



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

April 8, 2024

- Favorable safety and immunogenicity profile in ABCC6 Deficiency, with clinical improvements in vascular pathology, visual function and patient reported outcomes (PROs) -
- Natural history study highlights stroke as common feature among patients with early-onset ABCC6 Deficiency -
- Favorable safety, immunogenicity and clinical outcome data were maintained through 48 weeks in Cohorts 1-3 in ENPP1 Deficiency; Data from Cohort 4 support once weekly dosing in ongoing and future clinical trials -
- Company to host conference call and webcast today at 8:00 a.m. ET -

BOSTON, April 08, 2024 (GLOBE NEWSWIRE) -- [Inozyme Pharma, Inc.](#) (Nasdaq: INZY) ("the Company" or "Inozyme"), a clinical-stage rare disease biopharmaceutical company developing novel therapeutics for the treatment of pathologic mineralization and intimal proliferation, today announced positive topline 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 ABCC6 Deficiency (PXE, pseudoxanthoma elasticum) and ENPP1 Deficiency.

"We are excited by the excellent safety and preliminary efficacy profile of INZ-701 in adults with ABCC6 Deficiency," said Douglas A. Treco, Ph.D., CEO of Inozyme Pharma. "Our investigations into the natural history of this disease have identified a substantial and previously overlooked pediatric population with a high risk of stroke. We believe these patients represent a critical unmet need in this genetic disease and that changes observed in adults treated with INZ-701 will translate to clinical benefits in a future trial in children."

"The high risk of ischemic stroke in pediatric patients with ABCC6 Deficiency and its devastating consequences represents a serious unmet need in this population," commented Professor Zulf Mughal, M.D., Consultant in Paediatric Bone Disorders at Al Jalila Children's Specialty Hospital, Dubai, UAE. "I am very encouraged to see that INZ-701 may improve vascular pathology and believe that this effect may translate to clinical benefits in patients of all ages."

ABCC6 Deficiency Data

The ongoing Phase 1/2 trial in ABCC6 Deficiency enrolled 10 adults with heavy disease burden, as evidenced by serious cardiovascular disease and retinal disease. The patients were assigned to 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 Clinical and Efficacy Data

Exploratory markers of clinical benefit were collected throughout the study to provide evidence of the potential for disease modification with ongoing INZ-701 treatment. Notable changes were observed, including:

Carotid intima-media thickness (cIMT) stabilized and decreased

- cIMT, a predictive marker for cardiovascular disease and stroke, increases at a faster rate in people with PXE than in the general population. Reduction or stabilization of cIMT was observed across all dose cohorts (seven of eight evaluable patients), indicating a potential beneficial effect of INZ-701 on vascular pathology.

Choroidal thickness increased

- The choroid is the vascular layer between the sclera and retina. Choroidal thinning is associated with degenerative retinal changes in people with PXE and progresses with age. Increased choroidal thickness was observed across all dose cohorts (seven of eight evaluable patients), which indicates a potential beneficial effect of INZ-701 on retinal disease.

Global Visual Function Questionnaire (VFQ-25) scores indicated preservation and improvement of visual function over 48 weeks

- Four of six evaluable patients with VFQ-25 scores below normal at baseline improved over 48 weeks. Improvement in visual function was greater in older patients. A correlation between improvements in VFQ-25 and increases in choroidal thickness was preserved after 48 weeks.

Global Impression of Change Scale (GIC): Concordant improvement in GIC scores reported by patients (P-GIC) and clinicians (C-GIC) observed in all three dose cohorts

- All evaluable patients (nine of nine) showed improvement from baseline on C-GIC, and seven of nine evaluable patients showed improvement from baseline on P-GIC.

PD and PK Data

- Rapid increase in plasma pyrophosphate (PPi) levels observed at 1.8 mg/kg dose level and was sustained to levels

comparable to those observed in Inozyme's study of healthy subjects (n=10).

Safety Data

- INZ-701 was generally well tolerated and exhibited a favorable safety profile, with no serious or severe adverse events (AEs).
- All AEs were mild to moderate in severity. For previously reported data on AEs, please read [here](#).
- Eight patients remain in the trial and seven continue on home self-administration of INZ-701 treatment.
- Time on study ranged from 45 to over 631 days. Total time on treatment across all cohorts corresponds to approximately 12+ patient-years.

Anti-Drug Antibody (ADA) Data

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

Natural History Studies

The Company conducted a comprehensive retrospective, natural history study, and a prospective, longitudinal, observational study to characterize the natural progression of early-onset ABCC6 Deficiency and inform future clinical trial design. Findings indicate a substantial disease burden among pediatric patients with ABCC6 Deficiency, manifesting in a high incidence of major clinical events, notably stroke, severe neurological disease, and severe cardiovascular disease, occurring early in life. Seven out of 12 patients across the natural history studies either experienced stroke or are at risk, with strokes resulting in severe outcomes such as seizure disorders, paresis, and significant disability. Furthermore, 10 out of 12 patients were diagnosed with GACI Type 2, underscoring the considerable morbidity risk among pediatric survivors beyond the critical infancy period.

Development Plans for INZ-701 in Pediatric ABCC6 Deficiency

Given the high risk of cerebrovascular disease in the pediatric population, the Company believes that endpoints predictive of ischemic stroke (for example, progression of cerebral vasculopathy) may provide a suitable basis for Accelerated Approval in the US and Conditional Marketing Authorisation in the EU of INZ-701 in children with ABCC6 Deficiency. The Company plans to work expeditiously with the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA) on a pivotal trial design. Subject to regulatory review and sufficient funding, the Company expects to initiate a pivotal trial in pediatric patients with ABCC6 Deficiency in Q1 2025.

ENPP1 Deficiency Data

Thirteen adults with ENPP1 Deficiency were enrolled in the ongoing Phase 1/2 trial across three twice weekly dose cohorts (0.2 mg/kg [n=3], 0.6 mg/kg [n=3], and 1.8 mg/kg [n=3]) and one once-weekly dose cohort (1.2 mg/kg [n=4]) of INZ-701. 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. For previously reported exploratory biomarker data, please read [here](#). Notable changes in key biomarkers were observed and support Inozyme's clinical hypothesis, including:

- Significant reduction of fibroblast growth factor-23 (FGF-23) in the 1.8 mg/kg dose cohort (Cohort 3) through week 48. 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.
- Increase in bone specific alkaline phosphatase (BSAP) levels and decrease in c-telopeptide (CTX) in the 1.8 mg/kg dose cohort (Cohort 3) through week 48, which indicate the restoration of proper bone mineralization.

Exploratory Efficacy Data

Outcome measures were collected to assess the potential clinical benefit of ongoing treatment with INZ-701 and to inform the design and patient selection of future trials in adolescents and adults. For previously reported exploratory efficacy data, please read [here](#). Notable changes in PROs and functional outcomes were observed in all three twice-weekly dose cohorts, including:

- Favorable responses on the Patient-Reported Outcome Measurement Information Scales (PROMIS) of Pain Intensity, Fatigue and Pain Interference and P-GIC were maintained.

PD and PK Data

- Data from the once-weekly dose cohort showed increased PPI levels comparable to those observed in Inozyme's study of healthy subjects (n=10).
- Consistent exposure was observed with 1.2 mg/kg once weekly dosing when compared to 0.6 mg/kg twice weekly dosing.
- Long-term data showed a sustained increased PPI levels in the once-weekly dose cohort.

Safety Data

- INZ-701 was generally well-tolerated and exhibited a favorable safety profile, with no serious or severe AEs attributed to INZ-701 and no AEs leading to study withdrawal. For previously reported data on adverse events, please read [here](#).
- Eleven patients remain in the trial and 10 continue on home self-administration of INZ-701 treatment.

- Time on study ranged from 22 to over 742 days. Total time on treatment across all dose cohorts corresponds to approximately 12+ patient-years.

ADA Data

- INZ-701 exhibited a favorable immunogenicity profile with low titers of non-neutralizing ADAs observed in 11/14 patients.
- The ADA levels were transient in three of 11 patients.

Conference Call and Webcast Details

The live webcast and replay will be accessible through the [Investor Relations](#) section of Inozyme's website under [Events](#). Alternatively, the conference call may be accessed by dialing:

Domestic Dial-in Number: 1-833-816-1110

International Dial-in Number: 1-412-317-0686

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

For those unable to participate live, a replay will be available in the [Investor Relations](#) section of Inozyme's website for a limited time following the event.

About ABCC6 Deficiency

ABCC6 Deficiency is a progressively debilitating condition of the vasculature and soft tissue that is estimated to affect approximately 1 in 25,000 to 1 in 50,000 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. Pediatric patients who survive the first year of life may develop neurological disease, including stroke, and cardiovascular disease secondary to ongoing vascular calcification and stenosis. In older individuals, ABCC6 Deficiency presents as pseudoxanthoma elasticum (PXE), which is characterized by pathologic 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 10 adult patients with ABCC6 Deficiency at sites in the United States and Europe. The trial is primarily assessing the safety and tolerability of INZ-701 in adult patients with ABCC6 Deficiency, as well as characterizing the pharmacokinetic (PK) and pharmacodynamic (PD) profile of INZ-701, including the evaluation of levels of plasma pyrophosphate (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 that increases PPi levels for further development. 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 vascular, ophthalmologic, physical function, and patient-reported outcomes.

About ENPP1 Deficiency

ENPP1 Deficiency is a progressively debilitating condition of the vasculature, soft tissue, and skeleton with a prevalence of approximately 1 in 64,000 pregnancies worldwide. Although ENPP1 Deficiency was initially described in patients with biallelic ENPP1 Deficiency (homozygous or compound heterozygous mutations), many patients with monoallelic ENPP1 Deficiency (heterozygous mutations) have clinical symptoms, potentially increasing the worldwide prevalence. Individuals who present in utero or in infancy are typically diagnosed with generalized arterial calcification of infancy (GACI Type 1) and approximately 50% of infants 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 is primarily assessing the safety and tolerability of INZ-701 in adult patients with ENPP1 Deficiency, as well as characterizing 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 INZ-701

INZ-701, a recombinant Fc fusion protein, is an ENPP1 enzyme replacement therapy (ERT) in development for the treatment of rare disorders of the vasculature, soft tissue, and skeleton. INZ-701 metabolizes ATP to generate PPi, a natural inhibitor of mineralization, and AMP, which can be processed to phosphate and adenosine, the latter being a natural inhibitor of intimal proliferation. In preclinical studies, the experimental therapy has shown potential to prevent pathologic mineralization and intimal proliferation, which can drive morbidity and mortality in devastating disorders such as ENPP1 Deficiency, ABCC6 Deficiency and calciphylaxis. Clinical data to date have demonstrated that INZ-701 was generally well tolerated, exhibited a favorable safety profile, and meaningfully increased PPi levels in multiple clinical trials.

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 development for the treatment of ENPP1 Deficiency, ABCC6 Deficiency and calciphylaxis.

For more information, please visit <https://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 timing and contents of our planned topline data update, the initiation, timing, and design of our planned clinical trials, our regulatory strategy, including our plan to seek accelerated approval in the U.S. and conditional approval in the E.U, 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, ABCC6 Deficiency and calciphylaxis; 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 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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