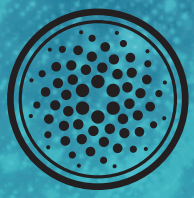

inozyme pharma

2024 Annual Report

To Our Shareholders:

It is with great optimism and purpose that I write to you at this important moment in Inozyme's evolution. Over the past year, we have sharpened our strategy, executed with rigor, and achieved major milestones that advance our vision of delivering the first approved treatment for ENPP1 Deficiency. The next twelve months promise to be defining for our company, as we prepare for pivotal data and begin laying the groundwork for commercialization.

At the heart of our efforts is INZ-701, our first-in-class enzyme replacement therapy targeting the PPi-Adenosine Pathway - a critical system regulating bone health and blood vessel function. INZ-701 is currently being studied in patients with ENPP1 Deficiency, a devastating genetic disease that presents in infancy with generalized arterial calcification (GACI) and progresses to severe skeletal disease (ARHR2) in childhood. With no approved therapies, high mortality in infancy, and progressive lifelong morbidity, this disease represents clear and urgent unmet medical need.

Over the past year, our team has made remarkable progress:

- We completed enrollment in ENERGY 3, our pivotal trial in pediatric patients with ENPP1 Deficiency, and expect topline data in Q1 2026. This study will serve as the cornerstone of our regulatory submission, supported by extensive data from our clinical studies in adults and infants. Achieving this milestone reflects the tireless efforts of our team and the trust of families around the world.
- We released highly encouraging early results from our infant studies (ENERGY 1 and ENERGY 2) and expanded access program, which showed improved survival beyond one year, stabilization of vascular calcification, and absence of changes associated with rickets in high-risk patients. These outcomes reinforce the potential of INZ-701 to meaningfully alter the course of disease when initiated early in life.
- We also advanced our patient identification and community-building efforts, having now identified more than 1,500 patients globally with confirmed or suspected ENPP1 Deficiency – a remarkable milestone given current levels of disease awareness and a strong indicator of the substantial addressable market for INZ-701.

Based on the severity of ENPP1 Deficiency, its clear genetic definition, lack of approved treatment, and orphan pricing dynamics, we believe INZ-701 could reach $1 billion in peak annual sales, even at modest market penetration. Internal epidemiology modeling suggests over 10,000 patients may be addressable across North America, Europe, Japan, Brazil, and the Gulf region. This is not just a compelling scientific opportunity - it is a significant, de-risked market where we hold global rights and have a clear path to commercial leadership.

As we progress toward potential approval, we have also been laying the foundation needed to reach patients as efficiently as possible. A major focus in 2024 was on patient identification and community engagement. We launched a global patient registry (the PROPEL Registry) in partnership with GACI Global to better understand the natural history of ENPP1 Deficiency and infantile ABCC6 Deficiency. We supported no-cost genetic testing and newborn screening programs in a number of countries to facilitate earlier and more accurate diagnoses, and we broadened our medical education and physician outreach efforts at key conferences and through scientific engagement. These initiatives have significantly expanded awareness of the disease, leading to the identification of over 1,500 patients with ENPP1 Deficiency to date and positioning Inozyme for a strong commercial launch.

These efforts not only help to identify patients who may benefit from INZ-701, but also build trusted relationships with families and healthcare providers ahead of a potential launch. We are heartened by the growing engagement in the ENPP1 Deficiency community, and are confident that these early investments in disease education and patient finding will pay dividends as we move closer to market. Understanding where patients are and how the disease impacts them enables us to forecast demand and ensure our supply chain and infrastructure are ready to meet the commercial needs on day one.

We have also taken steps to thoughtfully refocus our resources on ENPP1 Deficiency. In early 2025, we streamlined our operations to concentrate capital and talent on advancing INZ-701 through pivotal development and toward regulatory submission. While our data in ABCC6 Deficiency and calciphylaxis remain promising, we have paused new clinical studies and investments in these programs for now, with plans to revisit their advancement as financial resources allow. This approach reflects our commitment to financial discipline, extends our cash runway into Q1 2026, and positions us to build from a foundation of focus and strength.

Looking ahead, the opportunities are immense. In 2026, we aim to file for our first regulatory approval and prepare for commercial launch of INZ-701 for patients with ENPP1 Deficiency. We intend to build a focused, high-impact rare disease organization, initially centered on ENPP1 Deficiency, with the potential to expand into ABCC6 Deficiency, calciphylaxis, and other diseases driven by pathological calcification and the PPi-Adenosine pathway as the organization and our resources grow.

As we execute on our pivotal study and look toward topline data in early 2026, our prospects have never been stronger. We are advancing a therapy with a clear biological mechanism, a favorable clinical profile, and an urgent need among patients. ENPP1 Deficiency alone has the potential to support a standalone rare disease company, and we are determined to unlock that value.

In closing, I extend my deepest gratitude to our employees, our clinical collaborators, our Board of Directors, and our shareholders. Most importantly, I want to thank the patients and families who participate in our studies and who inspire our work every day - we carry their hope forward with determination and resolve.

Inozyme is at a pivotal inflection point, and we're just getting started.

Sincerely,

Douglas A. Treco, Ph.D.
Chief Executive Officer and Chairman

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, DC 20549

FORM 10-K

(Mark One)

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the fiscal year ended December 31, 2024

OR

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the transition period from _____ to _____

Commission File Number: 001-39397

INOZYME PHARMA, INC.

(Exact name of registrant as specified in its charter)

Delaware	**38-4024528**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. 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

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

Securities registered pursuant to Section 12(g) of the Act:
None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☐ No ☒

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 15(d) of the Act. Yes ☐ No ☒

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes ☒ No ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer ☐	Accelerated filer ☐
Non-accelerated filer ☒	Smaller reporting company ☒
	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. ☐

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☐

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements. ☐

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to § 240.10D-1(b). ☐

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes ☐ No ☒

As of June 28, 2024, the last business day of the registrant's most recently completed second fiscal quarter, the aggregate market value of the registrant's common stock held by non-affiliates of the registrant, based on the closing price of the registrant's common stock on the Nasdaq Global Select Market on June 28, 2024, was $199,349,178.

As of March 3, 2025, the registrant had 64,240,198 shares of common stock, $0.0001 par value per share, outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

The registrant intends to file a definitive proxy statement pursuant to Regulation 14A within 120 days of the end of the fiscal year ended December 31, 2024. Portions of such definitive proxy statement are incorporated by reference into Part III of this Annual Report on Form 10-K.

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CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS AND INDUSTRY DATA

This Annual Report on Form 10-K contains forward-looking statements, which reflect our current views with respect to, among other things, our operations and financial performance. All statements, other than statements of historical fact, contained in this Annual Report on Form 10-K, including statements regarding our strategy, future operations, future financial position, future revenue, projected costs, prospects, plans, objectives of management and expected market growth, are forward-looking statements. The words "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "might," "outlook," "plan," "potential," "predict," "project," "should," "target," "will," "would," and the negative version of these words and other similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Such forward-looking statements are subject to various risks and uncertainties. Accordingly, there are or will be important factors that could cause actual outcomes or results to differ materially from those indicated in these statements. We believe these factors include but are not limited to those described under the heading "Summary of Material Risks Associated with Our Business" and the "Risk Factors" section and include, among other things

- our ongoing Phase 1/2 clinical trials of INZ-701 for adults with ENPP1 and ABCC6 Deficiencies, our ongoing open label long-term safety study of INZ-701 in patients with ENPP1 or ABCC6 Deficiencies who have received INZ-701 in an existing study ("ADAPT"), our ongoing Phase 1b clinical trial of INZ-701 for infants with ENPP1 Deficiency ("ENERGY 1"), our ongoing pivotal trial of INZ-701 in pediatric patients with ENPP1 Deficiency ("ENERGY 3"), our ongoing Phase 1 clinical trial of INZ-701 in patients with end-stage kidney disease receiving hemodialysis ("SEAPORT 1"), and our ongoing pivotal clinical trial of INZ-701 in infants ("ENERGY 2"), including statements regarding the timing of enrollment and completion of the clinical trials and the period during which the results of the clinical trials will become available;
- the timing, design, and conduct of our planned clinical trials of INZ-701 for patients with ENPP1 Deficiency;
- our plans to conduct research, preclinical testing, and clinical trials of INZ-701 for additional indications;
- our plans to conduct research, preclinical testing, and clinical trials of other product candidates;
- our plans to engage in regulatory interactions with the U.S. Food and Drug Administration, the European Medicines Agency and other regulatory authorities;
- our plans with respect to regulatory filings;
- the timing of, and our ability to obtain and maintain, marketing approvals of INZ-701, and the ability of INZ-701 and our other product candidates to meet existing or future regulatory standards;
- our expectations regarding our ability to fund our cash flow requirements with our cash, cash equivalents and short-term investments;
- the potential advantages of our product candidates;
- the rate and degree of market acceptance and clinical utility of our product candidates;
- our estimates regarding the potential market opportunity for our product candidates;
- our commercialization and manufacturing capabilities and strategy;
- our intellectual property position;
- our ability to identify additional products, product candidates or technologies with significant commercial potential that are consistent with our commercial objectives;
- our estimates regarding expenses, future revenue, capital requirements and needs for additional financing;
- our ability to comply with the covenants under our loan agreement;
- the impact of government laws and regulations;
- our competitive position; and
- our expectations regarding the time during which we will be an emerging growth company under the Jumpstart our Business Startups Act of 2012.

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have included important factors in the cautionary statements included in this Annual Report on Form 10-K, particularly in the "Risk Factors" section, that we believe could cause actual results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, collaborations, joint ventures or investments we may make or enter into.

You should read this Annual Report on Form 10-K and the documents that we have filed as exhibits to this Annual Report on Form 10-K completely and with the understanding that our actual future results may be materially different from what we expect. The forward-looking statements contained in this Annual Report on Form 10-K are made as of the date of this Annual Report on Form 10-K, and we do not assume any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by applicable law.

This Annual Report on Form 10-K includes statistical and other industry and market data that we obtained from industry publications and research, surveys and studies conducted by third parties as well as our own estimates of potential market opportunities based on our analysis of these data, research, surveys and studies. All of the market data used in this Annual Report on Form 10-K involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such data. Industry publications and third-party research, surveys and studies generally indicate that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. Our estimates of the potential market opportunities for our product candidates include a number of key assumptions based on our industry knowledge, industry publications and third-party research, surveys and studies, which may be based on a small sample size and fail to accurately reflect market opportunities. While we believe that our internal assumptions are reasonable, no independent source has verified such assumptions.

Summary of Material Risks Associated with Our Business

Our business is subject to a number of risks that if realized could materially affect our business, prospects, operating results, and financial condition. These risks are discussed more fully in the "Risk Factors" section of this Annual Report on Form 10-K. These risks include the following:

- We have incurred significant losses since our inception. To date, we have not generated any revenue from product sales. We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future and may never achieve or maintain profitability. Our net losses were $102.0 million for the year ended December 31, 2024 and $71.2 million for the year ended December 31, 2023.

- We will need substantial additional funding. If we are unable to raise capital when needed or on attractive terms, we may be required to delay, limit, reduce or terminate our research and development programs or any future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves. Since our cash, cash equivalents and short-term investments as of December 31, 2024 are not sufficient to fund our operations for at least the next twelve months from the date of issuance of the consolidated financial statements included elsewhere in this Annual Report on Form 10-K, there is substantial doubt about our ability to continue as a going concern.

- We have a loan agreement that requires us to meet specified funding conditions for future draw downs and operating covenants and places restrictions on our operating and financial flexibility.

- We have a limited operating history and are early in our development efforts. We are heavily dependent on the success of our lead product candidate, INZ-701. If we are unable to commercialize INZ-701 or experience significant delays in doing so, our business will be materially harmed.

- We cannot be certain of the timely completion or outcome of our preclinical testing and clinical trials. The results of preclinical studies may not be predictive of the results of clinical trials, and preliminary interim topline results of clinical trials do not necessarily predict final results. The results of any early-stage clinical trials we conduct may not be predictive of the results of later-stage clinical trials and our product candidates could be associated with serious adverse events or undesirable side effects.

- Interim topline and preliminary results from our clinical trials that we announce or publish from time to time, such as interim data we have disclosed from our ongoing Phase 1/2 clinical trials of INZ-701 in adults with ENPP1 Deficiency and ABCC6 Deficiency, our ongoing Phase 1b clinical trial of INZ-701 for infants with ENPP1 Deficiency and our ongoing Phase 1 clinical trial of INZ-701 in patients with end-stage kidney disease ("ESKD") receiving hemodialysis, may change as more participant data become available and are subject to audit and verification procedures, which could result in material changes in the final data.

- If we are unable to obtain required marketing approvals for, commercialize, manufacture, obtain, maintain and enforce patent protection for, gain market acceptance of or obtain and maintain coverage, adequate pricing and adequate reimbursement from third-party payors for our product candidates, or experience significant delays in doing so, our business will be materially harmed and our ability to generate revenue from product sales will be materially impaired.

- The design and conduct of our clinical trials for the treatment of ENPP1 or ABCC6 Deficiencies or calciphylaxis may take longer, be more costly or be less effective as a result of the novelty of development in these diseases. We may use new or novel endpoints or methodologies and regulatory authorities may not consider the endpoints of our clinical trials to provide clinically meaningful results.

- We are conducting clinical trials for our product candidates at sites outside the United States. If the FDA determines that any such trial did not comply with all applicable U.S. laws and regulations, the FDA may not accept the data from that trial, in which case we would likely need to conduct one or more additional clinical trials.

- We focus our research and product development on treatments for rare diseases. Given the small number of patients who have the diseases that we are targeting, it is critical to our ability to grow and become profitable that we continue to successfully identify patients with these rare diseases and capture a significant market share.

- We rely, and expect to continue to rely, on third parties to conduct our clinical trials, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials, which may prevent or delay our ability to seek or obtain marketing approval for or commercialize our product candidates or otherwise harm our business. If we are not able to maintain these third-party relationships or if these arrangements are terminated, we may have to alter our development and commercialization plans and our business could be adversely affected.

- We rely, and expect to continue to rely, on third parties for the manufacture of our product candidates for preclinical testing and clinical trials, as well as for commercial manufacture if any of our product candidates receive marketing approval. This reliance on third parties may increase the risk that we will not have sufficient quantities of our product candidates or products or such quantities at an acceptable cost or quality, which could delay, prevent or impair our development or commercialization efforts.

- If we are unable to obtain, maintain, enforce and protect patent protection for our technology and products or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize technology and products similar or identical to ours, and our ability to successfully commercialize our technology and products may be adversely affected.

- We are highly dependent on the research and development, clinical, financial, operational and other business expertise of our executive officers, as well as the other principal members of our management, scientific and clinical teams. Our future success depends on our ability to retain key executives and to attract, retain and motivate qualified personnel.

The summary risk factors described above should be read together with the text of the full risk factors set forth in the section titled "Risk Factors" in Part I, Item 1A of this Annual Report on Form 10-K and the other information set forth in this Annual Report on Form 10-K, including our audited consolidated financial statements and the related notes, as well as in other documents that we file with the Securities and Exchange Commission. The risks summarized above or described in full below are not the only risks that we face. Additional risks and uncertainties not precisely known to us, or that we currently deem to be immaterial may also harm our business, financial condition, results of operations and future growth prospects.

PART I

Unless the context otherwise requires*, we use the term "Inozyme," "the Company," "we," "us," "our" and similar designations in this Annual Report on Form 10-K to refer to Inozyme Pharma, Inc. and its wholly owned subsidiaries.*

Item 1. BUSINESS

Overview

We are a clinical-stage biopharmaceutical company dedicated to developing innovative therapeutics for rare diseases that affect bone health and blood vessel function. Our expertise lies 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). It is well established that low levels of PPi drive pathologic mineralization and low levels of adenosine drive intimal proliferation in a number of rare diseases. 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").

We are initially focused on developing a novel therapy for diseases characterized by pathologic mineralization and intimal proliferation, including ENPP1 Deficiency and ABCC6 Deficiency as well as calciphylaxis. As part of our recent strategic review, we are prioritizing activities to support the planned Biologics License Application ("BLA") filing for INZ-701 for our lead indication, ENPP1 Deficiency. Patients with ABCC6 Deficiency being treated in our ADAPT long-term extension study, our expanded access program, or under investigator-sponsored INDs will continue to receive treatment. Any future trials in ABCC6 Deficiency and calciphylaxis will be postponed.

ENPP1 and ABCC6 Deficiencies are rare chronic, systemic, and progressive genetic diseases occurring over the course of a patient's lifetime, starting as early as fetal development and spanning into adulthood. These diseases represent a significant unmet medical need, with high mortality rates for infants with ENPP1 Deficiency and high levels of morbidity occurring for patients with these diseases throughout their lives. Calciphylaxis is a rare disorder with a high mortality rate that mostly affects patients with end-stage kidney disease ("ESKD"). There are currently no approved therapies for ENPP1 Deficiency, ABCC6 Deficiency, or calciphylaxis. Currently available treatments seek to minimize the manifestations of these diseases and do not address the underlying causes.

Our lead product candidate, INZ-701, is a soluble, recombinant, or genetically engineered, ENPP1 fusion protein that is designed to increase PPi and adenosine, to enable the potential treatment of multiple diseases caused by deficiencies in these molecules. By targeting the PPi-Adenosine Pathway, INZ-701 aims to correct pathologic mineralization and intimal proliferation, addressing the significant morbidity and mortality in these devastating diseases. We have generated robust proof of concept data in preclinical models of ENPP1 Deficiency, ABCC6 Deficiency and, in support of our calciphylaxis program, chronic kidney disease ("CKD") demonstrating that INZ-701 prevented pathologic mineralization and skeletal abnormalities, led to improvements in overall health and survival, and prevented intimal proliferation.

We are currently conducting clinical trials of INZ-701 for the treatment of ENPP1 Deficiency, ABCC6 Deficiency, and calciphylaxis. The U.S. Food and Drug Administration ("FDA") has granted Orphan Drug Designation and the European Medicines Agency ("EMA"), has granted Orphan Designation to INZ-701 for the treatment of ENPP1 Deficiency and ABCC6 Deficiency. The FDA has also granted fast track designation for INZ-701 for the treatment of ENPP1 Deficiency, for the treatment of ABCC6 Deficiency and for the treatment of calciphylaxis, and rare pediatric disease designation for INZ-701 for the treatment of ENPP1 Deficiency. Refer to the "Clinical Development of INZ-701 for ENPP1 Deficiency," "Clinical Development of INZ-701 for ABCC6 Deficiency" and "Clinical Development of INZ-701 for Calciphylaxis" sections below for further details on our clinical programs.

We retain worldwide, exclusive development and commercialization rights to our pipeline and programs, including INZ-701. Our current development programs are protected through exclusive intellectual property rights, including filed and issued patents covering composition of matter for ENPP1-Fc fusion proteins, including INZ-701, and methods of treatment. We obtained an exclusive, worldwide license to our foundational intellectual property rights from Yale University ("Yale") in January 2017. In July 2020, we entered into an intellectual property asset purchase agreement with Alexion Pharmaceuticals, Inc. ("Alexion") pursuant to which Alexion sold and assigned to us its right, title, and interest in and to specified patent rights and other specified assets solely related to ENPP1.

To date, we have funded our operations primarily with proceeds from the sales of convertible preferred stock, offerings of common stock and pre-funded warrants, and borrowings under our loan and security agreement (the "Loan Agreement") with K2 HealthVentures LLC ("K2HV").

Strategy

Our goal is to develop and commercialize safe and effective therapies for the treatment of patients suffering from a broad range of genetic and non-genetic diseases that impact bone health and blood vessel function. The critical components of our strategy to achieve this goal include:

- **Efficiently advance clinical development for our lead product candidate, INZ-701, with a focus on infants and children with ENPP1 Deficiency.** Our initial studies of INZ-701 in adult patients with ENPP1 Deficiency provided safety, pharmacokinetic, and pharmacodynamic data supporting clinical development in infants and children with this disease. We believe that these affected groups represent the most urgent unmet need in this disease. In September 2023, we opened the first site for our ENERGY 3 trial, a pivotal trial in pediatric patients with ENPP1 Deficiency, and patient enrollment was completed in January 2025. We are also currently enrolling infants with ENPP1 Deficiency in our ENERGY 1 Phase 1b clinical trial and patient recruitment is underway in our ENERGY 2 pivotal study. We plan to collect additional data evaluating the effects of INZ-701 in all ages with ENPP1 Deficiency to expand our safety database. While we are currently focusing our resources on our ongoing pivotal trial in ENPP1 Deficiency and refining our operational plans for development of INZ-701 for additional indications, we continue to work closely with regulatory authorities to define the optimal path forward for registrational trials in ABCC6 Deficiency and calciphylaxis. Any future trials in ABCC6 Deficiency and calciphylaxis will be postponed.

- **Build a patient-focused company to treat diseases that impact bone health and blood vessel function.** We intend to continue to engage with patient advocacy groups, medical centers of excellence, and medical specialists to fully understand the physical and economic burden these diseases have on patients. We have completed a burden of disease study in ENPP1 Deficiency and ABCC6 Deficiency with GACI Global, a patient advocacy organization dedicated to bettering the lives of families affected by generalized arterial calcification of infancy ("GACI") and autosomal-recessive hypophosphatemic rickets type 2 ("ARHR2") to understand the progression of the disease from the perspective of a patient and caregiver. We have completed a retrospective, cross-sectional natural history study of patients who had GACI or any presentation of ENPP1 Deficiency. We have several ongoing programs, including a retrospective, longitudinal natural history study of patients with ENPP1 Deficiency and ABCC6 Deficiency and a prospective, longitudinal natural history study of patients with ENPP1 Deficiency and ABCC6 Deficiency. Finally, we have launched a registry, in partnership with GACI Global, for all patients with ENPP1 Deficiency and infantile-onset ABCC6 Deficiency in order to expand our understanding of the burden of disease and disease progression across the entire disease population. We believe that the findings from these studies and others like it have been and will be important in supporting ongoing and future trial design and patient enrollment.

  We are also building awareness and understanding of the disease by promoting, through physician networks and patient organizations, the systematic genetic diagnosis of at-risk mothers, infants, and children to best intervene as early as possible in the disease. We have worked with multiple public and private organizations to introduce routine testing for ENPP1 and ABCC6 variants. Our partnership with the Rady Children's Institute for Genomic Medicine aims to expand newborn screening for genetic diseases to 1,000 diseases and sequence 3.7 million newborns annually. We successfully advocated for inclusion of *ENPP1* and *ABCC6* in the initial list of genes in the Genomic England's Generation Study, which aims to sequence the genomes of more than 100,000 infants and pave the way for potential widespread implementation of whole-genome sequencing in newborn screening.

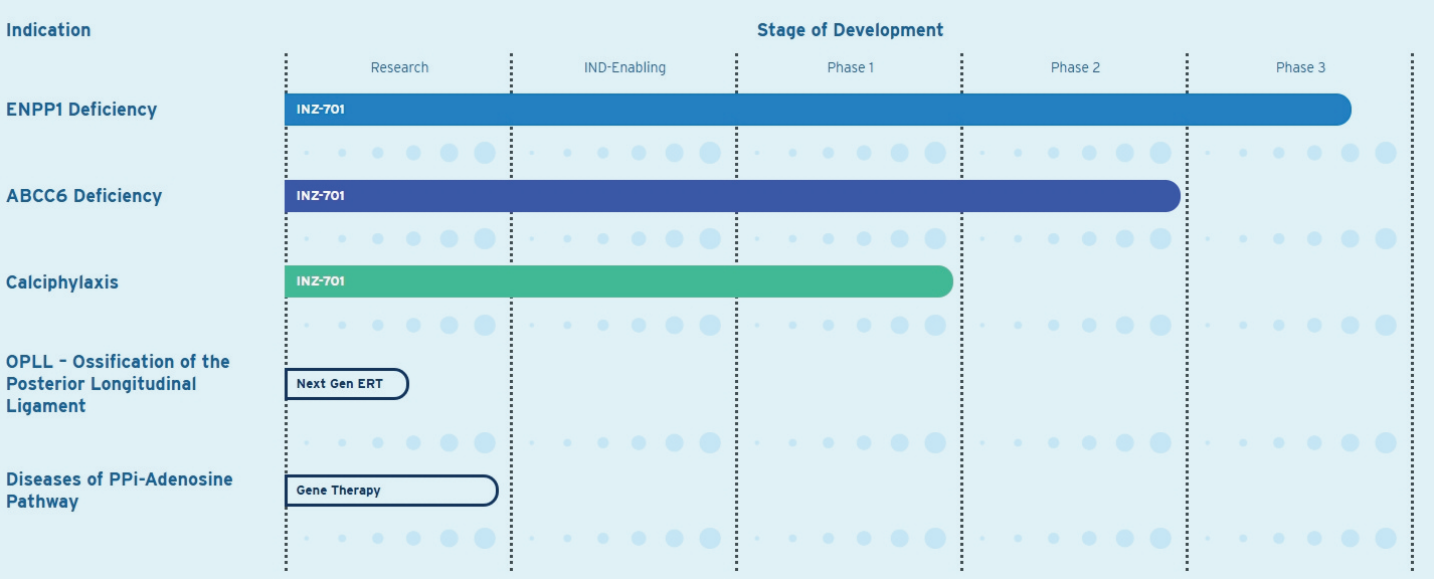
- **Establish commercialization infrastructure for the marketing and sale of INZ-701 for rare indications.** We retain worldwide, exclusive development and commercialization rights to INZ-701. Our current efforts focused on disease awareness and diagnosis, through our interactions with physician networks and patient organizations, as well as our patient registry, are laying the groundwork for an independent commercial organization. Given the limited number of specialists who treat the rare diseases we are initially pursuing, we believe that we will be able to commercialize INZ-701, if approved, in these indications with a small, targeted, internal sales and commercial organization in the United States and other major markets. Our executives have a strong track record and experience in building and managing biopharmaceutical companies and in rare disease research and development, developing new markets, and obtaining marketing approval for and commercializing therapies for previously unexplored rare diseases. We may explore the use of a variety of types of collaboration, co-promotion, distribution, and other marketing arrangements with one or more third parties to commercialize our product candidates in smaller markets outside the United States or for other situations in which a larger sales and marketing organization is required.

- **Expand our research and development efforts for INZ-701 in additional diseases impacting bone health and blood vessel function and for other therapies beyond INZ-701.** Based on its mechanism of action, we believe that INZ-701 has the potential to increase plasma PPi levels and provide therapeutic benefit to patients beyond those with monogenic defects in the ENPP1 or ABCC6 gene, including patients with calciphylaxis. 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. For instance, OPLL has been reported to cause myelopathy due to spinal cord compression, often necessitating surgery to alleviate symptoms - although surgery is not curative. We plan to investigate the potential of a next-generation INZ-701 molecule to address OPLL. Additionally, we believe there is potential to explore gene therapy approaches for disorders related to the PPi-Adenosine pathway in the future.

- **Continue to strengthen and expand our intellectual property portfolio and our rights to complementary technologies.** We intend to continue to pursue new scientific and therapeutic insights to position ourselves as leaders in the treatment of diseases impacting bone health and blood vessel function. In our Company's laboratory and in collaboration with academic and research institutions, we plan to continue to conduct translational experiments, validate disease models and evaluate new treatment modalities in our area of focus. Our current development programs are protected through exclusive intellectual property rights, including with filed and issued patents covering composition of matter for ENPP1-Fc fusion proteins, including INZ-701, and methods of treatment. We have expanded and expect to continue to expand the breadth of our intellectual property portfolio over time to incorporate novel insights we obtain through our research. In addition, we may further expand our development pipeline by opportunistically in-licensing or acquiring the rights to complementary technologies and product candidates. For example, in July 2020, we expanded our intellectual property portfolio when we acquired specified patent rights and other specified assets related to ENPP1 from Alexion.

Pipeline

Our lead development programs, for which we retain worldwide exclusive development and commercialization rights, are summarized in the table below. As part of our recent strategic review, we are prioritizing activities to support the planned BLA filing for INZ-701 for our lead indication, ENPP1 Deficiency. Patients with ABCC6 Deficiency being treated in our ADAPT long-term extension study, our expanded access program, or under investigator-sponsored INDs will continue to receive treatment. Any future trials in ABCC6 Deficiency and calciphylaxis will be postponed.



Diseases of the PPi-Adenosine Pathway: A Significant Unmet Need

The PPi-Adenosine Pathway plays a critical role in regulating bone health and blood vessel function. Disruptions in this pathway can lead to severe, life-threatening diseases characterized by abnormal calcium deposition or growth development, affecting bones, blood vessels, and soft tissues. These conditions, whether driven by genetic mutations or other factors, are associated with

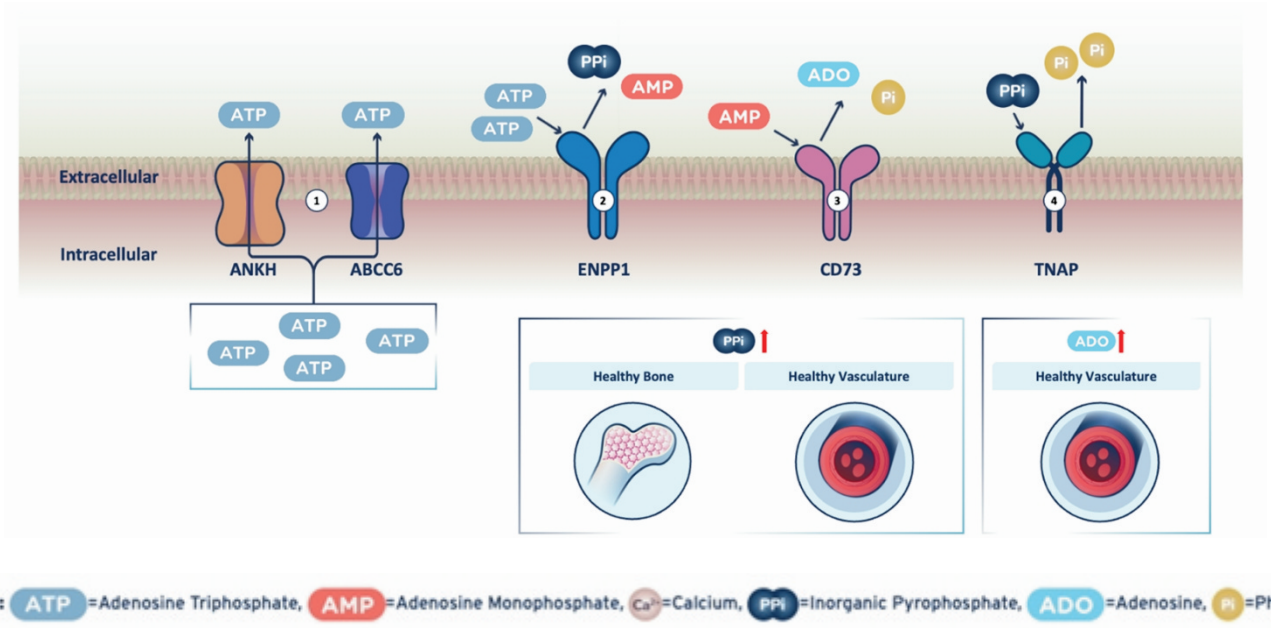
significant morbidity and mortality. Despite their devastating impact, there are currently no approved therapies that directly target the underlying pathway dysfunction, highlighting a significant unmet medical need and an urgent opportunity for innovation in treatment.

The PPi-Adenosine Pathway

The PPi-Adenosine Pathway has been conserved throughout evolution in higher organisms and is the key to keeping our bones and blood vessels healthy.

In a properly functioning PPi-Adenosine Pathway, the proteins encoded by the ABCC6 gene (ATP-Binding Cassette in the C6 family) and the ANKH gene (ANKilosis Homolog) located on the cellular membrane are responsible for modulating the transport of adenosine triphosphate ("ATP") from inside a cell to outside the cell. The enzyme encoded by the ENPP1 gene (ectonucleotide pyrophosphatase/phosphodiesterase 1) then cleaves extracellular ATP into PPi and adenosine monophosphate ("AMP"). PPi is a potent regulator of mineralization and, in particular, controls the rate of calcium crystal deposition in bone. AMP is further metabolized into adenosine, a potent regulator of cellular proliferation that, in particular, modulates a blood vessel's response to injury and is responsible for preventing intimal proliferation, or the overgrowth of smooth muscle cells inside blood vessels.

The normal function of the PPi-Adenosine Pathway is depicted in the figures below.



1. **ABCC6 and ANKH:** Transports adenosine triphosphate (ATP) from inside the cell and into the blood.
2. **ENPP1:** Breaks down ATP outside of the cell into two smaller molecules: AMP and PPi
3. **CD73:** Converts AMP into adenosine and phosphate.
4. **TNAP:** Breaks down PPi into phosphate.

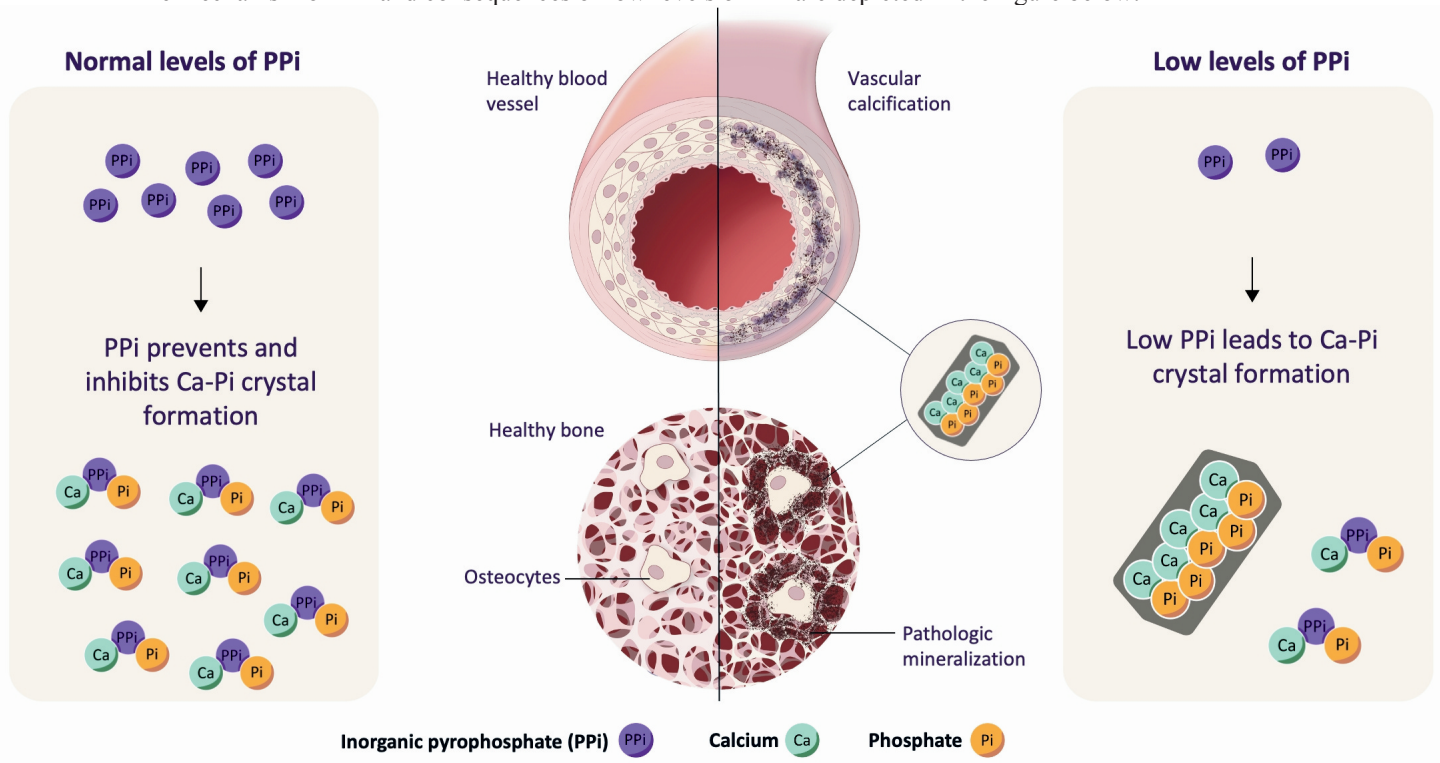
Pathology of Diseases of the PPi-Adenosine Pathway

Disruptions in the PPi-Adenosine Pathway—whether due to genetic mutations or other factors—can lead to severe diseases characterized by abnormal mineralization and vascular dysfunction, impacting bones, blood vessels, and soft tissues.

Mutations in ENPP1, a critical enzyme in this pathway, result in deficient levels of PPi and AMP, a precursor to adenosine. Similarly, mutations in ABCC6, a key transport protein, reduce extracellular ATP availability, indirectly leading to lower PPi and AMP levels. Low PPi levels drive pathologic mineralization, or ectopic calcification, in tissues where mineralization should not occur, including the heart, kidneys, skin, and vasculature. Calcification inside blood vessels within bones can also interfere with normal skeletal development and mineralization.

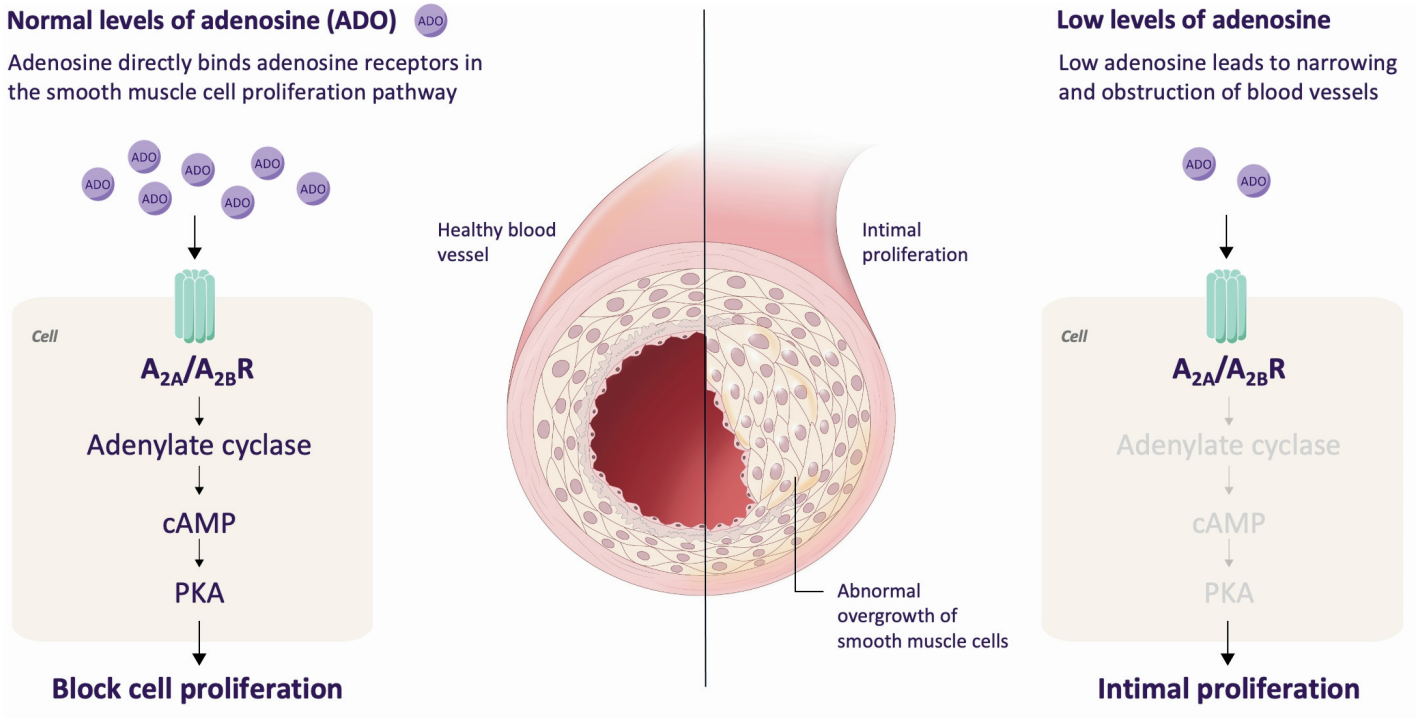
In addition to low PPi, low adenosine levels contribute to vascular dysfunction and intimal proliferation. This can lead to vascular narrowing, impaired blood flow, and increased cardiovascular risk, further exacerbating disease progression. The combined effects of pathologic mineralization and vascular complications highlight the urgent need for targeted therapies to restore PPi and adenosine balance, prevent disease progression, and improve patient outcomes.

The mechanism of PPi and consequences of low levels of PPi are depicted in the figure below.



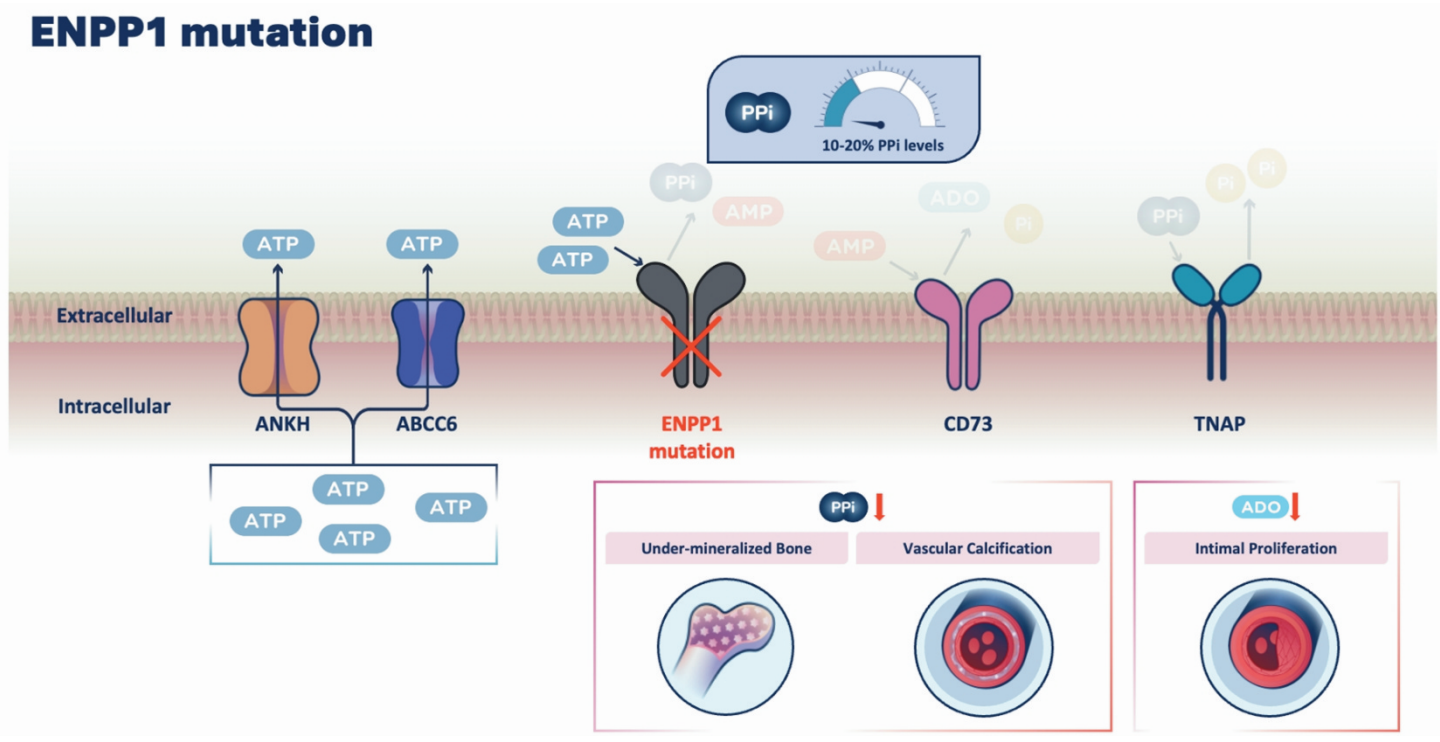
Low levels of adenosine lead to the narrowing and obstruction of blood vessels caused by intimal proliferation and potential development of cardiovascular complications.

The mechanism of adenosine and consequences of low levels of adenosine are depicted in the figure below.

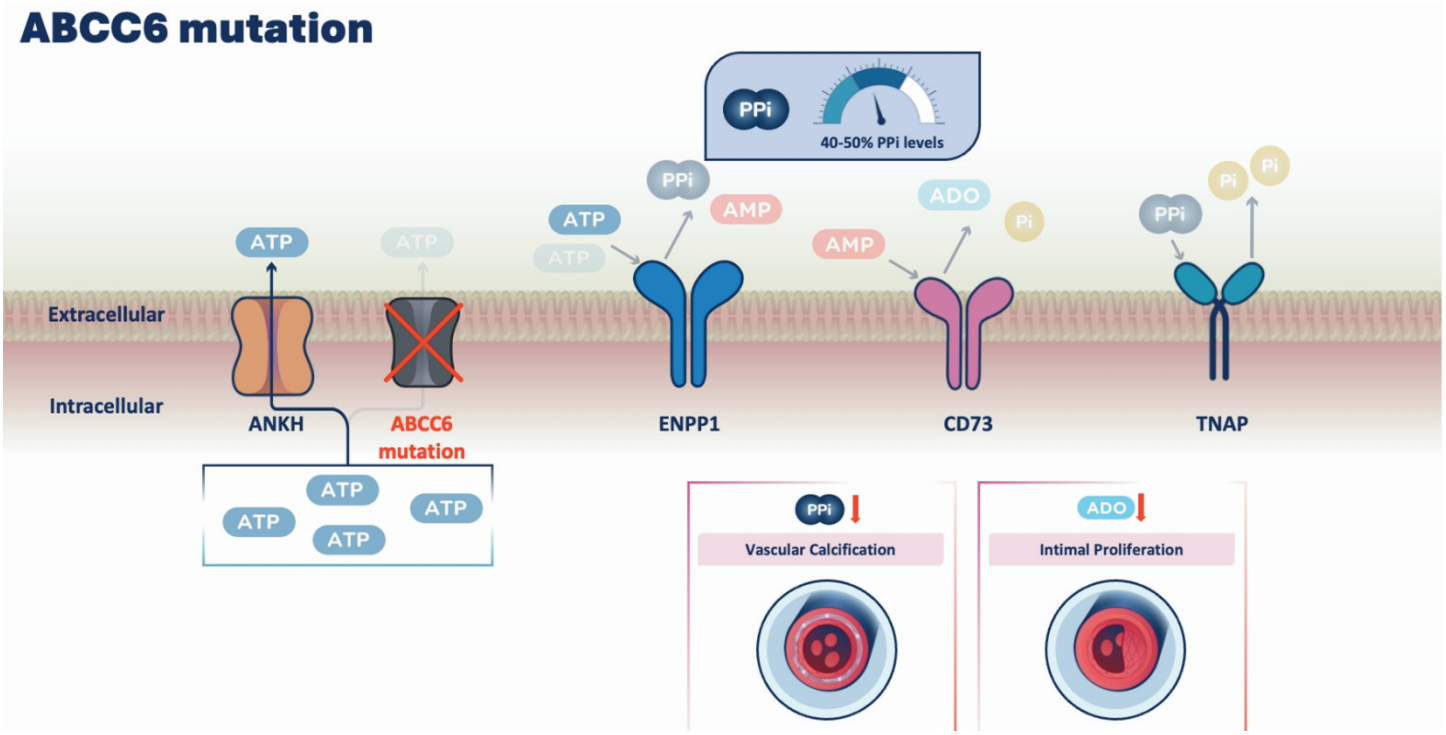


ENPP1 and ABCC6 Deficiencies are chronic, systemic, and progressive diseases occurring over the course of a patient's lifetime, starting as early as fetal development and spanning into adulthood.

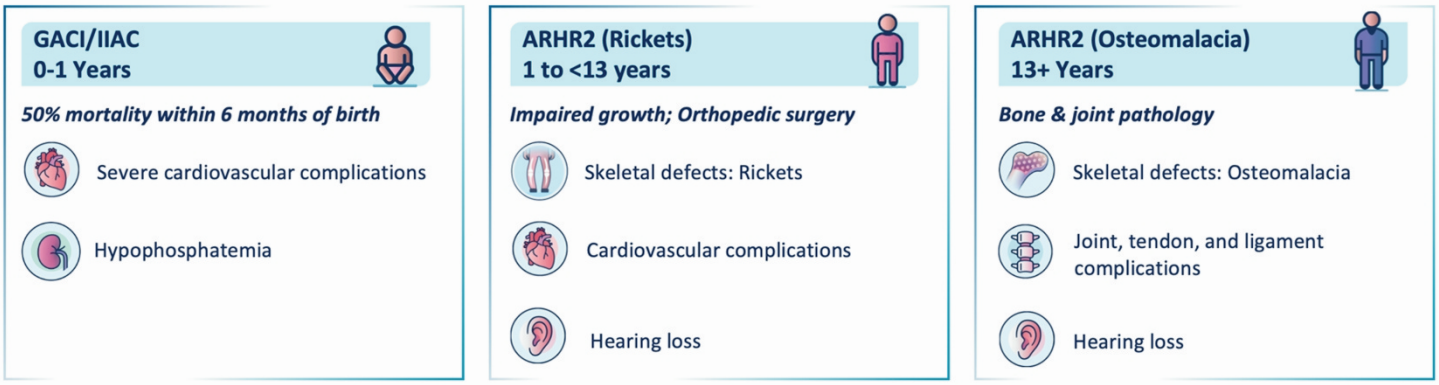
The consequences of genetic mutations affecting ENPP1 are depicted in the figure below.



The consequences of genetic mutations affecting ABCC6 are depicted in the figure below.



ENPP1 Deficiency and Disease Manifestations



ENPP1 Deficiency is a rare, inherited, genetic inborn error of metabolism caused by inactivating mutations in the ENPP1 gene. The condition is inherited as an autosomal recessive trait in which mutations in the ENPP1 gene result in decreased or absent activity of the ENPP1 enzyme. ENPP1 Deficiency results in low plasma levels of PPi, vascular calcification, and intimal proliferation, and is a single, chronic, systemic, and progressive disease with high mortality and morbidity. The spectrum of manifestations for ENPP1 Deficiency includes an infantile phase, a pediatric phase and an adult phase.

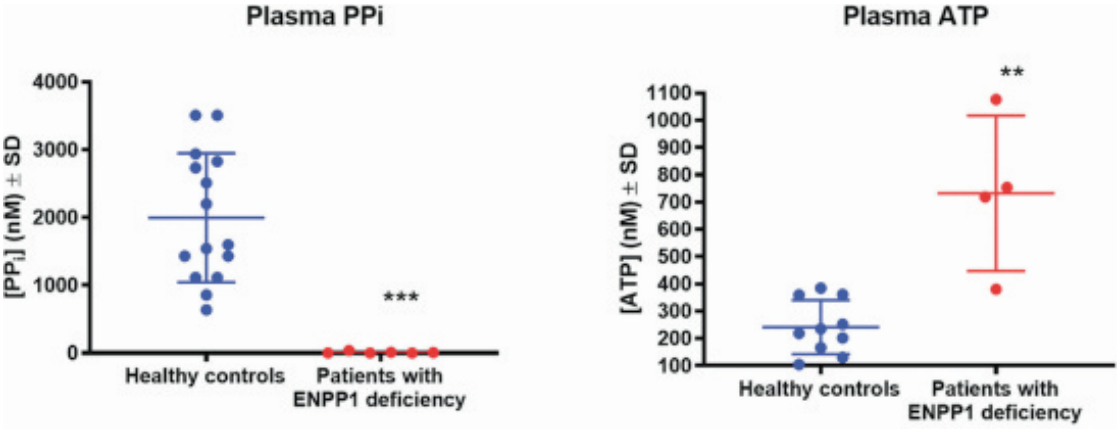
In the acute infantile phase, which has been referred to as GACI in the medical literature, ENPP1 Deficiency is characterized by narrowing of large and medium arteries caused by severe and pathologic vascular calcification and intimal proliferation, resulting in myocardial infarction, stroke, and dysfunction and potential failure of major organs, such as the heart and kidneys. The disease can be diagnosed prenatally when an ultrasound shows characteristic calcifications in the fetus. Infants with ENPP1 Deficiency have clinical signs of hypertension, heart disease and kidney disease even at birth. Mortality caused by ENPP1 Deficiency is at the highest during the infantile phase and occurs predominantly in the first 12 months of life. Approximately 50% of infants with ENPP1 Deficiency die within 6 months of birth. If they survive the crisis of infancy during the first 6 months of life,

individuals with ENPP1 Deficiency are likely to survive through adolescence and beyond, but with significant morbidity and a low quality of life.

In the pediatric phase, in addition to continuing vascular and organ calcification, ENPP1 Deficiency is characterized by the onset of rickets, which has been referred to in the medical literature as ARHR2. This is associated with an excess circulating concentration of a hormone known as fibroblast growth factor-23 (FGF23), which in turn causes the kidneys to waste phosphate, giving rise to rickets. ENPP1 Deficiency is also associated with severe skeletal deformities, short stature, and severe bone and joint pain. In addition, children with ENPP1 Deficiency may experience excess calcification in joints and ligaments and dental problems caused by disrupted tooth movement and exfoliation. Early onset of hearing loss has also been reported in these children. Patients with pediatric ENPP1 Deficiency experience impaired growth and development and generally decreased quality of life, including impaired ability to engage in normal childhood activities.

In the adult phase following closure of the bone growth plates at the end of adolescence, in addition to continuing vascular and organ calcification, patients with ENPP1 Deficiency have osteomalacia, severe bone and joint pain, fatigue, muscle weakness and risk of recurring bone fractures. Adults with ENPP1 Deficiency experience significant functional and cognitive impairment and generally decreased quality of life, including impaired activities of daily living.

The graphs below, adapted from a third-party study, show that patients with ENPP1 Deficiency have decreased levels of PPi and elevated levels of ATP in the plasma. This study measured plasma levels of PPi and plasma levels of ATP in healthy volunteers between 19 and 40 years of age and in patients with ENPP1 Deficiency between the ages of one month and 19 years of age. A p-value is a conventional statistical method for measuring the statistical significance of clinical results. A p-value of less than 0.05 is generally considered to represent statistical significance, meaning that there is a less than 5% likelihood that the observed results occurred by chance. Values are presented as the mean ± standard deviation ("SD"). In these graphs, the symbol ** represents a p-value of less than 0.005 and the symbol *** represents a p-value of less than 0.001.

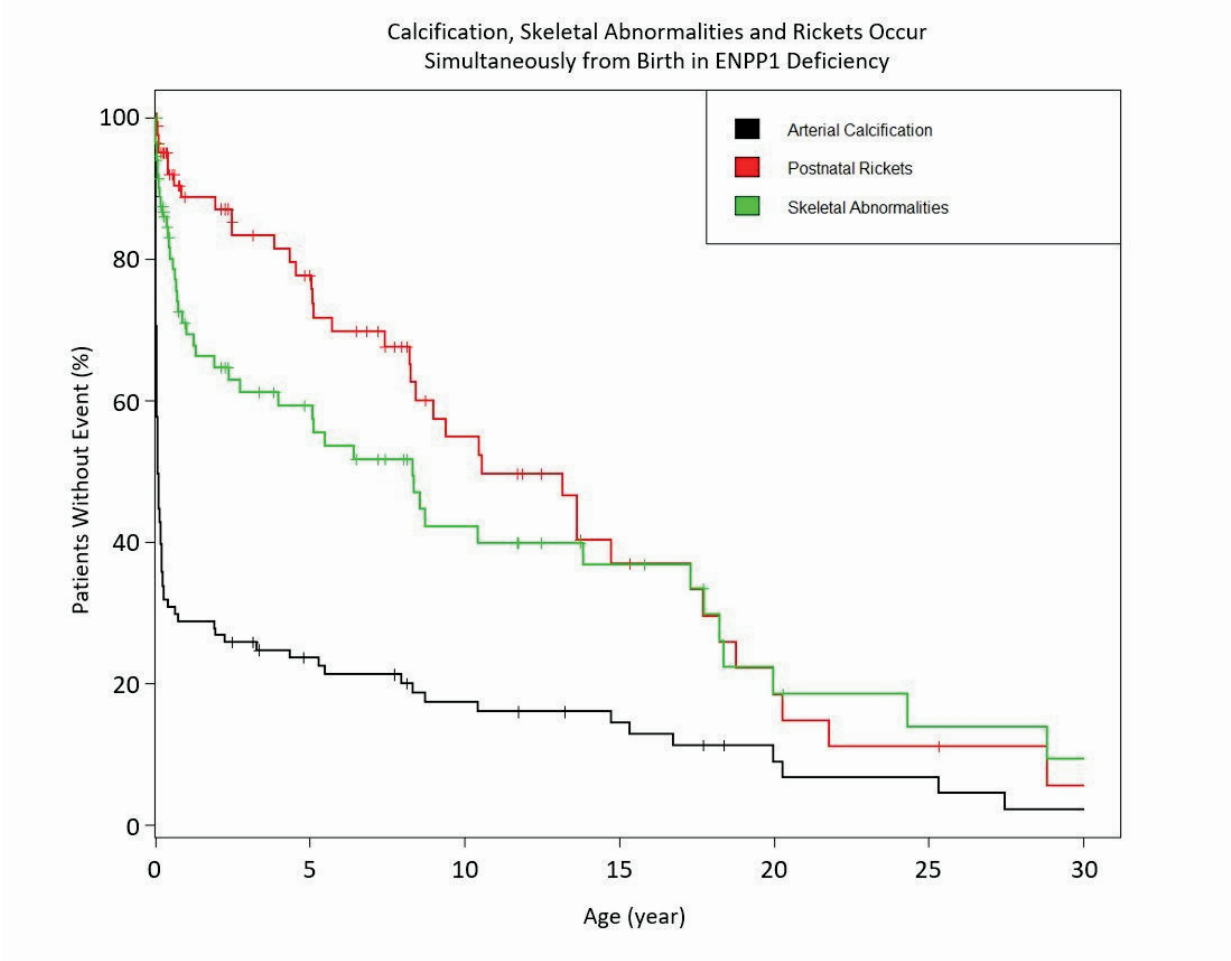


Source: Nitschke et al. Experimental & Molecular Medicine (2018)

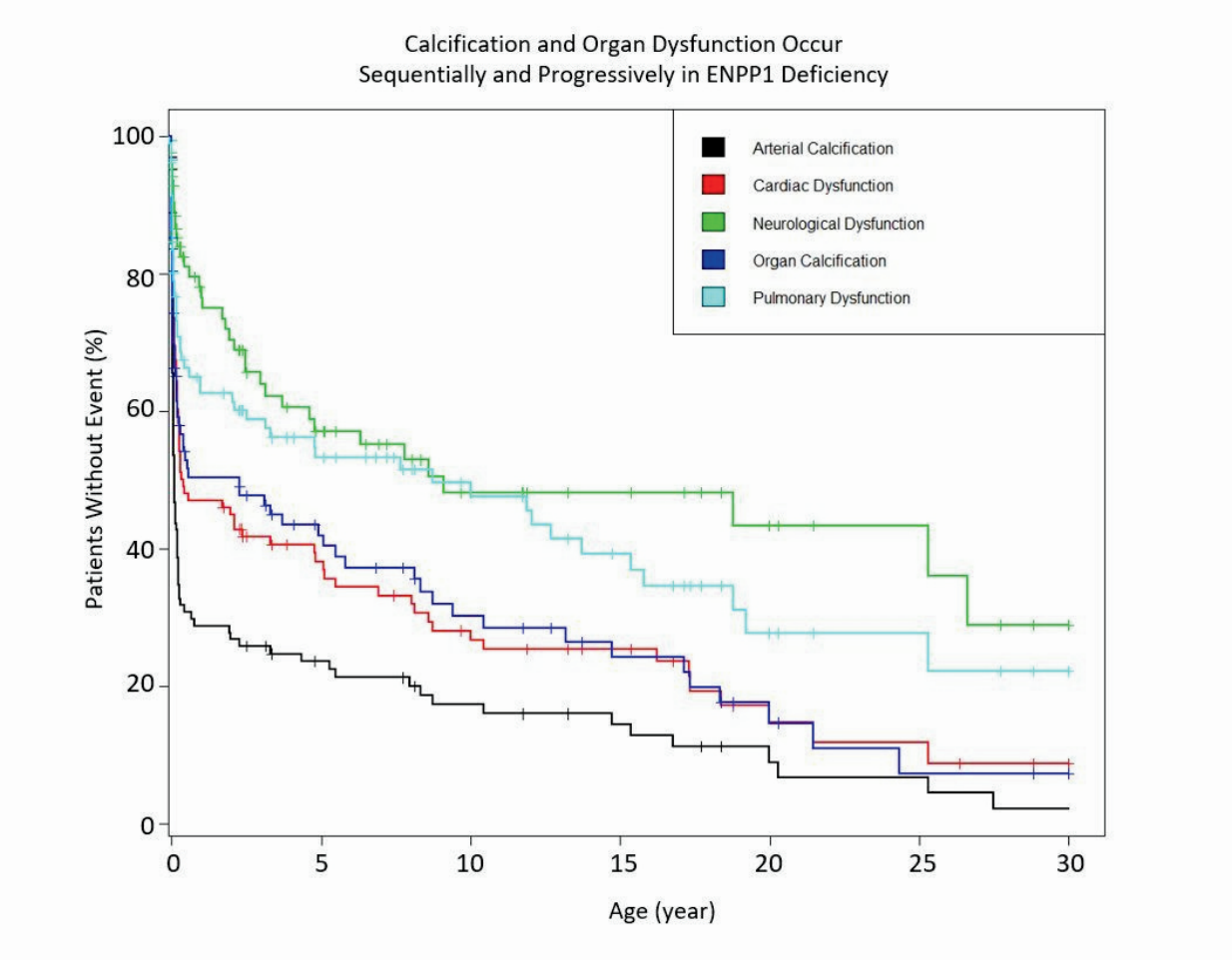
Retrospective Natural History Study

We conducted what we believe is the largest retrospective, cross-sectional, natural history study of infants, children and adults who had GACI or any presentation of ENPP1 Deficiency, including subjects with the acute form of ABCC6 Deficiency who were diagnosed with GACI as infants. The U.S. National Institutes of Health ("NIH") and the University of Münster in Germany contributed data on 127 subjects across 18 countries to this natural history study. Preliminary results from the study suggest that ENPP1 Deficiency, regardless of its phenotypic manifestation or original diagnosis as GACI or ARHR2, appears to be a chronic, systemic, and progressive disease that occurs over the course of a patient's lifetime.

As shown in the graph below, in our natural history study, arterial calcification preceded skeletal abnormalities, which preceded postnatal rickets. This data is shown using a Kaplan–Meier curve, also known as the product limit estimator, a non-parametric statistic used to estimate the probability of an event occurring given a defined time frame. While they occur at a defined rate, these manifestations occur simultaneously and concurrently following birth. The data indicate that the condition referred to as GACI in the medical literature is not independent of the condition referred to as ARHR2 in the medical literature. Preliminary results from our study suggest that arterial calcification and rickets are inseparable and dependent phenomena of ENPP1 Deficiency.



The data also suggest that patients who survive their first 12 months of life continue developing a systemic, progressive disease involving arterial, skeletal, and other organ calcifications, leading to physiological dysfunction across many systems. The graph below shows the Kaplan–Meier curve demonstrating systemic progression of the disease. The following manifestations of disease occur in progression: arterial calcification, cardiac dysfunction, organ calcification, pulmonary dysfunction, and neurological dysfunction.



The data suggest that arterial calcification, organ calcification, and organ dysfunction proceed in a progressive manner, with organ-specific symptoms emerging sequentially with time well into adulthood.

Based on our retrospective natural history study, we believe that ENPP1 Deficiency is characterized by concurrent onset of manifestations, albeit at different rates, and that ENPP1 Deficiency is a chronic, systemic, and progressive disease.

In 2022, we initiated a retrospective, longitudinal natural history study of patients with ENPP1 Deficiency and ABCC6 Deficiency and a prospective, longitudinal natural history study of patients with ENPP1 Deficiency and ABCC6 Deficiency. These studies are designed to test and validate our findings from our retrospective, cross-sectional natural history study. These studies are also designed to inform the design of pivotal trials and provide control data which may potentially be used in analysis of future therapeutic trials. In February 2025, we have completed a retrospective, cross-sectional natural history study of patients who had GACI or any presentation of ENPP1 Deficiency.

ENPP1 Deficiency Incidence and Prevalence; Current Standard of Care

ENPP1 Deficiency is estimated to occur in approximately one in 64,000 pregnancies worldwide, and we believe there are approximately 37,000 patients in addressable markets worldwide with ENPP1 Deficiency. In North America, the European Union ("EU"), Japan, Brazil, and the Gulf of Cooperation Council, we believe there are approximately 10,000 patients with ENPP1 Deficiency. In 2022, an analysis of all published cases of ENPP1 Deficiency patients diagnosed with GACI or ARHR2, and two

published natural history studies, reported a threefold increase in pathogenic/likely pathogenic *ENPP1* variants compared to those identified as of 2020.

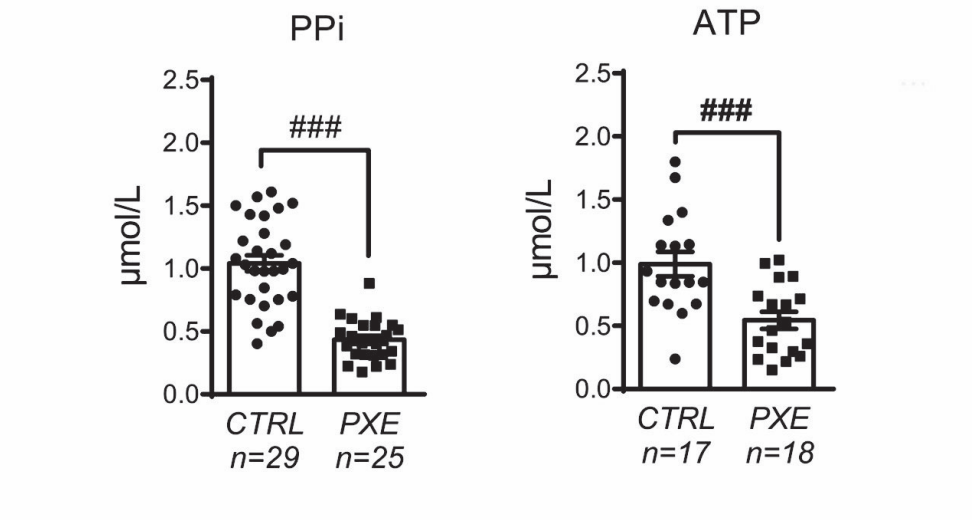
There are currently no approved therapies for ENPP1 Deficiency. Currently available treatments seek to minimize the manifestations of this disease. Some retrospective studies have reported potential therapeutic effect in infants of the bisphosphonate etidronate, a first-generation bisphosphonate developed to treat osteoporosis. However, these findings have been controversial due to selection bias in the study. In addition, etidronate has been discontinued in the United States, and bisphosphonate use can be associated with longer term adverse effects on skeletal development. Administration of active vitamin D3 and oral phosphate are sometimes used to address the rickets of ENPP1 Deficiency, although use of oral phosphate may actually increase the risk of pathologic calcification. In a third-party healthy volunteer study, treating PPi deficiency by adjusting the diet was an inefficient process, with only a small fraction of dietary PPi being absorbed.

ABCC6 Deficiency and Disease Manifestations

ABCC6 Deficiency is a rare, autosomal recessive gene disease characterized by a progressive ectopic deposition of calcium phosphate crystals on various extracellular matrices which leads to fragmentation of elastic fibers affecting the elastin-rich tissues such as the skin, the retina, and the vascular wall. Clinically diagnosed as pseudoxanthoma elasticum ("PXE") in adults, ABCC6 Deficiency has a high morbidity and cardiovascular and ophthalmological manifestations. Ocular changes include angioid streaks reflecting mineralization of Bruch’s membrane behind the pigmented retinal epithelium, which allows neovascularization of the retina, leading to loss of visual acuity, hemorrhage, and blindness. Cardiovascular manifestations include intermittent claudication, gastrointestinal ("GI") hemorrhages associated with stenoses of GI arteries, and stroke. Ectopic mineralization has also been noted in kidneys, joints, and tendons in patients with ABCC6 Deficiency, demonstrating this is a systemic and heterogenous disease. Infants with ABCC6 Deficiency may present with symptoms nearly identical to infants with ENPP1 Deficiency, and this syndrome is referred to as GACI-2.

Older pediatric patients with ABCC6 Deficiency may develop or present with ischemic stroke secondary to cerebrovascular stenosis and insufficiency, as well as other signs and symptoms observed in adult patients. In our natural history study of early onset ABCC6 Deficiency, we observed four of nine (44%) patients with biallelic ABCC6 mutations who suffered stroke at an early age, ranging from in utero to four years. These patients suffered significant disability, including residual paralysis and seizure disorders. Herring et al, have reported on a two-month-old girl with ABCC6 Deficiency caused by biallelic mutations who presented with multiple cerebral infarcts as well as extensive vascular calcification. Yasuhara described a 14-year-old girl with PXE who had no overt neurological deficits but exhibited occlusion of the right internal carotid artery, as well as other cerebral arterial occlusions. Bertamino et al reported on two pediatric patients with PXE who presented with cerebral vasculopathy and early onset stroke. Imaging of both patients revealed prominent narrowing of cerebral arteries. One of these patients remained undiagnosed until overt PXE developed later in life. Grossi et al systematically evaluated 38 pediatric patients with stroke of unknown etiology and screened them using a customized gene panel including 15 genes associated with genetic disease related to pediatric stroke. Four of the 38 patients had either heterozygous or compound heterozygous ABCC6 mutations. In addition, through our physician outreach program, we are aware of multiple other unpublished pediatric patients with ABCC6 Deficiency with either stroke or neurological symptoms. We suspect that many pediatric patients with unexplained stroke due to heterozygous and biallelic ABCC6 Deficiency remain undiagnosed. This information suggests we have identified a patient population with a severe unmet need who are in need of definitive treatment.

The graphs below, adapted from a third-party study, show that patients with PXE have decreased levels of PPi and ATP in the plasma. This study measured plasma levels of PPi and plasma levels of ATP in healthy volunteers with an average age of 45 years (SD ± 11 years) and in patients with PXE with an average age of 46 years (SD ± 13 years). A p-value is a conventional method for measuring the statistical significance of clinical results. Values are presented as the mean ± SD. In these graphs, the symbol ### represents a p-value of less than 0.005.



Source: *Kauffenstein, et al. J Inv Derm* ***2018***

ABCC6 Deficiency Incidence and Prevalence; Current Standard of Care

ABCC6 Deficiency is estimated to affect approximately one per 25,000 to 50,000 individuals, with the disease being diagnosed twice as frequently in females as in males, and we believe there are more than 67,000 patients worldwide with ABCC6 Deficiency. In North America, the EU, Japan, and Brazil, we believe there are approximately 24,400 patients with ABCC6 Deficiency.

There are currently no approved therapies for ABCC6 Deficiency. Currently available treatments seek to minimize the manifestations of this disease. Ophthalmic symptoms are typically treated with intravitreal injections of vascular endothelial growth factor inhibitors to slow the progression of choroidal neovascularization. However, damage to Bruch's membrane in these patients leads to continued and recurring choroidal neovascularization, causing vision loss. The current treatment approach for slowing or limiting the cardiovascular manifestations of PXE is based on the reduction of cardiovascular risk factors through lifestyle changes or in some cases by taking cholesterol-lowering agents. In the event of severe vascular disease, patients may undergo standard surgical bypass or angioplasty procedures.

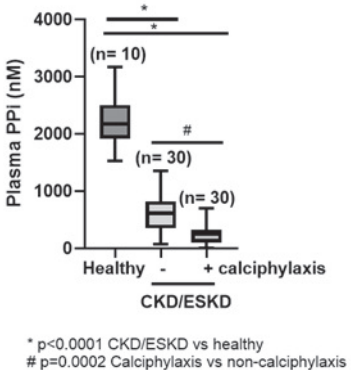
Calciphylaxis and Disease Manifestations

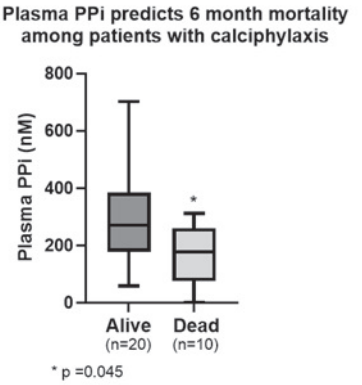
Calciphylaxis is a rare disease with a high mortality rate that mostly affects patients with ESKD. This disease is associated with low levels of PPi and is characterized by pathologic mineralization and intimal proliferation of the vasculature in the skin and fatty tissues leading to poor blood flow, blood clots, painful skin ulcers, serious infections, and death. Initial skin lesions typically present as extremely painful plaques and nodules, and progress to necrotic ulcers. This disease has a reported one-year survival rate of approximately 50%. The estimated incidence rate of calciphylaxis is approximately 3.5 per 1,000 patients with ESKD with approximately 5,000 new patients presenting annually across major geographies, including North America, the EU, Japan, and Brazil. There are currently no approved therapies for calciphylaxis, although use of sodium thiosulfate, a chelating agent intended to lower calcium content in the blood, reportedly improves wound healing. Patients also are often advised to maintain a low phosphate diet.

We have collaborated with a major academic institution to confirm that PPi levels are low in patients with calciphylaxis and to investigate associated manifestations that may be treated with INZ-701. Evidence of low PPi in calciphylaxis is supported by a longitudinal exploratory study designed to measure PPi in patients with calciphylaxis and to examine whether PPi levels are predictive of clinical outcomes. In this study, PPi was measured in patients with calciphylaxis at different stages of CKD/ESKD and matched for age, sex, race, and CKD/ESKD stage in patients without calciphylaxis. Results from this study revealed that PPi was significantly decreased in patients with calciphylaxis (both in those with and without dialysis-dependent CKD/ESKD) as compared to matched CKD/ESKD controls. The median PPi value was 248 nM in CKD/ESKD patients with calciphylaxis as compared to a median PPi value of 661 nM in CKD/ESKD patients without calciphylaxis, $p < 0.0001$. As shown in the graph below on the left, PPi levels in both

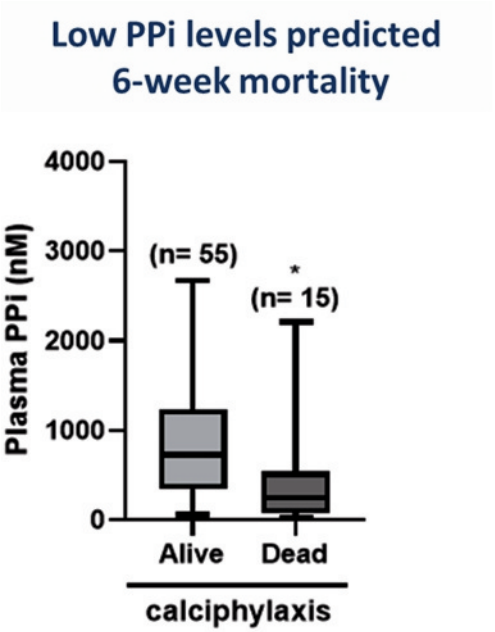
CKD/ESKD populations with and without calciphylaxis were significantly lower than PPi levels in healthy volunteers. Furthermore, as shown in the graph below on the right, lower PPi levels were associated with increased 6-month mortality among patients with calciphylaxis.

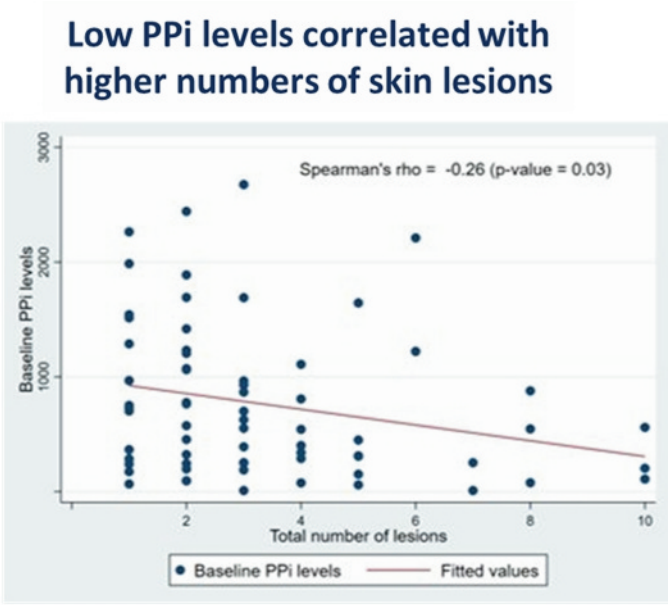
PPi levels in Healthy Volunteers and CKD/ESKD Patients with and without Calciphylaxis





In addition, a prospective cohort study conducted as part of the Partners Calciphylaxis Biorepository and Patient Registry (NCT03032835) enrolled 70 patients with calciphylaxis. Plasma PPi levels were measured using an ATP Sulfurylase/Luminescence-based method at enrollment (n=70) and at 6-week follow-up (n=30). In adjusted models, for every 10 nM decrease in PPi at enrollment, an approximately 25% increase in mortality was observed at 6 weeks. As shown in the graph below on the left, low PPi levels predicted 6-week mortality. In addition, as shown in the graph below on the right, low plasma PPi levels were correlated with higher numbers of skin lesions, suggesting a higher severity of calciphylaxis and predicting the mortality risk among patients with calciphylaxis (Chewcharat et al 2023).



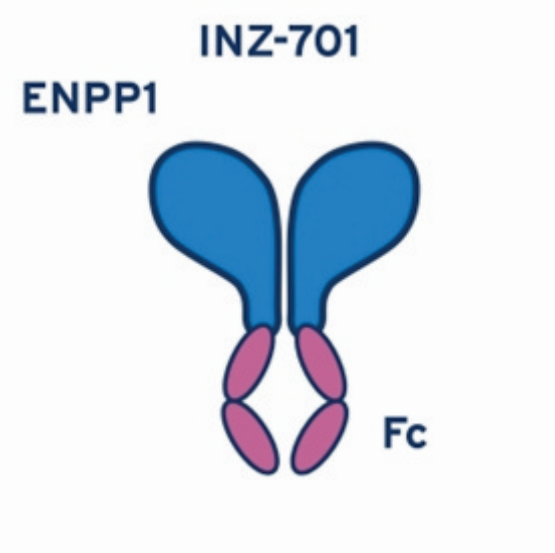


Our Solution: INZ-701

Overview of INZ-701

INZ-701 is a soluble, recombinant protein containing the extracellular domain of native human ENPP1 fused to the fragment crystallizable ("Fc") domain of the immunoglobulin IgG1. In its native form, ENPP1 is a transmembrane enzyme with a modular structure consisting of a short intracellular domain, a single transmembrane domain and an extracellular domain that contains a conserved catalytic site responsible for enzymatic activity. ENPP1 is expressed predominantly in the liver and, to a lesser extent, in the kidney and bone. INZ-701 contains the extracellular soluble domain of ENPP1 fused to the Fc domain of IgG1 to minimize immunogenicity, stabilize the construct, increase the plasma half-life, and allow ease of purification.

The presumed structure of INZ-701 is depicted in the figure below.



INZ-701 is designed to mimic the function of native ENPP1 protein, thus increasing PPi and adenosine, for ENPP1 Deficiency and providing therapeutic effect to treat other diseases, like ABCC6 Deficiency and calciphylaxis, involving low PPi levels. In contrast to native ENPP1, INZ-701 is a soluble protein that is designed to circulate throughout the body and access extracellular ATP and other nucleotide proteins. Like native ENPP1, INZ-701 cleaves ATP into PPi and AMP, a precursor of adenosine. Pharmacologically, INZ-701 is designed to have prolonged distribution and elimination phases, leading to steady-state concentrations in the blood over time and making dosing possible at infrequent intervals, potentially once-weekly dosing. INZ-701 is formulated for subcutaneous delivery.

In our preclinical studies conducted in Enpp1-deficient mouse models, dosing with INZ-701 resulted in increased plasma PPi levels, prevention of ectopic calcium deposits in a variety of tissues, prevention of calcification in the heart, aorta, lung, kidney, liver and spleen, prevention of skeletal abnormalities and improvements in overall health. In Abcc6-deficient mouse models, dosing with INZ-701 also increased plasma PPi levels and reduced calcification in key tissues. In addition to increasing levels of PPi, in preclinical studies, INZ-701 prevented intimal proliferation in both wild-type and Enpp1-deficient mice, which we believe is attributable to increased levels of adenosine. The nonclinical INZ-701 toxicology studies that we conducted in two animal species showed no systemic adverse effects at doses that significantly exceeded potential human doses.

The FDA has granted orphan drug designation, fast track designation, and rare pediatric disease designation to INZ-701 for the treatment of ENPP1 Deficiency and has granted orphan drug designation and fast track designation to INZ-701 for the treatment of ABCC6 Deficiency. The EMA has also granted orphan designation to INZ-701 for the treatment of ENPP1 Deficiency and ABCC6 Deficiency. The FDA has granted fast track designation to INZ-701 for the treatment of calciphylaxis. We have also been granted micro, small and medium-sized enterprise (SME) status by the EMA. We expect that SME status, combined with orphan designation, will result in substantial fee reduction during the EMA review process

INZ-701: Preclinical Results and Data

ENPP1 and ABCC6 Deficiencies

We demonstrated preclinical proof of concept for INZ-701 using multiple mouse models containing inactivated genes for ENPP1. In these Enpp1-deficient mouse models, the animals have an increased propensity for vascular calcification and replicate key aspects of human disease due to ENPP1 Deficiency. For example, an *asj* mouse contains a missense mutation in the ENPP1 gene and develops severe vascular calcification and skeletal abnormalities. In these mice, vascular calcification develops in newborn pups beginning around two weeks of age to fourteen weeks of age. This vascular calcification resembles that seen in human disease in infants due to ENPP1 Deficiency, although in humans, extensive vascular calcification begins as early as fetal development.

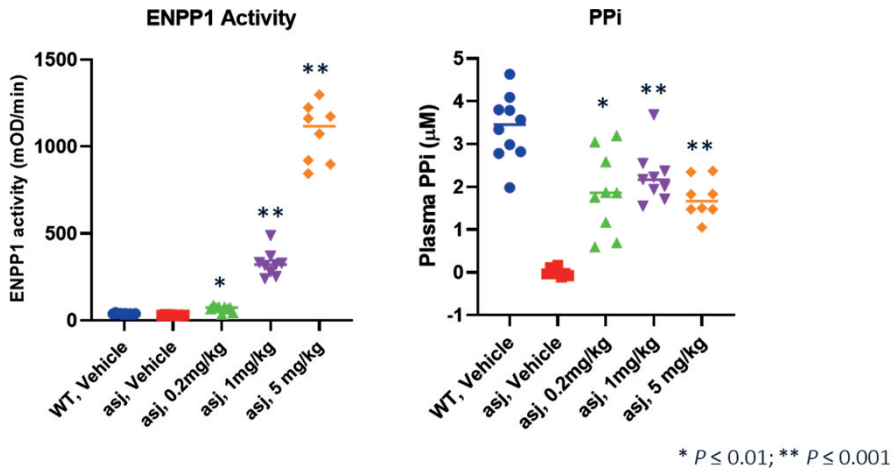
In another preclinical model of ENPP1 Deficiency in *ttw/ttw* mice, INZ-701 prevented intimal proliferation from developing and maintained proper vessel integrity.

In our preclinical studies, we also used an ABCC6 mouse model with targeted ablation of the ABCC6 gene. In these mice, ectopic calcification in tissues resembles that seen in human disease due to ABCC6 Deficiency. ABCC6 is primarily expressed in the liver. In mice, ABCC6 is responsible for approximately 90% of the levels of extracellular ATP, the primary source of extracellular PPi. Mice in which the gene for ABCC6 has been inactivated exhibit significantly reduced levels of extracellular PPi in blood.

Increase in PPi

As a result of an ENPP1 gene mutation, *asj* mice have very low or nondetectable levels of circulating PPi. Treatment of these mice with 0.2 mg/kg, 1 mg/kg or 5 mg/kg of INZ-701 by subcutaneous injection every other day for a period of eight weeks led to significant increases in ENPP1 enzyme activity and PPi levels in plasma to approximately wild-type levels. These increases compensated for the loss of ENPP1 activity in this strain of mice. Mice treated with vehicle control lacked any ENPP1 activity and plasma PPi, as expected.

The results of these initial studies are shown in the graphs below.

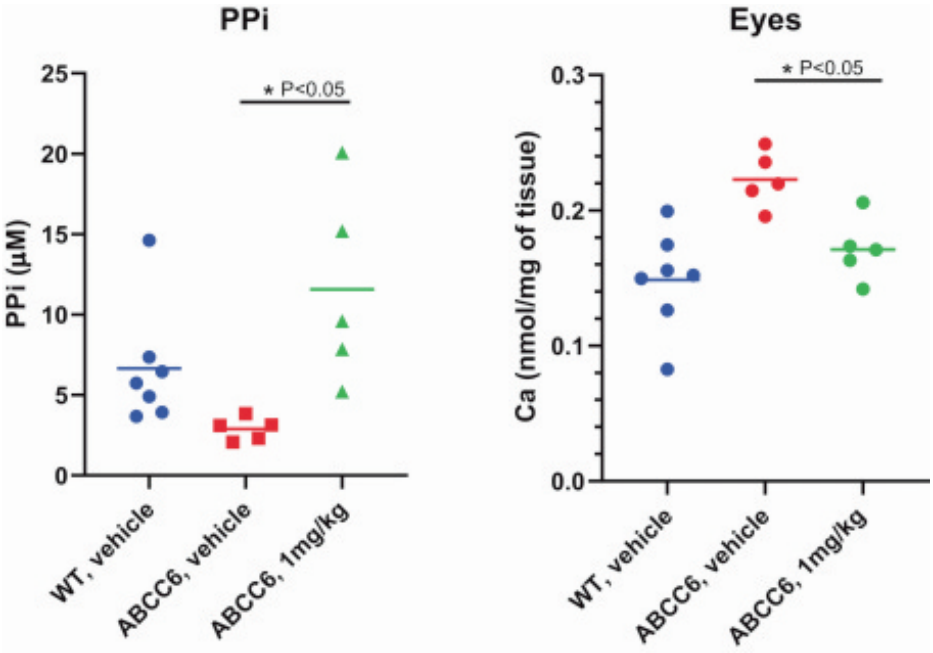


These initial studies showed that it is possible to administer doses of INZ-701 to increase PPi levels in mice and we believe that increasing the amount of ENPP1 enzymatic activity by administration of INZ-701 could lead to further increases of PPi. We further believe this suggests that INZ-701 has the potential to provide therapeutic benefit in non-genetic diseases that involve ectopic calcification.

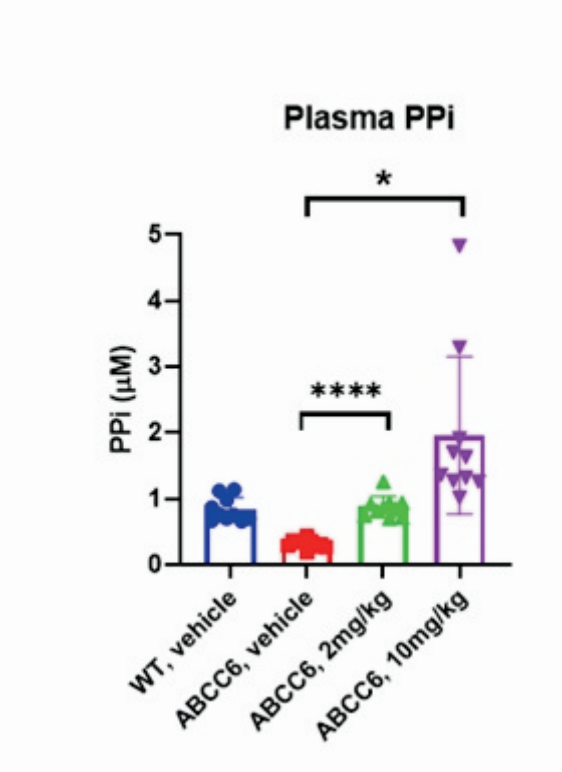
We also believe that our preclinical findings provide strong support for the eventual use of INZ-701 to treat patients with ABCC6 Deficiency. Individuals with PXE have dysfunctional ABCC6 and decreased levels of plasma PPi due to deficiencies in exporting ATP from within the cell. In studies in mice with defects in the ABCC6 gene, plasma PPi levels are significantly reduced relative to wild-type mice but still higher than those seen in *asj* mice, which have an inactivated ENPP1 gene. In other studies, overexpression of ENPP1 in *asj* mice containing inactivated ENPP1 normalized plasma PPi levels. Addition of the same transgene of ENPP1 in ABCC6 mutant mice normalized PPi levels, suggesting that even in the case of limiting extracellular ATP, an increase in ENPP1 activity led to the formation of additional PPi.

Studies in mice with a genetic defect in ABCC6 led to the hypothesis that low levels of plasma PPi in patients with ABCC6 Deficiency contributes to ectopic calcification. In studies in Abcc6-deficient mice, vascular calcification was correlated with plasma PPi level and overexpression of ENPP1 through transgene expression, led to high levels of PPi resulting in significant reductions in cardiac calcium deposits. We believe these findings confirm the link between ABCC6, PPi and calcification. It also suggests that increasing plasma PPi in PXE patients offers potentially significant therapeutic benefit.

To further illustrate the potential of our approach, we dosed Abcc6-deficient mice with 1 mg/kg of INZ-701 and vehicle control for eight weeks. Treatment with INZ-701 resulted in an increase in plasma PPi levels consistent with those in normal healthy mice. The increase in plasma PPi levels was also associated with a decrease in pathologic calcification of the eye, a target organ for ABCC6 Deficiency and patients with PXE. The results of this study are shown in the graphs below. We believe these data support the use of INZ-701 in patients who carry mutations in the gene for ABCC6 and have soft tissue calcification due to low PPi levels.

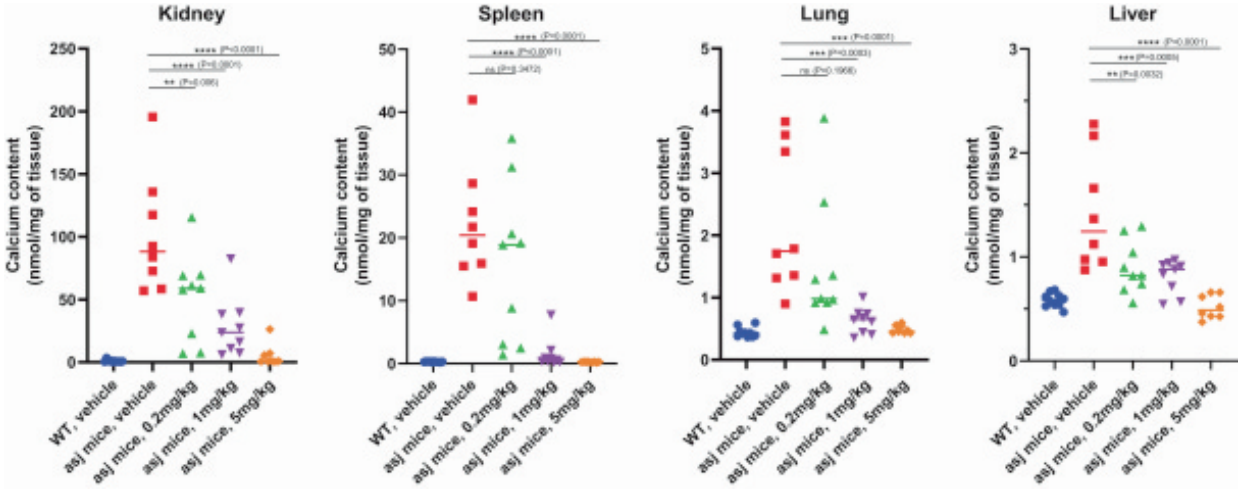


The above findings in Abcc6-deficient mice were also observed in another study, as shown in the graph below, where doses of INZ-701 ranging from 2 mg/kg to 10 mg/kg increased plasma PPi levels to wild-type levels. In the graph below, the symbol * represents a p-value of less than 0.05, and the symbol **** represents a p-value of less than 0.001 relative to Abcc6-deficient mice treated with vehicle. We believe that the data from these two studies in Abcc6-deficient mice suggest the potential of ENPP1-Fc fusion proteins to increase plasma PPi levels and thereby reduce pathologic tissue calcification.

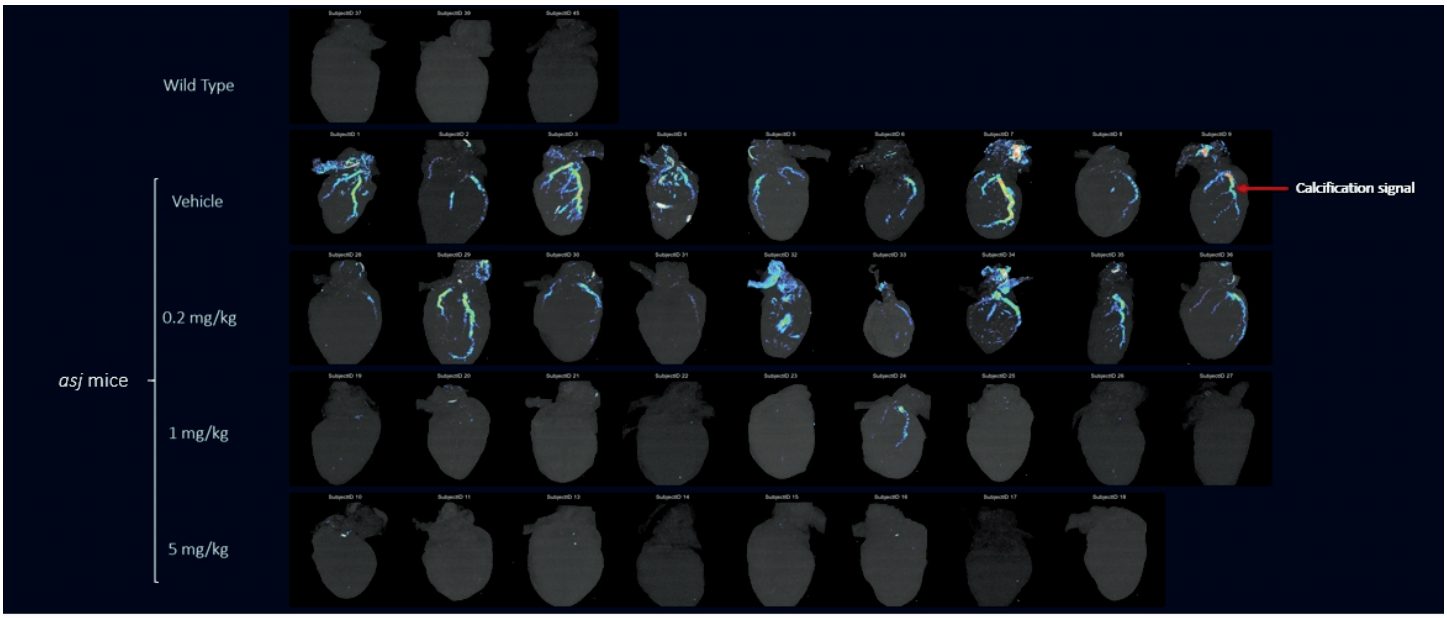


Reduction of Calcification

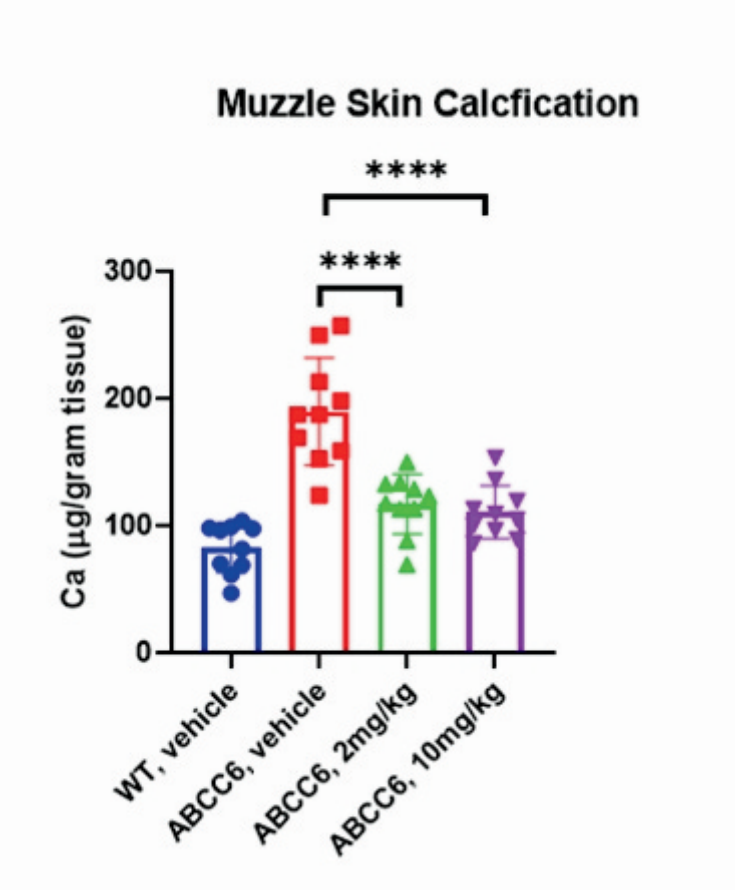
Asj mice fed a diet rich in phosphorous and low in magnesium, referred to as an acceleration diet, develop a number of complications due to calcification defects. These defects limit their locomotion, restrict their growth, cause calcium deposits in the vasculature and soft tissues and lead to a shortened lifespan. We dosed mice on the acceleration diet, starting at week two, with both INZ-701 and vehicle control every other day for eight weeks. INZ-701 delivered to *asj* mice at doses of 0.2 mg/kg, 1 mg/kg and 5 mg/kg significantly reduced ectopic calcification in the kidney, spleen, lung and liver. As shown in the graphs below, treatment with as little as 0.2 mg/kg of INZ-701 reduced calcium deposits in all tissues, and mice treated with 5 mg/kg of INZ-701 showed no differences in calcification compared to wild-type controls.



We obtained evidence of changes in vascular calcification in *asj* mice on the acceleration diet by carrying out scans of the heart and aorta using a technique known as high resolution micro computed tomography ("micro CT"). All nine *asj* mice dosed with vehicle control showed variable but extensive calcification in the aorta, coronary artery and heart. All nine *asj* mice dosed with 0.2 mg/kg of INZ-701 showed a pattern and intensity of calcification signals similar to that shown when mice were dosed with vehicle control. In almost all cases, increasing the dose of INZ-701 to 1 mg/kg or 5 mg/kg completely prevented calcification in the heart and in the aorta. Only one out of nine mice from the 1 mg/kg group showed some evidence of cardiovascular calcification. Treatment with 5 mg/kg of INZ-701 completely prevented calcification in the heart and aorta in all eight mice dosed in the 5 mg/kg group. The dose response and degree of calcification measured by micro CT of the heart and aorta for each mouse in this study are illustrated below in increasing shades of blue and green. We believe these results suggest that INZ-701 may have the ability to significantly reduce the extent of ectopic calcification due to ENPP1 Deficiency. In the study represented by the illustration below, the p-value for the degree of calcification for *asj* mice dosed with INZ-701 compared to *asj* mice dosed with vehicle control was 0.5341 for the 0.2 mg/kg group and 0.0004 for both the 1 mg/kg group and 5 mg/kg group.

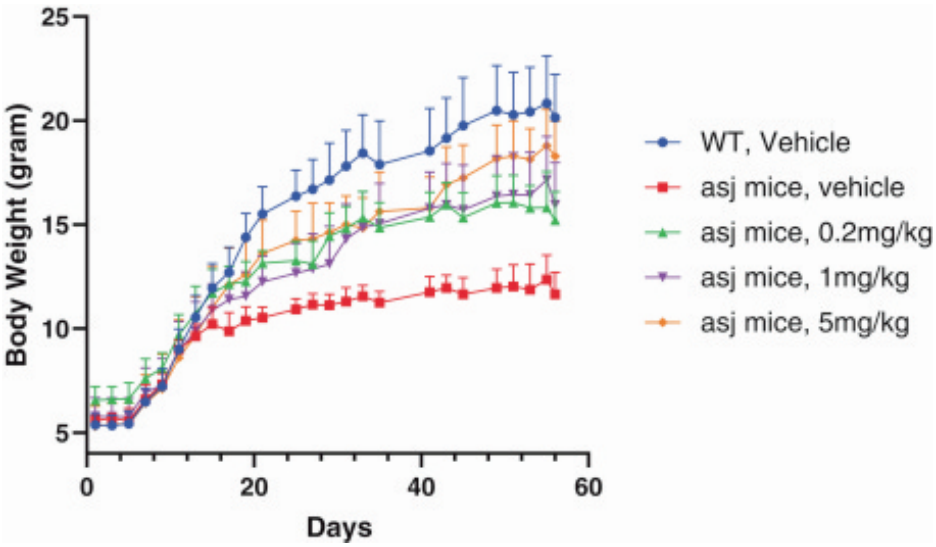


To investigate whether increasing plasma PPi levels would prevent ectopic calcification in Abcc6-deficient mice, we dosed Abcc6-deficient mice with 2 mg/kg of INZ-701, 10 mg/kg of INZ-701 or vehicle control from two weeks of age for eight weeks every other day. At 10 weeks of age, all of the mice were euthanized and the mineralization and blood biochemistry was measured. In this study, Abcc6-deficient mice exhibited low plasma PPi levels and significantly increased muzzle skin calcification. However, treatment of Abcc6-deficient mouse with INZ-701 caused a significant increase in plasma PPi at doses of 2 mg/kg and 10 mg/kg and a significant reduction in the extent of calcification noted in the muzzle skin to wild-type levels. This increase in plasma PPi levels in the Abcc6-deficient mice contributed to the reduction in pathologic tissue calcification. We believe that these data suggest that ABCC6 Deficiency contributes to increased ectopic calcification and that ENPP1, through PPi, may be able to reduce the extent of calcification. In the graph below, the symbol **** represents a p-value of less than 0.001 relative to Abcc6-deficient mice treated with vehicle.



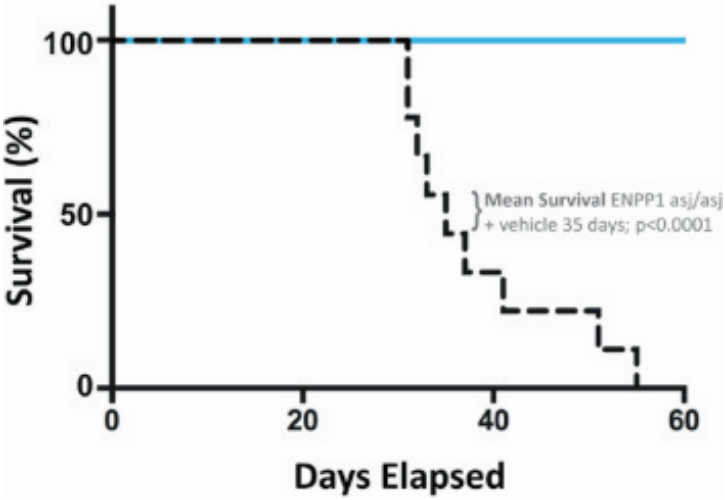
Overall Health and Survival

In addition to the measured changes in calcium deposition, treatment of *asj* mice with 0.2 mg/kg, 1 mg/kg, or 5 mg/kg of INZ-701 and vehicle control every other day also led to improvements in overall health. Mice treated with INZ-701 had a dose-dependent increase in body weight compared to mice treated with vehicle control, whose average weight at 27 to 56 days was only 60% that of wild-type mice. Compared to *asj* mice treated with vehicle control, mice treated with INZ-701 at 1 mg/kg and 5 mg/kg showed significant increases in body weight. The results of this study are shown in the graph below.

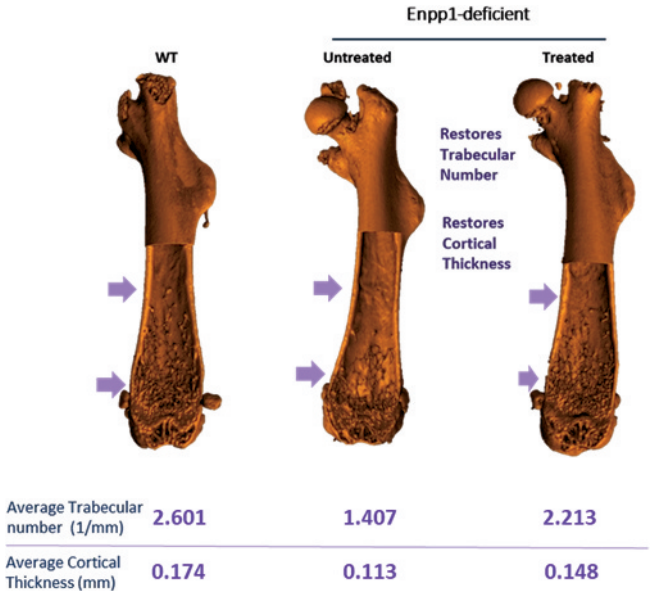


In addition to body weight, treatment of *asj* mice with INZ-701 at 1 mg/kg and 5 mg/kg every other day led to improvement in a number of clinical signs associated with ENPP1 Deficiency in mice, including pinned ear, hunched back, stilted and stiff legs, dehydration and rough hair coat. Treatment with INZ-701 also prevented *asj* mice from early mortality associated with becoming moribund.

In another experiment, we treated mice with either 1 mg/kg of mENPP1-Fc, a research version of INZ-701 containing a mouse Fc domain, or vehicle control starting on the fourteenth day of life and until day 55. In this experiment, all eight mice treated with mENPP1-Fc survived the full 55 days of the trial (represented by the blue line in the graph below), while the median lifespan of the untreated mice decreased from 58 days to 35 days (represented by the black hatched line in the graph below).



In another experiment, we treated *asj* mice with 0.2 mg/kg, 1 mg/kg, or 5 mg/kg of INZ-701 and vehicle control for 56 days to analyze by micro CT the femora and tibiae bones and measure both trabecular number and cortical thickness, which are two important contributors of bone strength. The strength of a bone and its ability to resist fracture is dependent upon these two structural parameters. Treatment of *asj* mice with INZ-701 corrected the bone defects, leading to a dose-dependent increase in bone length, trabecular number and cortical thickness as compared to *asj* mice treated with vehicle control.

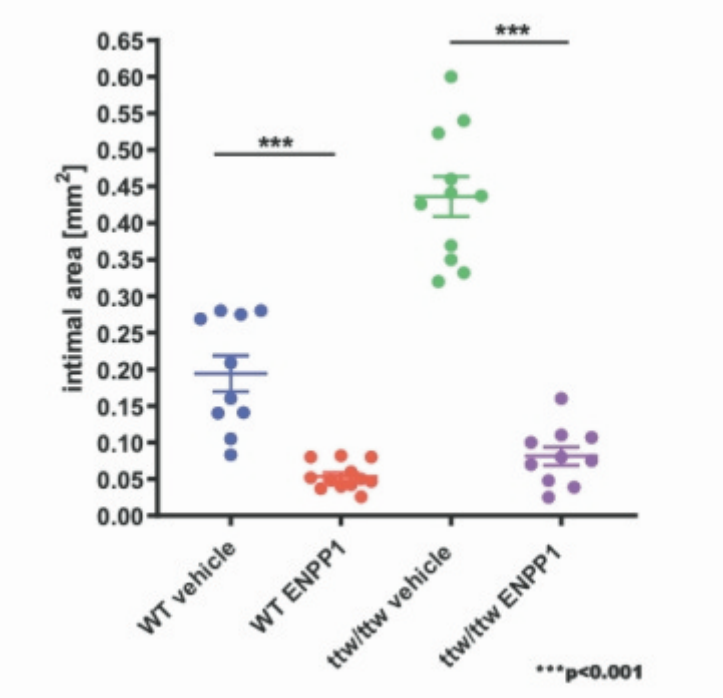


Intimal Proliferation

Intimal proliferation resulting from ENPP1 Deficiency was also replicated in corresponding animal models. In animal models, intimal proliferation is accelerated during conditions of injury including ligation of the artery. The exact mechanism linking ENPP1 Deficiency to intimal proliferation is under investigation but is believed to directly involve the adenosine pathway.

The increase in intimal proliferation can be observed in a strain of Enpp1-deficient mice known as *ttw/ttw* mice in a carotid artery ligation model. These mice have a single base pair change in the ENPP1 gene producing ENPP1 Deficiency. The *ttw/ttw* mice were treated with 10 mg/kg of INZ-701 or vehicle control every other day for seven days before carotid artery ligation surgery and for 14 days following carotid artery ligation surgery. Vehicle control-treated *ttw/ttw* mice showed a significant increase in intimal proliferation in the area of the artery at the sites of ligation. We believe these data, shown in the graph below, confirm that the INZ-701 treatment aligns with the earlier published findings indicating that ENPP1 treatment in mice inhibited ligation-induced intimal proliferation.

Importantly, as shown in the graph below, INZ-701 also inhibited ligation-induced intimal proliferation in wild-type mice without ENPP1 Deficiency. These important findings in wild-type mice suggest that increasing levels of ENPP1 above normal may be useful in diseases in which vascular intimal proliferation is increased.



To further evaluate INZ-701's effects on intimal proliferation, we conducted a pilot study in a swine model. In this study, three pigs underwent surgery in which stents were inserted into the coronary, profunda, and femoral arteries. At day 14, the stents were re-injured with balloon dilation to initiate additional intimal proliferation at the stented arterial sites. The sites were then evaluated with angiography and optimal coherence tomography ("OCT"). We dosed the pigs with vehicle control and 10 mg/kg of INZ-701 every four days, with the first dose administered on day 10. At day 42, the pigs again underwent angiography and OCT, and quantification of intimal proliferation was performed in the OCT images and compared to the day 14 OCT evaluation.

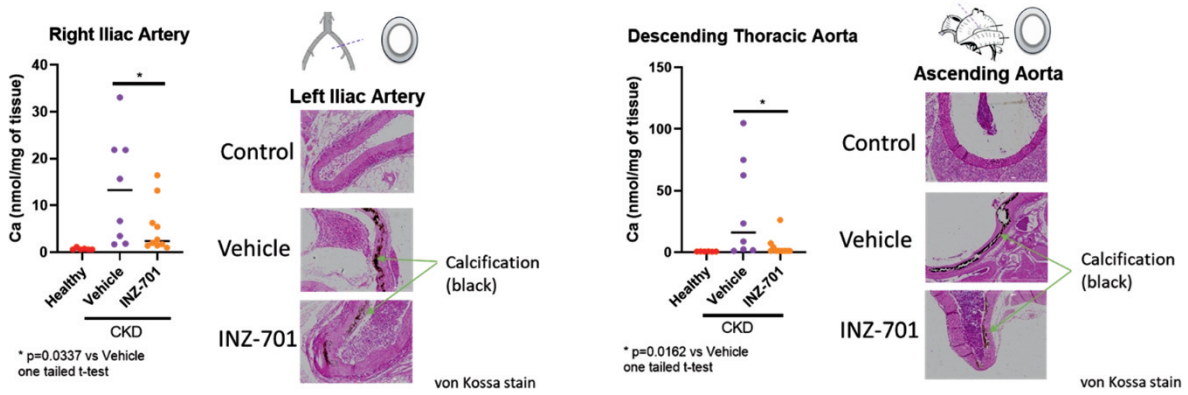
In this study, INZ-701 significantly ($p<0.05$) inhibited stenosis or intimal proliferation in the profunda artery over 28 days. These results in a large animal model of intimal proliferation support the results from the studies in the mouse model of intimal proliferation.

Chronic kidney disease (CKD)

Vascular calcification associated with ESKD and CKD, known as Monckeberg's sclerosis, have very similar pathophysiologies to GACI, as both diseases include vessel hardening with calcium deposits in the muscular layers of the medial vascular wall.

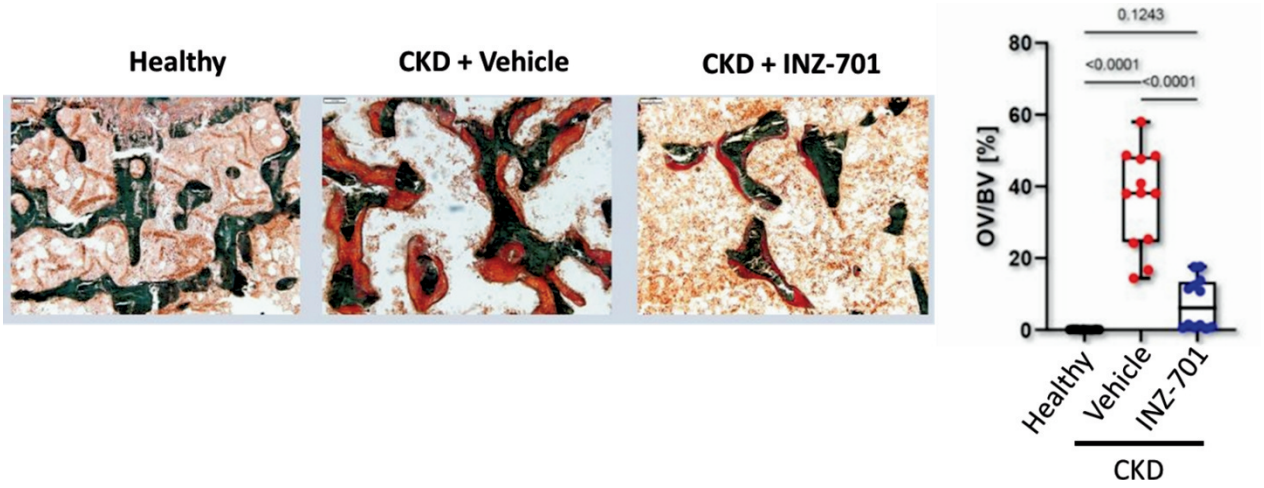
By modifying the adenine diet regimen previously described, we developed a rat model to induce uremia and enhance vascular calcification. Administration of 10 mg/kg of INZ-701 in uremic rats showed reduced total calcium content in the large arteries (between 61% and 86%) and organs (between 15% and 63%) as compared to the vehicle group. Histological examination of the arteries showed that uremic rats dosed with vehicle showed extensive, often circumferential, medial calcification that extended over multiple sections. In contrast, uremic rats dosed with INZ-701 had a reduction in calcification that was evident by von Kossa staining (black staining) as shown in the first figure below. In the treated group, calcification was segmented and frequently did not extend through multiple sections. Another complication associated with CKD is skeletal abnormalities such as high turnover bone disease or adynamic bone disease, known as mineral bone disorders. These abnormalities lead to under-mineralized bone which is evident as increased osteoid bone in bone sections. Histological examination of the femurs showed that uremic rats dosed with vehicle had increased osteoid volume. In contrast, uremic rats dosed with INZ-701 had a significantly lower osteoid volume that was evident by Goldner's trichrome staining (red staining) as shown in the second figure below. These results suggest that INZ-701 prevented vascular calcification and bone abnormalities in uremic rats and has the potential to be a treatment in patients with CKD. We believe that calciphylaxis very likely represents a continuum of vascular calcification complications with pain and skin changes, and that treatment with INZ-701 could potentially be beneficial in this disease.

Effect of INZ-701 on Vascular Calcification in a Rat Model of CKD



Ca=calcium

Effect of INZ-701 on Skeletal Abnormalities in a Rat Model of CKD



A cross-section of the trabecular area of the femur bone shows that CKD rats have thick osteoid (red staining). INZ-701 significantly prevented osteoid formation in CKD treated rats. Quantitation of the osteoid is shown in the graph above, wherein.

CKD=chronic kidney disease; OV=Osteoid volume; and BV=Bone volume.

Safety and Toxicology

We evaluated INZ-701 in toxicology studies in rats, mice, and non-human primates. In single and multiple administration studies in rats and non-human primates, the maximum tolerated doses of INZ-701 were determined to be 180 and 100 mg/kg, respectively. In these studies, no systemic adverse effects or pathologic effects were noted with INZ-701. Because both non-human primates and mice are relevant species, based on gene sequence homology and biologic activity, we subsequently conducted 28-day good laboratory practices ("GLP") investigational new drug application ("IND")-enabling studies in each species. In these studies, there were no adverse events and we observed normal histopathology and clinical pathology. In addition, we conducted a 28-day GLP cardiovascular study in non-human primates and a 28-day GLP central nervous system and respiratory risk study in mice. There were no adverse observations in any of these studies at doses up to 30 mg/kg of INZ-701, which was the highest dose tested. The 28-day studies were followed by three-month GLP IND enabling toxicology studies in mice and non-human primates. There were no adverse observations in these studies at doses up to 60 mg/kg of INZ-701 in mice and 30 mg/kg of INZ-701 in non-human primates, which were the highest doses tested in each species.

In addition, two GLP dose range-finding studies of INZ-701 were conducted in juvenile C57BL6 mice. In both studies INZ-701 was given by subcutaneous injection for 21 days every other day at doses up to 30 mg/kg. There were no adverse clinical observations, mortality, or moribundity in mice that received INZ-701; no test article-related changes in body weight, body weight gain, or food consumption; and no test article-related changes in hematology or coagulation in mice that received INZ-701 as compared to the concurrent control groups of the same sex (in either study).

A GLP multiple dose toxicity study of INZ-701 was also conducted in juvenile C57BL6 mice. The mice were given INZ-701 by subcutaneous injection every other day at doses of 5, 10, or 30 mg/kg from post-natal day 10 to post-natal day 100 and were followed for 4 additional weeks after dosing. Toxicokinetics, clinical observations, clinical chemistries, anti-drug antibodies ("ADAs"), neuro-assessment, macro and micropathology with the addition of neurohistological parameters, and reproductive endpoints were evaluated during the study. The study concluded there were no adverse findings related to INZ-701 throughout the study period at any dose level. The no-observed-adverse-effect level for the study was the highest dose tested, 30 mg/kg.

Overall, in our nonclinical toxicology studies, INZ-701 exhibited a good safety profile and an acceptable therapeutic index.

Clinical Development of INZ-701 for ENPP1 Deficiency

Phase 1/2 Clinical Trial in Adults with ENPP1 Deficiency

In November 2021, we initiated our Phase 1/2 clinical trial of INZ-701 in adult patients with ENPP1 Deficiency. The Phase 1/2 clinical trial of INZ-701 is an open-label, first-in-human, multiple ascending dose trial. The trial primarily assessed the safety and tolerability of INZ-701 in adult patients with ENPP1 Deficiency, as well as characterized the pharmacokinetic and pharmacodynamic profile of INZ-701, including evaluation of levels of plasma PPi and other biomarker levels. In the Phase 1 dose-escalation portion of the trial, we 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 per week, as well as at a dose of 1.2 mg/kg, administered via subcutaneous injection once per week, with three patients planned per dose cohort. Patients received a single dose and then began twice-weekly dosing one week later. The trial enrolled 13 patients with ENPP1 Deficiency at sites in North America and Europe. The Phase 1 dose-escalation portion of the trial sought to identify a safe and tolerable dose that increased plasma PPi levels, and that can be used for further clinical development. The Phase 1 dose-escalation portion of the trial is complete. The open-label Phase 2 extension portion of the trial assessed long-term safety, pharmacokinetics, and pharmacodynamics of continued treatment with INZ-701 for up to 48 weeks, where patients received doses of INZ-701 at home depending on site-specific protocols. Exploratory endpoints include evaluations of ectopic calcification, skeletal, vascular, and physical function, patient-reported outcomes and exploratory biomarkers. Exploratory biomarker data were collected to provide evidence of the potential for disease modification with ongoing treatment with INZ-701. Notable changes in patient reported outcomes and functional outcomes were observed in all cohorts, including concordant improvement in global impression of change scores reported by patients (“P-GIC”) and clinicians (“C-GIC”), and no patient showed a deterioration from baseline.

In February 2023, we reported interim pharmacokinetic, pharmacodynamic, and safety data from this trial. A rapid, significant, and sustained increase in plasma PPi was observed in all dose cohorts and in all patients, with a target plasma PPi threshold observed from the lowest dose of 0.2 mg/kg. Plasma PPi increased in all patients to levels comparable to those observed in our study of healthy subjects (n=10) (1002 nM to 2169 nM). The mean baseline plasma PPi across all three cohorts in the trial was 426±407 nM.

In September 2023, we reported positive interim safety, pharmacokinetic, pharmacodynamic, and exploratory efficacy data from this trial. A rapid, significant, and sustained increase in plasma PPi was observed in all dose cohorts and in all patients, and a significant elevation in plasma PPi was maintained for up to 18 months. INZ-701 activity increased in proportion to dose level and a 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. Exploratory biomarker data were collected to provide evidence of the potential for disease modification with ongoing treatment with INZ-701. Notable changes in key biomarkers support our clinical hypothesis. Clinical outcome measures were also collected to assess potential clinical benefit with ongoing treatment with INZ-701 and to inform the design and patient selection of future trials. Notable changes in patient reported outcomes and functional outcomes were observed in all cohorts, including concordant improvement in GIC scores reported by patients and clinicians, and no patient showed a deterioration from baseline. 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. Three of the nine patients experienced mild adverse events related to INZ-701 including injection site reactions (bruising or pain) occurring in two of nine patients, and other mild adverse events including decreased appetite and fatigue. There were two serious adverse events not related to INZ-701. INZ-701 exhibited a favorable immunogenicity profile with low titers of non-neutralizing ADAs observed in seven of the nine patients. All nine patients

enrolled in the Phase 2 portion of the trial, and two of them subsequently withdrew for personal reasons not related to adverse events. The ADA levels were transient in three of seven patients.

In the fourth quarter of 2023, we dosed two patients in a fourth cohort at 1.2 mg/kg to investigate the potential for once weekly dosing of INZ-701 in the ongoing trial. We completed enrollment of this fourth cohort in the fourth quarter of 2023. Data from the once-weekly dose cohort showed a sustained increase in plasma PPi levels comparable to those observed in our study of healthy subjects (n=10).

In April 2024, we reported positive topline safety, pharmacokinetic, pharmacodynamic, and exploratory efficacy data from this trial. Notable changes from baseline in key biomarkers were observed and support our clinical hypothesis. Significant reductions of fibroblast growth factor-23, increases in bone specific alkaline phosphatase levels, and decreases in c-telopeptide were observed in the 1.8 mg/kg dose cohort (Cohort 3) through week 48, which indicates the restoration of proper bone mineralization. Favorable responses on the Patient-Reported Outcome Measurement Information Scales of Pain Intensity, Fatigue and Pain Interference, and P-GIC were maintained. INZ-701 was generally well-tolerated and exhibited a favorable safety profile, with no serious or severe adverse events ("AEs") attributed to INZ-701 and no AEs leading to study withdrawal. Time on study ranged from 22 to over 742 days. Total time on treatment across all dose cohorts corresponds to approximately 12+ patient-years. INZ-701 exhibited a favorable immunogenicity profile with low titers of ADAs not impacting drug exposure observed in 10 of 13 patients. The ADA levels were transient in three of 10 patients. Plasma PPi levels observed after INZ-701 administration are shown in the table below:

			Mean Plasma PPi (nM) ± SEM		
			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±87	1438±146	1220±87
	2x/Week Dose	**Day 11-32**	1494±111	1745±170	1352±71
Phase 2	**2x/Week Dose**	**Day 32-672**	1118±93	1316±116	1598±322

Cohort 1 n=2 post day 84; Cohort 2 n=2 post day 336; Cohort 3 n=2 post day 252

The last patient's last visit occurred in the fourth quarter of 2024. All patients completing the extension phase are enrolled in our ongoing open label long term safety trial of INZ-701 in patients with ENPP1 or ABCC6 Deficiencies who have received INZ-701 in an existing trial ("ADAPT").

ENERGY 1 Clinical Trial in Infants with ENPP1 Deficiency and ABCC6 Deficiency and Expanded Access Program

In June 2023, we dosed the first infant patient in our Phase 1b, single arm, open-label clinical trial of INZ-701 (the "ENERGY 1 trial"), designed primarily to assess the safety, tolerability, pharmacokinetics, and pharmacodynamics of INZ-701 in infants with ENPP1 Deficiency and ABCC6 Deficiency. The ENERGY 1 study design was amended in the second quarter of 2024 to allow enrollment of infants with ABCC6 Deficiency and to increase the maximum number of patients. The ENERGY 1 trial is expected to enroll up to 16 infants between the ages of birth and 12 months across multiple sites in the United States and Europe. Patients will receive subcutaneous doses of INZ-701 during the treatment period of 52 weeks and may continue to receive INZ-701 in an extension period beyond 52 weeks. Doses range from 0.2 mg/kg once weekly through 2.4 mg/kg once weekly, with the ability to modify the dose depending on the results of pharmacokinetics, pharmacodynamics, and safety data. Other outcome measures include evaluation of plasma PPi levels, survival, growth, development, functional performance, cardiac function, and exploratory biomarkers.

Interim data from the ENERGY 1 trial (reporting data from three infants) and our expanded access program ("EAP") (reporting data from two infants and one child (2.5 years old)) evaluated patients with 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 (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 new safety signals observed. Anti-drug antibodies (ADA) impacting pharmacokinetics (PK) and pharmacodynamics (PD) were only seen in three infants and were not seen in any patient initiating treatment after 1 year of age. Where measured, PPi and drug levels were substantially elevated post-dose in these infants, consistent with the clinical effects observed. ADA were not associated with adverse events in any patient.

Global Development Strategy of INZ-701 for the Treatment of ENPP1 Deficiency

We initiated pivotal trial meetings with the FDA in the first quarter of 2023. In July 2023, we announced a regulatory update for our global development strategy of INZ-701 for the treatment of ENPP1 Deficiency following meetings with the FDA and the Paediatric Committee of the EMA ("PDCO"). Also in July 2023, we completed a scientific advice procedure and reached alignment with the Committee for Medicinal Products for Human Use ("CHMP") regarding our global development strategy.

We plan to conduct pivotal clinical trials of INZ-701 designed to support registration in infant, pediatric, and adult patient populations with ENPP1 Deficiency. Many companies pursuing marketing approval for enzyme replacement therapies in rare diseases have followed a similar clinical development strategy.

In the fourth quarter of 2024, we opened the first site for the ENERGY 2 trial, an open label, single arm, pivotal trial of INZ-701 in infants with ENPP1 Deficiency, outside of the United States and patient recruitment is underway. 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.

We have reached agreement with the PDCO on a Paediatric Investigational Plan for a pivotal trial of INZ-701 in pediatric patients with ENPP1 Deficiency. In September 2023, we opened the first site for the ENERGY 3 trial, a multicenter, randomized, open label trial, and in January 2025 completed enrollment with 27 patients between the ages of one and less than 13 years across sites globally. The trial is designed primarily to assess the efficacy and safety of INZ-701 in pediatric patients with ENPP1 Deficiency. Enrollment criteria for the trial includes 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 (which uses the conventional therapies, of 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 injection.

The ENERGY 3 trial is a single, multicenter, clinical trial with differences in the statistical treatment of endpoints, based on guidance from the FDA and CHMP. In the United States, the primary endpoint is change in plasma PPi from baseline, and the secondary endpoints are Radiographic Global Impression of Change ("RGI-C") score, Rickets Severity Score, Growth Z-score and pharmacokinetics. Based on recommendations from the FDA, the primary endpoint of change in plasma PPi should be supported by consistent trends in appropriate secondary endpoints and adequate overall scientific justification that plasma PPi is a clinically meaningful biomarker in patients with ENPP1 Deficiency. Based on the agreed Paediatric Investigational Plan with PDCO and CHMP advice, plasma PPi and RGI-C are co-primary endpoints in Europe, with a relaxed p-value of <0.2 for RGI-C. With 27 patients enrolled, the trial's 2:1 randomized design provides over 90% power to detect meaningful differences in RGI-C between the treatment and control groups.

In September 2023, we opened the first site for the ENERGY 3 trial. We completed enrollment in January 2025. We anticipate reporting topline data from the ENERGY 3 trial in the first quarter of 2026. Pending appropriate financial resources, we may conduct additional clinical trials of INZ-701 in adolescents and adults with ENPP1 Deficiency.

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 our submission of marketing applications in both the United States and the European Union. These data will include final results from our Phase 1/2 clinical trial in adult patients with ENPP1 Deficiency, available results from our ongoing ENERGY 1 trial, available results from the ongoing pivotal ENERGY 2 trial in infants which we are conducting outside of the United States, and final results from the ongoing pivotal ENERGY 3 trial in pediatric patients.

If these marketing applications are approved, we expect to commercially launch INZ-701 for infant and pediatric patients as early as the first half of 2027.

Clinical Development of INZ-701 for ABCC6 Deficiency

In April 2022, we initiated our Phase 1/2 clinical trial of INZ-701 in adult patients with ABCC6 Deficiency. The Phase 1/2 clinical trial of INZ-701 is an open-label multiple ascending dose trial, which enrolled 10 adult patients at sites in the United States and Europe. The trial primarily assessed the safety and tolerability of INZ-701 in adult patients with ABCC6 Deficiency, as well as characterized the pharmacokinetic and pharmacodynamic profile of INZ-701, including the evaluation of levels of plasma PPi and other biomarker levels. In the Phase 1 dose-escalation portion of the clinical trial, we 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, which doses were selected based on preclinical studies and pharmacokinetic/pharmacodynamic modeling. Patients received a single dose and then began twice-weekly dosing one week later. The Phase 1 dose-escalation portion of the trial sought to identify a safe and tolerable dose that increased plasma PPi levels for further clinical development. The open-label Phase 2 extension portion of the trial assessed long-term safety, pharmacokinetics, and pharmacodynamics of continued treatment with INZ-701 for up to 48 weeks, where patients received doses of INZ-701 at home depending on site-specific protocols. Exploratory endpoints included evaluations of ectopic calcification, vascular and retinal function, patient reported outcomes, and exploratory biomarkers.

Beginning in January 2023, self-administration of INZ-701 in the open-label Phase 2 extension portion of the trial was available.

In February 2023, we reported interim pharmacokinetic, pharmacodynamic, and safety data from this trial. A rapid, significant, and sustained increase in plasma PPi was observed in all cohorts with a dose response observed. Plasma PPi showed sustained increase in the highest dose cohort to levels comparable to those observed in our study of healthy subjects (n=10) (1002 nM to 2169 nM). Mean baseline plasma PPi across all three cohorts in the trial was 947±193 nM.

In September 2023, we reported positive interim safety, pharmacokinetic, pharmacodynamic, and exploratory efficacy data from this trial. A dose-dependent response in plasma PPi levels was observed, with a sustained increase in the highest dose cohort to levels comparable to those observed in our study of healthy subjects. INZ-701 activity in a greater-than-dose proportional manner was observed, and drug accumulation as shown by a greater-than-dose proportional exposure suggests the potential for once weekly dosing. Clinical outcome measures were collected to provide evidence of clinical benefit and to inform the design of future trials in adults. All patients showed improvements on clinician-reported GIC scores and seven of the nine patients showed improvement from baseline on patient-reported GIC scores at the last follow-up. INZ-701 was generally well-tolerated and exhibited a favorable safety profile, with no serious or severe adverse events attributed to INZ-701. Seven of the 10 patients experienced adverse events related to INZ-701 (including mild injection site reactions (discoloration, erythema, induration, pain, or pruritus) occurring in seven of the 10 patients and other adverse events included erythema, fatigue, night sweats, and urticaria). All adverse events were mild to moderate in severity. One patient from the highest dose cohort (1.8 mg/kg) was withdrawn from the Phase 1 portion of the trial at day 18 due to a moderate adverse event (erythema/urticaria) related to INZ-701. One patient withdrew from the trial during the Phase 2 portion for personal reasons not related to an adverse event. INZ-701 exhibited a favorable immunogenicity profile with low titers of non-neutralizing ADAs observed in eight of the 10 patients. The ADA levels were transient in three out of eight patients.

In April 2024, we reported positive topline safety, pharmacokinetic, pharmacodynamic, and exploratory efficacy data from this trial. Exploratory markers of clinical benefit were collected throughout the trial to provide evidence of the potential for disease modification with ongoing INZ-701 treatment. Reduction or stabilization of carotid intima-media thickness was observed across all dose cohorts (seven of eight evaluable patients), indicating a potential beneficial effect of INZ-701 on vascular pathology. Increased choroidal thickness was observed across all dose cohorts (seven of eight evaluable patients), which indicated a potential beneficial effect of INZ-701 on retinal disease. Four of six evaluable patients with Global Visual Function Questionnaire ("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. 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. The rapid increase in plasma PPi levels observed at the 1.8 mg/kg dose level (Cohort 3) was sustained to levels comparable to those observed in our study of healthy subjects (n=10). INZ-701 was generally well tolerated and exhibited a favorable safety profile, with no serious or severe AEs. All AEs were mild to moderate in severity. Time on study ranged from 45 to over 631 days, and total time on treatment across all cohorts corresponds to approximately 12+ patient-years. INZ-701 exhibited a favorable immunogenicity profile with low titers of ADAs not impacting drug exposure observed in eight of 10 patients. The ADA levels were transient in three of eight patients. Plasma PPi levels observed after INZ-701 administration are shown in the table below:

			Mean Plasma PPi (nM) ± SEM		
			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±162	1326±67	1540±169
	2x/Week Dose	**Day 11-32**	1023±99	1119±48	1312±122
Phase 2	**2x/Week Dose**	**Day 32-588**	1018±73	931±87	1613±188

Cohort 1 n=2 post day 504; Cohort 2 n=3; Cohort 3 n=2 post day 84

The last patient's last visit occurred in July 2024. All patients completing the extension phase have rolled over to the ADAPT trial.

As part of our recent strategic review, we are prioritizing activities to support the planned BLA filing for INZ-701 for our lead indication, ENPP1 Deficiency. Patients with ABCC6 Deficiency being treated in our ADAPT long-term extension study, our expanded access program, or under investigator-sponsored INDs will continue to receive treatment. Any future trials in ABCC6 Deficiency will be postponed.

Clinical Development of INZ-701 for Calciphylaxis

In February 2024, we initiated SEAPORT 1, a Phase 1 clinical trial designed to assess safety, tolerability, pharmacokinetics, and pharmacodynamics of INZ-701 in patients with ESKD receiving hemodialysis. Patients received 1.8 mg/kg of INZ-701 once weekly coinciding with their hemodialysis treatment for a total of 30 days. The trial's primary endpoint assessed safety and change from baseline plasma PPi concentration, with secondary endpoints including pharmacokinetic and pharmacodynamic parameters. In June 2024, SEAPORT 1 was fully enrolled.

In October 2024, we announced positive interim data from SEAPORT 1. The interim data demonstrated that INZ-701 significantly increased PPi levels in ESKD patients receiving hemodialysis, with levels rising into the normal range by week three of the trial's four-week dosing schedule. The largest changes occurred in patients with the lowest baseline PPi levels.

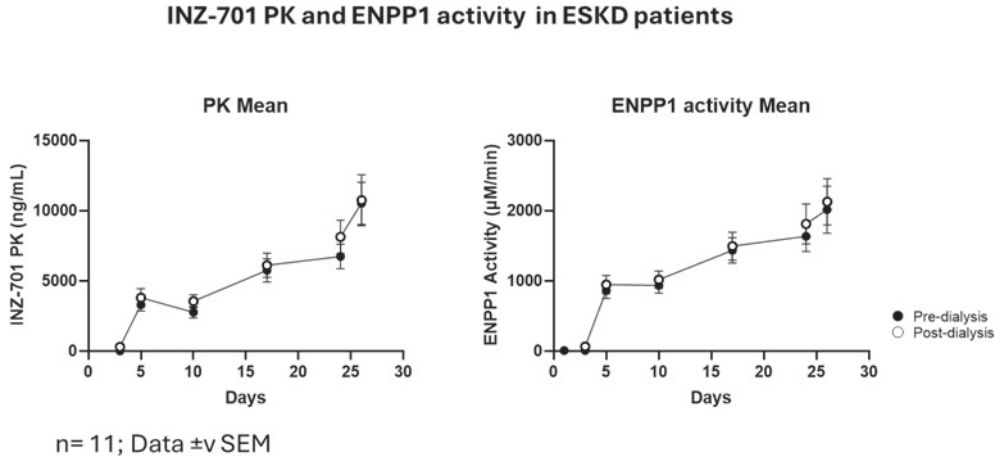
Timepoint	Mean PPi (nM) ± SEM (n=9)
Baseline-Day 3 pre-dose*	668±78
Day 10 pre-dose	876±231
Day 17 pre-dose	1270±240
Day 24 pre-dose	1582±240

*Baseline consists of three timepoints collected prior to the initiation of dosing

A prior study of healthy subjects (n=10) showed PPi levels between 1002 nM and 2169 nM.

The interim data demonstrated that INZ-701 also led to reductions in biomarkers of mineral metabolism, including serum phosphate and fibroblast growth factor-23, which are implicated in the pathogenesis of vascular calcification in ESKD. These findings suggest INZ-701 may mitigate the risk of pathologic calcification in these patients.

The interim data further demonstrated that INZ-701 was generally well-tolerated and exhibited a favorable safety profile, with no drug-related treatment-emergent adverse events ("TEAEs") reported in the 11 patients who completed the four-week treatment period. All observed TEAEs were mild to moderate in severity except for one case of hyperkalemia requiring urgent dialysis. Consistent drug exposure to INZ-701 was observed with 1.8 mg/kg weekly dosing and pharmacokinetic profiles were consistent with our prior studies in non-hemodialysis patients. We believe these results suggest consistent drug pharmacokinetic profiles can be maintained in dialysis patients, providing further confidence in dose selection for future trials.



Finally, low titers of ADAs were detected in three of 11 patients at the end-of-study timepoint, approximately 30 days after the last dose. Two of these patients became ADA-negative by day 60 after the last dose. The presence of ADAs was not associated with any AEs.

We plan to present additional follow-up data, including characterization of genetic markers associated with PPi and adenosine metabolism, at a later date.

As part of our recent strategic review, we are prioritizing activities to support the planned BLA filing for INZ-701 for our lead indication, ENPP1 Deficiency. Patients with ABCC6 Deficiency being treated in our ADAPT long-term extension study, our expanded access program, or under investigator-sponsored INDs will continue to receive treatment. Future trials in calciphylaxis will be postponed.

ADAPT Long-Term Safety Study in Patients with ENPP1 and ABCC6 Deficiencies

In June 2024, we initiated ADAPT, a multicenter, open-label, long-term safety trial of INZ-701 in patients with ENPP1 Deficiency or ABCC6 Deficiency who have received INZ-701 in an existing clinical trial and choose to continue dosing with INZ-701. Patients are eligible if they have completed the protocol-required safety and pharmacokinetic and pharmacodynamic and/or efficacy period(s) of a previous trial with INZ-701. Adult patients will receive once weekly subcutaneous doses of 1.8 mg/kg or a once weekly fixed dose of 150 mg; pediatric patients will receive once weekly subcutaneous doses of 2.4 mg/kg. Other outcome measures include evaluation of pharmacokinetic parameters and plasma PPi with long-term INZ-701 treatment. The ADAPT trial enrolled patients who have completed a Phase 1/2 trial in adults with ENPP1 and ABCC6 Deficiencies at the end of the fourth quarter of 2024.

Expanded Access Program

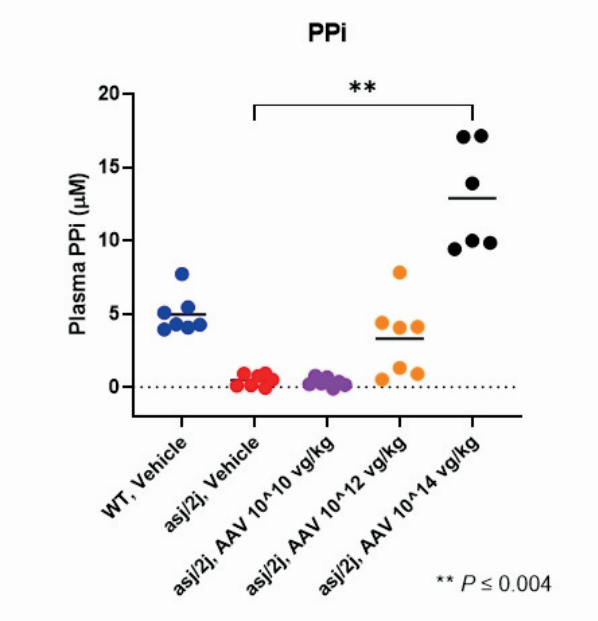
In February 2023, we dosed our first pediatric patient with ENPP1 Deficiency with INZ-701 under our expanded access program. Under this program, we can use INZ-701 outside of our clinical trials to treat patients with serious or immediately life-threatening diseases or conditions when there are no comparable or satisfactory alternative treatment options and when other criteria are met. Other criteria include, but are not limited to, lack of success from standard treatments, ineligibility for participation in any ongoing clinical trial of INZ-701 (including lack of access due to geographic limitations), and having a disease for which there is sufficient evidence of a projected benefit from the use of INZ-701. We expect that data collected from patients treated under our expanded access program will provide further support for the potential safety and clinical benefits of INZ-701.

ENPP1 Gene Therapy

Our future plans include developing new and innovative therapies to treat ENPP1 Deficiency. We believe we are well-positioned to do so because of our in-depth knowledge of the PPi-Adenosine Pathway. For example, we have identified a gene therapy construct having an optimized ENPP1-Fc sequence driven by a tissue specific promoter in our enzyme replacement therapy program that has shown restoration and sustained enzyme activity leading to an increase of plasma PPi levels in preclinical experiments without adverse effects. Our results to date encourage us to continue to optimize our gene therapy construct as a potential new modality to treat diseases of the PPi-Adenosine Pathway impacting the vasculature, soft tissue and skeleton, in furtherance of our mission to become leaders in the treatment of such diseases.

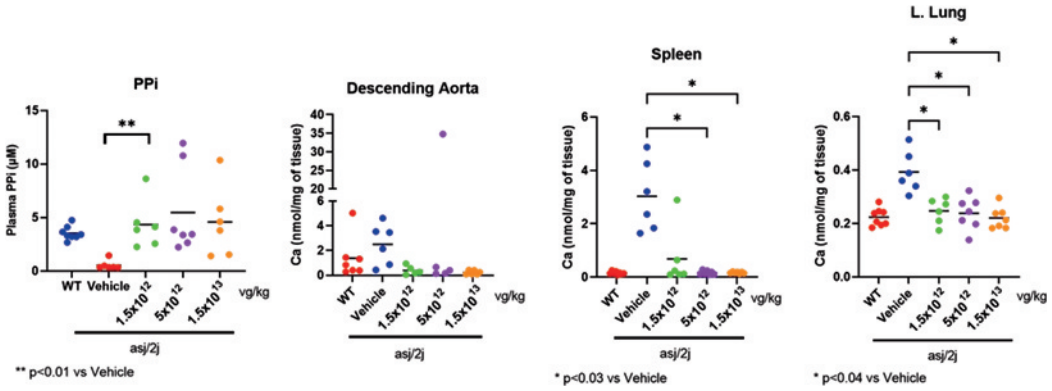
Treatment of asj/2j mice with, ENPP1 Deficiency with an AAV vector containing a modified ENPP1-Fc driven by a tissue specific promoter at three different doses by a single intravenous injection for a period of ten weeks led to a dose dependent increase in PPi levels. Mice treated with vehicle control lacked any plasma PPi, as expected.

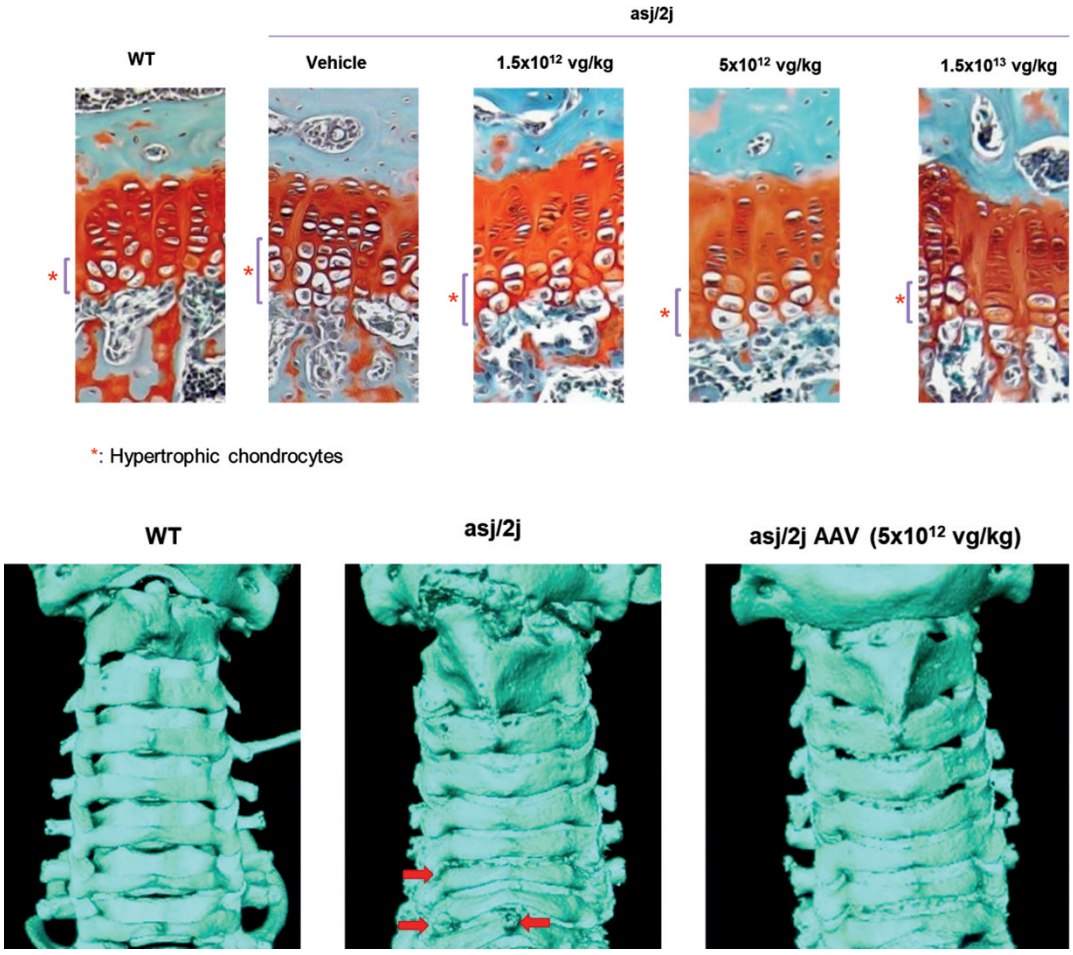
The results of this initial study are shown in the graph below:



In another study in asj/2j mice, we evaluated lower doses of an AAV vector containing a modified ENPP1-Fc driven by a tissue specific promoter at three different doses by a single intravenous injection for a period of ten weeks. These studies demonstrated increases in plasma PPi with corresponding prevention of calcification in various tissues, including the aorta, spleen and lung, as well as prevention of skeletal abnormalities such as rickets in the growth plate and ectopic calcification in the vertebrae as shown in the figures below. The vertebral phenotype in the asj/2j mice has similarities to OPLL where it is observed in ENPP1 deficient patients that have biallelic and monoallelic variants. These studies suggested that gene therapy is a potential therapeutic modality for ENPP1 Deficiency.

The results of this study are shown below:





Manufacturing and Supply

While we have personnel with substantial manufacturing experience, we do not own or operate, and currently have no plans to establish, any manufacturing facilities. We rely, and expect to continue to rely, on third parties for the manufacture of both drug substance and finished drug product for INZ-701 and any future product candidates for preclinical testing and clinical trials, as well as for commercial manufacture if any of our product candidates receive marketing approval. We also rely on these third parties for packaging, labeling, sterilization, storage, distribution and other production logistics. We have only limited supply agreements in place with respect to our product candidates, and these arrangements do not extend to commercial supply. We obtain supplies of drug substance and finished drug product for INZ-701 on a purchase order basis. We do not have long-term committed arrangements with respect to any of our product candidates or other materials.

Manufacturing biologics is complex, especially in large quantities. Biologic products must be made consistently and in compliance with a clearly defined manufacturing process. We have obtained from our third-party manufacturers a supply of INZ-701 that we believe is sufficient for our ongoing clinical trials of INZ-701 for ENPP1 Deficiency. However, we are continuing the process of scaling up our manufacturing processes and capabilities with our third-party manufacturers to support longer term clinical development. In addition, if we receive marketing approval for any of our product candidates, we will need to establish an agreement for commercial manufacture with a third party. If any of our current contract manufacturers cannot perform as agreed, we may be required to replace such manufacturers. Although we believe that there are several potential alternative manufacturers who could manufacture our product candidates, we may incur added costs and delays in identifying and qualifying any such replacement or be unable to reach agreement with an alternative manufacturer.

Commercialization

We retain worldwide exclusive development and commercialization rights to our pipeline and programs, including INZ-701. At this stage, we have not yet established our own commercial organization or distribution capabilities. We believe that we will be able to commercialize INZ-701, if approved, for ENPP1 Deficiency with a small, targeted, internal sales and commercial organization in the United States and other major markets. We may explore the use of a variety of types of collaboration, co-

promotion, distribution and other marketing arrangements with one or more third parties to commercialize our product candidates in smaller markets outside the United States or for other situations in which a larger sales and marketing organization is required.

We intend to continue to engage with patient advocacy groups, medical centers of excellence, and medical specialists in an effort to expeditiously bring our therapy to patients.

Competition

The pharmaceutical and biotechnology industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. While we believe that our technology, expertise, scientific knowledge and intellectual property provide us with competitive advantages, we face and will continue to face competition from many different sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions, governmental agencies and public and private research organizations that conduct research, seek patent protection, and establish collaborative arrangements for research, development, manufacturing, and commercialization. Any product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future. Moreover, our industry is characterized by the existence of large numbers of patents and frequent allegations of patent infringement.

The key competitive factors affecting the success of our product candidates, if approved, are likely to be their efficacy, safety, convenience and price, the level of competition and the availability of coverage and adequate reimbursement from third-party payors. If any of our product candidates are approved and successfully commercialized, it is likely that we will face increased competition as a result of other companies pursuing development of products to address similar diseases.

There are currently no approved therapies for the treatment of ENPP1 Deficiency. Currently available treatments are only seeking to minimize the manifestations of this disease. Although a number of companies generally are pursuing development of different enzyme replacement therapies or treatments for vascular calcification disorders and many other companies are focused on rare disease markets, we are not aware of any product candidate currently in clinical development for ENPP1 Deficiency. DS-1211b, a tissue-nonspecific alkaline phosphatase inhibitor, is currently in Phase 2 clinical development for PXE by Daiichi Sankyo Company.

Many of the companies against which we are competing or against which we may compete in the future have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller and other early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

We may pursue the in-license or acquisition of rights to complementary technologies and product candidates on an opportunistic basis. The acquisition and licensing of technologies and product candidates is a competitive area, and a number of more established companies also have similar strategies to in-license or acquire technologies and product candidates that we may consider attractive. These established companies may have a competitive advantage over us due to their size, cash resources, and greater development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to in-license or acquire the relevant technology or product candidate on terms that would allow us to make an appropriate return on our investment.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. In addition, our ability to compete may be affected in many cases by insurers or other third-party payors seeking to encourage the use of generic products. Because of our primary focus on rare diseases, if our product candidates achieve marketing approval, we expect to seek premium pricing.

Yale University License Agreement

In January 2017, we entered into a license agreement with Yale, which was amended in May 2020 and July 2020, pursuant to which Yale granted us (1) an exclusive, worldwide license, with specified rights to sublicense, under Yale's interest in specified intellectual property rights and materials for specified therapeutic and prophylactic products, (2) a nonexclusive, worldwide license under Yale's interest in the same intellectual property rights and materials for specified diagnostic products, and (3) a nonexclusive, worldwide license under Yale's interest in specified know-how for specified products, in each case that use any ectonucleotide pyrophosphatase/phosphodiesterase enzymes ("ENPPs"), or an agonist or antagonist of ENPP, its receptors, substrates, or ENPP enzymatic products, subject to certain exceptions. These licensed intellectual property rights, materials and know-how arose, and may in the future continue to arise, primarily from research conducted by Dr. Demetrios Braddock and members of his laboratory at Yale. During the period in which Professor Braddock serves as a member of our scientific advisory board or has another arrangement with us pursuant to which he provides regular advice to us or has an active consulting arrangement with us, and so long as he is an employee or faculty member (including emeritus faculty member) at Yale, Yale is restricted from granting any third party any rights for any therapeutic or prophylactic uses for any ENPP technology made, created, developed, discovered, conceived or first reduced to practice by or on behalf of Professor Braddock or his laboratory. Under the license agreement, we are obligated to use commercially reasonable efforts to pursue development and commercialization of specified ENPP products and licensed methods.

Pursuant to the license agreement, as partial upfront consideration, we paid to Yale approximately $0.1 million which amount reflected unreimbursed patent expenses incurred by Yale prior to the date of the license agreement. We are responsible for paying Yale an annual license maintenance fee in varying amounts throughout the term ranging from the low tens of thousands of dollars to the high tens of thousands of dollars. As of December 31, 2024, we have incurred a total of $0.5 million in license maintenance fees to Yale. We are required to pay Yale $3.0 million, based on the achievement of a specified net product sales milestone or specified development and commercialization milestones, for each therapeutic and prophylactic licensed product developed. In January 2022, we paid Yale an approximately $0.3 million milestone payment following dosing of the first patient in our Phase 1/2 clinical trial of INZ-701 in adult patients with ENPP1 Deficiency in November 2021. In March 2022, we paid Yale an approximately $0.3 million milestone payment following completion of the first cohort of our Phase 1/2 clinical trial of INZ-701 in adult patients with ENPP1 Deficiency. In March 2024, we incurred and paid a $0.5 million milestone payment following completion of dosing of the first patient in our pivotal clinical trial of INZ-701 in pediatric patients with ENPP1 Deficiency. In addition, we are required to pay Yale an amount in the several hundreds of thousands of dollars, based on the achievement of a specified net product sales milestone or specified development and commercialization milestones, for each diagnostic licensed product developed. While the agreement remains in effect, we are required to pay Yale low single-digit percentage royalties on aggregate worldwide net sales of certain licensed products, which may be subject to reductions. Yale is guaranteed a minimum royalty payment amount (ranging in dollar amounts from the mid six figures to low seven figures) for each year after the first sale of a therapeutic or prophylactic licensed product that results in net sales. Yale is guaranteed a minimum royalty payment amount (ranging from the low tens of thousands of dollars to the mid tens of thousands of dollars) for each year after the first sale of a diagnostic licensed product that results in net sales. Such minimum royalty payment amounts are summed for each year after the first sale of both a therapeutic or prophylactic licensed product and a diagnostic licensed product has occurred. We must also pay Yale a percentage in the twenties of certain types of income we receive from sublicensees. We are also responsible for costs relating to the prosecution and maintenance of the licensed patents. Finally, subject to certain conditions, all payments due by us to Yale will be tripled following any patent challenge or challenge to a claim by Yale that a product is a licensed product under the agreement made by us against Yale if Yale prevails in such challenge.

We have also agreed to pay for ENPP research support from Yale pursuant to a sponsored research agreement that we entered into with Yale in January 2017 and amended in February 2019, February 2022, May 2022, May 2023, January 2024, and December 2024. Under the sponsored research agreement, as amended, we agreed to pay Yale an aggregate of $3.4 million over nine years, ending in December 2025. The research was performed by and under the supervision and direction of Professor Braddock.

The license agreement remains in effect until the latest of, on a country-by-country basis, (a) the date on which the last claim of the licensed patents in such country expires; (b) 10 years after the last licensed know-how, licensed materials or licensed methods have been provided to us by Yale; and (c) 10 years after the first sale of a specified ENPP product; but in no event later than the date that is 30 years after the effective date of the agreement. We may terminate the agreement for Yale's uncured material breach of the agreement, we may terminate the agreement for convenience upon six months' prior notice, and Yale may terminate the agreement for our uncured material breach of certain provisions or if we fail to make a payment when due, fail to obtain or maintain adequate insurance coverage or fail to engage in specified development and regulatory activities. The agreement will automatically terminate if we become insolvent or the subject of a bankruptcy event. Upon termination for any reason other than Yale's breach of the agreement, in certain circumstances, Yale is permitted to use all regulatory approvals of, or clinical trials or other studies conducted by or on behalf of us on, and all filings made by or on behalf of us with regulatory agencies with respect to, certain licensed technology.

Alexion Intellectual Property Asset Acquisition

In July 2020, we entered into an intellectual property asset purchase agreement with Alexion pursuant to which Alexion sold and assigned to us Alexion's right, title and interest in and to specified patent rights and other specified assets solely related to ENPP1. We issued 8,294,360 shares of our Series A-2 Convertible Preferred Stock to Alexion in consideration for the sale and assignment to us of such assets, which shares of preferred stock converted into 1,109,910 shares of our common stock in connection with our IPO. Under the intellectual property asset purchase agreement, we also granted a non-exclusive license to Alexion and its affiliates to continue to use the assets we acquired for Alexion's and its affiliates' internal, non-clinical research purposes. In addition, subject to certain specified qualifications set forth in the intellectual property assets purchase agreement, Alexion is obligated to assign to us its rights with respect to any other assets owned by it that are solely related to ENPP1.

Intellectual Property

We strive to protect and enhance the proprietary technology, inventions and improvements that are commercially important to the development of our business, including by seeking, maintaining and defending patent rights, whether developed internally or licensed from third parties. We also rely on trade secrets, know-how, continuing technological innovation and in-licensing opportunities to develop, strengthen and maintain our proprietary position in our field. Additionally, we intend to rely on regulatory protection afforded through rare drug designations, data exclusivity and market exclusivity as well as patent term extensions, where available.

Our future commercial success depends, in part, on our ability to: obtain, maintain and enforce patent and other proprietary protection in the United States and other countries for commercially important technology, inventions and know-how related to our business; defend and enforce in our intellectual property rights, in particular our patents rights; preserve the confidentiality of our trade secrets; and operate without infringing, misappropriating or violating the valid and enforceable patents and proprietary rights of third parties. Our ability to stop third parties from making, using, selling, offering to sell or importing our products may depend on the extent to which we have rights under valid and enforceable patents or trade secrets that cover these activities.

The patent positions of pharmaceutical and biotechnology companies like ours are generally uncertain and can involve complex legal, scientific and factual issues. We cannot predict whether the patent applications we are currently pursuing will issue as patents in any particular jurisdiction or whether the claims of any issued patents will provide sufficient proprietary protection from competitors. We also cannot ensure that patents will issue with respect to any patent applications that we or our licensors may file in the future, nor can we ensure that any of our owned or licensed patents or future patents will be commercially useful in protecting our product candidates and methods of manufacturing the same. In addition, the coverage claimed in a patent application may be significantly reduced before a patent is issued, and its scope can be reinterpreted and even challenged after issuance. As a result, we cannot guarantee that any of our products will be protected or remain protectable by enforceable patents. Moreover, any patents that we hold may be challenged, circumvented or invalidated by third parties. See "Risk Factors—Risks Related to Our Intellectual Property" for a more comprehensive description of risks related to our intellectual property.

We generally file patent applications directed to our key programs in an effort to secure our intellectual property positions with respect to these programs. As of March 10, 2025, we owned or possessed exclusive rights to 25 issued U.S. patents, three pending U.S. provisional patent applications, 18 pending U.S. non-provisional patent applications, 36 issued foreign patents (including seven issued European patents), 180 pending foreign patent applications, and one pending Patent Cooperation Treaty application.

In addition, as of March 10, 2025, we owned two allowed U.S. trademark applications, one pending foreign trademark application, and 13 foreign registered trademarks.

INZ-701

The intellectual property portfolio for INZ-701, our most advanced program, as of March 10, 2025, is summarized below. Prosecution is a lengthy process, during which the scope of the claims initially submitted for examination by the U.S. Patent and Trademark Office may be significantly narrowed before issuance, if issued at all. We expect this may be the case with respect to some of our pending patent applications referred to below.

Currently, our patent protection includes patents and patent applications that we have exclusively licensed under our license agreement with Yale. This licensed patent portfolio includes:

- A patent family that includes seven issued U.S. patents relating to: (1) reducing and/or preventing progression of pathologic calcification, (2) reducing or preventing ectopic calcification of soft tissue, (3) reducing or preventing pathologic ossification, (4) treating, reversing or preventing progression of ossification of the posterior longitudinal ligament, (5) treating aging-related hardening of arteries (6) reducing or preventing progression of chronic kidney disease, end-stage renal disease, calcific uremic arteriolopathy, and calciphylaxis, and (7) reducing pathologic calcification of vascular tissue in a human subject in need thereof having reduced ENPP1 activity or a loss of function mutation in the gene encoding ENPP1. All such methods of treatment involve administration of soluble ENPP1 that lacks a bone targeting domain. These U.S. patents are expected to expire in 2034, absent any term adjustments or extensions. Corresponding foreign applications have been filed and are pending in Europe, and Japan. One patent has been granted in each of Europe and Hong Kong; three patents have been granted in Japan.

- A patent family that includes two issued U.S. patents covering certain compositions that contain ENPP1, including INZ-701. This U.S. patent is expected to expire in 2036, absent any term adjustments or extensions. Corresponding foreign applications have been filed and are pending in Europe, Japan, Australia, Canada, Brazil, South Korea, Mexico, New Zealand, and Russia. One patent has been granted in each Australia, Europe, Hong Kong, India, Mexico, and Russia; two patents have been granted in Japan.

Other

Through our acquisition of intellectual property assets from Alexion, we have acquired, among other assets:

- A patent family that includes one issued European patent relating to polypeptides comprising ENPP1 and the therapeutic use of such polypeptides, such as in the treatment of generalized arterial calcification of infancy. This European patent is expected to expire in 2031, absent any term adjustments or extensions.

- A patent family that includes two issued U.S. patents relating to compositions and fusion proteins comprising ENPP1 and a targeting moiety. These U.S. patents are expected to expire in 2031, absent any term adjustments or extensions.

- A patent family that includes one U.S. reissue patent and one European granted patent relate to the therapeutic use of ENPP1 to treat PXE. The U.S. patent is expected to expire in 2035, absent any term adjustments or extensions, and the European patent is expected to expire in 2035. Corresponding foreign applications are pending in Brazil, Canada, Europe, Japan, S. Korea, Russia and Mexico.

The term of individual patents depends upon the legal term of the patents in the countries in which they are obtained. In most countries in which we file, the patent term is 20 years from the earliest date of filing a non-provisional patent application.

In the United States, the term of a patent covering an FDA-approved drug may, in certain cases, be eligible for a patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984 as compensation for the loss of patent term during the FDA regulatory review process. The period of extension may be up to five years, but cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval. Only one patent relating to an approved drug may be extended among those patents eligible for an extension and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended. Similar provisions are available in Europe and in certain other jurisdictions to extend the term of a patent that covers an approved drug. It is possible that issued U.S. patents covering the use of INZ-701 and products from our intellectual property may be entitled to patent term extensions. If our use of product candidates or the product candidate itself receives FDA approval, we intend to apply for patent term extension, if available, to extend the patent term that covers the approved use or product candidate. We also intend to seek patent term extensions in any jurisdictions where available, however, there is no guarantee that the applicable authorities, including the FDA, will agree with our assessment of whether such extensions should be granted, and even if granted, the length of such extensions.

In addition to patent protection, we rely upon unpatented trade secrets and confidential know-how and continuing technological innovation to develop and maintain our competitive position. However, trade secrets and confidential know-how are difficult to protect. We seek to protect our proprietary information, in part, using confidentiality agreements with any collaborators, scientific advisors, employees and consultants and invention assignment agreements with our employees. We also have agreements requiring assignment of inventions with selected consultants, scientific advisors and collaborators. These agreements may not provide meaningful protection. These agreements may also be breached, and we may not have an adequate remedy for any such breach. In addition, our trade secrets and confidential know-how may become known or be independently developed by a third party, or misused by any collaborator to whom we disclose such information. Despite any measures taken to protect our intellectual property, unauthorized parties may attempt to copy aspects of our products or to obtain or use information that we regard as proprietary. Although we take steps to protect our proprietary information, third parties may independently develop the same or similar proprietary information or may otherwise gain access to our proprietary information. As a result, we may be unable to meaningfully protect our

trade secrets and proprietary information. See “Risk Factors—Risks Related to our Intellectual Property” for a more comprehensive description of risks related to our intellectual property.

Government Regulation

Government authorities in the United States, at the federal, state and local level, and in other countries and jurisdictions, including the European Union ("EU"), extensively regulate, among other things, the research, development, testing, manufacture, pricing, reimbursement, sales, quality control, approval, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, post-approval monitoring and reporting, and import and export of pharmaceutical products, including biological products. The processes for obtaining marketing approvals in the United States and in foreign countries and jurisdictions, along with subsequent compliance with applicable statutes and regulations and other regulatory authorities, require the expenditure of substantial time and financial resources and may have a significant impact on our business.

Licensure and Regulation of Biologics in the United States

In the United States, our product candidates are regulated as biological products, or biologics, under the Public Health Service Act ("PHSA") and the Federal Food, Drug and Cosmetic Act ("FDCA") and its implementing regulations and guidance. A company, institution, or organization which takes responsibility for the initiation and management of a clinical development program for such products, and for their regulatory approval, is typically referred to as a sponsor. The failure of a sponsor to comply with the applicable U.S. requirements at any time during the product development process, including preclinical testing, clinical testing, the approval process, or post-approval process, may subject a sponsor to delays in the conduct of the study, regulatory review, and approval, and/or administrative or judicial sanctions.

A sponsor seeking approval to market and distribute a new biologic in the United States generally must satisfactorily complete each of the following steps:

- preclinical laboratory tests, animal studies, and formulation studies all performed in accordance with the FDA’s GLP regulations and standards and other applicable regulations;
- completion of the manufacture, under current Good Manufacturing Practices ("cGMP") conditions, of the drug substance and drug product that the sponsor intends to use in human clinical trials along with required analytical and stability testing;
- design of clinical protocol and submission to the FDA of an IND application for human clinical testing, which must become effective before human clinical trials may begin;
- approval by an independent institutional review board ("IRB") representing each clinical site before each clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trials to establish the safety, potency, and purity of the product candidate for each proposed indication, in accordance with current Good Clinical Practices ("GCP");
- preparation and submission to the FDA of a BLA for a biologic product requesting marketing for one or more proposed indications, including submission of detailed information on the manufacture and composition of the product in clinical development and proposed labelling;
- review of the product by an FDA advisory committee, where appropriate or if applicable;
- satisfactory completion of one or more FDA inspections of the manufacturing facility or facilities, including those of third parties, at which the product, or components thereof, are produced to assess compliance with cGMP requirements and to assure that the chemistry, methods, and controls ("CMC") are adequate to preserve the product’s identity, strength, quality, and purity;
- satisfactory completion of any FDA audits of the preclinical studies and clinical trial sites to assure compliance with GLP, as applicable, and GCP, and the integrity of clinical data in support of the BLA;
- payment of user application and program fees pursuant to the Prescription Drug User Free Act ("PDUFA");
- FDA review and approval of a BLA licensing a biologic product for marketing for particular indications in the U.S.; and

- compliance with any post-approval requirements, including the potential requirement to implement a Risk Evaluation and Mitigation Strategy ("REMS"), and any post-approval studies or other post-marketing commitments required by the FDA.

Preclinical Studies

Before testing any biologic product candidate in humans, the product candidate must undergo preclinical testing. Preclinical tests include laboratory evaluations of product chemistry, formulation and stability, as well as studies to evaluate the potential for efficacy and toxicity in animal studies. These studies are generally referred to as IND-enabling studies. The conduct of the preclinical tests and formulation of the compounds for testing must comply with federal regulations and requirements, including GLP regulations and standards and the U.S. Department of Agriculture's Animal Welfare Act, if applicable. The results of the preclinical tests, together with manufacturing information and analytical data, are submitted to the FDA as part of an IND application. Some long-term preclinical testing, such as animal tests of reproductive adverse events and carcinogenicity, and long-term toxicity studies, may continue after the IND is submitted. With passage of the FDA's Modernization Act 2.0 in December 2022, Congress eliminated provisions in both the FDCA and PHSA that required animal testing in support of a BLA. While animal testing may still be conducted, the FDA was authorized to rely on alternative non-clinical tests, including cell-based assays, microphysiological systems or bioprinted or computer models.

Investigational New Drug Application

An IND is an exemption from the FDCA that allows an unapproved product candidate to be shipped in interstate commerce for use in an investigational clinical trial and a request for FDA authorization to administer such investigational product to humans. The IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions about the product or conduct of the proposed clinical trial, including concerns that human research subjects will be exposed to unreasonable health risks and issues surrounding CMC for the proposed product. In that case, the IND sponsor and the FDA must resolve any outstanding FDA concerns before the clinical trials can begin or recommence. As a result, submission of the IND may result in the FDA not allowing the trials to commence or allowing the trial to commence on the terms originally specified by the sponsor in the IND.

Following commencement of a clinical trial under an IND, the FDA may also place a clinical hold or partial clinical hold on the study if the FDA raises concerns or questions. Clinical holds are imposed by the FDA whenever there is concern for patient safety and may be a result of new data, findings, or developments in clinical, preclinical, and/or CMC. This order issued by the FDA would delay either a proposed clinical trial or cause suspension of an ongoing trial, until all outstanding concerns have been adequately addressed and the FDA has notified the company that investigations may proceed. This could cause significant delays or difficulties in completing our planned clinical trial or future clinical trials in a timely manner.

Following the issuance of a clinical hold or partial clinical hold, a clinical investigation may only resume once the FDA has notified the sponsor that the investigation may proceed. The FDA will base that determination on information provided by the sponsor correcting the deficiencies previously cited or otherwise satisfying the FDA that the investigation can proceed or recommence. Occasionally, clinical holds are imposed due to manufacturing issues that may present safety issues for the clinical study subjects.

Expanded Access to an Investigational Drug for Treatment Use

Expanded access, sometimes called "compassionate use," is the use of investigational products outside of clinical trials to treat patients with serious or immediately life-threatening diseases or conditions when there are no comparable or satisfactory alternative treatment options. The rules and regulations related to expanded access are intended to improve access to investigational products for patients who may benefit from investigational therapies. FDA regulations allow access to investigational products under an IND by the company or the treating physician for treatment purposes on a case-by-case basis for: individual patients (single-patient IND applications for treatment in emergency settings and non-emergency settings); intermediate-size patient populations; and larger populations for use of the investigational product under a treatment protocol or treatment IND application.

When considering an IND application for expanded access to an investigational product with the purpose of treating a patient or a group of patients, the sponsor and treating physicians or investigators will determine suitability when all of the following criteria apply: patient(s) have a serious or immediately life-threatening disease or condition, and there is no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the disease or condition; the potential patient benefit justifies the potential risks of the treatment and the potential risks are not unreasonable in the context or condition to be treated; and the expanded use of the investigational drug for the requested treatment will not interfere initiation, conduct, or completion of clinical investigations that could support marketing approval of the product or otherwise compromise the potential development of the product.

There is no obligation for a sponsor to make its drug products available for expanded access; however, as required by the 21st Century Cures Act, (the "Cures Act"), passed in 2016, if a sponsor has a policy regarding how it evaluates and responds to expanded access requests, sponsors are required to make such policies publicly available upon the earlier of initiation of a Phase 2 or

Phase 3 clinical trial, or 15 days after the investigational drug or biologic receives designation as a breakthrough therapy, fast track product, or regenerative medicine advanced therapy.

In addition to and separate from expanded access, on May 30, 2018, the Right to Try Act was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational products that have completed a Phase 1 clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a manufacturer to make its investigational products available to eligible patients as a result of the Right to Try Act.

Human Clinical Trials in Support of a BLA

Clinical trials involve the administration of the investigational product candidate to healthy volunteers or patients with the disease or condition to be treated under the supervision of a qualified principal investigator in accordance with GCP requirements. Clinical trials are conducted under protocols detailing, among other things, the objectives of the trial, inclusion and exclusion criteria, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND.

Further, each clinical trial must be reviewed and approved by an IRB either centrally or individually at each institution at which the clinical trial will be conducted. The IRB will consider, among other things, clinical trial design, patient informed consent, ethical factors, the safety of human subjects, and the possible liability of the institution. An IRB must operate in compliance with FDA regulations. The FDA, IRB, or the clinical trial sponsor may suspend or discontinue a clinical trial at any time for various reasons, including a finding that the clinical trial is not being conducted in accordance with FDA requirements or that the participants are being exposed to an unacceptable health risk. Clinical testing also must satisfy extensive GCP rules and the requirements for informed consent.

Additionally, some clinical trials are overseen by an independent group of qualified experts organized by the clinical trial sponsor, known as a data monitoring committee ("DMC"). This group may recommend continuation of the trial as planned, changes in trial conduct, or cessation of the trial at designated check points based on certain available data from the trial to which only the DMC has access. Suspension or termination of development during any phase of a clinical trial can occur if the DMC determines that the participants or patients are being exposed to an unacceptable health risk. Other reasons for suspension or termination may be made by us based on evolving business objectives and/or competitive climate.

Clinical trials typically are conducted in three sequential phases, but the phases may overlap or be combined. Additional studies may be required after approval.

- *Phase 1* clinical trials are initially conducted in a limited population to test the product candidate for safety, including adverse effects, dose tolerance, absorption, metabolism, distribution, excretion, and pharmacodynamics in healthy humans or, on occasion, in patients, such as cancer patients.

- *Phase 2* clinical trials are generally conducted in a limited patient population to identify possible adverse effects and safety risks, evaluate the efficacy of the product candidate for specific targeted indications, and determine dose tolerance and optimal dosage. Multiple Phase 2 clinical trials may be conducted by the sponsor to obtain information prior to beginning larger and more costly Phase 3 clinical trials.

- *Phase 3* clinical trials proceed if the Phase 2 clinical trials demonstrate that a dose range of the product candidate is potentially effective and has an acceptable safety profile. Phase 3 clinical trials are undertaken within an expanded patient population to further evaluate dosage, provide substantial evidence of clinical efficacy, and further test for safety in an expanded and diverse patient population at multiple, geographically dispersed clinical trial sites. A well-controlled, statistically robust Phase 3 trial may be designed to deliver the data that regulatory authorities will use to decide whether or not to approve, and, if approved, how to appropriately label a biologic; such Phase 3 studies are referred to as “pivotal.”

In some cases, the FDA may approve a BLA for a product but require the sponsor to conduct additional clinical trials to further assess the product’s safety and effectiveness after approval. Such trials are typically referred to as post-approval clinical trials. These studies are used to gain additional experience from the treatment of patients in the intended therapeutic indication and to document a clinical benefit in the case of biologics approved under accelerated approval regulations. If the FDA approves a product while a company has ongoing clinical trials that were not necessary for approval, a company may be able to use the data from these clinical trials to meet all or part of any post-approval clinical trial requirement or to request a change in the product labeling. The failure to exercise due diligence with regard to conducting post-approval clinical trials could result in withdrawal of approval for products.

A clinical trial may combine the elements of more than one phase and the FDA often requires more than one Phase 3 trial to support marketing approval of a product candidate. A company’s designation of a clinical trial as being of a particular phase is not

necessarily indicative that the study will be sufficient to satisfy the FDA requirements of that phase because this determination cannot be made until the protocol and data have been submitted to and reviewed by the FDA. Generally, pivotal trials are Phase 3 trials, but they may be Phase 2 trials if the design provides a well-controlled and reliable assessment of clinical benefit, particularly in an area of unmet medical need.

In December 2022, with the passage of Food and Drug Omnibus Reform Act ("FDORA") Congress required sponsors to develop and submit a diversity action plan for each Phase 3 clinical trial or any other "pivotal study" of a new drug or biological product. These plans are meant to encourage the enrollment of more diverse patient populations in late-stage clinical trials of FDA-regulated products. Specifically, action plans must include the sponsor's goals for enrollment, the underlying rationale for those goals, and an explanation of how the sponsor intends to meet them. In addition to these requirements, the legislation directs the FDA to issue new guidance on diversity action plans. In January 2024, the FDA issued draft guidance setting out its policies for the collection of race and ethnicity data in clinical trials. Unlike most guidance documents issued by the FDA, the diversity action plan guidance, when finalized, will have the force of the law because FDORA specifically dictates that the form and manner for submission of diversity action plans are specified in FDA guidance. In January 2025, in response to an executive order issued by President Trump on Diversity, Equity and Inclusion programs, the FDA removed this draft guidance from its website. The implications of this action are not yet known.

In June 2023, the FDA issued draft guidance with updated recommendations for GCPs aimed at modernizing the design and conduct of clinical trials. The updates are intended to help pave the way for more efficient clinical trials to facilitate the development of medical products. The draft guidance is adopted from the International Council for Harmonisation's ("ICH") recently updated E6(R3) draft guideline that was developed to enable the incorporation of rapidly developing technological and methodological innovations into the clinical trial enterprise. In addition, the FDA issued draft guidance outlining recommendations for the implementation of decentralized clinical trials.

Finally, sponsors of clinical trials are required to register and disclose certain clinical trial information on a public registry (clinicaltrials.gov) maintained by the NIH. In particular, information related to the product, patient population, phase of investigation, study sites and investigators and other aspects of the clinical trial is made public as part of the registration of the clinical trial. The PHSA grants the Secretary of Health and Human Services ("HHS") the authority to issue a notice of noncompliance to a responsible party to failure to submit clinical trial information as required. The responsible party, however, is allowed 30 days to correct the noncompliance and submit the required information. Although sponsors are also obligated to disclose the results of their clinical trials after completion, disclosure of the results can be delayed in some cases for up to two years after the date of completion of the trial. As of December 19, 2024, the FDA has issued six notices of non-compliance, signaling the government's willingness to enforce these requirements against non-compliant clinical trial sponsors. While these notices of non-compliance did not result in civil monetary penalties, the failure to submit clinical trial information to clinicaltrials.gov, as required, is a prohibited act under the FDCA with violations subject to potential civil monetary penalties of up to $10,000 for each day the violation continues. Violations may also result in injunctions and/or criminal prosecution or disqualification from federal grants.

Clinical Studies Outside the United States in Support of FDA Approval

In connection with our clinical development program, we may conduct trials at sites outside the United States. When a foreign clinical study is conducted under an IND, all IND requirements must be met unless waived. When a foreign clinical study is not conducted under an IND, the sponsor must ensure that the study complies with certain regulatory requirements of the FDA in order to use the study as support for an IND or application for marketing approval. Specifically, the studies must be conducted in accordance with GCP, including undergoing review and receiving approval by an independent ethics committee ("IEC") and seeking and receiving informed consent from subjects. GCP requirements encompass both ethical and data integrity standards for clinical studies. The FDA's regulations are intended to help ensure the protection of human subjects enrolled in non-IND foreign clinical studies, as well as the quality and integrity of the resulting data. They further help ensure that non-IND foreign studies are conducted in a manner comparable to that required for IND studies.

The acceptance by the FDA of study data from clinical trials conducted outside the United States in support of U.S. approval may be subject to certain conditions or may not be accepted at all. In cases where data from foreign clinical trials are intended to serve as the sole basis for marketing approval in the U.S., the FDA will generally not approve the application on the basis of foreign data alone unless (1) the data are applicable to the U.S. population and U.S. medical practice; (2) the trials were performed by clinical investigators of recognized competence and pursuant to GCP regulations; and (3) the data may be considered valid without the need for an on-site inspection by the FDA, or if the FDA considers such inspection to be necessary, the FDA is able to validate the data through an on-site inspection or other appropriate means.

In addition, even where the foreign study data are not intended to serve as the sole basis for approval, the FDA will not accept the data as support for an application for marketing approval unless the study is well-designed and well-conducted in accordance with GCP requirements and the FDA is able to validate the data from the study through an onsite inspection if deemed necessary. Many foreign regulatory authorities have similar approval requirements. In addition, such foreign trials are subject to the applicable local laws of the foreign jurisdictions where the trials are conducted.

Interactions with FDA During the Clinical Development Program

Following the clearance of an IND and the commencement of clinical trials, the sponsor will continue to have interactions with the FDA. A development safety update report ("DSUR") detailing the results of clinical trials must be submitted annually within 60 days of the anniversary dates that the IND went into effect and more frequently if serious adverse events occur. In addition, IND safety reports must be submitted to the FDA for any of the following: serious and unexpected suspected adverse reactions; findings from other trials or animal or in vitro testing that suggest a significant risk in humans exposed to the product; and any clinically important increase in the occurrence of a serious suspected adverse reaction over that listed in the protocol or investigator brochure.

In addition, sponsors are given opportunities to meet with the FDA at certain points in the clinical development program. Meetings at other times may also be requested. There are five types of meetings that occur between sponsors and the FDA. Type A meetings are those that are necessary for an otherwise stalled product development program to proceed or to address an important safety issue. Type B meetings include pre-IND and pre-BLA meetings, as well as end of phase meetings such as EOP2 meetings. A Type C meeting is any meeting other than a Type A or Type B meeting regarding the development and review of a product, including, for example, meetings to facilitate early consultations on the use of a biomarker as a new surrogate endpoint that has never been previously used as the primary basis for product approval in the proposed context of use. A Type D meeting is focused on a narrow set of issues, which should be limited to no more than two focused topics, and should not require input from more than three disciplines or divisions. Finally, INTERACT meetings are intended for novel products and development programs that present unique challenges in the early development of an investigational product.

At the conclusion of these meetings, the FDA will typically provide its responses to questions posed by the sponsor regarding the clinical development program. The FDA will not indicate whether a BLA will be approved, but it will provide guidance to the sponsor on various questions, including whether an application should be submitted in the first place on the basis of the studies and data proposed by the sponsor. The FDA has indicated that its responses, as conveyed in meeting minutes and advice letters, only constitute mere recommendations and/or advice made to a sponsor and, as such, sponsors are not bound by such recommendations and/or advice. Nonetheless, from a practical perspective, a sponsor's failure to follow the FDA's recommendations for design of a clinical program may put the program at significant risk of failure.

Pediatric Studies

Under the Pediatric Research Equity Act of 2003 ("PREA"), a BLA or supplement thereto must contain data that are adequate to assess the safety, potency, and purity of the product for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. Sponsors must also submit pediatric study plans prior to the assessment data. Those plans must contain an outline of the proposed pediatric study or studies the sponsor plans to conduct, including study objectives and design, any deferral or waiver requests, and other information required by regulation. The sponsor, the FDA, and the FDA's internal review committee must then review the information submitted, consult with each other, and agree upon a final plan. The FDA or the sponsor may request an amendment to the plan at any time.

The FDA may, on its own initiative or at the request of the sponsor, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements. A deferral may be granted for several reasons, including a finding that the product or therapeutic candidate is ready for approval for use in adults before pediatric trials are completed. The FDA is required to send a PREA Non-Compliance letter to sponsors who have failed to submit their pediatric assessments under PREA, have failed to seek or obtain a deferral or deferral extension or have failed to request approval for a required pediatric formulation. Unless otherwise required by regulation, the pediatric data requirements do not apply to products with orphan designation, although FDA has taken steps to limit what it considers abuse of this statutory exemption in PREA. The FDA also maintains a list of diseases that are exempt from PREA requirements due to low prevalence of disease in the pediatric population. In May 2023, the FDA issued new draft guidance that further describes the pediatric study requirements under PREA.

Compliance with cGMP Requirements

The FDA's regulations require that pharmaceutical products be manufactured in specific approved facilities and in accordance with cGMPs. The cGMP regulations include requirements relating to organization of personnel, buildings and facilities, equipment, control of components and product containers and closures, production and process controls, packaging and labeling controls, holding and distribution, laboratory controls, records and reports, and returned or salvaged products. Manufacturers and others involved in the manufacture and distribution of products must also register their establishments with the FDA and certain state agencies. Both domestic and foreign manufacturing establishments must register and provide additional information to the FDA upon their initial participation in the manufacturing process. Any product manufactured by or imported from a facility that has not registered, whether foreign or domestic, is deemed misbranded under the FDCA. Establishments may be subject to periodic unannounced inspections by government authorities to ensure compliance with cGMPs and other laws. Inspections must follow a "risk-based schedule" that may result in certain establishments being inspected more frequently. Manufacturers may also have to provide, on request, electronic or physical records regarding their establishments. Delaying, denying, limiting, or refusing inspection by the FDA may lead to a product being deemed to be adulterated. Changes to the manufacturing process, specifications or container closure system for an approved product are strictly regulated and often require prior FDA approval before being implemented. The FDA's regulations also require, among other things, the investigation and correction of any deviations from cGMP and the imposition

of reporting and documentation requirements upon the sponsor and any third-party manufacturers involved in producing the approved product.

The PREVENT Pandemics Act, which was enacted in December 2022, clarifies that foreign drug manufacturing establishments are subject to registration and listing requirements even if a drug or biologic undergoes further manufacture, preparation, propagation, compounding, or processing at a separate establishment outside the United States prior to being imported or offered for import into the United States.

Submission and Filing of a BLA

The results of product candidate development, preclinical testing, and clinical trials, including negative or ambiguous results as well as positive findings, are submitted to the FDA as part of a BLA requesting license to market the product. The BLA must contain extensive manufacturing information and detailed information on the composition of the product and proposed labeling as well as payment of a user fee. Under federal law, the submission of most BLAs is subject to an application user fee, which for federal fiscal year 2025 is $4.3 million for an application requiring clinical data. The sponsor of a licensed BLA is also subject to an annual program fee, which for federal fiscal year 2025 is $403,889. Certain exceptions and waivers are available for some of these fees, such as an exception from the application fee for products with orphan designation and a waiver for certain small businesses.

Following submission of a BLA, the FDA has 60 days to conduct a preliminary review of the application and it must inform the sponsor within that period of time whether the BLA is sufficiently complete to permit substantive review. In the event that FDA determines that an application does not satisfy this standard, it will issue a Refuse to File determination to the sponsor. The FDA may request additional information and studies, and the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing.

Once the submission has been accepted for filing, the FDA begins an in-depth review of the application. Under the goals and policies agreed to by the FDA under the PDUFA, the FDA has ten months in which to complete its initial review of a standard application and respond to the sponsor, and six months for a priority review of the application. The FDA does not always meet its PDUFA goal dates for standard and priority BLAs. The review process may often be significantly extended by FDA requests for additional information or clarification. The review process and the PDUFA goal date may be extended by three months if the FDA requests or if the sponsor otherwise provides additional information or clarification regarding information already provided in the submission within the last three months before the PDUFA goal date.

The FDA seeks to meet these timelines for review of an application but its ability to do so may be affected by a variety of factors. While the costs associated with review of an application are typically covered by the PDUFA user fee program, other activities, including government budget and funding levels, the ability to hire and retain key personnel and statutory, regulatory and policy changes, may impact the FDA's review and approval of marketing applications. Average review times at the agency have fluctuated in recent years, as a result. For example, during the past decade, the U.S. government has shut down several times and certain regulatory agencies, including the FDA, have had to furlough critical employees and stop critical activities. In connection with its review of an application, the FDA will typically submit information requests to the applicant and set deadlines for responses thereto. The FDA will also conduct a pre-approval inspection of the manufacturing facilities for the new product to determine whether the manufacturing processes and facilities comply with cGMPs. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and are adequate to assure consistent production of the product within required specifications. The FDA also may inspect the sponsor and one or more clinical trial sites to assure compliance with IND and GCP requirements and the integrity of the clinical data submitted to the FDA. With passage of FDORA, Congress clarified the FDA's authority to conduct inspections by expressly permitting inspections of facilities involved in the preparation, conduct, or analysis of clinical and non-clinical studies submitted to the FDA as well as other persons holding study records or involved in the study process.

Moreover, the FDA will review a sponsor's financial relationship with the principal investigators who conducted the clinical trials in support of the NDA or BLA. That is because, under certain circumstances, principal investigators at a clinical trial site may also serve as scientific advisors or consultants to a sponsor and receive compensation in connection with such services. Depending on the level of that compensation and any other financial interest a principal investigator may have in a sponsor, the sponsor may be required to report these relationships to the FDA. The FDA will then evaluate that financial relationship and determine whether it creates a conflict of interest or otherwise affects the interpretation of the trial or the integrity of the data generated at the principal investigator's clinical trial site. If so, the FDA may exclude data from the clinical trial site in connection with its determination of safety and efficacy of the investigational product.

The FDA may also refer the application to an advisory committee for review, evaluation, and recommendation as to whether the application should be approved. In particular, the FDA may refer applications for novel biologic products or biologic products that present difficult questions of safety or efficacy to an advisory committee. Typically, an advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates, and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

The FDA's Decision on a BLA

Under the PHSA, the FDA may approve a BLA if it determines that the product is safe, pure, and potent, and the facility where the product will be manufactured meets standards, including cGMP requirements, designed to ensure that it continues to be safe, pure, and potent. Specifically, the FDA must determine that the expected benefits of the proposed product outweigh its potential risks to patients. This "benefit-risk" assessment is informed by the extensive body of evidence about the proposed product in the BLA. The FDA will also consider the severity of the underlying condition and how well patients' medical needs are addressed by currently available therapies; uncertainty about how the premarket clinical trial evidence will extrapolate to real-world use of the product in the post-market setting; and whether risk management tools are necessary to manage specific risks.

On the basis of the FDA's evaluation of the application and accompanying information, including the results of the inspection of the manufacturing facilities and any FDA audits of preclinical and clinical trial sites to assure compliance with GCPs, the FDA may issue a complete response letter ("CRL") or an approval letter.

If the application is not approved, the FDA will issue a CRL, which will contain the conditions that must be met in order to secure final approval of the application, and when possible will outline recommended actions the sponsor might take to obtain approval of the application. Sponsors that receive a CRL may submit to the FDA information that represents a complete response to the issues identified by the FDA, withdraw the application or request a hearing. The FDA will not approve an application until issues identified in the CRL have been addressed. If a CRL is issued, the sponsor will have one year to respond to the deficiencies identified by the FDA, at which time the FDA can deem the application withdrawn or, in its discretion, grant the sponsor an additional six-month extension to respond. For those seeking to challenge FDA's CRL decision, the agency has indicated that sponsors may request a formal hearing on the CRL or they may file a request for reconsideration or a request for a formal dispute resolution. The FDA has committed to reviewing resubmissions in response to an issued CRL in either two or six months depending on the type of information included. Even with the submission of this additional information, however, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

An approval letter, on the other hand, authorizes commercial marketing of the product with specific prescribing information for specific indications. The FDA may limit the approved indication(s) for use of the product. It may also require that contraindications, warnings, or precautions be included in the product labeling. In addition, the FDA may call for post-approval studies, including Phase 4 clinical trials, to further assess the product's efficacy and/or safety after approval. The agency may also require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution restrictions or other risk management mechanisms, including REMS, to help ensure that the benefits of the product outweigh the potential risks. REMS can include medication guides, communication plans for healthcare professionals, and elements to assure safe use ("ETASU"). ETASU can include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring, and the use of patent registries. The FDA may prevent or limit further marketing of a product based on the results of post-market studies or surveillance programs. After approval, many types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

In the event that a sponsor wishes to make a change to a product that has been approved under a BLA, the sponsor must submit a supplemental application to the FDA. Such changes may include a revision of the labeling for the approved product, the addition of a new indication, a change in the dosage, strength or formulation of the product, or a modification of the manner in which the biologic is manufactured. Under the timelines established pursuant to PDUFA, the standard review time for a supplement to a BLA is generally 10 months from receipt of the application by the FDA.

Expedited Review Programs

The FDA is authorized to designate certain products for expedited review if they demonstrate the potential to address an unmet medical need in the treatment of a serious or life-threatening disease or condition. The purpose of these programs is to provide important new drugs to patients earlier than under standard review procedures. None of these expedited programs changes the standards for approval but each may help expedite the development or approval process governing product candidates.

Under the Fast Track program, the sponsor of a product candidate may request the FDA to designate the product for a specific indication as a Fast Track product concurrent with or after the filing of the IND. Candidate products are eligible for Fast Track designation if they are intended to treat a serious or life-threatening condition and demonstrate the potential to address unmet medical needs for the condition. Fast Track designation applies to the combination of the product candidate and the specific indication for which it is being studied. In addition to other benefits, such as the ability to have greater interactions with the FDA, the FDA may initiate review of sections of a Fast Track application before the application is complete, a process known as rolling review.

Any product candidate submitted to the FDA for marketing, including under a Fast Track program, may be eligible for other types of FDA programs intended to expedite development and review, such as breakthrough therapy designation, priority review and accelerated approval.

- Breakthrough therapy designation. To qualify for the breakthrough therapy program, product candidates must be intended to treat a serious or life-threatening disease or condition and preliminary clinical evidence must indicate that such product candidates may demonstrate substantial improvement on one or more clinically significant endpoints over existing therapies. The FDA will seek to ensure the sponsor of a breakthrough therapy product candidate receives intensive guidance on an efficient drug development program, intensive involvement of senior managers and experienced staff on a proactive, collaborative and cross-disciplinary review and rolling review.

- Priority review. A product candidate is eligible for priority review if it treats a serious condition and, if approved, it would be a significant improvement in the safety or effectiveness of the treatment, diagnosis or prevention compared to marketed products. Significant improvement may be illustrated by evidence of increased effectiveness in the treatment of a condition, elimination or substantial reduction of a treatment-limiting product reaction, documented enhancement of patient compliance that may lead to improvement in serious outcomes, and evidence of safety and effectiveness in a new subpopulation. FDA aims to complete its review of priority review applications within six months as opposed to 10 months for standard review.

- Accelerated approval. Drug or biologic products studied for their safety and effectiveness in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit over existing treatments may receive accelerated approval. Accelerated approval means that a product candidate may be approved on the basis of adequate and well controlled clinical trials establishing that the product candidate has an effect on a surrogate endpoint that is reasonably likely to predict a clinical benefit, or on the basis of an effect on a clinical endpoint other than survival or irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity and prevalence of the condition and the availability or lack of alternative treatments. As a condition of approval, the FDA may require that a sponsor of a drug or biologic product candidate receiving accelerated approval perform adequate and well controlled post-marketing clinical trials. In addition, the FDA currently requires as a condition for accelerated approval pre-approval of promotional materials. With passage of FDORA in December 2022, Congress modified certain provisions governing accelerated approval of drug and biologic products. Specifically, the new legislation authorized the FDA to: require a sponsor to have its confirmatory clinical trial underway before accelerated approval is awarded, require that a sponsor of a product granted accelerated approval to submit progress reports on its post-approval studies to FDA every six months (until the study is completed); and use expedited procedures to withdraw accelerated approval of an NDA or BLA if certain conditions are not met, including where the confirmatory trial fails to verify the product's clinical benefit or where evidence demonstrates the product is not shown to be safe or effective under the conditions of use. The FDA may also use such procedures to withdraw an accelerated approval if a sponsor fails to conduct any required post-approval trial of the product with due diligence, including with respect to "conditions specified by the Secretary." The new procedures include the provision of due notice and an explanation for a proposed withdrawal, and opportunities for a meeting with the FDA Commissioner or the Commissioner's designee and a written appeal, among other things. In March 2023, the FDA issued draft guidance that outlines its current thinking and approach to accelerated approval. Although single-arm trials have been commonly used to support accelerated approval, a randomized controlled trial is the preferred approach as it provides a more robust assessment and allows for direct comparisons to an available therapy. To that end, the FDA outlined considerations for designing, conducting, and analyzing data for trials intended to support accelerated approvals of oncology therapeutics. Subsequently, in December 2024 and January 2025, the FDA issued additional draft guidance relating to accelerated approval. This guidance describes the FDA's views on what it means to conduct a confirmatory trial with due diligence and how the agency plans to interpret whether such a study needs to be underway at the time of approval. While this guidance is currently only in draft form and will ultimately not be legally binding even when finalized, sponsors typically observe the FDA's guidance closely to ensure that their investigational products qualify for accelerated approval.

- Regenerative advanced therapy. With passage of the Cures Act, Congress authorized the FDA to accelerate review and approval of products designated as regenerative advanced therapies. A product is eligible for this designation if it is a regenerative medicine therapy that is intended to treat, modify, reverse or cure a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product candidate has the potential to address unmet medical needs for such disease or condition. The benefits of a regenerative advanced therapy designation include early interactions with the FDA to expedite development and review, benefits available to breakthrough therapies, potential eligibility for priority review and accelerated approval based on surrogate or intermediate endpoints.

Post-Approval Regulation

If regulatory approval for marketing of a product or new indication for an existing product is obtained, the sponsor will be required to comply with all regular post-approval regulatory requirements as well as any post-approval requirements that the FDA have imposed as part of the approval process. The sponsor will be required to report certain adverse reactions and production problems to the FDA, provide updated safety and efficacy information and comply with requirements concerning advertising and promotional labeling requirements. Manufacturers and certain of their subcontractors are required to register their establishments with the FDA and certain state agencies and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with ongoing regulatory requirements, including cGMP regulations, which impose certain procedural and documentation requirements upon manufacturers. Accordingly, the sponsor and its third-party manufacturers must continue to expend time, money, and effort in the areas of production and quality control to maintain compliance with cGMP regulations and other regulatory requirements.

A product may also be subject to official lot release, meaning that the manufacturer is required to perform certain tests on each lot of the product before it is released for distribution. If the product is subject to official lot release, the manufacturer must submit samples of each lot, together with a release protocol showing a summary of the history of manufacture of the lot and the results of all of the manufacturer's tests performed on the lot, to the FDA. The FDA may in addition perform certain confirmatory tests on lots of some products before releasing the lots for distribution. Finally, the FDA will conduct laboratory research related to the safety, purity, potency, and effectiveness of pharmaceutical products.

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending applications or supplements to approved applications, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

Although physicians may prescribe legally available products for unapproved uses or patient populations (i.e., "off-label uses"), manufacturers may not market or promote such uses. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

In September 2021, the FDA published final regulations which describe the types of evidence that the agency will consider in determining the intended use of a biologic product.

If a company is found to have promoted off-label uses, it may become subject to adverse public relations and administrative and judicial enforcement by the FDA, the Department of Justice, or the Office of the Inspector General of the Department of Health and Human Services, as well as state authorities. This could subject a company to a range of penalties that could have a significant commercial impact, including civil and criminal fines and agreements that materially restrict the manner in which a company promotes or distributes drug products.

It may be permissible, under very specific, narrow conditions, for a manufacturer to engage in nonpromotional, non-misleading communication regarding off-label information, such as distributing scientific or medical journal information. For example, in January 2025, the FDA published final guidance outlining its policies governing the distribution of scientific information to healthcare providers about unapproved uses of approved products. The final guidance calls for such communications to be truthful, non-misleading and scientifically sound and to include all information necessary for healthcare providers to interpret the strengths and

weaknesses and validity and utility of the information about the unapproved use of the approved product. If a company engages in such communications consistent with the guidance's recommendations, the FDA indicated that it will not treat such communications as evidence of unlawful promotion of a new intended use for the approved product. Moreover, with passage of the Pre-Approval Information Exchange Act in December 2022, sponsors of products that have not been approved may proactively communicate to payors certain information about products in development to help expedite patient access upon product approval.

In addition, the distribution of prescription pharmaceutical products is subject to the Prescription Drug Marketing Act ("PDMA") and its implementing regulations, as well as the Drug Supply Chain Security Act ("DSCSA"), which regulate the distribution and tracing of prescription drug samples at the federal level, and set minimum standards for the regulation of drug distributors by the states. The PDMA, its implementing regulations and state laws limit the distribution of prescription pharmaceutical product samples, and the DSCSA imposes requirements to ensure accountability in distribution and to identify and remove counterfeit and other illegitimate products from the market. Manufacturers were required by November 2023 to have such systems and processes in place to comply with the DSCSA, but, so as not to disrupt supply chains, the FDA has granted certain exemptions from enhanced drug distribution security requirements for eligible trading partners for particular periods of time.

Orphan Drug Designation and Exclusivity

Orphan drug designation in the United States is designed to encourage sponsors to develop products intended for rare diseases or conditions. In the United States, a rare disease or condition is statutorily defined as a condition that affects fewer than 200,000 individuals in the United States or that affects more than 200,000 individuals in the United States and for which there is no reasonable expectation that the cost of developing and making available the biologic for the disease or condition will be recovered from sales of the product in the United States.

Orphan drug designation qualifies a company for tax credits and market exclusivity for seven years following the date of the product's marketing approval if granted by the FDA. An application for designation as an orphan product can be made any time prior to the filing of an application for approval to market the product. A product becomes an orphan when it receives orphan drug designation from the Office of Orphan Products Development at the FDA based on acceptable confidential requests made under the regulatory provisions. The product must then go through the review and approval process like any other product.

A sponsor may request orphan drug designation of a previously unapproved product or new orphan indication for an already marketed product. In addition, a sponsor of a product that is otherwise the same product as an already approved orphan drug may seek and obtain orphan drug designation for the subsequent product for the same rare disease or condition if it can present a plausible hypothesis that its product may be clinically superior to the first drug. More than one sponsor may receive orphan drug designation for the same product for the same rare disease or condition, but each sponsor seeking orphan drug designation must file a complete request for designation.

If a product with orphan designation receives the first FDA approval for the disease or condition for which it has such designation or for a select indication or use within the rare disease or condition for which it was designated, the product generally will receive orphan drug exclusivity. Orphan drug exclusivity means that the FDA may not approve another sponsor's marketing application for the same product for the same indication for seven years, except in certain limited circumstances. If a product designated as an orphan drug ultimately receives marketing approval for an indication broader than what was designated in its orphan drug application, it may not be entitled to exclusivity.

The period of exclusivity begins on the date that the marketing application is approved by the FDA. Orphan drug exclusivity will not bar approval of another product under certain circumstances, including if a subsequent product with the same drug for the same condition is shown to be clinically superior to the approved product on the basis of greater efficacy or safety, or providing a major contribution to patient care, or if the company with orphan drug exclusivity is not able to meet market demand. Under Omnibus legislation enacted in December 2020, the requirement for a product to show clinical superiority applies to drugs and biologics that received orphan drug designation before enactment of the FDA Reauthorization Act of 2017 but have not yet been approved or licensed by FDA. In addition, the FDA may approve a second application for the same product for a different use or a second application for a clinically superior version of the product for the same use.

In September 2021, the Court of Appeals for the 11th Circuit in *Catalyst Pharms, Inc. v. Becerra ("Catalyst")* held that, for the purpose of determining the scope of orphan drug exclusivity, the term "same disease or condition" in the statute means the designated "rare disease or condition" and could not be interpreted by the FDA to mean the "indication or use." Although there have been legislative proposals to overrule this decision, they have not been enacted into law. On January 23, 2023, the FDA announced that, in matters beyond the scope of the *Catalyst* court order, the FDA will continue to apply its existing regulations tying orphan-drug exclusivity to the uses or indications for which the orphan drug is approved. More recently however, on February 14, 2025, a federal district court in Washington, D.C. fully embraced the reasoning of the *Catalyst* decision in another decision challenging the scope of orphan drug exclusivity. The implications of this decision, and its impact on the FDA's implementation of the Orphan Drug Act, are unclear at this point.

Pediatric Exclusivity

Pediatric exclusivity is another type of non-patent exclusivity in the United States and for biologics, if granted, provides for the attachment of an additional six months of regulatory exclusivity to the term of any existing regulatory exclusivity, including orphan exclusivity. This six-month exclusivity may be granted if a BLA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. The data do not need to show the product to be effective in the pediatric population studied; rather, if the clinical trial is deemed to fairly respond to the FDA's request, the additional protection is granted. If reports of requested pediatric studies are submitted to and accepted by the FDA within the statutory time limits, whatever statutory or regulatory periods of exclusivity that cover the product are extended by six months.

Biosimilars and Exclusivity

The 2010 Patient Protection and Affordable Care Act, which was signed into law in March 2010, included a subtitle called the Biologics Price Competition and Innovation Act of 2009 ("BPCIA"). The BPCIA established a regulatory scheme authorizing the FDA to approve biosimilars and interchangeable biosimilars.

Under the BPCIA, a manufacturer may submit an application for licensure of a biologic product that is "biosimilar to" or "interchangeable with" a previously approved biological product or "reference product." In order for the FDA to approve a biosimilar product, it must find that there are no clinically meaningful differences between the reference product and proposed biosimilar product in terms of safety, purity, and potency. For the FDA to approve a biosimilar product as interchangeable with a reference product, the agency must find that the biosimilar product can be expected to produce the same clinical results as the reference product, and (for products administered multiple times) that the biologic and the reference biologic may be switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic. To date, the FDA has licensed a number of biosimilar products, as well as a few interchangeable biosimilar products.

An application for a biosimilar product may not be submitted to the FDA until four years following the date of approval of the reference product. The FDA may not approve a biosimilar product until 12 years from the date on which the reference product was approved. Even if a product is considered to be a reference product eligible for regulatory exclusivity, another company could market a competing version of that product if the FDA approves a full BLA for such product containing the sponsor's own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity, and potency of their product. The BPCIA also created certain exclusivity periods for biosimilars approved as interchangeable products. There have been recent government proposals to reduce the 12-year reference product regulatory exclusivity period, but none has been enacted to date. At the same time, since passage of the BPCIA, many states have passed laws or amendments to laws, which address pharmacy practices involving biosimilar products. In December 2022, Congress clarified through FDORA that the FDA may approve multiple first interchangeable biosimilar biological products so long as the products are all approved on the first day on which such a product is approved as interchangeable with the reference product.

Federal and State Data Privacy and Security Laws

Under the federal Health Insurance Portability and Accountability Act of 1996 ("HIPAA"), HHS has issued regulations to protect the privacy and security of protected health information used or disclosed by covered entities including certain healthcare providers, health plans, and healthcare clearinghouses. HIPAA also regulates standardization of data content, codes, and formats used in healthcare transactions and standardization of identifiers for health plans and providers. HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 ("HITECH"), and their regulations, including the omnibus final rule published on January 25, 2013, also imposes certain obligations on the business associates of covered entities that obtain protected health information in providing services to or on behalf of covered entities. In addition to federal privacy regulations, there are a number of state laws governing confidentiality and security of health information that are applicable to our business. In addition to possible federal civil and criminal penalties for HIPAA violations, state attorneys general are authorized to file civil actions for damages or injunctions in federal courts to enforce HIPAA and seek attorney's fees and costs associated with pursuing federal civil actions. Accordingly, state attorneys general (along with private plaintiffs) have brought civil actions seeking injunctions and damages resulting from alleged violations of HIPAA's privacy and security rules. New laws and regulations governing privacy and security may be adopted in the future as well.

In addition to potential enforcement by HHS, we are also potentially subject to privacy enforcement from the FTC. The FTC has been particularly focused on the unpermitted processing of health and genetic data through its recent enforcement actions and is expanding the types of privacy violations that it interprets to be "unfair" under Section 5 of the FTC Act, as well as the types of activities it views to trigger the Health Breach Notification Rule (which the FTC also has the authority to enforce). The agency is also in the process of developing rules related to commercial surveillance and data security that may impact our business. We will need to account for the FTC's evolving rules and guidance for proper privacy and data security practices in order to mitigate our risk for a potential enforcement action, which may be costly. If we are subject to a potential FTC enforcement action, we may be subject to a settlement order that requires us to adhere to very specific privacy and data security practices, which may impact our business. We may also be required to pay fines as part of a settlement (depending on the nature of the alleged violations). If we violate any consent order that we reach with the FTC, we may be subject to additional fines and compliance requirements. Finally, both the FTC and

HHS's enforcement priorities (as well as those of other federal regulators) may be impacted by the change in administration and new leadership. These shifts in enforcement priorities may also impact our business. There are also increased restrictions at the federal level relating to transferring sensitive data outside of the United States to certain foreign countries. For example, in 2024, Congress passed H.B. 815, which included the Protecting Americans' Data from Foreign Adversaries Act of 2024. This law creates certain restrictions for entities that disclose sensitive data (including potential health data) to countries such as China. Failure to comply with these rules can lead to a potential FTC enforcement action. Additionally, the Department of Justice recently finalized a rule implementing Executive Order 14117, which creates similar restrictions related to the transfer of sensitive US data to countries such as China. These data transfer restrictions (and others that may pass in the future) may create operational challenges and legal risks for our business.

Additionally, California recently enacted legislation that has been dubbed the first "GDPR-like" law in the United States. Known as the California Consumer Privacy Act ("CCPA"), it creates new individual privacy rights for consumers (as that word is broadly defined in the law) and places increased privacy and security obligations on entities handling personal data of consumers or households. The CCPA went into effect on January 1, 2020 and requires covered companies to provide new disclosures to California consumers, provide such consumers new ways to opt-out of certain sales of personal information, and allow for a new cause of action for data breaches. The CCPA could impact our business activities depending on how it is interpreted and exemplifies the vulnerability of our business to not only cyber threats but also the evolving regulatory environment related to personal data and protected health information.

In November 2020, California voters passed a ballot initiative for the California Privacy Rights Act ("the CPRA"), which went into effect on January 1, 2023, and significantly expanded the CCPA to incorporate additional GDPR-like provisions including requiring that the use, retention, and sharing of personal information of California residents be reasonably necessary and proportionate to the purposes of collection or processing, granting additional protections for sensitive personal information, and requiring greater disclosures related to notice to residents regarding retention of information. The CPRA also created a new enforcement agency – the California Privacy Protection Agency – whose sole responsibility is to enforce the CPRA, which will further increase compliance risk. The provisions in the CPRA may apply to some of our business activities.

In addition to California, a number of other states have passed comprehensive privacy laws similar to the CCPA and CPRA. These laws are either in effect or will go into effect sometime over the next several years. Like the CCPA and CPRA, these laws create obligations related to the processing of personal information, as well as special obligations for the processing of "sensitive" data, which includes health data in some cases. Some of the provisions of these laws may apply to our business activities. There are also states that are strongly considering or have already passed comprehensive privacy laws that will go into effect over the next several years. Other states will be considering similar laws in the future, and Congress has also been debating passing a federal privacy law. There are also states that are specifically regulating health information that may affect our business. For example, the State of Washington passed the My Health My Data Act in 2023 which specifically regulated health information that is not otherwise regulated by the HIPAA rules, and the law also has a private right of action, which further increases the relevant compliance risk. Connecticut and Nevada have also passed similar laws regulating consumer health data, and more states are considering such legislation. These laws may impact our business activities, including our identification of research subjects, relationships with business partners and ultimately the marketing and distribution of our products.

Plaintiffs' lawyers are also increasingly using privacy-related statutes at both the state and federal level to bring lawsuits against companies for their data-related practices. In particular, there have been a significant number of cases filed against companies for their use of pixels and other web trackers. These cases often allege violations of the California Invasion of Privacy Act and other state laws regulating wiretapping, as well as the federal Video Privacy Protection Act. The rise in these types of lawsuits creates potential risk for our business.

Because of the breadth of these laws and the narrowness of the statutory exceptions and regulatory safe harbors available under such laws, it is possible that some of our current or future business activities, including certain clinical research, sales, and marketing practices and the provision of certain items and services to our customers, could be subject to challenge under one or more of such privacy and data security laws. The heightening compliance environment and the need to build and maintain robust and secure systems to comply with different privacy compliance and/or reporting requirements in multiple jurisdictions could increase the possibility that a healthcare company may fail to comply fully with one or more of these requirements. If our operations are found to be in violation of any of the privacy or data security laws or regulations described above that are applicable to us, or any other laws that apply to us, we may be subject to penalties, including potentially significant criminal, civil, and administrative penalties, damages, fines, imprisonment, contractual damages, reputational harm, diminished profits and future earnings, additional reporting requirements, and/or oversight if we become subject to a consent decree or similar agreement to resolve allegations of non-compliance with these laws, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations. To the extent that any of our product candidates, once approved, are sold in a foreign country, we may be subject to similar foreign laws.

Patent Term Restoration and Extension

In the United States, a patent claiming a new biologic product, its method of use or its method of manufacture may be eligible for a limited patent term extension under the Hatch-Waxman Act, which permits a patent extension of up to five years for patent term lost during product development and FDA regulatory review. Assuming grant of the patent for which the extension is

sought, the restoration period for a patent covering a product is typically one-half the time between the effective date of the IND clearing clinical studies and the submission date of the BLA, plus the time between the submission date of the BLA and the ultimate approval date. Patent term restoration cannot be used to extend the remaining term of a patent past a total of 14 years from the product's approval date in the United States. Only one patent applicable to an approved product is eligible for the extension, and the application for the extension must be submitted prior to the expiration of the patent for which extension is sought. A patent that covers multiple products for which approval is sought can only be extended in connection with one of the approvals. The USPTO reviews and approves the application for any patent term extension in consultation with the FDA.

FDA Approval of Companion Diagnostics

In August 2014, the FDA issued final guidance clarifying the requirements that will apply to approval of therapeutic products and *in vitro* companion diagnostics. According to the guidance, for novel drugs, a companion diagnostic device and its corresponding therapeutic should be approved or cleared contemporaneously by the FDA for the use indicated in the therapeutic product's labeling. Approval or clearance of the companion diagnostic device will ensure that the device has been adequately evaluated and has adequate performance characteristics in the intended population. In July 2016, the FDA issued a draft guidance intended to assist sponsors of the drug therapeutic and in vitro companion diagnostic device on issues related to co-development of the products.

The 2014 guidance also explains that a companion diagnostic device used to make treatment decisions in clinical trials of a biologic product candidate generally will be considered an investigational device, unless it is employed for an intended use for which the device is already approved or cleared. If used to make critical treatment decisions, such as patient selection, the diagnostic device generally will be considered a significant risk device under the FDA's Investigational Device Exemption, or IDE, regulations. Thus, the sponsor of the diagnostic device will be required to comply with the IDE regulations. According to the guidance, if a diagnostic device and a product are to be studied together to support their respective approvals, both products can be studied in the same investigational study, if the study meets both the requirements of the IDE regulations and the IND regulations. The guidance provides that depending on the details of the study plan and subjects, a sponsor may seek to submit an IND alone, or both an IND and an IDE.

In April 2020, the FDA issued additional guidance which describes considerations for the development and labeling of companion diagnostic devices to support the indicated uses of multiple biological oncology products, when appropriate. The 2020 guidance expands on the policy statement in the 2014 guidance by recommending that companion diagnostic developers consider a number of factors when determining whether their test could be developed, or the labeling for approved companion diagnostics could be revised through a supplement, to support a broader labeling claim such as use with a specific group of oncology therapeutic products (rather than listing an individual therapeutic product(s)).

Under the FDCA, *in vitro* diagnostics, including companion diagnostics, are regulated as medical devices. In the United States, the FDCA and its implementing regulations, and other federal and state statutes and regulations govern, among other things, medical device design and development, preclinical and clinical testing, premarket clearance or approval, registration and listing, manufacturing, labeling, storage, advertising and promotion, sales and distribution, export and import, and post market surveillance. Unless an exemption applies, diagnostic tests require marketing clearance or approval from the FDA prior to commercial distribution.

The FDA previously has required *in vitro* companion diagnostics intended to select the patients who will respond to the product candidate to obtain pre-market approval ("PMA") simultaneously with approval of the therapeutic product candidate. The PMA process, including the gathering of clinical and preclinical data and the submission to and review by the FDA, can take several years or longer. It involves a rigorous premarket review during which the sponsor must prepare and provide the FDA with reasonable assurance of the device's safety and effectiveness and information about the device and its components regarding, among other things, device design, manufacturing and labeling. PMA applications are subject to an application fee.

It is possible that an in vitro companion diagnostic device could be subject to FDA enforcement discretion from compliance with the FDCA if it meets the definition of a Laboratory Developed Test ("LDT"). However, FDA issued a final rule in April 2024 to end enforcement discretion for LDTs and actively regulate such products as medical devices. Under this final rule, LDTs are required to come into compliance with FDA's medical device regulatory requirements in a staged approach over the course of four years. The implementation of this LDT final rule could potentially be affected by the Executive Order, Regulatory Freeze Pending Review, issued by President Trump on January 20, 2025 and/or the anticipated change in leadership at FDA under the new administration. Further, while the final regulation is set to take effect on May 6, 2025, a number of parties have challenged the legality of the LDT regulation in a federal district court. That court held a hearing on this matter on February 19, 2025, and is expected to issue a ruling soon.

Regulation and Procedures Governing Approval of Medicinal Products in the European Union

In order to market any product outside of the United States, a company must also comply with numerous and varying regulatory requirements of other countries and jurisdictions regarding quality, safety, and efficacy, and governing, among other things, clinical trials, marketing authorization, commercial sales, and distribution of products. Whether or not it obtains FDA approval for a product, a sponsor will need to obtain the necessary approvals by the comparable foreign regulatory authorities before it can commence clinical trials or marketing of the product in those countries or jurisdictions. Specifically, the process governing approval of medicinal products in the European Union generally follows the same lines as in the United States. It entails satisfactory completion of preclinical studies and adequate and well-controlled clinical trials to establish the safety and efficacy of the product for each proposed indication. It also requires the submission to the relevant competent authorities of a marketing authorization application ("MAA") and granting of a marketing authorization by these authorities before the product can be marketed and sold in the European Union.

Clinical Trial Approval

On January 31, 2022, the new Clinical Trials Regulation (EU) No 536/2014 ("CTR") became effective in the EU and replaced the prior Clinical Trials Directive 2001/20/EC. The new regulation aims at simplifying and streamlining the authorization, conduct and transparency of clinical trials in the EU. Under the new coordinated procedure for the approval of clinical trials, the sponsor of a clinical trial to be conducted in more than one Member State of the European Union ("EU Member State") will only be required to submit a single application for approval. The submission will be made through the Clinical Trials Information System, a new clinical trials portal overseen by the EMA and available to clinical trial sponsors, competent authorities of the EU Member States and the public.

The main characteristics of the regulation include: a streamlined application procedure via a single entry point, the "EU Portal and Database"; a single set of documents to be prepared and submitted for the application as well as simplified reporting procedures for clinical trial sponsors; and a harmonized procedure for the assessment of applications for clinical trials, which is divided in two parts. Part I is assessed by the appointed reporting Member State, whose assessment report is submitted for review by the sponsor and all other competent authorities of all EU Member States in which an application for authorization of a clinical trial has been submitted, or concerned member states. Part II is assessed separately by each concerned member state. Strict deadlines have been established for the assessment of clinical trial applications. The role of the relevant ethics committees in the assessment procedure will continue to be governed by the national law of the concerned member state. However, overall related timelines will be defined by the Clinical Trials Regulation.

The new regulation did not change the preexisting requirement that a sponsor must obtain prior approval from the competent national authority of the EU Member State in which the clinical trial is to be conducted. If the clinical trial is conducted in different EU Member States, the competent authorities in each of these EU Member States must provide their approval for the conduct of the clinical trial. Furthermore, the sponsor may only start a clinical trial at a specific study site after the applicable ethics committee has issued a favorable opinion.

As of January 31, 2025, all clinical trials (including those which are ongoing) are subject to the provisions of the CTR. The failure to transition ongoing clinical trials to the Clinical Trials Regulation can result in corrective measures under Article 77 of the Clinical Trials Regulation, including revocation of the authorization of the clinical trial or suspension of the clinical trial as well as criminal sanctions and fines under national law of EU Member States.

Parties conducting certain clinical trials must, as in the United States, post clinical trial information in the European Union at the EudraCT website: https://eudract.ema.europa.eu.

PRIME Designation in the European Union

In March 2016, the EMA launched an initiative to facilitate development of product candidates in indications, often rare, for which few or no therapies currently exist. The PRIority MEdicines ("PRIME") scheme is intended to encourage drug development in areas of unmet medical need and provides accelerated assessment of products representing substantial innovation reviewed under the centralized procedure. Products from small- and medium-sized enterprises may qualify for earlier entry into the PRIME scheme than larger companies. Many benefits accrue to sponsors of product candidates with PRIME designation, including but not limited to, early and proactive regulatory dialogue with the EMA, frequent discussions on clinical trial designs and other development program elements, and accelerated marketing authorization application assessment once a dossier has been submitted. Importantly, a dedicated EMA contact and rapporteur from CHMP or Committee for Advanced Therapies are appointed early in the PRIME scheme facilitating increased understanding of the product at the EMA's Committee level.

Marketing Authorization

To obtain a marketing authorization for a product under the European Union regulatory system, a sponsor must submit an MAA, either under a centralized procedure administered by the EMA or one of the procedures administered by competent authorities in EU Member States (decentralized procedure, national procedure, or mutual recognition procedure). A marketing authorization may be granted only to a sponsor established in the European Union. Regulation (EC) No 1901/2006 provides that prior to obtaining a marketing authorization in the European Union, a sponsor must demonstrate compliance with all measures included in an EMA-approved Pediatric Investigation Plan ("PIP") covering all subsets of the pediatric population, unless the EMA has granted a product-specific waiver, class waiver, or a deferral for one or more of the measures included in the PIP.

The centralized procedure provides for the grant of a single marketing authorization by the European Commission that is valid for all EU Member States. Pursuant to Regulation (EC) No. 726/2004, the centralized procedure is compulsory for specific products, including for medicines produced by certain biotechnological processes, products designated as orphan medicinal products, advanced therapy products and products with a new active substance indicated for the treatment of certain diseases, including products for the treatment of cancer. For products with a new active substance indicated for the treatment of other diseases and products that are highly innovative or for which a centralized process is in the interest of patients, the centralized procedure may be optional. Manufacturers must demonstrate the quality, safety, and efficacy of their products to the EMA, which provides an opinion regarding the MAA. The European Commission grants or refuses marketing authorization in light of the opinion delivered by the EMA.

Specifically, the grant of marketing authorization in the European Union for products containing viable human tissues or cells such as gene therapy medicinal products is governed by Regulation 1394/2007/EC on advanced therapy medicinal products, read in combination with Directive 2001/83/EC of the European Parliament and of the Council, commonly known as the Community code on medicinal products. Regulation 1394/2007/EC lays down specific rules concerning the authorization, supervision, and pharmacovigilance of gene therapy medicinal products, somatic cell therapy medicinal products, and tissue engineered products. Manufacturers of advanced therapy medicinal products must demonstrate the quality, safety, and efficacy of their products to EMA which provides an opinion regarding the application for marketing authorization. The European Commission grants or refuses marketing authorization in light of the opinion delivered by EMA.

Under the centralized procedure, the CHMP established at the EMA is responsible for conducting an initial assessment of a product. Under the centralized procedure in the European Union, the maximum timeframe for the evaluation of an MAA is 210 days, excluding clock stops when additional information or written or oral explanation is to be provided by the sponsor in response to questions of the CHMP.

Conditional Marketing Authorization

In particular circumstances, EU legislation (Article 14–a Regulation (EC) No 726/2004 (as amended by Regulation (EU) 2019/5 and Regulation (EC) No 507/2006 on Conditional Marketing Authorizations for Medicinal Products for Human Use) enables sponsors to obtain a conditional marketing authorization prior to obtaining the comprehensive clinical data required for an application for a full MA. Such conditional approvals may be granted for product candidates (including medicines designated as orphan medicinal products) if (1) the product candidate is intended for the treatment, prevention, or medical diagnosis of seriously debilitating or life-threatening diseases; (2) the product candidate is intended to meet unmet medical needs of patients; (3) a marketing authorization may be granted prior to submission of comprehensive clinical data provided that the benefit of the immediate availability on the market of the medicinal product concerned outweighs the risk inherent in the fact that additional data are still required; (4) the risk-benefit balance of the product candidate is positive; and (5) it is likely that the sponsor will be in a position to provide the required comprehensive clinical trial data. A conditional MA may contain specific obligations to be fulfilled by the marketing authorization holder, including obligations with respect to the completion of ongoing or new clinical trials and with respect to the collection of pharmacovigilance data. Conditional MAs are valid for one year, and may be renewed annually, if the risk-benefit balance remains positive, and after an assessment of the need for additional or modified conditions or specific obligations. The timelines for the centralized procedure described above also apply with respect to the review by the CHMP of applications for a conditional MA.

Exceptional Circumstances

A MA may also be granted “under exceptional circumstances” when the applicant can show that it is unable to provide comprehensive data on the efficacy and safety under normal conditions of use even after the product has been authorized and subject to specific procedures being introduced. This may arise in particular when the intended indications are very rare and, in the present state of scientific knowledge, it is not possible to provide comprehensive information, or when generating data may be contrary to generally accepted ethical principles. This MA is similar to the conditional MA, as it is reserved to medicinal products to be approved for severe diseases or unmet medical needs and the applicant does not hold the complete data set legally required for the grant of a MA. However, unlike the conditional MA, the applicant does not have to provide the missing data and will never have to. Although the MA “under exceptional circumstances” is granted definitively, the risk-benefit balance of the medicinal product is reviewed annually and the MA is withdrawn in case the risk-benefit ratio is no longer favorable. Under these procedures, before granting the

MA, the EMA or the competent authorities of the member states make an assessment of the risk-benefit balance of the product on the basis of scientific criteria concerning its quality, safety, and efficacy.

Pediatric Trials

Prior to obtaining a marketing authorization in the EU, sponsors have to demonstrate compliance with all measures included in an EMA-approved PIP covering all subsets of the pediatric population, unless the EMA has granted a product-specific waiver, a class waiver, or a deferral for one or more of the measures included in the PIP. The respective requirements for all marketing authorization procedures are set forth in Regulation (EC) No 1901/2006, which is referred to as the Pediatric Regulation. This requirement also applies when a company wants to add a new indication, pharmaceutical form, or route of administration for a medicine that is already authorized. The Pediatric Committee of the EMA ("PDCO") may grant deferrals for some medicines, allowing a company to delay development of the medicine in children until there is enough information to demonstrate its effectiveness and safety in adults. The PDCO may also grant waivers when development of a medicine in children is not needed or is not appropriate because (a) the product is likely to be ineffective or unsafe in part or all of the pediatric population; (b) the disease or condition occurs only in adult population; or (c) the product does not represent a significant therapeutic benefit over existing treatments for the pediatric population. Before a marketing authorization application can be filed, or an existing marketing authorization can be amended, the EMA determines that companies actually comply with the agreed studies and measures listed in each relevant PIP.

Periods of Authorization and Renewals

A marketing authorization is valid for five years, in principle, and it may be renewed after five years on the basis of a reevaluation of the risk-benefit balance by the EMA or by the competent authority of the authorizing member state. To that end, the marketing authorization holder must provide the EMA or the competent authority with a consolidated version of the file in respect of quality, safety and efficacy, including all variations introduced since the marketing authorization was granted, at least six months before the marketing authorization ceases to be valid. Once renewed, the marketing authorization is valid for an unlimited period, unless the European Commission or the competent authority decides, on justified grounds relating to pharmacovigilance, to proceed with one additional five-year renewal period. Any authorization that is not followed by the placement of the drug on the European Union market (in the case of the centralized procedure) or on the market of the authorizing member state within three years after authorization ceases to be valid.

Regulatory Requirements after Marketing Authorization

Following approval, the holder of the marketing authorization is required to comply with a range of requirements applicable to the manufacturing, marketing, promotion and sale of the medicinal product. These include compliance with the European Union's stringent pharmacovigilance or safety reporting rules, pursuant to which post-authorization studies and additional monitoring obligations can be imposed. In addition, the manufacturing of authorized products, for which a separate manufacturer's license is mandatory, must also be conducted in strict compliance with the EMA's good manufacturing practice requirements and comparable requirements of other regulatory bodies in the European Union, which mandate the methods, facilities, and controls used in manufacturing, processing and packing of drugs to assure their safety and identity. Finally, the marketing and promotion of authorized products, including industry-sponsored continuing medical education and advertising directed toward the prescribers of drugs and/or the general public, are strictly regulated in the European Union under Directive 2001/83EC, as amended.

Regulatory Exclusivity

In the EU, new products authorized for marketing (i.e., reference products) qualify for eight years of data exclusivity and an additional two years of market exclusivity upon marketing authorization. The data exclusivity period prevents generic sponsors from relying on the preclinical and clinical trial data contained in the dossier of the reference product when applying for a generic marketing authorization in the EU during a period of eight years from the date on which the reference product was first authorized in the EU. The market exclusivity period prevents a successful generic sponsor from commercializing its product in the EU until 10 years have elapsed from the initial authorization of the reference product in the European Union. The 10-year market exclusivity period can be extended to a maximum of 11 years if, during the first eight years of those 10 years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies.

The EU pharmaceutical legislation is currently undergoing a complete review process, in the context of the Pharmaceutical Strategy for Europe initiative, launched by the European Commission in November 2020. The European Commission's proposal for revision of several legislative instruments related to medicinal products was published in April 2023 and includes, among other things, provisions that would potentially reduce the duration of regulatory data protection. The European

Parliament requested several amendments in April 2024. At this time, the proposed revisions remain to be agreed and adopted by the European Parliament and European Council and the proposals may therefore be substantially revised before adoption, which is not anticipated before early 2026. The revisions may, however, have a significant impact on the pharmaceutical industry in the long term, if and when adopted.

Orphan Drug Designation and Exclusivity

Regulation (EC) No 141/2000 and Regulation (EC) No. 847/2000 provide that a product can be designated as an orphan drug by the European Commission if its sponsor can establish: that the product is intended for the diagnosis, prevention or treatment of (1) a life-threatening or chronically debilitating condition affecting not more than five in 10,000 persons in the European Union when the application is made, or (2) a life-threatening, seriously debilitating or serious and chronic condition in the European Union and that without incentives it is unlikely that the marketing of the drug in the European Union would generate sufficient return to justify the necessary investment. For either of these conditions, the sponsor must demonstrate that there exists no satisfactory method of diagnosis, prevention, or treatment of the condition in question that has been authorized in the European Union or, if such method exists, the drug will be of significant benefit to those affected by that condition.

An orphan drug designation provides a number of benefits, including fee reductions, regulatory assistance, and the possibility to apply for a centralized European Union marketing authorization. Marketing authorization for an orphan drug leads to a ten-year period of market exclusivity. During this market exclusivity period, neither the EMA nor the European Commission or the member states can accept an application or grant a marketing authorization for a "similar medicinal product." A "similar medicinal product" is defined as a medicinal product containing a similar active substance or substances as contained in an authorized orphan medicinal product, and which is intended for the same therapeutic indication. The market exclusivity period for the authorized therapeutic indication may, however, be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for orphan drug designation because, for example, the product is sufficiently profitable not to justify market exclusivity.

Pediatric Exclusivity

If a sponsor obtains a marketing authorization in all EU Member States, or a marketing authorization granted in the centralized procedure by the European Commission, and the trial results for the pediatric population are included in the product information, even when negative, the medicine is then eligible for an additional six-month period of qualifying patent protection through extension of the term of the Supplementary Protection Certificate ("SPC") or alternatively a one-year extension of the regulatory market exclusivity from 10 to 11 years, as selected by the marketing authorization holder.

Patent Term Extensions in the European Union and Other Jurisdictions

The EU also provides for patent term extension through SPCs. The rules and requirements for obtaining an SPC are similar to those in the United States. An SPC may extend the term of a patent for up to five years after its originally scheduled expiration date and can provide up to a maximum of 15 years of marketing exclusivity for a drug. In certain circumstances, these periods may be extended for six additional months if pediatric exclusivity is obtained, which is described in detail below. Although SPCs are available throughout the EU, sponsors must apply on a country-by-country basis. Similar patent term extension rights exist in certain other foreign jurisdictions outside the EU.

Approval of Companion Diagnostic Devices

In the European Union, medical devices such as companion diagnostics must comply with the General Safety and Performance Requirements ("SPRs") detailed in Annex I of the European Union Medical Devices Regulation (Regulation (EU) 2017/745) ("MDR"), which came into force on May 26, 2021 and replaced the previously applicable European Union Medical Devices Directive (Council Directive 93/42/EEC). Compliance with SPRs, and additional requirements applicable to companion medical devices, is a prerequisite to be able to affix the CE Mark of Conformity to medical devices, without which they cannot be marketed or sold. To demonstrate compliance with SPRs, a manufacturer must undergo a conformity assessment procedure, which varies according to the type of medical device and its classification. The MDR is meant to establish a uniform, transparent, predictable, and sustainable regulatory framework across the European Union for medical devices.

Separately, the regulatory authorities in the European Union also adopted a new In Vitro Diagnostic Regulation (EU) 2017/746 ("IVDR"), which became effective in May 2022. The new regulation replaced the In Vitro Diagnostics Directive 98/79/EC. Manufacturers wishing to apply to a notified body for a conformity assessment of their in vitro diagnostic medical device had until May 2022 to update their Technical Documentation to meet the requirements and comply with the new, more stringent Regulation. The regulation will, among other things: strengthen the rules on placing devices on the market and reinforce surveillance once they are

available; establish explicit provisions on manufacturers' responsibilities for the follow-up of the quality, performance, and safety of devices placed on the market; improve the traceability of medical devices throughout the supply chain to the end-user or patient through a unique identification number; set up a central database to provide patients, healthcare professionals and the public with comprehensive information on products available in the European Union; and strengthen rules for the assessment of certain high-risk devices, such as implants, which may have to undergo an additional check by experts before they are placed on the market.

While the IVDR became effective in May 2022, it became clear in 2021 that Member States, health institutions, and economic operators were not ready to apply the IVDR as of that date. The European Commission therefore proposed a progressive or staggered roll-out of the rules of the IVDR. The current transition periods range from May 26, 2025 for high risk in vitro diagnostics to May 26, 2027 for lower risk in vitro diagnostics. Certain provisions for devices manufactured and used in health institutions would have to apply as of May 26, 2028. These transition periods only apply to so called "legacy devices," meaning devices covered by a certificate or declaration of conformity issued under the previous legal framework.

Brexit and the Regulatory Framework in the United Kingdom

The United Kingdom's withdrawal from the European Union took place on January 31, 2020. As of January 1, 2021, the Medicines and Healthcare Products Regulatory Agency (the "MHRA") became responsible for supervising medicines and medical devices in Great Britain, comprising England, Scotland and Wales under domestic law whereas Northern Ireland continues to be subject to European Union rules under the Northern Ireland Protocol.

As of January 1, 2025, the MHRA is responsible for approving all medicinal products destined for the UK market (i.e., Great Britain and Northern Ireland), and the EMA will no longer have any role in approving medicinal products destined for Northern Ireland. The MHRA relies on the Human Medicines Regulations 2012 (SI 2012/1916) (as amended), or the HMR, as the basis for regulating medicines.

As of January 1, 2024, a new international recognition procedure ("IRP") applies which intends to facilitate approval of pharmaceutical products in the UK. The IRP is open to applicants that have already received an authorization for the same product from one of the MHRA's specified Reference Regulators ("RRs"). The RR notably include EMA and regulators in the EEA member states for approvals in the EU centralized procedure and mutual recognition procedure as well as the FDA (for product approvals granted in the U.S.). The RR assessment must have undergone a full and standalone review. RR assessments based on reliance or recognition cannot be used to support an IRP application. A CHMP positive opinion or a positive end of procedure outcome is an RR authorisation for the purposes of IRP.

General Data Protection Regulation

The collection, use, disclosure, transfer, or other processing of personal data regarding individuals in the European Union, including personal health data, is subject to the European Union General Data Protection Regulation ("GDPR") which became effective on May 25, 2018. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, including requirements relating to processing health and other sensitive data, obtaining consent of the individuals to whom the personal data relates, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches, and taking certain measures when engaging third-party processors. The GDPR also imposes strict rules on the transfer of personal data to countries outside the European Union, including the U.S., and permits data protection authorities to impose large penalties for violations of the GDPR, including potential fines of up to €20 million or 4% of annual global revenues, whichever is greater. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. Compliance with the GDPR will be a rigorous and time-intensive process that may increase the cost of doing business or require companies to change their business practices to ensure full compliance. In July 2020, the Court of Justice of the European Union (the "CJEU") invalidated the EU-U.S. Privacy Shield framework, one of the mechanisms used to legitimize the transfer of personal data from the EEA to the United States. The CJEU decision also drew into question the long-term viability of an alternative means of data transfer, the standard contractual clauses, for transfers of personal data from the EEA to the United States.

Following the CJEU decision, in October 2022, President Biden signed an executive order to implement the EU-U.S. Data Privacy Framework, which would serve as a replacement to the EU-US Privacy Shield. The EU initiated the process to adopt an adequacy decision for the EU-U.S. Data Privacy Framework in December 2022, and the European Commission adopted the adequacy decision in July 2023. The adequacy decision permits U.S. companies who self-certify to the EU-U.S. Data Privacy Framework to rely on it as a valid data transfer mechanism for data transfers from the EU to the United States. However, some privacy advocacy groups have already suggested that they will be challenging the EU-U.S. Data Privacy Framework. If these challenges are successful, they

may not only impact the EU-U.S. Data Privacy Framework, but also further limit the viability of the standard contractual clauses and other data transfer mechanisms. The uncertainty around this issue has the potential to impact our business.

On June 23, 2016, the electorate in the UK voted in favor of leaving the EU, commonly referred to as Brexit. As with other issues related to Brexit, there are open questions about how personal data will be protected in the UK and whether personal information can transfer from the EU to the UK. Following the withdrawal of the UK from the EU, the UK Data Protection Act 2018 applies to the processing of personal data that takes place in the UK and includes parallel obligations to those set forth by GDPR. While the Data Protection Act of 2018 in the UK that "implements" and complements the GDPR has achieved Royal Assent on May 23, 2018 and is now effective in the UK, it is unclear whether transfer of data from the EEA to the UK will remain lawful under the GDPR, although these transfers currently are permitted by an adequacy decision from the European Commission. The UK government has already determined that it considers all 27 EU and EEA member states to be adequate for the purposes of data protection, ensuring that data flows from the UK to the EU/EEA remain unaffected. In addition, a recent decision from the European Commission appears to deem the UK as being "essentially adequate" for purposes of data transfer from the EU to the UK, although this decision may be re-evaluated in the future. The UK and the U.S. have also agreed to a U.S.-UK "Data Bridge," which functions similarly to the EU-U.S. Data Privacy Framework and provides an additional legal mechanism for companies to transfer data from the UK to the United States. In addition to the UK, Switzerland is also in the process of approving an adequacy decision in relation to the Swiss-U.S. Data Privacy Framework (which would function similarly to the EU-U.S. Data Privacy Framework and the U.S.-UK Data Bridge in relation to data transfers from Switzerland to the United States). Any changes or updates to these developments have the potential to impact our business.

Coverage, Pricing, and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any product candidates for which we may seek regulatory approval by the FDA or other government authorities. In the United States and markets in other countries, patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payors to reimburse all or part of the associated healthcare costs. Patients are unlikely to use any product candidates we may develop unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of such product candidates. Even if any product candidates we may develop are approved, sales of such product candidates will depend, in part, on the extent to which third-party payors, including government health programs in the United States such as Medicare and Medicaid, commercial health insurers, and managed care organizations, provide coverage, and establish adequate reimbursement levels for, such product candidates. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors are increasingly challenging the prices charged, examining the medical necessity, and reviewing the cost-effectiveness of medical products and services and imposing controls to manage costs. Third-party payors may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the approved products for a particular indication.

In order to secure coverage and reimbursement for any product that might be approved for sale, a company may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the product, in addition to the costs required to obtain FDA or other comparable marketing approvals. Nonetheless, product candidates may not be considered medically necessary or cost effective. A decision by a third-party payor not to cover any product candidates we may develop could reduce physician utilization of such product candidates once approved and have a material adverse effect on our sales, results of operations and financial condition. Additionally, a payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a product does not assure that other payors will also provide coverage and reimbursement for the product, and the level of coverage and reimbursement can differ significantly from payor to payor. Third-party reimbursement and coverage may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development. In addition, any companion diagnostic tests require coverage and reimbursement separate and apart from the coverage and reimbursement for their companion pharmaceutical or biological products. Similar challenges to obtaining coverage and reimbursement, applicable to pharmaceutical or biological products, will apply to any companion diagnostics.

The containment of healthcare costs also has become a priority of federal, state and foreign governments and the prices of pharmaceuticals have been a focus in this effort. Governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement, and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit a company's revenue generated from the sale of any approved products. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which a company or its collaborators receive marketing approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Outside the United States, ensuring adequate coverage and payment for any product candidates we may develop will face challenges. Pricing of prescription pharmaceuticals is subject to governmental control in many countries. Pricing negotiations with governmental authorities can extend well beyond the receipt of regulatory marketing approval for a product and may require us to conduct a clinical trial that compares the cost effectiveness of any product candidates we may develop to other available therapies. The conduct of such a clinical trial could be expensive and result in delays in our commercialization efforts.

In the European Union, pricing and reimbursement schemes vary widely from country to country. Some countries provide that products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost-effectiveness of a particular product candidate to currently available therapies (so called health technology assessments) in order to obtain reimbursement or pricing approval. For example, the European Union provides options for its member states to restrict the range of products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. EU Member States may approve a specific price for a product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the product on the market. Other member states allow companies to fix their own prices for products but monitor and control prescription volumes and issue guidance to physicians to limit prescriptions. Recently, many countries in the European Union have increased the amount of discounts required on pharmaceuticals and these efforts could continue as countries attempt to manage healthcare expenditures, especially in light of the severe fiscal and debt crises experienced by many countries in the European Union. The downward pressure on healthcare costs in general, particularly prescription products, has become intense. As a result, increasingly high barriers are being erected to the entry of new products. Political, economic, and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various EU Member States, and parallel trade (arbitrage between low-priced and high-priced member states), can further reduce prices. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products, if approved in those countries.

Healthcare Law and Regulation

Healthcare providers and third-party payors play a primary role in the recommendation and prescription of pharmaceutical products that are granted marketing approval. Arrangements with providers, consultants, third-party payors, and customers are subject to broadly applicable fraud and abuse, anti-kickback, false claims laws, reporting of payments to physicians and teaching physicians and patient privacy laws and regulations and other healthcare laws and regulations that may constrain our business and/or financial arrangements. Restrictions under applicable federal and state healthcare laws and regulations, include the following:

- the U.S. federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, paying, receiving, or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made, in whole or in part, under a federal healthcare program such as Medicare and Medicaid;

- the federal civil and criminal false claims laws, including the civil False Claims Act, and civil monetary penalties laws, which prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false, fictitious, or fraudulent or knowingly making, using, or causing to made or used a false record or statement to avoid, decrease, or conceal an obligation to pay money to the federal government;

- the Foreign Corrupt Practices Act, which prohibits companies and their intermediaries from making, or offering or promising to make improper payments to non-U.S. officials for the purpose of obtaining or retaining business or otherwise seeking favorable treatment; and

- the federal transparency requirements known as the federal Physician Payments Sunshine Act, under the Patient Protection and Affordable Care Act (the "ACA"), as amended by the Health Care Education Reconciliation Act, which requires certain manufacturers of drugs, devices, biologics and medical supplies to report annually to the Centers for Medicare & Medicaid Services ("CMS") within HHS, information related to payments and other transfers of value made by that entity to physicians, other healthcare providers, and teaching hospitals, as well as ownership and investment interests held by physicians, and their immediate family members.

Some state laws require pharmaceutical companies to comply with the pharmaceutical industry’s voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring pharmaceutical manufacturers to report information related to payments to physicians and other healthcare providers or marketing expenditures. In

addition, certain state and local laws require drug manufacturers to register pharmaceutical sales representatives in the jurisdiction. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal, and administrative penalties, damages, fines, disgorgement, exclusion from government funded healthcare programs, such as Medicare and Medicaid, integrity oversight and reporting obligations, and the curtailment or restructuring of our operations.

Healthcare Reform

A primary trend in the U.S. healthcare industry and elsewhere is cost containment. There have been a number of federal and state proposals during the last few years regarding the pricing of pharmaceutical and biopharmaceutical products, limiting coverage and reimbursement for drugs and other medical products, government control and other changes to the healthcare system in the United States.

In March 2010, the United States Congress enacted the ACA, which, among other things, includes changes to the coverage and payment for products under government healthcare programs.

Other legislative changes have been proposed and adopted in the United States since the ACA was enacted. For example, in August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2012 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers of up to 2% per fiscal year, which will remain in effect through 2031 pursuant to the Coronavirus Aid, Relief and Economic Security Act (the "CARES Act").

The American Taxpayer Relief Act of 2012, which was enacted in January 2013, among other things, further reduced Medicare payments to several providers, including hospitals, imaging centers, and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used. Indeed, under current legislation, the actual reductions in Medicare payments may vary up to 4%.

Since enactment of the ACA, there have been, and continue to be, numerous legal challenges and Congressional actions to repeal and replace provisions of the law. For example, with enactment of the Tax Cuts and Jobs Act of 2017, which was signed by President Trump on December 22, 2017, Congress repealed the "individual mandate." The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, became effective in 2019. On June 17, 2021, the U.S. Supreme Court dismissed the most recent judicial challenge to the ACA brought by several states without specifically ruling on the constitutionality of the ACA. During the first Trump Administration, Congress and the administration sought to overturn the ACA and related measures. Shortly after taking office in January 2025, President Trump revoked numerous executive orders issued by President Biden, including at least two executive orders (e.g., EO 14009, Strengthening Medicaid and the Affordable Care Act, and EO 14070, Continuing to Strengthen Americans' Access to Affordable, Quality Health Coverage) that were designed to further implement the ACA. We anticipate similar efforts to undermine the ACA, and the accompanying uncertainty, for the foreseeable future.

Pharmaceutical Prices

The prices of prescription pharmaceuticals have also been the subject of considerable discussion in the United States. There have been several United States congressional inquiries, as well as proposed and enacted state and federal legislation designed to, among other things, bring more transparency to pharmaceutical pricing, review the relationship between pricing and manufacturer patient programs, and reduce the costs of pharmaceuticals under Medicare and Medicaid.

In addition, in October 2020, HHS and the FDA published a final rule allowing states and other entities to develop a Section 804 Importation Program ("SIP") to import certain prescription drugs from Canada into the United States. That regulation was challenged in a lawsuit by the Pharmaceutical Research and Manufacturers of America ("PhRMA"), but the case was dismissed by a federal district court in February 2023 after the court found that PhRMA did not have standing to sue HHS. Several states have passed laws allowing for the importation of drugs from Canada. Several states have submitted Section 804 Importation Program proposals and are awaiting FDA approval. On January 5, 2023, the FDA approved Florida's plan for Canadian drug importation. Florida now has authority to import certain products from Canada for a period of two years once certain conditions are met. Florida will first need

to submit a pre-import request for each product selected for importation, which must be approved by the FDA. Florida will also need to relabel the products and perform quality testing of the products to meet FDA standards.

On August 16, 2022, the Inflation Reduction Act ("IRA") was signed into law by President Biden. The new legislation has implications for Medicare Part D, which is a program available to individuals who are entitled to Medicare Part A or enrolled in Medicare Part B to give them the option of paying a monthly premium for outpatient prescription drug coverage. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare (beginning in 2026), with prices that can be negotiated subject to a cap and replaces the Part D coverage gap discount program with a new discounting program (beginning in 2025). In addition, the IRA established inflation rebate programs under Medicare Part B and Part D. These programs require manufacturers to pay rebates to Medicare if they raise their prices for certain Part B and Part D drugs faster than the rate of inflation. On December 9, 2024, with issuance of its 2025 Physician Fee Schedule final regulation, CMS finalized its rules governing the IRA inflation rebate programs. The IRA permits the Secretary of the Department of HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years.

Specifically, with respect to price negotiations, Congress authorized Medicare to negotiate lower prices for certain costly single-source drug and biologic products that do not have competing generics or biosimilars and are reimbursed under Medicare Part B and Part D. CMS may negotiate prices for ten high-cost drugs paid for by Medicare Part D starting in 2026, followed by 15 Medicare Part D drugs in 2027, 15 Medicare Part B or Part D drugs in 2028, and 20 Medicare Part B or Part D drugs in 2029 and beyond. This provision applies to drug products that have been approved for at least 9 years and biologics that have been licensed for 13 years, but it does not apply to drugs and biologics that have been approved for a single rare disease or condition.

The IRA includes a provision, known as the orphan drug exclusion, that excludes from price negotiations those orphan drugs that have been designated for only one rare disease or condition and for which the only approved indication (or indications) is for such disease or condition. Thus, as CMS stated in final guidance in July 2023, a drug or biologic that is designated for more than one rare disease or condition will not qualify for the orphan drug exclusion, even if it is not approved for any indications for the additional diseases or conditions. Further, CMS will only consider active designations/approvals when evaluating a drug or biologic for the orphan drug exclusion. CMS has also clarified that, if a drug loses its orphan drug status, the agency will use the earliest date of approval/licensure to determine whether the product is a qualifying single source drug subject to price negotiations.

In August 2024, HHS published the results of the first Medicare drug price negotiations for ten selected drugs that treat a range of conditions and the prices will become effective January 1, 2026. In January 2025, CMS announced the next 15 drug and biologic prices that will be subject to the IRA’s price negotiation provisions. There has been uncertainty about the extent to which the new administration would support the price negotiation program. Following the change in administrations, CMS issued a public statement on January 2025, declaring that lowering the cost of prescription drugs is a top priority of the new administration and CMS is committed to considering opportunities to bring greater transparency in the negotiation program. The second cycle of negotiations with participating drug companies will occur during 2025, and any negotiated prices for this second set of drugs will be effective starting January 1, 2027.

Further, the legislation subjects drug manufacturers to civil monetary penalties and a potential excise tax for failing to comply with the legislation by offering a price that is not equal to or less than the negotiated “maximum fair price” under the law or for taking price increases that exceed inflation. The legislation also requires manufacturers to pay rebates for drugs in Medicare Part D whose price increases exceed inflation. The new law also caps Medicare out-of-pocket drug costs at an estimated $2,000 a year beginning in 2025.

In June 2023, Merck & Co. filed a lawsuit against the HHS and CMS asserting that, among other things, the IRA’s Drug Price Negotiation Program for Medicare constitutes an uncompensated taking in violation of the Fifth Amendment of the Constitution. Subsequently, a number of other parties, including Bristol Myers Squibb Company, the PhRMA, Astellas, Novo Nordisk, Janssen Pharmaceuticals, Novartis, AstraZeneca, and Boehringer Ingelheim, also filed lawsuits in various courts with similar constitutional claims against the HHS and CMS. There have been various decisions by the courts considering these cases since they were filed. We expect that litigation involving these and other provisions of the IRA will continue, with unpredictable and uncertain results.

At the state level, individual states are increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. A number of states, for example, require pharmaceutical manufacturers and other entities in the supply chain, including health carriers, pharmacy benefit managers, wholesale distributors, to disclose information about pricing of pharmaceuticals. This is increasingly true with respect to products approved pursuant to the accelerated approval pathway. State Medicaid programs and other payers are developing strategies and implementing significant coverage barriers, or refusing to cover these products outright, arguing that accelerated approval drugs have insufficient or limited evidence despite meeting the FDA's standards for accelerated approval. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

In the European Union, similar political, economic and regulatory developments to those in the United States may affect our ability to profitably commercialize our product candidates, if approved. In markets outside of the United States and the European Union, reimbursement and healthcare payment systems vary significantly by country and many countries have instituted price ceilings on specific products and therapies. In many countries, including those of the European Union, the pricing of prescription pharmaceuticals is subject to governmental control and access. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, pharmaceutical firms may be required to conduct a clinical trial that compares the cost-effectiveness of the product to other available therapies.

Human Capital

As of December 31, 2024, we had 67 employees, including a total of 21 employees with M.D. or Ph.D. degrees. Of these full-time employees, 48 are engaged in research and development activities. None of our employees are represented by labor unions or covered by collective bargaining agreements. We consider our relationship with our employees to be good.

In connection with our recent strategic review, we implemented a workforce reduction of approximately 25% of our employees in the first quarter of 2025.

Our future success is dependent on attracting, motivating and retaining a talented group of employees. We aim to create an inclusive and empowering work environment with different experiences, perspectives and backgrounds. Our human capital resources objectives include, as applicable, identifying, recruiting, retaining, incentivizing and integrating our existing and future employees. The principal purposes of our incentive plans are to attract, retain and motivate selected employees, consultants, advisors and directors through the granting of stock-based compensation awards and cash-based performance bonus awards, as applicable. We provide a comprehensive benefits package to help employees manage their health, well-being, finances, and life outside of work, including health insurance, dental and vision insurance, life insurance, accidental death and dismemberment issuance, short-term and long-term disability insurance, paid sick leave, a 401(k) plan, an employee stock purchase plan, a flexible spending account program, and paid vacation time. We value the health, safety, and wellbeing of our employees and their families.

Our Corporate Information

Our principal executive offices are located at 321 Summer Street, Suite 400, Boston, Massachusetts 02210, and our telephone number is (857) 330-4340. Our website address is http://www.inozyme.com. The information contained on, or that can be accessed through, our website is not a part of this Annual Report on Form 10-K. We have included our website address in this Annual Report on Form 10-K solely as an inactive textual reference.

We own or have rights to, or have applied for, trademarks, service marks and trade names that we use in connection with the operation of our business, including our corporate name, logos and website names. Other trademarks, service marks and trade names appearing in this Annual Report on Form 10-K are the property of their respective owners. Solely for convenience, some of the trademarks, service marks and trade names referred to in this Annual Report on Form 10-K are listed without the ® and ™ symbols.

Available Information

Through our website, we make available free of charge our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and amendments to those reports filed or furnished pursuant to Sections 13(a) and 15(d) of the

Exchange Act of 1934, as amended (the "Exchange Act"). We make these reports available through our website as soon as reasonably practicable after we electronically file such reports with, or furnish such reports to, the Securities and Exchange Commission. We also make available, free of charge on our website, the reports filed with the Securities and Exchange Commission by our executive officers, directors and 10% stockholders pursuant to Section 16 under the Exchange Act as soon as reasonably practicable after copies of those filings are provided to us by those persons. The information contained on, or that can be accessed through, our website is not a part of this Annual Report on Form 10-K. We have included our website address in this Annual Report on Form 10-K solely as an inactive textual reference.

Item 1A. Risk Factors.

Our future operating results could differ materially from the results described in this Annual Report on Form 10-K due to the risks and uncertainties described below. You should consider carefully the following information about risks in evaluating our business. If any of the following risks actually occur, our business, financial conditions, results of operations and future growth prospects would likely decline. In addition, we cannot assure investors that our assumptions and expectations will prove to be correct. Important factors could cause our actual results to differ materially from those indicated or implied by forward-looking statements. See page 1 of this Annual Report on Form 10-K for a discussion of some of the forward-looking statements that are qualified by these risk factors. Factors that could cause or contribute to such differences include those factors discussed below. The risks and uncertainties described below are not the only ones we face. Additional risks not presently known to us or other factors not perceived by us to present significant risks to our business at this time also may impair our business operations.

Risks Related to our Financial Position and Need for Additional Capital

We have incurred significant losses since our inception. We expect to continue to incur significant expenses and operating losses for the foreseeable future and may never achieve or maintain profitability.

Since inception, we have incurred significant operating losses. Our net losses were $102.0 million for the year ended December 31, 2024 and $71.2 million for the year ended December 31, 2023. As of December 31, 2024, we had an accumulated deficit of $388.0 million. To date, we have not yet commercialized any products or generated any revenue from product sales and have financed our operations primarily with proceeds from sales of convertible preferred stock, offerings of common stock and pre-funded warrants and borrowings under our loan and security agreement with K2 HealthVentures LLC (the “Loan Agreement"). We have devoted substantially all of our financial resources and efforts to pursuing research and development of our product candidates. We are currently conducting clinical development of our lead product candidate, INZ-701, and have initiated Phase 1/2 clinical trials of adults with ENPP1 Deficiency and ABCC6 Deficiency, a Phase 1b ENERGY 1 clinical trial of infants with ENPP1 Deficiency, a pivotal ENERGY 3 clinical trial in pediatric patients with ENPP1 Deficiency, a Phase 1 clinical trial of patients with end-stage kidney disease ("ESKD") receiving hemodialysis, and an ADAPT long-term safety study in patients with ENPP1 and ABCC6 Deficiencies who have received INZ-701.

We expect to continue to incur significant expenses and operating losses for the foreseeable future. We anticipate that our expenses will increase substantially if and as we:

- conduct our ongoing Phase 1/2 clinical trials of INZ-701 for adults with ENPP1 and ABCC6 Deficiencies, our ongoing open label long-term safety trial of INZ-701 in patients with ENPP1 or ABCC6 Deficiencies who have received INZ-701 in an existing study, our ongoing Phase 1b clinical trial of INZ-701 for infants with ENPP1 Deficiency, our ongoing pivotal clinical trial of INZ-701 in infants, our ongoing pivotal trial of INZ-701 in pediatric patients with ENPP1 Deficiency, and our ongoing Phase 1 clinical trial of INZ-701 in patients with ESKD receiving hemodialysis;
- prepare for, initiate, and conduct our planned clinical trials of INZ-701 for patients with ENPP1 Deficiency;
- conduct research, preclinical testing, and clinical trials of INZ-701 for additional indications;
- conduct research, preclinical testing, and clinical trials of other product candidates;
- engage in regulatory interactions with the U.S. Food and Drug Administration ("FDA"), the European Medicines Agency ("EMA"), and other regulatory authorities;
- submit regulatory filings and seek marketing approval for INZ-701 or any other product candidate if it successfully completes clinical trials;
- scale up our manufacturing processes and capabilities;
- establish a sales, marketing, and distribution infrastructure to commercialize any product candidate for which we may obtain marketing approval;
- in-license or acquire additional technologies or product candidates;

- make any payments to Yale University ("Yale") under our license agreement or sponsored research agreement with Yale;

- maintain, expand, enforce, and protect our intellectual property portfolio;

- hire additional clinical, regulatory, quality control, scientific, and commercial personnel;

- add operational, financial, and management information systems and personnel, including personnel to support our research, product development, and planned future commercialization efforts and our operations as a public company; and

- make any principal and interest payments when due under the terms of the Loan Agreement.

Because of the numerous risks and uncertainties associated with pharmaceutical product development, we are unable to accurately predict the timing or amount of increased expenses or when, or if, we will be able to achieve profitability. Our expenses could increase beyond our expectations if, among other things:

- we are required by regulatory authorities in the United States, Europe, or other jurisdictions to perform trials or studies in addition to, or different than, those that we currently expect;

- there are any delays in establishing appropriate manufacturing arrangements for or completing the development of any of our product candidates; or

- there are any third-party challenges to our intellectual property or we need to defend against any intellectual property-related claim.

Even if we obtain marketing approval for and are successful in commercializing one or more of our product candidates, we expect to incur substantial additional research and development and other expenditures to develop and market additional product candidates or to expand the approved indications of any marketed product. We may encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may adversely affect our business. The size of our future net losses will depend, in part, on the rate of future growth of our expenses and our ability to generate revenue.

We have never generated revenue from product sales and may never achieve or maintain profitability.

We are still in the early stages of clinical development of our first product candidate, INZ-701, and expect that it will be a number of years, if ever, before we have a product candidate ready for commercialization. We have no products that are approved for commercial sale and may never be able to develop marketable products. To become and remain profitable, we must succeed in completing development of, obtaining marketing approval for and eventually commercializing, one or more products that generates significant revenue. The ability to achieve this success will require us to be effective in a range of challenging activities, including completing clinical development of INZ-701 for ENPP1 Deficiency, ABCC6 Deficiency, and calciphylaxis, completing research, preclinical testing, and clinical development of INZ-701 for additional indications or of other product candidates, scaling up our manufacturing processes and capabilities to support clinical trials of INZ-701 or of other product candidates we develop, obtaining marketing approval for INZ-701 or any other product candidates, and manufacturing, marketing and selling any products for which we may obtain marketing approval. We may never succeed in these activities and, even if we do, may never generate revenues that are significant enough to achieve profitability. For example, we have determined to prioritize activities to support the planned Biologics License Application ("BLA") filing for INZ-701 for our lead indication, ENPP1 Deficiency. Patients with ABCC6 Deficiency being treated in our ADAPT long-term extension study, our expanded access program, or under investigator-sponsored INDs will continue to receive treatment, but any future trials in ABCC6 Deficiency and calciphylaxis will be postponed.

Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would depress the value of our company and could impair our ability to raise capital, expand our business, maintain our research and development efforts, diversify our pipeline of product candidates or even continue our operations. A decline in the value of our company could also cause our stockholders to lose all or part of their investment.

We are heavily dependent on the success of our lead product candidate, INZ-701, which will require significant clinical testing before we can seek marketing approval and potentially launch commercial sales. If INZ-701 does not receive marketing approval or is not successfully commercialized, or if there is significant delay in doing so, our business will be harmed.

We have no products that are approved for commercial sale and may never be able to develop marketable products. Our business currently depends heavily on the successful development, marketing approval and commercialization of INZ-701. We expect that a substantial portion of our efforts and expenditures for the foreseeable future will be devoted to advancing INZ-701. We cannot be certain that INZ-701 will achieve success in ongoing or future clinical trials, receive marketing approval or be successfully commercialized. For example, we have determined to prioritize activities to support the planned BLA filing for INZ-701 for our lead indication, ENPP1 Deficiency. Patients with ABCC6 Deficiency being treated in our ADAPT long-term extension study, our expanded access program, or under investigator-sponsored INDs will continue to receive treatment, but any future trials in ABCC6 Deficiency and calciphylaxis will be postponed.

If we were required to discontinue development of INZ-701, or if INZ-701 does not receive marketing approval for one or more of the indications we pursue, fails to achieve significant market acceptance, or fails to receive adequate reimbursement, we would be delayed by many years in our ability to achieve profitability, if ever, and may not be able to generate sufficient revenue to continue our business.

We will need substantial additional funding. If we are unable to raise capital when needed, we could be forced to delay, reduce or eliminate our product development programs or commercialization efforts.

We expect our expenses may increase substantially in connection with our ongoing and planned activities, particularly as we conduct our ongoing clinical trials of INZ-701 for ENPP1 Deficiency and ABCC6 Deficiency and calciphylaxis and initiate our planned clinical trials of INZ-701 for ENPP1 Deficiency, continue research and development and initiate additional clinical trials of, and seek marketing approval for, INZ-701 and any other product candidates we develop. In addition, if we obtain marketing approval for INZ-701 or any other product candidate we develop, we expect to incur significant commercialization expenses related to product manufacturing, sales, marketing and distribution. Furthermore, we have incurred and will continue to incur additional costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital or obtain adequate funds when needed or on acceptable terms, we may be required to delay, limit, reduce or terminate our research and development programs or any future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves. In addition, attempting to secure additional financing may divert the time and attention of our management from day-to-day activities and distract from our research and development efforts.

Our future capital requirements will depend on many factors, including:

- the progress, costs, and results of our ongoing clinical trials of INZ-701 for ENPP1 Deficiency, ABCC6 Deficiency, calciphylaxis, and any future clinical development of INZ-701 for these indications;
- the scope, progress, costs, and results of research, preclinical testing, and clinical trials of INZ-701 for additional indications;
- the number of and development requirements for additional indications for INZ-701 or for any other product candidates we develop;
- our ability to scale up our manufacturing processes and capabilities;
- our ability to execute on our global development strategy;
- the costs, timing, and outcome of regulatory review of INZ-701 and any other product candidates we develop;
- potential changes in the regulatory environment and enforcement rules;
- our ability to establish and maintain strategic collaborations, licensing, or other arrangements and the financial terms of such arrangements;
- the payment of license fees and other costs of our technology license arrangements;

- the extent of our debt service obligations and our ability, if desired, to refinance any of our existing debt on terms that are more favorable to us;

- the costs and timing of future commercialization activities, including product manufacturing, sales, marketing, and distribution, for INZ-701 and any other product candidates we develop for which we may receive marketing approval;

- the amount and timing of revenue, if any, received from commercial sales of INZ-701 and any other product candidates we develop for which we receive marketing approval;

- potential changes in pharmaceutical pricing and reimbursement infrastructure;

- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property and proprietary rights and defending any intellectual property-related claims; and

- the extent to which we in-license or acquire additional technologies or product candidates.

As of December 31, 2024, we had cash, cash equivalents, and short-term investments of approximately $113.1 million, and we had $45.0 million of outstanding principal indebtedness under our Loan Agreement. We believe that our cash, cash equivalents, and short-term investments as of December 31, 2024, along with the anticipated cost savings from our recent strategic prioritization, will enable us to fund our operating expenses and capital expenditures into the first quarter of 2026. Since our cash, cash equivalents and short-term investments as of December 31, 2024 are not sufficient to fund our operations for at least the next twelve months from the date of issuance of the consolidated financial statements included elsewhere in this Annual Report on Form 10-K, there is substantial doubt about our ability to continue as a going concern. Our future viability is dependent on our ability to raise additional capital to finance our operations. We expect to finance our operations through potential public or private equity financings, debt financings, collaboration agreements or other capital sources. Our inability to raise capital as and when needed could have a negative impact on our financial condition and ability to pursue our business strategies. There can be no assurance that our current operating plan will be achieved or that additional funding will be available on terms acceptable to us, or at all. We have based our assessment on assumptions that may prove to be wrong, and we could use our capital resources sooner than we currently expect. See "Going Concern" in Note 1 to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K. In addition, changing circumstances could cause us to consume capital significantly faster than we currently anticipate, and we may need to spend more than currently expected because of circumstances beyond our control. As a result, we could deplete our capital resources sooner than we currently expect. In addition, because the successful development of INZ-701 and any other product candidates that we pursue is highly uncertain, at this time we cannot reasonably estimate or know the nature, timing and costs of the efforts that will be necessary to complete the development of any product candidate.

Identifying potential product candidates and conducting preclinical testing and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve product sales. In addition, our product candidates, if approved, may not achieve commercial success. We will not generate commercial revenues unless and until we can achieve sales of products, which we do not anticipate for a number of years, if at all. Accordingly, we will need to obtain substantial additional financing to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms, or at all. Our ability to raise additional funds may be adversely impacted by general economic conditions, both inside and outside the U.S., including disruptions to, and instability and volatility in, the credit and financial markets in the U.S. and worldwide, heightened inflation, interest rate and currency rate fluctuations, and economic slowdown or recession as well as concerns related to health epidemics, and geopolitical events, including civil or political unrest. In addition, market instability and volatility, high levels of inflation and interest rate fluctuations may increase our cost of financing or restrict our access to potential sources of future liquidity. Alternatively, we may seek additional capital due to favorable market conditions or strategic considerations, even if we believe we have sufficient funds for our current or future operating plans.

We have a loan agreement that requires us to meet specified funding conditions for future draw downs and operating covenants and places restrictions on our operating and financial flexibility.

We currently have $45.0 million of outstanding principal indebtedness, and we may in the future draw down up to $25.0 million of additional principal indebtedness under the Loan Agreement, subject to specified conditions and lender discretion. Our ability to draw down an additional tranche commitment of $25.0 million is subject to use of proceeds limitations and the lender's consent in its discretion. As security for its obligations under the Loan Agreement, we granted the lenders a first priority security interest on substantially all of our assets (other than intellectual property), subject to certain exceptions. Because of the security

interest, the lender's rights to repayment from a liquidation of the assets subject to that security interest would be senior to the rights of other creditors.

The Loan Agreement contains customary representations and warranties, events of default and affirmative and negative covenants, including covenants that limit or restrict our ability to, among other things, dispose of assets, make changes to our business, management, ownership or business locations, merge or consolidate, incur additional indebtedness, incur additional liens, pay dividends or other distributions or repurchase equity, make investments, and enter into certain transactions with affiliates, in each case subject to certain exceptions.

We intend to satisfy our current and future debt service obligations with our existing cash and cash equivalents. However, we may not have sufficient funds or may be unable to arrange for additional financing to pay the amounts due under our outstanding debt. Funds from external sources may not be available on acceptable terms, if at all. In addition, a failure to comply with the conditions of our Loan Agreement, including a breach of any covenant, could result in an event of default thereunder. In the event of an acceleration of amounts due under our Loan Agreement as a result of an event of default, including upon the occurrence of an event or circumstance that could be expected to have a material adverse effect on our business, operations, properties, assets or financial condition or a failure to pay any amount due, we may not have sufficient funds or may be unable to arrange for additional financing to repay our indebtedness or to make any accelerated payments, and the lenders could seek to enforce security interests in the collateral securing such indebtedness. Any declaration by the lenders of an event of default could significantly harm our business and prospects and could cause the price of our common stock to decline.

In addition, our outstanding debt combined with our other financial obligations and contractual commitments could have significant adverse consequences, including:

- restricting the amount of our cash resources, after satisfaction of our debt service obligations, available to fund working capital, research and development efforts and other general corporate purposes;
- limiting our flexibility in planning for, or reacting to, changes in our business and our industry; and
- placing us at a competitive disadvantage compared to our competitors that have less debt or better debt servicing options.

Raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our technologies or product candidates.

Until such time, if ever, as we can generate substantial revenues from product sales, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances and marketing, distribution or licensing arrangements. We do not have any committed external source of funds, other than under our Loan Agreement. Our ability to borrow under our Loan Agreement is subject to our satisfaction of specified conditions and lender discretion. To the extent that we raise additional capital through the sale of equity or convertible debt securities or to the extent the lenders under our Loan Agreement elect to convert a portion of their outstanding principal into shares of our common stock or elect to purchase up to $5.0 million of shares of our common stock pursuant to the Loan Agreement, our stockholders' ownership interests will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect our stockholders' rights as common stockholders. Debt financing and equity financing, if available, may involve agreements that include covenants limiting or restricting our operations and ability to take specific actions, such as incurring additional indebtedness, making acquisitions, engaging in acquisition, merger or collaboration transactions, selling or licensing our assets, making capital expenditures, redeeming our stock, making certain investments or declaring dividends. The covenants under our Loan Agreement and the pledge of our assets as collateral limit our ability to take specific actions, including obtaining additional debt financing. If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or grant licenses on terms that may not be favorable to us.

Our limited operating history may make it difficult for stockholders to evaluate the success of our business to date and to assess our future viability.

Our operations to date have been limited to organizing and staffing our company, business planning, raising capital, securing intellectual property rights, conducting research and development activities, conducting preclinical studies and clinical trials, establishing arrangements for the manufacture of INZ-701 and longer-term planning for potential commercialization. As a company, we have limited experience in clinical development, having only advanced INZ-701 into the early stages of clinical development. Our prospects must be considered in light of the uncertainties, risks, expenses and difficulties frequently encountered by companies in their early stages of operations. We have not yet demonstrated our ability to successfully complete any clinical trials, obtain marketing approvals, manufacture a commercial scale product or arrange for a third party to do so on our behalf, or conduct sales, marketing, and

distribution activities necessary for successful product commercialization. Consequently, any predictions stockholders make about our future success or viability may not be as accurate as they could be if we had a longer operating history or a history of successfully developing, obtaining marketing approval for and commercializing products.

In addition, as our business grows, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown obstacles. We will need to transition at some point from a company with a research and development focus to a company capable of supporting commercial activities. We may not be successful in such a transition.

As we continue to build our business, we expect our financial condition and operating results to fluctuate significantly from quarter to quarter and year to year due to a variety of factors, many of which are beyond our control. Accordingly, stockholders should not rely upon the results of any quarterly or annual periods as indications of future operating performance.

We hold a portion of our cash and cash equivalents that we use to meet our working capital and operating expense needs in deposit accounts, and our liquidity and operations could be adversely affected if a financial institution holding such funds fails.

We hold a portion of our cash and cash equivalents that we use to meet our working capital and operating expense needs in deposit accounts at multiple financial institutions. The balance held in these accounts typically exceeds the Federal Deposit Insurance Corporation ("FDIC") standard deposit insurance limit of $250,000 per depositor and per institution. If a financial institution in which we hold such funds fails or is subject to significant adverse conditions in the financial or credit markets, we could be subject to a risk of loss of all or a portion of such uninsured funds or be subject to a delay in accessing all or a portion of our funds. Any such loss or lack of access to these funds could adversely impact our short-term liquidity and ability to meet our operating expense obligations, including payroll obligations.

For example, on March 10, 2023, Silicon Valley Bank ("SVB") was closed, and the FDIC was appointed receiver for the bank. The FDIC created a successor bridge bank, and all deposits of SVB were transferred to the bridge bank under a systemic risk exception approved by the United States Department of the Treasury, the Federal Reserve, and the FDIC. Access to and availability of deposits was delayed, though ultimately, in that case, restored. If financial institutions in which we hold funds for working capital and operating expenses were to fail, we cannot provide any assurances that the applicable governmental agencies would take action to protect our uninsured deposits or make deposits available in a similar manner.

We also maintain investment accounts with one or more financial institutions in which we hold our investments and, if access to the funds we use for working capital and operating expenses is impaired, we may not be able to open new operating accounts or to sell investments or transfer funds from our investment accounts to new operating accounts on a timely basis sufficient to meet our operating expense obligations. In addition, to the extent that the financial institutions with which we hold securities fail or are associated with banks that fail, there may be delays or other access restrictions with respect to such securities, similar to those described above for deposit accounts.

Changes in tax laws or in their implementation may adversely affect our business and financial condition.

Changes in tax law may adversely affect our business or financial condition. The Tax Cuts and Jobs Act (the "TCJA"), as amended by the Coronavirus Aid, Relief, and Economic Security Act ("CARES Act") significantly reformed the Internal Revenue Code of 1986, as amended ("the Code"). The TCJA, among other things, contains significant changes to corporate taxation, including a reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21% and the limitation of the deduction for net operating losses ("NOLs") to 80% of current-year taxable income for losses arising in taxable years beginning after December 31, 2017 (though any such NOLs may be carried forward indefinitely). In addition, beginning in 2022, the TCJA requires corporations to capitalize and amortize research and development expenditures over five years for domestic expenditures and fifteen years for foreign expenditures.

In addition to the CARES Act, as part of Congress’s response to the COVID-19 pandemic, economic relief legislation was enacted in 2020 and 2021 containing tax provisions. The Inflation Reduction Act ("IRA") was also signed into law in August 2022. The IRA introduced new tax provisions, including a 1% excise tax imposed on certain stock repurchases by publicly traded corporations. The 1% excise tax generally applies to any acquisition by the publicly traded corporation (or certain of its affiliates) of stock of the publicly traded corporation in exchange for money or other property (other than stock of the corporation itself), subject to a de minimis exception. Thus, the excise tax could apply to certain transactions that are not traditional stock repurchases. Regulatory guidance under the IRA, the TCJA, and such additional legislation is and continues to be forthcoming, and such guidance could

ultimately increase or lessen impact of these laws on our business and financial condition. In addition, it is uncertain if and to what extent various states will conform to the IRA, the TCJA, and additional tax legislation.

Our ability to use our NOLs and research and development tax credit carryforwards to offset future taxable income may be subject to certain limitations.

We have a history of cumulative losses and anticipate that we will continue to incur significant losses in the foreseeable future. As a result, we do not know whether or when we will generate taxable income necessary to utilize our NOLs or research and development tax credit carryforwards. As of December 31, 2024, we had federal and state NOL carryforwards of $201.3 million and $167.9 million, respectively, and federal and state research and development tax credit carryforwards totaling $28.1 million.

In general, under Sections 382 and 383 of the Code and corresponding provisions of state law, a corporation that undergoes an "ownership change," generally defined as a greater than 50 percentage point change (by value) in its equity ownership by certain stockholders over a three year period, is subject to limitations on its ability to utilize its pre-change NOLs and research and development tax credit carryforwards to offset future taxable income. We have not conducted a study to assess whether any such ownership changes have occurred. We may have experienced such ownership changes in the past and may experience such ownership changes in the future (which may be outside our control). As a result, if and to the extent we earn net taxable income, our ability to use our pre-change NOLs and research and development tax credit carryforwards to offset such taxable income may be subject to limitations.

Risks Related to Research and Development of our Product Candidates

We are early in our clinical development efforts. If we are unable to commercialize INZ-701 or experience significant delays in doing so, our business will be materially harmed.

We are early in our clinical development efforts and have recently determined to prioritize activities to support the planned BLA filing for INZ-701 for our lead indication, ENPP1 Deficiency. Patients with ABCC6 Deficiency being treated in our ADAPT long-term extension study, our expanded access program, or under investigator-sponsored INDs will continue to receive treatment. Any future trials in ABCC6 Deficiency and calciphylaxis will be postponed.

Our ability to generate revenues from product sales, which we do not expect will occur for a number of years, if ever, will depend heavily on the successful development, marketing approval and eventual commercialization of INZ-701 or other product candidates we develop, which may never occur. The success of INZ-701 and any other product candidate we develop will depend on several factors, including the following:

- successfully completing preclinical studies and initiating clinical trials;
- successfully enrolling patients in and completing clinical trials;
- scaling up manufacturing processes and capabilities to support our clinical trials of our product candidates;
- applying for and receiving marketing approvals from applicable regulatory authorities;
- obtaining and maintaining intellectual property protection and regulatory exclusivity for our product candidates;
- making arrangements for commercial manufacturing capabilities;
- establishing sales, marketing and distribution capabilities and launching commercial sales of our product candidates, if and when approved, whether alone or in collaboration with others;
- acceptance of our product candidates, if and when approved, by patients, the medical community and third-party payors;
- effectively competing with other therapies;
- obtaining and maintaining coverage, adequate pricing and adequate reimbursement from third-party payors, including government payors;

- maintaining, enforcing, defending and protecting our rights in our intellectual property portfolio;
- not infringing, misappropriating or otherwise violating others' intellectual property or proprietary rights; and
- maintaining a continued acceptable safety profile of our products following receipt of any marketing approvals.

If we do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully develop and commercialize INZ-701 or any other product candidate we develop, which would materially harm our business. As a company, we have limited experience in clinical development. Any predictions about the future success or viability of INZ-701 or any product candidates we develop may not be as accurate as they could be if we had a history of conducting clinical trials.

Drug development involves a lengthy and expensive process, with an uncertain outcome. The results of preclinical studies and early clinical trials may not be predictive of future results. We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of INZ-701 or any other product candidate. If our clinical trials do not meet safety or efficacy endpoints, or if we experience significant delays in clinical trials, our ability to commercialize INZ-701 or any other product candidates we develop and our financial position will be impaired.

We have limited experience in clinical development. The risk of failure for INZ-701 is high. It is impossible to predict when or if INZ-701 or any other product candidate that we develop will prove effective or safe in humans or will receive marketing approval. Before obtaining marketing approval from regulatory authorities for the sale of INZ-701 or any other product candidate we develop, we must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates in humans. Clinical trials may fail to demonstrate that INZ-701 or any other product candidates we develop is safe for humans and effective for indicated uses. As our clinical trials may advance to self- and/or home-administration for select patients, we may face difficulties in patient compliance or see increases in user error. Even if the clinical trials are successful, changes in marketing approval policies during the development period, changes in or the enactment or promulgation of additional statutes, regulations or guidance or changes in regulatory review for each submitted product application may cause delays in the approval or rejection of an application.

In order to obtain regulatory approval to market a new biological product, we must demonstrate proof of safety, purity and potency or efficacy in humans. To satisfy these requirements, we will have to conduct adequate and well-controlled clinical trials. Before we can commence clinical trials for a product candidate, we must complete extensive preclinical testing and studies that support our applications to regulatory authorities in North America and Europe to allow us to initiate clinical development. We cannot be certain of the timely completion or outcome of our preclinical testing and studies and cannot predict if the outcome of our preclinical testing and studies will ultimately support the further development of our current or future product candidates or whether regulatory authorities will accept our proposed clinical programs. As a result, we may not be able to submit applications to initiate clinical development of the other product candidates we develop on the timelines we expect, if at all, and the submission of these applications may not result in regulatory authorities allowing clinical trials to begin. For example, in August 2020, our IND for INZ-701 for the treatment of ENPP1 Deficiency was placed on clinical hold, until we submitted our final study report for our three-month toxicology studies in mice and non-human primates. Furthermore, product candidates are subject to continued preclinical safety studies, which may be conducted concurrently with our clinical testing. The outcomes of these safety studies may delay the launch of or enrollment in future clinical trials and could impact our ability to continue to conduct our clinical trials.

Clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to the outcome. We cannot guarantee that any of our clinical trials will be conducted as planned or completed on schedule, or at all. A failure of one or more clinical trials can occur at any stage of testing, which may result from a multitude of factors, including, among other things, flaws in study design, dose selection issues, placebo effects, patient enrollment criteria and failure to demonstrate favorable safety or efficacy traits. The outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and preliminary or interim results of a clinical trial do not necessarily predict final results. For example, our product candidates may fail to show the desired safety and efficacy in clinical development despite positive results in preclinical studies or having successfully advanced through initial clinical trials. As a result, we cannot assure stockholders that any clinical trials that we may conduct will demonstrate consistent or adequate efficacy and safety to support marketing approval.

Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials even after achieving promising results in preclinical testing and earlier-stage clinical trials, and we cannot be certain that we will not face similar setbacks. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their products. Furthermore, the failure of any of our product candidates to demonstrate safety and efficacy in any clinical trial could negatively impact the perception of our other product candidates or cause

regulatory authorities to require additional testing before approving any of our product candidates. In addition, results from compassionate use protocols or investigator-sponsored trials may not be confirmed in company-sponsored trials and/or may negatively impact the prospects for our programs.

We may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent our ability to receive marketing approval or commercialize any product candidates that we develop, including:

- regulators or institutional review boards ("IRBs"), may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site or at all;
- we may experience delays in reaching, or fail to reach, agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites;
- regulators may determine that the planned design of our clinical trials is flawed or inadequate;
- clinical trials of our product candidates may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon product development programs;
- we may be unable to establish clinical endpoints that applicable regulatory authorities consider clinically meaningful, or, if we seek accelerated approval, biomarker efficacy endpoints that applicable regulatory authorities consider likely to predict clinical benefit;
- preclinical testing may produce results based on which we may decide, or regulators may require us, to conduct additional preclinical studies before we proceed with certain clinical trials, limit the scope of our clinical trials, halt ongoing clinical trials or abandon product development programs;
- the number of patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate or participants may drop out of these clinical trials at a higher rate than we anticipate;
- third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- we may decide, or regulators or IRBs may require us, to suspend or terminate clinical trials of our product candidates for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks;
- regulators or IRBs may require us to perform additional or unanticipated clinical trials to obtain approval or we may be subject to additional post-marketing testing requirements to maintain marketing approval;
- regulators may revise the requirements for approving our product candidates, or such requirements may not be as we anticipate;
- the cost of clinical trials of our product candidates may be greater than we anticipate;
- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate;
- our product candidates may have undesirable side effects or other unexpected characteristics, causing us or our clinical investigators, regulators or IRBs to suspend or terminate the trials;
- regulators may withdraw their approval of a product or impose restrictions on its distribution.

If we are required to conduct additional clinical trials or other testing of our product candidates beyond those that we currently contemplate, if we are unable to successfully complete clinical trials of our product candidates or other testing, if the results

of these trials or tests are not positive or are only modestly positive, if there are safety concerns or if we determine that the observed safety or efficacy profile would not be competitive in the marketplace, we may:

- incur unplanned costs;
- be delayed in obtaining marketing approval for our product candidates;
- not obtain marketing approval at all;
- obtain marketing approval in some countries and not in others;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or safety warnings;
- be subject to additional post-marketing testing requirements; or
- have the product removed from the market after obtaining marketing approval.

Our product development costs will also increase if we experience delays in preclinical studies or clinical trials or in obtaining marketing approvals. We do not know whether any of our preclinical studies or clinical trials will begin as planned, will need to be restructured or will be completed on schedule, or at all. We may also determine to change the design or protocol of one or more of our clinical trials, including to add additional patients or arms, which could result in increased costs and expenses or delays. Significant preclinical study or clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do and impair our ability to successfully commercialize our product candidates and may harm our business and results of operations.

In addition, the FDA's and other regulatory authorities' policies with respect to clinical trials may change and additional government regulations may be enacted. For example, in December 2022, with the passage of Food and Drug Omnibus Reform Act ("FDORA"), Congress required sponsors to develop and submit a diversity action plan for each Phase 3 clinical trial or any other "pivotal study" of a new drug or biological product. These plans are meant to encourage the enrollment of more diverse patient populations in late-stage clinical trials of FDA-regulated products. In June 2024, as mandated by FDORA, the FDA issued draft guidance outlining the general requirements for diversity action plans. Unlike most guidance documents issued by the FDA, the diversity action plan guidance when finalized will have the force of law because FDORA specifically dictates that the form and manner for submission of the diversity action plans are specified in FDA guidance. In January 2025, in response to an Executive Order issued by President Trump on Diversity, Equity and Inclusion programs, the FDA removed this draft guidance from its website. This action raises questions about the applicability of statutory obligations to submit diversity action plans and the agency's current thinking on best practices for clinical development.

Similarly, the regulatory landscape related to clinical trials in the European Union ("EU") recently evolved. The EU Clinical Trials Regulation ("CTR") became effective on January 31, 2022. The CTR aims to simplify and streamline the authorization, conduct, and transparency of clinical trials in the EU. We have not previously secured authorization to conduct clinical studies in the EU pursuant to the CTR and, accordingly, there is a risk that we may be delayed in commencing any such studies. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies governing clinical trials, our development plans may be impacted.

Because we are developing INZ-701 for the treatment of diseases in which there is little clinical experience and, in some cases, using new endpoints or methodologies, the FDA or other regulatory authorities may not consider the endpoints of our clinical trials to predict or provide clinically meaningful results.

There are currently no therapies approved to treat ENPP1 or ABCC6 Deficiencies or calciphylaxis, and there may be no therapies approved to treat the underlying causes of other diseases that we attempt to address or may address in the future. As a result, the design and conduct of clinical trials of product candidates for the treatment of these diseases may take longer, be more costly or be less effective as a result of the novelty of development in these diseases. In some cases, we may use new or novel endpoints or methodologies, such as change in plasma PPi, which we are evaluating in our Phase 1/2 clinical trials of INZ-701 in adults with ENPP1 Deficiency and ABCC6 Deficiency, our ENERGY 3 trial of INZ-701, and our ENERGY 2 trial of INZ-701, and regulatory

authorities may not consider the endpoints of our clinical trials to predict or provide clinically meaningful results. Any such regulatory authority may require evaluation of additional or different clinical endpoints in our clinical trials or ultimately determine that these clinical endpoints do not support marketing approval. For example, based on recommendations from the FDA, the sole primary endpoint of changes in plasma PPi in our ENERGY 3 trial of INZ-701 in the United States should be supported by consistent trends in appropriate secondary endpoints. In addition, if we are required to use additional or different clinical endpoints by regulatory authorities, INZ-701 may not achieve or meet such clinical endpoints in our clinical trials.

Even if a regulatory authority finds our clinical trial success criteria to be sufficiently validated and clinically meaningful, we may not achieve the pre-specified endpoint to a degree of statistical significance in any pivotal or other clinical trials we may conduct for our product candidates. Further, even if we do achieve the pre-specified criteria, our trials may produce results that are unpredictable or inconsistent with the results of other efficacy endpoints in the trial. Regulatory authorities also could give overriding weight to other efficacy endpoints over a primary endpoint even if we achieve statistically significant results on that primary endpoint, if we do not do so on our secondary efficacy endpoints. Regulatory authorities also weigh the benefits of a product against its risks and may view the efficacy results in the context of safety as not being supportive of approval.

If we experience delays or difficulties in the enrollment of patients in our clinical trials for INZ-701 or any other product candidate we develop, our receipt of necessary marketing approvals could be delayed or prevented.

Identifying and qualifying patients to participate in clinical trials for INZ-701 and any other product candidate we develop is critical to our success. Successful and timely completion of clinical trials will require that we enroll a sufficient number of patients who remain in the trial until its conclusion. Because we primarily focus on rare diseases, we may have difficulty enrolling a sufficient number of eligible patients in future clinical trials of INZ-701 or any other product candidate. ENPP1 Deficiency is estimated to occur in approximately one in 64,000 pregnancies worldwide, and we believe there are approximately 37,000 patients in addressable markets worldwide with ENPP1 Deficiency. In North America, the EU, Japan, and Brazil we believe there are approximately 9,400 patients with ENPP1 Deficiency. ABCC6 Deficiency is estimated to affect approximately one per 25,000 to 50,000 individuals, and we believe there are more than 67,000 patients in addressable markets worldwide with ABCC6 Deficiency. In North America, the EU, Japan, and Brazil, we believe there are approximately 24,400 patients with ABCC6 Deficiency. The estimated incidence rate of calciphylaxis is approximately 3.5 per 1,000 patients with ESKD. In North America, the EU, Japan, and Brazil, we believe there are approximately 23,800 patients with ESKD receiving hemodialysis. We may not be able to initiate or continue clinical trials for our product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or similar regulatory authorities outside of the United States. We cannot predict how successful we will be at enrolling subjects in future clinical trials. Patient enrollment is affected by a variety of other factors, including:

- the prevalence and severity of the disease under investigation;
- the eligibility criteria for the trial in question and the process for identifying patients;
- the perceived risks and benefits of the product candidate under trial;
- the requirements of the trial protocols;
- the availability of existing treatments for the indications for which we are conducting clinical trials;
- the ability to recruit clinical trial investigators with the appropriate competencies and experience;
- the efforts to facilitate timely enrollment in clinical trials;
- the ability to identify specific patient populations based on specific genetic mutations or other factors;
- the challenges in recruiting critically ill infants, and the extensive logistical support and transportation required;
- the patient referral practices of physicians;
- the ability to monitor patients adequately during and after treatment;
- our ability to obtain and maintain patient consents;
- the proximity and availability of clinical trial sites for prospective patients;

- the conduct of clinical trials by competitors for product candidates that treat the same indications or address the same patient populations as our product candidates;

- the cost to, or lack of adequate compensation for, prospective patients; and

- the impact of any health epidemic.

Any inability to locate and enroll a sufficient number of patients for our clinical trials would result in significant delays, could require us to abandon one or more clinical trials altogether and could delay or prevent our receipt of necessary regulatory approvals. Enrollment delays in our clinical trials may result in increased development costs for our product candidates, which would cause the value of our company to decline and limit our ability to obtain additional financing.

If serious adverse events, undesirable side effects or unexpected characteristics are identified during the development of INZ-701 or any other product candidate we may develop, we may need to abandon or limit our further clinical development of those product candidates.

If INZ-701 or any other product candidate we develop is associated with serious adverse events or undesirable side effects in clinical trials or have characteristics that are unexpected in clinical trials or preclinical testing, we may need to abandon development of such product candidate or limit development to more narrow uses or subpopulations in which the serious adverse events, undesirable side effects or unexpected characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. In pharmaceutical development, many compounds that initially show promise in early-stage or clinical testing are later found to cause side effects that delay or prevent further development of the compound.

Additionally, if results of our clinical trials reveal undesirable side effects, we, regulatory authorities or the IRBs at the institutions in which our studies are conducted could suspend or terminate our clinical trials, regulatory authorities could order us to cease clinical trials or deny approval of our product candidates for any or all targeted indications or we could be forced to materially modify the design of our clinical trials. Treatment-related side effects could also affect patient recruitment or the ability of enrolled patients to complete any of our clinical trials. For example, one patient from the highest dose cohort (1.8 mg/kg) of our ongoing clinical trial of INZ-701 in adults with ABCC6 Deficiency was withdrawn from the Phase 1 portion of the trial at day 18 due to a moderate adverse event (erythema/urticaria) related to INZ-701. In addition, any treatment-related side effects could result in potential liability claims and may not be appropriately recognized or managed by the treating medical staff.

If we elect or are forced to suspend or terminate any clinical trial of our product candidates, the commercial prospects of such product candidate will be harmed, and our ability to generate revenues from sales of such product candidate will be delayed or eliminated. Any of these occurrences could materially harm our business.

Interim topline and preliminary results from our clinical trials that we announce or publish from time to time may change as more participant data become available and are subject to audit and verification procedures, which could result in material changes in the final data.

From time to time, we may publish interim topline or preliminary results from our clinical trials. Interim results from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as participant enrollment continues or more participant data become available. For example, the interim biomarker, safety, pharmacokinetic, pharmacodynamic, and/or exploratory efficacy data that we have disclosed in connection with our ongoing Phase 1/2 clinical trials of INZ-701 in adults with ENPP1 and ABCC6 Deficiencies, our ongoing Phase 1b clinical trial of INZ-701 for infants with ENPP1 Deficiency and our ongoing Phase 1 clinical trial of INZ-701 in patients with ESKD receiving hemodialysis may not be indicative of the full results of those trials obtained upon completion. We also make assumptions, estimations, calculations, and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully evaluate all data. Preliminary or topline results also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, interim and preliminary data should be viewed with caution until the final data are available. Adverse differences between preliminary or interim data and final data could be material and could significantly harm our reputation and business prospects and may cause the trading price of our common stock to fluctuate significantly.

In some instances, there can be significant variability in safety or efficacy results between different clinical trials of the same product candidate due to numerous factors, including changes in trial procedures set forth in protocols, differences in the size and type of the patient populations, changes in and adherence to the dosing regimen and other clinical trial protocols, and the rate of dropout among clinical trial participants.

If any of our product candidates receives marketing approval and we, or others, later discover that the drug is less effective than previously believed or causes undesirable side effects that were not previously identified, our ability to market the drug could be compromised.

Clinical trials are conducted in carefully defined subsets of patients who have agreed to enter into clinical trials. Consequently, it is possible that our ongoing, planned or future clinical trials may indicate an apparent positive effect of a product candidate that is greater than the actual positive effect, if any, or alternatively fail to identify undesirable side effects. If one or more of our product candidates receives marketing approval, and we, or others, later discover that they are less effective than previously believed, or cause undesirable side effects, a number of potentially significant negative consequences could result, including:

- withdrawal or limitation by regulatory authorities of approvals of such product;
- seizure of the product by regulatory authorities;
- recall of the product;
- restrictions on the marketing of the product or the manufacturing process for any component thereof;
- requirement by regulatory authorities of additional warnings on the label;
- requirement that we implement a risk evaluation and mitigation strategy or create a medication guide outlining the risks of such side effects for distribution to patients;
- commitment to expensive post-marketing studies as a prerequisite of approval by regulatory authorities of such product;
- the product may become less competitive;
- initiation of regulatory investigations and government enforcement actions;
- initiation of legal action against us to hold us liable for harm caused to patients; and
- harm to our reputation and resulting harm to physician or patient acceptance of our products.

Any of these events could prevent us from achieving or maintaining market acceptance of a particular product candidate, if approved, and could significantly harm our business, financial condition, and results of operations.

We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and managerial resources, we focus on research programs and product candidates that we identify for specific indications. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate. Failure to allocate resources or capitalize on strategies in a successful manner will have an adverse impact on our business.

We are conducting clinical trials for our product candidates at sites outside the United States, and the FDA may not accept data from clinical trials conducted in such locations.

We are conducting clinical trials of INZ-701 outside the United States, including our ongoing Phase 1/2 clinical trial of INZ-701 for adults with ENPP1 Deficiency in Europe and Canada, our ongoing Phase 1/2 clinical trial of INZ-701 for adults with ABCC6 Deficiency in Europe, our ongoing Phase 1b clinical trial of INZ-701 for infants with ENPP1 Deficiency in Europe, and our ongoing global pivotal ENERGY 3 trial, and we expect to conduct clinical trials at other sites outside the United States in the future. Although the FDA may accept data from clinical trials conducted outside the United States, acceptance of these data is subject to conditions imposed by the FDA. For example, in cases where data from foreign clinical trials are intended to serve as the sole basis for marketing approval in the U.S., the FDA will generally not approve the application on the basis of foreign data alone unless (1) the data are applicable to the U.S. population and U.S. medical practice; (2) the trials were performed by clinical investigators of recognized competence and pursuant to GCP regulations; and (3) the data may be considered valid without the need for an on-site inspection by the FDA, or if the FDA considers such inspection to be necessary, the FDA is able to validate the data through an on-site inspection or other appropriate means.

In addition, even where the foreign study data are not intended to serve as the sole basis for approval, the FDA will not accept the data as support for an application for marketing approval unless the study is well-designed and well-conducted in accordance with GCP requirements and the FDA is able to validate the data from the study through an onsite inspection if deemed necessary. Thus, our clinical trial outside the U.S. must be well designed and conducted and be performed by qualified investigators in accordance with ethical principles. The trial population must also adequately represent the U.S. population, and the data must be applicable to the U.S. population and U.S. medical practice in ways that the FDA deems clinically meaningful. In addition, while these clinical trials are subject to the applicable local laws, FDA acceptance of the data will depend on its determination that the trials also complied with all applicable U.S. laws and regulations. If the FDA does not accept the data from any trial that we conduct outside the United States, it would likely result in the need for additional trials, which would be costly and time-consuming and could delay or permanently halt our development of the applicable product candidates.

Many foreign regulatory authorities have similar approval requirements. In addition, such foreign trials would be subject to the applicable local laws of the foreign jurisdictions where the trials are conducted. There can be no assurance that the FDA or any comparable foreign regulatory authority will accept data from trials conducted outside of the U.S. or the applicable jurisdiction. If the FDA or any comparable foreign regulatory authority does not accept such data, it would result in the need for additional trials, which could be costly and time-consuming, and which may result in current or future product candidates that we may develop not receiving approval for commercialization in the applicable jurisdiction.

In addition, there are risks inherent in conducting clinical trials in multiple jurisdictions, inside and outside of the United States, such as:

- regulatory and administrative requirements of the jurisdiction where the trial is conducted that could burden or limit our ability to conduct our clinical trials;
- foreign exchange rate fluctuations;
- manufacturing, customs, shipment and storage requirements;
- cultural differences in medical practice and clinical research;
- the risk that the patient populations in such trials are not considered representative as compared to the patient population in the target markets where approval is being sought;
- diminished protection of intellectual property in some countries; and
- interruptions or delays in our trials resulting from geopolitical events, such as war or terrorism.

Because gene therapy is novel and the regulatory landscape that governs any product candidates we may develop is uncertain and may change, we cannot predict the time and cost of obtaining regulatory approval, if we receive it at all, for any product candidates we may develop.

The regulatory requirements that will govern any novel gene therapy product candidates we develop are not entirely clear and may change. Within the broader genetic medicine field, we are aware of a limited number of gene therapy products that have

received marketing authorization from the FDA and the EMA. Even with respect to more established products that fit into the categories of gene therapies or cell therapies, the regulatory landscape is still developing. Regulatory requirements governing gene therapy products and cell therapy products have changed frequently and will likely continue to change in the future. Moreover, there is substantial, and sometimes uncoordinated, overlap in those responsible for regulation of existing gene therapy products and cell therapy products. For example, in the United States, the FDA has established the Office of Therapeutic Products within its Center for Biologics Evaluation and Research ("CBER") to consolidate the review of gene therapy and related products, and the Cellular, Tissue and Gene Therapies Advisory Committee to advise CBER on its review. Gene therapy clinical trials are also subject to review and oversight by an institutional biosafety committee ("IBC"), a local institutional committee that reviews and oversees basic and clinical research conducted at the institution participating in the clinical trial. Gene therapy clinical trials conducted at institutions that receive funding for recombinant DNA research from the National Institutes of Health, or NIH, are also subject to review by the NIH Office of Biotechnology Activities' Recombinant DNA Advisory Committee. Although the FDA decides whether individual gene therapy protocols may proceed, the review process and determinations of other reviewing bodies can impede or delay the initiation of a clinical trial, even if the FDA has reviewed the trial and approved its initiation. The same applies in the European Union. The EMA's Committee for Advanced Therapies ("CAT") is responsible for assessing the quality, safety, and efficacy of advanced-therapy medicinal products. The role of the CAT is to prepare a draft opinion on an application for marketing authorization for a gene therapy medicinal candidate that is submitted to the EMA. In the European Union, the development and evaluation of a gene therapy medicinal product must be considered in the context of the relevant European Union guidelines. The EMA may issue new guidelines concerning the development and marketing authorization for gene therapy medicinal products and require that we comply with these new guidelines. As a result, the procedures and standards applied to gene therapy products and cell therapy products may be applied to any gene therapy product candidates we may develop, but that remains uncertain at this point.

Adverse public perception of genetic medicine, and gene therapy in particular, may negatively impact regulatory approval of, or demand for, our potential products.

The clinical and commercial success of our potential products will depend in part on public acceptance of the use of gene therapy for the prevention or treatment of human diseases. Public attitudes may be influenced by claims that gene therapy is unsafe, unethical, or immoral, and, consequently, our products may not gain the acceptance of the public or the medical community. Adverse public attitudes may adversely impact our ability to enroll clinical trials. Moreover, our success will depend upon physicians prescribing, and their patients being willing to receive, treatments that involve the use of product candidates we may develop in lieu of, or in addition to, existing treatments with which they are already familiar and for which greater clinical data may be available.

Risks Related to the Commercialization of our Product Candidates

Even if any of our product candidates receives marketing approval, it may fail to achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success, and the market opportunity for any of our product candidates, if approved, may be smaller than we estimate.

If any of our product candidates receives marketing approval, it may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. Efforts to educate the medical community and third-party payors on the benefits of our product candidates may require significant resources and may not be successful. If our product candidates do not achieve an adequate level of acceptance, we may not generate significant revenues from product sales and we may not become profitable. The degree of market acceptance of our product candidates, if approved for commercial sale, will depend on a number of factors, including:

- the efficacy and potential advantages of our product candidates compared to the advantages and relative risks of alternative treatments;
- the effectiveness of sales and marketing efforts;
- our ability to offer our products, if approved, for sale at competitive prices;
- our ability to manage the complex pricing and reimbursement negotiations that may arise with marketing the same product at potentially different doses for separate indications;
- the clinical indications for which the product is approved;
- the cost of treatment in relation to alternative treatments;

- the convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the strength of marketing and distribution support;
- the timing of market introduction of competitive products;
- the availability of third-party coverage and adequate reimbursement, and patients' willingness to pay out of pocket for required co-payments or in the absence of third-party coverage or adequate reimbursement;
- product labeling or product insert requirements of the FDA, the EMA or other regulatory authorities, including any limitations or warnings contained in a product's approved labeling;
- the prevalence and severity of any side effects;
- support from patient advocacy groups; and
- any restrictions on the use of our products, if approved, together with other medications.

Our assessment of the potential market opportunity for our product candidates is based on industry and market data that we obtained from industry publications, research, surveys and studies conducted by third parties and our analysis of these data, research, surveys and studies. Industry publications and third-party research, surveys and studies generally indicate that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. While we believe these industry publications and third-party research, surveys and studies are reliable, we have not independently verified such data. Our estimates of the potential market opportunities for our product candidates include a number of key assumptions based on our industry knowledge, industry publications and third-party research, surveys and studies, which may be based on a small sample size and fail to accurately reflect market opportunities. While we believe that our internal assumptions are reasonable, no independent source has verified such assumptions. If any of our assumptions or estimates, or these publications, research, surveys or studies prove to be inaccurate, then the actual market for any of our product candidates may be smaller than we expect, and as a result our revenues from product sales may be limited and it may be more difficult for us to achieve or maintain profitability.

If we are unable to establish sales, marketing and distribution capabilities or enter into sales, marketing and distribution agreements with third parties, we may not be successful in commercializing our product candidates if and when they are approved.

We do not have a sales or marketing infrastructure and have no experience as a company in the sale, marketing or distribution of pharmaceutical products. To achieve commercial success for any product for which we have obtained marketing approval, we will need to establish a sales, marketing and distribution organization, either ourselves or through collaborations or other arrangements with third parties.

We believe that we will be able to commercialize INZ-701, if approved, for ENPP1 Deficiency with a small, targeted, internal sales and commercial organization in the United States and other major markets. There are risks involved with establishing our own sales, marketing and distribution capabilities. For example, recruiting and training a sales force is expensive and time-consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. These efforts may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel. In general, the cost of establishing and maintaining a sales and marketing organization may exceed the cost-effectiveness of doing so.

Factors that may inhibit our efforts to commercialize our products on our own include:

- our inability to recruit, train and retain adequate numbers of effective sales, marketing, coverage or reimbursement, customer service, medical affairs and other support personnel;
- our inability to equip sales personnel with effective materials, including medical and sales literature to help them educate physicians and other healthcare providers regarding rare diseases and our future products;

- our inability to effectively manage a geographically dispersed sales and marketing team;
- the inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe any future products;
- the inability of reimbursement professionals to negotiate arrangements for formulary access, reimbursement and other acceptance by payors;
- the inability to price our products at a sufficient price point to ensure an adequate and attractive level of profitability;
- restricted or closed distribution channels that make it difficult to distribute our products to segments of the patient population;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

If we are unable to establish our own sales, marketing and distribution capabilities and we enter into arrangements with third parties to perform these services, our revenues from product sales and our profitability, if any, are likely to be lower than if we were to market, sell and distribute any products that we develop ourselves. In addition, we may not be successful in entering into arrangements with third parties to sell, market and distribute our product candidates or may be unable to do so on terms that are acceptable to us. We likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively. If we do not establish sales, marketing and distribution capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates.

We face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than we do, thus rendering our products non-competitive, obsolete or reducing the size of our market.

The pharmaceutical and biotechnology industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. We face and will continue to face competition from many different sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions, government agencies and public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization.

We are aware of a number of companies generally pursuing the development of different enzyme replacement therapies or treatments for vascular calcification disorders and many other companies are focused on rare disease markets. For example, DS-1211b, a tissue-nonspecific alkaline phosphatase inhibitor, is currently in Phase 2 clinical development for pseudoxanthoma elasticum by Daiichi Sankyo Company.

Many of the companies against which we are competing or against which we may compete in the future have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our development programs. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. In addition, our ability to compete may be affected in many cases by insurers or other third-party payors seeking to encourage the use of generic products. Because of our primary focus on rare disease, if our product candidates achieve marketing approval, we expect to seek premium pricing.

Technology in the pharmaceutical and biotechnology industries has undergone rapid and significant change, and we expect that it will continue to do so. Any compounds, products or processes that we develop may become obsolete or uneconomical before we recover any expenses incurred in connection with their development.

Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller and other early-stage companies may also prove to be significant

competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

We may pursue the in-license or acquisition of rights to complementary technologies and product candidates on an opportunistic basis. However, we may be unable to in-license or acquire any additional technologies or product candidates from third parties. The acquisition and licensing of technologies and product candidates is a competitive area, and a number of more established companies also have similar strategies to in-license or acquire technologies and product candidates that we may consider attractive. These established companies may have a competitive advantage over us due to their size, cash resources and greater development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to in-license or acquire the relevant technology or product candidate on terms that would allow us to make an appropriate return on our investment.

If the market opportunities for our product candidates are smaller than we currently believe, our revenue may be adversely affected, and our business may suffer. Because the target patient populations of our product candidates are small, we must be able to successfully identify patients and capture a significant market share to achieve profitability and growth.

We focus our research and product development on treatments for rare diseases. Given the small number of patients who have the diseases that we are targeting, it is critical to our ability to grow and become profitable that we continue to successfully identify patients with these rare diseases. Our projections of the number of people who have these diseases are based on our beliefs and estimates. These estimates have been derived from a variety of sources, including the scientific and medical literature, industry publications, third-party research, surveys and studies, patient registries, patient foundations, internal patient identification activities, or market research that we conducted, and may prove to be incorrect or contain errors. New studies may change the estimated incidence or prevalence of these diseases. The number of patients may turn out to be lower than expected. Our efforts to identify patients with diseases we seek to treat is in the early stages, and we cannot accurately predict the number of patients for whom treatment might be possible. Additionally, the potentially addressable patient population for each of our product candidates may be limited or may not be amenable to treatment with our product candidates, and new patients may become increasingly difficult to identify or gain access to, which would adversely affect our results of operations and our business.

Further, even if we obtain significant market share for our product candidates, because the potential target populations are very small, we may never achieve profitability despite obtaining such significant market share. For example, the estimated incidence of ENPP1 Deficiency is approximately one in 64,000 pregnancies worldwide. In North America, the EU, Japan, and Brazil we believe there are approximately 9,400 patients with ENPP1 Deficiency. ABCC6 Deficiency is estimated to affect approximately one per 25,000 to 50,000 individuals, and we believe there are more than 67,000 patients in addressable markets worldwide with ABCC6 Deficiency. In North America, the EU, Japan, and Brazil, we believe there are approximately 24,400 patients with ABCC6 Deficiency. The estimated incidence of calciphylaxis is approximately 3.5 per 1,000 patients with ESKD. In North America, the EU, Japan, and Brazil, we believe there are approximately 23,800 patients with ESKD receiving hemodialysis. In addition, while we are pursuing marketing approval for ENPP1 Deficiency, ABCC6 Deficiency, and calciphylaxis indications, the FDA may only grant approval for more narrow, specific disease indications that would result in a smaller market than we initially sought.

Because there are currently no products approved for the treatment of our target indications, such as ENPP1 and ABCC6 Deficiencies and calciphylaxis, the pricing and reimbursement of our product candidates, if approved, is uncertain, but must be adequate to support commercial infrastructure. In addition, while we are pursuing additional diseases of the PPi-Adenosine Pathway, including those without a clear genetic basis, such as calciphylaxis or calcifications as a result of ESKD, we may not receive approval for such indications or such indications may not expand the target population for INZ-701 in an amount sufficient to achieve profitability. Furthermore, if we are unable to obtain adequate levels of reimbursement, our ability to successfully market and sell our product candidates will be adversely affected.

Even if we are able to commercialize any product candidates, the products may become subject to unfavorable pricing regulations, third-party coverage or reimbursement practices or healthcare reform initiatives, which could harm our business.

The regulations that govern marketing approvals, pricing, coverage and reimbursement for new drug products vary widely from country to country. Current and future legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost effectiveness of our product candidate to other available therapies. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay our commercial launch of the product,

possibly for lengthy time periods, and negatively impact the revenues, if any, we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if our product candidates obtain marketing approval.

Our ability to commercialize any product candidates successfully also will depend in part on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers and other organizations. The availability of coverage and adequacy of reimbursement by governmental healthcare programs such as Medicare and Medicaid, private health insurers and other third-party payors are essential for most patients to be able to afford medical services and pharmaceutical products, including our product candidates. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. Coverage and reimbursement may not be available for any product that we commercialize and, even if these are available, the level of reimbursement may not be satisfactory. Reimbursement may affect the demand for, or the price of, any product candidate for which we obtain marketing approval. Obtaining and maintaining adequate reimbursement for our products may be difficult. We may be required to conduct expensive pharmacoeconomic studies to justify coverage and reimbursement or the level of reimbursement relative to other therapies. If coverage and adequate reimbursement are not available or reimbursement is available only to limited levels, we may not be able to successfully commercialize any product candidate for which we obtain marketing approval.

There may be significant delays in obtaining coverage and reimbursement for newly approved drugs, and coverage may be more limited than the purposes for which the drug is approved by the FDA or similar regulatory authorities outside of the United States. Reimbursement agencies in Europe may be more conservative than the Centers for Medicare & Medical Services ("CMS") in the United States. For example, a number of cancer drugs have been approved for reimbursement in the United States and have not been approved for reimbursement in certain European countries.

Moreover, eligibility for coverage and reimbursement does not imply that a drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution expenses. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs and may be incorporated into existing payments for other services. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies. Our inability to promptly obtain coverage and adequate reimbursement rates from both government-funded and private payors for any approved products that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

No uniform policy for coverage and reimbursement for products exists among third-party payors in the United States. Therefore, coverage and reimbursement for products can differ significantly from payor to payor. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our product candidates to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. Furthermore, rules and regulations regarding reimbursement change frequently, in some cases on short notice, and we believe that changes in these rules and regulations are likely.

There can be no assurance that our product candidates, even if they are approved for sale in the United States, in Europe or in other countries, will be considered medically reasonable and necessary for a specific indication or cost-effective by third-party payors, or that coverage and an adequate level of reimbursement will be available or that third-party payors' reimbursement policies will not adversely affect our ability to sell our product candidates profitably.

Our future growth depends, in part, on our ability to penetrate foreign markets, where we would be subject to additional regulatory burdens and other risks and uncertainties that, if they materialize, could harm our business.

Our future profitability will depend, in part, on our ability to commercialize our product candidates in markets outside of the United States and Europe. We are not permitted to market or promote INZ-701 or any other product candidates we develop before we receive approval from the applicable regulatory authority in that foreign market, and we may never receive such regulatory approval for any of our product candidates. To obtain separate marketing approvals in other countries we may be required to comply with numerous and varying regulatory requirements of such countries regarding the safety and efficacy of our product candidates and governing, among other things, clinical trials and commercial sales, pricing and distribution of our product candidates. If we commercialize our product candidates in these foreign markets, we will be subject to additional risks and uncertainties, including:

- economic weakness, including inflation, or political instability in particular economies and markets;
- the burden of complying with complex and changing foreign regulatory, tax, accounting and legal requirements, many of which vary between countries;
- different medical practices and customs in foreign countries affecting acceptance in the marketplace;
- tariffs and trade barriers, as well as other governmental controls and trade restrictions;
- other trade protection measures, import or export licensing requirements or other restrictive actions by U.S. or foreign governments;
- longer accounts receivable collection times;
- longer lead times for shipping;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- workforce uncertainty in countries where labor unrest is common;
- language barriers for technical training;
- reduced protection of intellectual property rights in some foreign countries, and related prevalence of generic alternatives to therapeutics;
- foreign currency exchange rate fluctuations and currency controls;
- differing foreign reimbursement landscapes;
- uncertain and potentially inadequate reimbursement of our products; and
- the interpretation of contractual provisions governed by foreign laws in the event of a contract dispute.

If risks related to any of these uncertainties materializes, it could have a material adverse effect on our business.

Clinical trial and product liability lawsuits against us could divert our resources and could cause us to incur substantial liabilities and to limit commercialization of any products that we may develop.

We face an inherent risk of clinical trial and product liability exposure related to the testing of our product candidates in human clinical trials and use of our product candidate through compassionate use, and we will face an even greater risk if we commercially sell any products that we may develop. While we currently have no products that have been approved for commercial sale, the ongoing, planned and future use of product candidates by us in clinical trials, and the sale of any approved products in the future, may expose us to liability claims. These claims might be made by patients that use the product, healthcare providers, pharmaceutical companies or others selling such products. On occasion, large judgments have been awarded in class action lawsuits based on products that had unanticipated adverse effects. If we cannot successfully defend ourselves against claims that our product candidates or products caused injuries, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for any product candidates or products that we may develop;
- termination of clinical trials;
- withdrawal of marketing approval, recall, restriction on the approval or a "black box" warning or contraindication for an approved drug;
- withdrawal of clinical trial participants;
- significant costs to defend any related litigation;
- substantial monetary awards to trial participants or patients;
- loss of revenue;
- injury to our reputation and significant negative media attention;
- reduced resources of our management to pursue our business strategy;
- distraction of management's attention from our primary business; and
- the inability to commercialize any products that we may develop.

We may need to obtain additional product liability insurance coverage as we expand our clinical trials or if we commence commercialization of our product candidates. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise. If a successful clinical trial or product liability claim or series of claims is brought against us for uninsured liabilities or in excess of insured liabilities, our assets may not be sufficient to cover such claims and our business operations could be impaired.

Risks Related to our Dependence on Third Parties

We rely, and expect to continue to rely, on third parties to conduct our clinical trials, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials, which may prevent or delay our ability to seek or obtain marketing approval for or commercialize our product candidates or otherwise harm our business. If we are not able to maintain these third-party relationships or if these arrangements are terminated, we may have to alter our development and commercialization plans and our business could be adversely affected.

We rely, and expect to continue to rely, on third-party clinical research organizations, in addition to other third parties such as research collaboratives, clinical data management organizations, medical institutions and clinical investigators, to conduct our ongoing clinical trials, our planned clinical trials, and any other clinical trials we conduct in the future. We do not plan to independently conduct clinical trials of INZ-701 or any other product candidate that we may develop. These contract research organizations and other third parties play a significant role in the conduct and timing of these trials and subsequent collection and analysis of data. These third-party arrangements might terminate for a variety of reasons, including a failure to perform by the third parties. If we need to enter into alternative arrangements, our product development activities might be delayed.

Our reliance on these third parties for research and development activities reduces our control over these activities but does relieve us of our responsibilities. For example, we remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA requires us to comply with standards, commonly referred to as good clinical practices, or GCPs, for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. Regulatory authorities in Europe and other jurisdictions have similar requirements. Regulatory authorities enforce these GCPs through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of our contract research organizations or trial sites fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable, and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We also are required to register ongoing clinical trials and post the results of completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within specified timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we will not be able to obtain, or may be delayed in obtaining, marketing approvals for our product candidates and will not be able to, or may be delayed in our efforts to, successfully develop and commercialize our product candidates. Furthermore, these third parties may also have relationships with other entities, some of which may be our competitors. In addition, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and may receive cash or equity compensation in connection with such services. If these relationships and any related compensation result in perceived or actual conflicts of interest, or the FDA concludes that the financial relationship may have affected the interpretation of the trial, the integrity of the data generated at the applicable clinical trial site may be questioned, and the utility of the clinical trial itself may be jeopardized, which could result in the delay or rejection of any marketing application we submit to the FDA. Any such delay or rejection could prevent us from commercializing our product candidates.

If any of our relationships with these third parties terminate, we may not be able to enter into arrangements with alternative third parties or do so on commercially reasonable terms. Switching or adding additional contract research organizations, investigators and other third parties involves additional cost and requires management time and focus. In addition, there is a natural transition period when a new contract research organization commences work. As a result, delays can occur, which could materially impact our ability to meet our desired clinical development timelines. For example, the COVID-19 pandemic and government measures taken in response have also had a significant impact on many contract research organizations. Although we plan to carefully manage our relationships with our contract research organizations, investigators and other third parties, we may nonetheless encounter challenges or delays in the future, which could have a material and adverse impact on our business, financial condition and prospects.

Manufacturing biologic products is complex and subject to product loss for a variety of reasons. We contract with third parties for the manufacture of our product candidates for preclinical testing and clinical trials and expect to continue to do so for commercialization. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or products or such quantities at an acceptable cost or quality, which could delay, prevent or impair our development or commercialization efforts.

We do not own or operate, and currently have no plans to establish, any manufacturing facilities. We rely, and expect to continue to rely, on third parties for the manufacture of both drug substance and finished drug product for INZ-701 and any future product candidates for preclinical testing and clinical trials, as well as for commercial manufacture if any of our product candidates receive marketing approval. We also rely on these third parties for packaging, labeling, sterilization, storage, distribution and other production logistics. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or products or such quantities at an acceptable cost or quality, which could delay, prevent or impair our development or commercialization efforts. We may be unable to establish any agreements with third-party manufacturers or to do so on acceptable terms. Even if we are able to establish agreements with third-party manufacturers, reliance on third-party manufacturers entails additional risks, including:

- reliance on the third party for regulatory compliance and quality assurance;
- the possible breach of the manufacturing agreement by the third party;
- the potential failure to manufacture our product candidate or product according to our specifications;
- the potential failure to manufacture our product candidate or product according to our schedule or at all;

- the possible misappropriation of our proprietary information, including our trade secrets and know-how; and
- the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us.

We have only limited supply agreements in place with respect to our product candidates, and these arrangements do not extend to commercial supply. We obtain supplies of drug substance and finished drug product for INZ-701 on a purchase order basis. We do not have long-term committed arrangements with respect to any of our product candidates or other materials. We are continuing the process of scaling up our manufacturing processes and capabilities with our third-party manufacturers to support ongoing and future clinical trials. In addition, if we receive marketing approval for any of our product candidates, we will need to establish an agreement for commercial manufacture with a third party.

We or our third-party manufacturers may encounter shortages in the raw materials or active pharmaceutical ingredients necessary to produce our product candidates in the quantities needed for our clinical trials or, if our product candidates are approved, in sufficient quantities for commercialization or to meet an increase in demand, as a result of capacity constraints or delays or disruptions in the market for the raw materials or active pharmaceutical ingredients, including shortages caused by the purchase of such raw materials or active pharmaceutical ingredients by our competitors or others. The failure of us or our third-party manufacturers to obtain the raw materials or active pharmaceutical ingredients necessary to manufacture sufficient quantities of our product candidates may have a material adverse effect on our business.

Our third-party manufacturers are subject to inspection and approval by regulatory authorities before we can commence the manufacture and sale of any of our product candidates, and thereafter subject to ongoing inspection from time to time. Third-party manufacturers may not be able to comply with current good manufacturing practices, or cGMP, regulations or similar regulatory requirements outside of the United States. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in regulatory actions, such as the issuance of FDA Form 483 notices of observations, warning letters or sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or products, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our products.

Manufacturing biologic products, such as INZ-701, is complex, especially in large quantities. Biologic products must be made consistently and in compliance with a clearly defined manufacturing process. Accordingly, it is essential to be able to validate and control the manufacturing process to assure that it is reproducible. The manufacture of biologics is extremely susceptible to product loss due to contamination, equipment failure or improper installation or operation of equipment, vendor or operator error, inconsistency in yields, variability in product characteristics and difficulties in scaling the product process. We have not yet scaled up the manufacturing process for any of our product candidates for potential commercialization. Even minor deviations from normal manufacturing processes could result in reduced production yields, product defects, and other supply disruptions. If microbial, viral, or other contaminations are discovered in our product candidates or in the manufacturing facilities in which our product candidates are made, such manufacturing facilities may need to be closed for an extended period of time to investigate and remedy the contamination, which could harm our results of operations and cause potential reputational damage. Our product candidates and any products that we may develop may compete with other product candidates and products for access to manufacturing facilities. As a result, we may not obtain access to these facilities on a priority basis or at all. There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us. Any performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval. If any of our current contract manufacturers cannot perform as agreed, we may be required to replace such manufacturers. Although we believe that there are several potential alternative manufacturers who could manufacture our product candidates, we may incur added costs and delays in identifying and qualifying any such replacement or be unable to reach agreement with an alternative manufacturer. In addition, a health epidemic, may impact our ability to procure sufficient supplies for the development of our product candidates.

Our current and anticipated future dependence upon others for the manufacture of our product candidates or products may adversely affect our future profit margins and our ability to commercialize any products that receive marketing approval on a timely and competitive basis.

We may enter into collaborations with third parties for the development or commercialization of our product candidates. If our collaborations are not successful, we may not be able to capitalize on the market potential of these product candidates and our business could be adversely affected.

While we retain worldwide, exclusive development and commercialization rights to our pipeline and programs, including INZ-701, we could in the future enter into development, distribution, marketing or funding arrangements with third parties with respect to our existing or future product candidates. Our likely collaborators for any sales, marketing, co-promotion, distribution, development, licensing or broader collaboration arrangements include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies. We are not currently party to any such arrangement. However, if we do enter into any such arrangements with any third parties in the future, we will likely have limited control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of our product candidates. Our ability to generate revenues from these arrangements will depend on our collaborators' abilities and efforts to successfully perform the functions assigned to them in these arrangements.

Collaborations that we enter into may not be successful, and any success will depend heavily on the efforts and activities of such collaborators. Collaborations pose a number of risks, including the following:

- collaborators have significant discretion in determining the amount and timing of efforts and resources that they will apply to these collaborations;
- collaborators may not perform their obligations as expected;
- collaborators may not pursue development of our product candidates or may elect not to continue or renew development programs based on results of clinical trials or other studies, changes in the collaborators' strategic focus or available funding, or external factors, such as an acquisition or business combination, that divert resources or create competing priorities;
- collaborators may not pursue commercialization of any product candidates that achieve marketing approval or may elect not to continue or renew commercialization programs based on results of clinical trials or other studies, changes in the collaborators' strategic focus or available funding, or external factors, such as an acquisition or business combination, that may divert resources or create competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- we may not have access to, or may be restricted from disclosing, certain information regarding product candidates being developed or commercialized under a collaboration and, consequently, may have limited ability to inform our stockholders about the status of such product candidates on a discretionary basis;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates and products if the collaborators believe that the competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- product candidates discovered in collaboration with us may be viewed by our collaborators as competitive with their own product candidates or products, which may cause collaborators to cease to devote resources to the commercialization of our product candidates; a collaborator may fail to comply with applicable regulatory requirements regarding the development, manufacture, distribution or marketing of a product candidate or product;
- a collaborator may seek to renegotiate or terminate their relationship with us due to unsatisfactory clinical results, manufacturing issues, a change in business strategy, a change of control or other reasons;
- a collaborator with marketing and distribution rights to one or more of our product candidates that achieve marketing approval may not commit sufficient resources to the marketing and distribution of such product or products;

- disagreements with collaborators, including disagreements over intellectual property or proprietary rights, contract interpretation or the preferred course of development, might cause delays or terminations of the research, development or commercialization of product candidates, might lead to additional responsibilities for us with respect to product candidates, or might result in litigation or arbitration, any of which would be time-consuming and expensive;

- collaborators may not properly obtain, maintain, enforce, defend or protect our intellectual property or proprietary rights or may use our proprietary information in such a way as to potentially lead to disputes or legal proceedings that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation;

- disputes may arise with respect to the ownership of intellectual property developed pursuant to our collaborations;

- collaborators may infringe, misappropriate or otherwise violate the intellectual property or proprietary rights of third parties, which may expose us to litigation and potential liability; and

- collaborations may be terminated for the convenience of the collaborator, and, if terminated, we could be required to raise additional capital to pursue further development or commercialization of the applicable product candidates.

Collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner, or at all. If any collaborations that we enter into do not result in the successful development and commercialization of products or if one of our collaborators terminates its agreement with us, we may not receive any future research funding or milestone or royalty payments under the collaboration. If we do not receive the funding we expect under these agreements, our development of our product candidates could be delayed and we may need additional resources to develop our product candidates. All of the risks relating to product development, regulatory approval and commercialization described herein also apply to the activities of our collaborators.

Additionally, subject to its contractual obligations to us, if a collaborator of ours is involved in a business combination, the collaborator might deemphasize or terminate the development or commercialization of any product candidate licensed to it by us. If one of our collaborators terminates its agreement with us, we may find it more difficult to attract new collaborators and our perception in the business and financial communities could be adversely affected.

If we are not able to establish or maintain collaborations, we may have to alter our development and commercialization plans and our business could be adversely affected.

We may decide to collaborate with pharmaceutical or biotechnology companies for the development and potential commercialization of one or more of our product candidates. We face significant competition in seeking appropriate collaborators, and a number of more established companies may also be pursuing strategies to license or acquire third-party intellectual property rights that we consider attractive. These established companies may have a competitive advantage over us due to their size, financial resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by the FDA or similar regulatory authorities outside the United States, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing products, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge, and industry and market conditions generally. The collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us for our product candidate. We may also be restricted under future license agreements from entering into agreements on certain terms with potential collaborators. Collaborations are complex and time-consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical and biotechnology companies that have resulted in a reduced number of potential future collaborators.

If we are unable to reach agreements with suitable collaborators on a timely basis, on acceptable terms or at all, we may have to curtail the development of a product candidate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to fund and undertake development or commercialization activities on our own, we may need to obtain additional expertise and additional capital, which may not be available to us on acceptable terms or at all. If we fail to enter into collaborations and do not have sufficient funds or expertise to undertake the necessary development and commercialization activities, we may not be able to further develop our product candidates or bring them to market.

We have agreements with Yale to supplement our internal research and development program. If Yale decides to discontinue or devote less resources to such research, our research efforts could be diminished.

Our set of arrangements with Yale provide us with access to certain of Yale's intellectual property and to Professor Demetrios Braddock's laboratory in a manner that we believe closely aligns our scientific interests with those of Yale. We are a party to both a license agreement and a sponsored research agreement with Yale. While Yale has contractual obligations to us, it is an independent entity and is not under our control or the control of our officers or directors. The license agreement is structured to provide Yale with license maintenance fees, development and regulatory milestone payments, royalties on net sales of products, and a portion of sublicense income that we receive. Upon the scheduled expiration of the Yale sponsored research agreement in December 2025, we may not be able to renew the research agreement or any renewal could be on terms less favorable to us than those contained in the existing agreement. Furthermore, either we or Yale may terminate the sponsored research agreement for convenience following a specified notice period. If Yale decides to not renew or to terminate the Yale sponsored research agreement or decides to devote fewer resources to such activities, our research efforts would be diminished, while our royalty obligations to Yale would continue unmodified.

Our license agreement with Yale also provides that so long as Professor Braddock remains meaningfully involved in our company by serving as a member of our scientific advisory board or has a similar advisory arrangement or has an active consulting arrangement with us, and so long as he is an employee or faculty member (including emeritus faculty member) at Yale, any future invention by Professor Braddock's laboratory in the license agreement's field is included in the licensed intellectual property. If Professor Braddock were to leave Yale or no longer be meaningfully involved with us, we would no longer have access to future inventions in the license agreement's field from Yale.

Additionally, the license granted under the license agreement terminates after a specified period following a qualifying change of control, unless we elect or our successor or assignee elects to continue the agreement. If the license is terminated after such a change of control, royalty payments would continue to be paid on certain licensed products.

Any acquisitions or in-license transactions that we complete could disrupt our business, cause dilution to our stockholders or reduce our financial resources.

We may enter into transactions to in-license or acquire other businesses, intellectual property, technologies, product candidates, or products. If we determine to pursue a particular transaction, we may not be able to complete the transaction on favorable terms, or at all. Any in-licenses or acquisitions we complete may not strengthen our competitive position, and these transactions may be viewed negatively by customers or investors. We may decide to incur debt in connection with an in-license or acquisition or issue our common stock or other equity securities to the stockholders of the target company, which would reduce the percentage ownership of our existing stockholders. We could incur losses resulting from undiscovered liabilities that are not covered by the indemnification we may obtain from the seller. In addition, we may not be able to successfully integrate the acquired personnel, technologies and operations into our existing business in an effective, timely and nondisruptive manner. In-license and acquisition transactions may also divert management attention from day-to-day responsibilities, increase our expenses and reduce our cash available for operations and other uses. For example, we completed an acquisition of specified patent rights and other specified assets related to ENPP1 from Alexion Pharmaceuticals, Inc. in July 2020. We cannot predict the number, timing or size of additional future in-licenses or acquisitions or the effect that any such transactions might have on our operating results.

Risks Related to our Intellectual Property

If we are unable to obtain, maintain and enforce patent protection for our technology and product candidates or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize technology and products similar or identical to ours, and our ability to successfully develop and commercialize our technology and product candidates may be adversely affected.

Our success depends in large part on our ability to obtain, maintain and enforce protection of the intellectual property we may own solely and jointly with others or may license from others, particularly patents, in the United States and other countries with respect to any proprietary technology and product candidates we develop. We seek to protect our proprietary position by filing patent applications in the United States and abroad related to our technologies and product candidates that are important to our business and by in-licensing intellectual property related to such technologies and product candidates. If we are unable to obtain, maintain or enforce patent protection with respect to any proprietary technology or product candidate, our business, financial condition, results of operations and prospects could be materially harmed.

The patent prosecution process is expensive, time-consuming and complex, and we may not be able to file, prosecute, maintain, defend or license all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Moreover, in some circumstances, we do not have the right to control the preparation, filing and prosecution of patent applications, or to maintain, enforce and defend the patents, covering technology that we license from third parties. Therefore, these in-licensed patents and applications may not be prepared, filed, prosecuted, maintained, defended and enforced in a manner consistent with the best interests of our business.

The patent position of pharmaceutical and biotechnology companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation. In addition, the scope of patent protection outside of the United States is uncertain and laws of foreign countries may not protect our rights to the same extent as the laws of the United States or vice versa. For example, European patent law restricts the patentability of methods of treatment of the human body more than United States law does. With respect to both owned and in-licensed patent rights, we cannot predict whether the patent applications we and our licensors are currently pursuing will issue as patents in any particular jurisdiction or whether the claims of any issued patents will provide sufficient protection from competitors. Further, we may not be aware of all third-party intellectual property rights potentially relating to our product candidates. In addition, publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not published at all. Therefore, neither we nor our licensors can know with certainty whether either we or our licensors were the first to make the inventions claimed in the patents and patent applications we own or in-license now or in the future, or that either we or our licensors were the first to file for patent protection of such inventions. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Moreover, our owned or in-licensed pending and future patent applications may not result in patents being issued which protect our technology and product candidates, in whole or in part, or which effectively prevent others from commercializing competitive technologies and products. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents and our ability to obtain, protect, maintain, defend and enforce our patent rights, narrow the scope of our patent protection and, more generally, could affect the value or narrow the scope of our patent rights.

Moreover, we or our licensors may be subject to a third-party preissuance submission of prior art to the United States Patent and Trademark Office ("USPTO") or become involved in opposition, derivation, revocation, reexamination, *inter partes* review, post-grant review or interference proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or product candidates and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize drugs without infringing third-party patent rights. If the breadth or strength of protection provided by our patents and patent applications is threatened, regardless of the outcome, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

Our owned or licensed patent estate includes patent applications, many of which are at an early stage of prosecution. The coverage claimed in a patent application can be significantly narrowed before the patent is issued, and its scope can be reinterpreted after issuance. Even if our owned or in-licensed patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our owned and in-licensed patents may be challenged in the courts or patent offices in the United States and abroad. Such challenges may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and product candidates. Such proceedings also may result in substantial cost and require significant time from our management and employees, even if the eventual outcome is favorable to us. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. Furthermore, our competitors may be able to circumvent our owned or in-licensed patents by developing similar or alternative technologies or products in a non-infringing manner. As a result, our patent portfolio may not provide us with sufficient rights to exclude others from commercializing technology and products similar or identical to any of our technology and product candidates.

Patent terms may be inadequate to protect our competitive position on our product candidates for an adequate amount of time.

Patents have a limited lifespan. In the United States, if all maintenance fees are timely paid, the natural expiration of a patent is generally 20 years from its earliest U.S. non-provisional filing date. Various extensions may be available, but the life of a patent, and the protection it affords, is limited. Even if patents covering our product candidates are obtained, once the patent life has expired, we may be open to competition from competitive products, including generics or biosimilars. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

If we are unable to obtain licenses from third parties on commercially reasonable terms or fail to comply with our obligations under such agreements, our business could be harmed.

It may be necessary for us to use the patented or proprietary technology of third parties to commercialize our products, in which case we would be required to obtain a license from these third parties. If we are unable to license such technology, or if we are forced to license such technology on unfavorable terms, our business could be materially harmed. If we are unable to obtain a necessary license, we may be unable to develop or commercialize the affected product candidates, which could materially harm our business and the third parties owning such intellectual property rights could seek either an injunction prohibiting our sales or an obligation on our part to pay royalties and/or other forms of compensation. Even if we are able to obtain a license, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us.

If we are unable to obtain rights to required third-party intellectual property rights or maintain the existing intellectual property rights we have, we may be required to expend significant time and resources to redesign our technology, product candidates, or the methods for manufacturing them or to develop or license replacement technology, all of which may not be feasible on a technical or commercial basis. If we are unable to do so, we may be unable to develop or commercialize the affected technology and product candidates, which could harm our business, financial condition, results of operations and prospects significantly.

Additionally, if we fail to comply with our obligations under any license agreements, our counterparties may have the right to terminate these agreements, in which event we might not be able to develop, manufacture or market, or may be forced to cease developing, manufacturing or marketing, any product that is covered by these agreements or may face other penalties under such agreements. Such an occurrence could materially adversely affect the value of the product candidate being developed under any such agreement. Termination of these agreements or reduction or elimination of our rights under these agreements, or restrictions on our ability to freely assign or sublicense our rights under such agreements when it is in the interest of our business to do so, may result in our having to negotiate new or reinstated agreements with less favorable terms, cause us to lose our rights under these agreements, including our rights to important intellectual property or technology or impede, or delay or prohibit the further development or commercialization of one or more product candidates that rely on such agreements.

Our product candidates may face competition from biosimilars approved through an abbreviated regulatory pathway.

The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010 (collectively the "ACA"), includes a subtitle called the Biologics Price Competition and Innovation Act of 2009 ("BPCIA") which created an abbreviated approval pathway for biological products that are biosimilar to or interchangeable with an FDA-approved reference biological product. Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA

until four years following the date that the reference product was first approved by the FDA. In addition, the approval of a biosimilar product may not be made effective by the FDA until 12 years from the date on which the reference product was first approved. During this 12-year period of exclusivity, another company may still market a competing version of the reference product if the FDA approves a full BLA for the competing product containing the sponsor's own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of the other company's product.

In December 2022, Congress clarified through FDORA that the FDA may approve multiple first interchangeable biosimilar biological products so long as the products are all approved on the same first day on which such a product is approved as interchangeable with the reference product and the exclusivity period may be shared amongst multiple first interchangeable products. There have been recent government proposals to reduce the 12-year reference product exclusivity period, but none has been enacted to date. At the same time, since passage of the BPCIA, many states have passed laws or amendments to laws which address pharmacy practices involving biosimilar products.

We believe that any product candidate of ours that may be approved as a biological product under a BLA should qualify for the 12-year period of exclusivity. Nonetheless, the approval of biosimilar products referencing any of our product candidates would have a material adverse impact on our business due to increased competition and pricing pressures. Moreover, there is a risk that any exclusivity we do receive could be shortened due to congressional action or otherwise, or that the FDA will not consider our product candidates to be reference products for competing products, potentially creating the opportunity for biosimilar competition sooner than anticipated. Other aspects of the BPCIA, some of which may impact the BPCIA exclusivity provisions, have also been the subject of recent litigation.

The extent to which a biosimilar, once approved, will be substituted for any one of our reference products in a way that is similar to traditional generic substitution for non-biological products is not yet clear, and will depend on a number of marketplace and regulatory factors that are still developing. The ultimate impact, implementation, and meaning of the BPCIA are subject to uncertainty, and any new regulations, guidance, policies, or processes adopted by the FDA to implement the law could have a material adverse effect on the future commercial prospects for our biological products.

In addition, foreign regulatory authorities may change their approval policies relating to regulatory exclusivity and new regulations may be enacted. For instance, the European Union pharmaceutical legislation is currently undergoing a complete review process, in the context of the Pharmaceutical Strategy for Europe initiative, launched by the European Commission in November 2020. The European Commission's proposal for revision of several legislative instruments related to medicinal products (including potentially reducing the duration of regulatory data protection and revising the eligibility for expedited pathways) was published in April 2023 and the European Parliament requested several amendments in April 2024. The proposed revisions remain to be agreed and adopted by the European Parliament and European Council, and the proposals may therefore be substantially revised before adoption, which is not anticipated before early 2026. The revisions may, however, have a significant impact on the pharmaceutical industry and our business in the long term.

If we do not obtain patent term extension for any product candidates we may develop, our business may be materially harmed.

In the United States, the term of a patent that covers an FDA-approved drug may, in certain cases, be eligible for a patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act, as compensation for the loss of a patent term during the FDA regulatory review process. The Hatch-Waxman Act permits a patent term extension of up to five years, but patent extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval. Only one patent among those eligible for an extension and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended. Similar provisions are available in Europe and certain other non-United States jurisdictions to extend the term of a patent that covers an approved drug. While, in the future, if and when our product candidates receive FDA approval, we expect to apply for patent term extensions on patents covering those product candidates, there is no guarantee that the applicable authorities, including the FDA, will agree with our assessment of whether such extensions should be granted, and even if granted, the length of such extensions. We may not be granted patent term extension either in the United States or in any foreign country because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. Moreover, the term of extension, as well as the scope of patent protection during any such extension, afforded by the governmental authority could be less than we request. If we are unable to obtain any patent term extension or the term of any such extension is less than we request, our competitors may obtain approval of competing products following the expiration of our patent rights, and our business, financial condition, results of operations and prospects could be materially harmed.

Changes to patent laws in the United States and other jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our products.

Changes in either the patent laws or interpretation of patent laws in the United States, including patent reform legislation such as the Leahy-Smith America Invents Act, or the Leahy-Smith Act, could increase the uncertainties and costs surrounding the prosecution of our owned or in-licensed patent applications and the maintenance, enforcement or defense of our owned or in-licensed issued patents. The Leahy-Smith Act includes a number of significant changes to United States patent law. These changes include provisions that affect the way patent applications are prosecuted, redefine prior art, provide more efficient and cost-effective avenues for competitors to challenge the validity of patents, and enable third-party submission of prior art to the USPTO during patent prosecution and additional procedures to attack the validity of a patent at USPTO-administered post-grant proceedings, including post-grant review, *inter partes* review, and derivation proceedings. Assuming that other requirements for patentability are met, prior to March 2013, in the United States, the first to invent the claimed invention was entitled to the patent, while outside the United States, the first to file a patent application was entitled to the patent. After March 2013, under the Leahy-Smith Act, the United States transitioned to a first-to-file system in which, assuming that the other statutory requirements for patentability are met, the first inventor to file a patent application will be entitled to the patent on an invention regardless of whether a third party was the first to invent the claimed invention. As such, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business, financial condition, results of operations and prospects.

In addition, the patent positions of companies in the development and commercialization of biologics and pharmaceuticals are particularly uncertain. Recent U.S. Supreme Court and Federal Appeals Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. This combination of events has created uncertainty with respect to the validity and enforceability of patents once obtained, including unexpired patents issued prior to such rulings. Depending on future actions by the U.S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that could have a material adverse effect on our patent rights and our ability to protect, defend and enforce our patent rights in the future.

The federal government retains certain rights in inventions produced with its financial assistance under the Bayh-Dole Act. The federal government retains a "nonexclusive, nontransferable, irrevocable, paid-up license" for its own benefit. The Bayh-Dole Act also provides federal agencies with "march-in rights". March-in rights allow the government, in specified circumstances, to require the contractor or successors in title to the patent to grant a "nonexclusive, partially exclusive, or exclusive license" to a "responsible applicant or applicants." If the patent owner refuses to do so, the government may grant the license itself. We collaborate with a number of universities with respect to certain of our research and development. While it is our policy to avoid engaging our university collaborators in projects in which there is a risk that federal funds may be commingled, we cannot be sure that any co-developed intellectual property will be free from government rights pursuant to the Bayh-Dole Act. If, in the future, we co-own or in-license technology which is critical to our business that is developed in whole or in part with federal funds subject to the Bayh-Dole Act, our ability to enforce or otherwise exploit patents covering such technology may be adversely affected.

Although we or our licensors are not currently involved in any litigation, we may become involved in lawsuits to protect or enforce our patent or other intellectual property rights, which could be expensive, time-consuming and unsuccessful.

Competitors and other third parties may infringe, misappropriate or otherwise violate our or our licensor's issued patents or other intellectual property. It may be difficult to detect infringers who do not advertise the components that are used in their products. Moreover, it may be difficult or impossible to obtain evidence of infringement in a competitor's product. To counter infringement or misappropriation, we or our licensors may need to file infringement, misappropriation or other intellectual property related claims, which can be expensive and time-consuming and can distract our management and scientific personnel. There can be no assurance that we will have sufficient financial or other resources to file and pursue such infringement claims, which typically last for years before they are concluded. Any claims we assert against perceived infringers could provoke such parties to assert counterclaims against us alleging that we infringe, misappropriate or otherwise violate their intellectual property.

In addition, in a patent infringement proceeding, such parties could counterclaim that the patents we or our licensors have asserted are invalid or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during prosecution. Third parties may institute such claims before administrative bodies in the United States or abroad, even outside the context of litigation. Such mechanisms include re-examination, post-grant review, *inter partes* review, interference proceedings, derivation proceedings, and equivalent proceedings in foreign jurisdictions, such as opposition proceedings. The outcome following legal assertions of invalidity and unenforceability is unpredictable. Similarly, if we or our licensors assert

trademark infringement claims, a court may determine that the marks we or our licensors have asserted are invalid or unenforceable, or that the party against whom we or our licensors have asserted trademark infringement has superior rights to the marks in question. In this case, we could ultimately be forced to cease use of such trademarks, which could materially harm our business and negatively affect our position in the marketplace.

An adverse result in any such proceeding could put one or more of our owned or in-licensed patents at risk of being invalidated or interpreted narrowly, could put any of our owned or in-licensed patent applications at risk of not yielding an issued patent, and could limit our or our licensor's ability to assert those patents against those parties or other competitors and curtail or preclude our ability to exclude third parties from developing and commercializing similar or competitive products. A court may also refuse to stop the third party from using the technology at issue in a proceeding on the grounds that our owned or in-licensed patents do not cover such technology. Even if we establish infringement, a court may not order the third party to stop using the technology at issue and instead award only monetary damages to us, which may not be an adequate remedy. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information or trade secrets could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions, or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of our common stock. Any of the foregoing could allow such third parties to develop and commercialize competing technologies and products and have a material adverse impact on our business, financial condition, results of operations and prospects.

Interference or derivation proceedings provoked by third parties or brought by us or declared by the USPTO may be necessary to determine the priority of inventions with respect to our patents or patent applications. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms or at all, or if a non-exclusive license is offered and our competitors gain access to the same technology. Our defense of litigation or interference or derivation proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees. In addition, the uncertainties associated with litigation could have a material adverse effect on our ability to raise the funds necessary to continue our clinical trials, continue our research programs, license necessary technology from third parties, or enter into development partnerships that would help us bring our product candidates to market.

Third parties may initiate legal proceedings alleging that we are infringing, misappropriating or otherwise violating their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business.

Our commercial success depends upon our ability and the ability of our collaborators to develop, manufacture, market and sell our product candidates and use our proprietary technologies without infringing, misappropriating or otherwise violating the intellectual property and proprietary rights of third parties. There is considerable patent and other intellectual property litigation in the pharmaceutical and biotechnology industries. We may become party to, or threatened with, adversarial proceedings or litigation regarding intellectual property rights with respect to our technology and product candidates, including interference proceedings, post grant review, *inter partes* review, and derivation proceedings before the USPTO and similar proceedings in foreign jurisdictions, such as opposition proceedings before the European Patent Office. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are pursuing development candidates. As the pharmaceutical and biotechnology industries expand and more patents are issued, the risk increases that our technologies or product candidates that we may identify may be subject to claims of infringement of the patent rights of third parties.

The legal threshold for initiating litigation or contested proceedings is low, so even lawsuits or proceedings with a low probability of success might be initiated and require significant resources to defend. Litigation and contested proceedings can also be expensive and time-consuming, and our adversaries in these proceedings may have the ability to dedicate substantially greater resources to prosecuting these legal actions than we can. The risks of being involved in such litigation and proceedings may increase if and as our product candidates near commercialization and as we gain the greater visibility associated with being a public company. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future, regardless of merit. Even if we diligently search third-party patents for potential infringement by our products or product candidates, we may not successfully find patents our products or product candidates may infringe. We may not be aware of all such intellectual property rights potentially relating to our technology and product candidates and their uses, or we may incorrectly conclude that third party intellectual property is invalid or that our activities and product candidates do not infringe such intellectual property. Thus, we do not know with certainty that our technology and product candidates, or our development and commercialization thereof, do not and will not infringe, misappropriate or otherwise violate any third party's intellectual property.

Third parties may assert that we are employing their proprietary technology without authorization. There may be third-party patents or patent applications with claims to materials, formulations or methods, such as methods of manufacture or methods for

treatment, related to the discovery, use or manufacture of the product candidates that we may identify or related to our technologies. Because patent applications can take many years to issue, there may be currently pending patent applications which may later result in issued patents that the product candidates that we may identify may infringe. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. Moreover, as noted above, there may be existing patents that we are not aware of or that we have incorrectly concluded are invalid or not infringed by our activities. If any third-party patents were held by a court of competent jurisdiction to cover, for example, the manufacturing process of the product candidates that we may identify, any molecules formed during the manufacturing process or any final product itself, the holders of any such patents may be able to block our ability to commercialize such product candidate unless we obtained a license under the applicable patents, or until such patents expire.

Parties making claims against us may obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize the product candidates that we may identify. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, pay royalties, redesign our infringing products or obtain one or more licenses from third parties, which may be impossible or require substantial time and monetary expenditure.

We may choose to take a license or, if we are found to infringe, misappropriate or otherwise violate a third party's intellectual property rights, we could also be required to obtain a license from such third party to continue developing, manufacturing and marketing our technology and product candidates. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors and other third parties access to the same technologies licensed to us and could require us to make substantial licensing and royalty payments. We could be forced, including by court order, to cease developing, manufacturing and commercializing the infringing technology or product. In addition, we could be found liable for significant monetary damages, including treble damages and attorneys' fees, if we are found to have willfully infringed a patent or other intellectual property right and could be forced to indemnify our customers or collaborators. A finding of infringement could prevent us from commercializing our product candidates or force us to cease some of our business operations, which could materially harm our business. In addition, we may be forced to redesign our product candidates, seek new regulatory approvals and indemnify third parties pursuant to contractual agreements. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar material adverse effect on our business, financial condition, results of operations and prospects.

If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected.

While we seek to protect the trademarks and trade names we use in the United States and in other countries, we may be unsuccessful in obtaining registrations or otherwise protecting these trademarks and trade names, which we need to build name recognition in our markets of interest and among potential partners or customers. We rely on both registration and common law protection for our trademarks. Our registered or unregistered trademarks or trade names may be challenged, infringed, diluted or declared generic, or determined to be infringing on other marks. At times, competitors may adopt trademarks and trade names similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trademark infringement claims brought by owners of other registered trademarks or trademarks that incorporate variations of our registered or unregistered trademarks. If we are unable to protect our rights to trademarks and trade names, we may be prevented from using such marks and names unless we enter into appropriate royalty, license or coexistence agreements, which may not be available or may not be available on commercially reasonable terms.

During trademark registration proceedings, we may receive rejections. Although we would be given an opportunity to respond to those rejections, we may be unable to overcome such rejections. In addition, in the USPTO and in comparable agencies in many foreign jurisdictions, third parties are given an opportunity to oppose pending trademark applications and to seek to cancel registered trademarks. Opposition or cancellation proceedings may be filed against our trademarks, and our trademarks may not survive such proceedings. Effective trademark protection may not be available or may not be sought in every country in which our products are made available. Any name we propose to use for our products in the United States must be approved by the FDA, regardless of whether we have registered it, or applied to register it, as a trademark. The FDA typically conducts a review of proposed product names, including an evaluation of potential for confusion with other product names. If the FDA objects to any of our proposed product names, we may be required to expend significant additional resources in an effort to identify a usable substitute name that would qualify under applicable trademark laws, not infringe the existing rights of third parties and be acceptable to the FDA, and such an effort may significantly delay our ability to market our products. If we are unable to establish name recognition based on our trademarks and trade names, we may not be able to compete effectively and our business may be adversely affected.

Intellectual property litigation or other legal proceedings relating to intellectual property could cause us to spend substantial resources and distract our personnel from their normal responsibilities.

Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses, and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and may also have an advantage in such proceedings due to their more mature and developed intellectual property portfolios. Uncertainties resulting from the initiation and continuation of intellectual property litigation or other proceedings could compromise our ability to compete in the marketplace.

Obtaining and maintaining patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

Periodic maintenance, renewal and annuity fees and various other government fees on any issued patent and pending patent application must be paid to the USPTO and foreign patent agencies in several stages or annually over the lifetime of our patents and patent applications. The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. In certain circumstances, we rely on our licensing partners to pay these fees to, or comply with the procedural and documentary rules of, the relevant patent agency. With respect to our patents, we rely on an annuity service, outside firms and outside counsel to remind us of the due dates and to make payment after we instruct them to do so. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of a patent or patent application include failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. In such an event, potential competitors might be able to enter the market with similar or identical products or technology. If we or our licensors fail to maintain the patents and patent applications covering our product candidates, it would have a material adverse effect on our business, financial condition, results of operations and prospects.

If we fail to comply with our obligations in our current and future intellectual property licenses and funding arrangements with third parties, or otherwise experience disruptions to our business relationships with our licensors, we could lose intellectual property rights that are important to our business.

We are party to a license agreement with Yale that provides us with the foundational intellectual property rights for our lead product candidate, INZ-701. This license agreement imposes diligence, development and commercialization timelines, and milestone payment, royalty, insurance and other obligations on us. If we fail to comply with such obligations, including achieving specified milestone events, Yale may have the right to terminate the license agreement or require us to grant them certain rights, in which event we might not be able to develop, manufacture or market any product that is covered by the intellectual property we in-license from them and may face other penalties. Any such occurrence could materially adversely affect the value of any product candidate being developed under any such agreement.

For a variety of purposes, we will likely enter into additional licensing and funding arrangement with third parties that may impose similar obligations on us. Termination of these agreements or reduction or elimination of our rights under these agreements may result in our having to negotiate new or reinstated agreements with less favorable terms, or cause us to lose our rights under these agreements, including our rights to important intellectual property or technology, which would have a material adverse effect on our business, financial condition, results of operations and prospects. While we still face all of the risks described herein with respect to those agreements, we cannot prevent third parties from also accessing those technologies. In addition, our licenses may place restrictions on our future business opportunities.

In addition to the above risks, intellectual property rights that we license in the future may include sublicenses under intellectual property owned by third parties, in some cases through multiple tiers. The actions of our licensors may therefore affect our rights to use our sublicensed intellectual property, even if we are in compliance with all of the obligations under our license agreements. Should our licensors or any of the upstream licensors fail to comply with their obligations under the agreements pursuant to which they obtain the rights that are sublicensed to us, or should such agreements be terminated or amended, our ability to develop and commercialize our product candidates may be materially harmed.

Disputes may arise regarding intellectual property subject to a licensing agreement, including:

- the scope of rights granted under the license agreement and other interpretation related issues;
- the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- the sublicensing of patent and other rights under our collaborative development relationships;
- our diligence obligations under the license agreement and what activities satisfy those diligence obligations;
- the inventorship and ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our partners; and
- the priority of invention of patented technology.

In addition, the agreements under which we currently license intellectual property or technology from third parties are complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology, or increase what we believe to be our financial or other obligations under the relevant agreement, either of which could have a material adverse effect on our business, financial condition, results of operations and prospects. Moreover, if disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on commercially acceptable terms, we may be unable to successfully develop and commercialize the affected technology and product candidates, which could have a material adverse effect on our business, financial conditions, results of operations and prospects.

Further, licensors could retain the right to prosecute and defend the intellectual property rights licensed to us, in which case we would depend on our licensors to control the prosecution, maintenance and enforcement of all of our licensed and sublicensed intellectual property, and even when we do have such rights, we may require the cooperation of our licensors and upstream licensors, which may not be forthcoming. For example, under the license agreement with Yale, any patent applications and issued patents under the agreement remain the property of Yale, and Yale has the right to choose patent counsel. Licensors may determine not to pursue litigation against other companies or may pursue such litigation less aggressively than we would. Our business could be adversely affected if we or our licensors are unable to prosecute, maintain and enforce our licensed and sublicensed intellectual property effectively.

Our current or future licensors may have relied on third-party consultants or collaborators or on funds from third parties such that our licensors are not the sole and exclusive owners of the patents and patent applications we in-license. If other third parties have ownership rights to patents or patent applications we in-license, they may be able to license such patents to our competitors, and our competitors could market competing products and technology. This could have a material adverse effect on our competitive position, business, financial conditions, results of operations and prospects.

In spite of our best efforts, our licensors might conclude that we have materially breached our license agreements and might therefore terminate the license agreements, thereby removing our ability to develop and commercialize product candidates and technology covered by these license agreements. If these in-licenses are terminated, or if the underlying intellectual property fails to provide the intended exclusivity, competitors would have the freedom to seek regulatory approval of, and to market, products and technologies identical to ours. This could have a material adverse effect on our competitive position, business, financial condition, results of operations and prospects.

We may not be able to protect our intellectual property and proprietary rights throughout the world.

Filing, prosecuting and defending patents on product candidates and trademark applications for our company name and product names in all countries throughout the world would be prohibitively expensive, and the laws of foreign countries may not protect our rights to the same extent as the laws of the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States, and even where such protection is nominally available, judicial and governmental enforcement of such intellectual property rights may be lacking. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection or licenses but enforcement is not as strong as that in the United States. These products may compete with our products, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets, and other intellectual property protection, particularly those relating to biotechnology products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our intellectual property and proprietary rights generally. In addition, certain jurisdictions do not protect to the same extent or at all inventions that constitute new methods of treatment.

Proceedings to enforce our intellectual property and proprietary rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly, could put our patent applications at risk of not issuing, and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property and proprietary rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Many countries have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, many countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If we or any of our licensors is forced to grant a license to third parties with respect to any patents relevant to our business, our competitive position may be impaired, and our business, financial condition, results of operations and prospects may be adversely affected.

We may be subject to claims challenging the inventorship or ownership of our patents and other intellectual property.

We or our licensors may be subject to claims that former employees, collaborators or other third parties have an interest in our owned or in-licensed patents, trade secrets or other intellectual property as an inventor or co-inventor. For example, we or our licensors may have inventorship disputes arise from conflicting obligations of employees, consultants or others who are involved in developing our product candidates. Litigation may be necessary to defend against these and other claims challenging inventorship or our or our licensors' ownership of our owned or in-licensed patents, trade secrets or other intellectual property. If we or our licensors fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, intellectual property that is important to our product candidates. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

We may be subject to claims by third parties asserting that our employees, consultants or contractors have wrongfully used or disclosed confidential information of third parties, or we have wrongfully used or disclosed alleged trade secrets of their current or former employers or claims asserting we have misappropriated their intellectual property, or claiming ownership of what we regard as our own intellectual property.

Many of our employees, consultants and contractors were previously employed at universities or other pharmaceutical or biotechnology companies, including our competitors or potential competitors. Although we try to ensure that our employees, consultants and contractors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that these individuals or we have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such individual's current or former employer. Litigation may be necessary to defend against these claims.

In addition, while it is our policy to require our employees, consultants and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact develops intellectual property that we regard as our own. Our intellectual property assignment agreements with them may not be self-executing or may be breached, and we may be forced to bring claims against third parties, or defend claims they may bring against us, to determine the ownership of what we regard as our intellectual property. Such claims could have a material adverse effect on our business, financial conditions, results of operations and prospects.

If we fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel, which could have a material adverse effect on our competitive business position and prospects. Such intellectual property rights could be awarded to a third party, and we could be required to obtain a license from such third party to commercialize our technology or products, which license may not be available on commercially reasonable terms, or at all, or such license may be non-exclusive. Even if we are successful in prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to our management and employees.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

In addition to seeking patents for some of our technology and product candidates, we also rely on trade secrets and confidentiality agreements to protect our unpatented know-how, technology and other proprietary information, to maintain our competitive position. We seek to protect our trade secrets and other proprietary technology, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, contract research organizations, contract manufacturers, consultants, advisors and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants, but we cannot guarantee that we have entered into such agreements with each party that may have or has had access to our trade secrets or proprietary technology. Despite these efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Detecting the disclosure or misappropriation of a trade secret and enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside of the United States are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor or other third party, we would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor or other third party, our competitive position would be materially and adversely harmed.

Intellectual property rights do not necessarily address all potential threats.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations and may not adequately protect our business or permit us to maintain our competitive advantage. For example:

- others may be able to make product candidates that are similar to ours but that are not covered by the claims of the patents that we own;
- we, or our license partners or current or future collaborators, might not have been the first to make the inventions covered by the issued patent or pending patent applications that we license or may own in the future;
- we, or our license partners or current or future collaborators, might not have been the first to file patent applications covering certain of our or their inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our owned or in-licensed intellectual property rights;
- it is possible that our owned or in-licensed pending patent applications or those we may own or in-license in the future will not lead to issued patents;
- issued patents that we hold rights to may be held invalid or unenforceable, including as a result of legal challenges by our competitors;
- our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;

- we cannot ensure that any of our patents, or any of our pending patent applications, if issued, or those of our licensors, will include claims having a scope sufficient to protect our product candidates;

- we cannot ensure that any patents issued to us or our licensors will provide a basis for an exclusive market for our commercially viable product candidates or will provide us with any competitive advantages;

- the U.S. Supreme Court, other federal courts, Congress, the USPTO or similar foreign authorities may change the standards of patentability, validity and enforcement, and any such changes could narrow or invalidate, change the scope of, or render unenforceable our or our licensors' patents;

- patent terms may be inadequate to protect our competitive position on our product candidates for an adequate amount of time;

- we cannot ensure that our commercial activities or product candidates will not infringe upon the patents of others;

- we cannot ensure that we will be able to successfully commercialize our product candidates on a substantial scale, if approved, before the relevant patents that we own or license expire;

- we may not develop additional proprietary technologies that are patentable;

- the patents of others may harm our business; and

- we may choose not to file a patent in order to maintain certain trade secrets or know-how, and a third party may subsequently file a patent covering such intellectual property.

Should any of these events occur, they could have a material adverse effect on our business, financial condition, results of operations and prospects.

Risks Related to Regulatory Approval and Other Legal Compliance Matters

Even if we complete the necessary preclinical studies and clinical trials, the marketing approval process of the FDA, the EMA and comparable foreign authorities is expensive, time-consuming, and uncertain and may prevent us from obtaining approvals for the commercialization of any product candidates we develop. If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals, we will not be able to commercialize, or will be delayed in commercializing, product candidates we develop, and our ability to generate revenue will be materially impaired.

Any product candidates we develop and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale, and distribution, are subject to comprehensive regulation by the FDA and other regulatory authorities in the United States, the EMA and other regulatory authorities in the European Union and by comparable authorities in other countries. Failure to obtain marketing approval for a product candidate will prevent us from commercializing the product candidate in a given jurisdiction. We have not received approval to market any product candidates from regulatory authorities in any jurisdiction. We have only limited experience in filing and supporting the applications necessary to gain marketing approvals and expect to rely on third-party contract research organizations to assist us in this process. Securing regulatory approval requires the submission of extensive preclinical and clinical data and supporting information, including manufacturing information, to the various regulatory authorities for each therapeutic indication to establish the biologic product candidate's safety, purity, and potency. Any product candidates we develop may not be effective, may be only moderately effective, or may prove to have undesirable or unintended side effects, toxicities, or other characteristics that may preclude our obtaining marketing approval or prevent or limit commercial use.

Moreover, principal investigators for our clinical trials may serve as scientific advisors or consultants to us and receive compensation in connection with such services. Under certain circumstances, we may be required to report some of these relationships to the FDA or comparable foreign regulatory authorities. The FDA or a comparable foreign regulatory authority may conclude that a financial relationship between us and a principal investigator has created a conflict of interest or otherwise affected interpretation of the study. The FDA or comparable foreign regulatory authority may therefore question the integrity of the data generated at the applicable clinical trial site and the utility of the clinical trial itself may be jeopardized. This could result in a delay in approval, or rejection, of our marketing applications by the FDA or comparable foreign regulatory authority, as the case may be, and may ultimately lead to the denial of marketing approval of one or more of our product candidates.

The process of obtaining marketing approvals, both in the United States and abroad, is expensive, may take many years if additional clinical trials are required, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity, and novelty of the product candidates involved. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application. The FDA, the EMA and comparable authorities in other countries have substantial discretion in the approval process and may refuse to accept any application or may decide that our data is insufficient for approval and require additional preclinical, clinical, or other studies. In addition, varying interpretations of the data obtained from preclinical testing and clinical trials could delay, limit, or prevent marketing approval of a product candidate. Any marketing approval we ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable.

Under the Pediatric Research Equity Act, a new drug application ("NDA"), a BLA or supplement to an NDA or BLA for certain drugs and biological products must contain data to assess the safety and effectiveness of the drug or biological product in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective, unless the sponsor receives a deferral or waiver from the FDA. A deferral may be granted for several reasons, including a finding that the product or therapeutic candidate is ready for approval for use in adults before pediatric trials are complete or that additional safety or effectiveness data needs to be collected before the pediatric trials begin. The applicable legislation in the European Union also requires sponsors to either conduct clinical trials in a pediatric population in accordance with a Pediatric Investigation Plan approved by the Pediatric Committee of the EMA, or to obtain a waiver or deferral from the conduct of these studies by this Committee. For any of our product candidates for which we are seeking regulatory approval in the United States or the European Union, we cannot guarantee that we will be able to obtain a waiver or alternatively complete any required studies and other requirements in a timely manner, or at all, which could result in associated reputational harm and subject us to enforcement action.

In addition, we could be adversely affected by several significant administrative law cases decided by the U.S. Supreme Court in 2024. In *Loper Bright Enterprises v. Raimondo*, for example, the court overruled *Chevron U.S.A., Inc. v. Natural Resources Defense Council, Inc.*, which for 40 years required federal courts to defer to permissible agency interpretations of statutes that are silent or ambiguous on a particular topic. The U.S. Supreme Court stripped federal agencies of this presumptive deference and held that courts must exercise their independent judgment when deciding whether an agency such as the FDA acted within its statutory authority under the Administrative Procedure Act, or the APA. Additionally, in *Corner Post, Inc. v. Board of Governors of the Federal Reserve System*, the court held that actions to challenge a federal regulation under the APA can be initiated within six years of the date of injury to the plaintiff, rather than the date the rule is finalized. The decision appears to give prospective plaintiffs a personal statute of limitations to challenge longstanding agency regulations. Another decision, *Securities and Exchange Commission v. Jarkesy*, overturned regulatory agencies' ability to impose civil penalties in administrative proceedings. These decisions could introduce additional uncertainty into the regulatory process and may result in additional legal challenges to actions taken by federal regulatory agencies, including the FDA and CMS, that we rely on. In addition to potential changes to regulations as a result of legal challenges, these decisions may result in increased regulatory uncertainty and delays and other impacts, any of which could adversely impact our business and operations.

Further, our ability to develop and market products may be threatened by the results of ongoing litigation challenging the FDA's approval of another company's drug, mifepristone. Specifically, in April 2023, the U.S. District Court for the Northern District of Texas invalidated the approval by the FDA of mifepristone, a product which was originally approved in 2000 and whose distribution is governed by various measures adopted under risk evaluation and mitigation strategy ("REMS"). The Court of Appeals for the Fifth Circuit declined to order the removal of mifepristone from the market but did hold that plaintiffs were likely to prevail in their claim that changes allowing for expanded access of mifepristone that the FDA authorized in 2016 and 2021 were arbitrary and capricious. In June 2024, the U.S. Supreme Court reversed and remanded that decision after unanimously finding that the plaintiffs did not have standing to bring this legal action against the FDA. In October 2024, the Attorneys General of three states filed an amended complaint in the district court in Texas challenging FDA's actions. In January 2025, the district court agreed to allow these states to file an amended complaint and continue to pursue this challenge. Depending on the outcome of this litigation, if it continues, our ability to develop new drug product candidates and to maintain approval of existing drug products and measures adopted under a REMS is at risk and our efforts to develop and market new drug products could be delayed, undermined or subject to protracted litigation.

Finally, with the change in presidential administrations in 2025, there is substantial uncertainty as to how, if at all, the new administration will seek to modify or revise the requirements and policies of the FDA and other regulatory agencies with jurisdiction over our product candidates. The impending uncertainty could present new challenges or potential opportunities as we navigate the clinical development and approval process for our product candidates.

If we experience delays in obtaining approval or if we fail to obtain approval of any product candidates we develop, the commercial prospects for those product candidates may be harmed, and our ability to generate revenues will be materially impaired.

Failure to obtain marketing approval in foreign jurisdictions would prevent any product candidates we develop from being marketed in such jurisdictions, which, in turn, would materially impair our ability to generate revenue.

In order to market and sell any product candidates we develop in the European Union and many other foreign jurisdictions, we or our collaborators must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The regulatory approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the United States, it is required that the product be approved for reimbursement before the product can be approved for sale in that country. We or these third parties may not obtain approvals from regulatory authorities outside the United States on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. The failure to obtain approval in one jurisdiction may negatively impact our ability to obtain approval elsewhere. We may not be able to file for marketing approvals and may not receive necessary approvals to commercialize our products in any jurisdiction, which would materially impair our ability to generate revenue.

Additionally, we could face heightened risks with respect to obtaining marketing authorization in the United Kingdom as a result of the withdrawal of the United Kingdom from the EU, commonly referred to as Brexit. The United Kingdom is no longer part of the European Single Market and EU Customs Union. As of January 1, 2025, the Medicines and Healthcare Products Regulatory Agency ("MHRA") is responsible for approving all medicinal products destined for the United Kingdom market (i.e., Great Britain and Northern Ireland). At the same time, a new international recognition procedure ("IRP") will apply, which intends to facilitate approval of pharmaceutical products in the United Kingdom. The IRP is open to applicants that have already received an authorization for the same product from one of the MHRA's specified Reference Regulators ("RRs"). The RRs notably include EMA and regulators in the EU/European Economic Area ("EEA") member states for approvals in the EU centralized procedure and mutual recognition procedure as well as the FDA (for product approvals granted in the U.S.). However, the concrete functioning of the IRP is currently unclear. Any delay in obtaining, or an inability to obtain, any marketing approvals may force us or our collaborators to restrict or delay efforts to seek regulatory approval in the United Kingdom for our product candidates, which could significantly and materially harm our business.

We expect that we will be subject to additional risks in commercializing any of our product candidates that receive marketing approval outside the United States, including tariffs, trade barriers and regulatory requirements; economic weakness, including inflation, or political instability in particular foreign economies and markets; compliance with tax, employment, immigration and labor laws for employees living or traveling abroad; foreign currency fluctuations, which could result in increased operating expenses and reduced revenue, and other obligations incident to doing business in another country; and workforce uncertainty in countries where labor unrest is more common than in the United States.

Fast track designation, breakthrough therapy designation and/or priority review designation by the FDA may not actually lead to a faster development or regulatory review or approval process, and does not assure FDA approval of our product candidates.

If a product candidate is intended for the treatment of a serious or life-threatening condition and the product candidate demonstrates the potential to address unmet medical need for this condition, the sponsor may apply to the FDA for fast track designation. For fast track products, sponsors may have greater interactions with the FDA and the FDA may initiate review of sections of a fast track product's application before the application is complete. This rolling review may be available if the FDA determines, after preliminary evaluation of clinical data submitted by the sponsor, that a fast track product may be effective.

In addition, a sponsor may seek designation of its product as a breakthrough therapy, which is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For drugs and biologics that have been designated as breakthrough therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens.

Designation as a breakthrough therapy is within the discretion of the FDA. Accordingly, even if we believe one of our product candidates meets the criteria for designation as a breakthrough therapy, the FDA may disagree and instead determine not to make such designation.

Further, if the FDA determines that a product candidate intended to treat a serious condition and, if approved, offers a significant improvement in safety or effectiveness, the FDA may designate the product candidate for priority review. Significant

improvement may be illustrated by evidence of increased effectiveness in the treatment of a condition, elimination or substantial reduction of a treatment-limiting product reaction, documented enhancement of patient compliance that may lead to improvement in serious outcomes, and evidence of safety and effectiveness in a new subpopulation. A priority review designation means that the goal for the FDA to review an application is six months, rather than the standard review period of 10 months.

In September 2020, we received fast track designation from the FDA for INZ-701 for the treatment of ENPP1 Deficiency, in July 2024, we received fast track designation from the FDA for INZ-701 for the treatment of ABCC6 Deficiency, and in January 2025, we received fast track designation from the FDA for INZ-701 for the treatment of calciphylaxis. We may seek other designations for that and other product candidates. The FDA has broad discretion with respect to whether or not to grant fast track designation, breakthrough therapy designation and/or priority review designation to a product candidate, so even if we believe a particular product candidate is eligible for such designation or status, the FDA may decide not to grant it. Moreover, a fast track designation, breakthrough therapy designation or priority review designation does not necessarily mean a faster regulatory review process, review or approval compared to conventional FDA procedures, or necessarily confer any advantage with respect to approval compared to conventional FDA procedures. Receiving priority review from the FDA does not guarantee approval within the six-month review cycle or thereafter. In addition, the FDA may withdraw these designations if it believes that the designation is no longer supported by data from our clinical development program.

Accelerated approval by the FDA or comparable foreign regulatory authorities, even if granted for our product candidates, may not lead to a faster development or regulatory review or approval process and it does not increase the likelihood that our product candidates will receive marketing approval.

A product may be eligible for accelerated approval if it treats a serious or life-threatening condition and generally provides a meaningful advantage over available therapies. In addition, it must demonstrate an effect on a biomarker efficacy endpoint that is reasonably likely to predict clinical benefit or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, or IMM, that is reasonably likely to predict an effect on IMM or other clinical benefit. The FDA or other applicable regulatory agency makes the determination regarding whether a biomarker efficacy endpoint is reasonably likely to predict long-term clinical benefit.

We may seek approval of our product candidates using the FDA's accelerated approval pathway. Prior to seeking such accelerated approval, we will seek feedback from the FDA and otherwise evaluate our ability to seek and receive such accelerated approval. As a condition of approval, the FDA may require that a sponsor of a drug or biologic product candidate receiving accelerated approval perform adequate and well-controlled post-marketing clinical trials. These confirmatory trials must be completed with due diligence and we may be required to evaluate different or additional endpoints in these post-marketing confirmatory trials. In addition, the FDA currently requires as a condition for accelerated approval pre-approval of promotional materials, which could adversely impact the timing of the commercial launch of the product.

There can be no assurance that the FDA will agree with any biomarker efficacy endpoints that we propose, or that we will decide to pursue or submit an NDA for accelerated approval or any other form of expedited development, review or approval. Similarly, there can be no assurance that, after feedback from FDA, we will continue to pursue or apply for accelerated approval or any other form of expedited development, review or approval, even if we initially decide to do so. Furthermore, if we decide to submit an application for accelerated approval or under another expedited regulatory designation, there can be no assurance that such submission or application will be accepted or that any expedited review or approval will be granted on a timely basis, or at all.

Moreover, as noted above, for drugs granted accelerated approval, the FDA typically requires post-marketing confirmatory trials to evaluate the anticipated effect on IMM or other clinical benefit. These confirmatory trials must be completed with due diligence. We may be required to evaluate additional or different clinical endpoints in these post-marketing confirmatory trials. These confirmatory trials may require enrollment of more patients than we currently anticipate and will result in additional costs, which may be greater than the estimated costs we currently anticipate.

With the passage of FDORA in December 2022, Congress modified certain provisions governing accelerated approval of drug and biologic products. Specifically, the legislation authorized the FDA to: require a sponsor to have its confirmatory clinical trial underway before accelerated approval is awarded, require a sponsor of a product granted accelerated approval to submit progress reports on its post-approval studies to FDA every six months until the study is completed; and use expedited procedures to withdraw accelerated approval of an NDA or BLA after the confirmatory trial fails to verify the product's clinical benefit. Moreover, FDORA established expedited procedures authorizing the FDA to withdraw an accelerated approval if certain conditions are met, including where a required confirmatory study fails to verify and describe the predicted clinical benefit or where evidence demonstrates the product is not shown to be safe or effective under the conditions of use. The FDA may also use such procedures to withdraw an accelerated approval if a sponsor fails to conduct any required post-approval study of the product with due diligence, including with respect to "conditions specified by the Secretary."

In March 2023, the FDA issued draft guidance that outlines its current thinking and approach to accelerated approval. The agency indicated that, although single-arm trials have been commonly used to support accelerated approval, a randomized controlled trial is the preferred approach as it provides a more robust efficacy and safety assessment and allows for direct comparisons to an available therapy. To that end, the FDA outlined considerations for designing, conducting, and analyzing data for trials intended to support accelerated approvals of oncology therapeutics. Subsequently, in December 2024 and January 2025, the FDA issued additional draft guidances relating to accelerated approval. These guidances describe FDA's latest thinking on what it means to conduct a confirmatory trial with due diligence and how the agency plans to interpret whether such a study needs to be underway at the time of approval. While these guidances are currently only in draft form and will ultimately not be legally binding even when finalized, sponsors typically observe the FDA's guidance closely to ensure that their investigational products qualify for accelerated approval.

The FDA may withdraw approval of a product candidate approved under the accelerated approval pathway if, for example, the trial required to verify the predicted clinical benefit of our product candidate fails to verify such benefit or does not demonstrate sufficient clinical benefit to justify the risks associated with the drug. The FDA may also withdraw approval if other evidence demonstrates that our product candidate is not shown to be safe or effective under the conditions of use, we fail to conduct any required post approval trial of our product candidate with due diligence or we disseminate false or misleading promotional materials relating to our product candidate. A failure to obtain accelerated approval or any other form of expedited development, review or approval for our product candidates, or withdrawal of a product candidate, would result in a longer time period for commercialization of such product candidate, could increase the cost of development of such product candidate and could harm our competitive position in the marketplace.

In the European Union, a "conditional" marketing authorization may be granted in cases where all the required safety and efficacy data are not yet available. A conditional marketing authorization is subject to conditions to be fulfilled for generating missing data or ensuring increased safety measures. A conditional marketing authorization is valid for one year and has to be renewed annually until fulfillment of all relevant conditions. Once the applicable pending studies are provided, a conditional marketing authorization can become a "standard" marketing authorization. However, if the conditions are not fulfilled within the timeframe set by the EMA, the marketing authorization will cease to be renewed.

Even if we do receive accelerated approval, we may not experience a faster development or regulatory review or approval process, and receiving accelerated approval does not provide assurance of ultimate FDA approval.

We may not be able to obtain or maintain orphan drug exclusivity for INZ-701 or any other product candidates we develop for one or more indications, and even if we do, that exclusivity may not prevent the FDA or the EMA from approving other competing products.

Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is a drug or biologic intended to treat a rare disease or condition. A similar regulatory scheme governs approval of orphan products by the EMA in the European Union. Generally, if a product candidate with an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the product is entitled to a period of marketing exclusivity, which precludes the FDA or the EMA from approving another marketing application for the same product for the same therapeutic indication for that time period. The applicable period is seven years in the United States and ten years in the European Union. The exclusivity period in the European Union can be reduced to six years if a product no longer meets the criteria for orphan drug designation, in particular if the product is sufficiently profitable so that market exclusivity is no longer justified.

The FDA and the EMA have granted orphan drug designation to INZ-701 for the treatment of ENPP1 Deficiency and ABCC6 Deficiency.

In order for the FDA to grant orphan drug exclusivity to one of our products, the agency must find that the product is indicated for the treatment of a condition or disease with a patient population of fewer than 200,000 individuals annually in the United States or that affects more than 200,000 individuals in the United States and for which there is no reasonable expectation that the cost of developing and making available the biologic for the disease or condition will be recovered from sales of the product in the United States. In order for the EMA to grant orphan drug designation, we must establish that the product is intended for the diagnosis, prevention or treatment of (1) a life-threatening or chronically debilitating condition affecting not more than five in 10,000 persons in the European Union when the application is made, or (2) a life-threatening, seriously debilitating or serious and chronic condition in the European Union and that without incentives it is unlikely that the marketing of the drug in the European Union would generate sufficient return to justify the necessary investment. For either of these conditions, we must demonstrate that there exists no satisfactory method of diagnosis, prevention, or treatment of the condition in question that has been authorized in the European Union or, if such method exists, the drug will be of significant benefit to those affected by that condition.

The FDA or the EMA may conclude that the condition or disease for which we seek orphan drug exclusivity does not meet the applicable standard. Even if we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different products can be approved for the same condition. In addition, even after an orphan drug is approved, the FDA can subsequently approve the same product for the same condition if the FDA concludes that the later product is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care. Under omnibus legislation signed by President Trump on December 27, 2020, the requirement for a product to show clinical superiority applies to drugs and biologics that received orphan drug designation before enactment of the FDA Reauthorization Act of 2017, but have not yet been approved or licensed by the FDA. Orphan drug exclusivity may also be lost if the FDA or the EMA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the product to meet the needs of the patients with the rare disease or condition.

The FDA may further reevaluate the Orphan Drug Act and its regulations and policies. This may be particularly true in light of a decision from the Court of Appeals for the 11th Circuit in September 2021 finding that, for the purpose of determining the scope of exclusivity, the term “same disease or condition” means the designated “rare disease or condition” and could not be interpreted by the FDA to mean the “indication or use.” Although there have been legislative proposals to overrule this decision, they have not been enacted into law.

On January 23, 2023, the FDA announced that, in matters beyond the scope of that court order, the FDA will continue to apply its existing regulations tying orphan-drug exclusivity to the uses or indications for which the orphan drug was approved. We do not know if, when, or how the FDA or Congress may change the orphan drug regulations and policies in the future, and it is uncertain how any changes might affect our business. Depending on what changes the FDA or Congress may make to its orphan drug regulations and policies, our business could be adversely impacted.

We may seek a Rare Pediatric Disease Designation for one or more of our product candidates. However, a BLA for one or more of our product candidates may not meet the eligibility criteria for a priority review voucher upon approval.

With enactment of the Food and Drug Administration Safety and Innovation Act in 2012, Congress authorized the FDA to award priority review vouchers ("PRVs") to sponsors of certain rare pediatric disease product applications that meet the criteria specified in the law. This provision is designed to encourage development of new drug and biological products for prevention and treatment of certain rare pediatric diseases. Specifically, under this program, a sponsor who receives an approval for a drug or biologic for a “rare pediatric disease” may qualify for a voucher that can be redeemed to receive a priority review of a subsequent marketing application for a different product. The sponsor of a rare pediatric disease drug product receiving a PRV may transfer (including by sale) the voucher to another sponsor. The voucher may be further transferred any number of times before the voucher is used, as long as the sponsor making the transfer has not yet submitted the application.

In order to receive a PRV upon BLA approval, the product must receive designation from the FDA as a product for a rare pediatric disease prior to submission of the marketing application. A “rare pediatric disease” is a disease that is serious or life-threatening, in which the serious or life-threatening manifestations primarily affect individuals aged from birth to 18 years and affects fewer than 200,000 people in the United States, or affects more than 200,000 people in the United States but there is no reasonable expectation that the cost of developing and making available in the United States a product for such disease or condition will be recovered from sales in the United States of such product. In addition to receiving rare pediatric disease designation, in order to receive a PRV, the BLA must be given priority review, rely on clinical data derived from studies examining a pediatric population and dosages of the product intended for that population, not seek approval for a different adult indication in the original rare pediatric disease product application and be for a product that does not include a previously approved active ingredient.

The Rare Pediatric Disease Priority Review Voucher program was not reauthorized by Congress in 2024 and expired on December 31, 2024. Thus, under the current statutory sunset provisions, FDA may only award PRVs for approved rare pediatric disease product applications if sponsors had rare pediatric disease designation for the drug or biologic granted by September 30, 2024. The FDA may not award any rare pediatric disease PRVs after September 30, 2026. In September 2020, we received rare pediatric disease designation from the FDA for INZ-701 for the treatment of ENPP1 Deficiency. However, the FDA may determine that a BLA for INZ-701 or one or more of our other product candidates does not meet the eligibility criteria for a PRV upon approval. Moreover, if we do not obtain approval of our BLA for INZ-701 by September 30, 2026, and if the program is not further extended by Congressional action, we will not receive a PRV.

The FDA, EMA, or other comparable foreign regulatory authorities could require the clearance or approval of a companion diagnostic device as a condition of approval for any product candidate that requires or would commercially benefit from such tests. Failure to successfully validate, develop and obtain regulatory clearance or approval for companion diagnostics on a timely basis or at all could harm our product development strategy and we may not realize the commercial potential of any such product candidate.

If safe and effective use of any of our other product candidates depends on an in vitro diagnostic, then the FDA generally will require approval or clearance of that diagnostic, known as a companion diagnostic, at the same time that the FDA approves our product candidates. The process of obtaining or creating such diagnostic is time consuming and costly. Companion diagnostics, which provide information that is essential for the safe and effective use of a corresponding therapeutic product, are subject to regulation by the FDA, EMA, and other comparable foreign regulatory authorities as medical devices and require separate regulatory approval from therapeutic approval prior to commercialization. The FDA previously has required in vitro companion diagnostics intended to select the patients who will respond to a product candidate to obtain pre-market approval ("PMA") simultaneously with approval of the therapeutic candidate. The PMA process, including the gathering of preclinical and clinical data and the submission and review by the FDA, can take several years or longer. It involves a rigorous pre-market review during which the sponsor must prepare and provide FDA with reasonable assurance of the device's safety and effectiveness and information about the device and its components regarding, among other things, device design, manufacturing, and labeling. After a device is placed on the market, it remains subject to significant regulatory requirements, including requirements governing development, testing, manufacturing, distribution, marketing, promotion, labeling, import, export, record-keeping, and adverse event reporting.

Given our limited experience in developing and commercializing diagnostics, we do not plan to develop companion diagnostics internally and thus will be dependent on the sustained cooperation and effort of third-party collaborators in developing and obtaining approval for these companion diagnostics. We may not be able to enter into arrangements with a provider to develop a companion diagnostic for use in connection with a registrational trial for our product candidates or for commercialization of our product candidates, or do so on commercially reasonable terms, which could adversely affect and/or delay the development or commercialization of our product candidates. We and our future collaborators may encounter difficulties in developing and obtaining approval for the companion diagnostics, including issues relating to selectivity/specificity, analytical validation, reproducibility, or clinical validation. Any delay or failure by our collaborators to develop or obtain regulatory approval of the companion diagnostics could delay or prevent approval of our product candidates. In addition, we, our collaborators or third parties may encounter production difficulties that could constrain the supply of the companion diagnostics, and both they and we may have difficulties gaining acceptance of the use of the companion diagnostics by physicians.

We believe that adoption of screening and treatment into clinical practice guidelines is important for payer access, reimbursement, utilization in medical practice and commercial success, but both our collaborators and we may have difficulty gaining acceptance of the companion diagnostic into clinical practice guidelines. If such companion diagnostics fail to gain market acceptance, it would have an adverse effect on our ability to derive revenues from sales, if any, of any of our product candidates that are approved for commercial sale. In addition, any companion diagnostic collaborator or third party with whom we contract may decide not to commercialize or to discontinue selling or manufacturing the companion diagnostic that we anticipate using in connection with development and commercialization of our product candidates, or our relationship with such collaborator or third party may otherwise terminate. We may not be able to enter into arrangements with another provider to obtain supplies of an alternative diagnostic test for use in connection with the development and commercialization of our product candidates or do so on commercially reasonable terms, which could adversely affect and/or delay the development or commercialization of our product candidates.

Even if we, or any collaborators we may have, obtain marketing approvals for any product candidates we develop, the terms of approvals and ongoing regulation of our products could require the substantial expenditure of resources and may limit how we, or they, manufacture and market our products, which could materially impair our ability to generate revenue.

Any product candidate for which we obtain marketing approval, along with the manufacturing processes, post-approval clinical data, labeling, advertising, and promotional activities for such product, will be subject to continual requirements of and review by the FDA, the EMA and other regulatory authorities. These requirements include submissions of safety and other post-marketing

information and reports, registration and listing requirements, cGMP requirements relating to quality control and manufacturing, quality assurance and corresponding maintenance of records and documents, and requirements regarding the distribution of samples to physicians and recordkeeping. Even if marketing approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the product, including the requirement to implement a REMS. We must also comply with requirements concerning advertising and promotion for any product candidate for which we obtain marketing approval.

Accordingly, assuming we, or any collaborators we may have, receive marketing approval for one or more product candidates we develop, we, and such collaborators, and our and their contract manufacturers will continue to expend time, money, and effort in all areas of regulatory compliance, including manufacturing, production, product surveillance, and quality control. If we and such collaborators are not able to comply with post-approval regulatory requirements, we and such collaborators could have the marketing approvals for our products withdrawn by regulatory authorities and our, or such collaborators', ability to market any future products could be limited, which could adversely affect our ability to achieve or sustain profitability. Further, the cost of compliance with post-approval regulations may have a negative effect on our business, operating results, financial condition, and prospects.

Any product candidate for which we obtain marketing approval could be subject to restrictions or withdrawal from the market, and we may be subject to substantial penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our products, when and if any of them are approved.

The FDA and other regulatory agencies closely regulate the post-approval marketing and promotion of products to ensure that they are marketed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA and other regulatory agencies impose stringent restrictions on manufacturers' communications regarding off-label use, and if we do not market our products for their approved indications, we may be subject to enforcement action for off-label marketing by the FDA and other federal and state enforcement agencies, including the Department of Justice. Violation of the Federal Food, Product, and Cosmetic Act and other statutes, including the False Claims Act, relating to the promotion and advertising of prescription products may also lead to investigations or allegations of violations of federal and state health care fraud and abuse laws and state consumer protection laws.

We will need to carefully navigate the FDA's various regulations, guidance and policies, along with recently enacted legislation, to ensure compliance with restrictions governing promotion of our products. In September 2021, the FDA published final regulations which describe the types of evidence that the agency will consider in determining the intended use of a drug or biologic. Moreover, with passage of the Pre-Approval Information Exchange Act in December 2022, sponsors of products that have not been approved may proactively communicate to payors certain information about products in development to help expedite patient access upon product approval. In addition, in January 2025, the FDA published final guidance outlining its policies governing the distribution of scientific information to healthcare providers about unapproved uses of approved products. The final guidance calls for such communications to be truthful, non-misleading and scientifically sound and to include all information necessary for healthcare providers to interpret the strengths and weaknesses and validity and utility of the information about the unapproved use of the approved product. If a company engages in such communications consistent with the guidance's recommendations, the FDA indicated that it will not treat such communications as evidence of unlawful promotion of a new intended use for the approved product. While this guidance only applies to communications about unapproved uses of approved products, it may be helpful in understanding the FDA's approach to communications about unapproved products.

In addition, later discovery of previously unknown problems with our products, manufacturers, or manufacturing processes, or failure to comply with regulatory requirements, may yield various results, including:

- restrictions on such products, manufacturers or manufacturing processes;
- restrictions on the labeling or marketing of a product;
- restrictions on the distribution or use of a product;
- requirements to conduct post-marketing clinical trials;
- receipt of warning or untitled letters;
- withdrawal of the products from the market;

- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of products;
- fines, restitution, or disgorgement of profits or revenue;
- suspension or withdrawal of marketing approvals;
- suspension of any ongoing clinical trials;
- refusal to permit the import or export of our products;
- product seizure; and
- injunctions or the imposition of civil or criminal penalties.

Similar restrictions apply to the approval of our products in the European Union. The holder of a marketing authorization is required to comply with a range of requirements applicable to the manufacturing, marketing, promotion and sale of medicinal products. These include: compliance with the European Union's stringent pharmacovigilance or safety reporting rules, which can impose post-authorization studies and additional monitoring obligations; the manufacturing of authorized medicinal products, for which a separate manufacturer's license is mandatory; and the marketing and promotion of authorized drugs, which are strictly regulated in the European Union and are also subject to European Union Member State laws. The failure to comply with these and other European Union requirements can also lead to significant penalties and sanctions.

Accordingly, any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. The occurrence of any event or penalty described above may inhibit our ability to commercialize any product candidates we develop and adversely affect our business, financial condition, results of operations, and prospects.

Our relationships with healthcare providers, physicians and third-party payors will be subject to applicable anti-kickback, fraud and abuse, and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm, and diminished profits and future earnings.

Healthcare providers, physicians, and third-party payors play a primary role in the recommendation and prescription of any product candidates that we develop for which we obtain marketing approval. Our future arrangements with third-party payors and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell, and distribute our products for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations include the following:

- the federal healthcare anti-kickback statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving, or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order, or recommendation of, any good or service, for which payment may be made under federal and state healthcare programs such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the federal Anti-Kickback Statute or specific intent to violate it in order to have committed a violation;
- the federal False Claims Act imposes criminal and civil penalties, including civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment or approval from Medicare, Medicaid, or other government payors that are false or fraudulent or making a false statement to avoid, decrease, or conceal an obligation to pay money to the federal government, with potential liability including mandatory treble damages and significant per-claim penalties. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act;
- the federal civil monetary penalties laws, which impose civil fines for, among other things, the offering or transfer of remuneration to a Medicare or state healthcare program beneficiary if the person knows or should know it is likely to

influence the beneficiary's selection of a particular provider, practitioner, or supplier of services reimbursable by Medicare or a state healthcare program, unless an exception applies;

- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, as further amended by the Health Information Technology for Economic and Clinical Health Act, which imposes certain requirements, including mandatory contractual terms, with respect to safeguarding the privacy, security, and transmission of individually identifiable health information without appropriate authorization by entities subject to the rule, such as health plans, health care clearinghouses, and health care providers;

- the federal false statements statute, which prohibits knowingly and willfully falsifying, concealing, or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items, or services;

- the Federal Food, Drug and Cosmetic Act, which prohibits, among other things, the adulteration or misbranding of drugs, biologics and medical devices;

- the federal transparency requirements under the federal Physician Payment Sunshine Act, which requires manufacturers of drugs, devices, biologics, and medical supplies to report to the U.S. Department of Health and Human Services, or HHS, information related to payments and other transfers of value to physicians, other healthcare providers, and teaching hospitals, and ownership and investment interests held by physicians and their immediate family members and applicable group purchasing organizations;

- federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers;

- analogous state laws and regulations, such as state anti-kickback and false claims laws, which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers, and certain state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring drug manufacturers to report information related to payments to physicians and other health care providers or marketing expenditures; and

- similar healthcare laws and regulations in the European Union and other jurisdictions, including reporting requirements detailing interactions with and payments to healthcare providers and laws governing the privacy and security of certain protected information, such as the General Data Protection Regulation ("GDPR"), which imposes obligations and restrictions on the collection and use of personal data relating to individuals located in the European Union (including health data).

Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available, it is possible that some of our business activities could be subject to challenge under one or more of such laws. If our operations are found to be in violation of any of the laws described above or any other government regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines, exclusion from participation in government health care programs, such as Medicare and Medicaid, imprisonment, and the curtailment or restructuring of our operations, any of which could adversely affect our business, financial condition, results of operations, and prospects.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices, including our relationships with physicians and other healthcare providers, may not comply with current or future statutes, regulations, or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal, and administrative penalties, damages, fines, exclusion from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. Further, defending against any such actions can be costly, time-consuming and may require significant personnel resources. Therefore, even if we are successful in defending against any such actions that may be brought against us, our business may be impaired. If any of the physicians or other providers or entities with whom we expect to do business are found to be not in compliance with applicable laws, they may be subject to criminal, civil, or administrative sanctions, including exclusions from government funded healthcare programs. Liabilities they incur pursuant to these laws could result in significant costs or an interruption in operations, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

Current and future legislation may increase the difficulty and cost for us and any collaborators to obtain marketing approval and commercialize our product candidates and affect the prices we, or they, may obtain.

In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could, among other things, prevent or delay marketing approval of our drug candidates, restrict or regulate post-approval activities, impact pricing and reimbursement and affect our ability, or the ability of any collaborators, to profitably sell or commercialize any product candidate for which we, or they, obtain marketing approval. In particular, there have been and continue to be a number of initiatives at the U.S. federal and state levels that seek to reduce healthcare costs and improve the quality of healthcare. We expect that current laws, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we, or any collaborators, may receive for any approved products.

Other legislative changes have been proposed and adopted since the ACA was enacted. These changes include the Budget Control Act of 2011, which, among other things, led to aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which will remain in effect through the first half of 2032. The American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to several types of providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used.

Under current legislation, the actual reductions in Medicare payments may vary up to 4%. The Consolidated Appropriations Act, which was signed into law by President Biden in December 2022, made several changes to sequestration of the Medicare program. Section 1001 of the Consolidated Appropriations Act delays the 4% Statutory Pay-As-You-Go Act of 2010 (PAYGO) sequester for two years, through the end of 2024. Triggered by enactment of the American Rescue Plan Act of 2021, the 4% cut to the Medicare program would have taken effect in January 2023. The Consolidated Appropriations Act's healthcare offset title includes Section 4163, which extends the 2% Budget Control Act of 2011 Medicare sequester for six months into 2032 and lowers the payment reduction percentages in years 2030 and 2031.

Since enactment of the ACA, there have been and continue to be, numerous legal challenges and Congressional actions to repeal and replace provisions of the law. For example, with enactment of the TCJA in 2017, Congress repealed the "individual mandate." The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, became effective in 2019. In June 2021, the U.S. Supreme Court dismissed this action after finding that the plaintiffs do not have standing to challenge the constitutionality of the ACA. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

In the European Union, on December 13, 2021, Regulation No 2021/2282 on Health Technology Assessment ("HTA"), amending Directive 2011/24/EU, was adopted. While the HTA entered into force in January 2022, it will only begin to apply from January 2025 onwards, with preparatory and implementation-related steps to take place in the interim. Once applicable, it will have a phased implementation depending on the concerned products. The HTA intends to boost cooperation among European Union member states in assessing health technologies, including new medicinal products as well as certain high-risk medical devices, and provide the basis for cooperation at the European Union level for joint clinical assessments in these areas. It will permit European Union member states to use common HTA tools, methodologies, and procedures across the European Union, working together in four main areas, including joint clinical assessment of the innovative health technologies with the highest potential impact for patients, joint scientific consultations whereby developers can seek advice from HTA authorities, identification of emerging health technologies to identify promising technologies early, and continuing voluntary cooperation in other areas. Individual European Union member states will continue to be responsible for assessing non-clinical (e.g., economic, social, ethical) aspects of health technology, and making decisions on pricing and reimbursement.

We expect that these healthcare reforms, as well as other healthcare reform measures that may be adopted in the future, may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies and additional downward pressure on the price that we receive for any approved product and/or the level of reimbursement physicians receive for administering any approved product we might bring to market. Reductions in reimbursement levels may negatively impact the prices we receive or the frequency with which our products are prescribed or administered. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. Accordingly, such reforms, if enacted, could have an adverse effect on anticipated revenue from product candidates that we may successfully develop and for which we may obtain marketing approval and may affect our overall financial condition and ability to develop or commercialize product candidates.

We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action in the United States, the European Union or any other jurisdiction. If we or any third parties we may engage are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we or such third parties are not able to maintain regulatory compliance, our product candidates may lose any regulatory approval that may have been obtained and we may not achieve or sustain profitability.

The prices of prescription pharmaceuticals in the United States and foreign jurisdictions are subject to considerable legislative and executive actions, which could impact the prices we obtain for our products, if approved.

The prices of prescription pharmaceuticals have also been the subject of considerable discussion in the United States. There have been several recent U.S. congressional inquiries, as well as proposed and enacted state and federal legislation designed to, among other things, bring more transparency to pharmaceutical pricing, review the relationship between pricing and manufacturer patient programs, and reduce the costs of pharmaceuticals under Medicare and Medicaid.

In addition, in October 2020, HHS and the FDA published a final rule allowing states and other entities to develop a Section 804 Importation Program, or SIP, to import certain prescription drugs from Canada into the United States. That regulation was challenged in a lawsuit by the Pharmaceutical Research and Manufacturers of America ("PhRMA"), but the case was dismissed by a federal district court in February 2023 after the court found that PhRMA did not have standing to sue HHS. Several states have passed laws allowing for the importation of drugs from Canada and a few states have passed legislation establishing workgroups to examine the impact of a state importation program. Several states have submitted Section 804 Importation Program proposals to the FDA. In January 2024, the FDA approved Florida's plan for Canadian drug importation. Florida now has authority to import certain drugs from Canada for a period of two years once certain conditions are met. Florida will first need to submit a pre-import request for each drug selected for importation, which must be approved by the FDA. Florida will also need to relabel the drugs and perform quality testing of the products to meet FDA standards.

Further, on November 20, 2020, HHS finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The final rule would eliminate the current safe harbor for Medicare drug rebates and create new safe harbors for beneficiary point-of-sale discounts and pharmacy benefit manager service fees. It originally was set to go into effect on January 1, 2022, but with passage of the IRA, it has been delayed by Congress to January 1, 2032.

The IRA has implications for Medicare Part D, which is a program available to individuals who are entitled to Medicare Part A or enrolled in Medicare Part B to give them the option of paying a monthly premium for outpatient prescription drug coverage. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare (beginning in 2026), with prices that can be negotiated subject to a cap; imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation (first due in 2023); and replaces the Part D coverage gap discount program with a new discounting program (beginning in 2025). The IRA permits the Secretary of HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years.

Specifically, with respect to price negotiations, Congress authorized Medicare to negotiate lower prices for certain costly single-source drug and biologic products that do not have competing generics or biosimilars and are reimbursed under Medicare Part B and Part D. CMS may negotiate prices for ten high-cost drugs paid for by Medicare Part D starting in 2026, followed by 15 Part D drugs in 2027, 15 Part B or Part D drugs in 2028, and 20 Part B or Part D drugs in 2029 and beyond. This provision applies to drug products that have been approved for at least 9 years and biologics that have been licensed for 13 years, but it does not apply to drugs and biologics that have been approved for a single rare disease or condition. Nonetheless, since CMS may establish a maximum price for these products in price negotiations, we would be fully at risk of government action if our products are the subject of Medicare price negotiations. Moreover, given the risk that could be the case, these provisions of the IRA may also further heighten the risk that we would not be able to achieve the expected return on our drug products or full value of our patents protecting our products if prices are set after such products have been on the market for nine years.

The first cycle of negotiations for the Medicare Drug Price Negotiation Program commenced in the summer of 2023. In August 2024, HHS published the results of the first Medicare drug price negotiations for ten selected drugs that treat a range of conditions, including diabetes, chronic kidney disease, and rheumatoid arthritis. The prices of these ten drugs will become effective in January 2026. In January 2025, CMS announced its selection of 15 additional drugs covered by Part D for the second cycle of negotiations. While there had been some questions about the Trump Administration’s position on this program, CMS issued a public statement in January 2025, declaring that lowering the cost of prescription drugs is a top priority of the new administration and CMS is committed to considering opportunities to bring greater transparency in the negotiation program. The second cycle of negotiations with participating drug companies will occur during 2025, and any negotiated prices for this second set of drugs will be effective starting January 2027.

The legislation subjects drug manufacturers to civil monetary penalties and a potential excise tax for failing to comply with the legislation by offering a price that is not equal to or less than the negotiated "maximum fair price" under the law or for taking price increases that exceed inflation. The legislation also requires manufacturers to pay rebates for drugs in Medicare Part D whose price increases exceed inflation. The law also caps Medicare out-of-pocket drug costs at an estimated $4,000 a year in 2024 and, thereafter beginning in 2025, at $2,000 a year. In addition, the IRA potentially raises legal risks with respect to individuals participating in a Medicare Part D prescription drug plan who may experience a gap in coverage if they required coverage above their initial annual coverage limit before they reached the higher threshold, or "catastrophic period" of the plan. Individuals requiring services exceeding the initial annual coverage limit and below the catastrophic period, must pay 100% of the cost of their prescriptions until they reach the catastrophic period. Among other things, the IRA contains many provisions aimed at reducing this financial burden on individuals by reducing the co-insurance and co-payment costs, expanding eligibility for lower income subsidy plans, and price caps on annual out-of-pocket expenses, each of which could have potential pricing and reporting implications.

On June 6, 2023, Merck & Co. filed a lawsuit against the HHS and CMS asserting that, among other things, the IRA's Drug Price Negotiation Program for Medicare constitutes an uncompensated taking in violation of the Fifth Amendment of the Constitution. Subsequently, a number of other parties, including the U.S. Chamber of Commerce, Bristol Myers Squibb Company, the PhRMA, Astellas, Novo Nordisk, Janssen Pharmaceuticals, Novartis, AstraZeneca, and Boehringer Ingelheim, also filed lawsuits in various courts with similar constitutional claims against the HHS and CMS. HHS has generally won the substantive disputes in these cases, and various federal district court judges have expressed skepticism regarding the merits of the legal arguments being pursued by the pharmaceutical industry. Certain of these cases are now on appeal and, on October 30, 2024, the Court of Appeals for the Third Circuit heard oral argument in three of these cases. We expect that litigation involving these and other provisions of the IRA will continue, with unpredictable and uncertain results.

Accordingly, while it is currently unclear how the IRA will be effectuated, we cannot predict with certainty what impact any federal or state health reforms will have on us, but such changes could impose new or more stringent regulatory requirements on our activities or result in reduced reimbursement for our products, any of which could adversely affect our business, results of operations and financial condition.

At the state level, individual states are increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. This is increasingly true with respect to products approved pursuant to the accelerated approval pathway. State Medicaid programs and other payers are developing strategies and implementing significant coverage barriers, or refusing to cover these products outright, arguing that accelerated approval drugs have insufficient or limited evidence despite meeting the FDA's standards for accelerated approval. In addition, regional health care authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription product and other health care programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

In the European Union, similar political, economic and regulatory developments may affect our ability to profitably commercialize our product candidates, if approved. In some countries, particularly the countries of the European Union, the pricing of prescription pharmaceuticals is subject to governmental control and access. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our products candidate to other available therapies. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be harmed, possibly materially.

In addition to continuing pressure on prices and cost containment measures, legislative developments at the European Union or member state level may result in significant additional requirements or obstacles that may increase our operating costs. The delivery of healthcare in the European Union, including the establishment and operation of health services and the pricing and reimbursement of medicines, is almost exclusively a matter for national, rather than European Union, law and policy. National governments and health service providers have different priorities and approaches to the delivery of healthcare and the pricing and reimbursement of products in that context. In general, however, the healthcare budgetary constraints in most European Union member states have resulted in restrictions on the pricing and reimbursement of medicines by relevant health service providers. Coupled with ever-increasing European Union and national regulatory burdens on those wishing to develop and market products, this could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to commercialize our product candidates, if approved.

Finally, in markets outside of the United States and the European Union, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies.

Inadequate funding for the FDA, the SEC, and other government agencies, including from government shut downs, or other disruptions to these agencies' operations, could hinder their ability to hire and retain key leadership and other personnel, prevent new products and services from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory and policy changes. Average review times at the agency have fluctuated in recent years as a result. Disruptions at the FDA and other agencies may also slow the time necessary for new product candidates to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. In addition, government funding of the Securities and Exchange Commission (the "SEC") and other government agencies on which our operations may rely, including those that fund research and development activities, is subject to the political process, which is inherently fluid and unpredictable.

In addition, disruptions may result from events similar to the COVID-19 pandemic. During the COVID-19 pandemic, a number of companies announced receipt of complete response letters due to the FDA's inability to complete required inspections for their applications. In the event of a similar public health emergency in the future, the FDA may not be able to continue its current pace and review timelines could be extended. Regulatory authorities outside the United States facing similar circumstances may adopt similar restrictions or other policy measures in response to a similar public health emergency and may also experience delays in their regulatory activities.

Disruptions at the FDA and other agencies may also slow the time necessary for new product candidates to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years the U.S. government has shut down several times and certain regulatory agencies, such as the FDA and the SEC, have had to furlough critical FDA, SEC and other government employees and stop critical activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, future government shutdowns could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

Compliance with global privacy and data security requirements could result in additional costs and liabilities to us or inhibit our ability to collect and process data globally, and the failure to comply with such requirements could subject us to significant fines and penalties, which may have a material adverse effect on our business, financial condition or results of operations.

The regulatory framework for the collection, use, safeguarding, sharing, transfer and other processing of information worldwide is rapidly evolving and is likely to remain uncertain for the foreseeable future. Globally, virtually every jurisdiction in which we operate has established its own data security and privacy frameworks with which we must comply. For example, the collection, use, disclosure, transfer, or other processing of personal data regarding individuals in the European Union, including personal health data, is subject to the GDPR, which took effect across all member states of the European Economic Area ("EEA") in May 2018. Beyond GDPR, there are privacy and data security laws in a growing number of countries around the world. While many follow GDPR as a model, other laws contain different or conflicting provisions. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, including requirements relating to processing health and other sensitive data, obtaining consent of the individuals to whom the personal data relates, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches, and taking certain measures when engaging third-party processors. The GDPR increases our obligations with respect to clinical trials conducted in the EEA by expanding the definition of personal data to include coded data and requiring changes to informed consent practices and more detailed notices for clinical trial subjects and investigators.

In addition, the GDPR also imposes strict rules on the transfer of personal data to countries outside the European Union, including the United States and, as a result, increases the scrutiny that clinical trial sites located in the EEA should apply to transfers of personal data from such sites to countries that are considered to lack an adequate level of data protection, such as the United States. There are ongoing concerns about the ability of companies to transfer personal data from the European Union to other countries. In July 2020, the Court of Justice of the European Union ("CJEU") invalidated the EU-U.S. Privacy Shield, one of the mechanisms used to legitimize the transfer of personal data from the EEA to the United States. This CJEU decision has resulted in increased scrutiny on data transfers generally and may increase our costs of compliance with data privacy legislation as well as our costs of negotiating appropriate privacy and security agreements with our vendors and business partners.

The GDPR also permits data protection authorities to require destruction of improperly gathered or used personal information and/or impose substantial fines for violations of the GDPR, which can be up to 4% of global revenues or 20 million Euros, whichever is greater, and it also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. In addition, the GDPR provides that European Union member states may make their own further laws and regulations limiting the processing of personal data, including genetic, biometric, or health data.

Additionally, in October 2022, President Biden signed an executive order to implement the EU-U.S. Data Privacy Framework, which would serve as a replacement to the EU-U.S. Privacy Shield. The European Commission initiated the process to adopt an adequacy decision for the EU-U.S. Data Privacy Framework in December 2022, and the European Commission adopted the adequacy decision on July 10, 2023. The adequacy decision will permit U.S. companies who self-certify to the EU-U.S. Data Privacy Framework to rely on it as a valid data transfer mechanism for data transfers from the EU to the U.S. However, some privacy advocacy groups have already suggested that they will be challenging the EU-U.S. Data Privacy Framework. If these challenges are successful, they may not only impact the EU-U.S. Data Privacy Framework, but also further limit the viability of the standard contractual clauses and other data transfer mechanisms. The uncertainty around this issue has the potential to impact our business internationally.

Following the withdrawal of the United Kingdom from the European Union, the United Kingdom's Data Protection Act 2018 applies to the processing of personal data that takes place in the United Kingdom and includes parallel obligations to those set forth by GDPR. In relation to data transfers, both the United Kingdom and the European Union have determined, through separate "adequacy" decisions, that data transfers between the two jurisdictions are in compliance with the United Kingdom's Data Protection Act 2018 and the GDPR, respectively. In October 2023, the United Kingdom and the United States implemented a US-UK "data bridge," which functions similarly to the EU-U.S. Data Privacy Framework and provides an additional legal mechanism for companies to transfer data from the United Kingdom to the United States. In addition to the United Kingdom, Switzerland is also in the process of approving an adequacy decision in relation to the Swiss-U.S. Data Privacy Framework (which would function similarly to the EU-U.S. Data Privacy Framework and the U.S.-UK "data bridge" in relation to data transfers from Switzerland to the United States). Any changes or updates to these developments have the potential to impact our business.

Similar actions are either in place or under way in the United States. There are a broad variety of data protection laws that are applicable to our activities, and a wide range of enforcement agencies at both the state and federal levels that can review companies for privacy and data security concerns based on general consumer protection laws. The Federal Trade Commission and state Attorneys General all are aggressive in reviewing privacy and data security protections for consumers. New laws also are being considered at both the state and federal levels. For example, the California Consumer Privacy Act ("CCPA"), which went into effect on January 1, 2020, is creating similar risks and obligations as those created by the GDPR, though the CCPA does exempt certain information collected as part of a clinical trial subject to the Federal Policy for the Protection of Human Subjects (the Common Rule). In November 2020, California voters passed a ballot initiative for the California Privacy Rights Act ("CPRA"), which went into effect on January 1, 2023, and significantly expanded the CCPA to incorporate additional GDPR-like provisions including requiring that the use, retention, and sharing of personal information of California residents be reasonably necessary and proportionate to the purposes of collection or processing, granting additional protections for sensitive personal information, and requiring greater disclosures related to notice to residents regarding retention of information. The CPRA also created a new enforcement agency – the California Privacy Protection Agency – whose sole responsibility is to enforce the CPRA, which will further increase compliance risk. The provisions in the CPRA may apply to some of our business activities.

In addition to California, a number of other states have passed comprehensive privacy laws similar to the CCPA and CPRA. These laws are either in effect or will go into effect sometime before the end of 2026. Like the CCPA and CPRA, these laws create obligations related to the processing of personal information, as well as special obligations for the processing of "sensitive" data, which includes health data in some cases. Some of the provisions of these laws may apply to our business activities, including our identification of research subjects, relationships with business partners and ultimately the marketing and distribution of our products. Other states will be considering similar laws in the future, and Congress has also been debating passing a federal privacy law. There are also states that are specifically regulating health information that may affect our business. For example, Washington state passed a health privacy law in 2023 that will regulate the collection and sharing of health information, and the law also has a private right of action, which further increases the relevant compliance risk. Connecticut and Nevada have also passed similar laws regulating consumer health data, and more states are considering such legislation. These laws may impact our business activities, including our identification of research subjects, relationships with business partners, and ultimately the marketing and distribution of our products.

A broad range of legislative measures also have been introduced at the federal level. Accordingly, failure to comply with federal and state laws (both those currently in effect and future legislation) regarding privacy and security of personal information could expose us to fines and penalties under such laws. There also is the threat of consumer class actions related to these laws and the

overall protection of personal data. Even if we are not determined to have violated these laws, government investigations into these issues typically require the expenditure of significant resources and generate negative publicity, which could harm our reputation and our business.

Given the breadth and depth of changes in data protection obligations, preparing for and complying with these requirements is rigorous and time intensive and requires significant resources and a review of our technologies, systems and practices, as well as those of any third-party collaborators, service providers, contractors or consultants that process or transfer personal data collected. The GDPR and other changes in laws or regulations associated with the enhanced protection of certain types of sensitive data, such as healthcare data or other personal information from our clinical trials, could require us to change our business practices and put in place additional compliance mechanisms, may interrupt or delay our development, regulatory and commercialization activities and increase our cost of doing business, and could lead to government enforcement actions, private litigation and significant fines and penalties against us and could have a material adverse effect on our business, financial condition or results of operations.

We cannot assure stockholders that our third-party service providers with access to our or our customers', suppliers', trial patients' and employees' personally identifiable and other sensitive or confidential information in relation to which we are responsible will not breach contractual obligations imposed by us, or that they will not experience data security breaches or attempts thereof, which could have a corresponding effect on our business, including putting us in breach of our obligations under privacy laws and regulations and/or which could in turn adversely affect our business, results of operations and financial condition. We cannot assure stockholders that our contractual measures and our own privacy and security-related safeguards will protect us from the risks associated with the third-party processing, storage and transmission of such information.

Laws and regulations governing any international operations we may have in the future may preclude us from developing, manufacturing, and selling certain product candidates outside of the United States and require us to develop and implement costly compliance programs.

We are subject to numerous laws and regulations in each jurisdiction outside the United States in which we operate. The creation, implementation and maintenance of international business practices compliance programs is costly and such programs are difficult to enforce, particularly where reliance on third parties is required.

The Foreign Corrupt Practices Act (the "FCPA") prohibits any U.S. individual or business from paying, offering, authorizing payment or offering of anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the United States to comply with certain accounting provisions requiring the company to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations. The anti-bribery provisions of the FCPA are enforced primarily by the Department of Justice. The SEC is involved with enforcement of the books and records provisions of the FCPA.

Compliance with the FCPA is expensive and difficult, particularly in countries in which corruption is a recognized problem. In addition, the FCPA presents particular challenges in the pharmaceutical industry, because, in many countries, hospitals are operated by the government, and doctors and other hospital employees are considered foreign officials. Certain payments to hospitals in connection with clinical trials and other work have been deemed to be improper payments to government officials and have led to FCPA enforcement actions.

Various laws, regulations and executive orders also restrict the use and dissemination outside of the United States, or the sharing with certain non-U.S. nationals, of information classified for national security purposes, as well as certain products and technical data relating to those products. Our expansion outside of the United States has required, and will continue to require, us to dedicate additional resources to comply with these laws, and these laws may preclude us from developing, manufacturing, or selling certain products and product candidates outside of the United States, which could limit our growth potential and increase our development costs. The failure to comply with laws governing international business practices may result in substantial penalties, including suspension or debarment from government contracting. Violation of the FCPA can result in significant civil and criminal penalties. Indictment alone under the FCPA can lead to suspension of the right to do business with the U.S. government until the pending claims are resolved. Conviction of a violation of the FCPA can result in long-term disqualification as a government contractor. The termination of a government contract or relationship as a result of our failure to satisfy any of our obligations under laws governing international business practices would have a negative impact on our operations and harm our reputation and ability to procure government contracts. The SEC also may suspend or bar issuers from trading securities on U.S. exchanges for violations of the FCPA's accounting provisions. For example, the provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order, or use of medicinal products is prohibited in the European Union. The provision of benefits or advantages to physicians is also governed by the national anti-bribery laws of European Union

Member States. Infringement of these laws could result in substantial fines and imprisonment. Payments made to physicians in certain European Union Member States must be publicly disclosed. Moreover, agreements with physicians often must be the subject of prior notification and approval by the physician' s employer, his or her competent professional organization, and/or the regulatory authorities of the individual European Union Member States. These requirements are provided in the national laws, industry codes, or professional codes of conduct applicable in the European Union Member States. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines, or imprisonment.

If we or any third-party manufacturer we engage now or in the future fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs or liabilities that could have a material adverse effect on our business.

We and third-party manufacturers we engage now are, and any third-party manufacturer we may engage in the future will be, subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties.

Although we maintain general liability insurance as well as workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials.

In addition, we may incur substantial costs in order to comply with current or future environmental, health, and safety laws and regulations. These current or future laws and regulations may impair our research, development or commercialization efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties, or other sanctions.

Further, with respect to the operations of our current and any future third-party contract manufacturers, it is possible that if they fail to operate in compliance with applicable environmental, health and safety laws and regulations or properly dispose of wastes associated with our products, we could be held liable for any resulting damages, suffer reputational harm or experience a disruption in the manufacture and supply of our product candidates or products. In addition, our supply chain may be adversely impacted if any of our third-party contract manufacturers become subject to injunctions or other sanctions as a result of their non-compliance with environmental, health and safety laws and regulations.

Risks Related to Employee Matters and Managing Growth

Our future success depends on our ability to retain key executives and to attract, retain and motivate qualified personnel.

We are highly dependent on the research and development, clinical, financial, operational and other business expertise of our executive officers, as well as the other principal members of our management, scientific and clinical teams. Although we have entered into employment agreements with our executive officers, each of them may terminate their employment with us at any time. We do not maintain "key person" insurance for any of our executives or other employees. Recruiting and retaining qualified scientific, clinical, manufacturing, accounting, legal and sales and marketing personnel will also be critical to our success.

The loss of the services of our executive officers or other key employees could impede the achievement of our research, development and commercialization objectives and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain marketing approval of and commercialize products. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. Our success as a public company also depends on implementing and maintaining internal controls and the accuracy and timeliness of our financial reporting. If we are unable to continue to attract and retain high quality personnel, our ability to pursue our growth strategy will be limited.

We expect to expand our development and regulatory capabilities and potentially implement sales, marketing, and distribution capabilities, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.

We expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of drug development, clinical, regulatory affairs, commercial, manufacturing, and quality control and, if any of our product candidates receives marketing approval, sales, marketing and distribution. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Future growth will impose significant added responsibilities on members of management, including:

- identifying, recruiting, integrating, maintaining and motivating additional employees;
- managing our internal development efforts effectively, including the clinical and regulatory review process for INZ-701 and any other product candidate we develop, while complying with our contractual obligations to contractors and other third parties; and
- improving our operational, financial and management controls, reporting systems and procedures.

Our future financial performance and our ability to advance development of and, if approved, commercialize INZ-701 and any other product candidate we develop will depend, in part, on our ability to effectively manage any future growth. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. If we do not effectively manage the expansion of our operations, we could experience weaknesses in our infrastructure, operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees. The expansion of our operations also could lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

Many of the pharmaceutical and biotechnology companies that we compete against for qualified personnel and consultants have greater financial and other resources, different risk profiles and a longer history in the industry than we do. If we are unable to continue to attract and retain high-quality personnel and consultants, the rate and success at which we can develop product candidates and operate our business will be limited.

Our internal computer systems, or those of our collaborators, vendors, suppliers, contractors, or consultants, may fail or suffer security breaches, which could result in a material disruption of our product development programs.

Our internal computer systems and those of any collaborators, vendors, suppliers, contractors or consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. Such systems are also vulnerable to service interruptions or to security breaches from inadvertent or intentional actions by our employees, third-party vendors and/or business partners, or from cyber-attacks by malicious third parties. Cyber-attacks are increasing in their frequency, sophistication and intensity, and have become increasingly difficult to detect. Cyber-attacks could include the deployment of harmful malware, ransomware, denial-of-service attacks, unauthorized access to or deletion of files, social engineering and other means to affect service reliability and threaten the confidentiality, integrity and availability of information. Cyber-attacks also could include phishing attempts or e-mail fraud to cause payments or information to be transmitted to an unintended recipient.

If we experience any material system failure, accident, cyber-attack, or security breach that causes interruptions in our operations, it could result in a material disruption of our development programs and our business operations, whether due to a loss of our trade secrets or other proprietary information or other similar disruptions. For example, the loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability, our competitive position could be harmed and the further development and commercialization of our product candidates could be delayed.

Our employees, independent contractors, including principal investigators, consultants and vendors and any third parties we may engage in connection with research, development, regulatory, manufacturing, quality assurance and other pharmaceutical functions and commercialization may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements and insider trading, which could cause significant liability for us and harm our reputation.

We are exposed to the risk of fraud or other misconduct by our employees, independent contractors, including principal investigators, consultants and vendors and any other third parties we engage. Misconduct by these partners could include intentional, reckless or negligent conduct or unauthorized activities that include failures to comply with FDA regulations or similar regulations of comparable foreign regulatory authorities, provide complete and accurate information to the FDA or comparable foreign regulatory authorities, comply with manufacturing standards, comply with federal and state data privacy, security, fraud and other healthcare fraud and abuse laws and regulations and similar laws and regulations established and enforced by comparable foreign regulatory authorities, report complete financial information or data accurately or disclose unauthorized activities to us. Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. This could include violations of HIPAA, other U.S. federal and state law, and requirements of non-U.S. jurisdictions, including the European Union Data Protection Directive. We are also exposed to risks in connection with any insider trading violations by employees or others affiliated with us. It is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws, standards, regulations, guidance or codes of conduct. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and results of operations, including the imposition of significant civil, criminal and administrative penalties, damages, monetary fines, disgorgements, possible exclusion from participation in Medicare, Medicaid, other U.S. federal healthcare programs or healthcare programs in other jurisdictions, integrity oversight and reporting obligations to resolve allegations of non-compliance, individual imprisonment, other sanctions, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations.

Risks Related to our Common Stock

Our executive officers, directors and principal stockholders, if they choose to act together, have the ability to control or significantly influence all matters submitted to stockholders for approval.

As of March 3, 2025, our executive officers and directors and our stockholders who owned more than 5% of our outstanding common stock, in the aggregate, owned shares representing approximately 49% of our capital stock. As a result, if these stockholders were to choose to act together, they would be able to control or significantly influence all matters submitted to our stockholders for approval, as well as our management and affairs. For example, these persons, if they choose to act together, would control the election of directors and approval of any merger, consolidation or sale of all or substantially all of our assets.

This concentration of ownership control may:

- delay, defer or prevent a change in control;
- entrench our management and board of directors; or
- delay or prevent a merger, consolidation, takeover or other business combination involving us that other stockholders may desire.

Provisions in our corporate charter documents and under Delaware law could make an acquisition of our company, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current directors and members of management.

Provisions in our certificate of incorporation and our bylaws may discourage, delay or prevent a merger, acquisition or other change in control of our company that stockholders may consider favorable, including transactions in which stockholders might otherwise receive a premium for their shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions:

- establish a classified board of directors such that only one of three classes of directors is elected each year;
- allow the authorized number of our directors to be changed only by resolution of our board of directors;
- limit the manner in which stockholders can remove directors from our board of directors;
- establish advance notice requirements for stockholder proposals that can be acted on at stockholder meetings and nominations to our board of directors;
- require that stockholder actions must be effected at a duly called stockholder meeting and prohibit actions by our stockholders by written consent;
- limit who may call stockholder meetings;
- authorize our board of directors to issue preferred stock without stockholder approval, which could be used to institute a “poison pill” that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our board of directors; and
- require the approval of the holders of at least 75% of the votes that all our stockholders would be entitled to cast to amend or repeal specified provisions of our certificate of incorporation or bylaws.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law (the "DGCL") which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner.

The price of our common stock is volatile and fluctuates substantially, which could result in substantial losses for our stockholders.

The trading price of our common stock has been, and is likely to continue to be, volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control. The stock market in general and the market for smaller biopharmaceutical companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. The market price for our common stock may be influenced by many factors, including:

- results of or developments in preclinical studies and clinical trials of our product candidates or those of our competitors or potential collaborators;
- our success in commercializing our product candidates, if and when approved;
- the success of competitive products or technologies;
- regulatory actions with respect to our product candidates;
- regulatory or legal developments in the United States and other countries;
- changes in physician, hospital, or healthcare provider practices;

- developments or disputes concerning patent applications, issued patents or other intellectual property or proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to any of our product candidates or clinical development programs;
- the results of our efforts to discover, develop, acquire or in-license products, product candidates or technologies, the costs of commercializing any such products, and the costs of development of any such product candidates or technologies;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- variations in our financial results or the financial results of companies that are perceived to be similar to us;
- announcements by us, our partners or our competitors of significant acquisitions, strategic partnerships, joint ventures, collaborations, or capital commitments;
- sales of common stock by us, our executive officers, directors or principal stockholders, or others;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry, and market conditions; and
- the other factors described in this "Risk Factors" section.

In the past, following periods of volatility in the market price of a company's securities, securities class-action litigation has often been instituted against that company. Any lawsuit to which we are a party, with or without merit, may result in an unfavorable judgment. We also may decide to settle lawsuits on unfavorable terms. Any such negative outcome could result in payments of substantial damages or fines, damage to our reputation or adverse changes to our offerings or business practices. Such litigation may also cause us to incur other substantial costs to defend such claims and divert management's attention and resources. Furthermore, negative public announcements of the results of hearings, motions or other interim proceedings or developments could have a negative effect on the market price of our common stock.

An active trading market for our common stock may not be sustained.

Although our common stock is listed on the Nasdaq Global Select Market, an active trading market for our shares may not continue to develop or be sustained. As a result, it may be difficult for our stockholders to sell their shares without depressing the market price for the shares, or at all.

If securities analysts do not publish or cease publishing research or reports or publish misleading, inaccurate or unfavorable research about our business or if they publish negative evaluations of our stock, the price and trading volume of our stock could decline.

The trading market for our common stock relies, in part, on the research and reports that industry or financial analysts publish about us or our business. There can be no assurance that existing analysts will continue to cover us or that new analysts will begin to cover us. There is also no assurance that any covering analyst will provide favorable coverage. Although we have obtained analyst coverage, if one or more of the analysts covering our business downgrade their evaluations of our stock or publish inaccurate or unfavorable research about our business, or provide more favorable relative recommendations about our competitors, the price of our stock could decline. If one or more of these analysts cease to cover our stock, we could lose visibility in the market for our stock, which in turn could cause our stock price and trading volume to decline.

If a significant portion of our total outstanding shares are sold into the market, the market price of our common stock could drop significantly, even if our business is doing well.

Sales of a substantial number of shares of our common stock in the public market, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock. Holders of a significant portion of our common stock have rights, subject to specified conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. We have also filed registration statements registering all shares of common stock that we may issue under our equity compensation plans. These shares can be freely sold in the public market upon issuance, subject to volume limitations applicable to affiliates.

We currently have on file with the SEC a universal shelf registration statement on Form S-3 which allows us to offer and sell up to $300.0 million of a variety of securities, including common stock, preferred stock, debt securities, depositary shares, subscription rights, warrants or units from time to time pursuant to one or more offerings at prices and terms to be determined at the time of sale. In addition, we have also entered into an Open Market Sale Agreement with Jefferies LLC, as sales agent, pursuant to which we may offer and sell shares of our common stock under a registration statement with an aggregate offering price of up to $50.0 million under an "at-the-market" offering program. To date, we have sold $31.8 million of securities pursuant to the Open Market Sale Agreement.

We are an "emerging growth company" and a "smaller reporting company," and the reduced disclosure requirements applicable to emerging growth companies and smaller reporting companies may make our common stock less attractive to investors.

We are an "emerging growth company," ("EGC") as defined in the Jumpstart Our Business Startups Act of 2012 (the "JOBS Act"). We will remain an EGC until December 31, 2025, although we would cease to be an EGC if we issue more than $1 billion of non-convertible debt over a three-year period. For so long as we remain an EGC, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not EGCs. These exemptions include:

- not being required to comply with the auditor attestation requirements in the assessment of our internal control over financial reporting;
- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements;
- reduced disclosure obligations regarding executive compensation; and
- exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved.

Further, even after we no longer qualify as an EGC, we may still qualify as a "smaller reporting company," which would allow us to take advantage of many of the same exemptions from disclosure requirements allowed for an EGC, including reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements. In addition, if we are a smaller reporting company with less than $100 million in annual revenue, we would not be required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404.

We may choose to take advantage of some or all of the available exemptions. We cannot predict whether investors will find our common stock less attractive if we rely on certain or all of these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

In addition, the JOBS Act permits an EGC to take advantage of an extended transition period to comply with new or revised accounting standards applicable to public companies until those standards would otherwise apply to private companies. We have elected to use the extended transition period for complying with new or revised accounting standards and will do so until such time that we either (1) irrevocably elect to "opt out" of such extended transition period or (2) no longer qualify as an EGC. As a result of this election, our consolidated financial statements may not be comparable to companies that comply with public company Financial Accounting Standards Board standards' effective dates.

We have incurred and will continue to incur increased costs as a result of operating as a public company, and our management will be required to devote substantial time to new compliance initiatives and corporate governance practices.

As a public company we have incurred, and particularly after we are no longer an EGC or a smaller reporting company, will continue to incur significant legal, accounting and other expenses that we did not incur as a private company. The Sarbanes-Oxley Act of 2002, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of the Nasdaq Global Select Market and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel will need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will increase our legal and financial compliance costs, particularly as we hire additional financial and accounting employees to meet public company internal control and financial reporting requirements, and will make some activities more time-consuming and costly. For example, we expect that these rules and regulations may make it more difficult and more expensive for us to obtain director and officer liability insurance, which in turn could make it more difficult for us to attract and retain qualified members of our board of directors.

We are evaluating these rules and regulations, and cannot predict or estimate the amount of additional costs we may incur or the timing of such costs. These rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

Pursuant to Section 404, we are required to furnish a report by our management on our internal control over financial reporting. However, while we remain an EGC or a smaller reporting company with less than $100 million in revenue, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404 within the prescribed period, we will be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, including through hiring additional financial and accounting personnel, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that we will not be able to conclude, within the prescribed timeframe or at all, that our internal control over financial reporting is effective as required by Section 404. If we identify one or more material weaknesses in our internal control over financial reporting, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

Because we do not anticipate paying any cash dividends on our capital stock in the foreseeable future, capital appreciation, if any, will be our stockholders' sole source of gain.

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. In addition, our ability to pay cash dividends is currently restricted by the terms of our Loan Agreement, and future debt financing arrangements may contain terms prohibiting or limiting the amount of dividends that may be declared or paid on our common stock. As a result, capital appreciation, if any, of our common stock will be our stockholders' sole source of gain for the foreseeable future.

Our certificate of incorporation designates the state courts in the State of Delaware as the sole and exclusive forum for certain types of actions and proceedings that may be initiated by our stockholders, which could discourage lawsuits against the company and our directors, officers and employees.

Our certificate of incorporation provides that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware (or, if the Court of Chancery of the State of Delaware does not have jurisdiction, the federal district court for the District of Delaware) will, to the fullest extent permitted by law, be the sole and exclusive forum for (1) any derivative action or proceeding brought on our behalf, (2) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers, employees or stockholders to our company or our stockholders, (3) any action asserting a claim arising pursuant to any provision of the DGCL or as to which the DGCL confers jurisdiction on the Court of Chancery of the State of Delaware or (4) any action asserting a claim arising pursuant to any provision of our certificate of incorporation or bylaws (in each case, as they may be amended from time to time) or governed by the internal affairs doctrine. These choice of forum provisions will not apply to claims arising under the Securities Act of 1933, as amended, the Securities Exchange Act of 1934, as amended, or any other claim for which federal courts have exclusive jurisdiction. Furthermore, our certificate of incorporation provides that, unless we consent in writing to the selection of an alternative forum, the federal district courts of the United States of America shall, to the fullest extent permitted by law, be the sole and exclusive forum for the resolution of any claims arising under the Securities Act of 1933, as amended.

These exclusive forum provisions may limit the ability of our stockholders to bring a claim in a judicial forum that such stockholders find favorable for disputes with us or our directors, officers or employees, which may discourage such lawsuits against us and our directors, officers and employees. If a court were to find such provisions contained in our certificate of incorporation to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could materially adversely affect our business, financial condition and operating results.

Item 1B. Unresolved Staff Comments.

None.

Item 1C. Cybersecurity.

We have certain processes for assessing, identifying, and managing cybersecurity risks, which are built into our overall information technology function and are designed to help protect our information assets and operations from internal and external cyber threats, protect information from unauthorized access or attack, as well as secure our network and systems. Such processes include physical, procedural, and technical safeguards, response plans, regular tests on our systems, incident simulations, and routine review of our policies and procedures to identify risks and improve our practices. We engage certain external parties, including consultants, computer security firms and risk management, peer companies, industry groups, and governance experts, to enhance our cybersecurity oversight. We consider the internal risk oversight programs of third-party service providers before engaging them to help protect us from any related vulnerabilities. As part of our overall risk mitigation strategy, we also maintain cyber insurance coverage; however, such insurance may not be sufficient in type or amount to cover us against claims related to security breaches, cyber attacks, and other related breaches.

The Audit Committee of our Board of Directors provides direct oversight over cybersecurity risk and provides periodic updates to the Board of Directors regarding such oversight. The Audit Committee receives periodic updates from management regarding cybersecurity matters and is notified between such updates regarding significant new cybersecurity threats or incidents.

Our Vice President of Information Technology leads the operational oversight of company-wide cybersecurity strategy, policy, standards, and processes and works across relevant departments to assess and help prepare us and our employees to address cybersecurity risks. The Vice President of Information Technology has over 25 years of experience working with life science companies and venture capital firms in the information technology field, a certificate from HarvardX (Cybersecurity: Managing Risk), and an active membership in Health-ISAC.

We have also established a cross-functional Cybersecurity Steering Committee, led by our Chief Executive Officer serving as the chair and consisting of other executive-level leaders, that is responsible for providing leadership in the protection of information assets and technology. The committee members advise on and prioritize the development of information security initiatives, projects, and policies as advocates for our stakeholders. This committee is also charged with helping to resolve security and compliance risk issues affecting us.

In order to help deter and detect cyber threats, we provide all employees, including part-time and temporary employees, with a monthly data protection, cybersecurity, and incident response and prevention training and compliance program, which covers timely

and relevant topics, including social engineering, phishing, password protection, confidential data protection, asset use, and mobile security, and educates employees on the importance of reporting all incidents immediately. We engage third-party vendors for 24/7 monitoring and comprehensive incident response measures. We also use technology-based tools to mitigate cybersecurity risks and to bolster our employee-based cybersecurity programs.

We do not believe that there are currently any known risks from cybersecurity threats that are reasonably likely to materially affect us or our business strategy, results of operations, or financial condition.

Item 2. Properties.

Our principal facilities consist of office and laboratory space in Boston, Massachusetts. We occupy approximately 8,499 square feet of office space under a lease that expires in October 2025. In addition, we occupy approximately 6,244 square feet of laboratory space under a lease that expires in December 2025. We do not own any real property. We believe that this office and laboratory space is sufficient to meet our current needs and that suitable additional space will be available as and when needed.

Item 3. Legal Proceedings.

We are not currently a party to any material legal proceedings.

Item 4. Mine Safety Disclosures.

Not applicable.

PART II

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities

Market Information

Our common stock commenced trading under the symbol "INZY" on the Nasdaq Global Select Market on July 24, 2020. Prior to that time, there was no public market for our common stock.

Holders of Our Common Stock

As of March 3, 2025, there were approximately 26 holders of record of shares of our common stock. This number does not include stockholders for whom shares are held in "nominee" or "street" name.

Dividend Policy

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all available funds and any future earnings to fund the development and expansion of our business. We do not anticipate paying any cash dividends for the foreseeable future. In addition, our ability to pay cash dividends is currently restricted by the terms of our Loan Agreement, and future debt financing arrangements may contain terms prohibiting or limiting the amount of dividends that may be declared or paid on our common stock. Any future determination to declare and pay dividends will be made at the discretion of our board of directors and will depend on then-existing conditions including our results of operations, financial condition, contractual restrictions, capital requirements, business prospects and other factors our board of directors may deem relevant.

Unregistered Sales of Equity Securities and Use of Proceeds

Recent Sales of Unregistered Equity Securities

We did not issue any securities that were not registered under the Securities Act of 1933, as amended (the "Securities Act"), during the 12 months ended December 31, 2024.

Issuer Purchases of Equity Securities

We did not purchase any of our registered securities during the period covered by this Annual Report on Form 10-K.

Item 6. [Reserved].

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations.

The following discussion and analysis of our financial condition and results of operations should be read together with our consolidated financial statements and the related notes appearing elsewhere in this Annual Report on Form 10-K. This discussion contains forward-looking statements that involve risks and uncertainties. As a result of many factors, including those factors set forth in the "Risk Factors" section of this Annual Report on Form 10-K, our actual results could differ materially from the results described in or implied by these forward-looking statements. For convenience of presentation some of the numbers have been rounded in the text below.

Overview

We are a clinical-stage biopharmaceutical company dedicated to developing innovative therapeutics for rare diseases that affect bone health and blood vessel function. Our expertise lies 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). It is well established that low levels of PPi drive pathologic mineralization and low levels of adenosine drive intimal proliferation in a number of rare diseases. 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").

We are initially focused on developing a novel therapy for diseases characterized by pathologic mineralization and intimal proliferation, including ENPP1 Deficiency and ABCC6 Deficiency as well as calciphylaxis. As part of our recent strategic review, we are prioritizing activities to support the planned Biologics License Application ("BLA") filing for INZ-701 for our lead indication, ENPP1 Deficiency. Patients with ABCC6 Deficiency being treated in our ADAPT long-term extension study, our expanded access program, or under investigator-sponsored INDs will continue to receive treatment. Any future trials in ABCC6 Deficiency and calciphylaxis will be postponed.

ENPP1 and ABCC6 Deficiencies are rare chronic, systemic, and progressive genetic diseases occurring over the course of a patient's lifetime, starting as early as fetal development and spanning into adulthood. These diseases represent a significant unmet medical need, with high mortality rates for infants with ENPP1 Deficiency and high levels of morbidity occurring for patients with these diseases throughout their lives. Calciphylaxis is a rare disorder with a high mortality rate that mostly affects patients with end-stage kidney disease ("ESKD"). There are currently no approved therapies for ENPP1 Deficiency, ABCC6 Deficiency, or calciphylaxis. Currently available treatments seek to minimize the manifestations of these diseases and do not address the underlying causes.

Our lead product candidate, INZ-701, is a soluble, recombinant, or genetically engineered, ENPP1 fusion protein that is designed to increase PPi and adenosine, to enable the potential treatment of multiple diseases caused by deficiencies in these molecules. By targeting the PPi-Adenosine Pathway, INZ-701 aims to correct pathologic mineralization and intimal proliferation, addressing the significant morbidity and mortality in these devastating diseases. We have generated robust proof of concept data in preclinical models of ENPP1 Deficiency, ABCC6 Deficiency and, in support of our calciphylaxis program, chronic kidney disease demonstrating that INZ-701 prevented pathologic mineralization and skeletal abnormalities, led to improvements in overall health and survival, and prevented intimal proliferation.

We are currently conducting clinical trials of INZ-701 for the treatment of ENPP1 Deficiency, ABCC6 Deficiency, and calciphylaxis. The U.S. Food and Drug Administration ("FDA") has granted Orphan Drug Designation and the European Medicines Agency ("EMA") has granted Orphan Designation to INZ-701 for the treatment of ENPP1 Deficiency and ABCC6 Deficiency. The FDA has also granted fast track designation for INZ-701 for the treatment of ENPP1 Deficiency, for the treatment of ABCC6 Deficiency and for the treatment of calciphylaxis, and rare pediatric disease designation for INZ-701 for the treatment of ENPP1 Deficiency.

In November 2021, we initiated our Phase 1/2 clinical trial of INZ-701 in adult patients with ENPP1 Deficiency. In February and September 2023, we reported positive interim pharmacokinetic, pharmacodynamic, safety, and exploratory efficacy data from this trial. In April 2024, we reported positive topline safety, pharmacokinetic, pharmacodynamic, and exploratory efficacy data from this trial.

In April 2022, we initiated our Phase 1/2 clinical trial of INZ-701 in adult patients with ABCC6 Deficiency. In February and September 2023, we reported positive interim safety, pharmacodynamic, pharmacokinetic, and exploratory efficacy data from this trial. In April 2024, we reported positive topline safety, pharmacokinetic, pharmacodynamic, and exploratory efficacy data from this trial.

In February 2023, we dosed our first pediatric patient with ENPP1 Deficiency with INZ-701 under our expanded access program. Under this program, we can use INZ-701 outside of our clinical trials to treat patients with serious or immediately life-threatening diseases or conditions when there are no comparable or satisfactory alternative treatment options and when other criteria are met.

In June 2023, we dosed the first infant patient in our Phase 1b, single arm, open-label clinical trial of INZ-701 (the "ENERGY 1 trial") designed primarily to assess the safety, tolerability, pharmacokinetics, and pharmacodynamics of INZ-701 in infants with ENPP1 Deficiency. In January 2025, we announced positive interim results in infants and young children with ENPP1 Deficiency from the ENERGY 1 trial and our expanded access program which 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.

In September 2023, we opened the first site for our pivotal trial of INZ-701 in pediatric patients with ENPP1 Deficiency (the "ENERGY 3 trial"). In January 2025, we completed enrollment with 27 patients between the ages of one and less than 13 years across multiple sites globally. We anticipate reporting topline data from the ENERGY 3 trial in the first quarter of 2026.

In February 2024, we initiated SEAPORT 1, a Phase 1 clinical trial designed to assess the safety, tolerability, pharmacokinetics, and pharmacodynamics of INZ-701 in patients with ESKD receiving hemodialysis. Patients received 1.8 mg/kg of INZ-701 once weekly coinciding with their hemodialysis treatment for a total of 30 days. The trial's primary endpoint assessed safety and change from baseline plasma PPi concentration, with secondary endpoints including pharmacokinetic and pharmacodynamic parameters. In October 2024, we announced positive interim data from SEAPORT 1. The interim data demonstrated that INZ-701 significantly increased PPi levels in ESKD patients receiving hemodialysis, with levels rising into the normal range by week three of the trial’s four-week dosing schedule.

In June 2024, we initiated ADAPT, a multicenter, open-label, long-term safety trial of INZ-701 in patients with ENPP1 Deficiency or ABCC6 Deficiency who have received INZ-701 in an existing clinical trial and choose to continue dosing for the potential treatment of their condition. ADAPT enrolled patients who have completed a Phase 1/2 trial in adults with ENPP1 and ABCC6 Deficiencies at the end of the fourth quarter of 2024.

In the fourth quarter of 2024, we opened the first site for the ENERGY 2 trial, an open label, single arm, pivotal trial of INZ-701 in infants with ENPP1 Deficiency, outside of the United States and patient recruitment is underway. 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.

Subject to successfully completing clinical development of INZ-701 in ENPP1 Deficiency, we plan to seek marketing approvals for INZ-701 on a worldwide basis. Beyond our development focus on INZ-701, we believe that our therapeutic approach has the potential to benefit patients suffering from additional diseases linked to the PPi-Adenosine Pathway.

Executive Summary

During the three months ended December 31, 2024, we continued to advance our ongoing clinical trials of INZ-701 in patients with ENPP1 and ABCC6 Deficiencies. Key highlights and accomplishments during the year ended December 31, 2024 through March 10, 2025, as well as upcoming anticipated milestones, include:

Key Highlights

- In January 2025, we received fast track designation from the FDA for INZ-701 for the treatment of calciphylaxis.
- In January 2025, we announced completion of enrollment in the ENERGY 3 pivotal trial of INZ-701 in pediatric patients with ENPP1 Deficiency. We expect topline data to follow in the first quarter of 2026 from the ENERGY 3 pivotal trial.
- In January 2025, we announced positive interim data for INZ-701 in infants and young children with ENPP1 Deficiency.
- In January 2025, we announced regulatory guidance from the FDA and EMA supporting further clinical development of INZ-701 in children with ABCC6 Deficiency.
- In October 2024, we announced positive interim data from our ongoing Phase 1 SEAPORT 1 Trial of INZ-701 in patients with ESKD receiving hemodialysis.

- In October 2024, we announced the appointment of Erik Harris to our Board of Directors. Mr. Harris, who currently serves as Chief Commercial Officer and Executive Vice President at Ultragenyx Pharmaceutical Inc., brings over 20 years of commercial expertise within the biopharmaceutical industry.

Our Operations

We have not yet commercialized any products or generated any revenue from product sales. Our operations to date have been limited to organizing and staffing our company, business planning, raising capital, securing intellectual property rights, conducting research and development activities, conducting preclinical studies and early-stage clinical trials, establishing arrangements for the manufacture of INZ-701, and longer-term planning for potential commercialization.

Since inception, we have incurred significant operating losses. Our ability to generate revenue from product sales sufficient to achieve profitability will depend heavily on the successful development and eventual commercialization of INZ-701 or one or more of our future product candidates and programs. Our net losses were $102.0 million and $71.2 million for the years ended December 31, 2024 and 2023, respectively. As of December 31, 2024, we had an accumulated deficit of $388.0 million.

Our total operating expenses were $104.0 million and $75.6 million for the years ended December 31, 2024 and 2023, respectively. We expect to continue to incur significant operating expenses for the foreseeable future. In addition, if we obtain marketing approval for INZ-701 or any other product candidate we develop, we expect to incur significant commercialization expenses related to product manufacturing, sales, marketing, and distribution. We have incurred and expect to continue to incur additional costs associated with operating as a public company.

As of December 31, 2024, we had cash, cash equivalents and short-term investments of $113.1 million, which along with the anticipated cost savings from our recent strategic prioritization, we believe will enable us to fund our operating expenses and capital expenditures into the first quarter of 2026. Since our cash, cash equivalents and short-term investments as of December 31, 2024 are not sufficient to fund our operations for at least the next twelve months from the date of issuance of the consolidated financial statements included elsewhere in this Annual Report on Form 10-K, there is substantial doubt about our ability to continue as a going concern. Our future viability is dependent on our ability to raise additional capital to finance our operations. We expect to finance our operations through potential public or private equity financings, debt financings, collaboration agreements or other capital sources. Our inability to raise capital as and when needed could have a negative impact on our financial condition and ability to pursue our business strategies. There can be no assurance that our current operating plan will be achieved or that additional funding will be available on terms acceptable to us, or at all. We have based our assessment on assumptions that may prove to be wrong, and we could use our capital resources sooner than we currently expect. See “Going Concern,” in Note 1 to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K.

Because of the numerous risks and uncertainties associated with pharmaceutical product development, we are unable to accurately predict the timing or amount of increased expenses or when, or if, we will be able to achieve profitability. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would depress the value of our company and could impair our ability to raise capital, expand our business, maintain our research and development efforts, diversify our pipeline of product candidates, or even continue our operations.

On July 25, 2022, we entered into the Loan Agreement with K2HV (which we refer to, together with any other lender from time to time party thereto, as the Lenders), K2HV, as administrative agent for the Lenders, and Ankura Trust Company, LLC, as collateral agent for the Lenders. The Loan Agreement provides up to $70.0 million principal in term loans consisting of (subject to certain customary conditions): (i) a first tranche commitment of $25.0 million, of which $5.0 million was funded at closing and of which the remaining $20.0 million was funded at our election on February 15, 2023, or collectively, the First Tranche Commitment, (ii) two subsequent tranche commitments totaling $20.0 million in the aggregate to be drawn at our option during certain availability periods, subject to the achievement, as determined by the administrative agent in its sole discretion, of certain time-based, financial, clinical and regulatory milestones relating to INZ-701, which were funded during June and December 2023, and (iii) a fourth tranche commitment of $25.0 million available to be drawn at our option through August 31, 2025, subject to use of proceeds limitations and Lender’s consent in its discretion.

The facility carries a 48-month term with interest only payments for 36 months and then interest and equal principal payments for the next 12 months. The term loan will mature on August 1, 2026 and bears a variable interest rate equal to the greater of (i) 7.85% and (ii) the sum of (A) the prime rate last quoted in The Wall Street Journal (or a comparable replacement rate if The Wall Street Journal ceases to quote such rate) and (B) 3.85%; provided that the interest rate cannot exceed 9.60%. We may prepay, at our option, all, but not less than all, of the outstanding principal balance and all accrued and unpaid interest with respect to the principal balance being prepaid of the term loans, subject to a prepayment premium to which the Lenders are entitled and certain notice requirements. We paid the Lenders certain customary fees and expenses at closing and are required to pay the Lenders additional fees

that may be due upon maturity or prepayment such as final payment fees and prepayment fees. As security for its obligations under the Loan Agreement, we granted the Lenders a first priority security interest on substantially all of our assets (other than intellectual property), subject to certain exceptions. The Lenders may elect, prior to the full repayment of the term loans, to convert up to $5.0 million of outstanding principal of the term loans into shares of our common stock, at a conversion price of $6.21 per share, subject to customary adjustments and 9.99% and 19.99% beneficial ownership limitations.

Subject to certain conditions, we granted the Lenders the right, prior to repayment of the term loans, to invest up to $5,000,000 in the aggregate in our future offerings of common stock, convertible preferred stock, or other equity securities that are broadly marketed and offered to multiple investors, on the same terms, conditions, and pricing afforded to others participating in any such financing.

On July 27, 2023, we entered into an underwriting agreement with BofA Securities, Inc., Cowen and Company, LLC and Piper Sandler & Co., as representatives of the several underwriters named therein , relating to an underwritten public offering of 14,375,000 shares of our common stock, which included 1,875,000 shares issued upon the exercise in full by the underwriters of their option to purchase additional shares (the "July 2023 Shares"). The closing of the offering took place on August 1, 2023. The offering price of the July 2023 Shares was $4.80 per share. Net proceeds from the sale and issuance of the July 2023 Shares were approximately $64.4 million, after deducting underwriting discounts and commissions and offering expenses.

On August 11, 2021, we filed a universal shelf registration statement on Form S-3, which was declared effective on August 23, 2021 (the "2021 Registration Statement"). Under the 2021 Registration Statement, we could offer and sell up to $200.0 million of a variety of securities, including common stock, preferred stock, depositary shares, debt securities, warrants, subscription rights or units from time to time pursuant to one or more offerings at prices and terms to be determined at the time of the sale. In connection with the filing of the 2021 Registration Statement, we entered into an Open Market Sale Agreement with Jefferies LLC, as sales agent, pursuant to which we may offer and sell shares of our common stock with an aggregate offering price of up to $50.0 million under an “at-the-market” offering program (the “At-the-Market Offering Program”). On November 7, 2023, we filed a universal shelf registration statement on Form S-3, which was declared effective on November 15, 2023 (the “2023 Registration Statement”). Under the 2023 Registration Statement, we may offer and sell up to $300.0 million of a variety of securities, including common stock, preferred stock, depositary shares, debt securities, warrants, subscription rights or units from time to time pursuant to one or more offerings at prices and terms to be determined at the time of the sale.

On August 6, 2024, in anticipation of the expiration of the 2021 Registration Statement, we filed a prospectus supplement (the “2024 Prospectus Supplement”) under the 2023 Registration Statement to register the offer and sale of the outstanding shares that could be sold under the At-the-Market Offering Program, which prospectus supplement superseded and replaced the sales agreement prospectus, dated August 23, 2021, under the 2021 Registration Statement. As of December 31, 2023, we had sold 3,553,995 shares of our common stock pursuant to the Open Market Sale Agreement for aggregate net proceeds of $21.2 million. As of the date of filing of the 2024 Prospectus Supplement, we had issued and sold 4,364,440 shares of common stock pursuant to the Open Market Sale Agreement for aggregate gross proceeds of approximately $26.2 million. Under the 2024 Prospectus Supplement, we may sell the shares of common stock under the Open Market Sale Agreement for an aggregate offering price of up to approximately $23.8 million. For the year ended December 31, 2024 we sold 2,100,903 shares of our common stock pursuant to the Open Market Sale Agreement for aggregate net proceeds of $10.5 million. Under the 2024 Prospectus Supplement, we may sell the shares of common stock under the Open Market Sale Agreement for an aggregate offering price of up to approximately $17.2 million.

To continue to finance our operations, we will need to raise additional capital, which cannot be assured. We anticipate that our expenses will increase substantially if and as we:

- conduct our ongoing Phase 1/2 clinical trials of INZ-701 for adults with ENPP1 and ABCC6 Deficiencies, our ongoing open label long-term safety trial of INZ-701 in patients with ENPP1 or ABCC6 Deficiencies who have received INZ-701 in an existing study, our ongoing Phase 1b clinical trial of INZ-701 for infants with ENPP1 Deficiency, our ongoing pivotal clinical trial of INZ-701 in infants, our ongoing pivotal trial of INZ-701 in pediatric patients with ENPP1 Deficiency, and our ongoing Phase 1 clinical trial of INZ-701 in patients with ESKD receiving hemodialysis;
- prepare for, initiate, and conduct our planned clinical trials of INZ-701 for patients with ENPP1;
- conduct research, preclinical testing, and clinical trials of INZ-701 for additional indications;
- conduct research, preclinical testing, and clinical trials of other product candidates;
- engage in regulatory interactions with the FDA, the EMA, and other regulatory authorities;
- submit regulatory filings and seek marketing approval for INZ-701 or any other product candidate if it successfully completes clinical trials;

- scale up our manufacturing processes and capabilities;
- establish a sales, marketing, and distribution infrastructure to commercialize any product candidate for which we may obtain marketing approval;
- in-license or acquire additional technologies or product candidates;
- make any payments to Yale University ("Yale") under our license agreement or sponsored research agreement with Yale;
- maintain, expand, enforce, and protect our intellectual property portfolio;
- hire additional clinical, regulatory, quality control, scientific, and commercial personnel;
- add operational, financial, and management information systems and personnel, including personnel to support our research, product development, and planned future commercialization efforts and our operations as a public company; and
- make any principal and interest payments when due under the terms of the Loan Agreement.

Financial Operations Overview

Research and Development Expenses

Research and development activities are central to our business model. Research and development costs consist of direct and indirect costs related to specific projects as well as fees paid to other entities that conduct certain research and development activities on our behalf and primarily relate to costs incurred in connection with the discovery and development of our lead product candidate, INZ-701.

We expense research and development costs as incurred. These expenses include:

- fees and expenses incurred in connection with the in-license of technology and intellectual property rights;
- expenses incurred under agreements with third parties, including contract research organizations ("CROs"), and other third parties that conduct research, preclinical, and clinical activities on our behalf as well as third parties that manufacture our product candidates for use in our preclinical studies and clinical trials;
- manufacturing scale-up expenses and the costs of acquiring and manufacturing preclinical trial materials, including manufacturing validation batches;
- personnel-related expenses, consisting primarily of salaries, related benefits, and stock-based compensation expense for employees engaged in research and development functions;
- the costs of acquiring laboratory supplies and developing preclinical studies and clinical trial materials;
- costs related to compliance with regulatory requirements; and
- an allocation of facilities costs, which include depreciation of equipment and expenses for rent, information technology, utilities, and other operating costs.

We recognize external development costs based on an evaluation of the progress to completion of specific tasks using information provided to us by our service providers. We do not currently track research and development expenses by specific indication.

We are currently conducting our Phase 1/2 clinical trials of INZ-701 for adults with ENPP1 Deficiency and ABCC6 Deficiency, our Phase 1b ENERGY 1 trial for infants with ENPP1 Deficiency, our pivotal ENERGY 3 trial of INZ-701 for pediatric patients with ENPP1 Deficiency, our Phase 1 SEAPORT 1 clinical trial of INZ-701 for patients with ESKD receiving hemodialysis, and our ongoing open label-long term safety trial ADAPT of INZ-701 in patients with ENPP1 or ABCC6 Deficiencies who have received INZ-701 in an existing study. Product candidates in later stages of clinical development generally have higher development costs than those in preclinical development or in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials. As a result of our recent strategic review and prioritization of activities in our ENPP1 Deficiency program, we expect that our research and development expenses will remain consistent in 2025 as compared to 2024.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries, related benefits, travel, and stock-based compensation expense for personnel in executive, finance, and administrative functions. General and administrative expenses also include professional fees for legal, consulting, accounting, tax, and audit services, and an allocation of facilities and information technology infrastructure costs. We incur, and anticipate that we will continue to incur, costs associated with being a public company, including costs of accounting, audit, legal, regulatory, compliance and tax-related services related to maintaining compliance with requirements of Nasdaq and the SEC; director and officer insurance costs; and investor and public relations costs. As a result of our strategic review and prioritization of activities in our ENPP1 Deficiency program, we expect that our general and administrative expenses will remain consistent in 2025 as compared to 2024.

Interest Income

Interest income consists of income from bank deposits and investments.

Interest Expense

Interest expense consists of interest expense related to our Loan Agreement, as well as amortization of debt discount and debt issuance costs.

Other Expense, net

Other expense, net primarily consists of realized gains and losses on marketable securities and foreign exchange gains or losses.

Results of Operations

Comparison of the Years Ended December 31, 2024 and 2023

The following table summarizes our results of operations for the years ended December 31, 2024 and 2023 (in thousands):

	Year Ended December 31,		
	2024	2023	Increase (Decrease)
Operating expenses:			
Research and development	$ 83,231	$ 54,847	$ 28,384
General and administrative	20,799	$ 20,798	1
Total operating expenses	104,030	75,645	28,385
Loss from operations	(104,030)	(75,645)	28,385
Other income (expense):			
Interest income	7,666	7,837	(171)
Interest expense	(5,558)	(3,333)	2,225
Other expense, net	(102)	(28)	74
Other income, net	2,006	4,476	(2,470)
Net loss	$ (102,024)	$ (71,169)	$ 30,855

Research and Development Expense

The following table summarizes our research and development expenses for the years ended December 31, 2024 and 2023 (in thousands):

	Year Ended December 31,		
	2024	2023	Increase
INZ-701-related research and development expense	$ 58,516	$ 33,564	$ 24,952
Unallocated expenses:			
Personnel-related expense (including stock-based compensation)	21,448	17,563	3,885
Facilities and administrative expense	3,267	3,720	(453)
Total	$ 83,231	$ 54,847	$ 28,384

Research and development expense increased $28.4 million for the year ended December 31, 2024 compared to the year ended December 31, 2023 primarily due to increases of $25.0 million in INZ-701-related research and development expense and $3.9 million in personnel-related costs, including stock-based compensation expense, offset by a $0.5 million decrease in facilities and administrative expense.

INZ-701-related research and development expense increased $25.0 million primarily due to a $10.1 million increase in chemistry, manufacturing, and controls expense to support our ongoing clinical trials and prepare for potential commercialization and a $14.9 million increase in clinical development and related consulting costs to support our ongoing clinical trials.

Personnel-related expense, including stock-based compensation expense, increased $3.9 million primarily due to increased headcount needed to support our ongoing clinical trials, offset by a $0.5 million decrease in facilities and administrative expense.

General and Administrative Expense

General and administrative expense remained relatively consistent for the year ended December 31, 2024 compared to the year ended December 31, 2023.

Interest Income

Interest income remained relatively consistent for the year ended December 31, 2024 compared to the year ended December 31, 2023.

Interest Expense

Interest expense increased $2.2 million for the year ended December 31, 2024 compared to the year ended December 31, 2023 primarily due to additional borrowings in 2023 under our Loan Agreement.

Other Expense, net

Other expense, net remained relatively consistent for the year ended December 31, 2024 compared to the year ended December 31, 2023.

Liquidity and Capital Resources

Sources of Liquidity

Since our inception, we have not generated any revenue and have incurred significant operating losses and negative cash flows from our operations. To date, we have funded our operations primarily with proceeds from the sales of convertible preferred stock, offerings of common stock and pre-funded warrants, and borrowings under our Loan Agreement. Until such time, if ever, as we can generate substantial revenues from product sales, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances, and marketing, distribution or licensing arrangements.

On August 11, 2021, we filed a universal shelf registration statement on Form S-3, which was declared effective on August 23, 2021 (the "2021 Registration Statement"). Under the 2021 Registration Statement, we could offer and sell up to $200.0 million of a variety of securities, including common stock, preferred stock, depositary shares, debt securities, warrants, subscription rights or units from time to time pursuant to one or more offerings at prices and terms to be determined at the time of the sale. In connection with the filing of the 2021 Registration Statement, we entered into an Open Market Sale Agreement with Jefferies LLC, as sales agent, pursuant to which we may offer and sell shares of our common stock with an aggregate offering price of up to $50.0 million under an “at-the-market” offering program (the “At-the-Market Offering Program”). On November 7, 2023, we filed a universal shelf registration statement on Form S-3, which was declared effective on November 15, 2023 (the “2023 Registration Statement”). Under the 2023 Registration Statement, we may offer and sell up to $300.0 million of a variety of securities, including common stock, preferred stock, depositary shares, debt securities, warrants, subscription rights or units from time to time pursuant to one or more offerings at prices and terms to be determined at the time of the sale. On August 6, 2024, in anticipation of the expiration of the 2021 Registration Statement, we filed a prospectus supplement (the “2024 Prospectus Supplement”) under the 2023 Registration Statement to register the offer and sale of the outstanding shares that could be sold under the At-the-Market Offering Program, which prospectus supplement superseded and replaced the sales agreement prospectus, dated August 23, 2021, under the 2021 Registration Statement. As of December 31, 2023, we had sold 3,553,995 shares of our common stock pursuant to the Open Market Sale Agreement for aggregate net proceeds of $21.2 million. As of the date of filing of the 2024 Prospectus Supplement, we had issued and sold 4,364,440 shares of common stock pursuant to the Open Market Sale Agreement for aggregate gross proceeds of

approximately $26.2 million. Under the 2024 Prospectus Supplement, we may sell the shares of common stock under the Open Market Sale Agreement for an aggregate offering price of up to approximately $23.8 million. For the year ended December 31, 2024 we sold 2,100,903 shares of our common stock pursuant to the Open Market Sale Agreement for aggregate net proceeds of $10.5 million. Under the 2024 Prospectus Supplement, we may sell the shares of common stock under the Open Market Sale Agreement for an aggregate offering price of up to approximately $17.2 million.

In July 2022, we entered into the Loan Agreement with K2 HealthVentures LLC (together with any other lender from time to time, "the Lenders"), which provides up to $70.0 million principal in term loans consisting of (subject to certain customary conditions): (i) a First Tranche Commitment of $25.0 million, of which $5.0 million was funded at closing and of which the remaining $20.0 million was funded at our election in February 2023, (ii) two subsequent tranche commitments totaling $20.0 million in the aggregate to be drawn at our option during certain availability periods, subject to the achievement, as determined by the administrative agent in its sole discretion, of certain time-based, financial, clinical, and regulatory milestones relating to INZ-701 of which $7.5 million was funded at our election in June 2023 and the remaining $12.5 million was funded at our election in December 2023, and (iii) a fourth tranche commitment of $25.0 million is available to be drawn at our option through August 31, 2025, subject to use of proceeds limitations and Lenders' consent in its discretion. We have an aggregate of $45.0 million principal in term loans outstanding. The Lenders may elect to purchase up to $5.0 million of shares of our common stock pursuant to the Loan Agreement. Additional information on the Loan Agreement is described in Note 8 to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K.

In August 2023, we closed an underwritten offering in which we sold 14,375,000 shares of common stock under the 2021 Registration Statement. Net proceeds from the offering were approximately $64.4 million, after deducting underwriting discounts and commissions and offering expenses.

Cash in excess of immediate requirements is invested primarily with a view to liquidity and capital preservation. The following table provides information regarding our total cash, cash equivalents, and short-term investments on December 31, 2024 and December 31, 2023 (in thousands):

	December 31, 2024	December 31, 2023
Cash and cash equivalents	$ 21,081	$ 34,588
Short-term investments	92,006	154,001
Total cash, cash equivalents, and short-term investments	$ 113,087	$ 188,589

Cash Flows

The following table provides information regarding our cash flows for the years ended December 31, 2024 and 2023 (in thousands):

	Year ended December 31,	
	2024	2023
Net cash used in operating activities	$ (91,907)	$ (70,675)
Net cash provided by (used in) investing activities	66,998	(53,646)
Net cash provided by financing activities	11,398	125,969
Net (decrease) increase in cash, cash equivalents, and restricted cash	$ (13,511)	$ 1,648

Net Cash Used in Operating Activities

Net cash used in operating activities increased approximately $21.2 million for the year ended December 31, 2024 compared to the year ended December 31, 2023 primarily due to a $30.9 million increase in our net loss offset by $4.8 million increase accounts payable and accrued expenses, $2.9 million decrease of prepaid expenses, $1.8 million adjustment for non-cash items, and $0.2 million in change of remaining operating assets and liabilities.

Net Cash Provided by (Used in) Investing Activities

Net cash provided by (used in) investing activities changed by approximately $120.6 million for the year ended December 31, 2024 compared to the year ended December 31, 2023, primarily due to a $114.3 million decrease in purchases of marketable securities, a decrease of $0.2 million in purchases of property and equipment, and a $6.1 million increase in maturities of marketable securities in the year ended December 31, 2024.

Net Cash Provided by Financing Activities

Net cash provided by financing activities decreased approximately $114.6 million for the year ended December 31, 2024 primarily due to year-over-year decreases of $40.0 million in net proceeds received from the issuance of long-term debt, $64.4 million related to the July 2023 equity offering, and $10.7 million from sales of common stock under our At-the-Market Offering Program, partially offset by an increase of $0.5 million from exercises of stock options.

Funding Requirements

We expect to devote substantial financial resources toward our ongoing and planned activities, particularly as we execute on our global development strategy, conduct our ongoing clinical trials of INZ-701 for ENPP1 Deficiency, ABCC6 Deficiency, and calciphylaxis, and continue research and development and initiate additional planned clinical trials of, and seek marketing approval for, INZ-701 and any other product candidates we develop. As part of our strategic review, we are prioritizing activities to support the planned BLA filing for INZ-701 for our lead indication, ENPP1 Deficiency. Any future trials in ABCC6 Deficiency and calciphylaxis will be postponed. As a result, we expect that our expenses will decrease in 2025 as compared to 2024. In addition, if we obtain marketing approval for INZ-701 or any other product candidates we develop, we expect to incur significant commercialization expenses related to product manufacturing, sales, marketing, and distribution. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital or obtain adequate funds when needed or on acceptable terms, we may be required to delay, limit, reduce, or terminate our research and development programs or any future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves. In addition, attempting to secure additional financing may divert the time and attention of our management from day-to-day activities and distract from our research and development efforts.

As of December 31, 2024, we had cash, cash equivalents, and short-term investments of approximately $113.1 million, and we had $45.0 million of outstanding principal indebtedness under our Loan Agreement. We believe that our existing cash, cash equivalents, and short-term investments as of December 31, 2024, along with our recent strategic prioritization, will enable us to fund our operating expenses and capital expenditures into the first quarter of 2026. Since our cash, cash equivalents and short-term investments as of December 31, 2024 are not sufficient to fund our operations for at least the next twelve months from the date of issuance of the consolidated financial statements included elsewhere in this Annual Report on Form 10-K, there is substantial doubt about our ability to continue as a going concern. Our future viability is dependent on our ability to raise additional capital to finance our operations. We expect to finance our operations through potential public or private equity financings, debt financings, collaboration agreements or other capital sources. Our inability to raise capital as and when needed could have a negative impact on our financial condition and ability to pursue our business strategies. There can be no assurance that our current operating plan will be achieved or that additional funding will be available on terms acceptable to us, or at all. We have based our assessment on assumptions that may prove to be wrong, and we could use our capital resources sooner than we currently expect. See “Going Concern,” in Note 1 to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K. In addition, changing circumstances could cause us to consume capital significantly faster than we currently anticipate, and we may need to spend more than currently expected because of circumstances beyond our control. As a result, we could deplete our capital resources sooner than we currently expect. In addition, because the successful development of INZ-701 and any other product candidates that we pursue is highly uncertain, at this time we cannot reasonably estimate or know the nature, timing and costs of the efforts that will be necessary to complete the development of any product candidate.

Identifying potential product candidates and conducting preclinical testing and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve product sales. In addition, our product candidates, if approved, may not achieve commercial success. We will not generate commercial revenues unless and until we can achieve sales of products, which we do not anticipate for a number of years, if at all. Accordingly, we will need to obtain substantial additional financing to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms. Our ability to raise additional funds may be adversely impacted by general economic conditions, both inside and outside the U.S., including disruptions to, and instability and volatility in, the credit and financial markets in the U.S. and worldwide, heightened inflation, interest rate and currency rate fluctuations, and economic slowdown or recession as well as concerns related to health epidemics and geopolitical events, including ongoing wars or civil or political unrest. In addition, market instability and volatility, high levels of inflation and interest rate fluctuations may increase our cost of financing or restrict our access to potential sources of future liquidity. In addition, market instability and volatility, high level of inflation and interest rate fluctuations may increase our cost of financing or restrict our access to potential sources of future liquidity.

Contractual Obligations, Commitments, and Contingencies

We currently lease office and laboratory space. Additional information about these leases and our commitments under them can be found in Note 7 to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K.

We have entered into a license agreement with Yale under which we are responsible to pay annual license maintenance fees, milestone payments and royalties. The amount, timing and likelihood of such milestone and royalty payments are not known. We have also entered into a sponsored research agreement with Yale under which we agreed to provide research support funding in the aggregate amount of $3.4 million over the nine year period from contract inception through December 2025. Additional information about these arrangements can be found in Note 6 to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K.

We have a Loan Agreement with K2HV under which we have borrowed $45.0 million as of the date of this Annual Report on Form 10-K. The term loan matures on August 1, 2026, and we are obligated to make interest only payments until September 1, 2025, at which point we will make monthly payments of equal principal and interest, in an amount which would fully amortize the principal amount of the term loan and accrued interest thereon as of the date of maturity. The loan bears a variable interest rate equal to the greater of (i) 7.85% and (ii) the sum of (A) the prime rate last quoted in The Wall Street Journal (or a comparable replacement rate if The Wall Street Journal ceases to quote such rate) and (B) 3.85%; provided that the interest rate cannot exceed 9.60%. Additional information about the Loan Agreement and our commitments under it can be found in Note 8 to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K.

Critical Accounting Policies and Estimates

Our management's discussion and analysis of our financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with generally accepted accounting principles in the United States. The preparation of these consolidated financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the consolidated financial statements, as well as the reported expenses incurred during the reporting periods. Our estimates are based on our historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are described in more detail in the notes to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K, we believe that the following critical accounting estimate is the most critical to the judgments and estimates used in the preparation of our consolidated financial statements.

Accrued Research and Development Expenses

As part of the process of preparing our consolidated financial statements, we are required to estimate our accrued research and development expenses. This process involves reviewing purchase orders and open contracts, communicating with our personnel and suppliers to identify services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the services when we have not yet been invoiced or otherwise notified of the actual cost. The majority of our service providers invoice us monthly in arrears for services performed or when contractual milestones are met; however, some require advance payments. We make estimates of our accrued expenses as of each balance sheet date in our consolidated financial statements based on facts and circumstances known to us at that time. We periodically confirm the accuracy of our estimates with the service providers and make adjustments if necessary. The significant estimates in our accrued research and development expenses include the costs incurred for services performed by CROs and contract manufacturing organizations ("CMOs"), among others, in connection with research and development activities for which we have not yet been invoiced.

We contract with CROs and CMOs to conduct clinical and manufacturing and other research and development services on our behalf. We base our expenses related to CROs and CMOs on our estimates of the services received and efforts expended pursuant to quotes and contracts with them. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to our CROs or CMOs will exceed the level of services provided and result in a prepayment of the research and development expense. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrual or amount of prepaid expense accordingly. Non-refundable advance payments for goods and services that will be used in future research and development activities are expensed when the activity has been performed or when the goods have been received rather than when the payment is made.

Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in us reporting amounts that are too high or too low in any particular period. To date, there have been no material differences between our estimates of such expenses and the amounts actually incurred.

Recently Issued Accounting Pronouncements

A description of recently issued accounting pronouncements that may potentially impact our financial position and results of operations is disclosed in Note 3 to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K.

Emerging Growth Company Status

The Jumpstart Our Business Startups Act of 2012 permits an "emerging growth company" such as us to take advantage of an extended transition period to comply with new or revised accounting standards applicable to public companies until those standards would otherwise apply to private companies. We have elected to use the extended transition period for complying with new or revised accounting standards and will do so until such time that we either (1) irrevocably elect to "opt out" of such extended transition period or (2) no longer qualify as an emerging growth company.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk

We are exposed to market risk related to changes in interest rates. As of December 31, 2024, our cash equivalents consisted primarily of short-term money market funds and U.S. Treasury securities. As of December 31, 2024 and 2023 our short-term investments consisted of U.S. Treasury securities and U.S. government agency debt securities with maturities of less than one year. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates. Due to the short-term nature of the investments in our portfolio and the low risk profile of our investments, an immediate change of 100 basis points in interest rates would not have a material effect on the fair market value of our investment portfolio or on our financial position or results of operations.

As of December 31, 2024, the aggregate principal amount outstanding under the Loan Agreement was $45.0 million, which bears interest at a variable rate equal to the greater of (i) 7.85% and (ii) the sum of (A) the prime rate last quoted in The Wall Street Journal (or a comparable replacement rate if The Wall Street Journal ceases to quote such rate) and (B) 3.85%; provided that the interest rate cannot exceed 9.60%. Of the $45.0 million aggregate principal amount outstanding, $5.0 million was funded at closing, and we borrowed an additional $20.0 million in February 2023, $7.5 million in June 2023, and $12.5 million in December 2023 under the Loan Agreement. The interest rate as of December 31, 2024 was 9.60%.

We are not currently exposed to significant market risk related to changes in foreign currency exchange rates; however, we have contracted with and may continue to contract with foreign vendors that are located in Europe. Our operations may be subject to fluctuations in foreign currency exchange rates in the future.

Inflation generally affects us by increasing our cost of labor and clinical trial costs. We do not believe that inflation had a material effect on our business, financial condition, or results of operations during the years ended December 31, 2024 and 2023.

Item 8. Financial Statements and Supplementary Data.

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Inozyme Pharma, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Inozyme Pharma, Inc. (the Company) as of December 31, 2024 and 2023, the related consolidated statements of operations and comprehensive loss, stockholders' equity and cash flows for each of the two years in the period ended December 31, 2024, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2024 and 2023, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2024, in conformity with U.S. generally accepted accounting principles.

The Company's Ability to Continue as a Going Concern

The accompanying consolidated financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 1 to the financial statements, the Company has suffered recurring losses from operations and has stated that substantial doubt exists about the Company's ability to continue as a going concern. Management's evaluation of the events and conditions and management's plans regarding these matters are also described in Note 1. The consolidated financial statements do not include any adjustments that might result from the outcome of this uncertainty.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2017.

Boston, Massachusetts

March 10, 2025

INOZYME PHARMA, INC.
CONSOLIDATED BALANCE SHEETS
(amounts in thousands, except share and per share data)

	December 31, 2024	December 31, 2023
Assets		
Current assets:		
Cash and cash equivalents	$ 21,081	$ 34,588
Short-term investments	92,006	154,001
Prepaid expenses and other current assets	7,278	7,661
Restricted cash	311	—
Total current assets	120,676	196,250
Property and equipment, net	784	1,466
Right-of-use assets	562	1,126
Restricted cash - noncurrent	—	311
Prepaid expenses, net of current portion	1,160	1,694
Total assets	$ 123,182	$ 200,847
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 2,530	$ 1,166
Accrued expenses	15,953	12,610
Operating lease liabilities	913	910
Current portion of long-term debt	14,502	—
Total current liabilities	33,898	14,686
Operating lease liabilities, net of current portion	—	913
Long-term debt, net	31,458	44,769
Total liabilities	65,356	60,368
Commitments and contingencies (Note 7)		
Stockholders' equity:		
Preferred Stock, $0.0001 par value - 5,000,000 shares authorized at December 31, 2024 and December 31, 2023; No shares issued and outstanding at December 31, 2024 or December 31, 2023	—	—
Common Stock, $0.0001 par value – 200,000,000 shares authorized at December 31, 2024 and December 31, 2023; 64,240,198 shares issued and outstanding at December 31, 2024 and 61,768,771 shares issued and outstanding at December 31, 2023	6	6
Additional paid in-capital	445,705	426,362
Accumulated other comprehensive income	69	41
Accumulated deficit	(387,954)	(285,930)
Total stockholders' equity	57,826	140,479
Total liabilities and stockholders' equity	$ 123,182	$ 200,847

The accompanying notes are an integral part of these consolidated financial statements.

INOZYME PHARMA, INC.
CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS
(amounts in thousands, except share and per share data)

	Year Ended December 31,	
	2024	**2023**
Operating expenses:		
Research and development	$ 83,231	$ 54,847
General and administrative	20,799	20,798
Total operating expenses	104,030	75,645
Loss from operations	(104,030)	(75,645)
Other income (expense):		
Interest income	7,666	7,837
Interest expense	(5,558)	(3,333)
Other expense, net	(102)	(28)
Other income, net	2,006	4,476
Net loss	$ (102,024)	$ (71,169)
Other comprehensive income (loss):		
Unrealized gains on available-for-sale securities	24	264
Foreign currency translation adjustment	4	(18)
Total other comprehensive income	28	246
Comprehensive loss	$ (101,996)	$ (70,923)
Net loss attributable to common stockholders—basic and diluted	$ (102,024)	$ (71,169)
Net loss per share attributable to common stockholders—basic and diluted	$ (1.62)	$ (1.37)
Weighted-average common shares outstanding—basic and diluted	62,811,814	51,839,131

The accompanying notes are an integral part of these consolidated financial statements.

INOZYME PHARMA, INC.
CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY
(amounts in thousands, except share data)

	Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Stockholders' Equity (Deficit)
	Shares	Amount				
Balance at December 31, 2022	40,394,363	$ 4	$ 333,356	$ (205)	$ (214,761)	$ 118,394
Stock-based compensation	—	—	7,037	—	—	7,037
Exercise of pre-funded warrants	3,325,644	—	—	—	—	—
Shares issued in at-the-market offering	3,553,995	1	21,235	—	—	21,236
Exercise of stock options	43,209	1	116	—	—	117
Issuance of common stock, net of issuance costs	14,375,000	—	64,412	—	—	64,412
Shares purchased in Employee Stock Purchase Plan	76,560	—	206		—	206
Other comprehensive loss:						
Unrealized loss on investments	—	—	—	264	—	264
Foreign currency translation adjustment	—	—	—	(18)	—	(18)
Net loss	—	—	—	—	(71,169)	(71,169)
Balance at December 31, 2023	61,768,771	$ 6	$ 426,362	$ 41	$ (285,930)	$ 140,479
Stock-based compensation	—	—	7,945	—	—	7,945
Exercise of stock options and RSU vesting	296,096	—	596	—	—	596
Shares issued in at-the-market offering	2,100,903	—	10,521	—	—	10,521
Shares purchased in Employee Stock Purchase Plan	74,428	—	281	—	—	281
Other comprehensive income (loss):						
Unrealized gain on investments	—	—	—	24	—	24
Foreign currency translation adjustment	—	—	—	4	—	4
Net loss	—	—	—	—	(102,024)	(102,024)
Balance at December 31, 2024	64,240,198	$ 6	$ 445,705	$ 69	$ (387,954)	$ 57,826

The accompanying notes are an integral part of these consolidated financial statements.

INOZYME PHARMA, INC.
CONSOLIDATED STATEMENTS OF CASH FLOWS
(amounts in thousands)

	Year Ended December 31,	
	2024	**2023**
Operating activities		
Net loss	$ (102,024)	$ (71,169)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation expense	742	833
Loss on disposal of fixed assets	—	20
Stock-based compensation expense	7,945	7,037
Amortization of premiums and discounts on marketable securities	(5,039)	(5,438)
Reduction in the carrying value of right-of-use assets	564	494
Non-cash interest expense and amortization of debt issuance costs	1,191	630
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	383	(4,134)
Accounts payable	1,364	(1,378)
Accrued expenses	3,343	1,255
Operating lease liabilities	(910)	(816)
Prepaid expenses, net of current portion	534	2,115
Other long-term liabilities	—	(124)
Net cash used in operating activities	(91,907)	(70,675)
Investing activities		
Purchases of marketable securities	(155,052)	(269,330)
Maturities of marketable securities	222,112	215,982
Purchases of property and equipment	(62)	(298)
Net cash provided by (used in) investing activities	66,998	(53,646)
Financing activities		
Net proceeds from issuance of common stock	10,521	85,647
Net proceeds from issuance of long-term debt	—	40,000
Proceeds from exercise of stock options	596	116
Proceeds from issuance of common stock for cash under employee stock purchase plan	281	206
Net cash provided by financing activities	11,398	125,969
Net decrease (increase) in cash, cash equivalents, and restricted cash	(13,511)	1,648
Effect of foreign currency exchange rate in cash	4	(18)
Cash, cash equivalents, and restricted cash at beginning of period	34,899	33,269
Cash, cash equivalents, and restricted cash at end of period	$ 21,392	$ 34,899
Supplemental cash flow information:		
Cash and cash equivalents	$ 21,081	$ 34,588
Restricted cash	311	311
Cash, cash equivalents, and restricted cash at end of period	$ 21,392	$ 34,899
Cash paid for interest	$ (4,350)	$ (2,347)

The accompanying notes are an integral part of these consolidated financial statements.

1. Organization and Basis of Presentation

Inozyme Pharma, Inc. (the "Company") is a clinical-stage biopharmaceutical company developing novel therapeutics for rare diseases impacting bone health and blood vessel function.

Through the Company's in-depth understanding of a key biological pathway, the PPi-Adenosine Pathway, the Company is pursuing the development of therapeutics that address pathologic mineralization and intimal proliferation, or smooth muscle cell overgrowth that leads to narrowing and the obstruction of blood vessels, to improve the underlying causes of these debilitating diseases. The ENPP1 enzyme is central to this pathway and generates plasma pyrophosphate ("PPi") and adenosine. It is well established that low levels of PPi drive pathologic mineralization and low levels of adenosine drive intimal proliferation in a number of rare diseases. 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"). The Company is initially focused on developing a novel therapy for diseases characterized by pathologic mineralization and intimal proliferation, including ENPP1 Deficiency and ABCC6 Deficiency as well as calciphylaxis.

The Company's lead product candidate, INZ-701, is a soluble, recombinant, or genetically engineered, ENPP1 fusion protein that is designed to increase PPi and adenosine, enabling the potential treatment of multiple diseases caused by deficiencies in these molecules. By targeting the PPi-Adenosine Pathway, INZ-701 aims to correct pathologic mineralization and intimal proliferation, addressing the significant morbidity and mortality in these devastating diseases.

As part of the Company's strategic review, it is prioritizing activities to support the planned Biologics License Application filing for its lead indication, ENPP1 Deficiency. Patients with ABCC6 Deficiency being treated in the Company's ADAPT long-term extension study, the Company's expanded access program, or under investigator-sponsored INDs will continue to receive treatment. Any future trials in ABCC6 Deficiency and calciphylaxis will be postponed.

Basis of Presentation

The accompanying consolidated financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America ("U.S. GAAP"). Any reference in these notes to applicable guidance is meant to refer to the authoritative U.S. GAAP as found in the Accounting Standards Codification ("ASC") and Accounting Standards Update ("ASU") of the Financial Accounting Standards Board ("FASB").

Going Concern

The accompanying consolidated financial statements have been prepared on a going concern basis, which contemplates the realization of assets and satisfaction of liabilities and commitments in the ordinary course of business. Since the Company's incorporation in 2017 and through December 31, 2024, the Company has devoted substantially all of its efforts to raising capital, building infrastructure, developing intellectual property and conducting research and development. The Company incurred net losses of $102.0 million and $71.2 million in the years ended December 31, 2024 and 2023, respectively, and had an accumulated deficit of $388.0 million as of December 31, 2024. The Company had net cash used in operating activities of $91.9 million and $70.7 million during the years ended December 31, 2024 and 2023, respectively. The Company had cash, cash equivalents, and short-term investments of $113.1 million as of December 31, 2024. Management believes that based on the Company's current cash, cash equivalents, and short-term investments as of December 31, 2024 and forecasted negative cash flows from operating activities over the next twelve months, there is substantial doubt about the Company's ability to continue as a going concern for one year after the date that these consolidated financial statements are issued.

The Company's ability to fund its operations is dependent upon management's plan, which include raising additional capital through potential public or private equity financings, debt financings, collaboration agreements or other capital sources. The Company's inability to raise capital as and when needed could have a negative impact on its financial condition and ability to pursue its business strategies. There can be no assurance that the current operating plan will be achieved or that additional funding will be available on terms acceptable to the Company, or at all.

Because of the numerous risks and uncertainties associated with product development, the Company is unable to predict the timing or amount of increased expenses or when or if the Company will be able to achieve or maintain profitability. Even if the Company is able to generate revenue from product sales, the Company may not become profitable. If the Company fails to become

profitable or is unable to sustain profitability on a continuing basis, then the Company may be unable to continue its operations at planned levels and be forced to reduce or terminate its operations.

The consolidated financial statements do not include any adjustments relating to the recoverability and classification of recorded asset amounts or the amounts and classification of liabilities that might result from the outcome of this uncertainty.

2. Summary of Significant Accounting Policies

Principles of Consolidation

The accompanying consolidated financial statements include the accounts of the Company and its wholly owned subsidiaries, Inozyme Securities Corp., which is a Massachusetts subsidiary created to buy, sell, and hold securities; Inozyme Ireland Limited; and Inozyme Pharma Switzerland GmbH. All intercompany transactions and balances have been eliminated.

Use of Estimates

The preparation of the Company's financial statements requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of expenses during the reporting period. Estimates and judgments are based on historical information and other market-specific or various relevant assumptions, including, in certain circumstances, future projections that management believes to be reasonable under the circumstances. Actual results could differ materially from estimates. Significant estimates and assumptions are used for, but not limited to the accruals for research and development expenses. The Company evaluates its estimates and assumptions on an ongoing basis. All revisions to accounting estimates are recognized in the period in which the estimates are revised and in any future periods affected.

Concentration of Credit Risk, Significant Suppliers, and Off-Balance Sheet Risk

Financial instruments that potentially subject the Company to significant concentrations of credit risk consist primarily of cash, cash equivalents, and short-term investments and, from time to time, long-term investments. The Company maintains deposits in federally insured financial institutions in excess of federally insured limits and limits its exposure to credit risk by placing its cash with high credit quality financial institutions. The Company's investments are composed of U.S. Treasury and U.S. government agency debt securities. The Company mitigates credit risk by maintaining a diversified portfolio and limiting the amount of investment exposure as to institution, maturity, and investment type.

The Company is dependent on third-party manufacturers and contract research organizations ("CROs") to supply product candidates and provide services for research and development activities in its programs. In particular, the Company relies and expects to continue to rely on a small number of manufacturers to supply it with its requirements for the active pharmaceutical ingredients and formulated drugs related to these programs. The Company also relies on CROs to conduct its clinical trials. The Company's programs could be adversely affected if a third-party manufacturer or a CRO is unable to successfully carry out their contractual obligations or meet expected deadlines. If a third-party manufacturer or a CRO needs to be replaced, the Company may not be able to complete its program development on its anticipated timelines and the Company may incur additional expenses as a result, which could be significant.

The Company has no significant off-balance sheet risk such as foreign exchange contracts, option contracts, or other foreign hedging arrangements.

Cash and Cash Equivalents

The Company considers all highly liquid investments with original maturities of three months or less at the date of purchase to be cash equivalents. Cash and cash equivalents include cash in readily available checking accounts, money market accounts, and certain marketable securities. Cash is carried at cost, which approximates its fair value. Cash equivalents are carried at fair market value.

Restricted Cash

Restricted cash is composed of amounts held to collateralize the letters of credit related to the Company's lease arrangements. Restricted cash is classified as either current or non-current based on the terms of the underlying lease arrangement.

Short-Term and Long-Term Investments

The Company classifies its investments as available-for-sale and records such assets at estimated fair value on the balance sheet, with unrealized gains and losses on marketable securities, if any, reported as a component of accumulated other comprehensive (loss) income. Realized gains and losses are calculated based on the specific-identification method and are recorded as a component of interest income. There have been no realized gains and losses for the years ended December 31, 2024 and 2023. The Company periodically reviews available-for-sale securities for other-than-temporary declines in fair value below the cost basis whenever events or changes in circumstances indicate the carrying amount of an asset may not be recoverable. Marketable securities with a maturity date of one year or less from the balance sheet date are classified by the Company as short-term investments. Marketable securities with a maturity date of greater than one year from the balance sheet date are classified as long-term investments and are available to fund operations as needed. As of December 31, 2024, the Company did not have any long-term investments. In accordance with the Company's investment policy, at the time of purchase, the final maturity of each security within the portfolio shall not exceed 18 months and the weighted average maturity of the portfolio will be no greater than 12 months.

Property and Equipment

Property and equipment are stated at cost, less accumulated depreciation. Depreciation is calculated using the straight-line method over the estimated useful lives of the assets. Leasehold improvements are amortized over the shorter of the lease term or the estimated useful life of the related asset. The estimated useful lives of the Company's property and equipment are as follows:

	Estimated Useful Life (In Years)
Laboratory equipment and manufacturing equipment	5
Furniture and fixtures	5
Computer equipment	3
Leasehold improvements	Lesser of asset life or lease term

Impairment of Long-lived Assets

As required under the applicable accounting guidance, the Company periodically reevaluates the original assumptions and rationale used in the establishment of the carrying value and estimated lives of all of its long-lived assets, including property and equipment. The Company reviews long-lived assets for impairment whenever events or changes in circumstances indicate that the carrying amount of the assets may not be recoverable. An impairment loss is recognized when the total of estimated future undiscounted cash flows, expected to result from the use of the asset and its eventual disposition, are less than its carrying amount. Impairment, if any, would be assessed using discounted cash flows or other appropriate measures of fair value. There were no impairments for the years ended December 31, 2024 and 2023.

Accrued Research and Development Costs

The Company records accrued liabilities for estimated costs of research and development activities conducted by service providers for sponsored research, preclinical studies, clinical operations, and contract manufacturing activities based upon the estimated amount of services provided but not yet invoiced and includes these costs in accrued expenses in the accompanying consolidated balance sheets and within research and development expense in the accompanying consolidated statements of operations and comprehensive loss.

The Company accrues for these costs based on factors such as estimates of the work completed and in accordance with agreements established with service providers. The Company makes significant judgments and estimates in determining the accrued liabilities balance in each reporting period. As actual costs become known, the Company adjusts its accrued liabilities. The Company has not experienced any material differences between accrued costs and actual costs incurred since its inception.

Research and Development Costs

Research and development costs are expensed as incurred. Research and development costs consist of direct and indirect internal costs related to specific projects as well as fees paid to other entities that conduct certain research and development activities on the Company's behalf.

Patent Costs

The Company expenses all costs as incurred in connection with patent applications, including direct application fees, and the legal and consulting expenses related to making such applications, and such costs are included in general and administrative expenses within the Company's consolidated statements of operations and comprehensive loss.

Stock-Based Compensation

Stock-based compensation expense represents the cost of the grant date fair value of employee and non-employee stock option grants recognized over the requisite service period of the awards on a straight-line basis. For service-based awards that are subject to graded vesting, the Company has elected to recognize compensation expense on a straight-line basis. The Company has elected to recognize forfeitures as they occur.

Income Taxes

Income taxes have been accounted for using the asset and liability method. Under the asset and liability method, deferred tax assets and liabilities are recognized for the future tax consequences attributable to differences between the financial carrying amounts of existing assets and liabilities and their respective tax bases and operating loss and tax credit carryforwards. Deferred tax assets and liabilities are measured using enacted tax rates applicable to taxable income in the years in which those temporary differences are expected to be recovered or settled. The effect on deferred tax assets and liabilities of a change in tax rates is recognized in the period that includes the enactment date. A valuation allowance against deferred tax assets is recorded if, based upon the weight of all available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized.

The Company accounts for income taxes in accordance with authoritative accounting guidance which states the impact of an uncertain income tax position is recognized at the largest amount that is "more likely than not" to be sustained upon audit by the relevant taxing authority. There are no unrecognized tax benefits included in the Company's consolidated balance sheets at December 31, 2024 or 2023. The Company's policy is to recognize interest and penalties related to income tax matters in income tax expense. The Company has not recognized any interest or penalties in its consolidated statements of operations and comprehensive loss since inception.

Leases

The Company determines if an arrangement is a lease at contract inception based on the facts and circumstances present in the arrangement. If a lease is identified in an arrangement, the Company recognizes a right-of-use asset and liability on its balance sheet and determines whether the lease should be classified as a finance or operating lease. Short-term leases, or leases that have a lease term of 12 months or less at the commencement date are excluded from this treatment and are recognized on a straight-line basis over the term of the lease. Additionally, the Company does not separate lease and non-lease components for all leases.

A lease qualifies as a finance lease if any of the following criteria are met at the inception of the lease: (i) there is a transfer of ownership of the leased asset to the Company by the end of the lease term, (ii) the Company holds an option to purchase the leased asset that it is reasonably certain to exercise, (iii) the lease term is for a major part of the remaining economic life of the leased asset, (iv) the present value of the sum of lease payments equals or exceeds substantially all of the fair value of the leased asset, (v) the nature of the leased asset is specialized to the point that it is expected to provide the lessor no alternative use at the end of the lease term. All other leases are recorded as operating leases.

Finance and operating lease assets and liabilities are recognized at the lease commencement date based on the present value of the lease payments over the lease term using the discount rate implicit in the lease. If the rate implicit is not readily determinable, the Company utilizes an estimate of its incremental borrowing rate at the lease commencement date. Operating lease assets are further adjusted for prepaid or accrued lease payments. Operating lease payments are expensed using the straight-line method as an operating expense over the lease term. Finance lease assets are amortized to depreciation expense using the straight-line method over the shorter of the useful life of the related asset or the lease term. Finance lease payments are bifurcated into (i) a portion that is recorded as imputed interest expense and (ii) a portion that reduces the finance liability associated with the lease. The Company did not have any finance leases recorded on its consolidated balance sheet as of December 31, 2024 and 2023.

Deferred Issuance Costs

The Company capitalizes certain legal, professional accounting, and other third-party fees that are directly associated with in-process equity financings as deferred issuance costs until such financings are consummated. After consummation of such an equity financing, these costs are recorded as a reduction of the proceeds generated as a result of the offering. Should a planned equity financing be abandoned, the deferred issuance costs would be expensed immediately as a charge to operating expenses in the consolidated statements of operations and comprehensive loss. The Company did not have any deferred issuance costs recorded at December 31, 2024 or December 31, 2023.

Net Loss Per Share

Basic net loss per share attributable to common stockholders is computed by dividing the net loss attributable to common stockholders by the weighted-average number of shares of common stock and pre-funded warrants outstanding during the period, without consideration for potentially dilutive securities. Diluted net loss per share is computed by dividing the net loss attributable to common stockholders by the weighted-average number of shares of common stock and pre-funded warrants and potentially dilutive securities outstanding during the period determined using the treasury-stock and if-converted methods. The Company has generated a net loss in all periods presented; therefore, the basic and diluted net loss per share attributable to common stockholders are the same as the inclusion of the potentially dilutive securities would be anti-dilutive.

Comprehensive Loss

The Company is required to report all components of comprehensive loss, including net loss, in the financial statements in the period in which they are recognized. Comprehensive loss is defined as the change in equity during a period from transactions and other events and circumstances from non-owner sources. Comprehensive loss consists of the Company's net loss, unrealized gains and losses on the Company's investments, and foreign currency translation adjustments and is presented within the consolidated statements of operations and comprehensive loss.

Foreign Currency Transactions

The Company maintains foreign bank accounts denominated in euros and Swiss francs and enters into transactions which are denominated in various currencies. Foreign currency transactions are initially recorded by the Company using the exchange rates prevailing at the date of the transaction. At the balance sheet date, recorded monetary balances denominated in foreign currencies are adjusted to U.S. dollars using the period-end rates of exchange. Exchange gains and losses arising from the translation of foreign currency items are included in other expense, net in the consolidated statements of operations and comprehensive loss.

Fair Value Measurements

The Company categorizes its assets and liabilities measured at fair value in accordance with the authoritative accounting guidance that establishes a consistent framework for measuring fair value, and expands disclosures for each major asset and liability category measured at fair value on either a recurring or nonrecurring basis. Fair value is defined as the exit price, representing the amount that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants. As such, fair value is a market-based measurement that should be determined based on assumptions that market participants would use in pricing an asset or liability. As a basis for considering such assumptions, the guidance establishes a three-tier fair value hierarchy, which prioritizes the inputs used in measuring fair value as follows:

- Level 1 – Unadjusted quoted prices in active markets that are accessible at the measurement date for identical assets or liabilities;

- Level 2 – Quoted prices for similar assets and liabilities in active markets, quoted prices in markets that are not active, or inputs which are observable, either directly or indirectly, for substantially the full term of the asset or liability; or

- Level 3 – Prices or valuation techniques that require inputs that are both significant to the fair value measurement and unobservable (i.e., supported by little or no market activity).

Emerging Growth Company Status

The Company is an "emerging growth company" ("EGC") as defined in the Jumpstart Our Business Startups Act of 2012 (the "JOBS Act"), and the Company may take advantage of certain exemptions from various reporting requirements that are applicable to other public companies that are not EGCs. As an EGC, the Company can elect to take advantage of the extended transition period afforded by the JOBS Act for the implementation of new or revised accounting standards. The Company has elected to use the extended transition period for complying with new or revised accounting standards, and as a result of this election, the Company's consolidated financial statements may not be comparable to companies that comply with public company FASB standards' effective dates. The Company will remain an EGC until December 31, 2025, although the Company would cease to be an EGC sooner if it issued more than $1 billion of non-convertible debt over a three-year period.

Debt and Debt Issuance Costs

Debt issuance costs are presented on the consolidated balance sheet as a direct deduction from the related debt liability. Debt issuance costs represent legal and other direct costs incurred in connection with the Company's term loan under the Loan Agreement. These costs are amortized as a non-cash component of interest expense using the effective interest method over the term of the loan. Any final payments are included in the cash flows to determine the effective interest rate and are recognized using the effective interest method over the term of the loan.

Warrants

The Company determines the accounting classification of warrants that are issued, as either liability or equity, by first assessing whether the warrants meet liability classification in accordance with ASC 480-10, *Accounting for Certain Financial Instruments with Characteristics of Both Liabilities and Equity*, and then in accordance with ASC 815-40, *Accounting for Derivative Financial Instruments Indexed to, and Potentially Settled in, a Company's Own Stock*. Under ASC 480-10, warrants are considered liability classified if the warrants are mandatorily redeemable, obligate the issuer to settle the warrants or the underlying shares by paying cash or other assets, or must or may require settlement by issuing variable number of shares.

If warrants do not meet liability classification under ASC 480-10, the Company assesses the requirements under ASC 815-40, which states that contracts that require or may require the issuer to settle the contract for cash are liabilities recorded at fair value, irrespective of the likelihood of the transaction occurring that triggers the net cash settlement feature. If the warrants do not require liability classification under ASC 815-40, in order to conclude equity classification, the Company assesses whether the warrants are indexed to its common stock and whether the warrants are classified as equity under ASC 815-40 or other applicable U.S. GAAP. After all relevant assessments are made, the Company concludes whether the warrants are classified as liability or equity. Liability classified warrants are required to be accounted for at fair value both on the date of issuance and on subsequent accounting period ending dates, with all changes in fair value after the issuance date recorded in the statements of operations as a gain or loss. Equity classified warrants are accounted for at fair value on the issuance date with no changes in fair value recognized after the issuance date.

3. Recent Accounting Pronouncements

From time to time, new accounting pronouncements are issued by the FASB or other standard setting bodies that are adopted by the Company as of the specified effective date. Unless otherwise discussed, the Company believes that the impact of recently issued standards that are not yet effective will not have a material impact on its financial position or results of operations upon adoption.

Recently Adopted Accounting Standard

In November 2023, the FASB issued ASU 2023-07 – Segment Reporting (Topic 280) – Improvements to Reportable Segment Disclosures, which improves segment disclosure requirements, primarily through enhanced disclosure requirements for significant segment expenses. The improved disclosure requirements apply to all public entities that are required to report segment information, including those with only one reportable segment. The Company adopted this standard effective for the year ending December 31, 2024 and the primary impact of which was the additional segment disclosures included in Note 13.

Recent Accounting Pronouncements

In December 2023, the FASB issued ASU 2023-09, Income Taxes (Topic 740): Improvements to Income Tax Disclosures, which is intended to provide enhancements to annual income tax disclosures. The standard will require more detailed information in the rate reconciliation table and for income taxes paid, among other enhancements. The standard is effective for years beginning after December 15, 2024 and early adoption is permitted. The Company is evaluating this standard to determine if adoption will have a material impact on the Company's consolidated financial statements.

In November 2024, the FASB issued ASU 2024-03, Income Statement—Reporting Comprehensive Income—Expense Disaggregation Disclosures (Subtopic 220-40), which requires disclosure, in the notes to the financial statements, of specified information about certain costs and expenses. This ASU is effective for public entities for annual reporting periods beginning after December 15, 2026 and interim reporting periods beginning after December 15, 2027. The Company is currently evaluating the impact ASU 2024-03 will have on its consolidated financial statements.

4. Balance Sheet Details

Short-term investments consisted of the following (dollar amounts in thousands):

		December 31, 2024			
Description	Maturity	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
U.S. Treasury securities	1 year or less	$ 52,408	$ 52	$ —	$ 52,460
U.S. government agency debt securities	1 year or less	39,506	42	(2)	39,546
		$ 91,914	$ 94	$ (2)	$ 92,006

		December 31, 2023			
Description	Maturity	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
U.S. Treasury securities	1 year or less	$ 80,160	$ 59	$ (1)	$ 80,218
U.S. government agency debt securities	1 year or less	73,774	17	(8)	73,783
		$ 153,934	$ 76	$ (9)	$ 154,001

The Company concluded that the declines in market value of available-for-sale securities were temporary in nature and did not consider any of the investments to be other-than-temporarily impaired. In accordance with its investment policy, the Company invests in investment grade securities with high credit quality issuers, and generally limits the amount of credit exposure to any one issuer. The Company evaluates securities for other-than-temporary impairment at the end of each reporting period. Impairment is evaluated considering numerous factors, and their relative significance varies depending on the situation. Factors considered include the length of time and extent to which fair value has been less than the cost basis, the financial condition and near-term prospects of the issuer, and the Company's intent and ability to hold the investment to allow for an anticipated recovery in fair value. Furthermore, the aggregate of individual unrealized losses that had been outstanding for 12 months or less was not significant as of December 31, 2024 and December 31, 2023. The Company does not intend to sell these investments and it is not more likely than not that the Company will be required to sell the investments before a recovery of their amortized cost bases, which may be maturity. The Company also believes that it will be able to collect both principal and interest amounts due at maturity.

Prepaid expenses and other current assets consisted of the following (dollar amounts in thousands):

	At December 31, 2024	At December 31, 2023
Interest receivable	$ 467	$ 385
Prepaid insurance	922	1,067
Prepaid research studies	5,272	5,339
Prepaid other	617	870
Total	$ 7,278	$ 7,661

Property and equipment consisted of the following (dollar amounts in thousands):

	At December 31, 2024	At December 31, 2023
Laboratory equipment and manufacturing equipment	$ 996	$ 947
Furniture and fixtures	284	284
Computer equipment	491	491
Leasehold improvements	2,167	2,157
	3,938	3,879
Less accumulated depreciation	(3,154)	(2,413)
Total	$ 784	$ 1,466

Depreciation expense for the years ended December 31, 2024 and 2023 totaled $0.7 million and $0.8 million, respectively.

Accrued expenses consisted of the following (dollar amounts in thousands):

	At December 31, 2024	At December 31, 2023
Payroll and related liabilities	$ 3,666	$ 3,838
Other professional fees	1,703	1,377
Clinical expenses	3,661	3,595
Research and development costs	6,192	2,917
Other	731	883
Total	$ 15,953	$ 12,610

5. Fair Value Measurement

The following tables represent the Company's financial assets measured at fair value on a recurring basis and indicate the level of fair value hierarchy utilized to determine such fair values (in thousands):

		Fair Value Measurements at Reporting Date Using		
Description	December 31, 2024	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Assets:				
Money market funds (included in cash and cash equivalents)	$ 20,273	$ 20,273	$ —	$ —
U.S. government agency debt securities	39,546	—	39,546	—
U.S. Treasury securities	52,460	52,460	—	—
Total assets	$ 112,279	$ 72,733	$ 39,546	$ —

Description	December 31, 2023	Fair Value Measurements at Reporting Date Using: Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Assets:				
Money market funds (included in cash and cash equivalents)	$ 33,830	$ 33,830	$ —	$ —
U.S. government agency debt securities	73,783	—	73,783	—
U.S. Treasury securities	80,218	80,218	—	—
Total assets	$ 187,831	$ 114,048	$ 73,783	$ —

There have been no transfers between fair value levels during the years ended December 31, 2024 and December 31, 2023.

6. License and Sponsored Research Agreements

In January 2017, the Company entered into a license agreement with Yale University ("Yale"), which was amended in May 2020 and July 2020, under which the Company licensed certain intellectual property related to ectonucleotide pyrophosphatase/phosphodiesterase enzymes that is the basis for the Company's INZ-701 development program. Pursuant to the license agreement, as partial upfront consideration, the Company made a payment of approximately $0.1 million to Yale, which amount reflected unreimbursed patent expenses incurred by Yale prior to the date of the license agreement. The Company is responsible for paying Yale an annual license maintenance fee in varying amounts throughout the term ranging from the low tens of thousands of dollars to the high tens of thousands of dollars. For each of the years ended December 31, 2024 and 2023, the Company incurred a total of $0.1 million in license maintenance fees to Yale.

The Company is required to pay Yale up to $3.0 million, based on the achievement of a specified net product sales milestone or specified development and commercialization milestones, for each therapeutic and prophylactic licensed product developed. In January 2022, the Company paid Yale an approximately $0.3 million milestone payment following dosing of the first patient in Company's Phase 1/2 clinical trial of INZ-701 in adult patients with ENPP1 Deficiency in November 2021. In March 2022, the Company paid Yale an approximately $0.3 million milestone payment following completion of the first cohort of the Company's Phase 1/2 clinical trial of INZ-701 in adult patients with ENPP1 Deficiency in January 2022. In March 2024, the Company incurred and paid a $0.5 million milestone payment following completion of dosing of the first patient in the Company's pivotal clinical trial of INZ-701 in pediatric patients with ENPP1 Deficiency. In addition, the Company is required to pay Yale an amount in the several hundreds of thousands of dollars, based on the achievement of a specified net product sales milestone or specified development and commercialization milestones, for each diagnostic licensed product developed. While the agreement remains in effect, the Company is required to pay Yale low single-digit percentage royalties on aggregate worldwide net sales of certain licensed products. Yale is guaranteed a minimum royalty payment amount (ranging in dollar amounts from the mid six figures to low seven figures) for each year after the first sale of a therapeutic or prophylactic licensed product that results in net sales. Yale is guaranteed a minimum royalty payment amount (ranging from the low tens of thousands of dollars to the mid tens of thousands of dollars) for each year after the first sale of a diagnostic licensed product that results in net sales. The Company must also pay Yale a percentage in the twenties of certain types of income it receives from sublicensees. The Company is also responsible for costs relating to the prosecution and maintenance of the licensed patents. Finally, subject to certain conditions, all payments due by the Company to Yale will be tripled following any patent challenge or challenge to a claim by Yale that a product is a licensed product under the agreement, made by the Company against Yale if Yale prevails in such challenge.

The Company has also agreed to pay for research support from Yale pursuant to a sponsored research agreement that the Company entered into with Yale in January 2017 and amended in February 2019, February 2022, May 2022, May 2023, January 2024, and December 2024. Under the sponsored research agreement, as amended, the Company agreed to pay Yale an aggregate of $3.4 million over nine years, ending in December 2025. As of December 31, 2024, the Company has incurred a total of $3.0 million for research support under this agreement since inception.

7. Commitments and Contingencies

Operating Leases

The Company held the following significant operating leases of office and laboratory space as of December 31, 2024:

- 8,499 square feet of office space in Boston, Massachusetts that expires in October 2025 with an option to extend the term for five years; and
- 6,244 square feet of laboratory space in Boston, Massachusetts that expires in December 2025 with an option to extend the term for five years.

The exercise of each option was determined not to be reasonably certain and thus neither option was included in the operating lease liability on the consolidated balance sheets as of December 31, 2024 or December 31, 2023.

Both leases are subject to yearly rent escalations. In connection with the Company's leases of office space and laboratory space, the Company provided security deposits to the landlords in the form of letters of credit totaling $0.3 million as of December 31, 2024. The cash collateralizing the letters of credit is included in restricted cash in the accompanying balance sheets as of December 31, 2024 and 2023.

At December 31, 2024, the weighted average incremental borrowing rate and the weighted average remaining lease term for the operating leases held by the Company were 8% and 0.92 years, respectively.

During the year ended December 31, 2024, cash paid for amounts included for the measurement of lease liabilities was $1.0 million and the Company recorded operating lease expense of $0.7 million. During the year ended December 31, 2023, cash paid for amounts included for the measurement of lease liabilities was $0.7 million and the Company recorded operating lease expense of $0.9 million.

Future lease payments under non-cancelable leases as of December 31, 2024 are as follows (dollar amounts in thousands):

Year Ending December 31,		
2025	$	944
Total future minimum lease payments		944
Less: interest		31
Present value of operating lease liabilities	$	913
Lease liability - current	$	913
Lease liability - long-term	$	-

The Company did not have any finance leases recorded on its consolidated balance sheet as of December 31, 2024 and 2023.

Indemnification Agreements

In the ordinary course of business, the Company may provide indemnification of varying scope and terms to vendors, lessors, business partners and other parties with respect to certain matters arising out of the relationship between such parties and the Company. In addition, the Company has entered into indemnification agreements with members of its board of directors and senior management that will require the Company, among other things, to indemnify them against certain liabilities that may arise by reason of their status or service as directors or officers. To date, the Company has not incurred any material costs as a result of such indemnifications. The Company is not aware of any claims under indemnification arrangements, and it has not accrued any liabilities related to such obligations as of December 31, 2024 or December 31, 2023.

Legal Proceedings

The Company is not currently a party to any material legal proceedings. At each reporting date, the Company evaluates whether or not a potential loss amount or a potential range of loss is probable and reasonably estimable under the provisions of the authoritative guidance that addresses accounting for contingencies. The Company expenses the costs related to its legal proceedings as they are incurred. No such costs have been incurred during the years ended December 31, 2024 and 2023.

8. Convertible Debt

Loan Agreement with K2 HealthVentures LLC

On July 25, 2022, the Company, as borrower, entered into the Loan Agreement with K2 HealthVentures LLC ("K2HV", together with any other lender from time to time, the "Lenders"), K2HV, as administrative agent for the Lenders, and Ankura Trust Company, LLC, as collateral agent for the Lenders. The Loan Agreement provides up to $70.0 million principal in term loans, subject to certain customary conditions. The Company received $5.0 million from the first tranche commitment upon closing. The first tranche commitment contained an additional $20.0 million available to be drawn at the Company's option through March 31, 2023. The Company borrowed the remaining $20.0 million in February 2023. Two subsequent tranche commitments totaling $20.0 million in the aggregate were available to be drawn at the Company's option during certain availability periods, subject to the achievement of certain clinical and regulatory milestones relating to INZ-701. The Company borrowed $7.5 million under the second tranche commitment in June 2023 and borrowed $12.5 million under the third tranche commitment in December 2023. A fourth tranche commitment of $25.0 million may be made available to be drawn down at the Company's option through August 31, 2025, subject to use of proceeds limitations and Lender's consent at its discretion. The fourth tranche commitment is subject to an additional 0.75% facility fee.

As of December 31, 2024, a total of $25.0 million of borrowing capacity remained available under the Loan Agreement, subject to the terms and conditions set forth therein. As security for its obligations under the Loan Agreement, the Company granted the Lenders a first priority security interest on substantially all of the Company's assets (other than intellectual property), subject to certain exceptions.

The term loan matures on August 1, 2026, and the Company is obligated to make interest only payments until September 1, 2025, at which point the Company will make monthly payments of equal principal and interest, in an amount which would fully amortize the principal amount of the term loan and accrued interest thereon as of the date of maturity. The term loan bears a variable interest rate equal to the greater of (i) 7.85%, and (ii) the sum of (A) the prime rate last quoted in The Wall Street Journal (or a comparable replacement rate if The Wall Street Journal ceases to quote such rate) and (B) 3.85%; provided that the interest rate cannot exceed 9.60%. The interest rate as of December 31, 2024 was 9.60%. The Company has the option to prepay all, but not less than all of the outstanding principal balance and all accrued and unpaid interest with respect to the principal balance being repaid of the term loans, subject to a prepayment premium to which the Lenders are entitled. The prepayment fee is 3% prior to the second anniversary of the July 25, 2022 funding date, 2% after the second anniversary but prior to the third anniversary of the funding date, and 1% thereafter if prior to the maturity date. Upon final payment or prepayment of the loans, the Company must pay a final payment equal to 6.25% of the loans borrowed ("Final Fee"), which is being accrued as interest expense over the term of the loan using the effective interest method.

The Lenders may elect, prior to the full repayment of the term loans, to convert up to $5.0 million of outstanding principal of the term loans into shares of the Company's common stock, at a conversion price of $6.21 per share, subject to customary adjustments and 9.99% and 19.99% beneficial ownership limitations. The Company determined that the embedded conversion option was not required to be separated from the term loan. The embedded conversion option met the derivative accounting scope exception since the embedded conversion option is indexed to the Company's own common stock and qualifies for classification within stockholders' equity.

The Loan Agreement contains customary representations and warranties, events of default and affirmative and negative covenants, including covenants that limit or restrict the Company's ability to, among other things, dispose of assets, make changes to the Company's business, management, ownership or business locations, merge or consolidate, incur additional indebtedness, incur additional liens, pay dividends or other distributions or repurchase equity, make investments, and enter into certain transactions with affiliates, in each case subject to certain exceptions. Upon the occurrence of an event of default, a default interest rate of an additional 5.00% per annum may be applied to the outstanding loan balances, and the Lender may declare all outstanding obligations immediately due and payable and exercise all of its rights and remedies as set forth in the Loan Agreement and under applicable law. As of December 31, 2024, the Company was in compliance with all covenants under the Loan Agreement.

Subject to certain conditions, the Company granted the Lenders the right, prior to repayment of the term loans, to invest up to $5.0 million in the aggregate in future offerings of common stock, convertible preferred stock or other equity securities of the Company that are broadly marketed and offered to multiple investors, on the same terms, conditions and pricing afforded to others participating in any such financing.

The Company incurred debt issuance costs of $0.5 million in connection with the term loan. In addition, at the time of closing the Company paid to the Lenders a facility fee of $0.4 million, as well as $0.1 million of other expenses incurred by the

Lenders and reimbursed by the Company ("Lender Expenses"). The debt issuance costs, Lender Expenses, and the Final Fee are being amortized as additional interest expense over the term of the loan using the effective interest method. At December 31, 2024, the carrying value of the Loan Agreement approximates the fair value of the term loan, considering that it bears interest that is similar to prevailing market rates.

The following table summarizes the impact of the term loan on the Company's consolidated balance sheet at December 31, 2024:

	December 31, 2024 (in thousands)
Gross proceeds	$ 45,000
Unamortized debt issuance costs and accretion of final payments, net	960
Total debt	$ 45,960
Less: current portion	14,502
Long-term debt	$ 31,458

Future principal payments, which include the Final Fee, in connection with the Loan Agreement as of December 31, 2024 are as follows (dollar amounts in thousands):

Fiscal Year	
2025	14,508
2026	33,305
Total	$ 47,813

9. Stockholders' Equity

July 2023 Underwritten Offering

On July 27, 2023, the Company entered into an underwriting agreement with BofA Securities, Inc., Cowen and Company, LLC and Piper Sandler & Co., as representatives of the several underwriters named therein (collectively, the "Underwriters"), relating to an underwritten public offering of 14,375,000 shares of the Company's common stock, which included 1,875,000 shares issued upon the exercise in full by the Underwriters of their option to purchase additional shares (the "July 2023 Shares"). The closing of the offering took place on August 1, 2023. All of the July 2023 Shares were sold by the Company. The offering price of the July 2023 Shares was $4.80 per share. Net proceeds from the sale and issuance of the July 2023 Shares were approximately $64.4 million, after deducting underwriting discounts and commissions and offering expenses.

Open Market Sale Agreement

On August 11, 2021, the Company filed a universal shelf registration statement on Form S-3, which was declared effective on August 23, 2021 (the "2021 Registration Statement"). Under the 2021 Registration Statement, the Company could offer and sell up to $200.0 million of a variety of securities, including common stock, preferred stock, depositary shares, debt securities, warrants, subscription rights or units from time to time pursuant to one or more offerings at prices and terms to be determined at the time of the sale. In connection with the filing of the 2021 Registration Statement, the Company entered into an Open Market Sale Agreement with Jefferies LLC, as sales agent, pursuant to which the Company may offer and sell shares of its common stock with an aggregate offering price of up to $50.0 million under an "at-the-market" offering program (the "At-the-Market Offering Program"). On November 7, 2023, the Company filed a universal shelf registration statement on Form S-3, which was declared effective on November 15, 2023 (the "2023 Registration Statement"). Under the 2023 Registration Statement, the Company may offer and sell up to $300.0 million of a variety of securities, including common stock, preferred stock, depositary shares, debt securities, warrants, subscription rights or units from time to time pursuant to one or more offerings at prices and terms to be determined at the time of the sale. On August 6, 2024, in anticipation of the expiration of the 2021 Registration Statement, the Company filed a prospectus supplement (the "2024 Prospectus Supplement") under the 2023 Registration Statement to register the offer and sale of the outstanding shares that could be sold under the At-the-Market Offering Program, which prospectus supplement superseded and replaced the sales agreement prospectus, dated August 23, 2021, under the 2021 Registration Statement. As of December 31, 2023, the Company had sold 3,553,995 shares of its common stock pursuant to the Open Market Sale Agreement for aggregate net proceeds of

$21.2 million. As of the date of filing of the 2024 Prospectus Supplement, the Company had issued and sold 4,364,440 shares of common stock pursuant to the Open Market Sale Agreement for aggregate gross proceeds of approximately $26.2 million. Under the 2024 Prospectus Supplement, the Company may sell the shares of common stock under the Open Market Sale Agreement for an aggregate offering price of up to approximately $23.8 million. For the year ended December 31, 2024 the Company sold 2,100,903 shares of its common stock pursuant to the Open Market Sale Agreement for aggregate net proceeds of $10.5 million. Under the 2024 Prospectus Supplement, we may sell the shares of common stock under the Open Market Sale Agreement for an aggregate offering price of up to approximately $17.2 million.

Equity Incentive Plans

In January 2017, the Company's board of directors and stockholders adopted the 2017 Equity Incentive Plan, which was amended and restated in July 2017, (as so amended and restated, the "2017 Plan"), which provided for the grant of incentive stock options, non-statutory stock options, stock appreciation rights, restricted stock awards, restricted stock unit awards and other stock awards. The maximum number of shares of common stock that were authorized for issuance under the 2017 Plan was 2,730,496 shares.

On July 17, 2020, the Company's stockholders approved the 2020 Stock Incentive Plan (the "2020 Plan"), which became effective on July 23, 2020. The 2020 Plan provides for the grant of incentive stock options, non-statutory stock options, stock appreciation rights, restricted stock awards, restricted stock units, and other stock-based awards.

The number of shares of the Company's common stock reserved for issuance under the 2020 Plan was 1,588,315 shares, plus the 426,065 shares of common stock remaining available for issuance under the 2017 Plan as of July 23, 2020. The number of shares reserved under the 2020 Plan will be annually increased on each January 1 through January 1, 2030 by the lower of (i) 4% of the number of shares of common stock outstanding on the first day of such fiscal year and (ii) an amount determined by the Company's board of directors.

As of the effective date of the 2020 Plan, no further awards will be made under the 2017 Plan. Any options or awards outstanding under the 2017 Plan are governed by their existing terms. The shares of the Company's common stock subject to outstanding awards under the 2017 Plan that expire, terminate, or are otherwise surrendered, cancelled, forfeited, or repurchased by the Company at their original issuance price pursuant to a contractual repurchase right will be added back to the shares of common stock available for issuance under the 2020 Plan. No more than 1,588,315 shares of the Company's common stock may be granted subject to incentive stock options under the 2020 Plan. On January 1, 2025 and 2024, the number of shares of common stock reserved under the 2020 Plan was increased by 2,569,607 shares and 2,470,750 shares, respectively.

On February 27, 2023, the Company's board of directors adopted the 2023 Inducement Stock Incentive Plan (the "Inducement Plan"). The Inducement Plan provides for the grant of non-statutory stock options, stock appreciation rights, restricted stock awards, restricted stock units, and other stock-based awards to persons who (a) were not previously an employee or director or (b) are commencing employment with the Company following a bona fide period of non-employment, in either case, as an inducement material to such person's entry into employment with the Company and in accordance with the requirements of the Nasdaq Stock Market Rule 5635(c)(4). As of December 31, 2024, the maximum number of shares of the Company's common stock reserved for issuance under the Inducement Plan is 1,000,000 shares.

For the years ended December 31, 2024 and 2023, the Company recognized stock-based compensation expense of $7.9 million and $7.0 million, respectively. The fair value of shares vested for the years ended December 31, 2024 and 2023 was $8.5 million and $7.6 million, respectively.

Stock Options

The following table summarizes stock option activity under the Company's equity incentive plans since December 31, 2023:

	Options Outstanding	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term (in years)	Aggregate Intrinsic Value (1) (in thousands)
Outstanding at December 31, 2023	7,036,666	$ 6.68	7.71	$ 4,615
Granted	2,967,000	5.43		
Exercised	(271,096)	2.01		
Forfeited	(523,557)	7.44		
Outstanding at December 31, 2024	9,209,013	$ 6.37	7.76	$ 833
Exercisable at December 31, 2024	4,765,649	$ 7.59	6.82	$ 751
Vested and expected to vest at December 31, 2024	9,209,013	$ 6.37	7.76	$ 833

(1) The aggregate intrinsic value of stock options is calculated as the difference between the exercise price of the stock options and the fair value of the Company's common stock for those stock options that had exercise prices lower than the fair value of the Company's common stock.

The weighted average grant date fair value of stock options granted in the years ended December 31, 2024 and 2023 was $4.10 per share and $3.47 per share, respectively. The aggregate intrinsic value of stock options exercised during the years ended December 31, 2024 and 2023 was $0.8 million and $0.1 million, respectively.

The total unrecognized compensation cost related to outstanding employee option awards as of December 31, 2024 was $14.9 million and is expected to be recognized over a weighted average period of 2.7 years.

For purposes of calculating stock-based compensation expense, the Company estimates the fair value of stock options using the Black-Scholes option-pricing model. This model incorporates various assumptions, including the expected volatility, expected term, and interest rates. The underlying assumptions used to value stock options granted to participants using the Black-Scholes option-pricing were as follows:

	Years Ended December 31,	
	2024	2023
Risk-free interest rate range	3.53% to 4.59%	3.36% to 4.67%
Dividend yield	0%	0%
Expected term of options (years)	5.5 to 6.08	5.5 to 6.48
Volatility rate range	88.25% to 90.59%	87.26% to 89.67%

Expected Term – The expected term of stock options represents the weighted average period the stock options are expected to be outstanding. The Company uses the simplified method for estimating the expected term, which calculates the expected term as the average time-to-vesting and the contractual life of the options for stock options issued to participants.

Expected Volatility – Due to the Company's limited operating history and lack of company-specific historical or implied volatility, the expected volatility assumption was determined by examining the historical volatilities of a group of industry peers whose share prices are publicly available. The Company expects to continue using this approach until such time as it has adequate historical data regarding the volatility of its own traded stock price.

Risk-Free Interest Rate – The risk-free rate assumption is based on U.S. Treasury instruments, the terms of which were consistent with the expected term of the Company's stock options.

Expected Dividend – The expected dividend assumption is based on the Company's history and expectation of dividend payouts. The Company has not paid any dividends to date and does not intend to pay dividends.

Fair Value of Common Stock – Following the Company's initial public offering, the fair value of the Company's common stock has been determined based on the closing price of the Company's common stock on the Nasdaq Global Select Market on the grant date, with consideration of whether there is material nonpublic information that could impact that estimated fair value when it is released.

Restricted Sock Units

Activity related to restricted stock units ("RSUs") for the year ended December 31, 2024 is summarized in the table below:

	Number of Shares
Outstanding as of December 31, 2023	100,000
Granted	—
Canceled / Forfeited	—
Vested / Settled	(25,000)
Outstanding as of December 31, 2024	75,000

The weighted-average grant date fair value of RSUs granted in the year ended December 31, 2024 and 2023 was $5.73 per share. The total unrecognized compensation cost related to outstanding RSUs as of December 31, 2024 was $0.3 million and is expected to be recognized over a weighted-average period of 2.2 years.

The total compensation cost recognized in the consolidated statements of operations associated with all the stock-based compensation awards granted by the Company is as follows:

	Year Ended December 31,	
	2024	2023
Research and development	$ 3,896	$ 3,430
General and administrative	4,049	3,607
Total	$ 7,945	$ 7,037

Employee Stock Purchase Plan

On July 17, 2020, the Company's stockholders approved the 2020 Employee Stock Purchase Plan (the "ESPP"), which became effective on July 23, 2020. The ESPP initially provided participating employees with the opportunity to purchase up to an aggregate of 198,539 shares of the Company's common stock. The number of shares of common stock reserved for issuance under the ESPP will increase each January 1 through January 1, 2031, in an amount equal to the lowest of (1) 397,079 shares of the Company's common stock, (2) 1% of the number of shares of the Company's common stock outstanding on the first day of such fiscal year, and (3) an amount determined by the Company's board of directors. On January 1, 2024 and 2023, the number of shares of common stock reserved under the ESPP was increased by 397,079 shares and 397,079 shares, respectively. The Company activated its first six month offering period under the ESPP on April 1, 2022. As of December 31, 2024, 191,400 shares have been purchased by employees under the ESPP.

10. Income Taxes

During the years ended December 31, 2024 and 2023, the Company recorded pre-tax net losses of $102.0 million and $71.2 million, respectively. Since it maintains a full valuation allowance on its deferred tax assets, the Company did not record an income tax provision for the years ended December 31, 2024 and 2023.

A reconciliation of the U.S. federal statutory income tax rate to the Company's effective income tax rate is as follows:

	Year Ended December 31,	
	2024	2023
Federal income tax at statutory rate	21.0 %	21.0 %
Stock compensation	(1.4)	(0.9)
Permanent differences	(0.1)	(0.1)
State income tax, net of federal benefit	6.2	8.1
Federal and state research and development tax credits	9.6	9.1
Valuation allowance	(35.3)	(37.2)
Effective income tax rate	— %	— %

Deferred taxes are recognized for temporary differences between the bases of assets and liabilities for financial statement and income tax purposes. The significant components of the Company's deferred tax assets as of December 31, 2024 and 2023 are composed of the following (dollar amounts in thousands):

	December 31,	
	2024	2023
Deferred tax assets:		
Net operating losses	$ 52,767	$ 42,999
Research and development credits	27,509	16,903
Stock options	2,384	1,930
Accrued expenses	963	916
Amortization	3,418	3,759
Lease liability	250	499
Capitalized research and experimental expenditures	37,667	21,959
Other	543	351
Gross deferred tax assets	125,501	89,316
Less: Valuation allowance	(125,347)	(88,906)
Net deferred tax assets	154	410
Deferred tax liabilities:		
Depreciation of fixed assets	—	(64)
Right of use assets	(154)	(308)
Other	—	(38)
Gross deferred tax liabilities	(154)	(410)
Non-current net deferred tax assets (liabilities)	—	—

As of December 31, 2024, the Company had gross federal net operating loss carryforwards ("NOLs") of $201.3 million, which may be available to offset future taxable income. Of the federal NOLs, $5.6 million expire in 2037 and $195.7 million do not expire. As of December 31, 2024, the Company had gross state NOLs of $167.9 million, which may be available to offset future taxable income and which begin to expire in 2037.

As required by FASB ASC Topic 740, *Income Taxes*, management of the Company has evaluated the positive and negative evidence bearing upon the realizability of its deferred tax assets, which are composed principally of capitalized research and experimental ("R&E") expenditures, NOLs, and research and development credits. Under the applicable accounting standards, management has considered the Company's history of losses and concluded that it is more likely than not that the Company will not recognize the benefits of federal and state deferred tax assets. Accordingly, a full valuation allowance of $125.3 million and $88.9 million has been established at December 31, 2024 and December 31, 2023, respectively. The increase in the valuation allowance of $36.4 million during 2024 was primarily due to increases in capitalized R&E expenditures, NOLs, and research and development credits generated by the Company.

The Company also has federal and state research and development credit carryforwards totaling $28.1 million as of December 31, 2024. The federal research and development credit carryforwards will begin to expire in 2038, unless previously utilized. The state research and development credit carryforwards will begin to expire in 2032, unless previously utilized. The Company has generated research and development credits but has not conducted a study to document the qualified activity. This study may result in an adjustment to the Company's research and development credit carryforwards; however, until a study is completed and any adjustment is known, no amounts are being presented as an uncertain tax position. A full valuation allowance has been provided against the Company's research and development credits and, if an adjustment is required, this adjustment would be offset by an adjustment to the deferred tax asset established for the research and development credit carryforwards and the valuation allowance.

Effective January 1, 2022, a provision of the Tax Cuts and Jobs Act ("TCJA") changed the treatment of R&E expenditures under Section 174 of the United States Internal Revenue Code (the "Internal Revenue Code"). Prior to the TCJA being effective, businesses have had the option of deducting Section 174 expenses in the year incurred or capitalizing and amortizing the costs over five years. The new TCJA provision, however, eliminates this option and requires Section 174 expenses associated with research conducted in the United States to be capitalized and amortized over a five-year period. For expenses associated with research outside of the United States, Section 174 expenses will be capitalized and amortized over a 15-year period.

The Company's ability to use its NOLs and tax credit carryforwards to offset taxable income is subject to restrictions under Sections 382 and 383 of the Internal Revenue Code. Under the Internal Revenue Code provisions, certain substantial changes in the Company's ownership, including the sale of the Company or significant changes in ownership due to sales of equity, have limited and may limit in the future, the amount of NOLs which could be used annually to offset future taxable income. The Company has not yet conducted an analysis of ownership changes. The Company may also experience ownership changes in the future as a result of subsequent shifts in its stock ownership, some of which may be outside the Company's control. As a result, the Company's ability to use its pre-change NOLs to offset U.S. federal taxable income may be subject to limitations, which could potentially result in increased future tax liability to the Company. In addition, at the state level, there may be periods during which the use of NOLs is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed. Under the TCJA, the use of federal NOLs arising in taxable years beginning after December 31, 2017 is limited to 80% of current year taxable income and NOLs arising in taxable years ending after December 31, 2017 may not be carried back (though any such NOLs may be carried forward indefinitely).

The Company establishes reserves for uncertain tax positions based on management's assessment of exposures associated with tax positions taken on tax return filings. The tax reserves are analyzed periodically and adjustments are made as events occur that warrant adjustment to the reserves. The Company does not have any reserves for uncertain tax positions as of December 31, 2024 and any change in position would result in a change in the valuation allowance maintained against its net deferred tax assets.

Interest and penalty charges, if any, related to unrecognized tax benefits are classified as income tax expense in the accompanying consolidated statements of operations and comprehensive loss. As of December 31, 2024, the Company had no accrued interest related to uncertain tax positions. Since the Company is in a loss carryforward position, the Company is generally subject to examination by the U.S. federal, state, and local income tax authorities for all tax years in which a loss carryforward is available.

11. Net Loss per Share

Net Loss per Share Attributable to Common Stockholders

The following table sets forth the computation of basic and diluted net loss per share for the years ended December 31, 2024 and 2023 (in thousands, except share and per share amounts):

	Year Ended December 31,	
	2024	2023
Net loss attributable to common stockholders	$ (102,024)	$ (71,169)
Net loss per share attributable to common stockholders	$ (1.62)	$ (1.37)
Weighted-average common shares and pre-funded warrants outstanding	62,811,814	51,839,131

The Company has generated a net loss in all periods presented; therefore, the basic and diluted net loss per share attributable to common stockholders are the same as the inclusion of the potentially dilutive securities would be anti-dilutive. Since the shares underlying the pre-funded warrants are issuable for nominal consideration, they are considered outstanding for both basic and diluted earnings per share from the date of issuance. The Company excluded the following potential dilutive securities, presented based on amounts outstanding at each period end, from the computation of diluted net loss per share attributable to common stockholders for the periods indicated:

	Year Ended December 31,	
	2024	2023
Options to purchase common stock	9,209,013	7,036,666
Unvested RSUs	75,000	100,000
Total	9,284,013	7,136,666

12. Employee Benefit Plans

The Company established a defined contribution savings plan in 2018 for all eligible U.S. employees under Section 401(k) of the Internal Revenue Code. Employees can designate the investment of their 401(k) accounts into several mutual funds. Effective January 1, 2021, the Company implemented a matching policy under which the Company matches 50% of an employee's contributions to the 401(k) plan, up to a maximum of 6% of the employee's base salary and bonus paid during the year. For the years ended December 31, 2024 and 2023, the Company made employer contributions to the 401(k) plan of $0.4 million and $0.3 million, respectively.

13. Segment Reporting

The Company manages its operations as a single segment, focused on developing novel therapeutics for rare diseases impacting bone health and blood vessel function. The Company's Chief Executive Officer ("CEO"), as the Company's chief operating decision maker ("CODM"), manages and allocates resources at a consolidated level.

The CODM assesses performance, monitors budget versus actual results, and decides how to allocate resources based on net loss that also is reported on the consolidated statement of operations and comprehensive loss as consolidated net loss.

The accounting policies of the Company's single operating segment are the same as those described in the summary of significant accounting policies in Note 2. The measure of segment assets is reported on the consolidated balance sheet as total consolidated assets. In 2024 and 2023, all the Company's long-lived assets were held in the United States. Expenditures for the addition of long-lived assets are reported on the consolidated statements of cash flows as purchases of property and equipment.

The company does not have intra-entity sales or transfers.

The following table presents reportable segment profit and loss, including significant expense categories, attributable to the Company's reportable segment for the periods presented:

	Year Ended December 31,	
	2024	2023
Clinical	$ 26,857	$ 15,084
CMC	20,931	10,483
Other research and development expense [(1)]	12,043	9,940
Personnel expense - R&D	17,552	14,133
Personnel expense - G&A	6,226	6,674
Share-based compensation expense	7,945	7,037
Administrative & facilities expense [(2)]	12,476	12,294
Interest income	(7,666)	(7,837)
Interest expense	5,558	3,333
Other expense, net	102	28
Net loss	$ 102,024	$ 71,169

(1) Other research and development expenses primarily consist of consulting, regulatory support, toxicology, sponsored research costs, and other research and development activities.

(2) Administrative & facilities expense primarily consists of facilities expenses, depreciation expense, legal costs, insurance, consulting, and other administrative costs.

14. Subsequent Events

On March 6, 2025, the Company implemented a plan to reduce operating costs and better align its workforce to support the prioritization of activities for its lead indication, ENPP1 Deficiency. As a result of these prioritization activities, the Company reduced its workforce by approximately 25%. The Company estimates that it will incur one-time restructuring charges of approximately $1.8 million including employee severance, benefits and related termination costs, the majority of which the Company expects to pay by the end of the third quarter of 2025.

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure.

None.

Item 9A. Controls and Procedures.

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our Chief Executive Officer and our Chief Financial Officer (our principal executive officer and principal financial officer, respectively), evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2024. The term "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended, or the Exchange Act, means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company's management, including its principal executive and principal financial officers, or persons performing similar functions, as appropriate to allow timely decisions regarding required disclosure. Our management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and our management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on the evaluation of our disclosure controls and procedures as of December 31, 2024, our Chief Executive Officer and Chief Financial Officer concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

Management's Annual Report on Internal Control Over Financial Reporting and Attestation Report of Registered Public Accounting Firm

Our management is responsible for establishing and maintaining adequate internal control over financial reporting for our company. Internal control over financial reporting is defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act as a process designed by, or under the supervision of, a company's principal executive officer and principal financial officer, or persons performing similar functions, and effected by a company's board of directors, management, and other personnel, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles and includes those policies and procedures that:

- pertain to the maintenance of records that in reasonable detail accurately and fairly reflect the transactions and dispositions of a company's assets;
- provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that a company's receipts and expenditures are being made only in accordance with authorizations of a company's management and directors; and
- provide reasonable assurance regarding prevention or timely detections of unauthorized acquisition, use or disposition of a company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Therefore, even those systems determined to be effective can provide only reasonable assurance with respect to financial statement preparation and presentation. Projections of any evaluation of effectiveness to future periods are subject to the risk that controls become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Under the supervision of and with the participation of our principal executive officer and principal financial officer, our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2024 based on the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) in Internal Control - Integrated Framework (2013 framework). Based on this assessment, management concluded that our internal control over financial reporting was effective as of December 31, 2024.

This Annual Report on Form 10-K does not include an attestation report of our independent registered public accounting firm due to an exemption established by the JOBS Act for "emerging growth companies".

Changes in Internal Control Over Financial Reporting

There was no change in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) that occurred during the three months ended December 31, 2024 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information.

(b)Director and Officer Trading Arrangements

None of our directors or officers adopted or terminated a Rule 10b5-1 trading arrangement or a non-Rule 10b5-1 trading arrangement (as defined in Item 408(c) of Regulation S-K) during the fourth quarter of 2024.

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections.

Not applicable.

Part III

Item 10. Directors, Executive Officers and Corporate Governance.

Except to the extent provided below, the information required under this Item 10 is incorporated by reference to our definitive proxy statement for our 2025 Annual Meeting of Stockholders, which we intend to file with the Securities and Exchange Commission not later than 120 days after the end of the fiscal year ended December 31, 2024.

We post our Code of Business Conduct and Ethics, which applies to our directors, officers and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions, in the "Governance" sub-section of the "Investors" section of our corporate website at http://www.inozyme.com. We intend to disclose on our website any amendments to, or waivers from, the Code of Business Conduct and Ethics that are required to be disclosed pursuant to the disclosure requirements of Item 5.05 of Form 8-K.

Item 11. Executive Compensation.

The information required under this Item 11 is incorporated by reference to our definitive proxy statement for our 2025 Annual Meeting of Stockholders, which proxy statement we intend to file with the Securities and Exchange Commission not later than 120 days after the end of the fiscal year ended December 31, 2024.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholders Matters.

The information required under this Item 12 is incorporated by reference to our definitive proxy statement for our 2025 Annual Meeting of Stockholders, which proxy statement we intend to file with the Securities and Exchange Commission not later than 120 days after the end of the fiscal year ended December 31, 2024.

Item 13. Certain Relationships and Related Transactions, and Director Independence.

The information required under this Item 13 is incorporated by reference to our definitive proxy statement for our 2025 Annual Meeting of Stockholders, which proxy statement we intend to file with the Securities and Exchange Commission not later than 120 days after the end of the fiscal year ended December 31, 2024.

Item 14. Principal Accountant Fees and Services.

The information required under this Item 14 is incorporated by reference to our definitive proxy statement for our 2025 Annual Meeting of Stockholders, which proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the close of the end of the fiscal year ended December 31, 2024.

PART IV

Item 15. Exhibits and Financial Statement Schedules.

1. Financial Statements

For a list of financial statements included herein, see Index to the Consolidated Financial Statements on page F-1 of this Annual Report on Form 10-K.

2. Financial Statement Schedules

All financial statement schedules have been omitted because they are not applicable, not required, or the information required is shown in the consolidated financial statements or the notes thereto.

3. Exhibits

The following is a list of exhibits filed as part of this Annual Report on Form 10-K.

Exhibit Number	Description of Exhibit
2.1†	Intellectual Property Asset Purchase Agreement, dated July 17, 2020, by and between the Registrant and Alexion Pharmaceuticals, Inc. (incorporated by reference to Exhibit 2.1 to Amendment No. 1 to the Registrant's Registration Statement on Form S-1 (File No. 333-239648) filed with the Securities and Exchange Commission on July 20, 2020).
3.1	Restated Certificate of Incorporation of the Registrant (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K (File No. 001-39397) filed with the Securities and Exchange Commission on July 28, 2020).
3.2	Amended and Restated Bylaws of the Registrant (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K (File No. 001-39397) filed with the Securities and Exchange Commission on June 14, 2023).
4.1	Specimen Stock Certificate evidencing the shares of common stock (incorporated by reference to Exhibit 4.1 to Amendment No. 1 to the Registrant's Registration Statement on Form S-1 (File No. 333-239648) filed with the Securities and Exchange Commission on July 20, 2020).
4.2	Description of the Registrant's Securities Registered under Section 12 of the Exchange Act (incorporated by reference to Exhibit 4.2 to the Registrant's Annual Report on Form 10-K (File No. 001-39397) filed with the Securities and Exchange Commission on March 25, 2021).
4.3	Form of Amended and Restated Pre-Funded Warrant (incorporated by reference to Exhibit 4.1 to the Registrant's Current Report on Form 8-K (File No. 001-39397) filed with the Securities and Exchange Commission on June 10, 2022).
10.1	Second Amended and Restated Investor Rights Agreement, dated as of November 9, 2018, by and among the Registrant and the other parties thereto, as amended (incorporated by reference to Exhibit 10.1 to Amendment No. 1 to the Registrant's Registration Statement on Form S-1 (File No. 333-239648) filed with the Securities and Exchange Commission on July 20, 2020).
10.2	Registration Rights Agreement, dated as of June 1, 2016, by and among the Registrant and the other parties thereto (incorporated by reference to Exhibit 10.2 to the Registrant's Registration Statement on Form S-1 (File No. 333-239648) filed with the Securities and Exchange Commission on July 2, 2020).
10.3#	Amended and Restated 2017 Equity Incentive Plan, as amended (incorporated by reference to Exhibit 10.3 to the Registrant's Registration Statement on Form S-1 (File No. 333-239648) filed with the Securities and Exchange Commission on July 2, 2020).
10.4#	Form of Stock Option Agreement Granted under Amended and Restated 2017 Equity Incentive Plan (incorporated by reference to Exhibit 10.4 to the Registrant's Registration Statement on Form S-1 (File No. 333-239648) filed with the Securities and Exchange Commission on July 2, 2020).
10.5#	2020 Stock Incentive Plan (incorporated by reference to Exhibit 10.5 to Amendment No. 1 to the Registrant's Registration Statement on Form S-1 (File No. 333-239648) filed with the Securities and Exchange Commission on July 20, 2020).
10.6#	Form of Stock Option Agreement under the 2020 Stock Incentive Plan (incorporated by reference to Exhibit 10.6 to Amendment No. 1 to the Registrant's Registration Statement on Form S-1 (File No. 333-239648) filed with the Securities and Exchange Commission on July 20, 2020).

10.7#	Form of Restricted Stock Unit Agreement under the 2020 Stock Incentive Plan (incorporated by reference to Exhibit 10.7 to Amendment No. 1 to the Registrant's Registration Statement on Form S-1 (File No. 333-239648) filed with the Securities and Exchange Commission on July 20, 2020).
10.8#	2020 Employee Stock Purchase Plan (incorporated by reference to Exhibit 10.8 to Amendment No. 1 to the Registrant's Registration Statement on Form S-1 (File No. 333-239648) filed with the Securities and Exchange Commission on July 20, 2020).
10.9*#	Summary of Non-Employee Director Compensation Policy.
10.10†	License Agreement, dated January 6, 2017, by and between Yale University and the Registrant, as amended by Amendment No. 1 to License Agreement, dated May 2, 2020, by and between Yale University and the Registrant and Amendment No. 2 to License Agreement, dated July 1, 2020, by and between Yale University and the Registrant (incorporated by reference to Exhibit 10.10 to the Registrant's Registration Statement on Form S-1 (File No. 333-239648) filed with the Securities and Exchange Commission on July 2, 2020).
10.11#	Corporate Sponsored Research Agreement, dated January 6, 2017, by and between Yale University and the Registrant, as amended by Amendment No. 1 to Corporate Sponsored Research Agreement, dated February 19, 2019, by and between Yale University and the Registrant, as amended by Amendment No. 2 to Corporate Sponsored Research Agreement, effective December 31, 2021, by and between Yale University and the Registrant and as amended by Amendment No. 3 to Corporate Sponsored Research Agreement, dated May 31, 2022, by and between Yale University and the Registrant and as amended by Amendment No. 4 to Corporate Sponsored Research Agreement, dated March 24, 2023, by and between Yale University and the Registrant, as amended by Amendment No. 5 to Corporate Sponsored Research Agreement, dated January 24, 2024, by and between Yale University and the Registrant (incorporated by reference to Exhibit 10.11 to the Registrant's Annual Report on Form 10-K (File No. 001-39397) filed with the Securities and Exchange Commission on March 12, 2024).
10.12*†	Amendment No. 6 to Corporate Sponsored Research Agreement, dated December 19, 2024, by and between Yale University and the Registrant)
10.13#	Form of Restricted Stock Agreement between the Registrant and Axel Bolte (incorporated by reference to Exhibit 10.12 to the Registrant's Registration Statement on Form S-1 (File No. 333-239648) filed with the Securities and Exchange Commission on July 2, 2020).
10.14	Lease, dated December 13, 2019, by and between 321 Summer Street LLC and the Registrant (incorporated by reference to Exhibit 10.13 to the Registrant's Registration Statement on Form S-1 (File No. 333-239648) filed with the Securities and Exchange Commission on July 2, 2020).
10.15	Lease, dated May 13, 2020, by and between RREF II 451D, LLC and the Registrant (incorporated by reference to Exhibit 10.14 to the Registrant's Registration Statement on Form S-1 (File No. 333-239648) filed with the Securities and Exchange Commission on July 2, 2020).
10.16#	Form of Indemnification Agreement between the Registrant and each of its Executive Officers and Directors (incorporated by reference to Exhibit 10.15 to Amendment No. 1 to the Registrant's Registration Statement on Form S-1 (File No. 333-239648) filed with the Securities and Exchange Commission on July 20, 2020).
10.17#	Employment Contract, dated March 24, 2021, between Inozyme Pharma Switzerland GmbH and Axel Bolte (incorporated by reference to Exhibit 10.16 to the Registrant's Annual Report on Form 10-K (File No. 001-39397) filed with the Securities and Exchange Commission on March 25, 2021).
10.18#	Transition and Separation Letter Agreement, dated March 21, 2023, by and between the Registrant and Axel Bolte (incorporated by reference to Exhibit 10.2 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-39397) filed with the Securities and Exchange Commission on May 9, 2023).
10.19#	Consulting Agreement, dated April 30, 2023, by and between the Registrant and Axel Bolte (incorporated by reference to Exhibit 10.3 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-39397) filed with the Securities and Exchange Commission on May 9, 2023).
10.20#	Employment Agreement, dated March 2, 2022, by and between the Registrant and Sanjay Subramanian (incorporated by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-39397) filed with the Securities and Exchange Commission on May 10, 2022).
10.21	Open Market Sale Agreement[SM], dated August 11, 2021, by and between the Registrant and Jefferies LLC (incorporated by reference into Exhibit 1.2 to the Registrant's Registration Statement on Form S-3 (File No. 333-258702) filed with the Securities and Exchange Commission on August 11, 2021).

10.22#†	Loan and Security Agreement, dated July 25, 2022, by and among the Registrant, K2 HealthVentures LLC, as lender, K2 HealthVentures LLC, as administrative agent, and Ankura Trust Company, LLC, as collateral agent (incorporated by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-39397) filed with the Securities and Exchange Commission on August 15, 2022).
10.23#	Employment Agreement, dated March 21, 2023, by and between the Registrant and Douglas Treco (incorporated by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-39397) filed with the Securities and Exchange Commission on May 9, 2023).
10.24#	Employment Agreement, dated March 14, 2023, by and between the Registrant and Matthew Winton (incorporated by reference to Exhibit 10.4 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-39397) filed with the Securities and Exchange Commission on May 9, 2023).
10.25#	2023 Inducement Stock Incentive Plan (incorporated by reference to Exhibit 99.3 to the Registrant's Registration Statement on Form S-8 (File No. 333-270733) filed with the Securities and Exchange Commission on March 22, 2023).
10.26#	Form of Nonstatutory Stock Option Agreement under 2023 Inducement Stock Incentive Plan (incorporated by reference to Exhibit 10.7 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-39397) filed with the Securities and Exchange Commission on May 9, 2023).
10.27#	Form of Restricted Stock Unit Agreement under 2023 Inducement Stock Incentive Plan (incorporated by reference to Exhibit 10.8 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-39397) filed with the Securities and Exchange Commission on May 9, 2023).
10.28#	Form of Restricted Stock Unit Agreement under the 2020 Stock Incentive Plan (incorporated by reference to Exhibit 10.27 to the Registrant's Annual Report on Form 10-K (File No. 001-39397) filed with the Securities and Exchange Commission on March 12, 2024).
19.1*	Amended and Restated Insider Trading Policy
21.1*	Subsidiaries of the Registrant
23.1*	Consent of Ernst & Young LLP, independent registered public accounting firm
31.1*	Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
31.2*	Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
32.1+	Certification of Principal Executive Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
32.2+	Certification of Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
97.1	Dodd-Frank Compensation Recovery Policy (incorporated by reference to Exhibit 97.1 to the Registrant's Annual Report on Form 10-K (File No. 001-39397) filed with the Securities and Exchange Commission on March 12, 2024).
101.INS	Inline XBRL Instance Document
101.SCH	Inline XBRL Taxonomy Extension Schema Document
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document
104	Cover Page Interactive Data File (formatted as Inline XBRL with applicable taxonomy extension information contained in Exhibits 101).

* Filed herewith.

+ Furnished herewith.

# Indicates a management contract or any compensatory plan, contract or arrangement.

† Certain portions of this exhibit have been omitted because they are not material and contain information that the Registrant customarily and actually treats as private or confidential.

Item 16. Form 10-K Summary

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

Date: March 10, 2025

INOZYME PHARMA, INC.

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

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

Signature	Title	Date
/s/ Douglas A. Treco Douglas A. Treco	Chief Executive Officer and Chairman (Principal Executive Officer)	March 10, 2025
/s/ Sanjay Subramanian Sanjay Subramanian	Chief Financial Officer (Principal Financial Officer and Principal Accounting Officer)	March 10, 2025
/s/ Sarah Bhagat Sarah Bhagat	Director	March 10, 2025
/s/ Axel Bolte Axel Bolte	Director	March 10, 2025
/s/ Reinaldo Diaz Reinaldo Diaz	Director	March 10, 2025
/s/ Martin Edwards Martin Edwards	Director	March 10, 2025
/s/ Erik Harris Erik Harris	Director	March 10, 2025
/s/ Robert Hopfner Robert Hopfner	Director	March 10, 2025
/s/ Edward Mathers Edward Mathers	Director	March 10, 2025
/s/ Lynne Sullivan Lynne Sullivan	Director	March 10, 2025

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Boston, Massachusetts 02210
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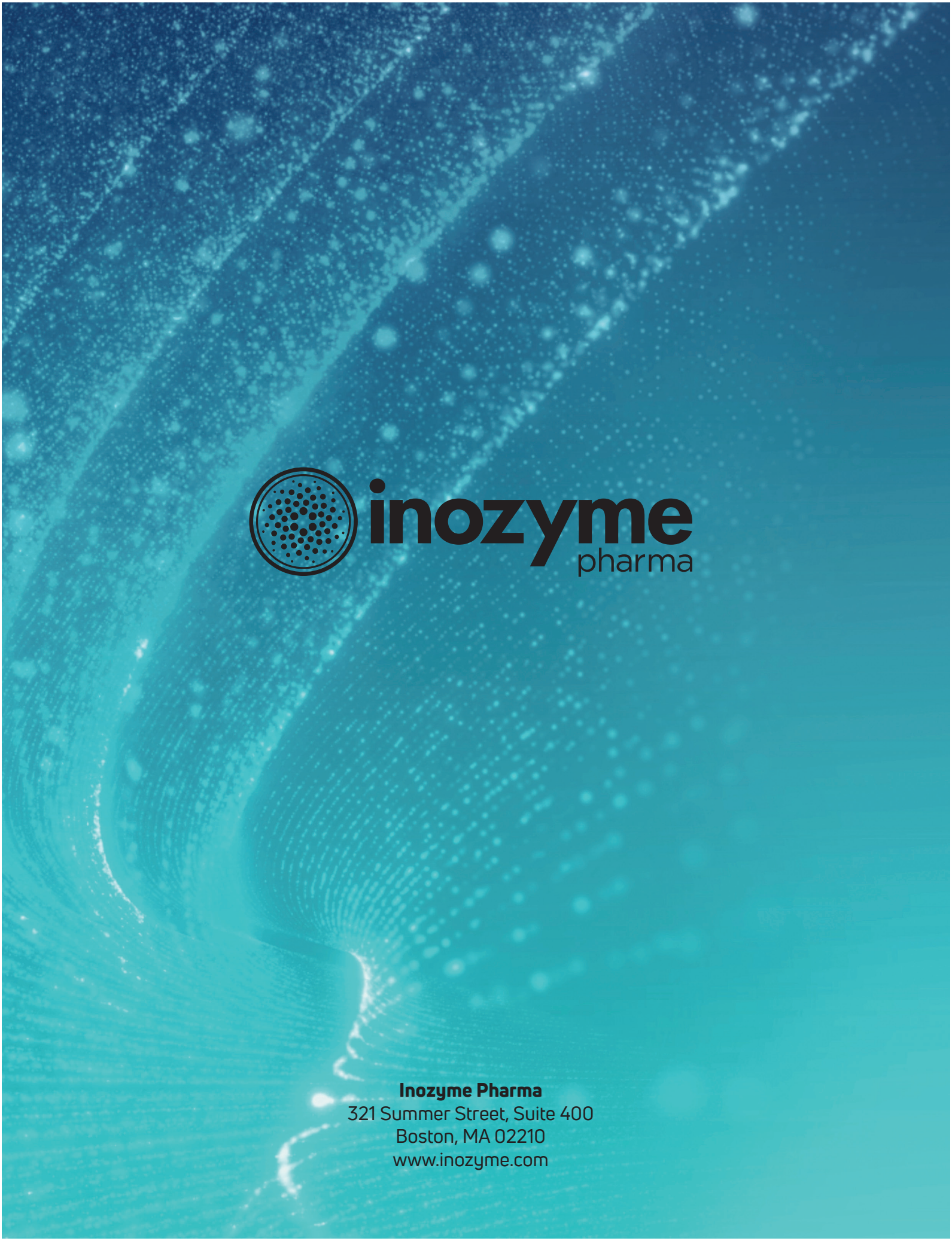
www.inozyme.com

Forward-Looking Statements

This annual report contains forward-looking statements within the meaning of applicable federal securities laws and regulations. Any statements contained in this annual report that are not statements of historical fact may be deemed to be forward-looking statements. Without limiting the foregoing, the words “believes,” “intends,” “anticipates,” “plans,” “expects,” “seeks,” “estimates,” “would,” “should,” “likely,” “will,” “may,” “continue,” “could,” or similar expressions are intended to identify forward-looking statements. While we may elect to update forward-looking statements in the future, we specifically disclaim any obligation to do so, even if our expectations change. A number of factors could cause our results to differ materially from those indicated by such forward-looking statements, including those detailed under the heading “Risk Factors” in Part I, Item 1A in the accompanying Annual Report on Form 10-K for the fiscal year ended December 31, 2023 and our subsequent filings with the U.S. Securities and Exchange Commission.



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