	2.213
Average Cortical Thickness (mm)	0.174	0.113	0.148

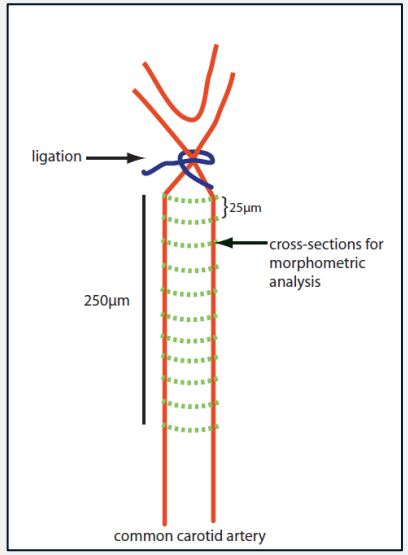
2 *Rescued growth defect*



Sources: *Internal, Unpublished Data.*

INZ-701 Prevented Neointimal Proliferation in ENPP1-Deficient Mouse Model (ttw)

Proof of Concept Achieved in Mouse Model Supporting Normalization of Adenosine Pathway



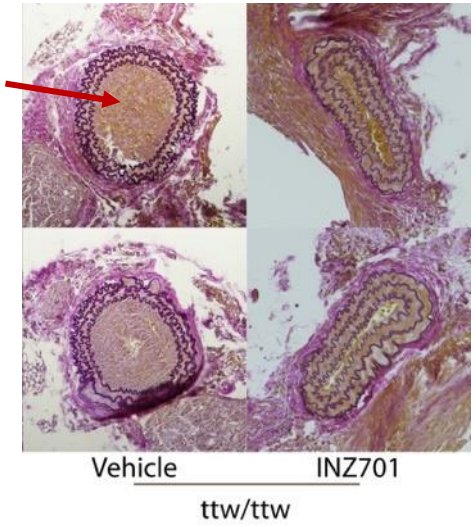
ttw-Mouse Model:

- Severe calcification of the cartilage and arterial walls
- Marked intimal vascular smooth muscle cell proliferation in response to arterial injury
- Mimics human disease

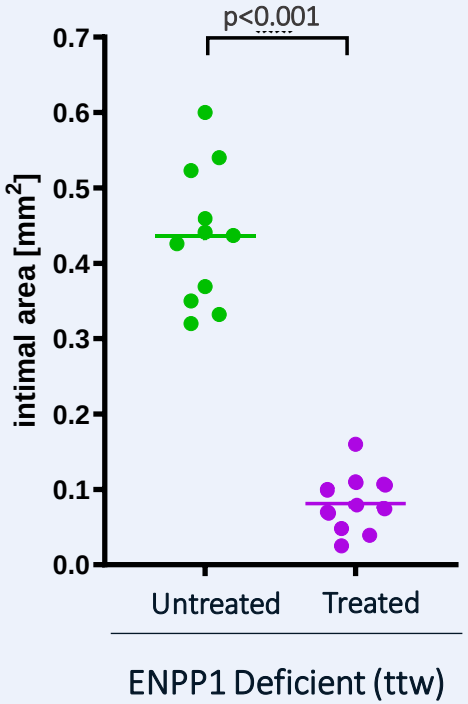
1 *Histology*

Histological Analysis of Preventive Treatment in Mice Ligated for 14 Days

Intimal area



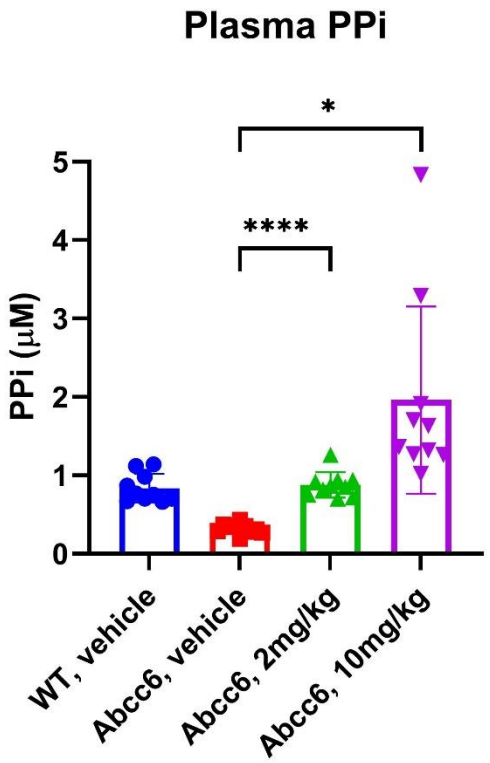
2 *Intimal Area*

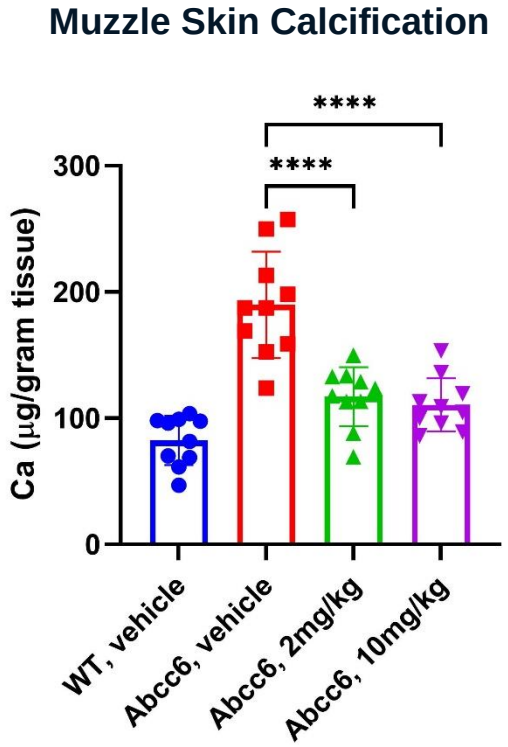


Sources: *Internal, Unpublished Data.*

INZ-701 Reduced Tissue Calcification and Normalized PPi in ABCC6-Deficient Murine Model

Proof of Concept Achieved in Representative Animal Model





- Dose: 2 and 10mg/kg, SC, QOD
- Duration: ~4wk of age to ~12 wk of age
- All animals are given anti-CD4
- All animals on normal diet

** P≤ 0.05; **** P≤ 0.0001*

Abcc6 – Mouse Model:

- Calcification in aorta and arteries of soft tissues
- Spontaneously developed
- Calcification of elastic fibers in blood vessel walls
- Calcification in Bruch's membrane in the eye
- Mimics human disease

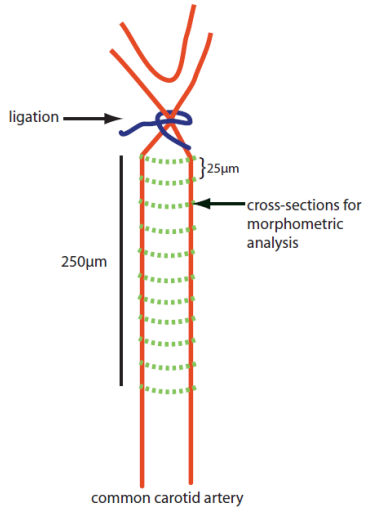
Sources: *Internal, Unpublished Data.*

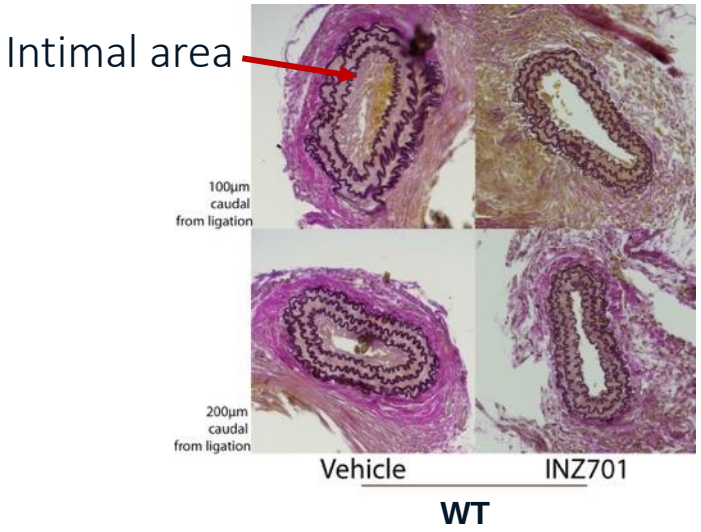
INZ-701 Treatment Prevented Neointimal Proliferation in Normal Mice

Potential for Future Expansion in Non-Genetic Diseases

1 *Histology*

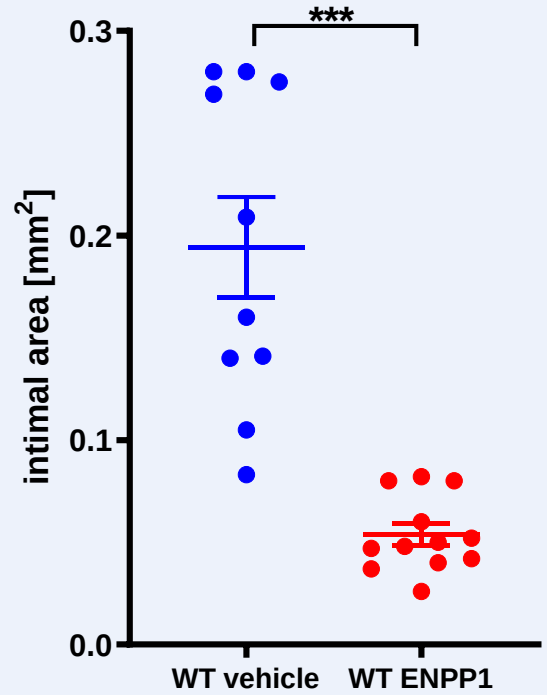
Histological Analysis of Preventive Treatment in Mice Ligated for 14 Days





WT = wild-type

2 *Intimal Area*



*** $P \leq 0.001$

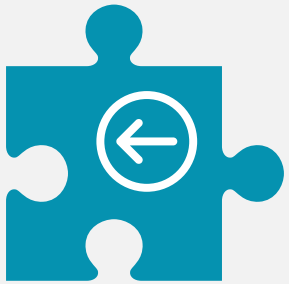
Our Solution: INZ-701
Clinical Development

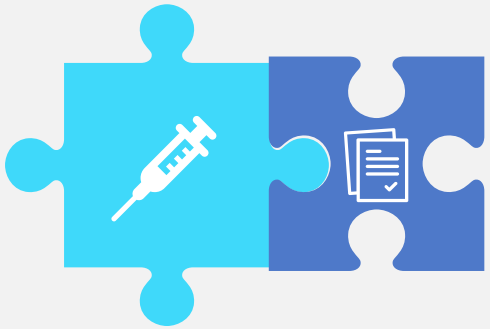
Aim to Understand ENPP1- and ABCC6-Deficiencies from All Angles

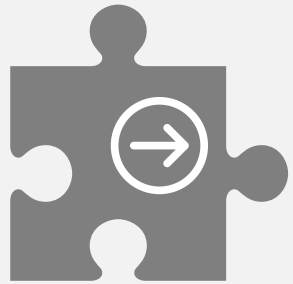
☑ **Retrospective Natural History Study**
Believed to be largest retrospective, cross-sectional study in ENPP1 Deficiency

❑ **INZ-701 Interventional Studies**
Expect Ph. 1/2 initiations in both ENPP1- and ABCC6-Deficiencies H1'21

❑ **Normal Healthy Volunteer PPi Study**
Expected by preliminary Ph. 1/2 data read out







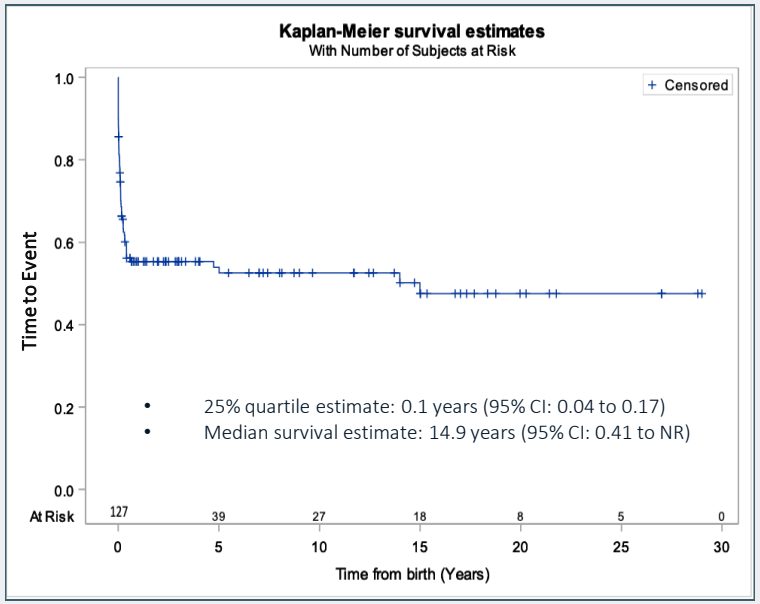
☑ **Burden of Disease Study**
Intend to understand disease from perspective of ENPP1 and ABCC6 patients and caregivers. Expect to share data in 2021.

❑ **Prospective Natural History Study**
Expect initiation H1'21

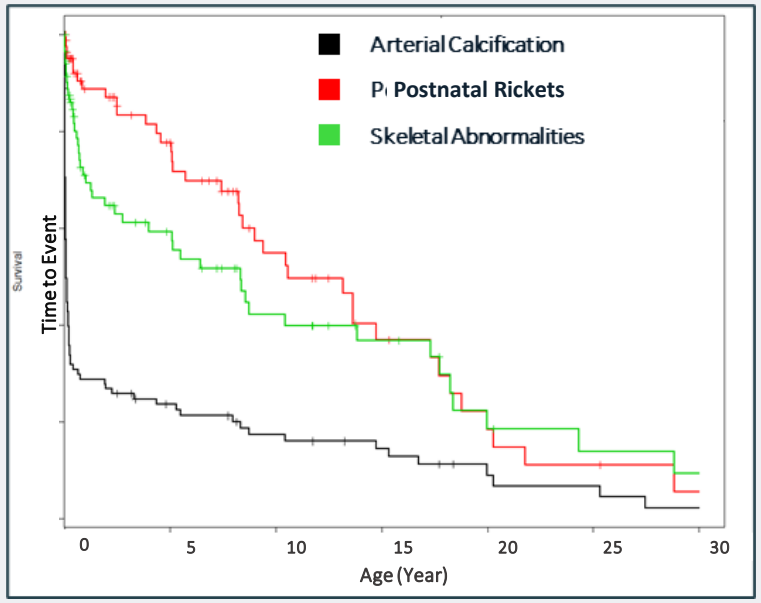
inozyme pharma

Retrospective Natural History Study Showed ENPP1 Deficiency is Single Disease with Three Manifestations (Infantile, Pediatric, Adult)

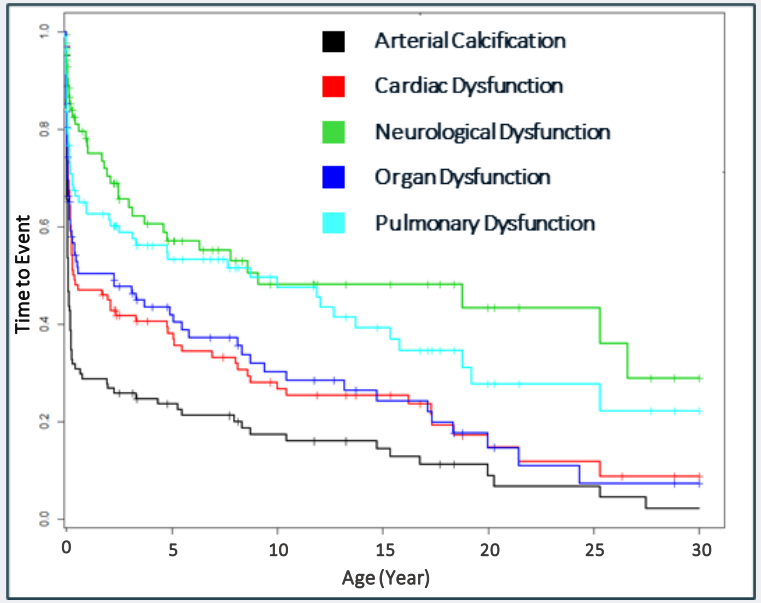
1 Over 40% Mortality in First 12 Months of Life



2 Calcification, Skeletal Abnormalities, and Rickets Occur Simultaneously From Birth



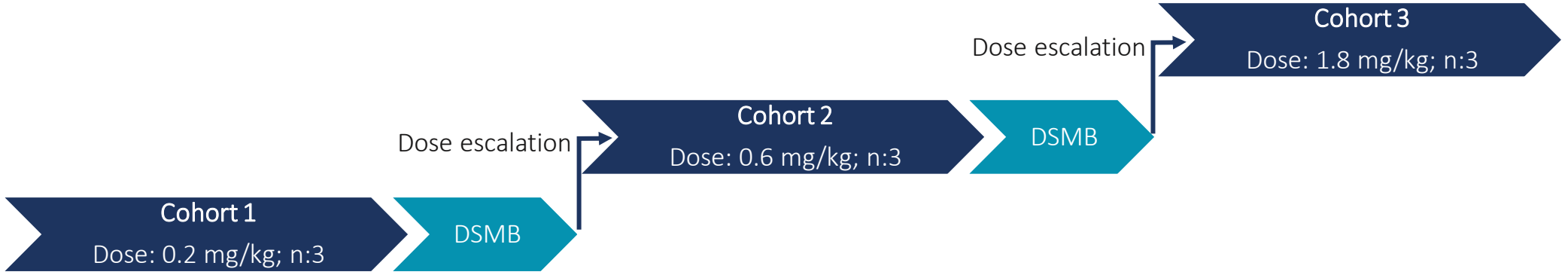
3 Calcification and Organ Dysfunction Occur Sequentially and Progressively



Believed to be largest retrospective, cross-sectional study in ENPP1 Deficiency – Data collected at NIH and Universität Münster (n=127)

Sources: *Internal, Unpublished Data.*

First-in-Human Phase 1/2 Study with Dose Escalation Design Expected to Initiate H1'21



ENPP1 Deficiency Ph. 1/2	
Eligibility Criteria	• Confirmed clinical and genetic diagnosis of ENPP1 Deficiency • Age 18-65 years
Primary Endpoint(s)	• **Safety and tolerability of INZ-701** • Establish dosing regimen for future clinical development
Exploratory Biomarkers	• Plasma PPi • Other disease-relevant biomarkers
Planned Doses	• 0.2 mg/kg, 0.6 mg/kg, and 1.8 mg/kg; twice weekly subcutaneous
Duration	• 7 weeks duration per subject; staggered recruitment per cohort (DSMB)
Upcoming Milestones	• H1'21 – Study initiation • H2'21 – Preliminary safety and biomarker data

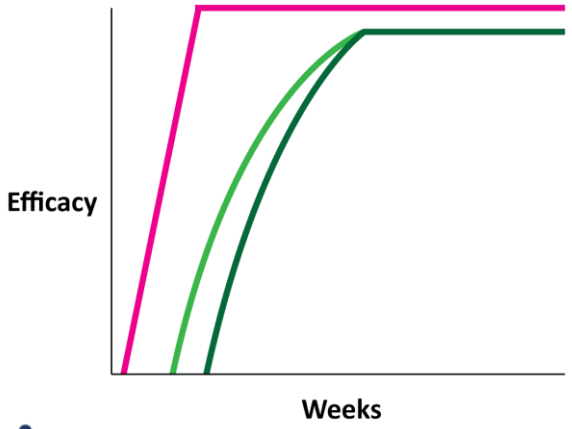
DSMB = Data Safety Monitoring Board

ENPP1 Deficiency: Clinical Strategy for INZ-701 is to Link Restoration of Plasma PPi to Measures of Physiological and Clinical Efficacy

Illustrative Goals of our Planned Trials

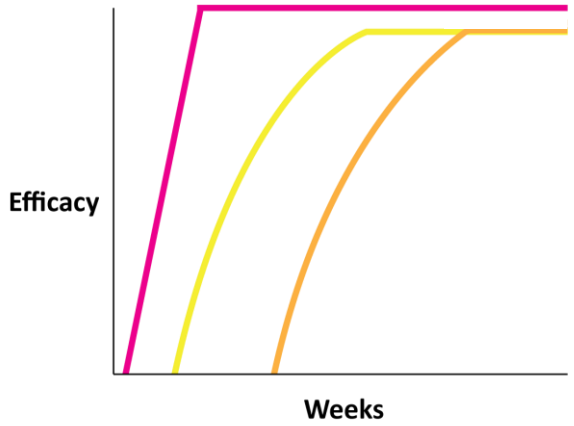
0 – 3 Years

Endpoint	Measurement
PPi	Blood Biochemistry
Calcification	High resolution radiography
Survival	Alive After 6 Months



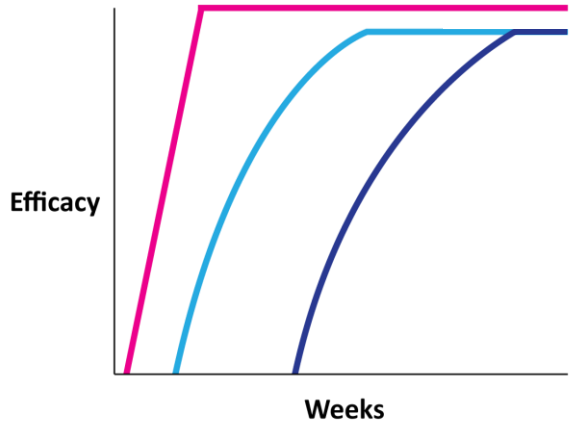
3 – 18 Years

Endpoint	Measurement
PPi	Blood Biochemistry
BMD	High resolution radiography
Rickets, Growth, Organ Function	MRI, RGI-C, RSS, Dexa



18+ Years

Endpoint	Measurement
PPi	Blood Biochemistry
Bone Pain	Pain Scores
Osteomalacia	MRI, Bone biopsies



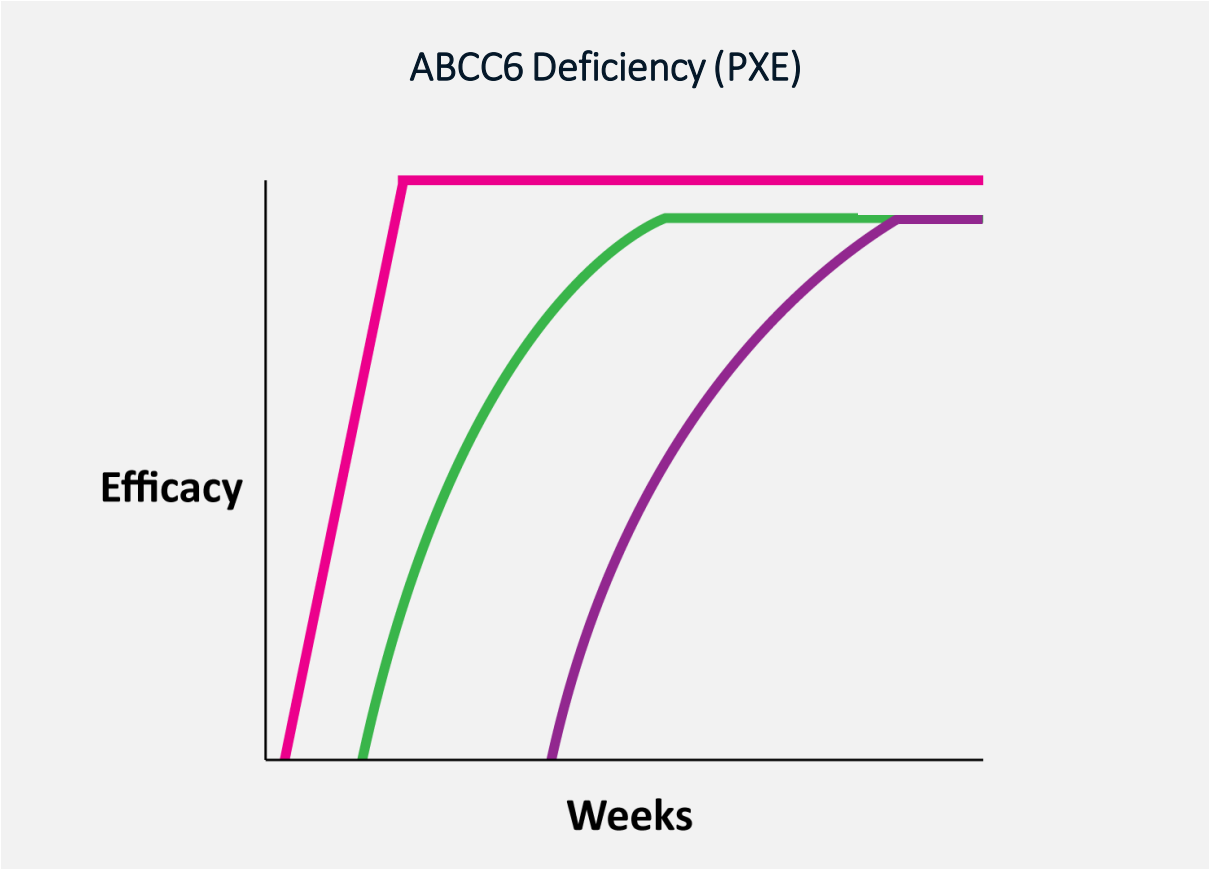
inozyme pharma

ABCC6 Deficiency: Clinical Strategy for INZ-701 is to Link Restoration of Plasma PPi to Measures of Physiological and Clinical Efficacy

Illustrative Goals of our Planned Trials

18+ Years

Endpoint	Measurement
PPi	Blood Biochemistry
Calcification	High resolution radiography
Cardiac Function/Pain	Doppler, ECG, CT scan, Pain scores



Market and Finance

International Physician Survey Identified Significant Numbers of Treatable ENPP1 Deficiency Patients

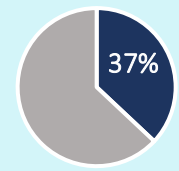
1,367 Target **Physicians** in 7 Key Markets Responded to Survey

SCREENING SURVEY COMPLETES:

# of Physicians	US	Canada	UK	France	Germany	Italy	Spain
Geneticists	42	5	10	7	4	19	11
Endocrinologists	160	25	63	54	35	97	72
Ped Endos	33	3	10	9	6	13	16
Ped Cardiologists	24	--	1	4	7	3	5
Orthopedists	174	8	56	33	78	33	24
Neonatologists	75	8	34	22	35	18	31
TOTAL	**508**	**49**	**174**	**129**	**165**	**183**	**159**

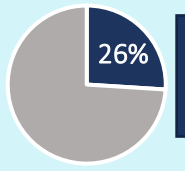
Source: Global online survey, conducted in local language, March 22 to April 15, 2019.

1,367 Physician Responses



Confirmed Patients
(N=506 Physicians)

2,976 Confirmed Patients



Managing Patients
(N=355 Physicians)

1,682 Managed Patients

1,001 Patient Profiles Collected

Over **600** Patients Alive

Financial Overview and Upcoming Anticipated Milestones

Funding History	Pre IPO	• $116 M in Private Financings : $49 M January 2017, $67 M March 2019
	IPO	• July 2020 – Net proceeds of approximately $116.5 M
	Cash Position	• Cash of $171.7 million as of September 30, 2020

ENPP1 Deficiency

- ☑ **Clearance of IND and CTAs**
  Early 2021
- ❑ **Initiation of Phase 1/2 clinical trial**
  H1 2021
- ❑ **Initiation of prospective natural history study**
  H1 2021
- ❑ **Preliminary safety and biomarker data from Phase 1/2 clinical trial**
  H2 2021

ABCC6 Deficiency

- ❑ **Clearance of CTAs**
  Early 2021
- ❑ **Initiation of Phase 1/2 clinical trial**
  H1 2021
- ❑ **Preliminary safety and biomarker data from Phase 1/2 clinical trial**
  H2 2021

New Indications and Pipeline

- ❑ **Neointimal proliferation**
  Pre-clinical POC
- ❑ **Calciphylaxis**
  Pre-clinical POC
- ❑ **Gene Therapy Program**
  Select development candidate

inozyme pharma

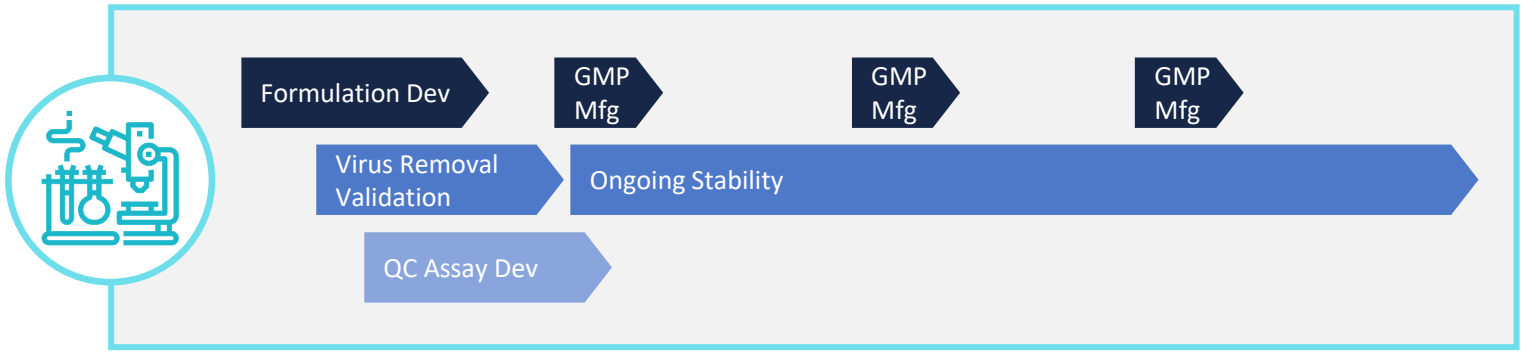
Thank You!

Inozyme Pharma, Inc.
321 Summer Street, Suite 400
Boston, MA 02210

Appendix

Robust CMC Process Designed for Stability and Scalability

Produced Enough GMP Material to Support Phase 1/2 Trials



- ✓ Recombinant Fc-fusion protein with the soluble extracellular domain of ENPP1 produced in CHO cells, titers ranging from 800 to 900 mg/L
- ✓ Fully tested master cell bank stored in multiple locations for redundancy
- ✓ Large scale production confirmed (GMP run at 1000L scale)
- ✓ Protein purified using a well-defined process suitable for cGMP manufacturing, Protein A purification with multiple virus removal and virus inactivation steps
- ✓ Final product concentrated to 50 mg/mL for SQ injections (Once weekly)
- ✓ Consistent process performance through scale-up—process easily scalable, supply chain established
- ✓ Produced enough GMP material to support planned Phase 1/2 clinical trials in both ENPP1 and ABCC6 deficiencies

Ongoing Physician Identification and Educational Activities

Building KOL Relationships and Educating the Scientific and Patient Community

Discussing

Advocating

GACI Global
circulating hope

Presenting

Educating

inozyme pharma