Inozyme Pharma Publishes Data Supporting INZ-701 as a Potential Treatment for ENPP1 Deficiency

April 29, 2021

- Peer-reviewed article in Journal of Bone and Mineral Research *showed INZ-701 increased pyrophosphate (PPi) levels, improved disease markers, and decreased mortality in an ENPP1-deficient mouse model -*

- Preclinical findings support increase of PPi levels as a predictive marker of therapeutic benefit -

BOSTON, April 29, 2021 (GLOBE NEWSWIRE) -- Inozyme Pharma, Inc., a rare disease biopharmaceutical company developing novel therapeutics for the treatment of abnormal mineralization, today announced the online pre-publication release of preclinical data suggesting the potential of its lead development candidate, INZ-701, as a treatment for ENPP1 Deficiency. As reported in the *Journal of Bone and Mineral Research (JBMR)*, in an article titled, "INZ -701 prevents ectopic tissue calcification and restores bone architecture and growth in ENPP1 deficient mice", treatment with INZ-701 was associated with increased plasma levels of pyrophosphate (PPi), a potent regulator of mineralization, as well as improvements in several other disease markers and decreased mortality in a mouse model of ENPP1 Deficiency. The publication is the first to present data on INZ-701 in a peer-reviewed journal.

"In addition to boosting circulating levels of PPi, INZ-701 prevented pathological calcification in all tested organs, improved growth parameters, corrected bone defects, improved clinical signs, and decreased mortality in ENPP1-deficient mice. These results strengthen the rationale for INZ-701 as a potential treatment for ENPP1 Deficiency and support the endpoints for our planned clinical trials," said Yves Sabbagh, Ph.D., Senior Vice President and Chief Scientific Officer of Inozyme Pharma. "We are pleased that the editors of the *JBMR* recognize the importance of these preclinical data and their potential implications for patients and families affected by ENPP1 Deficiency."

ENPP1 Deficiency is a progressive condition that manifests as a spectrum of disease. The most extreme manifestation seen in newborns and infants, generalized arterial calcification of infancy (GACI), is characterized by severe vascular calcification and neointimal proliferation (overgrowth of smooth muscle cells inside blood vessels), resulting in dysfunction and failure of major organs such as the heart and kidneys. The condition is lethal in an estimated 50% of affected babies. Children and adults with ENPP1 Deficiency are affected by autosomal-recessive hypophosphatemic rickets type 2 (ARHR2), which is characterized by bone defects such as rickets and osteomalacia (softened bones), and often exhibit a range of signs and symptoms that can include hearing loss, arterial calcification, cardiac and neurological involvement.

The *JBMR* publication highlights the following preclinical findings with INZ-701:

- Increase of PPi:
  - Durable increases in PPi levels were observed after subcutaneous administration of a single dose of INZ-701 (5 mg/kg) in ENPP1-deficient mice.
  - In a dose-response study, animals injected with INZ-701 (0.2, 1, or 5 mg/kg every other day for eight weeks) showed a dose-dependent elevation in plasma ENPP1 activity and an average increase of approximately 2 µM in plasma PPi. Those findings suggested that INZ-701 at a dose as low as 0.2 mg/kg every other day was sufficient to maintain increased plasma PPi levels after eight weeks.
- Prevention of calcification:
  - Repeated dosing of INZ-701 at 0.2 mg/kg tended to reduce tissue calcium levels in the kidney, spleen, lung, and liver.
  - Dosing at 1 mg/kg significantly reduced calcification in most of the tissues.
  - Dosing at 5 mg/kg completely prevented calcification in all tissues.
- Correction of bone defects:
  - INZ-701 treatment led to a dose-dependent increase in trabecular number (a measure of bone texture correlated with bone microarchitecture), cortical thickness, bone volume, and bone mineral density.
- Restoration of growth parameters:
  - INZ-701 treatment resulted in a clear dose response in rescuing slow growth in ENPP1-deficient mice during the first four weeks of the study.
  - By the end of the study (day 56), mice treated with INZ-701 gained significant weight and reached approximately 15-16 grams in the 0.2 and 1 mg/kg dosing groups, and approximately 18 grams in the 5 mg/kg dosing group, compared to approximately 20 grams in wild-type (WT) mice.
  - ENPP1-deficient mice dosed with vehicle failed to gain weight from roughly four weeks of age to the end of the study.
- Improvements in other clinical signs:
  - Compared to the vehicle-treated group, ENPP1-deficient mice dosed with 0.2 mg/kg of INZ-701 showed less severe clinical signs associated with ENPP1 deficiency (dehydration, hunched back, stilted gait, rough hair coat and pinned ears) from day 27.
  - Mice dosed with 1 mg/kg of INZ-701 did not show any signs of morbidity until the eighth week of the study.

- No abnormalities were observed in any WT mice or in ENPP1-deficient mice treated with 5 mg/kg of INZ-701.

About ENPP1 Deficiency
The ENPP1 gene produces a critical enzyme called ectonucleotide pyrophosphatase/phosphodiesterase 1 (ENPP1), which regulates inorganic pyrophosphate (PPi) levels in plasma. PPi is essential for preventing harmful soft tissue calcification and for regulating normal bone mineralization. ENPP1 Deficiency affects patients across the age spectrum and manifests as either generalized arterial calcification of infancy (GACI) type 1 or autosomal recessive hypophosphatemic rickets type 2 (ARHR2). GACI type 1 is a devastating and often fatal disease affecting infants and is characterized by calcification and narrowing of large and medium-sized arteries, resulting in heart failure and death in about half of patients within the first six months of life. Mutations in the ABCC6 gene can also cause an infantile onset of the disease called GACI type 2. ARHR2 manifests in the post-infancy stage and causes rickets, weakened bones, repeated bone fractures, skeletal deformities, short stature, muscle weakness, fatigue, and bone pain.

About INZ-701
INZ-701 is an enzyme replacement therapy in development for the treatment of mineralization disorders of the circulatory system, bones, and kidneys. In preclinical studies, the experimental therapy has shown potential to generate plasma pyrophosphate (PPi) and to restore it to appropriate physiological levels, thereby preventing calcification in the vasculature and kidneys, while at the same time normalizing bone mineralization. Inozyme is developing INZ-701 for certain rare, life-threatening, and devastating genetic disorders such as ENPP1 Deficiency and ABCC6 Deficiency in which PPi levels are below the normal physiological levels.

Inozyme is preparing to initiate a Phase 1/2 clinical trial in patients with ENPP1 Deficiency in the first half of 2021 and a separate Phase 1/2 clinical trial in patients with ABCC6 Deficiency in mid-2021.

About Inozyme Pharma
Inozyme Pharma (Nasdaq: INZY) is a rare disease biopharmaceutical company developing novel therapeutics for the treatment of diseases of abnormal mineralization impacting the vasculature, soft tissue, and skeleton. Through our in-depth understanding of the biological pathways involved in mineralization, we are pursuing the development of therapeutics to address the underlying causes of these debilitating diseases. It is well established that two genes, *ENPP1* and *ABCC6*, play key roles in a critical mineralization pathway and that defects in these genes lead to abnormal mineralization. We are initially focused on developing a novel therapy to treat the rare genetic diseases of ENPP1 and ABCC6 Deficiencies.

Inozyme Pharma was founded in 2017 by Joseph Schlessinger, Ph.D., Demetrios Braddock, M.D., Ph.D., and Axel Bolte, MSc, MBA, with technology developed by Dr. Braddock and licensed from Yale University. For more information, please visit www.inozyme.com.

Cautionary Note Regarding Forward-Looking Statements
Statements in this press release about future expectations, plans, and prospects, as well as any other statements regarding matters that are not historical facts, may constitute "forward-looking statements" within the meaning of The Private Securities Litigation Reform Act of 1995. These statements include, but are not limited to, statements relating to the potential of our lead product candidate, INZ-701, the initiation and timing of our future clinical trials and our research and development programs. The words "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "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. Any forward-looking statements are based on management's current expectations of future events and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in, or implied by, such forward-looking statements. These risks and uncertainties include, but are not limited to, risks associated with the Company's ability to initiate its planned Phase 1/2 clinical trials of INZ-701 for ENPP1 Deficiency and ABCC6 Deficiency; obtain and maintain necessary approvals from the FDA and other regulatory authorities; continue to advance its product candidates in preclinical studies and clinical trials; replicate in later clinical trials positive results found in preclinical studies and early-stage clinical trials of its product candidates; advance the development of its product candidates under the timelines it anticipates in planned and future clinical trials; obtain, maintain and protect intellectual property rights related to its product candidates; manage expenses; and raise the substantial additional capital needed to achieve its business objectives. For a discussion of other risks and uncertainties, and other important factors, any of which could cause the Company's actual results to differ from those contained in the forward-looking statements, see the "Risk Factors" section, 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 press release represent the Company's views as of the date hereof and should not be relied upon as representing the Company's views as of any date subsequent to the date hereof. The Company anticipates that subsequent events and developments will cause the Company's views to change. However, while the Company may elect to update these forward-looking statements at some point in the future, the Company specifically disclaims any obligation to do so.

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