Inozyme

Exceptional science. Breakthrough medicines.

Company Overview

- Inozyme Pharma is a biotechnology company **developing novel medicines** to treat rare and life-threatening calcification disorders
- These disorders are characterized by **mineral imbalances** that lead to over-calcified soft tissues and under-mineralized bone
- Our initial focus is on **enzyme replacement therapies (ERTs)** to address hypopyrophosphatemia, or low PPi, which is responsible for a broad range of rare calcification disorders that threaten and limit life
- Our lead drug candidate, **INZ-701**, is a first-in-class therapy designed to increase PPi levels and regulate calcification in multiple metabolic diseases
- INZ-701 for ENPP1 deficiency has received Orphan Drug Designation, Fast Track Designation, and Rare Pediatric Disease Designation in the US and Orphan Drug Designation in the EU
- **We expect to begin our clinical trials for both ENPP1 deficiency and ABCC6 deficiency in the first half of 2021**

Contact

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Corporate Brochure

inozyme pharma

Hypopyrophosphatemia/Adenosinemia

Our focus is on the biology of pyrophosphate and adenosine. Pyrophosphate is the body's natural inhibitor of calcification. A decrease in an individual's pyrophosphate permits pathological mineralization in tissues other than bone and teeth including the vasculature and joints. Adenosine is another important chemical in the body with multiple functions in the body. In blood vessels, adenosine prevents neointimal proliferation, the infilling of blood vessels with soft tissue. Neointimal proliferation that blocks blood flow occurs when adenosine levels in the body are low. When both pyrophosphate and adenosine are significantly reduced, this combination contributes to significant morbidity and mortality.

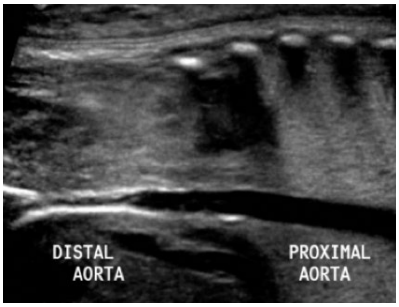
Key Genes Implicated in Hypopyrophosphatemia

ENPP1 regulates PPi levels in the blood by converting adenosine triphosphate (ATP) to PPi and adenosine monophosphate (AMP). ABCC6 channels ATP from inside a cell to outside the cell. Mutations in the *ENPP1* gene and the *ABCC6* gene lead to low PPi, which is responsible for the calcification disorders, causing ENPP1 deficiency and ABCC6 deficiency respectively.

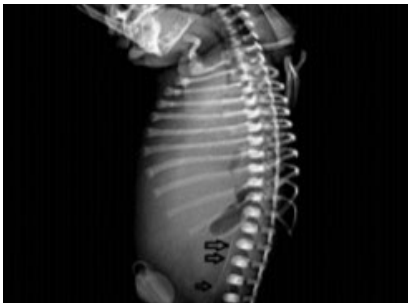
Genes	Disorders	Diseases
ENPP1 gene	ENPP1 Deficiency	Generalized arterial calcification of infancy type 1 (GACI type 1) in infants Autosomal recessive hypophosphatemic rickets type 2 (ARHR2) post-infancy
ABCC6 gene	ABCC6 Deficiency	GACI type 2 in infants Pseudoxanthoma elasticum (PXE)

Phenotypes of ENPP1 Deficiency

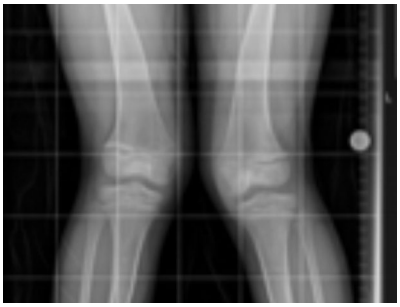
- In infants with **GACI**, calcium builds abnormally in soft tissues, especially blood vessels, often resulting in death by one year of up to 50% of infants with ENPP1 deficiency.
- In children and adults with **ARHR2**, low PPi can lead to severe muscle/bone/joint pain, limited movement of the spine and hips, short stature, and often bowed legs or knocked knees.



An ultrasound from an infant patient shows echo-brightness of the distal aorta, a reflection of the calcium deposit in that artery.



A lateral radiograph of the neonate showing calcification of descending aorta and its bifurcation (arrows).



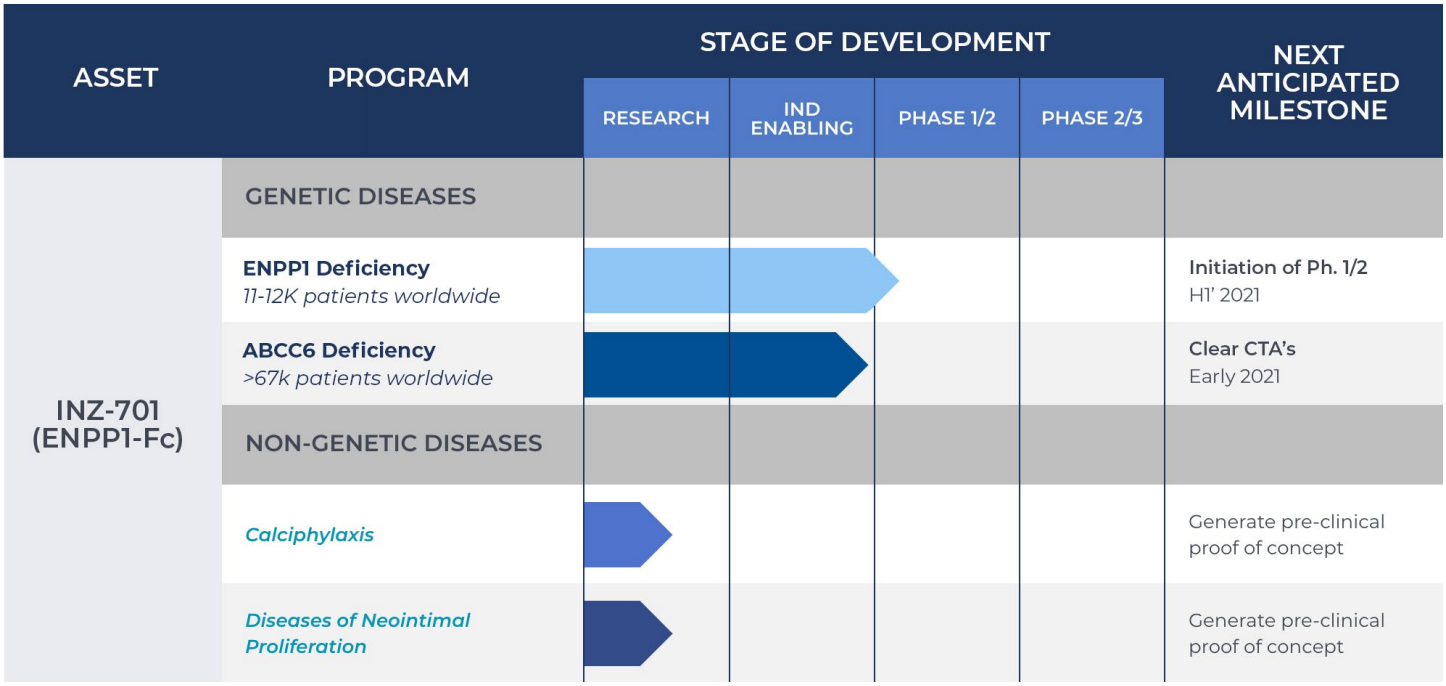
A radiograph of the lower extremities of a patient with ARHR2. The child presented with short stature and bilateral genu valgum.

Phenotypes of ABCC6 Deficiency

- **PXE** is a rare genetic disease leading to ectopic calcification of elastic tissues including arteries, skin and the Bruch's membrane in the retina.
- Similar to GACI type 1, in infants with **GACI type 2,** calcification leads to narrowing of large and medium-sized arteries, often resulting in heart failure and death by one year.

Our Pipeline

Our lead product candidate is INZ-701, an ENPP1 enzyme replacement therapy (ERT) in preclinical development for the potential treatment of patients with a variety of calcification disorders linked primarily to mutations in the ENPP1 and ABCC6 genes, or ENPP1 deficiency and ABCC6 deficiency respectively. We have generated robust preclinical proof of concept data demonstrating that in animal models INZ-701 prevented pathological calcification, led to improvements in overall health and survival and prevented neointimal proliferation. We expect to initiate clinical trials in both ENPP1 and ABCC6 deficiencies in the first half of 2021.



Free Genetic Testing Program: Early Detection is Key

- **In partnership with PreventionGenetics**, Inozyme Pharma provides a no-cost, global genetic testing program to improve detection and understanding of two rare and debilitating calcification disorders, **ENPP1 deficiency and ABCC6 deficiency**
- The purpose of the genetic testing program is to increase awareness, reduce barriers to genetic testing, and **help people and their healthcare providers make more informed decisions** about these rare conditions
- Individuals who meet eligibility criteria can receive a **no-cost, third-party genetic test** to determine if they have or are a carrier for ENPP1 deficiency or ABCC6 deficiency
- For more information about the program, please visit **inozyme.com/patients-hcps/genetic-testing-program/** or email **clinicaldnatesting@preventiongenetics.com.**

The Genetic Testing Process

An HCP will determine if the patient meets the eligibility criteria for a no-cost genetic test.

The HCP will order the test.

A genetic laboratory will process the test and share the results with the HCP.

Natural History Study, Burden of Disease Study and Ongoing Clinical Trials

- **The National Human Genome Research Institute (NHGRI)**, a division of the National Institutes of Health (NIH), and the Münster University Children's Hospital, Münster, Germany, have completed a natural history study and the results have been submitted for publication.
    - The natural history study was designed to enhance our understanding of the natural progression of GACI and ARHR2 in affected individuals, and of how genes might play a role in the presentation of these conditions. This information could help in the development of new treatments for GACI and ARHR2.
- Inozyme, along with GACI Global and Engage Health, have completed a Burden of Disease Study in ENPP1 and infantile onset ABCC6 deficiency. These data are currently being analyzed and will be submitted for publication in the first half of 2021.
- There will soon be **clinical trials for patients with ENPP1 or ABCC6 deficiencies**. If you have questions, please contact Inozyme at **clinicaltrials@inozyme.com**.

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