Inozyme Pharma Announces Updates on Global Development Strategy of INZ-701 for the Treatment of ENPP1 Deficiency

July 26, 2023

- Change in plasma pyrophosphate (PPi) as primary endpoint in the U.S. and co-primary endpoint in the EU for planned ENERGY-3 pivotal trial in pediatric patients -

- ENERGY-3 pivotal trial in pediatric patients expected to initiate in October 2023, topline data expected to be reported in mid-2025 -

- Updated cash runway expected to fund cash flow requirements into Q1 2025 -

- Company to host conference call today at 8am ET -

BOSTON, July 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 a regulatory update for its global development strategy of INZ-701 for the treatment of ENPP1 Deficiency following recent meetings with the United States (U.S.) Food and Drug Administration (FDA) and the Paediatric Committee (PDCO) of the European Medicines Agency (EMA).

"We are pleased to have finalized our pediatric pivotal trial design with PPi, a well-established natural inhibitor of mineralization, as a primary endpoint in the U.S. and a co-primary endpoint in the EU. We have already observed that INZ-701 meaningfully increased PPi levels in our ongoing trial of INZ-701 in adults with ENPP1 Deficiency and, based on our discussions with regulators in the U.S. and EU, we believe we have a clear path forward in our clinical development program for the treatment of ENPP1 Deficiency," said Douglas A. Treco, Ph.D., CEO of Inozyme Pharma.

ENERGY-3 Trial Design – Planned Pivotal Trial in Pediatric Patients with ENPP1 Deficiency

The Company plans to initiate the ENERGY-3 pivotal trial, a multicenter, randomized, open label trial in pediatric patients with ENPP1 Deficiency in October 2023. The ENERGY-3 trial is expected to enroll up to 33 patients between the ages of one and less than 13 years across multiple sites globally and is designed primarily to assess the efficacy and safety of INZ-701 in pediatric patients with ENPP1 Deficiency. Enrollment criteria for the trial include a confirmed genetic diagnosis of ENPP1 Deficiency, radiographic evidence of skeletal abnormalities and low plasma PPi. Patients will be randomized in a 2:1 ratio to an INZ-701 arm or a control arm (conventional therapy, i.e., oral phosphate and active vitamin D) for 52 weeks, followed by an open label extension period during which all patients may receive INZ-701. INZ-701 will be administered at a 2.4 mg/kg once weekly dose via subcutaneous (SC) injection.

ENERGY-3 is a single, multicenter, clinical trial with differences in the statistical treatment of endpoints, based on guidance from the FDA and PDCO, as follows:

U.S.	EU
Primary Endpoint – Change in plasma PPi from baseline	**Co-Primary Endpoints –** Change in plasma PPi from baseline and Radiographic Global Impression of Change (RGI-C) score ($p<0.2$)
Secondary Endpoints - RGI-C score, Rickets Severity Score (RSS), Growth Z-score and pharmacokinetics (PK)	**Secondary Endpoints –** RSS, Growth Z-score and PK

Based on recommendations from the FDA, the primary endpoint of plasma PPi should be supported by consistent trends in appropriate secondary endpoints. Based on the agreed Paediatric Investigational Plan (PIP) with PDCO, plasma PPi and RGI-C are co-primary endpoints, with a relaxed p-value of <0.2 for RGI-C.

Planned Pivotal Trials in Infants and Adolescent/Adult Patients with ENPP1 Deficiency

The Company plans to conduct the ENERGY-2 pivotal trial, an open label, single arm trial in infants with ENPP1 Deficiency, based on the Paediatric Investigational Plan (PIP) agreed upon by PDCO. The trial is expected to be initiated outside of the U.S. The trial's co-primary endpoints will be change in plasma PPi from baseline and survival. The trial is expected to enroll up to 12 infants between birth and up to 12 months of age. Primary endpoint data from this trial will be compared to a natural history control group with patients matched on covariates associated with mortality. Discussions are ongoing with the FDA regarding the design of a potential pivotal trial of INZ-701 in infants with ENPP1 Deficiency in the U.S.

Pending regulatory discussions and appropriate financial resources, the Company also plans to conduct the ENERGY-4 pivotal trial, a multicenter, randomized, controlled trial in adolescents and adults with ENPP1 Deficiency. In the U.S., the trial's sole primary endpoint is expected to be change in plasma PPi from baseline, supported by trends in appropriate secondary endpoints, and in the EU, the trial's co-primary endpoints are expected to be change in plasma PPi from baseline and bone mineral content/density. Subject to regulatory review, the trial is expected to enroll up to 30 patients 13 years and older, and patients will be randomized in a 2:1 ratio to an INZ-701 arm or a control arm (conventional therapy, i.e., oral phosphate and active vitamin D).

Basis for Planned Marketing Applications

Based on regulatory feedback from the FDA and EMA, positive data from the ongoing and planned clinical trials of INZ-701 in patients with ENPP1 Deficiency, including comprehensive data demonstrating clinical impact of plasma PPi, could provide the basis for the Company's submission of marketing applications in both the U.S. and EU. These data will include final results from the Company's ongoing Phase 1/2 trial in adult patients with ENPP1 Deficiency, available results from the Company's ongoing ENERGY-1 trial, a Phase 1b trial of INZ-701 in infants with ENPP1 Deficiency, available results from the planned pivotal ENERGY-2 trial in infants to be initiated ex-U.S., and final results from the planned pivotal ENERGY-3 trial in

pediatric patients.

If these marketing applications are approved, the Company expects to commercially launch INZ-701 for infant and pediatric patients as early as the second half of 2026. Data from the planned ENERGY-4 trial in adolescent and adult patients with ENPP1 Deficiency may provide a basis for a supplemental marketing application.

Anticipated Milestones for ENPP1 Deficiency Program

- Interim data from Cohorts 1-3 in the Phase 2 portion of the ongoing Phase 1/2 trial in adults – September 2023
- Initiation of ENERGY-3 trial, a pivotal trial in pediatric patients – October 2023
- Topline data from Cohorts 1-3 in the Phase 2 portion of the ongoing Phase 1/2 trial in adults – Q1 2024
- Initiation of ENERGY-2 trial, a pivotal trial in infants, ex U.S. - Q2 2024
- Interim data from ENERGY-1 trial, a Phase 1b trial in infants – 2H 2024
- Topline data from ENERGY-3 trial, a pivotal trial in pediatric patients – Mid-2025

Cash Runway Guidance

The Company expects to report cash, cash equivalents, and short-term investments of approximately $140.2 million as of June 30, 2023. 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 quarter ended June 30, 2023 and does not present all necessary information for a complete understanding of the Company's financial condition as of June 30, 2023, or the Company's results of operations for the quarter ended June 30, 2023. 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 June 30, 2023, will enable the Company to fund cash flow requirements into the first quarter of 2025.

Conference Call

Inozyme will host a conference call and webcast to discuss its global development strategy for INZ-701 in patients with ENPP1 Deficiency today, July 26, 2023 at 8am ET. The live webcast will be accessible through the Investor Relations section of Inozyme's website under News & Events. To access the live call by phone, dial 1-877-270-2148 (domestic) or 1-412-902-6510 (international) and ask to be connected to 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 ENPP1 Deficiency

ENPP1 Deficiency is a progressive condition that manifests as a spectrum of diseases. The estimated genetic prevalence of ENPP1 Deficiency is approximately 1 in 64,000 pregnancies worldwide. 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 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.

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. (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 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** 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 and design of our clinical trials, the potential benefits of INZ-701, the timing and contents of our planned global development strategy, the availability and timing of clinical trial data, planned regulatory filings and the basis for such filings, the timing of the planned commercial launch of INZ-701, if approved, and the period over which we believe that our existing cash, cash equivalents and short term investments will be sufficient to fund our cash flow requirements. 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, EMA, 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; obtain clinically meaningful results with respect to novel endpoints; 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 filed with the Securities and Exchange Commission (SEC), as well as discussions of potential risks, uncertainties, and other important factors, in the Company's most recent filings with the SEC. 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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