Inozyme Pharma Announces Presentation of Data from ENPP1 Deficiency Development Program at the ASBMR 2021 Annual Meeting

October 4, 2021

- Natural History Study shows ectopic calcification and/or cardiovascular disease could serve as distinguishing characteristics of ENPP1 Deficiency in some children with rickets -

- Preclinical data support AAV-ENPP1 gene therapy as a potential treatment for ENPP1 Deficiency -

BOSTON, Oct. 04, 2021 (GLOBE NEWSWIRE) -- Inozyme Pharma, Inc. (Nasdaq: INZY), a rare disease biopharmaceutical company developing novel therapeutics for the treatment of abnormal mineralization, today announced the presentation of data from the Company's ENPP1 Deficiency Natural History Study and its gene therapy program for the treatment of ENPP1 Deficiency. The data were presented at the American Society for Bone and Mineral Research (ASBMR) 2021 Annual Meeting held October 1-4.

"Results from these studies deepen our understanding of ENPP1 Deficiency and underscore the urgent need for novel interventions," said Axel Bolte, MSc, MBA, Inozyme's co-founder, president, and chief executive officer. "With conventional therapies for FGF23-mediated hypophosphatemia associated with worsening calcification, identifying distinguishing characteristics of ENPP1 Deficiency is imperative for ensuring quick and proper diagnosis and treatment of patients suffering from this disease. We firmly believe that our pipeline candidates hold strong potential to play a meaningful role in the treatment of multiple underserved populations, and we look forward to commencing the Phase 1/2 clinical trials of INZ-701 in ENPP1 Deficiency and ABCC6 Deficiency in the fourth quarter."

ENPP1 Deficiency is a progressive condition that manifests as a spectrum of disease. Those who present in utero or infancy are typically diagnosed with generalized arterial calcification of infancy (GACI), which is characterized by extensive vascular calcification and neointimal proliferation (overgrowth of smooth muscle cells inside blood vessels), resulting in myocardial infarction or cardiac or multiorgan failure. The condition is lethal in an estimated 50% of affected babies. Children and adults with ENPP1 Deficiency typically experience rickets and osteomalacia (softened bones), also termed autosomal-recessive hypophosphatemic rickets type 2 (ARHR2), and can exhibit a range of signs and symptoms that can include hearing loss, arterial calcification, cardiac, and neurological involvement. There are no approved treatments for ENPP1 Deficiency.

Summary of Data Presented

Title: ENPP1-Deficient Patients Present With Both Skeletal Complications and Ectopic Calcification
Lead Author: Frank Rutsch, M.D., Muenster University Children's Hospital, Münster, Germany

- This cross-sectional, retrospective study assessed data from 74 patients with confirmed *ENPP1* variants. A total of 46% of patients demonstrated skeletal disease (median age of initial reporting: 4.3 years), with an estimated 90% of all patients expected to develop skeletal complications by 25 years. Cardiac disease was reported in 58% of patients with skeletal complications, as well as high rates of calcification of the aorta (68%) and other arteries (71%). GACI was not reported in 25% (9/34) of patients with skeletal complications; however, some of these individuals reported arterial calcification (n=2) or cardiac complications [heart valve defect (n=4), cardiac failure (n=2)]. Thirty patients received conventional therapy with calcitriol and phosphate. Young ENPP1-deficient patients are at risk for skeletal complications over a broad age spectrum, warranting continued monitoring well into adolescence. As skeletal manifestations have a similar phenotype to other forms of FGF23-mediated hypophosphatemia, a history of calcification or cardiovascular disease should trigger consideration of ENPP1 Deficiency as the etiology. These data highlight implications for the appropriate diagnosis and treatment of patients with ENPP1 Deficiency.

Title: Treatment with an AAV vector expressing ENPP1-Fc prevents ectopic tissue calcification and restores bone parameters in Enpp1-deficient mice
Presenter: Yves Sabbagh, Ph.D., Inozyme Pharma

- This dose-response study assessed the pharmacological effects of AAV-ENPP1-Fc, an adeno-associated virus vector expressing a modified human ENPP1-Fc under a tissue-specific promoter, when administered to murine mouse models of ENPP1 Deficiency. Clinically relevant endpoints, including plasma PPi levels, tissue calcium content assessed by a colorimetric assay, and bone parameters, were measured after 10 weeks. At 12 weeks of age, vehicle-treated mutant mice showed profound defects in long bones, including lower trabecular number and thickness and thinner cortical bone in femora, and clear signs of rickets in the growth plate. One single intravenous injection of AAV-ENPP1-Fc resulted in a robust and durable increase in plasma ENPP1 activity for the duration of the study. AAV-ENPP1-Fc administration also led to a dose-dependent increase in plasma PPi levels and prevention of soft tissue calcification. Treatment at high dose prevented pathological calcification in all the tested organs and restored bone parameters. Findings demonstrate the potential of AAV-ENPP1-Fc gene therapy to treat ENPP1 Deficiency.

About INZ-701

INZ-701 is an ENPP1 enzyme replacement therapy (ERT) 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 correcting bone abnormalities. 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.

About Inozyme Pharma

Inozyme Pharma, Inc. (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 initiation and timing of our clinical trials, the initiation and timing of our natural history study, our research and development programs, the availability of preclinical study and clinical trial data, the timing of our regulatory applications and the period over which we believe that our existing cash, cash equivalents and investments will be sufficient to fund our operating expenses. 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 in the Company's 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 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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