



Inozyme Pharma Reports Positive Topline Data from Ongoing Phase 1/2 Trials of INZ-701

February 16, 2023

- Rapid, significant, and sustained increase in plasma pyrophosphate (PPi) observed and encouraging patient reported outcome data in all dose cohorts in ENPP1 Deficiency trial -
- Rapid and significant increase in PPi observed in all dose cohorts with sustained increase observed in highest dose cohort in ABCC6 Deficiency (PXE) trial -
- INZ-701 was generally well-tolerated and exhibited a favorable safety profile in both trials -
- Company updates its cash runway guidance to fund cash flow requirements into fourth quarter of 2024 -
- Company to host virtual investor and analyst event at 8:00 a.m. ET on February 16, 2023 -

BOSTON, Feb. 16, 2023 (GLOBE NEWSWIRE) -- [Inozyme Pharma, Inc.](#) (Nasdaq: INZY), a clinical-stage rare disease biopharmaceutical company developing novel therapeutics for the treatment of pathologic mineralization and intimal proliferation, today announced positive topline pharmacokinetic (PK), pharmacodynamic (PD), and safety data from the ongoing Phase 1/2 clinical trials of INZ-701 in ENPP1 Deficiency and ABCC6 Deficiency (PXE). The Company also reported encouraging patient reported outcome data as measured by global impression of change (GIC) in the ENPP1 Deficiency trial.

"We are pleased to share topline data today demonstrating that INZ-701 rapidly restored PPi to normal levels in all dose cohorts in the ENPP1 Deficiency trial, with normal PPi levels sustained during the trial. Additionally, emerging patient-reported outcome data, as measured by GIC, showed six of eight patients reported concordant improvements in overall health compared to baseline on clinician-GIC and patient-GIC," said Axel Bolte, MSc, MBA, Inozyme's co-founder, president and chief executive officer. "In the ABCC6 Deficiency trial, we saw pharmacodynamic activity in all dose cohorts and we were particularly encouraged to see sustained PPi levels in the highest dose cohort."

"Data reported today are highly encouraging and show that INZ-701 significantly increased PPi levels into normal physiological ranges with a favorable safety profile," 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. "The data presented today represent strong evidence to warrant continued clinical development of INZ-701 in ENPP1 Deficiency and ABCC6 Deficiency."

Kurt Gunter, M.D., senior vice president and chief medical officer at Inozyme, added, "People suffering from ENPP1 Deficiency and ABCC6 Deficiency are in desperate need of an effective therapeutic option. INZ-701 has shown in our ongoing clinical trials encouraging safety data, a predictable pharmacokinetic profile, and significant pharmacodynamic activity, all of which provide a strong foundation for advancing our trials. We are grateful to patients, families, and investigators for their continued support and participation in our research."

"We aim to achieve multiple key milestones in 2023, including the initiation of a pivotal trial of INZ-701 for pediatric patients with ENPP1 Deficiency," added Mr. Bolte. "With our estimated cash position expected to fund cash flow requirements into the fourth quarter of 2024, we believe we are well positioned for success."

Phase 1/2 Clinical Trial in Adults with 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.

Pharmacodynamic Data¹

- Mean baseline PPi across all three cohorts was 426±407 nM.
- Rapid, significant, and sustained increase in PPi was observed in all patients, with a target PPi threshold observed from the lowest dose of 0.2 mg/kg.
- PPi increased in all patients to levels comparable to those observed in a study of healthy subjects (n=10), which showed PPi levels between 1002 nM and 2169 nM.

Table 1: PPi levels after INZ-701 administration in ENPP1 Deficiency.

			Mean PPi (nM) ± SD		
			Cohort 1 (0.2 mg/kg)*	Cohort 2 (0.6 mg/kg)	Cohort 3 (1.8 mg/kg)
Phase 1	Single Dose	Day 1-8	1229±410	1438±715	1220±426
	2x/Week Dose	Day 11-32	1494±498	1745±780	1341±330
Phase 2	2x/Week Dose	Day 32-338	1299±490	1472±516	1462±233

*Cohort 1 – n=2 post week 12

Pharmacokinetic Data¹

- INZ-701 activity in a dose proportional manner was observed.

- 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 Data²

- 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 or pain) 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 Phase 2, one of whom subsequently withdrew from the study following week 12 due to travel reasons. Eight patients continue on INZ-701 treatment.

Anti-Drug Antibody (ADA) Data¹

INZ-701 exhibited a favorable immunogenicity profile with low titers of non-neutralizing ADAs observed in 7/9 patients.

Emerging Exploratory Clinical Data³

GIC is a patient reported outcome measure (PRO) in the ongoing Phase 1/2 clinical trial of INZ-701 in ENPP1 Deficiency. The measurement is performed by the clinician (C-GIC) and the patient (P-GIC) and assesses overall change in health from baseline on a 7-point scale as measured from "very much worse" (-3) to "very much improved" (+3). GIC is an exploratory endpoint and an early indicator of potential clinical outcomes.

- 6/8 patients showed concordant improvements on overall health on C-GIC and P-GIC.
- 5/8 patients showed "much improved" (+2) or "very much improved" (+3) on P-GIC.
- No patients showed a deterioration in overall health from baseline on C-GIC or P-GIC.

Phase 1/2 Clinical Trial in Adults with ABCC6 Deficiency

Nine patients were initially 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=3)). For trial design details, please see the section entitled "INZ-701 in ABCC6 Deficiency Phase 1/2 Clinical Trial Design" below.

Pharmacodynamic Data²

- Mean baseline PPI across all three cohorts was 947±193 nM.
- Rapid and significant increase in PPI was 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 (n=10), which showed PPI levels between 1002 nM and 2169 nM.

Table 2: PPI levels after INZ-701 administration in ABCC6 Deficiency.

			Mean PPI (nM) ± SD		
			Cohort 1 (0.2 mg/kg)	Cohort 2 (0.6 mg/kg)	Cohort 3 (1.8 mg/kg)
Phase 1	Single Dose	Day 1-8	1087±796	1326±330	1589±1065
	2x/Week Dose	Day 11-32	1023±454	1119±216	1415±509
Phase 2	2x/Week Dose	Day 32-252	900±253	1011±121	1498±465*

*P<0.05 vs 0.2 mg/kg – Cohort 3 – n=2 post day 18.

Pharmacokinetic Data²

- INZ-701 activity in a greater than dose proportional manner was observed.
- 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 Data⁴

- 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.
- 7/9 patients experienced adverse events related to INZ-701.
 - Injection site reactions (discoloration, erythema, induration, pain, or pruritus) occurred in 4/9 patients and were mild.

- Other related adverse events were erythema, fatigue, night sweats, pruritus, 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.
- 8/9 patients enrolled in Phase 2 and continue on INZ-701 treatment.

Anti-Drug Antibody (ADA) Data²

INZ-701 exhibited a favorable immunogenicity profile with low titers of non-neutralizing ADAs observed in 6/9 patients.

Anticipated Milestones

- **ENPP1 Deficiency**
 - Start of FDA pivotal trial meetings—Q1 2023
 - Initiation of ENERGY-1 - Phase 1b clinical trial of INZ-701 to evaluate the safety, tolerability, pharmacokinetics, and pharmacodynamics of INZ-701 in infants—Q2 2023
 - Interim clinical data from ongoing Phase 1/2 trial in adults—Q3 2023
 - Initiation of pivotal trial in pediatric patients, subject to regulatory approval—Q3 2023
 - Start of EMA protocol assistance meetings—Q4 2023
- **ABCC6 Deficiency**
 - Interim clinical data from ongoing Phase 1/2 trial in adults—Q4 2023
 - Initiation of Phase 2/3 clinical trial, subject to regulatory approval—2024

Cash Runway Guidance

The Company expects to report cash, cash equivalents, and short-term investments of approximately \$127.9 million as of December 31, 2022. The estimated cash, cash equivalents, and short-term investments amount is preliminary and unaudited, represents management's estimate as of the date of this press release, is subject to completion of the Company's financial closing procedures for the fourth quarter and fiscal year ended December 31, 2022, and does not present all necessary information for a complete understanding of the Company's financial condition as of December 31, 2022, or the Company's results of operations for the year ended December 31, 2022. The actual financial results may differ materially from the preliminary estimated financial information.

Based on its current plans, the Company anticipates its cash, cash equivalents, and short-term investments as of December 31, 2022, together with the additional \$20 million borrowed on February 15, 2023, under its existing debt facility, will enable the Company to fund cash flow requirements into the fourth quarter of 2024. This represents an increase of two quarters over the Company's previous guidance.

Investor and Analyst Event – Webcast and Conference Call Details

The Company will host an Investor and Analyst Event today, Thursday, February 16, 2023, at 8:00 a.m. ET to present the topline results from the trials in greater detail as well as provide an overview of the opportunity and planned development milestones in each indication. Joining the call will be members of the Inozyme management team as well as the following key opinion leaders:

- Michael A. 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
- Wilko Spiering, M.D., Ph.D., Associate Professor, Division of Internal Medicine and Dermatology, Department of Vascular Medicine, at the University Medical Center Utrecht of Utrecht University
- Mark Kiel, M.D., Ph.D., Founder and Chief Science Officer of Genomenon

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: 1-877-317-6789
- International Dial-in Number: 1-412-317-6789
- Participants should ask to be joined into 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 experience rickets, a condition also known as autosomal-recessive hypophosphatemic rickets type 2 (ARHR2), while adults experience osteomalacia (softened bones), 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.

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 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 with three patients per dose cohort. Patients received a single dose and then began twice weekly dosing one week later. 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 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 ectopic calcification, skeletal, vascular, and physical function, patient-reported outcomes, and exploratory biomarkers.

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 initially enrolled nine 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 with three patients per dose cohort. Patients received a single dose and then began twice weekly dosing one week later. 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 for further development that increases PPi levels. The open-label Phase 2 portion of the trial will assess 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 ectopic calcification, vascular and retinal function, patient-reported outcomes and exploratory biomarkers.

About INZ-701

INZ-701 is a clinical-stage enzyme 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 Phase 1/2 clinical trials for the treatment of adult ENPP1 Deficiency and ABCC6 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 impacting the vasculature, soft tissue, and skeleton. We are developing INZ-701, an enzyme therapy, to address pathologic mineralization and intimal proliferation which can drive morbidity and mortality in these severe diseases. INZ-701 is currently in Phase 1/2 clinical trials for the treatment of ENPP1 Deficiency and ABCC6 Deficiency.

For more information, please visit www.inozyme.com and follow us on [LinkedIn](#), [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 timing of our planned clinical trials, the availability of data from clinical trials, timing of planned regulatory meetings, the potential benefits of INZ-701, and the sufficiency of the Company's cash resources. 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 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; comply with the 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 and Quarterly Report on Form 10-Q 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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¹Data as of January 25, 2023

²Data as of January 10, 2023

³Data as of January 27, 2023

⁴Data as of January 16, 2023