Inozyme Pharma Announces Positive Interim Data from Ongoing Phase 1/2 Trials of INZ-701 in Adults with ENPP1 Deficiency and ABCC6 Deficiency (PXE)

September 26, 2023

- Data from ongoing trial suggest clinical benefit for ENPP1 Deficiency, including improvement in key biomarkers, patient reported outcomes (PROs) and functional outcomes -

- Improvement in the Global Impression of Change (GIC) observed in all three dose cohorts in ABCC6 Deficiency (PXE) trial -

- INZ-701 was generally well tolerated and exhibited a favorable safety and immunogenicity profile in both trials -

- Company to host conference call and webcast today at 8:00 a.m. ET -

BOSTON, Sept. 26, 2023 (GLOBE NEWSWIRE) -- **Inozyme Pharma, Inc.** (Nasdaq: INZY) ("Inozyme" or the "Company"), a clinical-stage rare disease biopharmaceutical company developing novel therapeutics for the treatment of pathologic mineralization and intimal proliferation, today announced positive interim safety, pharmacokinetic (PK), pharmacodynamic (PD) and exploratory efficacy data from the Company's ongoing Phase 1/2 clinical trials of INZ-701 in adults with ENPP1 Deficiency and ABCC6 Deficiency (PXE, pseudoxanthoma elasticum).

"We are pleased that these trials have achieved their primary goals of demonstrating that INZ-701 was generally safe and well tolerated and meaningfully increased PPi levels in patients with ENPP1 Deficiency and ABCC6 Deficiency. We have also observed trends of clinical improvement which gives us confidence that we can design an informative pivotal trial in adults with ENPP1 Deficiency," said Kurt Gunter, M.D., senior vice president and chief medical officer of Inozyme Pharma. "The trends towards improvement in clinically meaningful markers of bone metabolism in adults with ENPP1 Deficiency point to the potential for INZ-701 to treat rickets in our planned pivotal trial in pediatric patients with the condition."

"Data from these first-in-human trials of INZ-701 are highly encouraging for both patients and physicians in the ENPP1 Deficiency and ABCC6 Deficiency communities. I am particularly excited to see early signs that INZ-701 may address symptoms in the adult population of ENPP1 Deficiency, which could translate to clinical benefits in the infant and adolescent patients who are in urgent need of a therapeutic option," said Michael Levine, M.D., Professor Emeritus, Pediatrics and Medicine and Chief Emeritus, Division of Endocrinology and Diabetes at the Center for Bone Health at the Children's Hospital of Philadelphia Research Institute.

ENPP1 Deficiency

Nine patients were initially enrolled in the ongoing Phase 1/2 clinical trial across three dose cohorts of INZ-701 (0.2 mg/kg (n=3), 0.6 mg/kg (n=3), and 1.8 mg/kg (n=3)). For trial design details, please see the section entitled "INZ-701 in ENPP1 Deficiency Phase 1/2 Clinical Trial Design" below.

Exploratory Biomarker Data

Exploratory biomarker data were collected throughout the study to provide evidence of the potential for disease modification with ongoing treatment with INZ-701. Notable changes in key biomarkers were observed and support the clinical hypothesis, including:

- Meaningful reduction of fibroblast growth factor-23 (FGF-23) observed. Most patients with ENPP1 Deficiency have elevated levels of FGF-23, which leads to increased phosphate wasting and hypophosphatemia, a key driver of osteomalacia and rickets.
- Serum phosphate (Pi) levels increased over time, in the absence of phosphate and active vitamin D supplementation, which were withheld from patients during the study.
- Statistically significant correlation between increase in plasma pyrophosphate (PPi) and decrease in FGF-23 observed at one week post first dose.
- Upward trends observed in bone specific alkaline phosphatase (BSAP) levels from baseline, which signal biological activity in bone tissue.

Exploratory Efficacy Data

Outcome measures were collected to assess potential clinical benefit with ongoing treatment with INZ-701 and to inform the design and patient selection of future trials in adolescents and adults. Notable changes in PROs and functional outcomes were observed in all cohorts, including:

- Concordant improvement in GIC scores reported by patients (P-GIC) and clinicians (C-GIC), and no patient showed a deterioration from baseline.
- High responder rates in Patient-Reported Outcome Measurement Information Scales (PROMIS) of Pain Intensity, Fatigue and Pain Interference.[1]
- Trend of improvement in 6-minute walk test (6-MWT). Subgroup analysis of 6-MWT results showed greater improvement in patients with lower baseline values and stable results over time in patients with higher baseline values.
- Subgroup analysis of patients who presented with arthritis/arthralgia at baseline showed improvement in 6-MWT, and increased spine bone mineral density (BMD) and bone mineral content (BMC), as measured by dual x-ray absorptiometry (DEXA).

Pharmacodynamic (PD) and Pharmacokinetic (PK) Data

- Rapid, significant, and sustained increase in PPi levels observed in all patients and significant elevation in PPi maintained for up to 18 months.
- Long half-life of approximately 126 hours and drug accumulation as shown by a greater than dose proportional exposure suggests the potential for once weekly dosing.

Safety Data

- INZ-701 was generally well-tolerated and exhibited a favorable safety profile, with no serious or severe adverse events attributed to INZ-701 and no adverse events leading to study withdrawal.
- 3/9 patients experienced mild adverse events related to INZ-701.
    - Injection site reactions (bruising, hemorrhage, pain, pruritus, and/or swelling) occurred in 2/9 patients.
    - Other related adverse events included decreased appetite and fatigue.
- There were two serious adverse events not related to INZ-701.
- All nine patients enrolled in the Phase 2 portion of the trial, two of whom subsequently withdrew from the study. The study withdrawals were not related to an adverse event.
- Seven patients remain in the trial and continue on home self-administration of INZ-701 treatment.
- Time on study ranged from 98 to over 638 days. Total time on treatment across all cohorts corresponds to approximately 9 patient-years.

Anti-Drug Antibody (ADA) Data

INZ-701 exhibited a favorable immunogenicity profile with low titers of non-neutralizing ADAs observed in 7/9 patients. The ADA levels were transient in 3/7 patients.

ABCC6 Deficiency

Ten patients were enrolled in the ongoing Phase 1/2 trial across three dose cohorts of INZ-701 (0.2 mg/kg (n=3), 0.6 mg/kg (n=3), and 1.8 mg/kg (n=4)). For trial design details, please see the section entitled “INZ-701 in ABCC6 Deficiency Phase 1/2 Clinical Trial Design” below.

Exploratory Efficacy Data

Clinical outcome measures were collected to provide evidence of clinical benefit and to inform the design of future trials in adults. Notable changes in GIC, a PRO, were observed, including:

- The majority of timepoints showed improvement in GIC scores reported by P-GIC and C-GIC.
- All patients (9/9) showed improvement on C-GIC, and 7/9 patients showed improvement from baseline on P-GIC at last follow-up.

Pharmacodynamic (PD) and Pharmacokinetic (PK) Data

- Rapid and significant increase in PPi levels observed in all cohorts with a dose response observed.
- PPi showed sustained increase in the highest dose cohort to levels comparable to those observed in a study of healthy subjects.[2]
- PK properties were consistent with those observed in the Phase 1/2 clinical trial in adults with ENPP1 Deficiency.

Safety Data

- INZ-701 was generally well-tolerated and exhibited a favorable safety profile, with no serious or severe adverse events.
- All adverse events were mild to moderate in severity.
- 7/10 patients experienced adverse events related to INZ-701.
    - Injection site reactions (discoloration, discomfort, erythema, induration, pain, pruritus, warmth) occurred in 7/10 patients.
    - Other related adverse events were fatigue, night sweats and urticaria.
- One patient from the highest dose cohort was withdrawn from Phase 1 at day 18 due to a moderate adverse event (erythema/urticaria) related to INZ-701.
- One patient withdrew from the trial during Phase 2, which was not related to an adverse event.
- Eight patients remain in the trial and seven continue on home self-administration of INZ-701 treatment.
- Time on study ranged from 18 to over 518 days. Total time on treatment across all cohorts corresponds to approximately 9.1 patient-years.

ADA Data

- INZ-701 exhibited a favorable immunogenicity profile with low titers of non-neutralizing ADAs observed in 8/10 patients.
- The ADA levels were transient in 3/8 patients.

Webcast and Conference Call Details

Inozyme will host a conference call and webcast to discuss these updates today, Tuesday, September 26th, 2023, at 8:00 a.m. ET.

The live webcast and replay will be accessible here and through Inozyme's website under News and Events. Alternatively, the conference call may be accessed by dialing:

Domestic Dial-in Number: 1-877-270-2148
International Dial-in Number: 1-412-902-6510

Participants should ask to join the **Inozyme Pharma** call.

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 intimal proliferation (overgrowth of smooth muscle cells inside blood vessels), resulting in myocardial infarction, stroke, or cardiac or multiorgan failure. Approximately 50% of infants with ENPP1 Deficiency die within six months of birth. Children with ENPP1 Deficiency typically develop rickets, a condition diagnosed as autosomal-recessive hypophosphatemic rickets type 2 (ARHR2), while adolescents and adults can develop osteomalacia (softened bones). ARHR2 and osteomalacia lead to pain and mobility issues. Patients can also exhibit signs and symptoms of hearing loss, arterial and joint calcification, and cardiovascular complications. There are no approved therapies for ENPP1 Deficiency.

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

The ongoing Phase 1/2 open-label clinical trial initially enrolled 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 pharmacokinetic (PK) and pharmacodynamic (PD) profile of INZ-701, including evaluation of the PD marker, plasma pyrophosphate (PPi) and other biomarker levels. In the Phase 1 dose-escalation portion of the trial, Inozyme assessed 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 sought to identify a safe, tolerable dose that increases PPi levels, and that can be used for further clinical development. Following completion of the Phase 1 portion of the first three cohorts, Inozyme dosed patients in a fourth cohort at 1.2 mg/kg to investigate the potential for once-weekly dosing of INZ-701. The open-label Phase 2 extension portion of the trial is assessing long-term safety, PK, and PD of continued treatment with INZ-701 for at least 48 weeks, where patients may self-administer INZ-701. Exploratory endpoints include evaluations of skeletal, vascular, physical function and patient-reported outcomes.

About ABCC6 Deficiency

ABCC6 Deficiency is a rare, severe, inherited disorder caused by mutations in the ABCC6 gene, leading to low levels of PPi. PPi is essential for preventing harmful soft tissue calcification and regulating bone mineralization. ABCC6 Deficiency is a systemic and progressively debilitating condition, which affects more than 67,000 individuals worldwide. Infants with ABCC6 Deficiency are diagnosed with generalized arterial calcification of infancy (GACI) type 2, a condition that resembles GACI type 1, the infant form of ENPP1 Deficiency. In older individuals, ABCC6 Deficiency presents as pseudoxanthoma elasticum (PXE), which is characterized by pathological mineralization in blood vessels and soft tissues clinically affecting the skin, eyes, and vascular system. There are no approved therapies for ABCC6 Deficiency.

INZ-701 in ABCC6 Deficiency Phase 1/2 Clinical Trial Design

The ongoing Phase 1/2 open-label clinical trial enrolled ten adult patients with ABCC6 Deficiency at sites in the United States and Europe. The trial will primarily assess the safety and tolerability of INZ-701 in adult patients with ABCC6 Deficiency, as well as characterize the pharmacokinetic (PK) and pharmacodynamic (PD) profile of INZ-701, including the evaluation of levels of plasma PPi and other biomarkers. In the Phase 1 dose-escalation portion of the trial, Inozyme assessed 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 sought to identify a safe, tolerable dose for further development that increases PPi levels. The open-label Phase 2 extension portion of the trial is assessing long-term safety, PK, and PD of continued treatment with INZ-701 for at least 48 weeks, where patients may self-administer INZ-701. Exploratory endpoints will include evaluations of vascular, ophthalmologic, physical function and patient-reported outcomes.

About INZ-701

INZ-701, a recombinant Fc fusion protein, is an ENPP1 enzyme replacement therapy in development for the treatment of rare disorders of the vasculature, soft tissue, and skeleton. In preclinical studies, the experimental therapy has shown potential to prevent pathologic mineralization and intimal proliferation (the overgrowth of smooth muscle cells inside blood vessels), which can drive morbidity and mortality in devastating genetic disorders such as ENPP1 Deficiency and ABCC6 Deficiency. INZ-701 is currently in clinical trials for the treatment of ENPP1 Deficiency and ABCC6 Deficiency.

About Inozyme Pharma

Inozyme Pharma, Inc. is a clinical-stage rare disease biopharmaceutical company developing novel therapeutics for the treatment of diseases impacting the vasculature, soft tissue, and skeleton. Inozyme is developing INZ-701, an enzyme replacement therapy, to address pathologic mineralization and intimal proliferation which can drive morbidity and mortality in these severe diseases. INZ-701 is currently in clinical trials for the treatment of ENPP1 Deficiency and ABCC6 Deficiency.

For more information, please visit **www.inozyme.com** or follow Inozyme on **LinkedIn**, **X (formerly Twitter)**, and **Facebook**.

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 availability of data from clinical trials, 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 conduct its ongoing clinical trials of INZ-701 for ENPP1 Deficiency and ABCC6 Deficiency; enroll patients in ongoing and planned trials; 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; comply with covenants under its outstanding loan agreement; 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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[1] “Responder” is defined as exhibiting improvement from baseline in >50% of timepoints evaluated.

[2] Khursigara, et al, Bone 2023