Inozyme Pharma Presents Preclinical Data Suggesting Utility of INZ-701 as a Potential Treatment for ABCC6 Deficiency

May 7, 2021

Results presented at the European Calcified Tissue Society Congress provide first evidence of increased plasma pyrophosphate (PPi) levels and reduced calcification with an enzyme replacement therapy in an animal model of PXE

BOSTON, May 07, 2021 (GLOBE NEWSWIRE) -- Inozyme Pharma, Inc. (Nasdaq: INZY), a rare disease biopharmaceutical company developing novel therapeutics for the treatment of abnormal mineralization, today presented preclinical data suggesting the utility of its lead clinical development candidate, INZ-701, as a potential treatment for ABCC6 Deficiency. The data, presented at the virtual European Calcified Tissue Society Annual Congress (ECTS, May 6-8), are the first to show that an enzyme replacement therapy (ERT) increased plasma pyrophosphate (PPi) levels and reduced calcification in an animal model of ABCC6 Deficiency.

ABCC6 Deficiency is a rare, inherited disorder that can present as generalized arterial calcification of infancy (GACI) type 2 in infants and as pseudoxanthoma elasticum (PXE) in children and adults. This is one of several disorders with significant decrease in plasma PPi levels, a potent regulator of mineralization. In patients with ABCC6 Deficiency, the abnormal calcification caused by low PPi can result in vision loss and life-threatening cardiovascular complications, among other morbidities. There is no approved treatment for ABCC6 Deficiency.

“In patients with ABCC6 Deficiency, the reduced levels of PPi that lead to pathological mineralization suggest an overlap between ENPP1 and ABCC6 Deficiencies,” explained Yves Sabbagh, Ph.D., Senior Vice President and Chief Scientific Officer of Inozyme Pharma. “This supports the rationale for an enzyme replacement therapy aimed at raising PPi to treat these serious genetic disorders. The data show that INZ-701 increased plasma PPi levels and prevented abnormal calcification in an ABCC6-deficient mouse model, demonstrating its potential for treating patients with PXE, a chronic form of ABCC6 Deficiency with no approved therapeutic options.”

This study was performed in collaboration with Thomas Jefferson University. Subcutaneous administration of INZ-701 (2 and 10 mg/kg every other day for two or eight weeks) was initiated in ABCC6-deficient mice at five to six weeks of age, the time where initiation of ectopic mineralization in this model is observed. INZ-701 led to a dose-dependent increase in plasma PPi levels at both two and eight weeks after initiation of treatment, leading to significantly lower levels of soft tissue mineralization. Histopathologic examination of tissue biopsies from vehicle-treated mice revealed extensive mineralization in the muzzle skin containing vibrissae, a biomarker of the mineralization process in this model. Compared to vehicle-treated mice, a quantitative calcium assay demonstrated that the amount of calcium in muzzle skin biopsies was reduced by 68% and 74% in mice receiving INZ-701 at dose levels of 2 and 10 mg/kg, respectively ($p < 0.01$).

“It is encouraging to see an ENPP1 enzyme replacement having an effect on tissue calcification in this PXE animal model. The patients suffering from this disease currently have no treatment options and collaborating with Inozyme to use our in-house expertise on this disease with their drug discovery efforts is exciting,” said Jouni Uitto, M.D., Ph.D., Professor and Chair of Dermatology and Cutaneous Biology, and Biochemistry and Molecular Biology, at Thomas Jefferson University. "This study will help Inozyme further characterize the therapeutic potential of INZ-701 in PXE and other manifestations of ABCC6 Deficiency, which may offer hope to patient communities that have been waiting many years for a viable treatment option.”

About ABCC6 Deficiency and Pseudoxanthoma Elasticum (PXE)
ABCC6 Deficiency is a rare, inherited disorder caused by mutations in the *ABCC6* gene, resulting in decreased or absent activity of the ABCC6 protein. A systemic and progressively debilitating condition estimated to affect more than 67,000 individuals worldwide, ABCC6 Deficiency leads to low levels of pyrophosphate (PPi) and is associated with pathological mineralization in blood vessels and soft tissues throughout the body. These effects can result in devastating medical problems including blindness, life-threatening cardiovascular complications, and skin calcification.

Some infants with ABCC6 Deficiency are diagnosed with generalized arterial calcification of infancy (GACI) type 2, a vascular condition that resembles GACI type 1, the acute infantile form of ENPP1 Deficiency. In older patients, ABCC6 Deficiency presents as pseudoxanthoma elasticum (PXE), a rare, inherited disorder in which individuals develop calcification of soft connective tissues, including in the eyes, cardiovascular system, and skin. Individuals with PXE often have abnormalities in the eyes, such as changes in the pigmented cells of the retina; angioid streaks (tiny cracks in Bruch’s membrane, the inner layer of the retina); and choroidal vascularization (bleeding and scarring of the retina), possibly leading to vision loss. Patients with PXE may also exhibit yellowish bumps, papules, on the neck, underarms, and other areas of the skin which becomes leathery and sagging. The skin findings indicate a general, systemic, pathological process of soft tissue calcification.

About INZ-701
INZ-701 is an ENPP1 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 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.

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.

Contacts

Investors:
Inozyme Pharma
Stefan Riley, Director of Investor Relations
Stefan.riley@inozyme.com

Media:
SmithSolve
Alex Van Rees
(973) 442-1555 ext. 111
Alex.vanrees@smithsolve.com