UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): January 10, 2025

INOZYME PHARMA, INC.
(Exact name of Registrant as Specified in Its Charter)

Delaware	**001-39397**	**38-4024528**
(State or Other Jurisdiction of Incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

321 Summer Street **Suite 400** **Boston, Massachusetts**	**02210**
(Address of Principal Executive Offices)	**(Zip Code)**

Registrant's Telephone Number, Including Area Code: (857) 330-4340

(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common stock, par value $0.0001 per share	INZY	Nasdaq Global Select Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 2.02 Results of Operations and Financial Condition.

Inozyme Pharma, Inc. (the "Company") expects to report cash, cash equivalents, and short-term investments of approximately $113.1 million as of December 31, 2024.

The financial statements for the Company for the year ended December 31, 2024 are not yet available. The estimated cash, cash equivalents, and short-term investments amount as of December 31, 2024 is preliminary and unaudited, represents management's estimate as of the date of this report, is subject to completion of the Company's financial closing procedures for the year ended December 31, 2024, and does not present all necessary information for a complete understanding of the Company's financial condition as of December 31, 2024, or the Company's results of operations for the year ended December 31, 2024. The actual financial results may differ materially from the preliminary estimated financial information.

The information in this Item 2.02 shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended (the "Securities Act"), or the Exchange Act, except as expressly set forth by specific reference in such a filing.

Item 7.01 Regulation FD Disclosure.

On January 10, 2025, the Company issued a press release announcing positive interim data for INZ-701 in infants and young children with ENPP1 Deficiency and key program updates. A copy of the press release is attached as Exhibit 99.1 to this Current Report on Form 8-K and is incorporated herein by reference. On January 10, 2025, the Company also posted a presentation related to interim clinical and safety data of INZ-701 treatment in infants and young children with ENPP1 Deficiency and key program updates under "Events and Presentations" on the "Investors" section of the Company's website (www.inozyme.com). The information contained in, or that can be accessed through, the Company's website is not a part of this filing. A copy of the presentation is attached as Exhibit 99.2 to this Current Report on Form 8-K and is incorporated herein by reference.

The information in this Item 7.01, including Exhibits 99.1 and 99.2, shall not be deemed "filed" for purposes of Section 18 of the Exchange Act or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act or the Exchange Act, except as expressly set forth by specific reference in such a filing.

Item 8.01 Other Events.

On January 10, 2025, the Company announced positive interim data from its ENERGY 1 trial and Expanded Access Program ("EAP") evaluating INZ-701 in infants and young children with ENPP1 Deficiency, completion of enrollment in the Company's ENERGY 3 pivotal trial in pediatric patients with ENPP1 Deficiency and regulatory guidance for the Company's planned ASPIRE pivotal trial in children with ABCC6 Deficiency.

ENERGY 1 Trial and Expanded Access Program

Interim data from the ENERGY 1 trial (three infants) and the EAP (two infants and one child - 2.5 years old) evaluated patients with generalized arterial calcification of infancy ("GACI"), a severe manifestation of ENPP1 Deficiency. Patients were treated with INZ-701 for periods of three weeks to 22 months. Key results include:

- **Improved Survival:** 80% of infants treated with INZ-701 survived beyond their first year, compared to a historical survival rate of approximately 50%.
- **Reduction in Arterial Calcifications:** Substantial reductions or stabilization of arterial calcifications were observed in all surviving patients, including complete resolution in some instances. There was no evidence of progression of arterial calcification in any patient.
- **Improved Heart Function:** Stabilization or improvement in left ventricular ejection fraction was noted in all surviving patients.
- **Reduced Risk of Rickets:** No radiographic evidence of rickets was observed in patients evaluated beyond one year of age and at-risk of rickets development (n=3), supported by stabilization or increases in serum phosphate levels.
- **Favorable Safety Profile:** INZ-701 was well-tolerated, with no serious treatment-related adverse events in infants and young children. Observed treatment-related events were limited to mild injection site reactions. Across studies to-date, low, often transient, anti-drug antibody ("ADA") levels were noted in some children and adults, with no impact on pharmacokinetics ("PK") or pharmacodynamics ("PD"). In the ENERGY 1 trial and EAP, higher ADA levels in some infants significantly

affected PK and PD. In infants with high ADA levels, data collected pre- and post-dosing demonstrated substantial transient increases in PPi and drug exposure following INZ-701 administration, consistent with the clinical effects observed. ADAs were not associated with adverse events in any patient.

Enrollment Complete in ENERGY 3 Pivotal Trial

The Company today announced completion of enrollment in its ENERGY 3 pivotal trial of INZ-701 in patients with ENPP1 Deficiency aged >1 to <13 years. Based on recommendations from the U.S. Food and Drug Administration ("FDA"), the primary endpoint of plasma PPi should be supported by consistent trends in appropriate clinical endpoints, such as radiographic global impression of change ("RGI-C"), a measure for progression or improvement of rickets. As per agreement with the European Medicines Agency ("EMA"), plasma PPi and RGI-C are co-primary endpoints, with a relaxed p-value of <0.2 for RGI-C.

With 25 patients enrolled, the trial's 2:1 randomized design provides >90% power to detect meaningful differences in RGI-C between treatment and control groups. Strong patient interest and scheduled screenings may result in the enrollment of additional participants in January 2025. The Company anticipates completing the one-year dosing period for all patients by January 2026, with topline data expected in early 2026.

Regulatory Progress for Planned ASPIRE Pivotal Trial in Children with ABCC6 Deficiency

The Company is advancing the development of INZ-701 in ABCC6 Deficiency. In April 2024, the Company reported topline data from an open-label, dose-escalation study in adults, along with findings from a natural history study documenting the significant disease burden in patients with the early-onset form of the disease, known as GACI Type 2 (GACI-2). The adult study demonstrated positive improvements in vascular and retinal pathology after 48 weeks of treatment with INZ-701, as well as normalization of PPi levels at the highest dose tested, supporting further development in additional age groups. The natural history study revealed a high disease burden characterized by childhood strokes, arteriopathy, cardiovascular complications, and early mortality. Further research has identified a substantial pediatric population with ABCC6 Deficiency, underscoring the significant unmet medical need in this group.

The natural history study data, supplemented by literature reports, has informed the design of the Company's planned randomized, controlled ASPIRE trial of INZ-701 in children with ABCC6 Deficiency. The proposed primary endpoint, comprising major adverse clinical events over a two-year treatment period, has been reviewed and received preliminary support from U.S. and EU regulators. The trial is expected to enroll approximately 70 patients from infancy up to <18 years old with biallelic or monoallelic ABCC6 Deficiency. The Company is currently refining the trial design to harmonize feedback from the FDA and EMA.

The Company plans to continue regulatory engagement over the coming months to finalize the trial protocol. Pending ongoing regulatory review and the availability of financial resources, the Company aims to initiate the ASPIRE trial in early 2026.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits:

Exhibit	Description
99.1	Press Release dated January 10, 2025
99.2	Company Presentation dated January 2025
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

Cautionary Note Regarding Forward-Looking Statements

Statements in this Current Report on Form 8-K 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 initiation, enrollment, timing, and design of the Company's planned clinical trials, enrollment and availability of data from clinical trials, the potential benefits of INZ-701 and the Company's regulatory strategy. 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 Current Report on Form 8-K 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.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Date: January 10, 2025

By: /s/ Douglas A. Treco
Name: Douglas A. Treco
Title: Chief Executive Officer

Exhibit 99.1

Inozyme Pharma Announces Positive Interim Data for INZ-701 in Infants and Young Children with ENPP1 Deficiency and Key Program Updates

- Positive interim results in infants and young children with ENPP1 Deficiency showed improvements from baseline in multiple measures of disease, including survival, heart function, and stabilization or reduction in ectopic calcification and hypophosphatemia, with no radiographic evidence of rickets –

- Enrollment complete in ENERGY 3 pivotal trial in pediatric patients with ENPP1 Deficiency; on track to complete dosing in January 2026, with topline data to follow in early 2026 –

- Regulatory guidance from FDA and EMA supports planned ASPIRE pivotal trial focused on addressing severe complications of ABCC6 Deficiency in children –

BOSTON, Jan. 10, 2025 – Inozyme Pharma, Inc. (Nasdaq: INZY) ("the Company" or "Inozyme"), a clinical-stage biopharmaceutical company developing innovative therapeutics for rare diseases that affect bone health and blood vessel function, today announced positive interim data from its ENERGY 1 trial and Expanded Access Program (EAP) evaluating INZ-701 in infants and young children with ENPP1 Deficiency, completion of enrollment in the ENERGY 3 pivotal trial in pediatric patients with ENPP1 Deficiency and regulatory guidance for the ASPIRE pivotal trial in children with ABCC6 Deficiency.

"We believe these highly encouraging outcomes in infants and young children, combined with previously reported data from adult studies, provide strong support for the potential impact of INZ-701 on rickets, a key clinical endpoint in the ongoing pivotal ENERGY 3 trial, and underscore its potential to address the significant needs of pediatric patients," said Douglas A. Treco, Ph.D., CEO and Chairman of Inozyme Pharma.

Matt Winton, Ph.D., Senior Vice President and COO of Inozyme Pharma added, "Our team and global collaborators worked tirelessly to identify and diagnose these rare patients and initiate treatment as quickly as possible. Tragically, in some cases, we have been unable to begin treatment before the infant passed. This only deepens our commitment to the patient community and strengthens our resolve to address unmet needs across all populations as we advance INZ-701."

Positive Interim Data from the ENERGY 1 trial and Expanded Access Program

Interim data from the ENERGY 1 trial (three infants) and the EAP (two infants and one child ~2.5 years old) evaluated patients with generalized arterial calcification of infancy (GACI), a severe manifestation of ENPP1 Deficiency. Patients were treated with INZ-701 for periods of three weeks to 22 months. The data presentation can be accessed here on Inozyme's Investor Relations site. Key results include:

- **Improved Survival:** 80% of infants treated with INZ-701 survived beyond their first year, compared to a historical survival rate of approximately 50%.
- **Reduction in Arterial Calcifications:** Substantial reductions or stabilization of arterial calcifications were observed in all surviving patients, including complete resolution in some instances. There was no evidence of progression of arterial calcification in any patient.
- **Improved Heart Function:** Stabilization or improvement in left ventricular ejection fraction (LVEF) was noted in all surviving patients.
- **Reduced Risk of Rickets:** No radiographic evidence of rickets was observed in patients evaluated beyond one year of age and at-risk of rickets development (n=3), supported by stabilization or increases in serum phosphate levels.
- **Favorable Safety Profile:** INZ-701 was well-tolerated, with no serious treatment-related adverse events in infants and young children. Observed treatment-related events were limited to mild injection site reactions. Across studies to-date low, often transient, anti-drug antibody (ADA) levels were noted in some children and adults, with no impact on pharmacokinetics (PK) or pharmacodynamics (PD). In the ENERGY 1 trial and EAP, higher ADA levels in some infants significantly affected PK and PD. In infants with high ADA levels, data collected pre- and post-dosing demonstrated substantial transient increases in PPi and drug exposure following INZ-701 administration, consistent with the clinical effects observed. ADAs were not associated with adverse events in any patient.

Enrollment Complete in ENERGY 3 Pivotal Trial

The Company today announced completion of enrollment in its ENERGY 3 pivotal trial of INZ-701 in patients with ENPP1 Deficiency aged >1 to <13 years. Based on recommendations from the U.S. Food and Drug Administration (FDA), the primary endpoint of plasma PPi should be supported by consistent trends in appropriate clinical endpoints, such as radiographic global impression of change (RGI-C), a measure for progression or improvement of rickets. As per agreement with the European Medicines Agency (EMA), plasma PPi and RGI-C are co-primary endpoints, with a relaxed p-value of <0.2 for RGI-C.

With 25 patients enrolled, the trial's 2:1 randomized design provides >90% power to detect meaningful differences in RGI-C between treatment and control groups. Strong patient interest and scheduled screenings may result in the enrollment of additional participants in January 2025. Inozyme anticipates completing the one-year dosing period for all patients by January 2026, with topline data expected in early 2026.

Regulatory Progress for ASPIRE Pivotal Trial in Children with ABCC6 Deficiency: Preliminary Support from U.S. and EU Regulators

Inozyme is advancing the development of INZ-701 in ABCC6 Deficiency. In April 2024, the Company reported topline data from an open-label, dose-escalation study in adults, along with findings from a natural history study documenting the significant disease burden in patients with the early-onset form of the disease, known as GACI Type 2 (GACI-2). The adult study demonstrated positive improvements in vascular and retinal pathology after 48 weeks of treatment with INZ-701, as well as normalization of PPi levels at the highest dose tested, supporting further development in additional age groups. The natural history study revealed a high disease burden characterized by childhood strokes, arteriopathy, cardiovascular complications, and early mortality. Further research has identified a substantial pediatric population with ABCC6 Deficiency, underscoring the significant unmet medical need in this group.

The natural history study data, supplemented by literature reports, has informed the design of the Company's planned randomized, controlled ASPIRE trial of INZ-701 in children with ABCC6 Deficiency. The proposed primary endpoint, comprising major adverse clinical events over a two-year treatment period, has been reviewed and received preliminary support from U.S. and EU regulators. The trial is expected to enroll approximately 70 patients from infancy up to <18 years old with biallelic or monoallelic ABCC6 Deficiency. Inozyme is currently refining the study design to harmonize feedback from the FDA and EMA.

The Company plans to continue regulatory engagement over the coming months to finalize the trial protocol. Pending ongoing regulatory review and the availability of financial resources, Inozyme aims to initiate the ASPIRE trial in early 2026.

About ENPP1 Deficiency

ENPP1 Deficiency is a serious and progressive rare disease that affects blood vessels, soft tissues, and bones. Individuals who present in utero or in infancy are typically diagnosed with generalized arterial calcification of infancy (GACI Type 1), with about 50% of these infants not surviving beyond six months. Children with this condition typically develop rickets, specifically autosomal-recessive hypophosphatemic rickets type 2 (ARHR2), while adolescents and adults may develop osteomalacia, or softened bones. ARHR2 and osteomalacia cause pain and difficulty with movement. Additionally, patients may experience hearing loss, calcification in arteries and joints, and heart problems.Biallelic ENPP1 Deficiency affects approximately 1 in 64,000 pregnancies worldwide. Initially, it was believed to only impact individuals with two copies of the mutated gene. However, many individuals with just one copy of the mutated gene (monoallelic ENPP1 Deficiency) also exhibit severe symptoms. This suggests that the worldwide prevalence of ENPP1 Deficiency may be much higher than current estimates, which are based solely on biallelic cases. Currently, there are no approved therapies for ENPP1 Deficiency.

About ABCC6 Deficiency

ABCC6 Deficiency is a progressive and debilitating rare disease that affects blood vessels and soft tissues. Infants with ABCC6 Deficiency are diagnosed with generalized arterial calcification of infancy (GACI Type 2), which is similar to GACI Type 1, the infant form of ENPP1 Deficiency. Pediatric patients who survive beyond the first year of life may develop neurological disease, including strokes, and cardiovascular diseases due to ongoing vascular calcification and stenosis. In older individuals, ABCC6 Deficiency manifests as pseudoxanthoma elasticum (PXE), characterized by abnormal mineralization in blood vessels and soft tissues, affecting the skin, visual function, and vascular system. Biallelic ABCC6 Deficiency is estimated to affect 1 in 25,000 to 1 in 50,000 individuals worldwide. Initially, it was believed to only impact individuals with two copies of the mutated gene. However, many people with just one copy of the mutated gene (monoallelic ABCC6 Deficiency) also exhibit severe symptoms. This suggests that the worldwide prevalence of ABCC6 Deficiency may be much higher than current estimates, which are based solely on biallelic cases. Currently, there are no approved therapies for ABCC6 Deficiency.

About Inozyme Pharma

Inozyme Pharma is a pioneering clinical-stage biopharmaceutical company dedicated to developing innovative therapeutics for rare diseases that affect bone health and blood vessel function. We are experts in the PPi-Adenosine Pathway, where the ENPP1 enzyme generates inorganic pyrophosphate (PPi), which regulates mineralization, and adenosine, which controls intimal proliferation (the overgrowth of smooth muscle cells inside blood vessels). Disruptions in this pathway impact the levels of these molecules, leading to severe musculoskeletal, cardiovascular, and neurological conditions, including ENPP1 Deficiency, ABCC6 Deficiency, calciphylaxis, and ossification of the posterior longitudinal ligament (OPLL).

Our lead candidate, INZ-701, is an ENPP1 Fc fusion protein enzyme replacement therapy (ERT) designed to increase PPi and adenosine, enabling the potential treatment of multiple diseases caused by deficiencies in these molecules. It is currently in clinical development for the treatment of ENPP1 Deficiency, ABCC6 Deficiency, and calciphylaxis. By targeting the PPi-Adenosine Pathway, INZ-701 aims to correct pathological mineralization and intimal proliferation, addressing the significant morbidity and mortality in these devastating diseases.

For more information, please visit https://www.inozyme.com/ or follow Inozyme on LinkedIn, X, 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 initiation, timing, and design of our planned clinical trials, enrollment and availability of data from clinical trials, the potential benefits of INZ-701 and our regulatory strategy. 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 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.

Contacts

Investors:
Inozyme Pharma
Stefan Riley, Senior Director of IR and Corporate Communications
(617) 461-2442
stefan.riley@inozyme.com

Media:
Biongage Communications
Todd Cooper
(617) 840-1637
todd@biongage.com

Exhibit 99.2

Interim clinical and safety data of INZ-701 treatment in infants and young children with ENPP1 Deficiency and key program updates

January 2025

Ella
Living with ENPP1 Deficiency

Legal disclaimer

This presentation and any statements made orally during this presentation contain estimates and other statistical data made by independent parties and by us relating to market size and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such data and estimates. In addition, projections, assumptions and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk. Neither Inozyme Pharma, Inc. nor its affiliates, advisors or representatives make any representations as to the accuracy or completeness of that data or undertakes to update such data after the date of this presentation.

Forward-Looking Statement Disclaimer

Statements in this presentation about future expectations, plans, and prospects, as well as any other statements regarding matters that are not historical facts, may constitute forward-looking statements that involve substantial risks and uncertainties. These statements include, but are not limited to, statements relating to the initiation, timing, and design of our planned clinical trials, the potential benefits of INZ-701 and our regulatory strategy.

The words “anticipate,” “believe,” “continue,” “could,” “estimate,” “expect,” “intend,” “may,” “might,” “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. We may not actually achieve the plans, intentions or expectations disclosed in these forward-looking statements, and you should not place undue reliance on these forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in these forward-looking statements. For a discussion of risks and uncertainties, and other important factors, any of which could cause our actual results to differ from those contained in the forward-looking statements, see the “Risk Factors” section in our 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 presentation represent our views as of the date of this presentation. We anticipate that subsequent events and developments will cause our views to change. However, while we may elect to update these forward-looking statements in the future, we specifically disclaim any obligation to do so. These forward-looking statements should not be relied upon as representing our views as of any date subsequent to the date of this presentation.

Strong progress advancing INZ-701 across multiple indications and demographics

Milestones to Date

- ✓ Positive clinical effects observed in adults with ENPP1 Deficiency and ABCC6 Deficiency in Phase 1/2 trials
- ✓ Favorable safety profile in adults with ENPP1 Deficiency, ABCC6 Deficiency and calciphylaxis
- ✓ Low, often transient, ADAs detected in some adults in ENPP1 Deficiency and ABCC6 Deficiency Phase 1/2 Trials
- ✓ >5,000 doses of INZ-701 (>57 Patient Years)
- ✓ Convenient at-home dosing regimen

January 2025 Updates

- Clinical improvements in multiple measures of disease from baseline observed in infants and children with ENPP1 Deficiency with INZ-701 treatment
- Favorable safety profile in infants and children
- Enrollment complete in ENERGY 3 pivotal trial in pediatric patients with ENPP1 Deficiency
- Preliminary support from U.S. and EU regulators for ASPIRE pivotal trial in children with ABCC6 Deficiency

Generalized arterial calcification of infancy (GACI): A severe manifestation of ENPP1 Deficiency in infants

Significant morbidity and mortality in infants and children with GACI

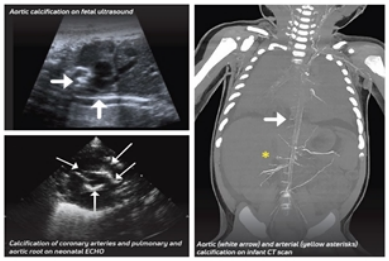
~10%
of normal PPi levels

50%
Mortality within the first 6 months due to severe cardiovascular complications

95%
Present with ectopic calcification

100%
Develop hypophosphatemic rickets in childhood
Expected to develop after 1 year

Vascular Calcification



Calcification, intimal proliferation, and stenosis

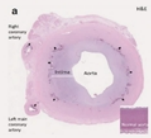


Image reproduced from Ferreira 2021.

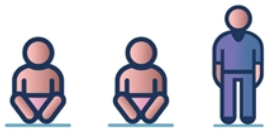
INZ-701 treatment in infants and very young children with GACI

Two ongoing programs evaluating safety and clinical effects

ENERGY 1
3 infants treated

- Phase 1b, global, open-label study in patients <1 yr old
- GACI-1 (ENPP1 Deficiency) or GACI-2 (ABCC6 Deficiency)
- No fixed dose; intra- and inter-patient dose escalation over time based on safety and tolerability data

Expanded Access Program
2 infants + 1 toddler treated



- Open-label treatment for ENPP1 Deficiency
  - Patients <1 yr old with unstable conditions where transport is not possible
  - Patients of any age in countries where no trial site is open to new patient accrual

Clinical improvements in multiple measures of disease from baseline observed with INZ-701 treatment

Natural history	INZ-701 treatment
50% Mortality within the first 6 months due to severe cardiovascular complications	**80%** of treated infants thriving beyond 1 year of age Improved survival observed
95% Present with ectopic calcification	Substantial reduction or stabilization of arterial calcifications Evidence of improved heart function
100% Develop hypophosphatemic rickets in childhood Expected to develop after 1 year	**0%** Evidence of rickets in at-risk children Increase/stabilization of serum phosphate levels

ENERGY 1 data cut: 14 Oct 2024; EAP data cut: 13 Dec 2024

Significant disease burden at baseline in GACI infants and children

Impaired heart function, substantial ectopic calcifications, hypophosphatemia and systemic hypertension are common; Some patients entering age for rickets development

Study Patient ID/ [Time on Tx]	Age at diagnosis	Age at Tx Start	Status	Arterial calcifications		LVEF		Systemic Hypertension		Hypophosphatemia		Joint/soft tissue calcifications		Age for rickets risk	Rickets
			Alive/ Dead	Baseline	Treatment	Baseline	Treatment	Baseline	Treatment	Baseline	Treatment	Baseline	Treatment	Current Status	
E1 Pt1 [16 mo]	2.6 mo	8.5 mo		Yes (M)		62%		NR		Yes		Yes		Yes	
E1 Pt2 [15 mo]	4.4 mo	10.5 mo		NR		64%		NR		Yes		Yes		Yes	
E1 Pt3* [3 wks]	26 d	1 mo		Yes (M)		29%		Yes		Yes		Yes		NA	
EAP-01 [22 mo]	1.5 mo	2 yrs 5 mo		Yes (M)		71%		Yes		Yes		NR		Yes	
EAP-02 [14 mo]	19 d	3 mo		Yes (M)		40%, CHF		Yes		Yes		NR		No	
EAP-03 [11 mo]	Birth	2 mo		Yes (M)		52%		Yes		No		Yes		No	

ENERGY 1 data cut: 14 Oct 2024; EAP data cut: 13 Dec 2024; BL: Baseline; D/C: discontinued; anti-HTN: ant-hypertension medication; M: Multiple; NA=Not applicable; NR: Not reported; CHF: Congestive heart failure; LVEF: Left ventricular ejection fraction, *Patient expired at 3 weeks of dosing, not evaluable

INZ-701 treatment observations in GACI infants and children

Evidence of improved heart function, stabilization or reduction in ectopic calcifications and hypophosphatemia, and prevention of rachitic changes

Study Patient ID/ [Time on Tx]	Age at diagnosis	Age at Tx Start	Status	Arterial calcifications		LVEF		Systemic Hypertension		Hypophosphatemia		Joint/soft tissue calcifications		Age for rickets risk	Rickets
			Alive/ Dead	Baseline	Treatment	Baseline	Treatment	Baseline	Treatment	Baseline	Treatment	Baseline	Treatment	Current Status	
E1 Pt1 [16 mo]	2.6 mo	8.5 mo	A	Yes (M)	Stable	62%	Stable	NR	NR	Yes	↑ to/near normal	Yes	Stable	Yes	No
E1 Pt2 [15 mo]	4.4 mo	10.5 mo	A	NR	Stable	64%	Stable	NR	NR	Yes	Stable	Yes	Stable	Yes	No
E1 Pt3* [3 wks]	26 d	1 mo	D	Yes (M)	NA	29%	NA	Yes	Stable on pro-panolol	Yes	↑ to normal/ nr. normal	Yes	NA	NA	NA
EAP-01 [22 mo]	1.5 mo	2 yrs 5 mo	A	Yes (M)	Stable	71%	Stable	Yes	Stable on catopril	Yes	↑ to normal/ nr. normal	NR	NR	Yes	No
EAP-02 [14 mo]	19 d	3 mo	A	Yes (M)	↓↓	40%, CHF	↑ (68%)	Yes	Stable on catopril, pro-panolol	Yes	Stable	NR	NR	No	NA
EAP-03 [11 mo]	Birth	2 mo	A	Yes (M)	↓↓	52%	↑ (61%)	Yes	Anti-HTN tx D/C	No	Stable	Yes	Stable	No	NA

ENERGY 1 data cut: 14 Oct 2024; EAP data cut: 13 Dec 2024; BL: Baseline; D/C: discontinued; anti-HTN: ant-hypertension medication; M: Multiple; NA=Not applicable; NR: Not reported; CHF: Congestive heart failure; LVEF: Left ventricular ejection fraction, *Patient expired at 3 weeks of dosing, not evaluable

Improved survival in GACI observed:

80% of treated infants thriving with 11+ months of treatment

Study Patient ID/ [Time on Tx]	Age at diagnosis	Age at Tx Start	Status
			Alive/Dead
E1 Pt1 [16 mo]	2.6 mo	8.5 mo	A
E1 Pt2 [15 mo]	4.4 mo	10.5 mo	A
E1 Pt3 [3 wks]	26 d	1 mo	D
EAP-01 [22 mo]	1.5 mo	2 yrs 5 mo	A
EAP-02 [14 mo]	19 d	3 mo	A
EAP-03 [11 mo]	Birth	2 mo	A

ENERGY 1 data cut: 14 Oct 2024; EAP data cut: 13 Dec 2024

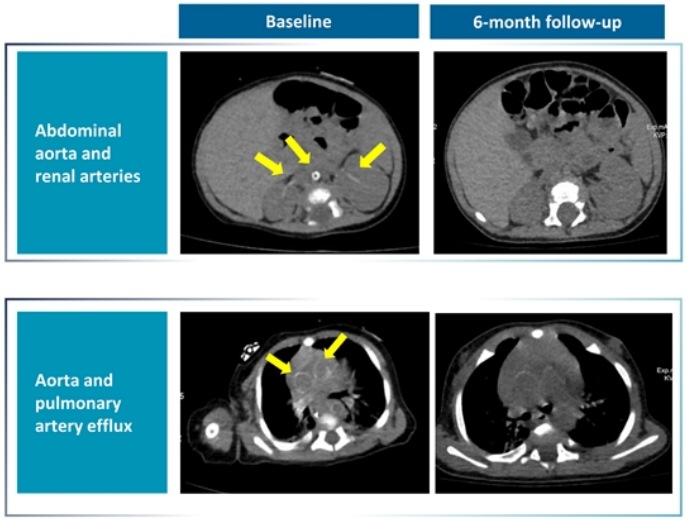
Reduced or stabilized arterial calcifications observed:

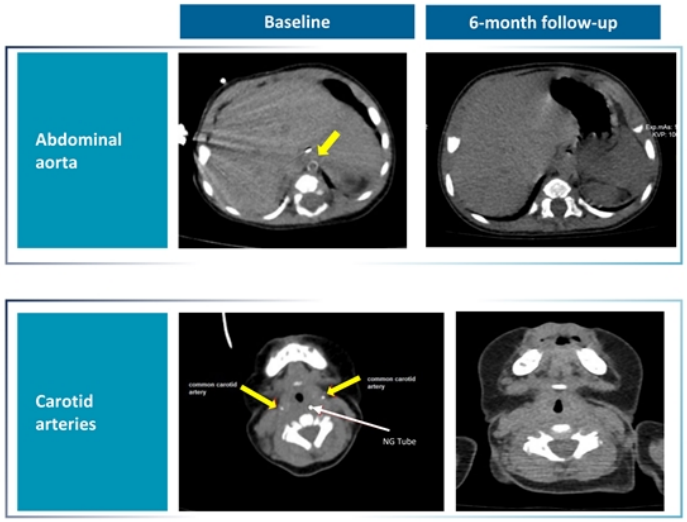
Key driver of morbidity and mortality in GACI addressed

Study Patient ID/ [Time on Tx]	Age at diagnosis	Age at Tx Start	Arterial calcifications	
			Baseline	Treatment
E1 Pt1 [16 mo]	2.6 mo	8.5 mo	Yes (M)	Stable
E1 Pt2 [15 mo]	4.4 mo	10.5 mo	NR	Stable
E1 Pt3 [3 wks]	26 d	1 mo	Yes (M)	NA
EAP-01 [22 mo]	1.5 mo	2 yrs 5 mo	Yes (M)	Stable
EAP-02 [14 mo]	19 d	3 mo	Yes (M)	↓↓
EAP-03 [11 mo]	Birth	2 mo	Yes (M)	↓↓

ENERGY 1 data cut: 14 Oct 2024; EAP data cut: 13 Dec 2024; M=Multiple sites; NR=Not reported ; NA = Not applicable; Patient expired at 3 weeks of dosing

Case EAP-03: Evidence of complete resolution of arterial calcification observed





EAP data cut: 13 Dec 2024

Calcification

Evidence of improved heart function observed:

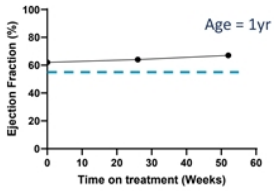
Stabilization or improvement in left ventricular ejection fraction (LVEF) in all surviving patients observed

Study Patient ID/ [Time on Tx]	Age at diagnosis	Age at Tx Start	LVEF	
			Baseline	Treatment
E1 Pt1 [16 mo]	2.6 mo	8.5 mo	62%	Stable
E1 Pt2 [15 mo]	4.4 mo	10.5 mo	64%	Stable
E1 Pt3 [3 wks]	26 d	1 mo	29%	NA
EAP-01 [22 mo]	1.5 mo	2 yrs 5 mo	71%	Stable
EAP-02 [14 mo]	19 d	3 mo	40%	↑ (68%)
EAP-03 [11 mo]	Birth	2 mo	52%	↑ (61%)

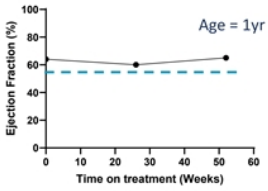
ENERGY 1 data cut: 14 Oct 2024; EAP data cut: 13 Dec 2024; M=Multiple sites; NR=Not reported; NA = Not applicable, Patient expired at 3 weeks of dosing

Ejection fraction was stable or improved with INZ-701 treatment

E1 Pt1

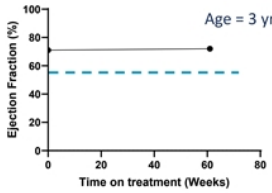


E1 Pt2

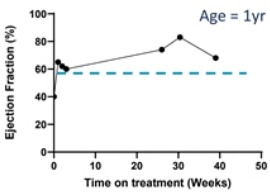


Normal infant EF % (Tissot et al, Front Pediatr. 2018 Apr 4;6:79)

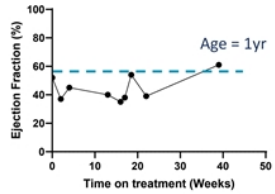
EAP-01



EAP-02



EAP-03



ENERGY 1 data cut: 14 Oct 2024; EAP data cut: 13 Dec 2024

Reduced risk of rickets observed:

Increased or stabilized phosphate levels in all patients

Study Patient ID/ [Time on Tx]	Age at diagnosis	Age at Tx Start	Hypophosphatemia		Age for rickets risk	Rickets
			Baseline	Treatment	Current Status	
E1 Pt1 [16 mo]	2.6 mo	8.5 mo	Yes	↑ to/near normal	Yes	No
E1 Pt2 [15 mo]	4.4 mo	10.5 mo	Yes	Stable	Yes	No
E1 Pt3 [3 wks]	26 d	1 mo	Yes	↑ to/near normal	NA	NA
EAP-01 [22 mo]	1.5 mo	2 yrs 5 mo	Yes	↑ to/near normal	Yes	No
EAP-02 [14 mo]	19 d	3 mo	Yes	Stable	No	NA
EAP-03 [11 mo]	Birth	2 mo	No	Stable	No	NA

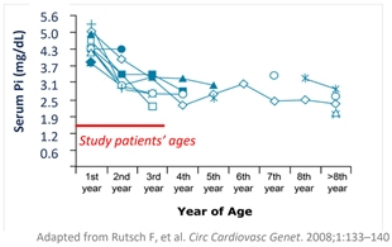
- Radiographic evidence of rickets expected after 1 year of age
- Co-incident with progressive hypophosphatemia
- X-Rays pending for patients EAP-02 and EAP-03

ENERGY 1 data cut: 14 Oct 2024; EAP data cut: 13 Dec 2024; M=Multiple sites; NA=Not applicable; Patient expired at 3 weeks of dosing; NR=Not reported.

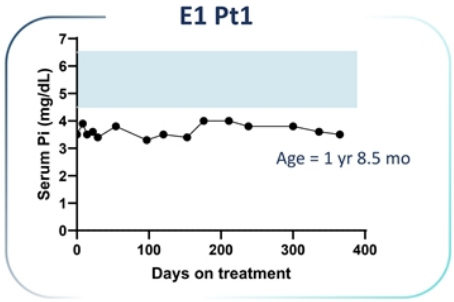
Serum phosphate was stable with INZ-701 treatment in all patients at risk for ARHR2

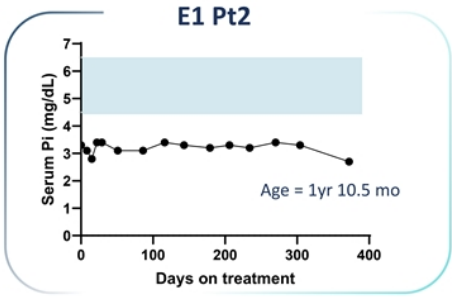
Natural History: Patients with ENPP1 Deficiency who survive the critical period of infancy develop hypophosphatemia

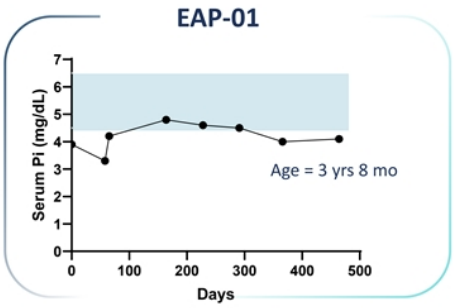
Serum Phosphate Levels

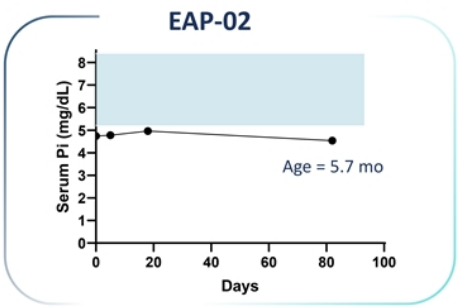


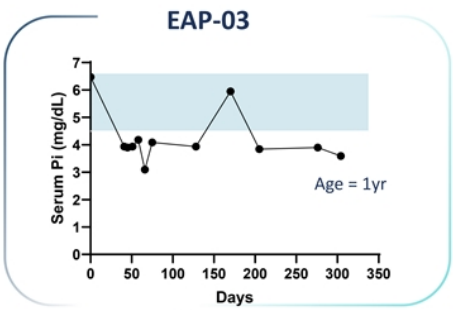
Adapted from Rutsch F, et al. *Circ Cardiovasc Genet*. 2008;1:133–140







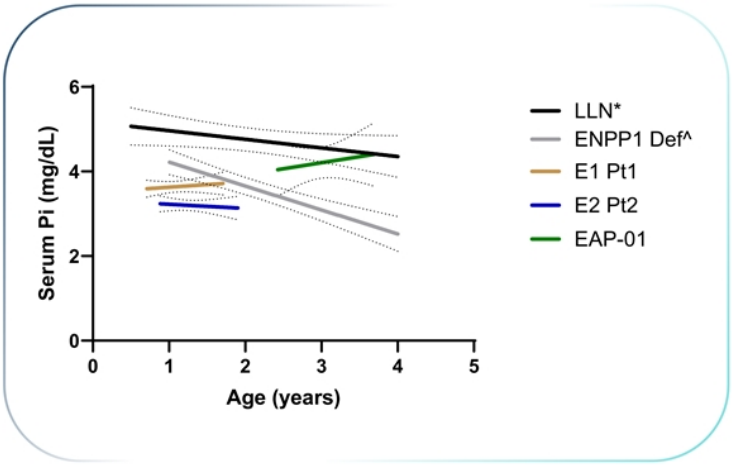




Age-specific normal range*

* Am J Kidney Dis 46: S1-S122, 2005; Pediatrics 77:891-896, 1986, ENERGY 1 data cut: 14 Oct 2024; EAP data cut: 13 Dec 2024

Serum phosphate was stable or improved with INZ-701 treatment in patients at risk for rickets



- Serum phosphate levels (LLN) decreased slightly over time in healthy individuals (black line)
- By 1 year of age, ENPP1 deficient patients are already hypophosphatemic
- Serum phosphate levels decrease in a more pronounced way over time in ENPP1 deficient patients (grey line)
- **INZ-701 showed stabilization or improvement of serum phosphate levels in infants (brown and blue line) or children (green line)**

* LLN = lower limit of normal: Am J Kidney Dis 46: S1-S122, 2005, Pediatrics 77:891-896, 1986; ^ Adapted from Rutsch F, et al. *Circ Cardiovasc Genet.*1:133–140, 2008, ENERGY 1 data cut: 14 Oct 2024; EAP data cut: 13 Dec 2024

Data presented as linear regression; ····· 95% confidence interval

INZ-701 exhibited a favorable safety profile in ENERGY 1 and EAP patients

		No. of Patients			
No. of Patients with AEs	Total adverse events (AEs) reported	AEs related to INZ-701	AEs not related to INZ-701	Serious AEs (SAEs) related to INZ-701	SAEs not related to INZ-701
ENERGY 1 (n=3)	34	0	2[2]	0	1[4]
Expanded Access (n=2)	12	2[1]	Not reported[3]	0	1[5]

[1] Includes 9 low grade injection site reactions

[2] All AEs were mild (grade 1)

[3] Limited AE reporting in EAP patients; All SAEs reported regardless of relationship to INZ-701; other AEs reported only if related to INZ-701.

[4] 1 SAE: MI resulting in death

[5] 3 SAEs: Sepsis with MI; viral infection; GI bleed

ENERGY 1 data cut: 14 Oct 2024; EAP data cut: 13 Dec 2024

ADA response observed in youngest patients

ADAs absent in toddler and transient in one infant

	Anti-Drug Antibody (ADA) Status/Titers																
Weeks	5	13	19	20	21	24	26	27	29	30	34	37	38	39	43	52	79
Subject ID																	
E1 Pt1		320			80		40			80							
E1 Pt2		2,560			10,240		10,240			10,240				40,960	20,480	81,920	
EAP-01																	
EAP-02		1,280					40,960	81,920		163,840			163,840				
EAP-03		2,560	5,120	10,240	10,240	20,480			40,960		81,920		163,840				

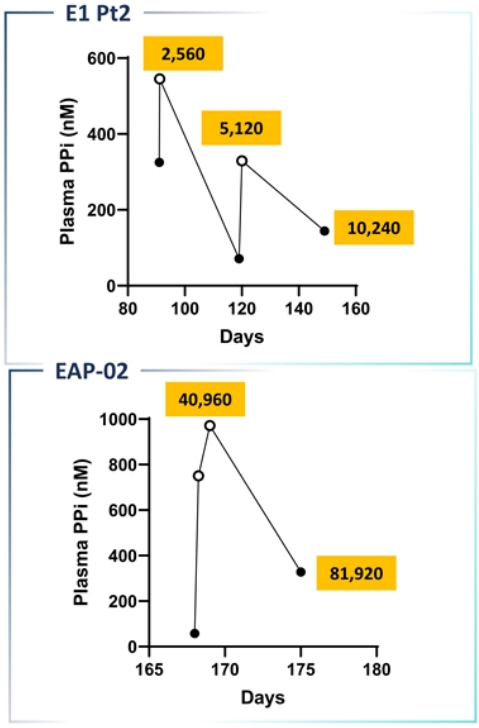
- High ADA titers in some infants significantly affected PK and PD
- ADAs were not associated with adverse events in any patient
- Data collected pre- and post-dosing demonstrated substantial transient increases in PPi and drug exposure following INZ-701 administration, consistent with the clinical effects observed

ADA Negative
ADA Positive

ENERGY 1 data cut: 16 Aug 2024; EAP data cut: 13 Dec 2024

ADAs blunt but do not eliminate potentially beneficial post-dose PPi increases

Subject ID	Day	PPi (nM)	Fold change
E1 Pt2	91 pre-dose	325	--
	91+4 hrs post-dose	545	1.7X
	119 pre-dose	71	--
	119 +24 hrs post-dose	329	4.6X
EAP-02	168 pre-dose	58	--
	168 +6hrs post-dose	750	13X
	168 +24 hrs post-dose	971	16.7X

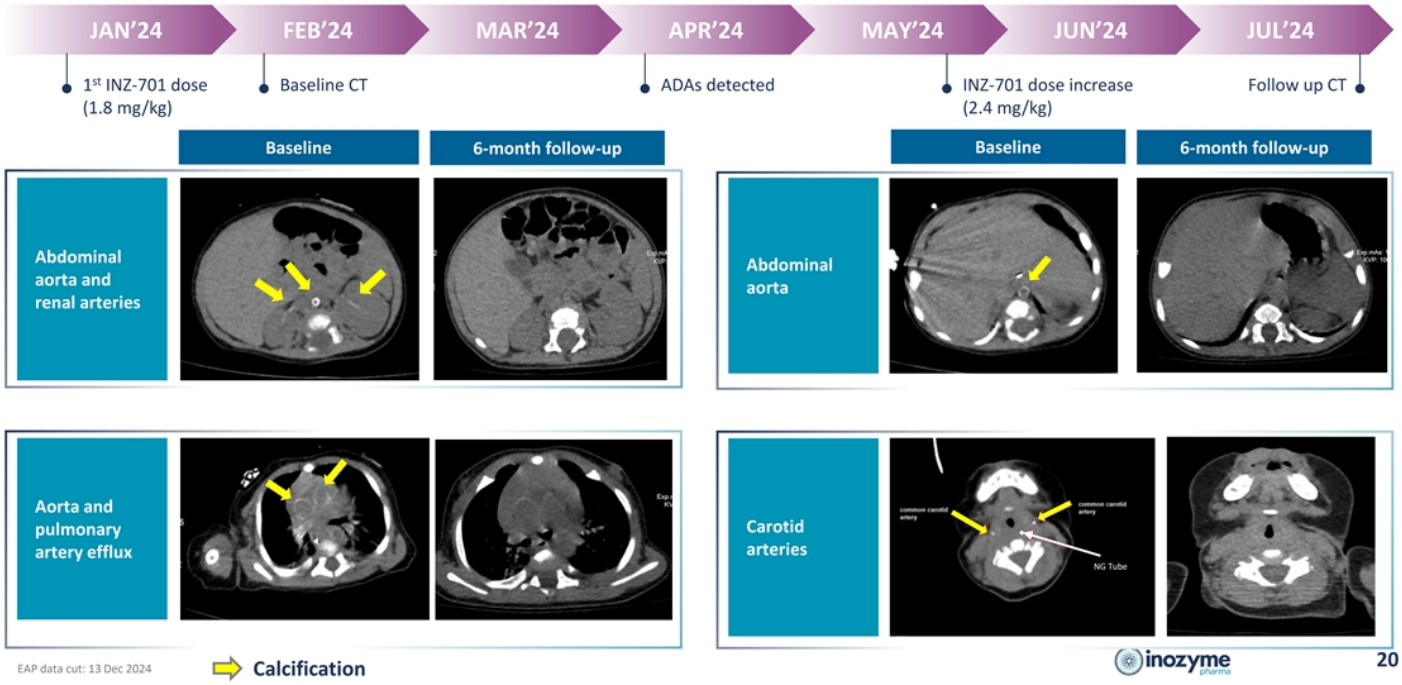


Antibody titers

Closed symbols = pre-dose; Open symbols = post-dose

ENERGY 1 data cut: 14 Oct 2024; EAP data cut: 13 Dec 2024

Case EAP-03: Evidence of complete resolution of arterial calcification observed despite ADA detection



EAP data cut: 13 Dec 2024

Calcification

Five patients continue receiving long-term, home administration of INZ-701

Data Review Committee recommended continuing treatment of all patients following review of interim laboratory and clinical data

- No safety signals
- Transient exposure and PPi response expected following each dose
- Potential for tolerization with long-term exposure

Clinically-relevant ADA response limited to infants

- Most ENPP1 and ABCC6 deficient adults show no ADA response or a transient, low titer response with no impact on PK
- Monitoring of ENPP1 deficient pediatric patients (ENERGY 3 trial) has shown no evidence of hypersensitivity or immune-related adverse events

Positive interim data in infants and very young children supports growing body of evidence for INZ-701 use in all age groups

Positive interim safety and exploratory efficacy data

- Well-tolerated when administered to infants and very young children
- Evidence of improved heart function, stabilization or reduction in ectopic calcifications and hypophosphatemia, and prevention of rachitic changes
  - Absence of rachitic changes support potential benefit in ENERGY 3 pediatric pivotal trial
- ADAs impacting exposure only seen in some patients less than 1 year of age and not observed in older patients

Infant data intended to support approval package for broad commercial label

- ENPP1 Deficiency can severely affect patients at all ages
- Clinical studies comprising the INZ-701 development program address ENPP1 Deficiency across all age groups
  - ENERGY 1, ENERGY 2, EAP: Infants
  - ENERGY 3, EAP: Pediatric (1-12 yrs.)
  - 101, ADAPT: Adults
  - ENABLE: >1 yr.

ASPIRE: Planned Pivotal Study in Pediatric Patients with ABCC6 Deficiency

ASPIRE: Planned pivotal study in pediatric patients with ABCC6 Deficiency

Preliminary support from U.S. and EU regulators for ASPIRE pivotal trial in children with ABCC6 Deficiency

Population: Infants and pediatrics birth to <18 yrs

- Mono or biallelic
- At risk for stroke or CV events based on at least 1 of the following:
  - History of GACI or GACI symptoms
  - Prior stroke/TIA
  - History of CV disease
  - Cerebral arteriopathy documented by imaging
  - Family member with ABCC6 variant and GACI, stroke, cardiovascular disease or arteriopathy

Design: Multicenter, multinational, randomized (1:1), open label, conventional therapy control

Sample size estimate: 70 patients (35/arm); 85% Power

Primary

Composite endpoint:

1. Death (any cause)
2. Stroke
3. Myocardial infarction
4. Cardiac hospitalization
5. Severe disease-related AEs

Secondary

- PPi concentration
- Retinal disease progression
- Change from BL: arterial calcium score
- Change from BL: transcranial doppler
- Pediatric PROs
- PK and enzyme activity
- Safety

inozyme pharma

Thank you