Inozyme Pharma Announces Positive Preliminary Data from Phase 1/2 Clinical Trial of INZ-701 in Patients with ENPP1 Deficiency

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- Rapid, significant, and sustained increase in plasma pyrophosphate (PPi) levels observed in all three patients in lowest dose cohort (0.2 mg/kg) –

- PPi increased in all three patients to levels comparable to those observed in a study of healthy subjects -

- INZ-701 was generally well-tolerated and exhibited a favorable initial safety profile –

- Second cohort underway at next dose level (0.6 mg/kg) –

BOSTON, April 04, 2022 (GLOBE NEWSWIRE) -- Inozyme Pharma, Inc. (Nasdaq: INZY), a clinical-stage rare disease biopharmaceutical company developing novel therapeutics for the treatment of abnormal mineralization, today announced positive preliminary biomarker, safety, and pharmacokinetic (PK) data from the first three patients treated in the Phase 1 portion of its ongoing first-in-human Phase 1/2 clinical trial of INZ-701 in adult patients with ENPP1 Deficiency. At the 0.2 mg/kg dose level of INZ-701, all three patients showed rapid, significant, and sustained increases in PPi levels. Preclinical findings demonstrated PPi as a key predictive biomarker of therapeutic benefit in ENPP1 Deficiency.

“ENPP1 Deficiency is a devastating disease, and patients currently have no approved therapies,” said Axel Bolte, MSc, MBA, Inozyme’s co-founder, president, and chief executive officer. “We are greatly encouraged by the data reported today, as they represent the first clinical evidence supporting the potential of INZ-701 to address an urgent medical need. The data from the lowest dose cohort demonstrated that INZ-701 was able to rapidly and significantly increase PPi levels in these patients, with a potential for therapeutic benefit. We look forward to additional data from patients at the next dose levels in our ongoing clinical trial.”

Summary of Preliminary Data

- The range of PPi levels across three patients at screening was 132-333 nM.
- The range of PPi levels measured at six hours after the first dose was 581-1239 nM, an approximately 4-fold mean increase from screening across the three patients.
- The mean PPi level during the 32-day dose evaluation period across the three patients was 1356 nM, an approximately 5-fold mean increase from screening across the three patients.
- The range of peak PPi levels observed during the 32-day dose evaluation period across the three patients was 1082-2416 nM, and was comparable to data from our study of healthy subjects (n=10), which showed PPi levels between 1002 nM and 2169 nM.

PPi levels observed after dosing of INZ-701 correlated to systemic exposure and activity of INZ-701. PK analysis showed INZ-701 nearing steady-state by Day 29 with an approximately 4-fold accumulation from Day 1, based on $AUC_{0\text{-}72}$. The half-life of INZ-701 observed in this trial suggests the potential for once-weekly dosing. INZ-701 was generally well-tolerated, with no serious adverse events reported, and otherwise exhibited a favorable initial safety profile.

All three patients from the first cohort enrolled in the open-label Phase 2 48-week extension portion of the trial. At Week 12, low titers of anti-drug antibodies were observed in two out of three patients. The significantly increased PPi levels observed during the 32-day dose evaluation period were sustained in all three patients through Week 12 of the extension portion of the trial.

Following conclusion of the 32-day dose evaluation period, an independent Data Safety Monitoring Board (DSMB) reviewed preliminary data from the ongoing trial. Based on this review, the DSMB recommended the trial continue as planned. Dosing is underway at the 0.6 mg/kg dose level of INZ-701 in the second cohort of the trial.

Inozyme plans to report topline data from the ongoing trial in the second half of 2022.

About the PPi Assay and Healthy Subject Study

Inozyme conducted a controlled study in healthy subjects to establish a highly sensitive, reproducible PPi assay and to determine factors that may influence PPi measurements. The assay was validated in accordance with the Clinical Laboratory Improvement Amendments (CLIA) and is being used in the ongoing Phase 1/2 trial as a laboratory-developed test (LDT).

Key objectives of the healthy subject study were to determine if and how exercise and timing of meals, respectively, affect PPi levels in each subject. Results demonstrated intra-subject variability of PPi levels during the day with the timing of meals. In addition, exercise was shown to increase PPi levels in all subjects. Samples collected after an overnight fast had consistent PPi measurements with low intra-subject variability.

Data from this study of healthy subjects (n=10), using the same sample processing protocol employed in the ongoing and planned Phase 1/2 clinical trials of INZ-701 in ENPP1 Deficiency and ABCC6 Deficiency, showed PPi levels between 1002 nM and 2169 nM. Additional data from this study is expected to be presented at the European Calcified Tissue Society Congress (ECTS), being held on the 7-10^{th} of May 2022.

INZ-701 in ENPP1 Deficiency Phase 1/2 Clinical Trial Design

The ongoing Phase 1/2 open-label clinical trial is expected to enroll up to nine adult patients with ENPP1 Deficiency at sites in North America and

Europe. The trial will primarily assess the safety and tolerability of INZ-701 in adult patients with ENPP1 Deficiency, as well as characterize the PK and pharmacodynamic (PD) profile of INZ-701, including evaluation of PPi and other biomarker levels. In the Phase 1 dose-escalation portion of the trial, Inozyme is assessing INZ-701 for 32-days at doses of 0.2 mg/kg, 0.6 mg/kg, and 1.8 mg/kg administered via subcutaneous injection twice weekly, with three patients per dose cohort. Doses were selected based on preclinical studies and PK/PD modeling. The Phase 1 dose-escalation portion of the trial seeks to identify a safe, tolerable dose that increases PPi levels, and that can be used for further clinical development. The open-label Phase 2 extension portion of the trial is assessing long-term safety, pharmacokinetics, and pharmacodynamics of continued treatment with INZ-701 for up to 48 weeks, where patients may receive doses of INZ-701 at home depending on site-specific protocols. Exploratory endpoints will include evaluations of skeletal, vascular, physical function and patient-reported outcomes.

About ENPP1 Deficiency

ENPP1 Deficiency is a progressive condition that manifests as a spectrum of diseases. Individuals who present in utero or in 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, stroke, or cardiac or multiorgan failure. Approximately 45% to 50% of infants with ENPP1 Deficiency die within six months of birth. Children and adults with ENPP1 Deficiency typically experience rickets and osteomalacia (softened bones), a condition also known as autosomal-recessive hypophosphatemic rickets type 2 (ARHR2), and they can exhibit a range of signs and symptoms that include hearing loss, arterial calcification, and cardiac and/or neurological involvement. There are no approved therapies for ENPP1 Deficiency.

About INZ-701

INZ-701 is a clinical-stage 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 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. INZ-701 is currently in a Phase 1/2 clinical trial for the treatment of ENPP1 Deficiency.

About Inozyme Pharma

Inozyme Pharma, Inc. (Nasdaq: INZY) is a clinical-stage 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, INZ-701, to treat the rare genetic diseases of ENPP1 and ABCC6 Deficiencies.

INZ-701 is currently in a Phase 1/2 clinical trial for ENPP1 Deficiency. 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 trial results, trial design, the availability of clinical trial data and the potential benefits of INZ-701. 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 and conduct its ongoing and 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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