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, 2025

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: 001-43080

Polaryx Therapeutics, Inc.

(Exact name of registrant as specified in its charter)

Nevada	47-3393659
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification Number)**

South Tower, 140 E Ridgewood Avenue, Suite 415
Paramus, NJ 07652
(201) 940-7236

(Address including zip code, and telephone number including area code, of registrant's principal executive offices)

Former name, former address and former fiscal year, if changed since last report: N/A

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

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, par value $0.0001 per share	PLYX	The Nasdaq Capital Market

Securities registered pursuant to Section 12(g) of the Exchange 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 Section 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 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, a 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). ☐

The registrant was not a public company as of the last business day of its most recently completed second fiscal quarter and therefore cannot calculate the aggregate market value of the voting and non-voting common equity held by non-affiliates as of such date.

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 February 1, 2026, the registrant had 47,343,297 shares of common stock, $0.0001 par value per share, outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

None.

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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K (this "Annual Report") contains forward-looking statements that can involve substantial risks and uncertainties. All statements other than statements of historical facts contained in this Annual Report, including statements regarding our future results of operations and financial position, business plan and strategy, future revenue, timing and likelihood of success, plans and objectives of management for future operations, future results of anticipated products and prospects, plans and objectives of management are forward-looking statements. These statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements.

In some cases, you can identify forward-looking statements by terms such as "anticipate," "believe," "contemplate," "continue," "could," "estimate," "expect," "intend," "may," "plan," "potential," "predict," "project," "should," "target," "will," or "would" or the negative of these terms or other similar expressions, although not all forward-looking statements contain these words. Forward-looking statements contained in this Annual Report include, but are not limited to, statements about:

- our plans to develop and commercialize our product candidate pipeline for the treatment of rare, pediatric lysosomal storage disorders ("LSDs");
- our ability to obtain funding for our operations, including funding necessary to complete the development and commercialization of our programs;
- the timing and focus of our ongoing and future preclinical studies and clinical trials and the reporting of data from those studies and trials;
- the beneficial characteristics, safety, efficacy and therapeutic effects of our product candidates;
- our plans relating to the further development of our product candidates;
- the size of the market opportunity for our product candidates, including our estimates of the number of patients who suffer from the diseases we are targeting;
- our continued reliance on third parties to conduct additional preclinical studies and clinical trials of our product candidates and for the manufacture of our product candidates for preclinical studies and clinical trials;
- the success, cost and timing of our preclinical and clinical development activities and planned clinical trials;
- our plans regarding, and our ability to obtain, and negotiate favorable terms of, any collaboration, licensing or other arrangements that may be necessary or desirable to develop, manufacture or commercialize our product candidates;
- the timing of and our ability to obtain and maintain regulatory approvals for our product candidates, as well as future programs;
- the rate and degree of market acceptance and clinical utility of our product candidates;
- the success of competing treatments that are or may become available;
- our ability to attract and retain key management and technical personnel;
- our expectations regarding our ability to obtain, maintain and enforce intellectual property protection for our product candidates;
- our financial performance;
- the period over which we estimate our existing cash will be sufficient to fund our future operating expenses and capital expenditure requirements; and
- our expectations regarding the period during which we will qualify as an emerging growth company under the Jumpstart Our Business Startups Act of 2012 (the "JOBS Act").

We have based these forward-looking statements largely on our current expectations and projections about our business, the industry in which we operate and financial trends that we believe may affect our business, financial condition, results of operations and prospects, and these forward-looking statements are not guarantees of future performance or development. These forward-looking statements speak only as of the date of this Annual Report and are subject to a number of risks, uncertainties and assumptions, including, but not limited to, those described in the section titled "*Risk Factors*" and elsewhere in this Annual Report. Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified, you should not rely on these forward-looking statements as predictions of future events. The events and circumstances reflected in our forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein until after we distribute this Annual Report, whether as a result of any new information, future events or otherwise.

In addition, statements that "we believe" and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this Annual Report, and while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain and you are cautioned not to unduly rely upon these statements.

PART I

As used in this Annual Report, unless the context otherwise requires, references to "we," "us," "our," the "Company," "Polaryx" and similar references refer to Polaryx Therapeutics, Inc. Additionally, references to our "Board" refer to the board of directors of Polaryx Therapeutics, Inc.

Item 1. Business

Overview

We are a clinical-stage biotechnology company committed to the discovery, development, and commercialization of novel, disease-modifying therapies for rare, pediatric LSDs. Our therapeutic philosophy is centered on delivering safe, effective, and patient-friendly treatments that address the underlying pathophysiology of these catastrophic diseases and their significant unmet need. Our multi-modal approach integrates small molecule therapies, including a combination therapy, and a gene therapy, positioning us to potentially address both the genetic and downstream pathological features of LSDs. Our small molecule drug candidates share target indications, as well as similar modes of action, that have been demonstrated to address lysosomal dysfunction, neuroinflammation, and neuronal loss in our validated animal models that closely mimic human clinical phenotypes. Our most advanced product candidate, PLX-200, targets several LSDs and we intend to launch a Phase 2 proof-of-concept basket trial which we expect will enhance PLX-200's potential to become the standard of care across multiple LSDs. Our drug candidate pipeline includes:

- **PLX-200** (gemfibrozil), our most advanced drug candidate, is an oral small molecule for the treatment of LSDs. PLX-200 is a repurposed, reformulated drug that we are pursuing through a 505(b)(2) regulatory pathway and is designed to be administered through a novel and proprietary oral solution. We are advancing PLX-200 through a Phase 2 proof-of-concept basket trial, which we refer to as SOTERIA (PLX-200-600), and expect to initiate this trial in the second half of 2026. SOTERIA is an open-label, multi-indication, master study for the treatment of certain LSDs, which we believe represent approximately one quarter of the LSD population, including Classic Late Infantile Neuronal Ceroid Lipofuscinosis ("CLN2") and Juvenile Neuronal Ceroid Lipofuscinosis ("CLN3") subtypes of neuronal ceroid lipofuscinosis ("NCLs"), Krabbe disease, and Sandhoff disease. We held a pre-investigational new drug ("IND") submission meeting in April 2025. We submitted an IND application to the U.S. Food and Drug Administration ("FDA") for the SOTERIA trial in August 2025 and received a safe to proceed letter in October 2025. For more information regarding the 505(b)(2) regulatory pathway, see "*Business — Government Regulation — 505(b)(2) New Drug Applications*".

  Data readouts from SOTERIA are expected to provide guidance and a clear pathway for each of the four indications towards potentially registrable trials. We believe there may also be an opportunity to seek accelerated approval for CLN2 and CLN3 from the FDA based on precedent approval for a third-party drug with a similar trial design. Products studied for their safety and effectiveness in treating serious or life-threatening diseases or conditions may receive accelerated approval upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. As a condition of accelerated approval, the FDA will generally require the sponsor to perform adequate and well-controlled post-marketing clinical studies to verify and describe the anticipated effect on irreversible morbidity or mortality or other clinical benefit.

  PLX-200 has already received authorization under two separate INDs to initiate potentially single pivotal trials in CLN2 and CLN3, the most prevalent subtypes of NCLs, which we filed on December 20, 2019 and March 6, 2020 and received authorization for on January 17, 2020 and April 6, 2020. Initiation of these trials was delayed due to the COVID-19 pandemic and a subsequent shift in our strategy. We currently do not expect to commence the trials in the near term while we focus our resources on SOTERIA. To date, the FDA has granted three orphan drug designations ("ODD") to PLX-200, for the treatment of all 13 subtypes of NCLs, GM2 gangliosidoses, such as Tay-Sachs and Sandhoff diseases, and Krabbe disease. PLX-200 has also received fast track ("Fast Track") designation for

the treatment of CLN2 (for SOTERIA) and CLN3 (for STARLIGHT). For more information, see "*Business — Government Regulation — Expedited Development and Review Programs*" below. The receipt of such designations does not guarantee a faster development process, regulatory review, or approval as compared to the conventional FDA approval process.

- **PLX-300** (cinnamic acid) is a novel, oral small molecule therapy in IND-enabling studies for the treatment of LSDs. PLX-300 is an unsaturated carboxylic acid that occurs naturally in several plants as a deaminated product of phenylalanine. To date, the FDA has granted three ODDs to PLX-300 for the treatment of GM2 gangliosidosis, Krabbe disease, and Niemann-Pick Disease ("NPD") type A and type B. PLX-300 has also received rare pediatric drug designation ("RPD") for the treatment of GM2 gangliosidosis, Krabbe disease, and NPD type A and type B. The receipt of such designations does not guarantee a faster development process, regulatory review, or approval as compared to the conventional FDA approval process.

- **PLX-100** is a preclinical stage orally administrable combination therapy comprised of our proliferator-activated receptor alpha ("PPARα") agonist, PLX-200, and vitamin A, a retinoid X receptor alpha ("RXRα") agonist. PLX-100 is being developed for the treatment of LSDs. To date, the FDA has granted one ODD to PLX-100 for the treatment of classic late infantile neuronal ceroid lipofuscinoses, or CLN2. The receipt of such designation does not guarantee a faster development process, regulatory review, or approval as compared to the conventional FDA approval process.

- **PLX-400** is a preclinical stage novel gene therapy being developed for the treatment of LSDs. We are exploring PLX-400 as a monotherapy or in combination with oral administration of PLX-200 and expect to determine any clinical development plans for PLX-400 at a later date.

LSDs are a heterogeneous group of nearly 50 inherited rare, catastrophic, metabolic diseases caused by mutations in genes encoding lysosomal enzymes or associated proteins. These mutations result in the accumulation of undegraded substrates within lysosomes, leading to cellular dysfunction, chronic inflammation, and cell apoptosis. LSDs often manifest in infancy or early childhood and are associated with severe clinical outcomes, including developmental regression, seizures, blindness, motor impairment, and premature death. We believe that there are approximately 50,000 LSD patients in the United States, Europe and select regions of the rest of the world ("ROW"), assuming an incidence rate of one in 5,000 births.

The LSDs addressed by our pipeline of drug candidates are currently treated for symptomatic relief and palliative care, and, with few exceptions, lack approved disease-modifying therapies. Our drug candidates have been validated in gold standard preclinical animal models for CLN2, CLN3, Sandhoff disease, Krabbe disease and NPD type A and type B. With similar broad disease pathology shared across multiple LSDs in terms of substrate accumulation, neuroinflammation, and neuronal loss, we believe our small molecule drug candidates have the potential to demonstrate high therapeutic benefit in other targeted indications.

Our development program is focused on a subset of rare LSDs with particularly high unmet need, including:

- **Neuronal Ceroid Lipofuscinoses:** A group of 13 genetically distinct subtypes categorized according to the associated gene (CLN1 – 8; CLN10 – 14), we believe that NCLs represent approximately 15% of the LSD population, roughly 7,700 patients in the United States, Europe and select regions of ROW. NCLs are characterized by progressive neurodegeneration, vision loss, and early mortality. The three most common forms of NCLs are CLN1, CLN2, and CLN3. Of the 13 NCL sub-types, only one, CLN2, has an established standard of care in the form of an enzyme replacement therapy.

- **Krabbe Disease:** Krabbe disease, also known as globoid cell leukodystrophy, is caused by mutations in the galactosylceramidase ("GALC") gene, leading to GALC deficiency and an inability to break down certain lipids in the body. This results in accumulation of toxic substances in the brain and other areas of the nervous system leading to demyelination and severe neurological decline. The incidence rate of Krabbe disease varies significantly, affecting 0.3 to 2.6 per 100,000 live births. We believe that there are approximately 6,700 Krabbe disease patients in the United States, Europe and select regions of the ROW. Hematopoietic stem cell transplantation ("HSCT") is considered the current standard of care.

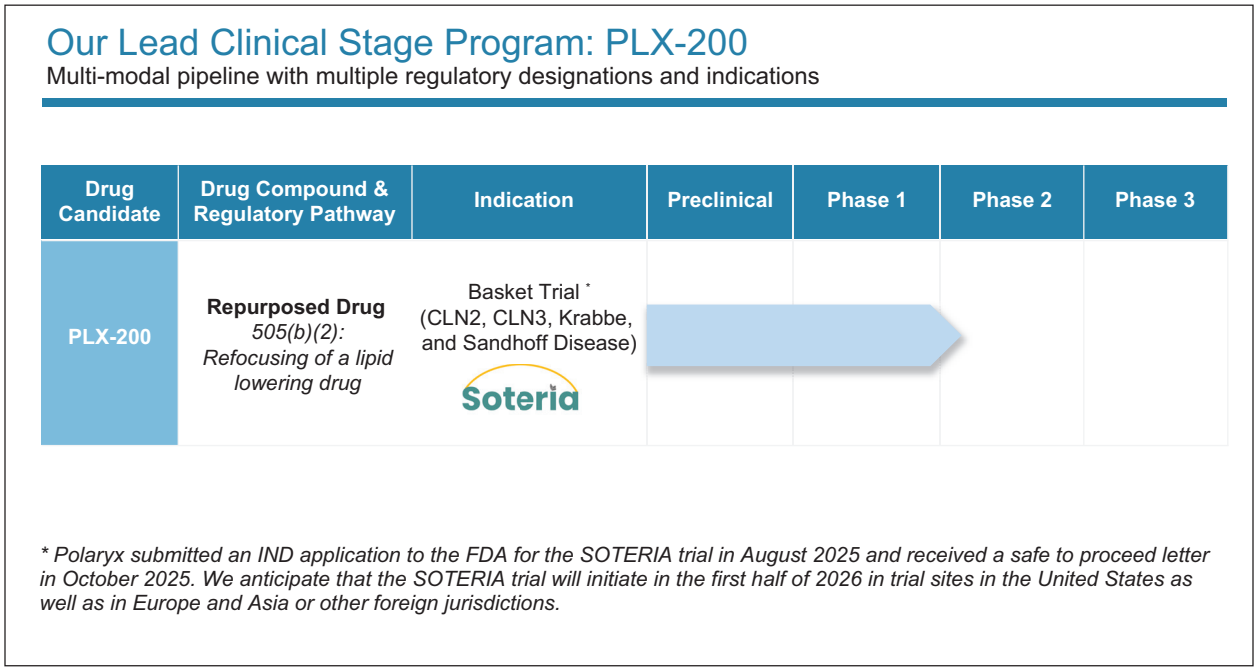
- **Tay-Sachs and Sandhoff Diseases:** Tay-Sachs and Sandhoff Diseases are part of a group of inherited disorders called GM2 gangliosidoses, resulting from deficiencies in the hexosaminidase enzyme. This mutation leads to an accumulation of GM2 ganglioside in nerve cells, resulting in rapid neurodegeneration. While the prevalence of Tay-Sachs disease is approximately one in 100,000 births, Sandhoff Disease is much rarer with a prevalence of approximately 0.67 per 100,000 births. We believe that there are approximately 1,200 Sandhoff disease patients in the United States, Europe and select regions of the ROW. There is currently no established standard of care for these diseases.
- **Niemann-Pick Disease Types A and B:** NPD is caused by mutations in the sphingomyelin phosphodiesterase 1 ("SMPD1") gene. This causes acid sphingomyelinase enzyme deficiency, leading to lipid accumulation in multiple organs, including the brain. The prevalence for NPD types A and B is one in 250,000 births, with a high prevalence found within the Ashkenazi Jewish population. An enzyme replacement therapy has been approved for the treatment of NPD type A and type B, but is not intended to treat neurological symptoms.

Our Pipeline

Our therapeutic pipeline includes PLX-200, PLX-300, and PLX-100, which are orally available small molecule drug candidates designed to address core pathological mechanisms common to LSDs. With shared modes of action involving transcription factor EB ("TFEB") activation leading to increased lysosomal biogenesis and autophagy, decreased neuroinflammation, and decreased neuronal loss, our small molecule therapies possess the potential to benefit multiple indications within the LSD spectrum. However, if PLX-200 encounters safety or efficacy problems, manufacturing or supply interruptions, developmental delays, regulatory issues or other problems, its development plans and business related to those other indications for PLX-200 as well as PLX-300 and PLX-100 could be significantly harmed. See the risk factor entitled "*We are substantially dependent on the success of our most advanced drug candidate, PLX-200, and our clinical trials of PLX-200 may not be successful*."

Our pipeline also includes PLX-400, a preclinical gene therapy program. Our multi-modal approach positions us to potentially address both the genetic and downstream pathological features of LSDs.

Figure 1. Our Lead Clinical Stage Program



Our Small Molecule Pipeline Demonstrates Multiple Critical Modes of Action

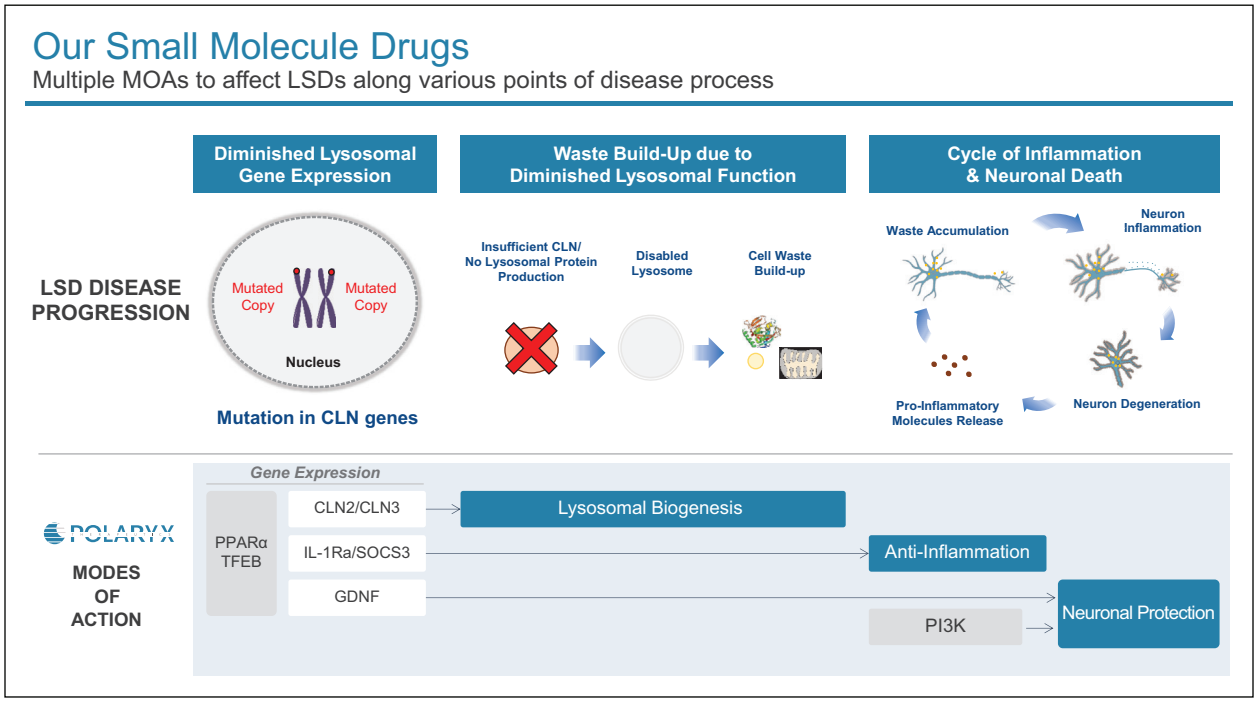
Our small molecule pipeline is represented by PLX-200, PLX-300, and PLX-100, all of which exert their therapeutic effects through a constellation of complementary modes of action, each of which is relevant to the pathophysiology of NCLs and other LSDs. All of our small molecule drug candidates in the portfolio work through a common mechanism of action which involves PPARα-dependent upregulation of TFEB. As a master regulator of lysosomal biogenesis, TFEB translocates to the nucleus and binds to the promoter regions of lysosomal and autophagy-related genes, initiating their transcription and enhancing lysosomal function.

As demonstrated in well-established animal models that closely mimic the human disease, our drug candidates exhibit the potential for therapeutic value via the following modes of action:

- **Lysosomal Biogenesis:** LSDs are characterized by deficiency in lysosomal function. Our small molecule drug candidates, including our most advanced drug candidate PLX-200, have demonstrated the ability to upregulate the abundance and activity of lysosomes and related autophagy of cellular waste through TFEB-mediated lysosomal biogenesis and clearance of accumulated substrates, enhancing cellular homeostasis.
- **Reduction in Neural Inflammation:** Our small molecules, including PLX-200, demonstrated PPARα-driven suppression of neuroinflammation caused by microglial and astroglial activation, mitigating secondary damage associated with lysosomal dysfunction.
- **Neuronal Support:** PLX-200 and our other small molecule drug candidates mediate neuronal survival, which promotes resilience in vulnerable neuronal populations through PI3K pathway activation and contributes to anti-apoptotic signaling and neuroprotection.

Collectively, these mechanisms target multiple nodes in the pathological cascade of LSDs, offering a multi-pronged therapeutic strategy. We believe that our lead drug candidate, PLX-200, with a noninvasive and dose-controlled administration could potentially position our drug to become the standard of care in multiple LSDs. The integrated impact of these pathways across disease stages is illustrated in Figure 2. Should PLX-200 fail to achieve positive results, our small molecule portfolio's sharing of modes of action and targeted indications increases risks related to PLX-100 and PLX-300's development and prospects for regulatory approval in similar indications.

Figure 2. Our Small Molecule Drug Candidates Demonstrate Multiple Modes of Action



Our History and Our People

We were founded in August 2014 as a Wyoming corporation and completed the Redomestication to convert into a Nevada corporation on October 24, 2025. Since our inception through the date of this Annual Report, we have raised $21.7 million supported by institutional and private investors.

We have assembled an executive team with deep experience advancing private and publicly-listed clinical-stage and commercial-stage companies. Our leadership brings a proven track record in designing and executing patient-centric drug development programs and clinical trials, particularly in the rare and orphan disease space.

Our senior management team is supported by an experienced team of professionals who manage our current operations and is expected to continue to provide these mission-critical services. To maximize efficiency and control cost, we signed the Services Agreement ("Service Agreement") in November 2021 with our controlling stockholder, Mstone Partners Healthcare Limited (together with its affiliates, "Mstone"), to receive critical consulting and advisory services. Mstone is a Hong Kong-based biotechnology, healthcare, and AI incubator structured as a holding company. Mstone manages a portfolio of seven companies and has a record of advancing early-to late-stage rare, neurological and pediatric life science ventures. Mstone also has experience in managing strategic exits, including the sale of Epygenix Therapeutics, Inc., a rare pediatric biopharmaceutical portfolio company to Nasdaq-listed Harmony Biosciences Holdings, Inc. in a transaction valued at up to $680 million.

A team of eleven Mstone professionals, many with advanced degrees and experience in small-molecule drug discovery and clinical development in rare orphan indications, provide comprehensive operational support across key functions, including: preclinical and clinical development; regulatory engagement; scientific and medical affairs; business development, licensing, and strategic partnerships; intellectual property management; and investor relations and capital markets engagement.

Our Strategy

Our objective is to establish a leading position globally in the research, development, and commercialization of disease-modifying therapies targeting LSDs, which represent a significant and largely unaddressed global medical need. To this end, we intend to strategically leverage the expertise of our executive leadership and external collaborators to advance the development of therapeutic candidates that are safe, effective, and patient-friendly.

To advance this mission, we intend to pursue the following strategic initiatives:

- **Advance the development of PLX-200 through SOTERIA, a clinical trial designed to be flexible, resource-efficient, and provide important data and information important to PLX-200's future clinical development.** We intend to prioritize the clinical development of PLX-200, our lead drug candidate, through the initiation of SOTERIA. We submitted an IND application to the FDA for the SOTERIA trial in August 2025 and received a safe to proceed letter in October 2025. We anticipate that SOTERIA will initiate in the second half of 2026. SOTERIA is a Phase 2, open-label trial intended to assess the safety, tolerability, and clinical activity of PLX-200 in CLN2, CLN3, Krabbe disease, and Sandhoff disease, four different LSDs whose patient populations we believe represent approximately one quarter of the LSD population. Designed with a high degree of flexibility, SOTERIA represents a resource-efficient opportunity to validate PLX-200's preclinical science across multiple LSDs while gathering data that we believe will be invaluable in planning PLX-200's future development pathway, including the initiation of potentially pivotal trials. For the CLN2 and CLN3, cohorts although the entire trial is open label, these cohorts will incorporate analyses comparing natural history data as a control arm to PLX-200's treated arm. A natural history study is a preplanned observational study intended to track the course of the disease. Should the data demonstrate compelling clinical activity, we may seek conditional marketing authorization.

- **Advance potentially single pivotal trials in CLN2 and CLN3.** We intend to optimize the design of our potentially single pivotal clinical trials for PLX-200 in the CLN2 and CLN3 subtypes of NCLs, which represent the largest patient populations among the 13 known NCL subtypes. PLX-200 has received authorization under two separate INDs to initiate these trials in CLN2 and CLN3, which may serve as registrational studies later, which we filed on December 20, 2019 and March 6, 2020 and

received authorization for on January 17, 2020 and April 6, 2020. Initiation of these trials was delayed due to the COVID-19 pandemic and a subsequent shift in our strategy. We currently do not expect to commence the trials in the near term while we focus our resources on SOTERIA. Our management team plans to focus on maximizing operational efficiency with respect to time, cost, and resource allocation. We intend to align CLN2 and CLN3 trial timelines with emerging data from SOTERIA as data readouts from SOTERIA are expected to provide guidance and a clear pathway for each of the four indications towards potentially registrable trials, including CLN2, CLN3, Krabbe disease and Sandhoff disease.

- **Pursue approval for PLX-200 through the 505(b)(2) regulatory pathway while strengthening PLX-200's competitive positioning.** In our Type B, pre-IND meeting with the FDA for our CLN2 trial held on June 16, 2017, the FDA indicated that the 505(b)(2) application is the appropriate marketing application to use for PLX-200. The 505(b)(2) pathway is a streamlined FDA drug approval process that allows the use of existing data. This pathway is covered by section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act. While a drug seeking 505(b)(2) New Drug Approval requires full reports of investigations of safety and effectiveness, some of the information required for approval comes from studies not conducted by or for the applicant and for which the applicant has not obtained a right of reference. Such information may include an FDA finding of safety or effectiveness of a listed drug, clinical data produced by other entities, or published literature. By utilizing the 505(b)(2) pathway as indicated in our IND correspondences, we expect that PLX-200 will benefit from an accelerated clinical development pathway that leverages gemfibrozil's existing safety record as an approved drug and reduces development time and cost. Because gemfibrozil has never been approved for pediatric patients and the only approved dosage forms of gemfibrozil are oral capsules and tablets solely for administration to adult patients, we have completed juvenile toxicity studies to identify and establish an optimal pediatric dosing regimen, which is required for PLX-200 to be the first-to-market as a commercial form of gemfibrozil approved for pediatric patients. We have further differentiated PLX-200 from its approved form through a novel alternative oral solution formulation with a unique and proprietary buffer system. The physical and chemical properties of gemfibrozil make it challenging to formulate the drug product as an oral solution. Grinding commercially available gemfibrozil tablets for reconstitution in aqueous solution is unsuitable for pediatric administration due to poor content uniformity and resultant inaccurate dosing. Our development of a pediatric patient-friendly oral solution formulation is critical for compliance purposes given decreased swallowing function in pediatric patients suffering from NCLs and is essential to determining appropriate doses for safety and efficacy by using a weight-based titration scheme. We expect to continue to refine our proprietary oral formulation of PLX-200 to ensure suitability for pediatric administration and patient compliance with a focus on increasing the concentration of gemfibrozil oral solution and enhancing dose control with minimal volume intake. As part of the 505(b)(2) submission pathway, we expect to be able to rely on referenced studies instead of engaging in a new Phase 1 study. The referenced studies may include published safety studies, juvenile animal studies, publicly available information that is scientifically relevant to the PLX-200 program including the LOPID package insert, bridging studies and/or comparative bioavailability data. For more information regarding the 505(b)(2) regulatory pathway, see "*Business — Government Regulation — 505(b)(2) New Drug Applications*".

- **Further develop our pipeline and expand our targeted indications.** While PLX-200 is our most advanced drug candidate, we intend to broaden our development efforts across our pipeline candidates, including our preclinical gene therapy candidate, and study those candidates across an expanded slate of LSDs characterized by high unmet medical need. Our preclinical studies have been conducted in well established, validated animal models representing these single gene mutations and, more importantly, they closely mimic the human disease. Our multi-modal pipeline offers the prospect of addressing the genetic and downstream pathological features of select LSDs by increasing clinical flexibility and enhancing our likelihood of therapeutic success. The three drug candidates in our small molecule portfolio possess similar mechanisms, such as storage material degradation, reduction in inflammation, and increased protection of neurons, that address key LSD disease processes and uniquely provide us with the potential to become the standard of care for multiple rare, orphan and pediatric LSDs.

- **Expand and protect our intellectual property portfolio.** We will continue to expand and vigorously defend our global intellectual property portfolio to safeguard our proprietary technologies and therapeutic assets across key jurisdictions.

Disease and Industry Background

Lysosomes are ubiquitous membrane-enclosed organelles in the body that are integral for major cellular processes, such as waste management and nutritional responses. The diverse functionality of this single organelle requires a complex and coordinated regulation of its activity with the transcription factor TFEB, a key regulator of lysosomal biogenesis. Defects in lysosomal genes and associated gene products (enzymes and other proteins) can result in accumulation of toxic waste materials within the cells.

LSDs are a heterogeneous group of nearly 50 inherited metabolic diseases caused by mutations in genes encoding lysosomal enzymes or associated proteins. These mutations result in the accumulation of undegraded substrates within lysosomes, leading to cellular dysfunction, chronic inflammation, and cell apoptosis. LSDs often manifest in infancy or early childhood and are associated with severe debilitating clinical outcomes, including developmental regression, seizures, blindness, motor impairment, and premature death. These disorders are typically treated for symptomatic relief and palliative care and, with the exception of CLN2, lack approved disease-modifying therapies.

We believe that there are approximately 50,000 LSD patients in the United States, Europe and select regions of ROW, based on an incidence rate of one in 5,000 births. Of the broader universe of LSDs, we are focused on developing therapies for NCLs, of which there are 13 subtypes; Krabbe disease; Tay-Sachs and Sandhoff diseases; and NPD type A and type B diseases. Virtually all of the LSDs on which we focus lack patient-friendly, disease-modifying therapies and are characterized by devastating symptoms such as developmental delays, neurodegeneration, blindness, seizures, and early death.

Neuronal Ceroid Lipofuscinoses

NCLs are a heterogeneous group of 13 LSDs generally characterized by the excessive accumulation of lipofuscin. Lipofuscins are made up of fats and proteins, and they are found inside cellular lysosomes of the brain and the eye as well as in skin, muscle, and many other tissues. The cellular accumulation of lipofuscin results in lysosomal dysfunction and causes devastating neurodegeneration.

Despite being genetically heterogeneous, NCLs share similar histopathological and clinical characteristics and clinical manifestations of NCLs include progressive mental deterioration, cognitive impairment, visual failure, seizures, and deteriorating motor function, accompanied by histological findings such as the accumulation of auto-fluorescent storage material in neurons or other cell types.

NCLs arise from genetic mutations within one of 13 different genes from CLN1-8 and CLN10-14. The three most common forms of NCLs are CLN1, CLN2, and CLN3. We believe that NCLs represent approximately 15% of the LSD population, or roughly 7,700 patients. Of the 13 NCL sub-types, only CLN2 has an established standard of care.

Our current areas of disease focus within NCLs include:

- CLN2 Disease

CLN2 disease, also known as late infantile neuronal ceroid lipofuscinosis (“LINCL”), is associated with mutations in the CLN2 gene, which encodes lysosomal tripeptidyl-tripeptidase I (“TPP1”), a 46-kDa protein that functions in the acidic environment of the lysosomal compartment to remove tripeptides from the amino terminus of proteins. This mutation in the CLN2 gene results in a deficiency and/or loss of function of the TPP1 protein that leads to intralysosomal accumulation of auto-fluorescent lipopigments known as ceroid-lipofuscin.

Globally, the classical form of CLN2 disease has a prevalence of 0.6 to 0.7 per million inhabitants. CLN2 is a rare neurodegenerative genetic disease that affects children in early life. Its classic form is rapidly progressive and the most common clinical manifestations in CLN2 disease at disease onset include unprovoked seizures and ataxia, leading to death within the first ten years. The average age at diagnosis is four years old, and by the age of six years, most children are completely dependent on caregivers for all of their daily needs. Life expectancy ranges from eight to 12 years.

- CLN3 Disease

CLN3 disease, also known as juvenile neuronal ceroid lipofuscinosis ("JNCL") or juvenile Batten disease, is a rare inherited LSD that primarily affects the nervous system in childhood. With a prevalence of one in 100,000 births worldwide, CLN3 disease is caused by mutations in the CLN3 gene which encodes a lysosomal transmembrane protein, Battenin. The most common genetic defect is a ~1-kb deletion in CLN3, leading to a loss of protein function. The disorder follows an autosomal recessive inheritance pattern, requiring two defective copies of CLN3 for disease manifestation. Due to impaired lysosomal function, neurons accumulate waste material and progressively deteriorate, resulting in a neurodegenerative disease course.

Several subtypes of CLN3 disease exist, varying in age. CLN3 typically manifests between the ages of four and eight years, with the first symptom usually being progressive vision loss due to retinal degeneration. For late and protracted CLN3, patients may face a slower disease progression and delayed onset of symptoms. Seizures, progressive neurological deterioration, and severe motor and cognitive decline continue to develop during the course of the disease, with death occurring in the second decade of life.

Tay-Sachs and Sandhoff Diseases

Tay-Sachs and Sandhoff disease are the two most common types of GM2 gangliosidosis, a group of inherited LSDs. There is currently no established standard of care. Tay-Sachs and Sandhoff diseases are both rare autosomal recessive LSDs caused by a mutation in either the HEXA gene for Tay-Sachs disease or the HEXB gene for Sandhoff disease. This mutation results in a deficiency of a functional HEXA enzyme, while Sandhoff disease results in deficiencies of both HEXA and HEXB enzymes due to the role of the HEXB gene. While the prevalence of Tay-Sachs disease is approximately one in 100,000 births, Sandhoff Disease is much rarer with a prevalence of approximately 0.67 per 100,000 births. We believe that there are approximately 1,200 Sandhoff disease patients in the United States, Europe and select regions of the ROW.

Tay-Sachs disease is caused by mutations in the HEXA gene, which disrupt the function of β-hexosaminidase A enzyme. This deficiency leads to the accumulation of GM2 gangliosides in neurons, causing progressive neurodegeneration. Several subtypes of Tay-Sachs disease exist: infantile, juvenile, and adult-onset, with infantile Tay-Sachs disease being the most severe. Symptom onsets begin within the first six months of life, with symptoms such as motor weakness, developmental delay, and the hallmark "cherry-red spot" visible in the retina. Compared to the infantile variant, the juvenile and adult-onset forms of the disease progress more slowly and may present psychiatric symptoms during adulthood. Infantile Tay-Sachs patients experience an aggressive loss of motor function and vision as the disease progresses, often succumbing by the age of four or five. For other variants, progressive neurological deterioration will eventually transition patients into a vegetative state, with death occurring by the age of 10 to 15.

Sandhoff disease, a more severe form of Tay-Sachs disease, is caused by mutations in the HEXB gene, which impair the function of β-hexosaminidase enzymes. This deficiency causes the accumulation of GM2 gangliosides in neurons, resulting in progressive neurodegeneration. Several subtypes of Sandhoff disease exist, varying depending on the age of onset. The infantile form typically manifests between three and six months of age and is the most severe. The first symptom is often hypotonia, accompanied by an exaggerated startle response to auditory stimuli, followed by developmental regression. Acute infantile and sub-acute juvenile Sandhoff disease patients begin regressing significantly after the onset of symptoms, with death usually occurring between two and three years for the infantile cohort and early to late teens for the juvenile cohort. Life expectancy for late-onset Sandhoff patients is not significantly impacted.

Krabbe Disease

Krabbe disease, also known as globoid cell leukodystrophy, is caused by mutations in the GALC gene, encoding galactosylceramidase, an enzyme critical for breaking down galactolipids in myelin. Deficiency in galactosylceramidase leads to the toxic accumulation of psychosine, resulting in widespread demyelination and neurodegeneration in the central and peripheral nervous systems. The incidence rate of Krabbe disease varies significantly, affecting 0.3 to 2.6 per 100,000 live births. We believe that there are approximately 6,700 Krabbe disease patients in the United States, Europe and select regions of the ROW. Krabbe disease is categorized into

four subtypes based on age of symptom onset. Classic infantile form has the earliest onset, typically at birth to six months, and is the most severe. Late infantile form, with an onset of six months to three years, has slightly slower progression but early loss of motor and cognitive functions. Juvenile form, with onset between three to 16 years, presents with gait abnormalities, motor decline, and vision loss. Adult form, with onset over the age of 16, presents with progressive weakness, cognitive decline, and psychiatric symptoms, with variable life expectancy. HSCT is considered the current standard of care.

Niemann-Pick disease

NPD, also known as acid sphingomyelinase deficiency, is a rare and catastrophic pediatric neurodegenerative lipid metabolism disorder caused by genetic mutations in acidic sphingomyelinase ("ASMase"), an enzyme found in lysosomes and important in the degradation of sphingomyelin or proteins involved in lipid transport. It is characterized by progressive cerebellar ataxia and dementia. Based on the genetic origin and the signs and symptoms of this rare condition, NPD is divided into four subtypes: types A, B, C1, and C2. We are focused on NPD types A and B, which are caused by mutations in the SMPD1 gene encoding ASMase. The prevalence for NPD types A and B is one in 250,000 births, with a high prevalence found within the Ashkenazi Jewish population. An enzyme replacement therapy has been approved for the treatment of NPD type A and type B, but is not intended to treat neurological symptoms.

Children with NPD type A exhibit hepatosplenomegaly and profound central nervous system ("CNS") deficits in infancy. These patients rarely survive beyond two to three years of age. Patients with NPD type B also have hepatosplenomegaly and significant lung pathology, but there are usually no CNS deficits. The age of onset and rate of disease progression vary greatly among patients with NPD type B. Although patients with NPD type B may live into adulthood, some patients can develop significant life-threatening complications.

Our Drug Candidates

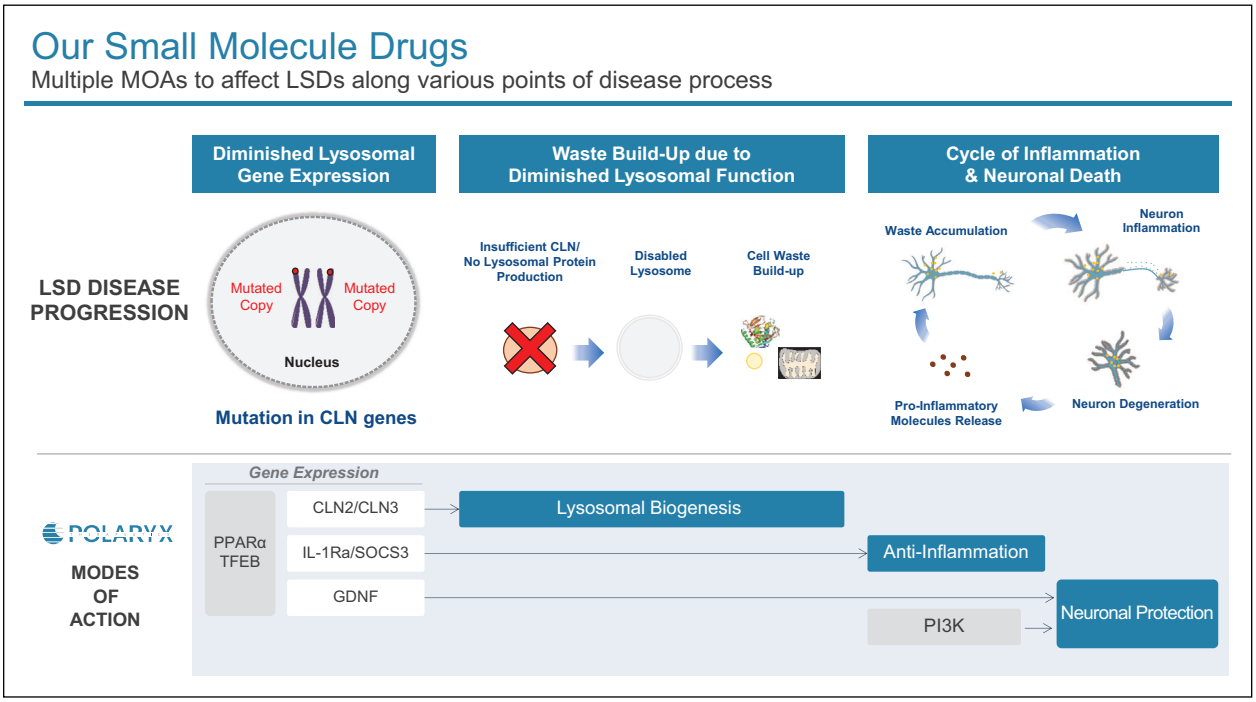
Our small molecule drug candidates, PLX-200, PLX-300, and PLX-100, exert therapeutic effects through multiple modes of action demonstrated in all three compounds, which have unique relevance for the treatment of NCLs as well as other LSDs.

These modes of action include:

- PPARα/TFEB-mediated lysosomal biogenesis and removal of storage materials,
- PPARα/TFEB-mediated suppression of inflammation, and
- PPARα/TFEB mediated neuronal survival and PI3Kinase mediated protection and anti-apoptosis.

The critical mechanism of action is PPARα-dependent upregulation of TFEB. As a master regulator of lysosomal biogenesis, the subsequent TFEB binding to the promoter region of genes involved in lysosomal biogenesis activates their production. Together, these mechanisms affect LSDs along important points of the disease process as shown in Figure 2. With mechanisms that address key pathophysiological characteristics, we believe our drug candidates possess the potential to become the standard of care in multiple rare, orphan, and pediatric LSDs. Should PLX-200 fail to achieve positive results, our small molecule portfolio's sharing of modes of action and targeted indications increases risks related to PLX-100 and PLX-300's development and prospects for regulatory approval in similar indications.

Figure 2. Illustration of PLX Candidates' Multiple Modes of Action



PLX-200

Description

Our lead drug candidate, PLX-200, is a liquid orally available compound comprised of gemfibrozil. Gemfibrozil is an FDA-approved lipid regulating agent in the fibrate family which has only been approved in a capsule form for adult patients with very high elevations of serum triglyceride levels to decrease serum triglycerides and very low-density lipoprotein cholesterol and increase high density lipoprotein cholesterol. The ability of gemfibrozil to cross the blood-brain barrier ("BBB") has also been documented in third-party preclinical trials and safe use of gemfibrozil in adults has also been well-established over several decades of clinical investigation and commercial use, which we believe accelerates clinical development and reduces associated costs. Although pediatric patients have been treated with gemfibrozil through small studies across several pediatric indications, including CLN2, gemfibrozil has never been approved to treat any indications in pediatric patients. We believe the unique ability of PLX-200 to cross the BBB, along with its widely applicable mechanism of action, positions PLX-200 to potentially address the immense unmet need in multiple rare, catastrophic LSD indications.

We are pursuing PLX-200 through the 505(b)(2) regulatory pathway as a repurposed drug. In our Type B, pre-IND meeting with the FDA for our CLN2 trial held on June 16, 2017, the FDA indicated that the 505(b)(2) application is the appropriate marketing application to use for PLX-200. We expect this guidance will apply to all of our product candidates since all of our planned studies have cross-referenced the CLN2 study and each product candidate shares the same dosage form as PLX-200. For more information regarding the 505(b)(2) regulatory pathway, see "*Business — Government Regulation — 505(b)(2) New Drug Applications*". The therapeutic potential of PLX-200 in neurodegenerative disorders was identified by Dr. Kalipada Pahan, the scientist behind our therapeutic pipeline and a member of our Scientific and Clinical Advisory Board. Dr. Pahan has worked extensively on the science of peroxisome proliferator-activated receptors for more than three decades. To pursue his interest in neurodegenerative disorders and neuroinflammation, Dr. Pahan studied and evaluated a long list of PPARα agonists and discovered that gemfibrozil maintains a superior safety profile among other fibrates.

We believe PLX-200 is clearly differentiated as a potential disease-modifying therapy with patient-friendly characteristics as demonstrated in our animal studies and anecdotal evidence through anecdotal off-label use in CLN2 patients. As an orally administered, small molecule drug candidate with multiple modes of action, we

believe that PLX-200 possesses the potential to gain leadership in the treatment of multiple NCLs. Unlike enzyme replacement therapies, which are limited to treating a specific disorder by replacing a deficient or missing enzyme, PLX-200 possesses the prospect of treating multiple indications due to its multiple modes of action.

Patient-friendly administration is a further point of differentiation as patients with NCLs commonly suffer from decreased swallowing function. Currently, the only form of gemfibrozil is an oral tablet. There are limitations on the use of grounded oral tablets for pediatric administration in patients with NCLs given the hydrophobic physicochemical properties of gemfibrozil. Our development of a patient-friendly oral solution for PLX-200 is designed to overcome these challenging properties and enhance patient compliance, while providing accurate pediatric dosing in a home environment. We continue to further optimize our proprietary oral solution by, among other things, increasing gemfibrozil concentration, and aim to further deepen patient adherence by lowering administered volumes. In comparison, BRINEURA® (cerliponase alfa), an enzyme replacement therapy and the only available standard of care for patients with CLN2, requires a regularly scheduled intracerebroventricular administration injected in a hospital environment. In addition, the administration of cerliponase alfa has also been associated with device-related complications, including infections, leakage, and an increased white-cell count in cerebrospinal fluid.

To date, the FDA has granted three ODD to PLX-200 for the treatment of all 13 sub-types of NCLs, Tay-Sachs and Sandhoff diseases, and Krabbe disease. PLX-200 has also received Fast Track designation for the treatment of CLN3. The receipt of such designations does not guarantee a faster development process, regulatory review, or approval as compared to the conventional FDA approval process.

PLX-200 Mechanism of Action

PLX-200 is a potent activator of PPARα, which promotes the expression of TFEB genes. TFEB is a master regulator of CLN1, CLN2, and CLN3, and is known to be involved in coordinated regulation of several lysosomal genes via CLEAR elements leading to lysosomal biogenesis, improving the cellular clearance of accumulated storage materials in neurodegenerative diseases.

PLX-200 also promotes anti-inflammatory gene expression to facilitate reduction of inflammation. Our compounds activate PPARα, which also promote the transcription of anti-inflammatory genes such as IL-1Ra and SOSC3. Since neuroinflammation accelerates neuronal loss in LSDs, reducing inflammation may protect neurons and prolong survival.

PLX-200 Preclinical Data Summary

We have evaluated the tolerability and clinical activity of PLX-200 in proof-of-concept preclinical models that support PLX-200's therapeutic potential to address multiple LSDs, including CLN2, CLN3, Krabbe, and Sandhoff Diseases. Our preclinical studies in well-established mouse models that closely mirror clinical phenotypes suggest that PLX-200 has the potential to be a well-tolerated and disease-modifying drug. In all animal models, PLX-200 has been demonstrated to upregulate the deficient gene function associated with the human disease, attenuate neuroinflammation, suppresses apoptosis, and improve neuronal survival.

CLN3

We believe that PLX-200 has the potential to address unmet needs in CLN3 disease. In our preclinical studies, PLX-200 was shown to activate PPARα and stimulate TFEB, a key regulator of lysosomal biogenesis and autophagy, improving cellular clearance and reducing the toxic accumulation of storage materials containing subunit c of mitochondrial ATP synthase ("SCMAS") (Figure 3). In our *in vivo* studies with the $CLN3^{\Delta ex7/8}$ animal model, activation of PPARα by PLX-200 suppressed the activation of microglia and astroglia and reduced the level of proinflammatory molecule inducible nitric oxide synthase ("iNOS") (Figure 4). Chronic neuroinflammation contributes to disease progression in CLN3. PLX-200 mediated reduction in neuroinflammation protected neurons from further cell death and slowed down disease progression.

Figure 3. Effect of PLX-200 on TFEB and Storage Material Levels in CLN3 Mice Model

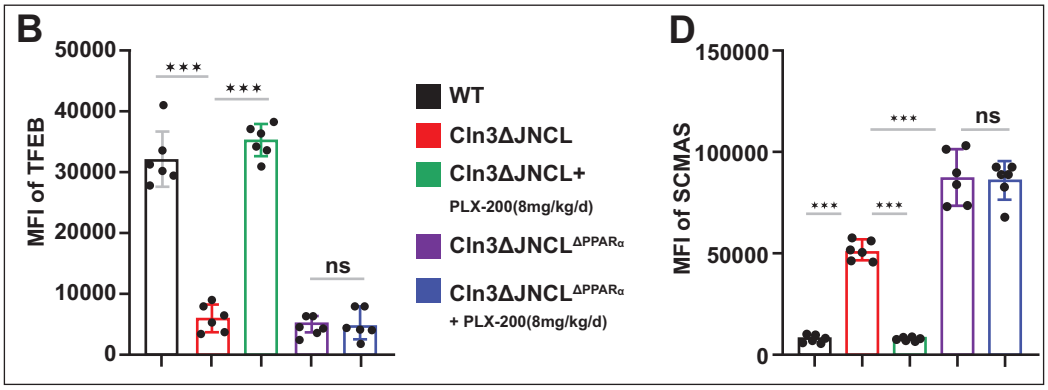
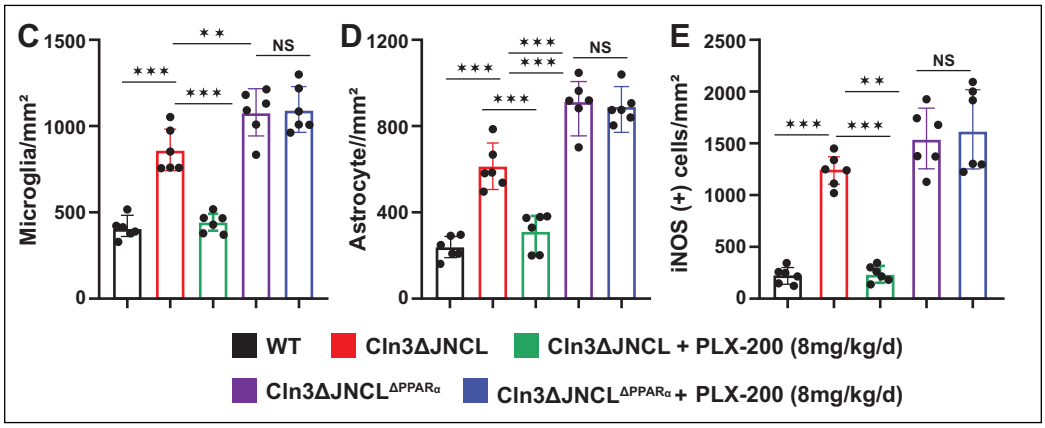
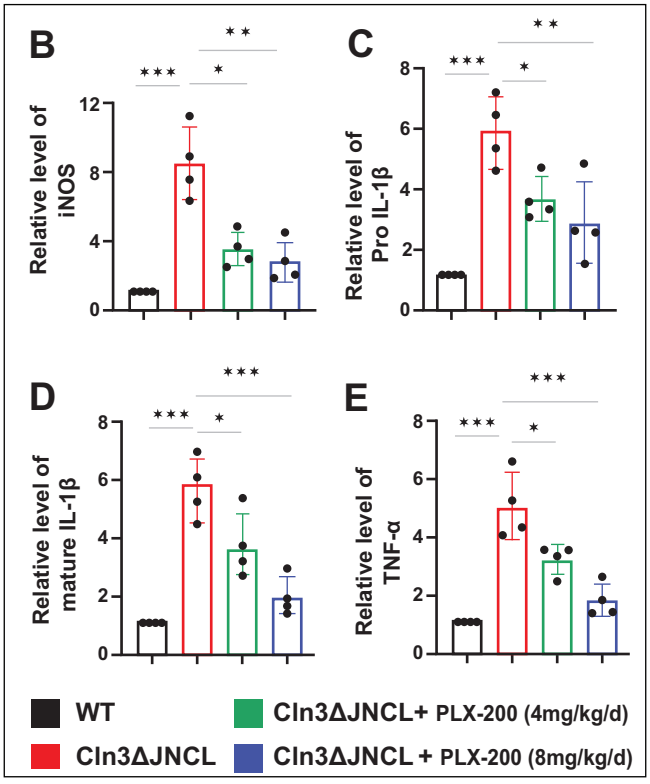


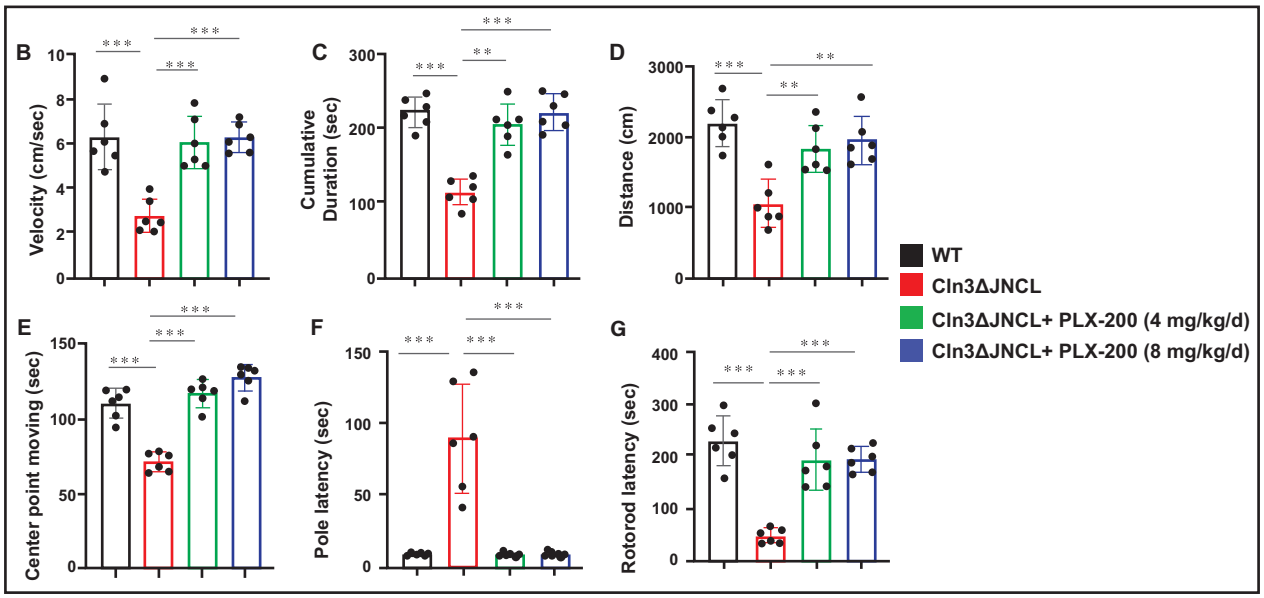
Figure 4. PLX-200 Reduces Glial Activation and Neuroinflammation in CLN3 Mice Model





In the gold standard mouse model of CLN3 (CLN3ΔJNCL mouse model), PLX-200 improved locomotor activity and motor coordination (Figure 5), suggesting potential benefits in preserving neuronal function and delaying disease progression. By activating PPARα, upregulating TFEB, reducing neuroinflammation, enhancing lysosomal function, protecting neurons and slowing down disease progression, we believe PLX-200 shows promise as a therapeutic candidate for CLN3.

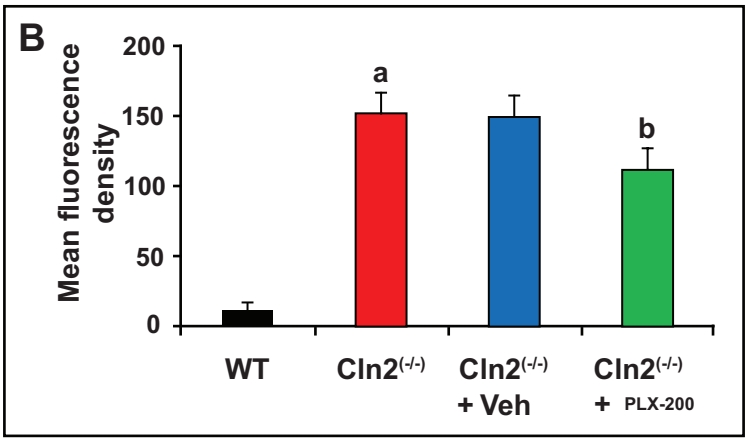
Figure 5. Effect of PLX-200 in Improving Locomotor Activity



CLN2

We believe that PLX-200, as a PPARα agonist, also has high therapeutic importance for CLN2 and we are targeting to address some of the limitations of current therapies. We have completed preclinical studies using CLN2 mouse and human primary astrocytes. In these studies, $CLN2^{-/-}$ mice treated with PLX-200 have been shown to reduce the accumulation of storage materials, quantified by SCMAS positive immunofluorescence (Figure 6).

Figure 6. PLX-200 Reduces Buildup of Storage Materials



In a mouse model of LINCL ($CLN2^{-/-}$ model), PLX-200 has been demonstrated to upregulate levels of antiapoptotic phosphorylated BCL2-associated Death Protein ("pBAD") in the striatum and motor cortex, leading to BCL-2 mediated suppression of apoptosis and reduction of neuronal death (Figure 7). The activation of PI3K has been documented to phosphorylate BAD via Akt. Through PI3K-pBAD pathway, PLX-200 suppresses apoptosis in the CNS of $CLN2^{-/-}$ mice. In the same preclinical study, treatment with PLX-200 has also been shown to improve locomotor activities (Figure 8).

Figure 7. PLX-200 Suppresses Apoptosis Through Activation of PI3K-pBAD Pathway

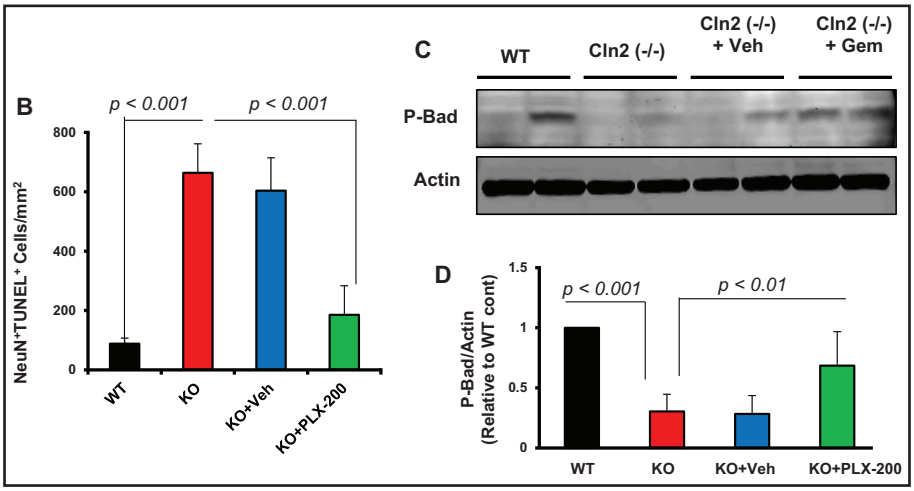
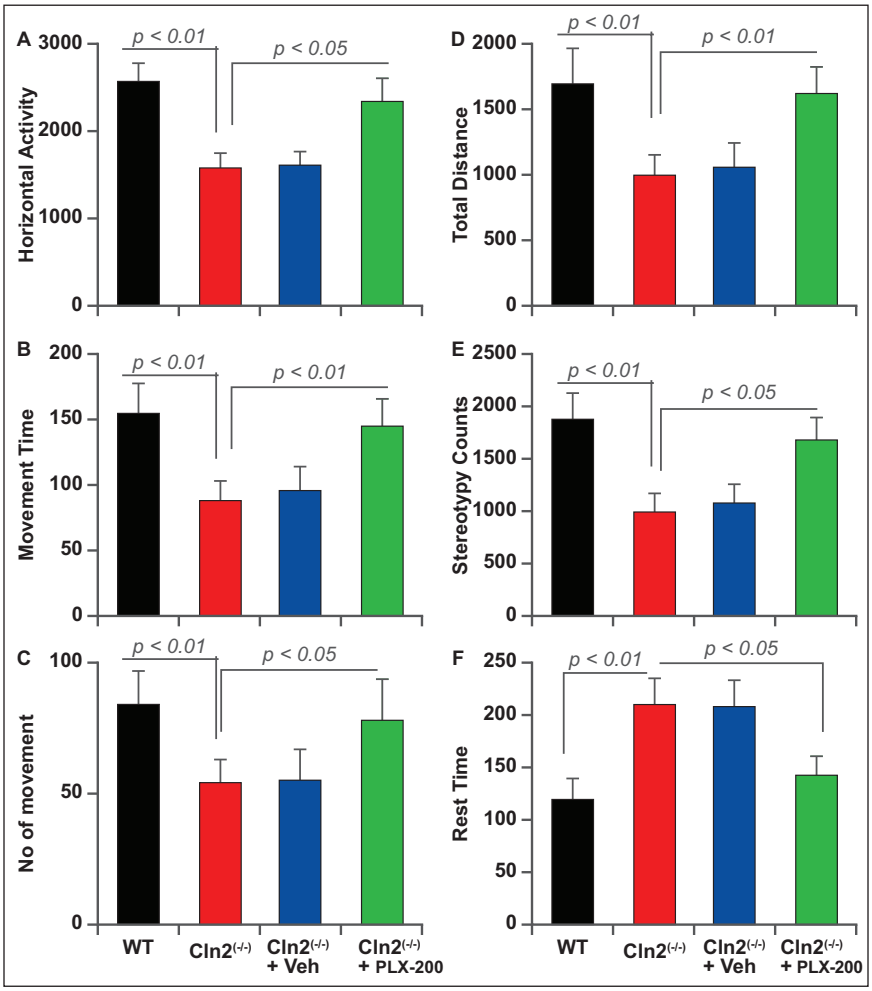
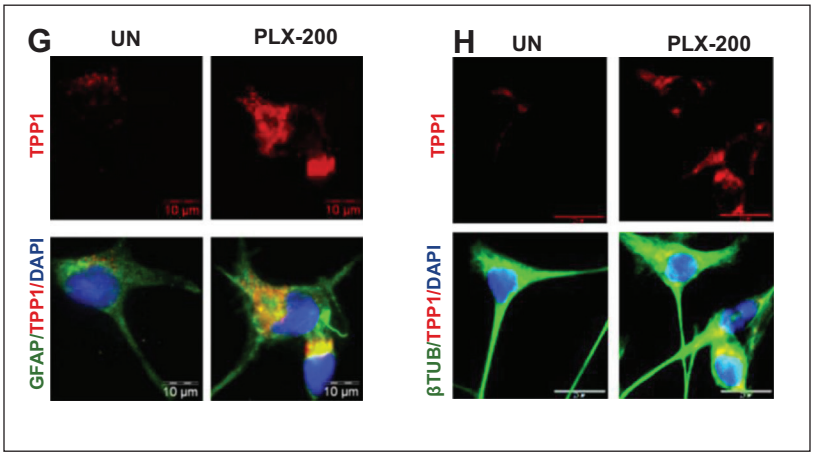


Figure 8: Treatment with PLX-200 Improves Locomotor Activities



Human primary astrocytes were treated with 25µm PLX-200 for 24 hours under similar culture conditions and were double-labeled for TPP1 (red) and glial fibrillary acidic protein ("GFAP") (green) (Figure 9 (G)). SH-SY5Y cells were treated with 25µm PLX-200 in B27-AO containing Neurobasal media for 24 h and were double-labeled for TPP1 (red) and β-tubulin (green) (Figure 9 (H)).

Figure 9. PLX-200 Upregulation of TPP1 via PPARα



By activating PPARα, upregulating TPP1, promoting lysosomal biogenesis, and reducing neuroinflammation, PLX-200 has shown to mitigate the pathological accumulation of undigested proteins in CLN2 neurons of animal model studies.

Krabbe Disease

In Krabbe Disease, increase in myelination in the CNS has therapeutic importance. In our preclinical studies, PLX-200 has been demonstrated to restore myelin in cerebellum and corpus callosum of GALC$^{-/-}$ animal model. Oral administration of PLX-200 increased the level of myelin basic protein ("MBP") and proteolipid protein ("PLP"), which are markers for myelin, in both cerebellum and corpus callosum of GALC$^{-/-}$ mice (Figure 10). PLX-200 has also been shown to attenuate glial activation by reducing GFAP and iNOS levels, a hallmark of neurodegenerative diseases, resulting in reduced inflammation (Figure 11). Treatment with PLX-200 has also exhibited significant improvement in hypolocomotion and increased longevity of GALC$^{-/-}$ mice by 11-13 days (Figure 12).

Figure 10. PLX-200 Increases MBP and PLP Levels in the Brain

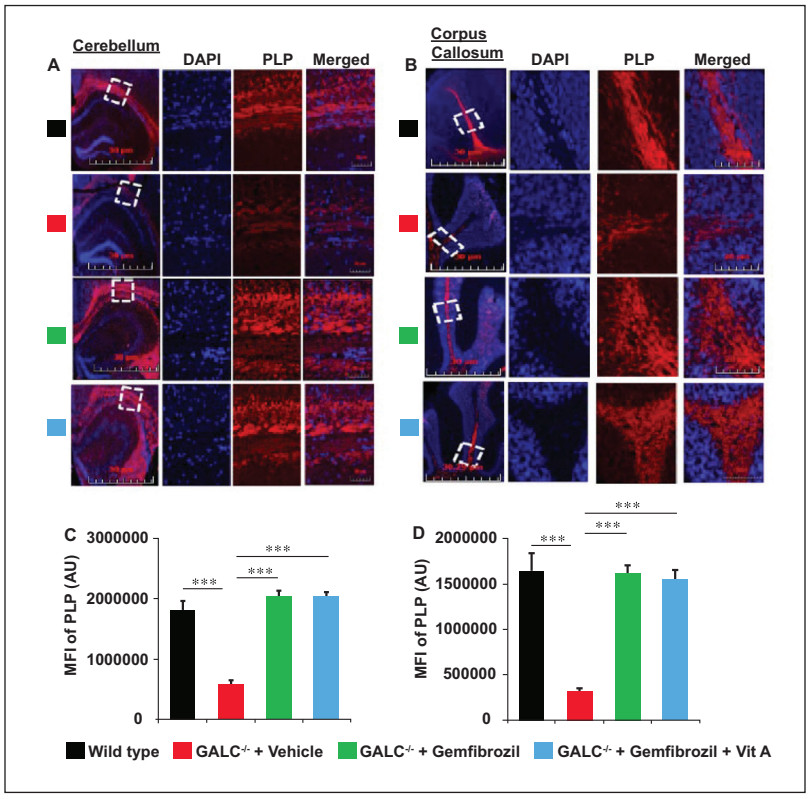


Figure 11. PLX-200 Decreases GFAP and iNOS Levels

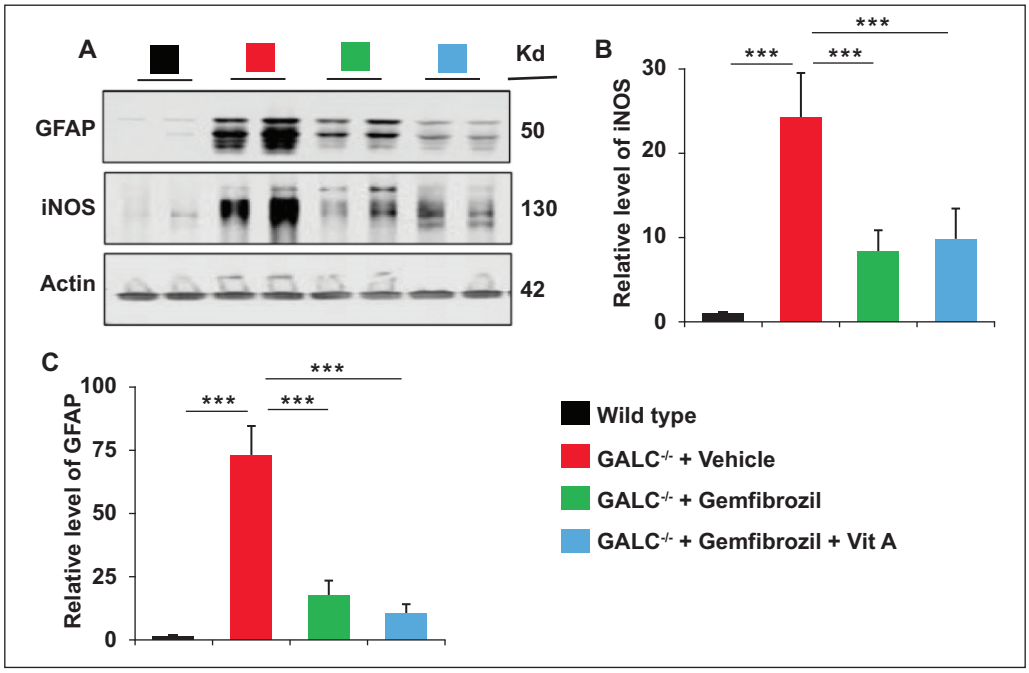
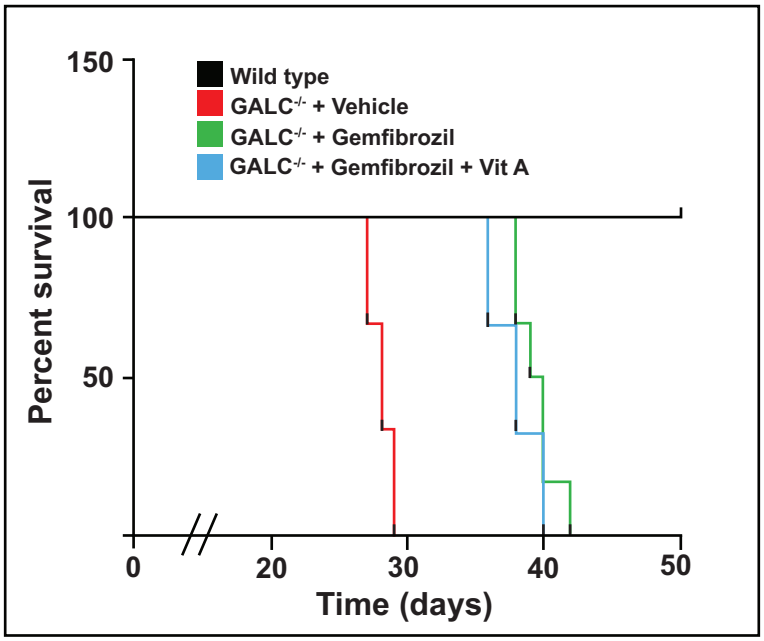


Figure 12. PLX-200 Increases Life Span in GALC-deficient Mice



Tay-Sachs and Sandhoff Diseases

We have conducted preclinical studies to determine the therapeutic potential of PLX-200 for GM2 gangliosidoses, such as Sandhoff Disease. In GM2 gangliosidosis, the accumulation of undegraded ganglioside is directly linked to the activation of microglial cells, triggering apoptosis and contributing to the disease progression. In our preclinical studies, oral treatment of PLX-200 at 8 mg/kg/day dose has been demonstrated to attenuate neuronal apoptosis and reduce glycoconjugates (magenta stained), a hallmark of GM2 gangliosides (Figure 13; Figure 14).

Figure 13. PLX-200 Lowers Storage Materials

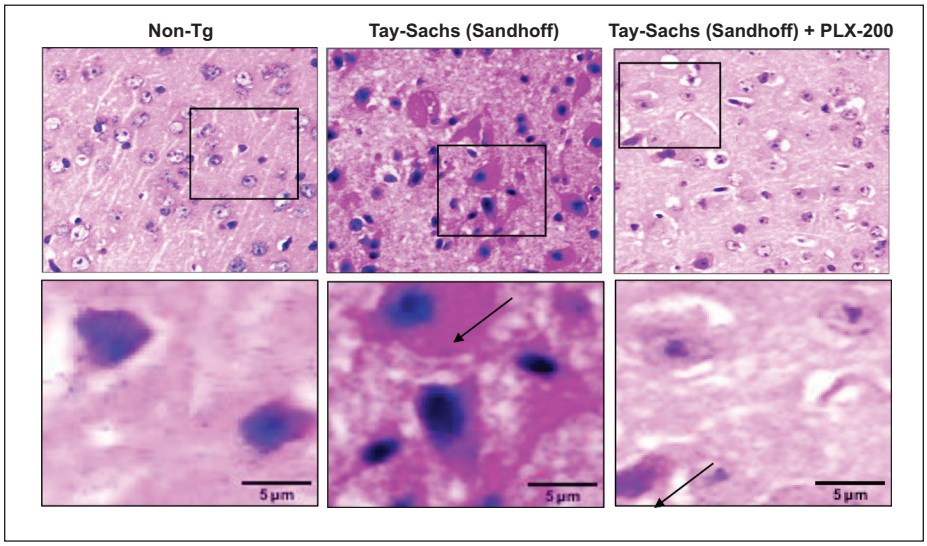
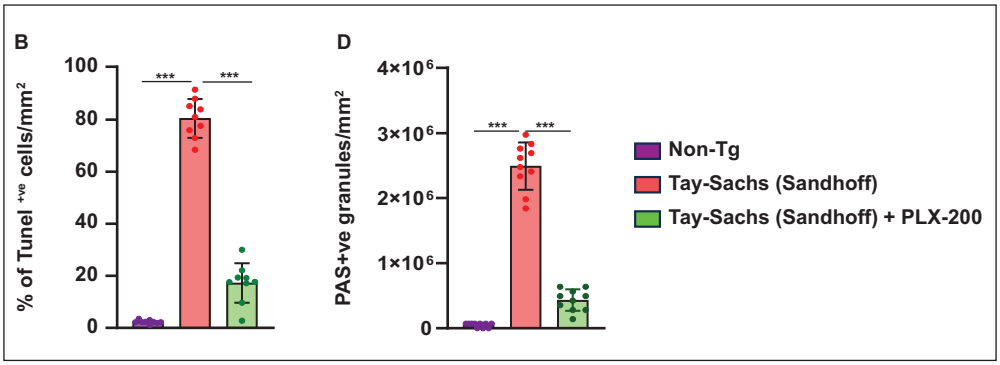


Figure 14. PLX-200 Reduces TUNEL Positive Cells and PAS Positive Granules



In the same study, widely dispersed swollen dystrophic axons, neurites, and spheroids were observed in various tissues, along with severe vacuolation. These pathological findings were markedly reduced after treatment with PLX-200 (Figure 15). PLX-200 has also been shown to reduce iNOS and GFAP levels (Figure 16), a hallmark of inflammation in neurodegenerative disorders, including Sandhoff disease.

Figure 15. PLX-200 Preserves Neuronal Function and Structure

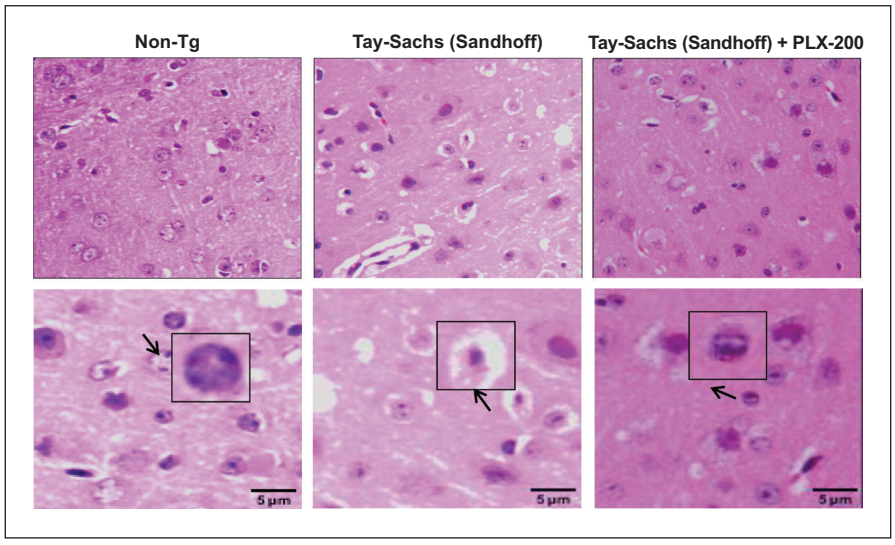
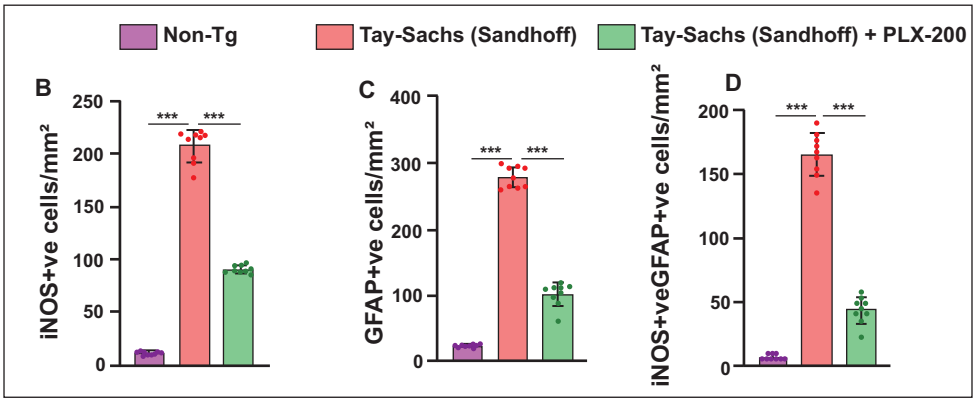


Figure 16. PLX-200 Reduces iNOS and GFAP Levels



Juvenile Toxicology Study (Covance)

We have completed juvenile rate pharmacokinetic ("PK") and toxicology studies with PLX-200. In this *in vivo* study using Sprague-Dawley rats, doses of 0, 100, 300, and 1000/600 mg/kg/day of PLX-200 were administered via oral gavage from postnatal day 21 to 105. Based on the findings of repeated-dose toxicity studies, the no observed adverse effect level was identified. Estimated corresponding pediatric doses are calculated based on weight tiers. Assessment of toxicity was based on mortality, clinical observations, body weights, food consumption, ophthalmic examinations, neurobehavioral assessments, gross pathology, organ weights, and microscopic pathology. Satellite animals were included for toxicokinetic assessments.

PLX-200 Clinical Programs

PLX-200 Clinical Development Strategy

PLX-200's clinical development strategy prioritizes the launch of Phase 2 SOTERIA, for which we received FDA authorization to initiate in October 2025, over the launch of PLX-200-001 and PLX-200-003, two potentially single pivotal trials which received Study May Proceed letters from the FDA in January and April 2020, respectively. The onset and prolonged impact of the COVID-19 pandemic delayed the launch of these two IND approved trials. Following the conclusion of the pandemic period and recognizing financial constraints, we decided to pause the trials while conducting additional studies to investigate the effectiveness of PLX-200 across other LSDs beyond CLN2 and CLN3, such as Krabbe disease and Sandhoff disease. The results from these preclinical studies confirmed PLX-200's potential therapeutic value beyond CLN2 and CLN3 to include multiple LSDs. Our clinical development strategy now focuses on a Phase 2 trial to target a number of indications which we believe will provide useful data on PLX-200. Based on these findings, we may find relevant information that can be used to optimize the PLX-200-001 and PLX-200-003 trials within the context of their existing INDs. We believe the optimization will require an amendment to the existing INDs, which may provide for different trial design elements such as trial center identification and patient recruitment, enrollment criteria, primary and secondary endpoints, relevant biomarkers, and trial duration. See the risk factor entitled "*Preclinical and clinical development involves a lengthy and expensive process that is subject to delays and uncertain outcomes, and results of earlier studies and trials may not be predictive of future clinical trial results. If our preclinical studies and clinical trials are not sufficient to support regulatory approval of any of our drug candidates, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development of such drug candidate*."

We anticipate that SOTERIA will initiate in the second half of 2026. Our regulatory approval and commercialization strategy for PLX-200 would prioritize the United States, followed by Europe and other foreign jurisdictions. However, we cannot guarantee that an FDA approval will result in the expedited approvals in other foreign jurisdictions.

PLX-200-600 (SOTERIA) Phase 2 Basket Clinical Trial

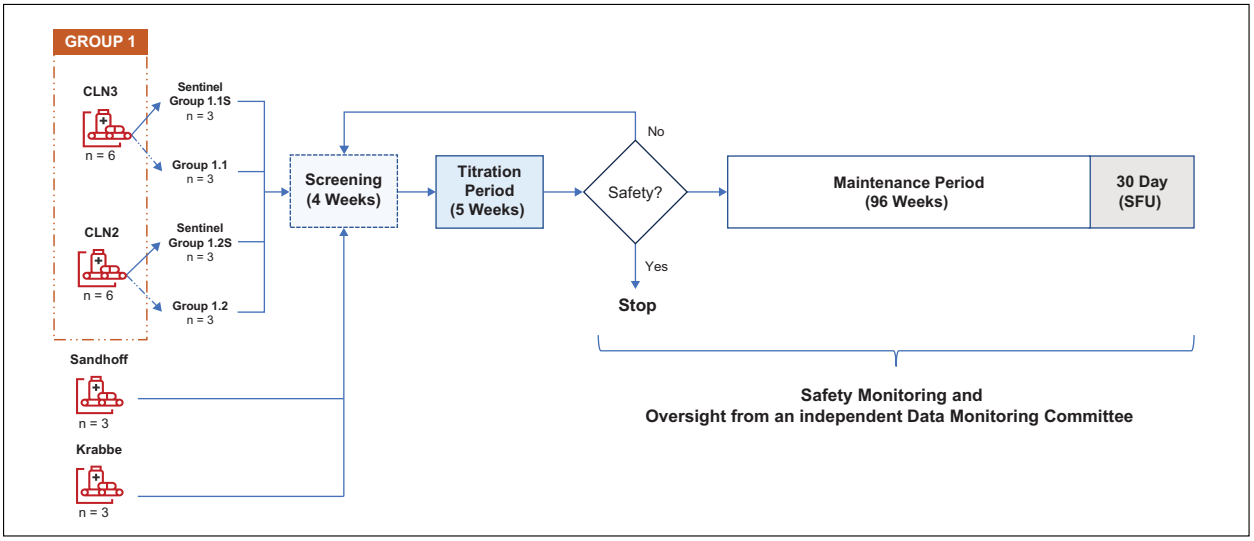
SOTERIA is a small-scale, proof-of-concept, open-label Phase 2 basket trial intended to study PLX-200 for up to 101 weeks. We held a pre-IND submission meeting in April 2025. We submitted an IND application to the FDA for the SOTERIA trial in August 2025 and received a safe to proceed letter in October 2025. SOTERIA is a Phase 2, open-label trial intended to assess the safety, tolerability, and clinical activity of PLX-200 in CLN2, CLN3, Krabbe disease, and Sandhoff disease, four different LSDs whose patient populations we believe represent approximately one quarter of the LSD population. Designed with a high degree of flexibility, SOTERIA represents a resource-efficient opportunity to validate PLX-200's preclinical science across multiple LSDs while gathering data that we believe will be invaluable in planning PLX-200's future development pathway, including the initiation of potentially pivotal trials. For the CLN2 and CLN3 cohorts, although the entire trial is open-label, these cohorts will incorporate analyses comparing natural history data as a control arm to PLX-200's treated arm. A natural history study is a preplanned observational study intended to track the course of the disease. Should the data demonstrate compelling efficacy, we may seek conditional marketing authorization.

SOTERIA's purpose is to collect positive patient data across several indications, with an additional focus on identifying safety parameters and clinical outcome assessments. SOTERIA has been designed to provide key data and information important to PLX-200's future clinical development. Data readouts from are expected to provide guidance and a clear pathway for each of the four indications towards potentially registrable trials. Further, with the precedent approval of Brineura, a drug approved to treat CLN2 on the basis of a single-arm, natural history comparator, open-label trial, we believe there may be an opportunity for CLN2 and CLN3 to seek accelerated approval from the FDA based on precedent approval for a third-party drug with a similar trial design. Products studied for their safety and effectiveness in treating serious or life-threatening diseases or conditions may receive accelerated approval upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. As a condition of accelerated approval, the FDA will generally require the sponsor to perform adequate and well-controlled post-marketing clinical studies to verify and describe the anticipated effect on irreversible morbidity or mortality or other clinical benefit.

We anticipate this trial will initiate in the second half of 2026. For CLN2 and CLN3 cohorts, enrollment is expected to begin in the second half of 2026, with the first interim analysis anticipated one year after the enrollment of the last patient. Given the flexible design of SOTERIA, enrollment timeline for the remaining indications (Krabbe disease and Sandhoff disease) may also begin in 2026 but may be adjusted at the discretion of management once initial sentinel data from Group 1 (CLN2 and CLN3) is provided.

SOTERIA's Phase 2 basket trial design is illustrated below in Figure 17.

Figure 17. Proposed PLX-200-600 (SOTERIA) Trial Design



As depicted above, this basket trial is expected to have a total of four cohorts. The CLN2 and CLN3 cohorts will be enrolled first, with the first three patients in each of the cohorts designed as the sentinel group. The remaining cohorts, which include the Sandhoff and Krabbe cohorts, will initiate after CLN2 and CLN3 participants' safety data is reviewed. All cohorts are expected to undergo titration and 96-week maintenance periods, followed by safety follow-up. An interim analysis is expected to be used to determine the statistical power of the trial, triggered by various milestones.

SOTERIA's primary objective is expected to be the evaluation of the safety and tolerability of PLX-200 in a total of 18 trial participants, ranging from two to fifteen years of age, with LSDs during the treatment period. Secondary objectives are expected to include evaluation of clinical activity of PLX-200 in trial participants as measured by respective instruments, as well as evaluation of PK and pharmacodynamic and biomarker data.

PLX-200-003 CLN3 Phase 3 Clinical Trial

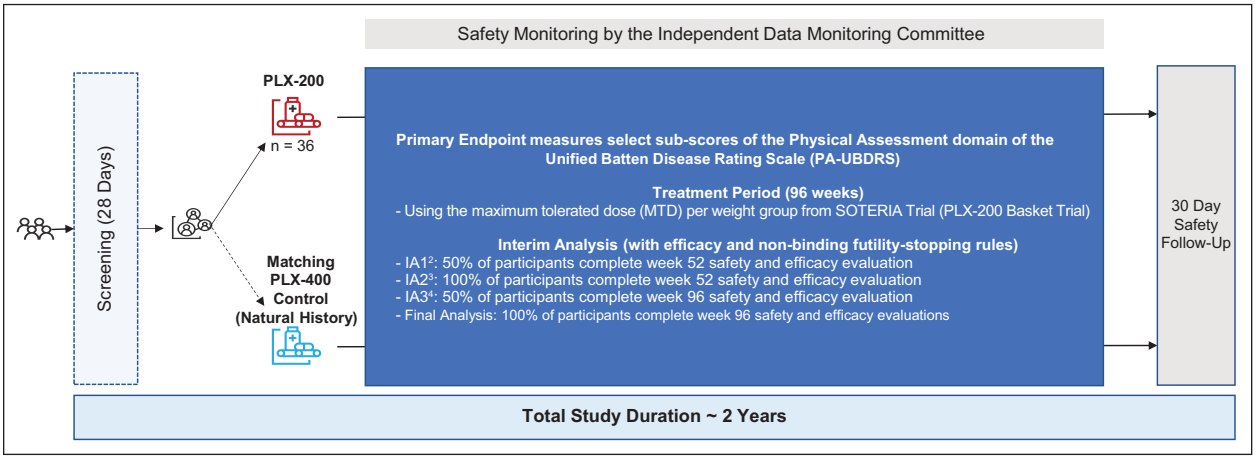
PLX-200-003, our IND-approved Phase 3 clinical trial of PLX-200 for the treatment of CLN3, is a single registrable, randomized, double-blind, placebo-controlled clinical trial for participants with mild to moderate CLN3 disease. In March 2020, we submitted an IND for PLX-200 for the treatment of CLN3 and, in April 2020, the FDA determined that the Phase 3 clinical trial may proceed. The primary objectives are to evaluate the safety and tolerability of PLX-200 compared with the placebo group and to evaluate the efficacy of PLX-200 using the motor score of Hamburg Rating Scale compared with the placebo group after 60 weeks of maintenance therapy.

PLX-200-003 Optimization

After extensive engagement with the CLN3 community, we have determined that a clinical trial design optimization exercise is warranted with a possible change in trial design to a single-arm, open-label trial. We plan to continue to actively engage with the FDA to seek alignment on the proposed trial optimization.

The primary efficacy objective of the proposed single arm, open-label clinical trial would be to evaluate the efficacy of PLX-200 in trial participants four to 18 years old with mild to moderate CLN3 disease as measured by the Gait and Speech Clarity subdomains of the Physical Assessment of the Unified Batten Disease Rating Scale after 96 weeks of treatment administration (maintenance period), while the secondary objective is to evaluate the safety and tolerability of PLX-200 in CLN3 patients.

Figure 18. Proposed PLX-200-003 (CLN3) Trial Design



1 Maximum tolerated dose is based on age and weight categories.
2,3,4 IA1, IA2 and IA3 allow potential accelerated approval depending on the result of evaluation.

We plan to continue optimizing our clinical trial design based on the findings from SOTERIA and inputs from clinical experts in the CLN3 landscape before continuing to actively align with the FDA. If the SOTERIA trial generates evidence of safety and effectiveness, it may help support the regulatory pathway and NDA submission for PLX-200 as the treatment of CLN3.

PLX-200-001 CLN2 Phase 2 Clinical Trial

PLX-200-001, our IND-approved Phase 2 clinical trial of PLX-200 for the treatment of CLN2, is a potentially single pivotal, single arm, open-label, synthetic control clinical trial in participants with mild-to-moderate "classic" CLN2 disease.

In December 2019, we submitted an IND for PLX-200 for the treatment of CLN2 and, in January 2021, the FDA determined that the Phase 2 clinical trial may proceed. PLX-200-001's primary endpoint aims to measure the mean difference in the rate of decline in the Total Disability Score of the Adapted Hamburg Rating Scale, which contains the motor, visual, and language domains, between matched populations (PLX-200 participants with similar baseline CLN2 motor score, genotype, and age (age three to 16) within three months as analyzable DEM-CHILD data), at Week 96 of treatment exposure. The current total trial duration is expected to be approximately two years, although we may amend the clinical trial design to improve patient/caregiver experience in the trial, reduce the length of the trial, and ensure that patients are exposed to an effective and safe treatment.

PLX-300

Description

PLX-300 (cinnamic acid) is an unsaturated carboxylic acid that occurs naturally in several plants as a deaminated product of phenylalanine. Cinnamic acid has a long history of human use as a component of plant-derived scents and is one of many compounds in the common spice cinnamon, which has been used for millennia for its medicinal properties. To date, the FDA has granted three ODDs to PLX-300 for the treatment of GM2 gangliosidosis, Krabbe disease, and NPD types A and B. PLX-300 has also received RPD for the treatment of GM2 gangliosidosis, Krabbe disease, and NPD type A and type B. The receipt of such designations does not guarantee a faster development process, regulatory review, or approval as compared to the conventional FDA approval process.

We have completed preclinical animal model studies for PLX-300 and are evaluating the potential for clinical advancement, which will be contingent upon a positive readout and successful commercialization of our most advanced drug candidate, PLX-200.

PLX-300 Mechanism of Action

Cinnamic acid, the main component of PLX-300, has been documented to have antioxidant and anti-inflammatory activities that are important for protecting brain cells from neurodegeneration, a common pathology in LSDs. Additional biological activities of cinnamic acid have been identified, including stimulation of suppressor of cytokine signaling 3 activity, which inhibits the activation of microglia. Our preclinical studies demonstrate that PLX-300 is also capable of activating PPARα and stimulating autophagy. Through these mechanisms, we believe that PLX-300 has potential to address unmet needs within the LSD landscape.

PLX-300 Preclinical Data Summary

Tay-Sachs and Sandhoff Diseases

We have completed preclinical studies using PLX-300 in a $HEXB^{-/-}$ mice model, a gene mutation animal model of Sandhoff disease, a severe form of Tay-Sachs disease. Our animal studies demonstrated that oral administration of PLX-300 reduced glycoconjugate accumulation (Figure 19), astroglial and microglial activations (Figure 20), and apoptosis in the brain of $HEXB^{-/-}$ mice, which led to improved neurobehavioral scores in open-field activities and enhanced rotarod performance, and normalized both footprints and gating (Figure 21). Based on these preclinical data, we believe that PLX-300 has therapeutic potential to halt the progression of Sandhoff Disease.

Figure 19. PLX-300 Reduces Neuronal Apoptosis and Cerebral Glycoconjugates Accumulation

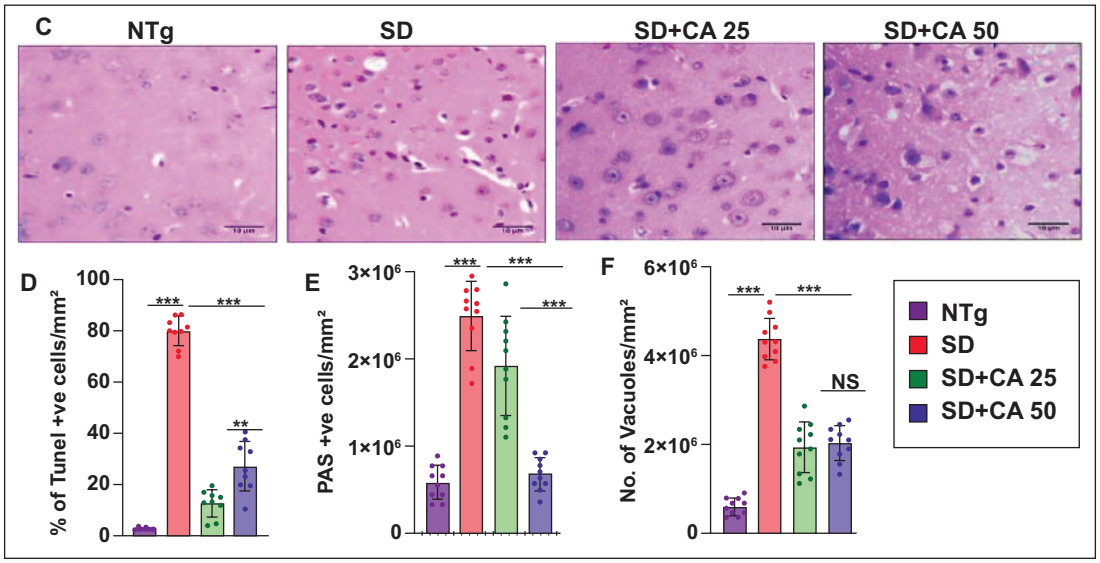


Figure 20. PLX-300 Reduces Neuroinflammation

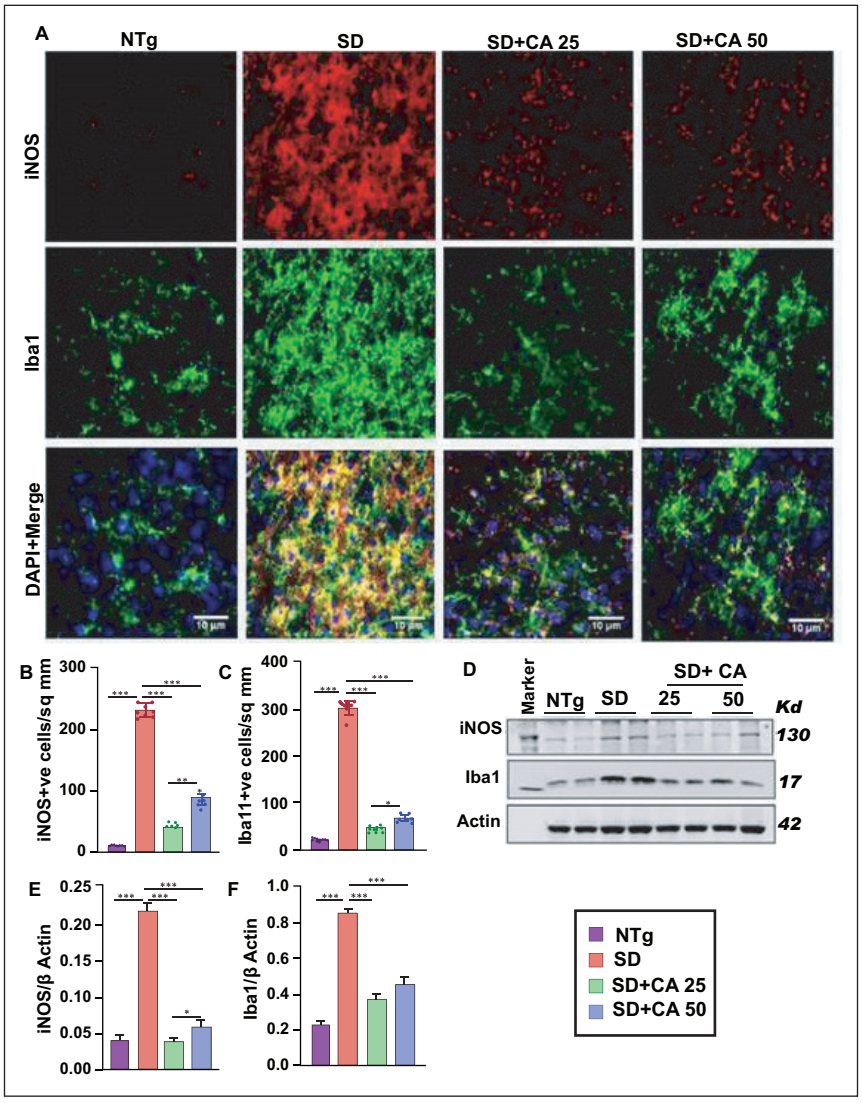
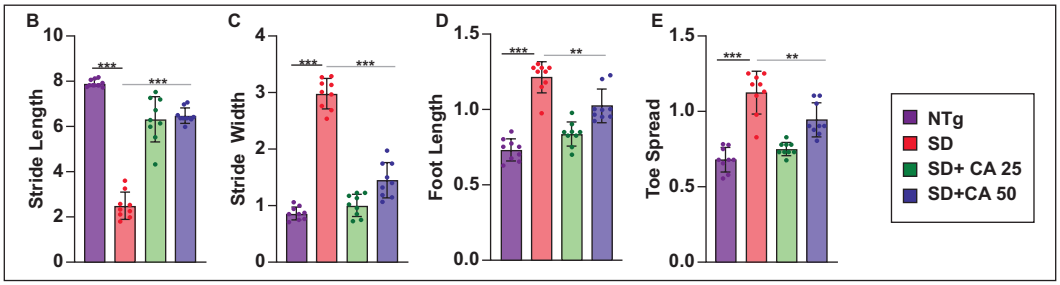


Figure 21. PLX-300 Improves Locomotor Function



Krabbe Disease

We have also completed *in vivo* studies using PLX-300 in GALC$^{-/-}$ mice, in which we observed that treatment with PLX-300 increased the level of MBP and PLP, markers of myelin, in cerebellum and corpus callosum (Figure 22), indicating the restoration of myelin. This finding was confirmed by immunostaining with antibodies against PLP. PLX-300 has also been demonstrated to reduce astroglial activation and neuroinflammation, as observed by decreased level of iNOS and GFAP, in vivo in the cerebellum of GALC$^{-/-}$ mice (Figure 23). Based on these preclinical data and the fact that Krabbe Disease is associated with lipid accumulation and glial activation, we believe that PLX-300 has the potential for high therapeutic value in treating Krabbe Disease.

Figure 22. Treatment with PLX-300 Restores Myelin in Cerebellum and Corpus Callosum of GALC$^{-/-}$ Mice

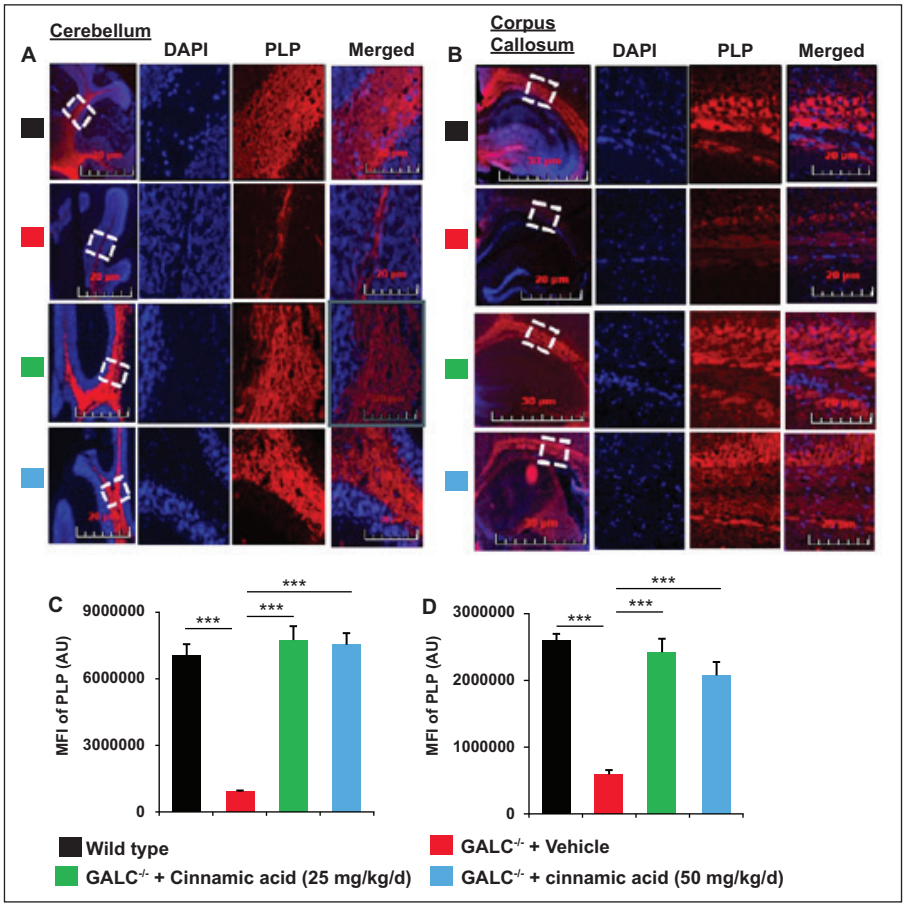
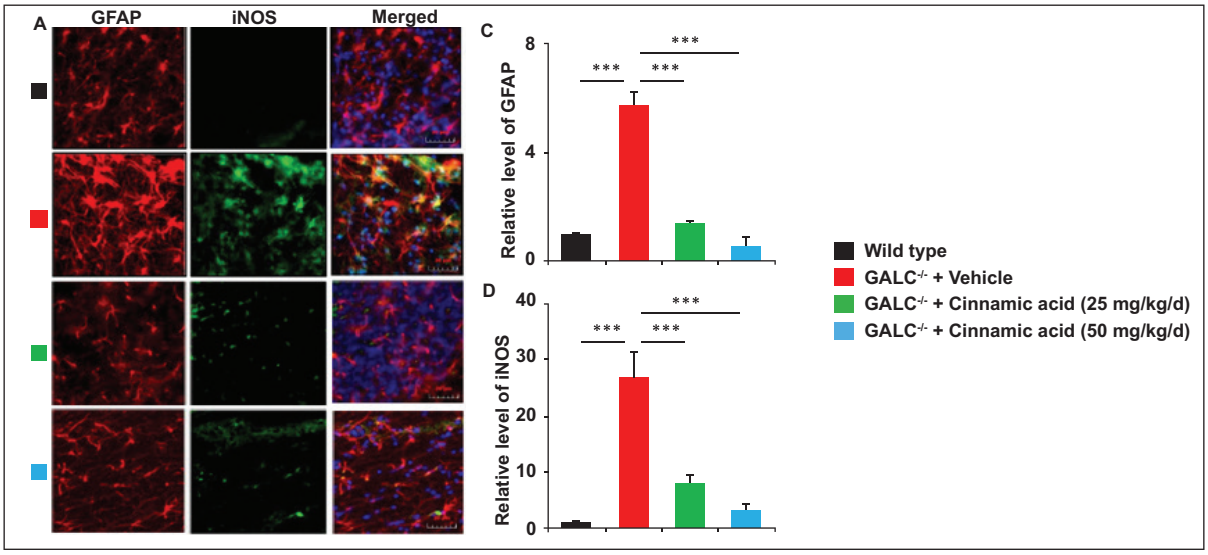


Figure 23. PLX-300 Reduces Astroglial Activation In Vivo in Cerebellum and Corpus Callosum of GALC$^{-/-}$ Mice



NPD type A and type B

We have also evaluated the effects of PLX-300 on both glial activation and neurodegeneration in ASMase knock out mice (ASMase$^{-/-}$ mice). Our preclinical studies demonstrated that orally administered PLX-300 reduced accumulation of neural sphingomyelin, a pathological hallmark of NPD (Figure 24), activated astroglial and microglial in the cerebellum, decreased neural apoptosis (Figure 25) and improved the locomotor activities (Figure 26) in treated ASMase$^{-/-}$ mice.

Figure 24. PLX-300 Reduces the Accumulation of Sphingomyelin in ASMase$^{-/-}$ Mice

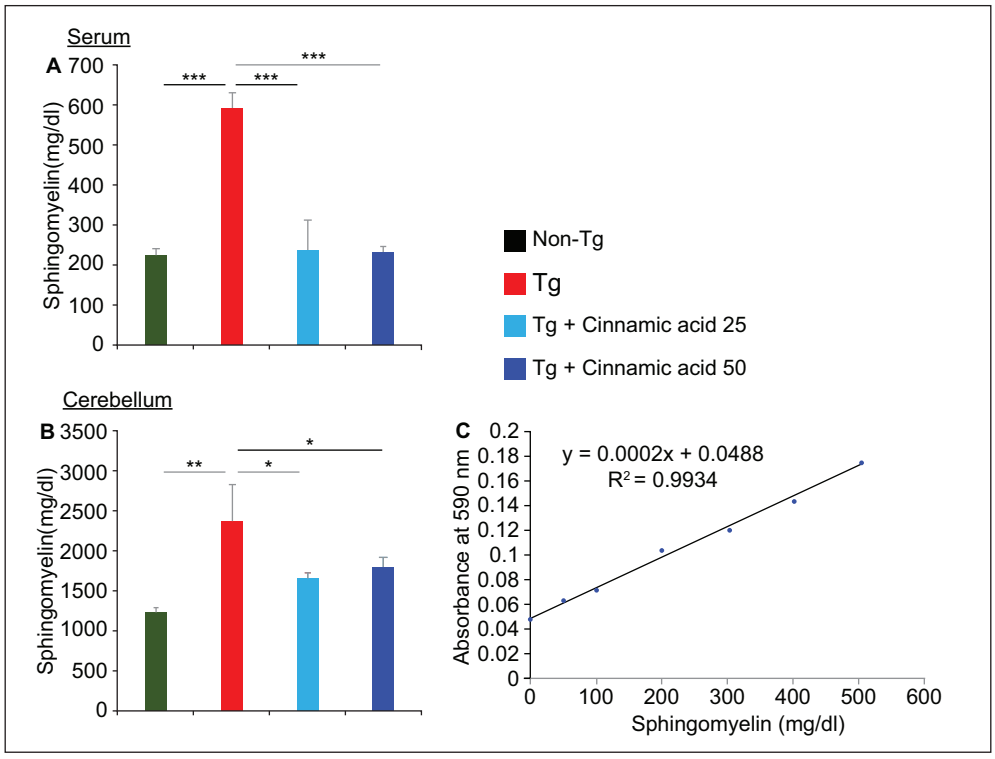


Figure 25. PLX-300 Decreases Neural Apoptosis in ASMase$^{-/-}$ Mice

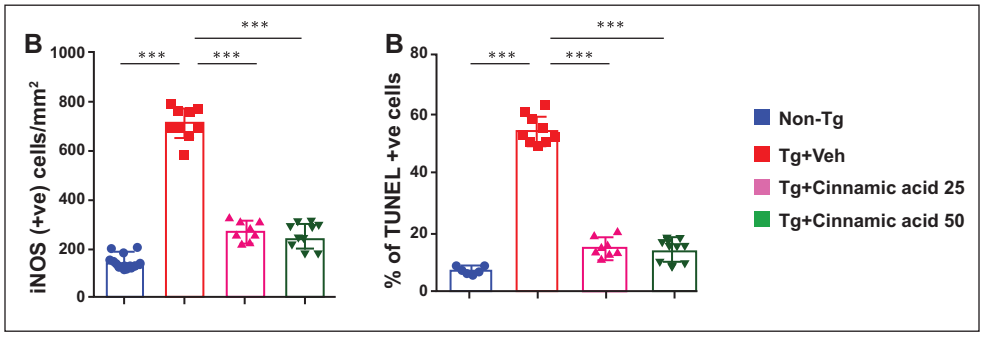
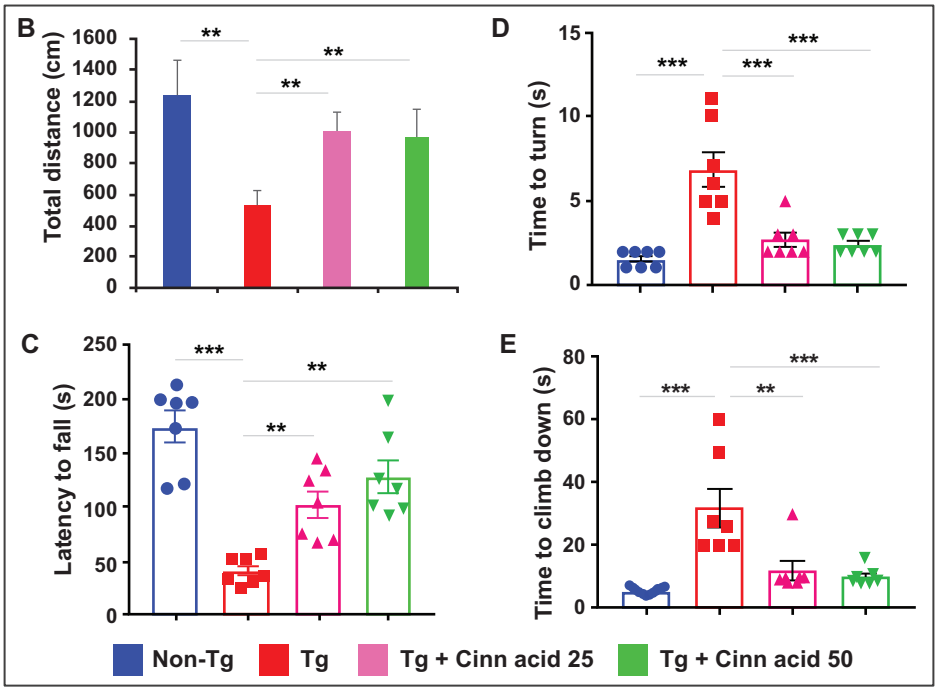


Figure 26. PLX-300 Improves Locomotor Activities in ASMase$^{-/-}$ Mice



PLX-300 Anticipated Clinical Programs

We have completed preclinical animal model studies for PLX-300 and are evaluating the potential for clinical advancement, which will be contingent upon a positive readout and successful commercialization of our most advanced drug candidate, PLX-200.

PLX-100

Description

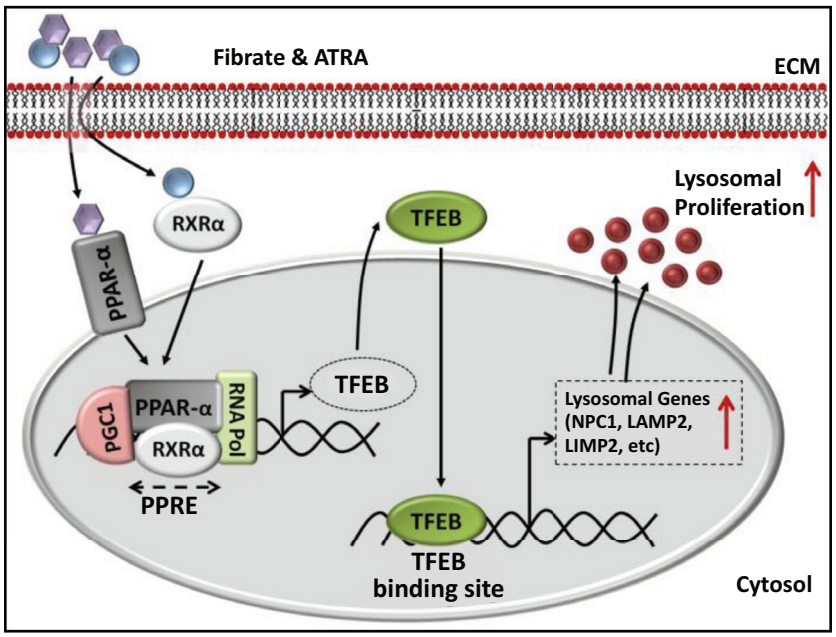
PLX-100 is a novel oral therapy comprised of our PPARα agonist, PLX-200, and vitamin A, a RXRα agonist. We believe that the unique mechanism of lysosomal biogenesis in PLX-200 and the role of vitamin A, a group of fat-soluble retinoids in major biological processes such as cellular communication, work synergistically to improve relevant enzymatic activities in multiple LSD indications while minimizing exposure levels. PLX-100 allows for an alternative to PLX-200 and may show improved efficacy. We are developing PLX-100 with the goal of addressing some of the limitations of therapies currently available in the LSD landscape. To date, the FDA has granted one ODD to PLX-100 for the treatment of CLN2. The receipt of such designation does not guarantee a faster development process, regulatory review, or approval as compared to the conventional FDA approval process.

We have completed preclinical animal model studies for PLX-100 and are evaluating the potential for clinical advancement, which will be contingent upon a positive readout and successful commercialization of our most advanced drug candidate, PLX-200.

PLX-100 Mechanism of Action

PLX-100 forms a PPARα/RXRα heterodimer with PLX-200 binding to PPARα and retinoic acid activating RXRα. PPARα/RXRα heterodimer has been documented to show DNA binding activity and activate transcription of genes involved in lipid homeostasis, cell growth, and differentiation. Our preclinical studies demonstrated that PPARα/RXRα heterodimer binds to PPRE-and RXR-binding sites in the TFEB promoter and, thereby, upregulates TFEB and lysosomal genes. Moreover, retinoic acid supports vision, which is lost in Batten disease patients.

Figure 27. Mode of Action of PLX-100



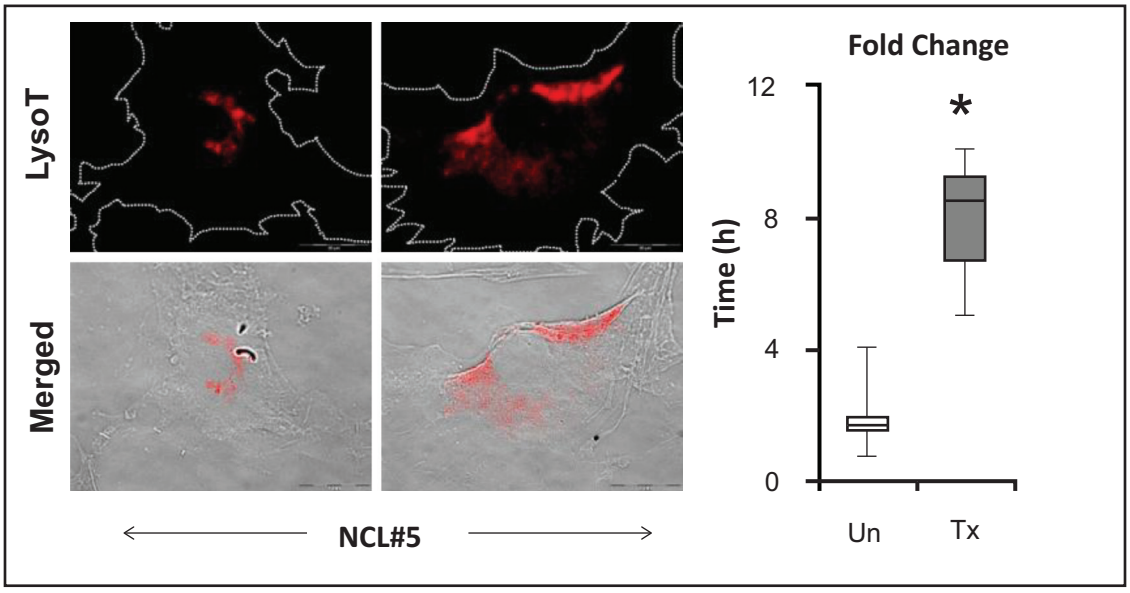
The potential therapeutic benefits of PLX-200, one of the main components of PLX-100, has been studied in multiple preclinical studies across various LSD indications. As our preclinical studies in animal models demonstrated that PLX-100 as a combination therapy may provide improved efficacy over PLX-200 alone, we believe that PLX-100 also has a strong therapeutic value in treating other catastrophic LSD indications beyond CLN2 and Krabbe Diseases, such as CLN3, Tay-Sachs and Sandhoff Diseases.

PLX-100 Preclinical Data Summary

CLN2

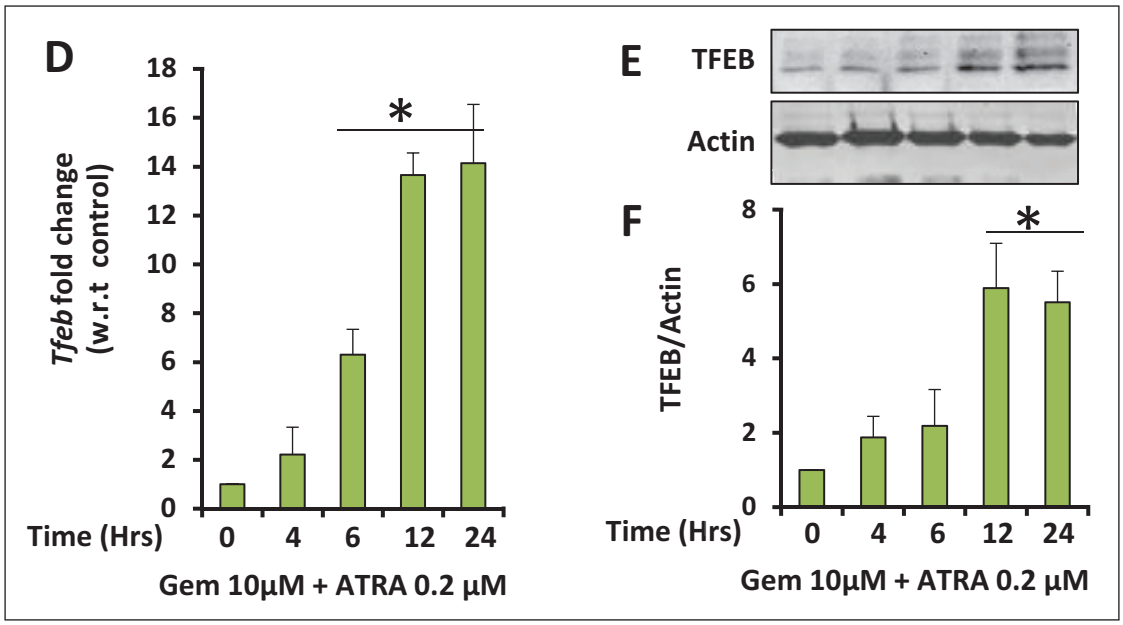
Our preclinical studies using a CLN2 animal model showed that PLX-100 up-regulated TPP1 mRNA, protein, and enzymatic activity in mouse and human primary astrocyte cultures via activation of the PPARα in a dose and time dependent manner. Activation of PPARα induced lysosomal biogenesis in mouse brain cells. Protein levels of TPP1 were also increased in both human astrocytes and SH-SY5Y human neuroblastoma cell lines as determined by immunofluorescence (Figure 28). Our animal model suggested that the upregulation of TPP1 occurs via formation of PPARα/RXRα heterodimer. Based on these data, we believe that PLX-100 may provide benefit to patients with CLN2, which is characterized by deficiency and/or loss of function of the TPP1 lysosomal protein.

Figure 28. PLX-100 Increases Lysosomal Biogenesis in LINCL Patient Fibroblasts



Our preclinical studies also demonstrated that PLX-100 upregulates TFEB in brain cells via PPARα/RXRα pathway. Primary astrocytes treated with PLX-100 for 4, 6, 12, and 24 hours demonstrated enhanced expression of TPP1 by almost more than three-fold relative to the levels achieved by PLX-200 alone. Figure 29 below shows improvement in TFEB level when treated with PLX-100. Given the increased potency, we believe PLX-100 has therapeutic value in the treatment of LSDs in which the autophagy-lysosome pathway plays an important role.

Figure 29. PLX-100 Upregulates TFEB via PPARα/RXR



Krabbe Disease

Oral administration of PLX-100 has been shown to markedly protect and/or increase the level of myelin markers, MBP and PLP in the cerebellum and corpus callosum of GALC$^{-/-}$ mice (Figure 30; Figure 31). We believe this increase in MBP and PLP has therapeutic importance in Krabbe disease as we have also seen a marked decrease in MBP and PLP in cerebellum and corpus callosum of GALC$^{-/-}$ mice as compared to wild type mice (Figure 30; Figure 31).

Figure 30. PLX-100 Increases MBP and PLP Levels in Cerebellum

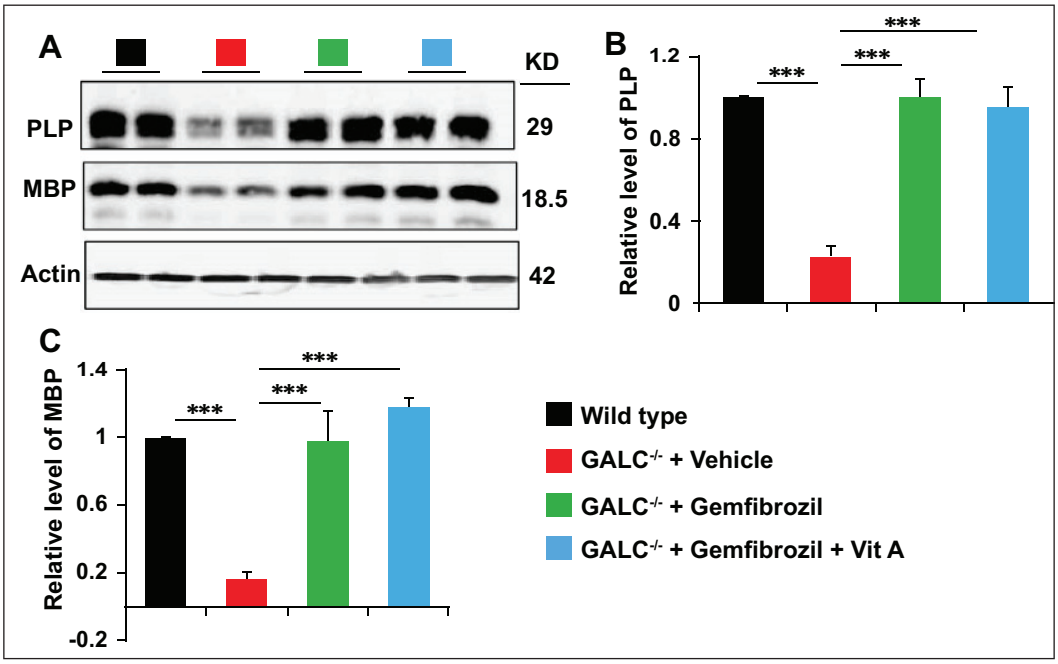
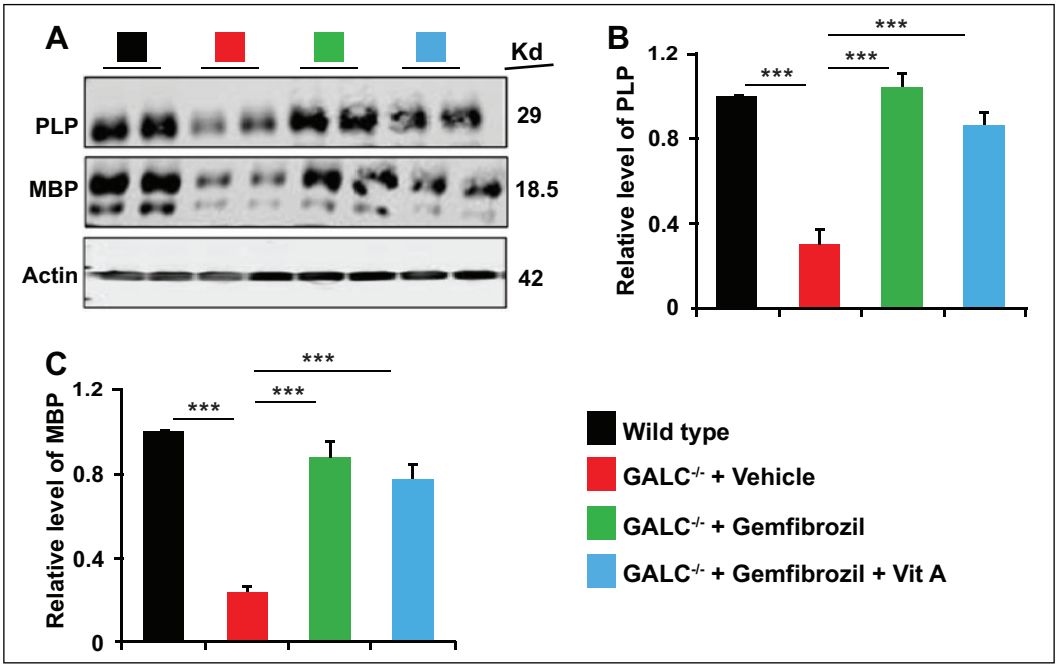


Figure 31. PLX-100 Increases MBP and PLP Levels in Corpus Callosum



In the same study, oral administration of PLX-100 has also been shown to reduce glial activation, a hallmark of many neurodegenerative diseases, including Krabbe Disease. Our preclinical studies showed that PLX-100 decreased the astroglial marker GFAP and proinflammatory marker iNOS levels in both the cerebellum and corpus callosum (Figure 32; Figure 33). Administration of PLX-100 has also shown to significantly improve hypolocomotion in GALC-deficient mice (Figure 34).

Figure 32. PLX-100 Decreases iNOS and GFAP Levels in Cerebellum

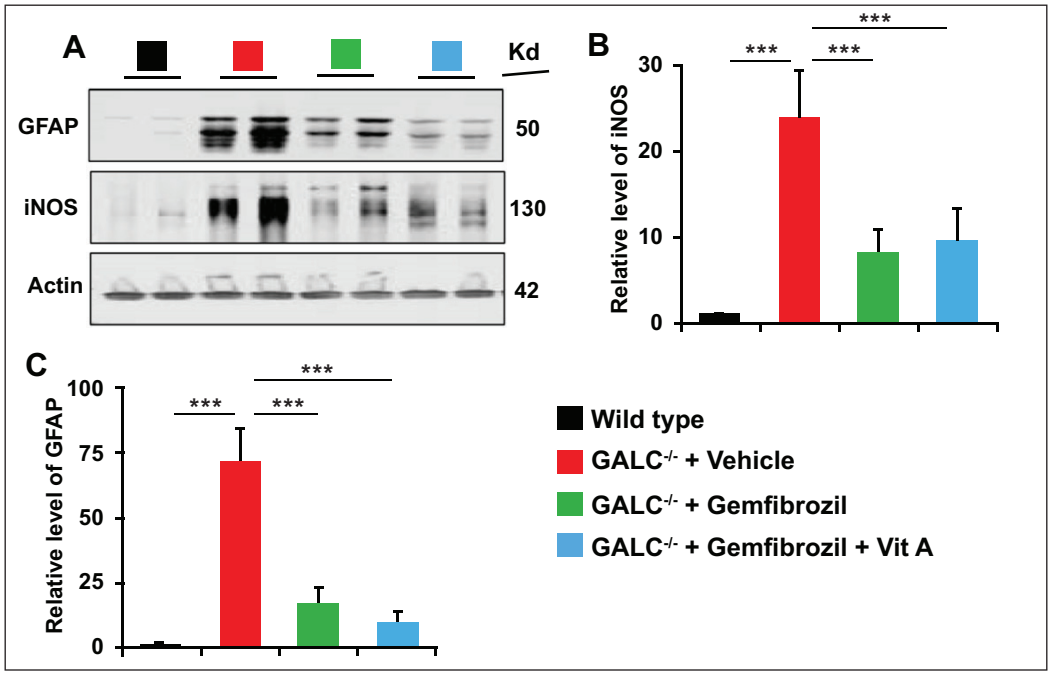


Figure 33. PLX-100 Decreases iNOS and GFAP Levels in Corpus Callosum

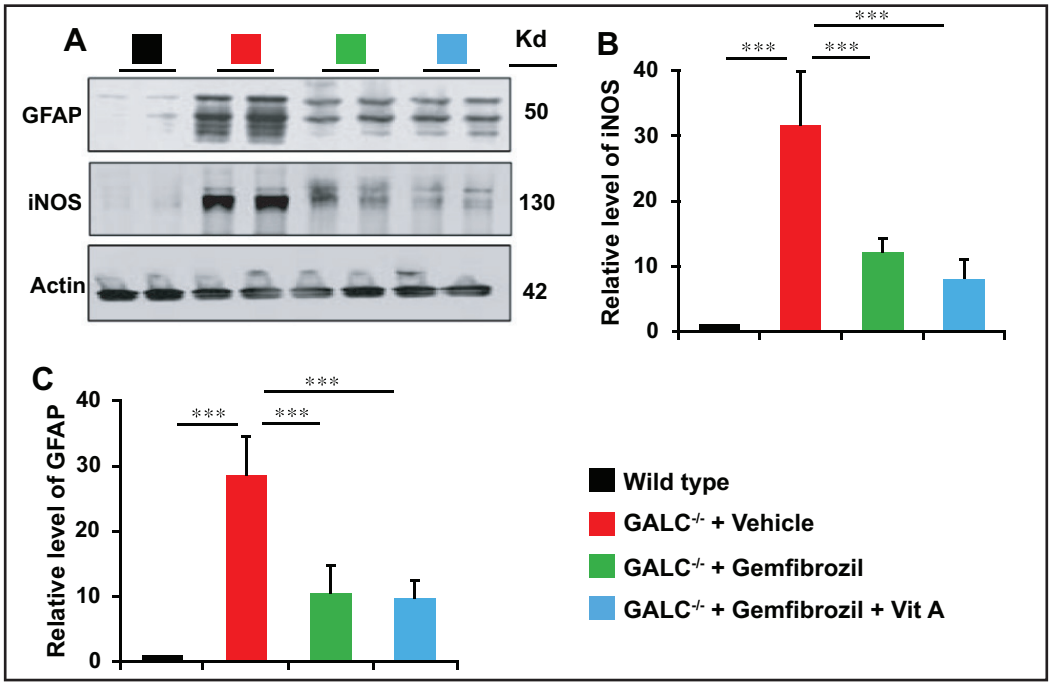
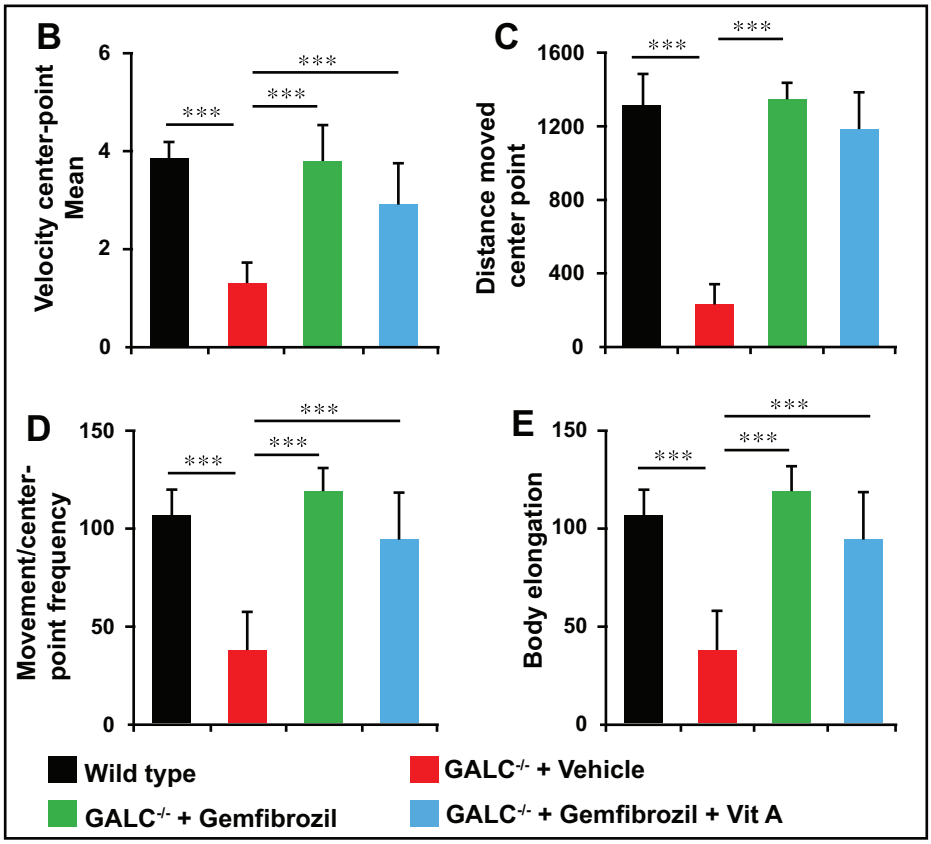


Figure 34. PLX-100 Improves Locomotor Function in GALC-deficient Mice



PLX-100 Anticipated Clinical Programs

We have completed preclinical animal model studies for PLX-100 and are evaluating the potential for clinical advancement, which will be contingent upon a positive readout and successful commercialization of our most advanced drug candidate, PLX-200.

PLX-400

Description

PLX-400 is a novel intranasally deliverable gene therapy candidate. It is designed to deliver lysosomal genes in appropriate adeno-associated viral vectors. We are initially developing PLX-400 for the treatment of CLN2 and CLN3 and are actively conducting additional preclinical animal studies with the goal of advancing the program toward clinical development.

Intra-nasal delivery takes advantage of the "nose-to-brain" ("N2B") transport systems in which several possibilities exist for bypassing the BBB for direct delivery to the brain. These include the draining of drugs absorbed in the nasal mucosa into the sinus and eventually to the carotid artery, where a "counter-current transfer" from venous blood to the brain may occur. Lymphatic drainage into the perivascular space from the olfactory trigeminal nerves have also been postulated as the mechanism of N2B transport. PLX-400 is designed to deliver lysosomal genes via intranasal delivery system to address the limitations of therapies currently available in the LSD market.

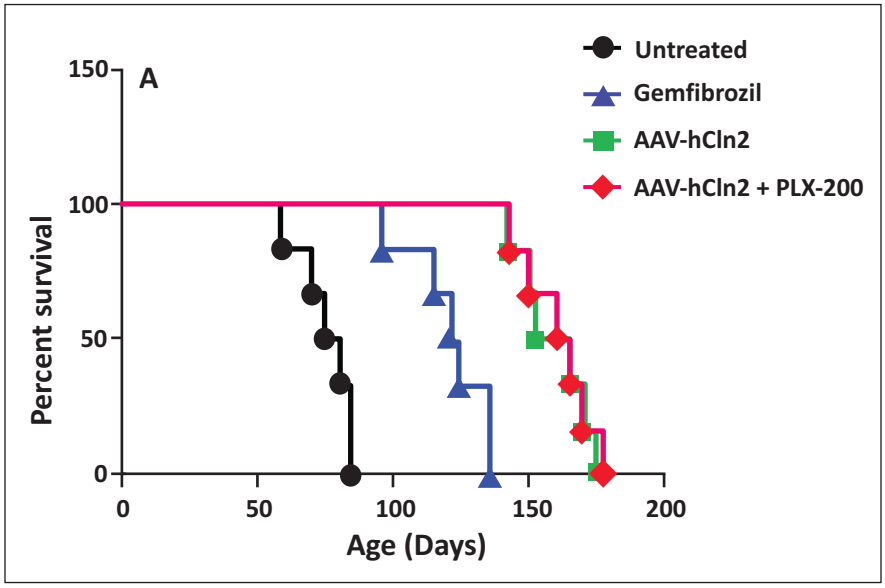
PLX-400 Mechanism of Action

PLX-400 is a self-complementary intranasally deliverable adeno-associated virus ("AAV") gene replacement therapy with a human cytomegalovirus ("CMV") promoter. PLX-400 is designed to express the relevant missing human gene for the treatment of LSDs, such as CLN2 transgene for the treatment of CLN2 disease.

PLX-400 Preclinical Data Summary

In our preclinical studies using a CLN2 single gene mutation animal model, PLX-400 as a monotherapy as well as in combination with oral administration of PLX-200, was demonstrated to prolong the life span $CLN2^{-/-}$ mice (Figure 35).

Figure 35. Improved Life Span with PLX-400 as a Monotherapy and in Combination with Oral PLX-200



PLX-400 Anticipated Clinical Programs

We intend to undertake further preclinical animal model studies for PLX-400 and evaluate clinical advancement potential, whether as a monotherapy or in combination with oral administration of PLX-200, at a later date.

Manufacturing and Supply

We do not own or operate, and currently have no immediate plans to establish, any manufacturing facilities for the clinical or commercial scale production of our product candidates. We currently rely, and expect to continue to rely for the foreseeable future, on third-party CMOs for the manufacturing of our product candidates for preclinical and clinical testing, as well as for commercial manufacture of any products that we may commercialize. We currently obtain our supplies from our CMOs on a purchase order basis and do not have long-term supply arrangements in place. Should any of our CMOs become unavailable to us for any reason, we believe that there are a number of potential replacements, although we may face delays in identifying and qualifying such replacements. We intend to qualify manufacturers to provide the active pharmaceutical ingredients and drug products prior to submission of an NDA to the FDA or other marketing authorization applications to other regulatory authorities.

Given our stage of development, we have not yet defined our sales, marketing or product distribution capabilities and strategy for our product candidates. We intend to build a commercial infrastructure to support the sale of any of our approved products and our commercial strategy may include the establishment of our own commercial sales force or third-party relationships, including the use of strategic partners, distributors, and a contract sales force. While we may commit significant financial and management resources to commercial activities, we may also consider enhancing our capabilities by collaborating with one or more pharmaceutical companies. We plan to further evaluate these alternatives as we approach approval for our product candidates.

Licensing, Collaboration and Other Agreements

We actively pursue strategic licensing and collaboration opportunities with biopharmaceutical companies and academic institutions to expand our product pipeline and support the advancement of our product candidates. Below is an overview of our licensing and collaboration agreements that are expected to have a material impact on our financial results in the near term.

2016 License Agreement with Rush University Medical Center

In April 2016, we entered into a License Agreement with Rush, which was subsequently amended by the First Amendment in July 2019, the Second Amendment in September 2019, and the Third Amendment in December 2021 (as amended, the "2016 Rush License Agreement"). Pursuant to the 2016 Rush License Agreement, we received an exclusive, sublicensable license to certain of Rush's rights in certain technologies (the "Licensed Patents") in the fields of composition and method of treating certain neurodegenerative disorders (the "Licensed Field") to make, use, formulate, import, export, sell and offer to sell certain products within the Licensed Field, worldwide. We also granted non-exclusive licenses to Rush, with the right to grant sublicenses to non-profit institutions and governmental agencies, to make and use the Licensed Patents and certain improvements solely for non-commercial research and education purposes.

As consideration for the license, we paid Rush an upfront payment of $70 thousand and issued common stock to Rush equal to 15% of our then-outstanding common stock. Pursuant to the 2016 Rush License Agreement, we are obligated to pay Rush (i) up to $150 thousand upon the achievement of specific milestones and (ii) an annual royalty equal to 3.5% of net sales. In the event we sublicense the rights under the 2016 Rush License Agreement, we are also obligated to pay Rush (i) an annual royalty equal to 3.5% of such sublicensee's net sales and (ii) a percentage of all non-royalty considerations we receive from such sublicensee in the mid-double-digit range.

The 2016 Rush License Agreement will continue indefinitely or until the expiration of the last Licensed Patent, unless terminated (i) by us at any time upon 90 days' written notice to Rush or (ii) by Rush for certain conditions, including our insolvency, material breach of the agreement, or failure to appoint a new chief executive officer or president within six months following the termination or resignation of the current chief executive officer or president that remain uncured for 90 days after written notice. The last licensed patent underlying the 2016 Rush License Agreement is estimated to expire in 2044.

Master Services Agreement with Rush University Medical Center

In June 2016, we entered into a Master Services Agreement with Rush (the "Rush MSA"), pursuant to which Rush provides services regarding the development and regulatory approval process for products currently under development by us, under statements of work for such services agreed to by the parties from time to time.

The Rush MSA will continue until the completion of all services, unless terminated by either party (i) upon 30 days' prior written notice for any reason, (ii) upon 30 days' prior written notice of the other party's material breach that remains uncured during that period, or (iii) upon written notice of the other party's bankruptcy, liquidation, or insolvency. We may also terminate the Rush MSA upon 30 days' written notice to Rush if we decide not to proceed with the development of our products.

In April 2025, the Company paid $109 thousand under two statements of work pursuant to the Rush MSA. Total expenses incurred for the years ended December 31, 2025 and 2024 were $133 thousand and zero, respectively, which is recorded in research and development in the statement of operations and comprehensive loss. As of December 31, 2025 and 2024, there was $23 thousand and zero due to Rush, respectively, which is recorded in accrued expenses — related party in the balance sheet.

2022 License Agreement with Rush University Medical Center

In May 2022, Somaryx Therapeutics Limited ("Somaryx"), an affiliate of Mstone, entered into a License Agreement with Rush (as amended, the "2022 Rush License Agreement"), which was subsequently novated to us by Somaryx in January 2025 and amended in February 2025. Under the 2022 Rush License Agreement, we received an exclusive, sublicensable license to certain of Rush's rights in certain technologies (the "Patent Rights") in the

fields of composition and method of treating certain disorders (the "Licensed Field") to make, use, formulate, import, export, sell and offer to sell certain products within the Licensed Field, worldwide including a gene therapy to treat various lysosomal storage disorders. In consideration for the license, we issued 277,823 shares to Rush and 3,426,484 shares to Mstone.

Pursuant to the 2022 Rush License Agreement, we are obligated to pay Rush (i) up to $75 thousand upon the achievement of specific milestones for an orphan indication, (ii) up to $650 thousand upon the achievement of specific milestones for a non-orphan indication, and (iii) an annual royalty equal to 1.75% of net sales. In the event we sublicense the rights under the 2022 Rush License Agreement, we are also obligated to pay Rush (i) an annual royalty equal to 1.75% of such sublicensee's net sales and (ii) 7.5% of all non-royalty considerations we receive from such sublicensee.

The 2022 Rush License Agreement will continue indefinitely or until the expiration of the last Patent Rights, unless terminated (i) by us at any time upon 90 days' written notice to Rush or (ii) by Rush for certain conditions, including our insolvency, material breach of the agreement, or failure to appoint a new chief executive officer or president within six months following the termination or resignation of the current chief executive officer or president that remain uncured for 90 days after written notice. The last licensed patent underlying the 2022 Rush License Agreement is expected to expire in 2040.

Intellectual Property

Intellectual property, including patents, trade secrets, trademarks and copyrights, is a critical component of our business. Our commercial success depends, in part, on our ability to obtain and maintain robust intellectual property protections for our current and future product candidates, as well as for our proprietary discoveries, development technologies, and know-how. It also depends on, in part, on our ability to protect our intellectual property from unauthorized use. We pursue a strategy to develop and maintain protection of our proprietary position by, among other methods, filing patent applications in the United States and other key jurisdictions relating to our product candidates and their methods of use. A comprehensive discussion on risk relating to intellectual property is provided under the section of this Annual Report entitled "*Risk Factors — Risks Related to Intellectual Property*."

Our patent portfolio is built with a strategic objective of establishing layered protection around our product candidates through claims on compositions of matter, pharmaceutical formulations, and methods of treatment. Along with our Licensor (Rush), we are actively prosecuting patents in principal jurisdictions with strong IP enforcement and commercial relevance, specifically the United States, Europe, Canada and China (including Hong Kong, SAR). As of January 12, 2026, our patent portfolio consists of six distinct patent application families protecting the compositions of matter and methods of treatment of our product candidates. This includes five issued patents in the United States, six issued patents in foreign jurisdictions (excluding validated European patents in individual countries), one allowed patent, and 25 pending patent applications, of which four are U.S. filings, with the remainder filed internationally. We also hold two proprietary patent families protecting the pharmaceutical formulations of our lead candidate, PLX-200.

PLX-200/PLX-100

We hold exclusive rights to four patent families that disclose and cover the methods of using a fibrate, including gemfibrozil, all-trans retinoic acid, or a combination of a fibrate and all-trans retinoic acid for the treatment of lysosomal storage disorders, which represent our key areas of immediate clinical development.

U.S. Patent No. US 9,750,712 B2 and its divisional, U.S. Patent No. US 10,357,471 B2, contain issued claims directed to methods of treating NCLs comprising administering a fibrate (*e.g.,* gemfibrozil), all-trans retinoic acid, or a combination of a fibrate and all-trans retinoic acid. A continuation of this family, U.S. Patent No. US 11,351,142 B2, contains issued claims directed to methods of treating Tay-Sachs disease comprising administering a fibrate (*e.g.,* gemfibrozil), or a combination of a fibrate and all-trans retinoic acid. This patent family is estimated to expire in 2034.

A separate patent family discloses the treatment of lysosomal storage disorders, specifically neuronal ceroid lipofuscinosis, comprising administering a fibrate such as gemfibrozil. The patent family is issued in the United States (US 11,020,366 B2), Australia (2017388399), and Canada (CA 3043921 C), with additional applications from this family pending in China (including Hong Kong), and estimated expiration dates in 2034 and 2037 on granted claims.

A patent family that discloses methods of administering or using gemfibrozil alone or in combination with Vitamin A to treat globoid cell leukodystrophy (a/k/a Krabbe disease) is filed in the United States (U.S. Ser. No. 18/261,959), Europe, Canada, and China (including Hong Kong), and once granted will have an estimated expiration date in 2041. Another patent family discloses the treatment of juvenile neuronal ceroid lipofuscinosis with PLX-200 is filed in the United States (U.S. Ser. No. 19/149,297), Europe, Canada, China, Korea, and Japan, with an estimated expiry date in 2044 on any granted claims.

With respect to the formulation of gemfibrozil, we hold issued patents disclosing a gemfibrozil salt composition in Australia (2021224133) and Japan (JP 7538557 B2), both with projected expiration dates in 2041. Additional patent applications from this family are pending in the United States, Europe, and Canada, with projected expiration dates in 2041. We are also pursuing a patent application directed to a liquid pharmaceutical composition of gemfibrozil in an aqueous solvent in the United States (U.S. Application No. 18/871,396), with a projected expiration date in 2043.

Orphan Drug Designation

PLX-200 has obtained orphan drug designation from the FDA as well as the EMA for the treatment of all 13 sub-types of neuronal ceroid lipofuscinoses. PLX-200 has obtained additional orphan drug designation status from the FDA for the treatment of GM2 gangliosidoses or Tay-Sachs and Sandhoff diseases, and globoid cell leukodystrophy or Krabbe disease. PLX-100 has obtained orphan drug designation from the FDA for treatment of neuronal ceroid lipofuscinoses. Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if, in relevant part, it is a drug intended to treat a rare disease or condition, defined as a patient population of fewer than 200,000 in the United States. If PLX-200 receives the first marketing approval for the treatment of any of the 13 sub-types of neuronal ceroid lipofuscinoses, Tay-Sachs and Sandhoff diseases, and/or Krabbe disease, then it would be entitled to marketing exclusivity for seven years, which precludes the FDA from approving another marketing application for the same drug for the same use or indication for seven years after PLX-200's marketing approval. We may seek an additional six months of market exclusivity pursuant to The Best Pharmaceuticals for Children Act ("BPCA"). Among the other benefits of orphan drug designation are tax credits for certain research and fee waivers. The receipt of such designation does not guarantee a faster development process, regulatory review, or approval as compared to the conventional FDA approval process.

PLX-300

We hold exclusive rights to an issued patent covering the administration of cinnamic acid or in combination with either all-trans retinoic acid or Vitamin A to treat a lysosomal storage disorder in the United States (US 12,023,345 B2), Europe (EP 3,220,906 B1), Japan (JP 2021107404 A) and Australia (2015350223). Currently, this patent family includes an allowed patent in Canada (2967066), and pending divisional applications in Europe, Canada, and the United States. The granted claims in this patent family are estimated to expire in 2035. In addition, along with our Licensor (Rush), we are pursuing patent protection for the method of using cinnamic acid to treat globoid cell leukodystrophy or Krabbe disease under a related patent family filed for PLX-200. This family shares the same application as noted above and is filed in the United States (U.S. Ser. No. 18/261,959), Europe, Canada and China (including Hong Kong), with estimated expiration dates in 2041.

Orphan Drug Designation

We have obtained orphan drug designation from the FDA for the treatment of GM2 gangliosidosis, Krabbe disease, and NPD disease type A and type B. Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if, in relevant part, it is a drug intended to treat a rare disease or condition, defined as a patient population of fewer than 200,000 in the United States. If PLX-300 receives the first marketing approval for the treatment of GM2 gangliosidosis, Krabbe disease or NPD type A or type B then it would be entitled to marketing

exclusivity for seven years, which precludes the FDA from approving another marketing application for the same drug for the same use or indication for seven years after PLX-300's marketing approval. The receipt of such designation does not guarantee a faster development process, regulatory review, or approval as compared to the conventional FDA approval process.

PLX-400

We hold exclusive rights to an issued patent disclosing methods of treating lysosomal storage disorders by administering a combination of nasal gene delivery and a pharmaceutical agent, including oral cinnamic acid, oleamide, or gemfibrozil in Australia (2020245415). The patent is pending in the United States (U.S. Ser. No. 17/441,029), Canada, China, Japan, and the Republic of Korea. Any granted claims from this patent family will have an estimated expiration date in 2040.

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 date of filing the non-provisional application. In the United States, a patent's term may be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the USPTO in granting a patent or may be shortened if a patent is terminally disclaimed over an earlier-filed patent. The term of a patent that covers an FDA-approved drug may also be eligible for patent term extension, which permits patent term restoration of a U.S. patent as compensation for the patent term lost during the FDA regulatory review process. The Hatch-Waxman Act permits a patent term extension of up to five years beyond the expiration of the patent. The length of the patent term extension is related to the length of time the drug is under regulatory review. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval and only one patent applicable to an approved drug may be extended. Moreover, a patent can only be extended once, and thus, if a single patent is applicable to multiple products, it can only be extended based on one product. Similar provisions are available in Europe and other foreign jurisdictions to extend the term of a patent that covers an approved drug. When possible, we expect to apply for patent term extensions for patents covering our product candidates and their methods of use.

We may also rely on trade secrets relating to our discovery programs and product candidates, and seek to protect and maintain the confidentiality of proprietary information to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection. It is our policy to require our employees, consultants, outside scientific collaborators, sponsored researchers and other advisors to execute confidentiality agreements upon the commencement of employment or consulting relationships with us, and for employees and consultants to enter into invention assignment agreements with us.

Competition

The pharmaceutical and biotechnology industries are characterized by rapidly advancing technologies, fierce competition, and a strong defense of intellectual property. While we believe that our platform, knowledge, scientific resources and experience provides us with competitive advantages, we face competition with respect to our current product candidates and will face competition with respect to any other product candidates that we may seek to develop or commercialize in the future, from, among others, major pharmaceutical companies, specialty pharmaceutical and biotechnology companies, academic institutions, governmental agencies and public and private research institutions worldwide. It is also possible that we will face competition from other pharmaceutical approaches as well as other types of therapies. The key competitive factors affecting the success of our product candidates are likely to be the efficacy and safety of our product candidates, the scope and limitations of marketing approval, the success of regulatory approval, the successful protection of our intellectual property, and the availability of funding and reimbursement.

With respect to products and product candidates in the treatment of the 13 sub-types of NCLs, there is currently one established standard of care for one sub-type. On April 17, 2017, cerliponase alfa was approved for the treatment of CLN2 disease. We are also aware of companies that are currently developing product candidates that can be competitive, including Tern Therapeutics, Inc. For the remaining sub-types of NCLs, while direct competition is limited as there is currently no established standard of care, we are aware of companies that are developing product candidates, including THX Pharma (formerly known as Theranexus) in the treatment of CLN3.

With respect to products and product candidates in the treatment of Tay-Sachs and Sandhoff diseases, while direct competition is limited as there is currently no established standard of care, we are aware of companies that are developing product candidates that can be competitive, including IntraBio, Inc.

With respect to products and product candidates in the treatment of Krabbe disease, hematopoietic stem cell transplantation is considered the current standard of care. We are aware of other companies that are developing product candidates that can be competitive, including Forge Biologics (Ajinomoto).

With respect to products and product candidates in the treatment of NPD type A or type B, there is currently one established standard of care. On August 31, 2022, olipudase alfa was approved for the treatment of NPD type A and type B. We are unaware of other companies developing treatments for NPD type A or type B that can be competitive.

Additional potential competitors include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization.

There are a number of large pharmaceutical and biotechnology companies that currently market and sell products or are pursuing the development of product candidates for the treatment of the indications that we are pursuing. More established companies may have a competitive advantage over us due to their greater size, resources and institutional experience. In particular, these companies have greater experience and expertise in securing reimbursement, government contracts, relationships with key opinion leaders, conducting testing and clinical trials, obtaining and maintaining regulatory approvals and distribution relationships to market products, and marketing approved drugs. These companies also have significantly greater research and marketing capabilities than we do.

Government Regulation

The FDA and other regulatory authorities at federal, state and local levels, as well as in foreign countries, extensively regulate, among other things, the research, development, testing, manufacture, quality control, import, export, safety, effectiveness, labeling, packaging, storage, distribution, record keeping, approval, advertising, promotion, marketing, post-approval monitoring and post-approval reporting of drug product candidates, such as those we are developing. We, along with third-party contractors, will be required to navigate the various preclinical, clinical and commercial approval requirements of the governing regulatory agencies of the countries in which we wish to conduct studies or seek approval or licensure of our product candidates. Generally, before a new therapeutic product can be marketed, considerable data demonstrating a biological product candidate's quality, safety, purity and potency, or a small molecule drug candidate's quality, safety and efficacy, must be obtained, organized into a format specific for each regulatory authority, submitted for review and approved by the regulatory authority. For biological product candidates, potency is similar to efficacy and is interpreted to mean the specific ability or capacity of the product, as indicated by appropriate laboratory tests or by adequately controlled clinical data obtained through the administration of the product in the manner intended, to effect a given result.

Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or post-marketing may subject an applicant to administrative or judicial sanctions. These sanctions could include, among other actions, the FDA's refusal to approve pending applications from the sponsor, withdrawal of an approval, a clinical hold, untitled or warning letters, product recalls or market withdrawals, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement and civil or criminal penalties. Any agency or judicial enforcement action could have a material adverse effect on our company and our products or product candidates.

U.S. Government Regulation

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act ("FDCA") and its implementing regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, and local statutes and regulations requires the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or following approval may subject an applicant to administrative action and judicial sanctions. The process required by the FDA before a drug may be marketed in the United States generally involves the following:

- completion of preclinical laboratory tests and animal studies performed in accordance with the FDA's current Good Laboratory Practices regulation;
- submission to the FDA of an IND, which must become effective before clinical trials may begin and must be updated annually or when significant changes are made;
- approval by an independent IRB, or ethics committee at each clinical site before the trial is commenced;
- manufacture of the proposed biologic candidate in accordance with current good manufacturing practices("cGMP");
- performance of adequate and well-controlled human clinical trials in accordance with GCP requirements to establish the safety, purity and potency of the proposed biologic product candidate for its intended purpose;
- preparation of and submission to the FDA of an NDA (or a BLA for a biological product), after completion of all pivotal clinical trials;
- satisfactory completion of an FDA Advisory Committee review, if applicable;
- a determination by the FDA within 60 days of its receipt of an NDA or BLA to file the application for review (if applicable);
- satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities at which the proposed product is produced to assess compliance with cGMPs, and to assure that the facilities, methods and controls are adequate to preserve the biological product's continued safety, purity and potency, and of selected clinical investigation sites to assess compliance with GCPs; and
- FDA review and approval of the NDA or BLA to permit commercial marketing of the product for particular indications for use in the United States.

Preclinical and Clinical Development

Prior to beginning any clinical trial with a product candidate in the United States, we must submit an IND to the FDA. An IND is a request for authorization from the FDA to administer an investigational new drug product to humans. The central focus of an IND submission is on the general investigational plan and the protocol or protocols for preclinical studies and clinical trials. The IND also includes results of animal and in vitro studies assessing the toxicology, pharmacokinetics, pharmacology and pharmacodynamic characteristics of the product, CMC information, and any available human data or literature to support the use of the investigational product. In April 2025, the FDA published a roadmap to reduce animal testing in preclinical safety studies, including those required in INDs, with scientifically validated new approach methodologies ("NAMs"). An IND must become effective before human clinical trials may begin. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day period, raises safety concerns or questions about the proposed clinical trial. In such a case, the IND may be placed on clinical hold and the IND sponsor and the FDA must resolve any outstanding concerns or questions before the clinical trial can begin. Submission of an IND therefore may or may not result in FDA authorization to begin a clinical trial.

In addition to the IND submission process, supervision of human gene transfer trials includes evaluation and assessment by an IBC, a local institutional committee that reviews and oversees research utilizing recombinant or synthetic nucleic acid molecules at that institution. The IBC assesses the safety of the research and identifies any potential risk to public health or the environment and such review may result in some delay before initiation of a clinical trial.

Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators in accordance with GCPs, which include the requirement that all research subjects provide their informed consent for their participation in any clinical study. Clinical trials are conducted under protocols detailing, among other things, the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. A separate submission to the existing IND must be made for each successive clinical trial conducted during product development and for any subsequent protocol amendments. Furthermore, an independent IRB for each site proposing to conduct the clinical trial must review and approve the plan for any clinical trial and its informed consent form before the clinical trial begins at that site, and must monitor the study until completed. Regulatory authorities, the IRB or the sponsor may suspend a clinical trial at any time on various grounds, including a finding that the subjects are being exposed to an unacceptable health risk or that the trial is unlikely to meet its stated objectives. Some studies also include oversight by an independent group of qualified experts organized by the clinical study sponsor, known as a data safety monitoring board, which provides authorization for whether or not a study may move forward at designated check points based on access to certain data from the study and may halt the clinical trial if it determines that there is an unacceptable safety risk for subjects or other grounds, such as no demonstration of efficacy. There are also requirements governing the reporting of ongoing preclinical studies and clinical trials and clinical study results to public registries.

Human clinical trials are typically conducted in three sequential phases that may overlap.

- Phase 1. The investigational product is initially introduced into healthy human subjects or patients with the target disease or condition. These studies are designed to test the safety, dosage tolerance, absorption, metabolism and distribution of the investigational product in humans, the side effects associated with increasing doses, and, if possible, to gain early evidence on effectiveness.
- Phase 2. The investigational product is administered to a limited patient population with a specified disease or condition to evaluate the preliminary efficacy, optimal dosages and dosing schedule and to identify possible adverse side effects and safety risks. Multiple Phase 2 clinical trials may be conducted to obtain information prior to beginning larger and more expensive Phase 3 clinical trials.
- Phase 3. The investigational product is administered to an expanded patient population to further evaluate dosage, to provide statistically significant evidence of clinical efficacy and to further test for safety, generally at multiple geographically dispersed clinical trial sites. These clinical trials are intended to establish the overall risk/benefit ratio of the investigational product and to provide an adequate basis for product approval.

In some cases, the FDA may require, or companies may voluntarily pursue, additional clinical trials after a product is approved to gain more information about the product. These so-called Phase 4 studies may be made a condition to approval of an NDA or BLA. Concurrent with clinical trials, companies may complete additional animal studies and develop additional information about the biological characteristics of the product candidate, and must finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, must develop methods for testing the identity, strength, quality and purity of the final product, or for biologics, the safety, purity and potency. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life.

A sponsor may choose, but is not required, to conduct a foreign clinical study under an IND. When a foreign clinical study is conducted under an IND, all IND requirements must be met unless waived. When the foreign clinical study is not conducted under an IND, the sponsor must ensure that the study complies with certain FDA regulatory requirements in order to use the study as support for an IND or application for marketing approval or licensure, including that the study was conducted in accordance with GCP, including review and approval by an

independent ethics committee and use of proper procedures for obtaining informed consent from subjects, and the FDA is able to validate the data from the study through an onsite inspection if the FDA deems such inspection necessary. The GCP requirements encompass both ethical and data integrity standards for clinical studies.

BLA Submission and Review

Assuming successful completion of all required testing in accordance with all applicable regulatory requirements, the results of product development, nonclinical studies and clinical trials are submitted to the FDA as part of a BLA requesting approval to market the product for one or more indications. The BLA must include all relevant data available from pertinent preclinical studies and clinical trials, including negative or ambiguous results as well as positive findings, together with detailed CMC information, and proposed labeling, among other things. Data can come from company-sponsored clinical studies intended to test the safety and effectiveness of the product, or from a number of alternative sources, including studies initiated and sponsored by investigators. The submission of a BLA requires payment of a substantial application user fee to the FDA, unless a waiver or exemption applies.

In addition, under the Pediatric Research Equity Act ("PREA"), a BLA or supplement to a BLA must contain data to assess the safety and effectiveness of the biological product candidate 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. The Food and Drug Administration Safety and Innovation Act requires that a sponsor who is planning to submit a marketing application for a biological product that includes a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration submit an initial pediatric study plan within sixty days after an end-of-Phase 2 meeting or as may be agreed between the sponsor and FDA. Unless otherwise required by regulation, PREA does not apply to any biological product for an indication for which orphan designation has been granted, except that the PREA will apply to an original BLA for a new active ingredient that is orphan-designated if the biologic is a molecularly targeted cancer product intended for the treatment of an adult cancer and is directed at a molecular target that the FDA determines to be substantially relevant to the growth or progression of a pediatric cancer.

Within 60 days following submission of the application, the FDA reviews a BLA submitted to determine if it is substantially complete before the agency accepts it for filing. The FDA may refuse to file any BLA that it deems incomplete or not properly reviewable at the time of submission and may request additional information. In this event, the BLA must be resubmitted with the additional information. Once a BLA has been accepted for filing, the FDA's goal is to review standard applications within ten months after the filing date, or, if the application qualifies for priority review, six months after the FDA accepts the application for filing. In both standard and priority reviews, the review process may also be extended by FDA requests for additional information or clarification. The FDA reviews a BLA to determine, among other things, whether a product is safe, pure and potent and the facility in which it is manufactured, processed, packed or held meets standards designed to assure the product's continued safety, purity and potency. The FDA may convene an advisory committee to provide clinical insight on application review questions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions. Before approving a BLA, the FDA will typically inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving a BLA, the FDA will typically inspect one or more clinical sites to assure compliance with GCPs. If the FDA determines that the application, manufacturing process or manufacturing facilities are not acceptable, it will outline the deficiencies in the submission and often will request additional testing or information. Notwithstanding the submission of any requested additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

After the FDA evaluates a BLA and conducts inspections of manufacturing facilities where the investigational product and/or its drug substance will be produced, the FDA may issue an approval letter or a Complete Response letter. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A Complete Response letter will describe all of the deficiencies that the FDA has identified in the BLA, except that where the FDA determines that the data supporting the application are inadequate to support approval, the FDA may issue the Complete Response letter without first conducting required inspections, testing

submitted product lots and/or reviewing proposed labeling. In issuing the Complete Response letter, the FDA may recommend actions that the applicant might take to place the BLA in condition for approval, including requests for additional information or clarification. The FDA may delay or refuse approval of a BLA if applicable regulatory criteria are not satisfied, require additional testing or information and/or require post-marketing testing and surveillance to monitor safety or efficacy of a product.

If regulatory approval of a product is granted, such approval will be granted for particular indications and may entail limitations on the indicated uses for which such product may be marketed. For example, the FDA may approve the BLA with a risk evaluation and mitigation strategy ("REMS") to ensure the benefits of the product outweigh its risks. A REMS is a safety strategy to manage a known or potential serious risk associated with a product and to enable patients to have continued access to such medicines by managing their safe use, and could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. The FDA also may condition approval on, among other things, changes to proposed labeling or the development of adequate controls and specifications. Once approved, the FDA may withdraw the product approval if compliance with pre-and post-marketing requirements is not maintained or if problems occur after the product reaches the marketplace. The FDA may require one or more Phase 4 post-market studies and surveillance to further assess and monitor the product's safety and effectiveness after commercialization, and may limit further marketing of the product based on the results of these post-marketing studies.

NDA Submission and Review

Following successful completion of the required clinical testing and the results of the pre-clinical and clinical studies, together with detailed CMC information and proposed labeling, among other information, are submitted to the FDA as part of an NDA requesting approval to market the product for one or more indications. In most cases, the submission of an NDA is subject to an application user fee. Under the Prescription Drug User Fee Act guidelines, the FDA has a target of ten months from the date of "filing" of a standard NDA for a new molecular entity to review and act on the submission. This review typically takes twelve months from the date the NDA is submitted to the FDA. Therapies that have Orphan Drug Designation are granted Priority Review. Under the Prescription Drug User Fee Act guidelines, the FDA has a target of six months from the date of "filing" of a standard NDA for a new molecular entity to review and act on the submission. This review typically takes ten months from the date the NDA is submitted to the FDA.

The BPCA is a U.S. federal law enacted in 2002 (and made permanent in 2012) that incentivizes pharmaceutical companies to conduct pediatric clinical trials by offering six months of additional market exclusivity for drugs studied in children. The program works through FDA-issued "Written Requests" that specify needed pediatric studies. While the FDA may issue a Written Requests on their own, generally a company must request the Written Requests by submitting a Proposed Pediatric Study Request to the FDA. If the FDA agrees to issue the Written Requests in response to the Proposed Pediatric Study Request and the company completes these studies, they receive the exclusivity extension regardless of whether the drug proves safe or effective in children.

In addition, under the Pediatric Research Equity Act of 2003, certain NDAs or supplements to an NDA must contain data that is adequate to assess the safety and effectiveness of the drug 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. The FDA may, on its own initiative or at the request of the applicant, 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. Therapies that have Orphan Drug Designation are exempt from PREA.

The FDA also may require submission of a REMS plan to ensure that the benefits of the drug outweigh its risks. REMS plans typically include medication guides, physician communication plans, assessment plans, and/or elements to assure safe use, such as restricted distribution methods, patient registries, or other risk minimization tools.

The FDA conducts a preliminary review of all NDAs within the first 60 days after submission, before accepting them for filing, to determine whether they are sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA for filing. In this event, the application must be resubmitted with the requested information. The resubmitted application is also subject to review before the

FDA accepts it for filing. After the submission is accepted for filing, the FDA begins a substantive review. The FDA reviews an NDA to determine whether the drug is safe and effective and whether the facility in which it is manufactured, processed, packaged or held meets standards designed to assure the product's continued safety, quality and purity.

The FDA may refer an application for a novel drug to an advisory committee. 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.

Before approving an NDA, the FDA typically will inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA may inspect one or more clinical trial sites to assure compliance with GCP requirements.

After evaluating the NDA and all related information, including the advisory committee recommendation, if any, and inspection reports regarding the manufacturing facilities and clinical trial sites, the FDA may issue an approval letter or a Complete Response letter. A Complete Response letter generally contains a statement of specific conditions that must be met in order to secure final approval of the NDA and may require additional clinical or pre-clinical testing for the FDA to reconsider the application. Even after submission of this additional information, the FDA may decide that the application does not satisfy the regulatory criteria for approval. If and when those conditions have been met to the FDA's satisfaction, the FDA will typically issue an approval letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications.

Even if the FDA approves a product, it may limit the approved indications for use of the product. It may also require that contraindications, warnings or precautions be included in the product labeling or require that post-approval studies, including Phase 4 clinical trials, be conducted to further assess a drug's safety after approval. In addition, the FDA may mandate testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution and use restrictions or other risk management mechanisms under a REMS. This can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-marketing studies or surveillance programs. After approval, some types of alterations, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Additional Considerations for Gene Therapy Products

In addition to the regulations discussed above, there are a number of additional considerations that apply to clinical trials involving the use of gene therapy. Supervision of human gene transfer trials includes evaluation and assessment by an institutional biosafety committee, a local institutional committee that reviews and oversees research utilizing recombinant or synthetic nucleic acid molecules at that institution. The IBC assesses the safety of the research and identifies any potential risk to public health or the environment, and such review may result in some delay before initiation of a clinical trial. The FDA has issued various guidance documents regarding gene therapies, which outline additional factors that the FDA will consider at each of the above stages of development and relate to, among other things: the proper preclinical assessment of gene therapies; the CMC information that should be included in an IND application; the proper design of tests to measure product efficacy or potency in support of an IND or BLA application; and measures to observe delayed adverse effects in subjects who have been exposed to investigational gene therapies when the risk of such effects is high. For instance, the FDA usually recommends that sponsors observe all surviving subjects who receive treatment using gene therapies that are based on adeno-associated virus vectors in clinical trials for potential gene therapy-related delayed adverse events for a minimum five-year period. FDA does not require the long-term tracking to be complete prior to its review of the BLA.

Expedited Development and Review Programs

The FDA offers a number of expedited development and review programs for qualifying product candidates. The Fast Track program is intended to expedite or facilitate the process for reviewing new products that meet certain criteria. Specifically, new products are eligible for Fast Track designation if they are intended to treat a serious or life-threatening disease or condition and data demonstrate the potential to address unmet medical needs for the disease or condition. Fast track designation applies to the combination of the product and the specific indication for which it is being studied. The sponsor of a Fast Track product has opportunities for more frequent interactions with the review team during product development and, once a BLA is submitted, the product may be eligible for priority review. A Fast Track product may also be eligible for rolling review, where the FDA may consider for review sections of the BLA or NDA on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the BLA or NDA, the FDA agrees to accept sections of the BLA or NDA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the BLA or NDA. We have received Fast Track designation for PLX-200 for the treatment of CLN2 (for SOTERIA) and CLN3 (for STARLIGHT).

Additionally, products studied for their safety and effectiveness in treating serious or life-threatening diseases or conditions may receive accelerated approval upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. As a condition of accelerated approval, the FDA will generally require the sponsor to perform adequate and well-controlled post-marketing clinical studies to verify and describe the anticipated effect on irreversible morbidity or mortality or other clinical benefit. Under the Food and Drug Omnibus Reform Act of 2022, the FDA may require, as appropriate, that such studies be underway prior to approval or within a specific time period after the date of approval for a product granted accelerated approval. Products receiving accelerated approval may be subject to expedited withdrawal procedures if the sponsor fails to conduct the required post-marketing studies or if such studies fail to verify the predicted clinical benefit. 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.

In 2017, the FDA established a new RMAT designation as part of its implementation of the 21st Century Cures Act (the "Cures Act"). The RMAT designation program is intended to fulfill the Cures Act requirement that the FDA facilitate an efficient development program for, and expedite review of, any drug that meets the following criteria: (i) the drug qualifies as a RMAT, which is defined as a cell therapy, therapeutic tissue engineering product, human cell and tissue product, or any combination product using such therapies or products, with limited exceptions; (ii) the drug is intended to treat, modify, reverse, or cure a serious or life-threatening disease or condition; and (iii) preliminary clinical evidence indicates that the drug has the potential to address unmet medical needs for such a disease or condition. RMAT designation provides all the benefits of breakthrough therapy designation, including more frequent meetings with the FDA to discuss the development plan for the product candidate and eligibility for rolling review and priority review.

Products granted RMAT designation may also be eligible for accelerated approval on the basis of a surrogate or intermediate endpoint reasonably likely to predict long-term clinical benefit, or reliance upon data obtained from a meaningful number of sites, including through expansion to additional sites. When appropriate, the FDA can permit fulfillment of post-approval requirements for an RMAT that has received accelerated approval through: the submission of clinical evidence, preclinical studies, clinical trials, patient registries or other sources of real world evidence such as electronic health records; the collection of larger confirmatory datasets; or post-approval monitoring of all patients treated with the therapy prior to approval. A product intended to treat a serious or life-threatening disease or condition may also be eligible for breakthrough therapy designation to expedite its development and review. A product can receive breakthrough therapy designation if preliminary clinical evidence indicates that the product, alone or in combination with one or more other drugs or biologics, may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The designation includes all of the Fast Track program features, as well as more intensive FDA interaction and guidance beginning as early as Phase 1 and an organizational commitment to expedite the development and review of the product, including involvement of senior managers.

Any marketing application for a drug product submitted to the FDA for approval, including a product with a Fast Track designation and/or breakthrough therapy designation, may be eligible for other types of FDA programs intended to expedite the FDA review and approval process, such as priority review and accelerated approval. A product is eligible for priority review if there is evidence it has the potential to provide a significant improvement in the treatment, diagnosis or prevention of a serious disease or condition. For original BLAs and NDAs, priority review designation means the FDA's goal is to take action on the marketing application within six months of the 60-day filing date (as compared to ten months under standard review). We have not sought priority review for any of our product candidates to date, but may do so in the future.

Fast track designation, breakthrough therapy designation, RMAT designation and priority review do not change the standards for approval but may expedite the development or approval process. Even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

Orphan Drug Designation and Exclusivity

Under the Orphan Drug Act of 1983, the FDA may grant orphan drug designation to a product candidate intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000 individuals in the United States, or 200,000 or more individuals in the United States for which there is no reasonable expectation that the cost of developing and making available in the United States a drug or biologic for this type of disease or condition will be recovered from sales in the United States for that product candidate. Orphan drug designation must be requested before submitting a BLA or NDA. After the FDA grants orphan drug designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. The orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review or approval process.

If a product that has orphan drug designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to orphan drug exclusive approval (or exclusivity), which means that the FDA may not approve any other applications to market the same product for the same approved use or indication for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity by means of greater effectiveness, greater safety or providing a major contribution to patient care or if the holder of the orphan drug exclusivity cannot assure the availability of sufficient quantities of the orphan drug to meet the needs of patients with the same use or indication for which the already-approved or licensed product was approved or licensed. Orphan drug exclusivity does not prevent the FDA from approving a different drug or biologic for the same disease or condition, or the same drug or biologic for a different disease or condition. Among the other benefits of orphan drug designation are tax credits for certain research and fee waivers.

A designated orphan drug may not receive orphan drug exclusivity if it is approved for a use that is broader than the indication for which it received orphan drug designation. In addition, exclusive marketing rights in the United States may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition.

There is some uncertainty with respect to the FDA's interpretation of the scope of orphan drug exclusivity. Historically, exclusivity was specific to the orphan indication for which the drug was approved. As a result, the scope of exclusivity was interpreted as preventing approval of a competing product. However, in 2021, the federal court in *Catalyst Pharmaceuticals, Inc. v. Becerra* suggested that orphan drug exclusivity covers the full scope of the orphan-designated "disease or condition" regardless of whether a drug obtained approval for a narrower use.

Combination Therapy

Combination therapy is a treatment modality that involves the use of two or more drugs to be used in combination to treat a disease or condition. If those drugs are combined in one dosage form, such as one pill, that is known as a fixed dose combination product and it is reviewed pursuant to the FDA's Combination Rule at 21 CFR 300.50. The rule provides that two or more drugs may be combined in a single dosage form when each

component contributes to the claimed effects and the dosage of each component (amount, frequency, duration) is such that the combination is safe and effective for a significant patient population requiring such concurrent therapy as defined in the labeling for the drug.

But not all combination therapy falls under the category of a fixed dose combination. For example, the FDA recognizes that two drugs in separate dosage forms and in separate packaging, that otherwise might be administered as monotherapy for an indication, also may be used in combination for the same indication. In 2013, the FDA issued guidance to assist sponsors that were developing the range of combination therapies that fall outside the category of fixed dose combinations. That guidance provides recommendations and advice on such topics as: (i) assessment at the outset whether two or more therapies are appropriate for use in combination; (ii) guiding principles for nonclinical and clinical development of the combination; (iii) options for regulatory pathways to seek marketing approval of the combination; and (iv) post-marketing safety monitoring and reporting obligations. Given the wide range of potential combination therapy variations, the FDA indicated it intends to assess each potential combination on a case-by case basis and encouraged sponsors to engage in early and regular consultation with the relevant review division at the agency throughout the development process for its proposed combination.

Post Approval Requirements

Any products manufactured or distributed by us pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to record-keeping, reporting of adverse experiences, periodic reporting, product sampling and distribution, and advertising and promotion of the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA review and approval. There also are continuing user fee requirements, under which the FDA assesses an annual program fee for any marketed products. The FDA may impose a number of post-approval requirements as a condition of approval of an NDA or BLA. For example, the FDA may require post-marketing testing, including Phase 4 clinical trials, and surveillance to further assess and monitor the product's safety and effectiveness after commercialization.

In addition, product manufacturers and 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 cGMPs, which impose certain procedural and documentation requirements upon us and our third-party manufacturers. Changes to the manufacturing process are strictly regulated, and, depending on the significance of the change, may require prior FDA approval before being implemented.

FDA regulations also require investigation and correction of any deviations from cGMPs and impose reporting requirements upon us and any third-party manufacturers that we may decide to use. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain compliance with cGMPs and other aspects of regulatory compliance.

The FDA may withdraw 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 studies to assess new safety risks; or imposition of distribution restrictions or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of a product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical studies;
- refusal of the FDA to approve pending applications or supplements to approved applications, or suspension or revocation of existing product approvals;
- product seizure or detention, or refusal of the FDA to permit the import or export of products;

- consent decrees, corporate integrity agreements, debarment or exclusion from federal healthcare programs;
- mandated modification of promotional materials and labeling and the issuance of corrective information;
- the issuance of safety alerts, Dear Healthcare Provider letters, press releases and other communications containing warnings or other safety information about the product; or
- injunctions or the imposition of civil or criminal penalties.

The FDA closely regulates the marketing, labeling, advertising and promotion of biologics. A company can make only those claims relating to safety and efficacy, purity and potency that are approved by the FDA and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses. Failure to comply with these requirements can result in, among other things, adverse publicity, warning letters, corrective advertising and potential civil and criminal penalties. Physicians may prescribe legally available products for uses that are not described in the product's labeling and that differ from those tested by us and approved by the FDA. Such off-label uses are common across medical specialties. Physicians may believe that such off-label uses are the best treatment for many patients in varied circumstances. The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, restrict manufacturer's communications on the subject of off-label use of their products.

Biosimilars and Reference Product Exclusivity

The Affordable Care Act ("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 highly similar, or "biosimilar," to or interchangeable with an FDA-approved reference biological product. The FDA has issued several guidance documents outlining an approach to review and approval of biosimilars.

Biosimilarity, which requires that there be no clinically meaningful differences between the biological product and the reference product in terms of safety, purity, and potency, is generally shown through analytical studies, animal studies, and a clinical study or studies. Interchangeability requires that a product is biosimilar to the reference product and the product must demonstrate that it can be expected to produce the same clinical results as the reference product in any given patient and, for products that are administered multiple times to an individual, the biologic and the reference biologic may be alternated or switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic. A product shown to be biosimilar or interchangeable with an FDA-approved reference biological product may rely in part on the FDA's previous determination of safety and effectiveness for the reference product for approval, which can potentially reduce the cost and time required to obtain approval to market the product. Complexities associated with the larger, and often more complex, structures of biological products, as well as the processes by which such products are manufactured, pose significant hurdles to implementation of the abbreviated approval pathway that are still being worked out by the FDA.

The FDA has issued guidance documents intended to inform prospective applicants and facilitate the development of proposed biosimilars and interchangeable biosimilars, as well as to describe the FDA's interpretation of certain statutory requirements added by the BPCIA.

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 licensed 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 licensed. 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 that applicant's own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of its product. The BPCIA also created certain exclusivity periods for biosimilars approved as interchangeable products. At this juncture, it is unclear whether products deemed "interchangeable" by the FDA will, in fact, be readily substituted by pharmacies, which are governed by state pharmacy law.

A reference biologic is granted twelve years of exclusivity from the time of first licensure of the reference product. The first biologic product submitted under the abbreviated approval pathway that is determined to be interchangeable with the reference product has exclusivity against other biologics submitted under the abbreviated approval pathway for the lesser of (i) one year after the first commercial marketing, (ii) 18 months after approval if there is no legal challenge, (iii) 18 months after the resolution in the applicant's favor of a lawsuit challenging the biologics' patents if an application has been submitted, or (iv) 42 months after the application has been approved if a lawsuit is ongoing within the 42-month period.

A biological product can also obtain pediatric market exclusivity in the United States. Pediatric exclusivity, if granted, adds six months to existing exclusivity periods and patent terms. This six-month exclusivity, which runs from the end of other exclusivity protection or patent term, may be granted based on the voluntary completion of a pediatric study in accordance with an FDA-issued "Written Request" for such a study.

The BPCIA is complex and continues to be interpreted and implemented by the FDA. On December 20, 2020, Congress amended the Public Health Service Act ("PHSA") as part of the COVID-19 relief bill to further simplify the biosimilar review process by making it optional to show that conditions of use proposed in labeling have been previously approved for the reference product, which used to be a requirement of the application. In addition, government proposals have sought to reduce the 12-year reference product exclusivity period. Other aspects of the BPCIA, some of which may impact the BPCIA exclusivity provisions, have also been the subject of recent litigation. As a result, the ultimate impact, implementation, and impact of the BPCIA is subject to significant uncertainty.

As discussed below, the Inflation Reduction Act of 2022 ("IRA") is a significant new law that intends to foster generic and biosimilar competition and to lower drug and biologic costs.

Abbreviated New Drug Applications for Generic Drugs

In 1984, with passage of the Drug Price Competition and Patent Term Restoration Act of 1984 ("Hatch-Waxman Amendments") amending the FDCA, Congress authorized the FDA to approve generic drugs that are the same as drugs previously approved by the FDA under the NDA provisions of the statute. To obtain approval of a generic drug, an applicant must submit an abbreviated new drug application ("ANDA") to the agency. Upon approval of an ANDA, the FDA indicates that the generic product is "therapeutically equivalent" to the drug product previously approved under an NDA, known as the reference listed drug ("RLD"), and it assigns a therapeutic equivalence rating to the approved generic drug in its publication "Approved Drug Products with Therapeutic Equivalence Evaluations," also referred to as the "Orange Book." Physicians and pharmacists consider the therapeutic equivalence rating to mean that a generic drug is fully substitutable for the RLD. In addition, by operation of certain state laws and numerous health insurance programs, the FDA's designation of a therapeutic equivalence rating often results in substitution of the generic drug without the knowledge or consent of either the prescribing physician or patient.

Under the Hatch-Waxman Amendments, the FDA may not approve an ANDA until any applicable period of nonpatent exclusivity for the RLD has expired. The FDCA provides a period of five years of data exclusivity for NDAs containing a new chemical entity. In cases where such exclusivity has been granted, an ANDA may not be filed with the FDA until the expiration of five years unless the submission is accompanied by a Paragraph IV certification (discussed further below), in which case the applicant may submit its application four years following the original product approval. The FDCA also provides for a period of three years of exclusivity if the NDA includes reports of one or more new clinical investigations, other than bioavailability or bioequivalence studies, that were conducted by or for the applicant and are essential to the approval of the application. This three-year exclusivity period often protects changes to a previously approved drug product, such as a new dosage form, route of administration, combination or indication.

Hatch-Waxman Patent Certification and the 30 Month Stay

Upon approval of an NDA or a supplement thereto, NDA sponsors are required to list with the FDA each patent with claims that cover the applicant's product or a method of using the product. When an ANDA applicant files its application with the FDA, the applicant is required to certify to the FDA concerning any patents listed for the reference product in the Orange Book, except for patents covering methods of use for which the ANDA applicant is not seeking approval.

A certification that the new product will not infringe the already approved product's listed patents or that such patents are invalid or unenforceable is called a Paragraph IV certification. If the applicant does not challenge the listed patents or indicate that it is not seeking approval of a patented method of use, the ANDA application will not be approved until all the listed patents claiming the referenced product have expired. If the ANDA applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA and patent holders once the ANDA has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days after the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA until the earlier of 30 months, expiration of the patent, settlement of the lawsuit or a decision in the infringement case that is favorable to the ANDA applicant.

505(b)(2) New Drug Applications

As an alternative path to FDA approval for modifications to formulations or uses of products previously approved by the FDA pursuant to an NDA, an applicant may submit an NDA under Section 505(b)(2) of the FDCA. Section 505(b)(2) was enacted as part of the Hatch-Waxman Amendments and permits the filing of an NDA where at least some of the information required for approval comes from studies not conducted by, or for, the applicant, and for which the applicant has not obtained a right of reference. If the 505(b)(2) applicant can establish that reliance on the FDA's previous findings of safety and effectiveness is scientifically and legally appropriate, it may eliminate the need to conduct certain preclinical studies or clinical trials of the new product. The FDA may also require companies to perform additional bridging studies or measurements, including clinical trials, to support the change from the previously approved reference drug. The FDA may then approve the new drug candidate for all, or some, of the label indications for which the reference drug has been approved, as well as for any new indication sought by the 505(b)(2) applicant.

To the extent that a Section 505(b)(2) applicant is relying on studies conducted for an already approved product, the applicant is required to certify to the FDA concerning any patents listed for the approved product in the Orange Book to the same extent that an ANDA applicant would. As a result, approval of a 505(b)(2) NDA can be stalled until all the listed patents claiming the referenced product have expired, until any non-patent exclusivity, such as exclusivity for obtaining approval of a new chemical entity, listed in the Orange Book for the referenced product has expired, and, in the case of a Paragraph IV certification and subsequent patent infringement suit, until the earlier of 30 months, settlement of the lawsuit or a decision in the infringement case that is favorable to the Section 505(b)(2) applicant.

Patent Term Extension

In the United States, owners of relevant drug patents may apply for up to a five-year patent extension, which permits patent term restoration as compensation for the patent term lost during the FDA regulatory process. The length of the patent term extension is related to the length of time the drug is under regulatory review. The time can be shortened if the FDA determines that the applicant did not pursue licensure with due diligence. The total patent term after the extension may not exceed 14 years from the date of product licensure. Only one patent applicable to a licensed product is eligible for extension and only those claims covering the product, a method for using it, or a method for manufacturing it may be extended and the application for the extension must be submitted prior to the expiration of the patent in question. However, we may not be granted an extension 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. Some, but not all, foreign jurisdictions possess patent term extension or other additional patent exclusivity mechanisms that may be more or less stringent and comprehensive than those of the United States.

Rare Pediatric Disease Designation and Priority Review Vouchers

Under the FDCA, as amended, the FDA incentivizes the development of drugs and biologics intended to treat conditions that meet the definition of a "rare pediatric disease," defined to mean a serious or life-threatening disease in which the serious or life-threatening manifestations primarily affect individuals aged from birth to 18 years and the disease affects fewer than 200,000 individuals in the United States or affects more than 200,000 in the United States and for which there is no reasonable expectation that the cost of developing and making in the United States a drug for such disease or condition will be received from sales in the United States of such drug.

We have received rare pediatric disease designation for PLX-300 for the treatment of Tay-Sachs and Sandhoff disease, Krabbe disease, and Niemann-Pick disease Type A and B, and we may request such designation for future product candidates if the diseases they are intended to treat meet the definition of a rare pediatric disease.

Other Healthcare Laws and Compliance Requirements

Pharmaceutical companies are subject to additional healthcare regulation and enforcement by the federal government and by authorities in the states and foreign jurisdictions in which they conduct their business. Such laws include, without limitation: the federal Anti-Kickback Statute ("AKS"); the federal False Claims Act ("FCA"); the Health Insurance Portability and Accountability Act of 1996 ("HIPAA") and similar foreign, federal and state fraud, abuse and transparency laws.

The AKS prohibits, among other things, persons and entities from knowingly and willfully soliciting, receiving, offering or paying remuneration, to induce, or in return for, either the referral of an individual, or the purchase or recommendation of an item or service for which payment may be made under any federal healthcare program. The term remuneration has been interpreted broadly to include anything of value. The AKS has been interpreted to apply to arrangements between pharmaceutical manufacturers on one hand, and prescribers and purchasers on the other. The government often takes the position that to violate the AKS, only one purpose of the remuneration need be to induce referrals, even if there are other legitimate purposes for the remuneration. There are a number of statutory exceptions and regulatory safe harbors protecting some common commercial activities from AKS prosecution, but they are drawn narrowly and practices that involve remuneration, such as consulting agreements, or persons in a position to refer or recommend federally reimbursable healthcare business may be alleged to be intended to induce prescribing, purchasing or recommending, and may be subject to scrutiny if they do not qualify for an exception or regulatory safe harbor. Qualifying for a statutory exception or regulatory safe harbor requires satisfying all of the criteria for the exception or safe harbor. Our practices may not in all cases meet all of the criteria for protection under a statutory exception or regulatory safe harbor. Failure to meet all of the requirements of a particular applicable statutory exception or regulatory safe harbor does not make the conduct per se illegal under the AKS but it does increase the risk of regulatory scrutiny. Ultimately, the legality of the arrangement will be evaluated on a case-by-case basis based on a cumulative review of all of its facts and circumstances. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.

The FCA, which can be enforced through civil whistleblower or qui tam actions, prohibits, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment of federal government funds, including in federal healthcare programs, that are false or fraudulent. Pharmaceutical and other healthcare companies have been prosecuted under these laws for engaging in a variety of different types of conduct that caused the submission of false claims to federal healthcare programs. Under the AKS, for example, a claim resulting from a violation of the AKS is deemed to be a false or fraudulent claim for purposes of the FCA.

HIPAA created additional federal criminal statutes that prohibit, among other things, executing a scheme to defraud any healthcare benefit program, including private third-party payors, and making false statements relating to healthcare matters. A person or entity does not need to have actual knowledge of the healthcare fraud statute implemented under HIPAA or specific intent to violate the statute in order to have committed a violation.

The FDCA addresses, among other things, the design, production, labeling, promotion, manufacturing, and testing of drugs, biologics and medical devices, and prohibits such acts as the introduction into interstate commerce of adulterated or misbranded drugs or devices. The PHSA also prohibits the introduction into interstate commerce of unlicensed or mislabeled biological products.

The U.S. federal Physician Payments Sunshine Act requires certain manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program, with specific exceptions, to annually report to the Centers for Medicaid & Medicare Services ("CMS") information related to payments or other transfers of value to various healthcare professionals including physicians, physician assistants, nurse practitioners, clinical nurse specialists, certified nurse anesthetists, certified nurse-midwives, and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Beginning on January 1, 2023, California Assembly Bill 1278 requires California physicians and surgeons to notify patients of the Open Payments database established under the federal Physician Payments Sunshine Act.

We are also subject to federal price reporting laws and federal consumer protection and unfair competition laws. Federal price reporting laws require manufacturers to calculate and report complex pricing metrics to government programs, where such reported prices may be used in the calculation of reimbursement and/or discounts on approved products. Federal consumer protection and unfair competition laws broadly regulate marketplace activities and activities that potentially harm consumers.

We are also subject to additional similar U.S. state and foreign law equivalents of each of the above federal laws, which, in some cases, differ from each other in significant ways, and may not have the same effect, thus complicating compliance efforts. If our operations are found to be in violation of any of such laws or any other governmental regulations that apply, we may be subject to penalties, including, without limitation, civil, criminal and administrative penalties, damages, fines, exclusion from government-funded healthcare programs, such as Medicare and Medicaid or similar programs in other countries or jurisdictions, integrity oversight and reporting obligations to resolve allegations of non-compliance, disgorgement, individual imprisonment, contractual damages, reputational harm, diminished profits and the curtailment or restructuring of our operations.

Data Privacy and Security

Numerous state, federal, and foreign laws govern the collection, dissemination, use, access to, confidentiality, and security of personal information, including health-related information. In the United States, numerous federal and state laws and regulations, including state data breach notification laws, state health information privacy laws, and federal and state consumer protection laws and regulations, govern the collection, use, disclosure, and protection of health-related and other personal information and could apply to our operations or the operations of our partners.

For example, HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act ("HITECH"), and their respective implementing regulations impose data privacy, security, and breach notification obligations on certain health care providers, health plans, and health care clearinghouses, known as covered entities, as well as their business associates and their covered subcontractors that perform certain services that involve using, disclosing, creating, receiving, maintaining, or transmitting individually identifiable protected health information ("PHI") for or on behalf of such covered entities. These requirements imposed by HIPAA and HITECH on covered entities and business associates include entering into agreements that require business associates protect PHI provided by the covered entity against improper use or disclosure, among other things; following certain standards for the privacy of PHI, which limit the disclosure of a patient's past, present, or future physical or mental health or condition or information about a patient's receipt of health care if the information identifies, or could reasonably be used to identify, the individual; ensuring the confidentiality, integrity, and availability of all PHI created, received, maintained, or transmitted in electronic form, to identify and protect against reasonably anticipated threats or impermissible uses or disclosures to the security and integrity of such PHI; and reporting of breaches of PHI to individuals and regulators.

Entities that are found to be in violation of HIPAA may be subject to significant civil, criminal, and administrative fines and penalties and/or additional reporting and oversight obligations if required to enter into a resolution agreement and corrective action plan with HHS to settle allegations of HIPAA non-compliance. A covered entity or business associate is also liable for civil money penalties for a violation that is based on an act or omission of any of its agents, which may include a downstream business associate, as determined according to the federal common law of agency. HITECH also increased the civil and criminal penalties applicable to covered entities and business associates and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce HIPAA and seek attorneys' fees and costs associated with pursuing federal civil actions. To the extent that we submit electronic healthcare claims and payment transactions that do not comply with the electronic data transmission standards established under HIPAA and HITECH, payments to us may be delayed or denied.

In addition, state health information privacy laws, such as California's Confidentiality of Medical Information Act and Washington's My Health My Data Act, that govern the privacy and security of health-related information, specifically, may apply even when HIPAA does not and impose additional requirements.

Even when HIPAA and state health information privacy laws do not apply, according to the FTC and state attorney general, violating consumers' privacy rights or failing to take appropriate steps to keep consumers' personal information secure may constitute unfair acts or practices in or affecting commerce in violation of Section 5(a) of the Federal Trade Commission Act and state consumer protection laws.

In addition, certain state laws, such as the California Consumer Privacy Act of 2018 ("CCPA"), as amended by the California Privacy Rights Act of 2020, govern the privacy and security of personal information, including health-related information in certain circumstances, some of which are more stringent than HIPAA in various ways. Numerous other states have passed similar laws, but many differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts. The CCPA applies to personal data of consumers, business representatives, and employees, and imposes obligations on certain businesses that do business in California, including to provide specific disclosures in privacy notices, and affords rights to California residents in relation to their personal information. Health information falls under the CCPA's definition of personal information where it identifies, relates to, describes, or is reasonably capable of being associated with or could reasonably be linked, directly or indirectly, with a particular consumer or household and is included under a new category of personal information, "sensitive personal information," which is offered greater protection. The CCPA and numerous other comprehensive privacy laws that have passed or are being considered in other states, as well as at the federal and local levels, exempt PHI that is subject to HIPAA; and others exempt covered entities and business associates subject to HIPAA altogether, further complicating compliance efforts, and increasing legal risk and compliance costs for us and the third parties upon whom we rely.

Failure to comply with these laws, where applicable, can result in the imposition of significant civil and/or criminal penalties and private litigation. Privacy and security laws, regulations, and other obligations are constantly evolving, may conflict with each other to complicate compliance efforts, and can result in investigations, proceedings, or actions that lead to significant civil and/or criminal penalties and restrictions on data processing.

Coverage and Reimbursement

In the United States and markets in other countries, patients generally rely on third-party payors to reimburse all or part of the costs associated with their treatment. Adequate coverage and reimbursement from governmental healthcare programs, such as Medicare and Medicaid, and commercial payors is critical to new product acceptance. Our ability to successfully commercialize our product candidates 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. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow it to establish or maintain pricing sufficient to realize a sufficient return on its investment. 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.

Significant uncertainty exists as to the coverage and reimbursement status of any pharmaceutical or biological product for which we obtain regulatory approval. Sales of any product, if approved, depend, in part, on the extent to which such product will be covered by third-party payors, such as federal, state, and foreign government healthcare programs, commercial insurance and managed healthcare organizations, and the level of reimbursement, if any, for such product by third-party payors. Decisions regarding whether to cover any of our product candidates, if approved, the extent of coverage and amount of reimbursement to be provided are made on a plan-by-plan basis. Further, no uniform policy for coverage and reimbursement exists in the United States, and coverage and reimbursement can differ significantly from payor to payor. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement rates, but also have their own methods and approval process apart from Medicare determinations. 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. Factors payors consider in determining reimbursement are based on whether the product is:

- a covered benefit under its health plan;
- safe, effective and medically necessary;
- cost-effective; and
- neither experimental nor investigational.

Third-party payors are increasingly challenging the prices charged for medical products and services, examining the medical necessity and reviewing the cost effectiveness of pharmaceutical or biological products, medical devices and medical services, in addition to questioning safety and efficacy. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit sales of any product that receives approval. Decreases in third-party reimbursement for any product or a decision by a third-party not to cover a product could reduce physician usage and patient demand for the product.

For products administered under the supervision of a physician, obtaining coverage and adequate reimbursement may be particularly difficult because of the higher prices often associated with such drugs. Additionally, separate reimbursement for the product itself or the treatment or procedure in which the product is used may not be available, which may impact physician utilization. In addition, 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 companion diagnostics.

In addition, the U.S. government, state legislatures and foreign governments have continued implementing cost-containment programs, including price controls, restrictions on coverage and reimbursement and requirements for substitution of generic products. The IRA provides CMS with significant new authorities intended to curb drug costs and to encourage market competition. For the first time, CMS will be able to directly negotiate prescription drug prices and to cap out-of-pocket costs. Each year, CMS will select and negotiate a preset number of high-spend drugs and biologics that are covered under Medicare Part B and Part D that do not have generic or biosimilar competition. On August 29, 2023, HHS announced the list of the first ten drugs subject to price negotiations. These price negotiations occurred in 2024. In January 2025, CMS announced a list of 15 additional Medicare Part D drugs that will be subject to price negotiations. The IRA also provides a new "inflation rebate" covering Medicare patients that took effect in 2023 and is intended to counter certain price increases in prescriptions drugs. The inflation rebate provision requires drug manufacturers to pay a rebate to the federal government if the price for a drug or biologic under Medicare Part B and Part D increases faster than the rate of inflation. To support biosimilar competition, beginning in October 2022, qualifying biosimilars may receive a Medicare Part B payment increase for a period of five years. Separately, if a biologic drug for which no biosimilar exists delays a biosimilar's market entry beyond two years, CMS will be authorized to subject the biologics manufacturer to price negotiations intended to ensure fair competition. Notwithstanding these provisions, the IRA's impact on commercialization and competition remains largely uncertain.

In addition, 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. 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. We cannot be sure that reimbursement will be available for any product candidate that we may commercialize and, if reimbursement is available, the level of reimbursement. In addition, many pharmaceutical manufacturers must calculate and report certain price reporting metrics to the government, such as average sales price and best price. Penalties may apply in some cases when such metrics are not submitted accurately and timely. Further, these prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs.

Finally, in some foreign countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. For example, the EU provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. To obtain reimbursement or pricing approval, some of these countries may require the completion of clinical trials that compare the cost effectiveness of a particular product candidate to currently available therapies. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. 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 product candidates. Historically, products launched in the EU do not follow price structures of the United States and generally prices tend to be significantly lower.

Healthcare Reform

The United States and some foreign jurisdictions are considering or have enacted a number of reform proposals to change the healthcare system. There is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality or expanding access. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by federal and state initiatives, including those designed to limit the pricing, coverage, and reimbursement of pharmaceutical and biopharmaceutical products, especially under government-funded health care programs, and increased governmental control of drug pricing.

The ACA, which was enacted in March 2010, substantially changed the way healthcare is financed by both governmental and private insurers in the United States, and significantly affected the pharmaceutical industry. The ACA contains a number of provisions of particular import to the pharmaceutical and biotechnology industries, including, but not limited to, those governing enrollment in federal healthcare programs, a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected, and annual fees based on pharmaceutical companies' share of sales to federal health care programs. Since its enactment, there have been judicial and Congressional challenges to certain aspects of the ACA, and we expect there will be additional challenges and amendments to the ACA in the future. For example, the IRA, among other things, extends enhanced subsidies for individuals purchasing health insurance coverage in ACA marketplaces through plan year 2025. The IRA also eliminates the "donut hole" under the Medicare Part D program beginning in 2025 by significantly lowering the beneficiary maximum out-of-pocket cost and creating a new manufacturer discount program.

Other legislative changes have been proposed and adopted since the ACA was enacted, including automatic aggregate reductions of Medicare payments to providers of on average 2% per fiscal year as part of the federal budget sequestration under the Budget Control Act of 2011. These reductions went into effect in April 2013 and, due to subsequent legislative amendments, will remain in effect until 2032 unless additional action is taken by Congress. In addition, the Bipartisan Budget Act of 2018, among other things, amended the Medicare Act (as amended by the ACA) to increase the point-of-sale discounts that manufacturers must agree to offer under the Medicare Part D coverage discount program from 50% to 70% off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs being covered under Medicare Part D.

Moreover, there has recently been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed and enacted federal and state measures designed to, among other things, reduce the cost of prescription drugs, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products. For example, in May 2019, CMS adopted a final rule allowing Medicare Advantage Plans the option to use step therapy for Part B drugs, permitting Medicare Part D plans to apply certain utilization controls to new starts of five of the six protected class drugs, and requiring the Explanation of Benefits for Part D beneficiaries to disclose drug price increases and lower cost therapeutic alternatives, which went into effect on January 1, 2021. In May 2025, the Trump Administration renewed the idea of international reference pricing through an executive order entitled "Delivering Most-Favored-Nation Prescription Drug Pricing to American Patients," which, among other things, directs the HHS and other agencies to communicate most-favored-nation price targets to pharmaceutical manufacturers to bring prices for U.S. patients in line with comparably developed nations and to facilitate direct-to-consumer purchasing programs. The HHS subsequently issued guidance indicating the MFN target price will be the lowest price paid in an Organisation for Economic Co-operation and Development country with a gross domestic product ("GDP") per capita of at least 60% of the U.S. GDP per capital. In addition, in December 2025, CMS proposed new drug payment models to lower drug prices for Medicare beneficiaries; under the models, CMS would explore potential adjustments to Medicare drug inflation rebate calculations by comparison to international drug pricing information. It is currently unclear whether and to what extent these measures will be implemented and what impact any such implementation would have on our business.

Notwithstanding the IRA, continued legislative and enforcement interest exists in the United States with respect to specialty drug pricing practices. Specifically, we expect government authorities to continue pushing for transparency to drug pricing, reducing the cost of prescription drugs under Medicare, reviewing the relationship between pricing and manufacturer patient programs, and reforming government program reimbursement methodologies for drugs.

Individual states in the United States have also become increasingly active in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain drug access and marketing cost disclosure and transparency measures, and designed to encourage importation from other countries and bulk purchasing. Legally mandated price controls on payment amounts by third-party payors or other restrictions could harm our business, financial condition, results of operations and prospects. 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. This could reduce the ultimate demand for its drugs or put pressure on its drug pricing, which could negatively affect our business, financial condition, results of operations and prospects.

Other Government Regulation Outside of the United States

In addition to regulations in the United States, we are subject to a variety of regulations in other jurisdictions governing, among other things, research and development, clinical trials, testing, manufacturing, safety, efficacy, quality control, labeling, packaging, storage, record keeping, distribution, reporting, export and import, advertising, marketing and other promotional practices involving biological products as well as authorization, approval as well as post-approval monitoring and reporting of our products. Because biologically sourced raw materials are subject to unique contamination risks, their use may be restricted in some countries.

Whether or not we obtain FDA approval for a product, we must obtain the requisite approvals from regulatory authorities in foreign countries prior to the commencement of clinical trials or marketing of the product in those countries. Certain countries outside of the United States have a similar process that requires the submission of a clinical trial application much like the IND prior to the commencement of human clinical trials.

The requirements and process governing the conduct of clinical trials, including requirements to conduct additional clinical trials, product licensing, safety reporting, post-authorization requirements, marketing and promotion, interactions with healthcare professionals, pricing and reimbursement may vary widely from country to country. No action can be taken to market any product in a country until an appropriate approval application has been approved by the regulatory authorities in that country. The current approval process varies from country to country, and the time spent in gaining approval varies from that required for FDA approval. In certain countries, the sales price of a product must also be approved. The pricing review period often begins after market approval is granted. Even if a product is approved by a regulatory authority, satisfactory prices may not be approved for such product, which would make launch of such products commercially unfeasible in such countries.

Regulation in the European Union

European Data Laws

The processing of personal data, including health-related personal data in the European Economic Area ("EEA") is mainly governed by the provisions of the European General Data Protection Regulation (EU) 2016/679 ("GDPR"), and related data protection laws in individual EEA countries. In the UK, the processing of personal data is mainly governed by the GDPR as incorporated into UK law pursuant to the European Union (Withdrawal) Act 2018 (the UK GDPR). The GDPR and UK GDPR impose. The GDPR imposes a number of strict obligations and requirements for the processing, including collecting, analyzing and transferring, of personal data of individuals in the EEA or in the UK, in particular with respect to health data from clinical trials and adverse event reporting. The GDPR and UK GDPR include requirements relating to the legal basis of the processing (such as consent of the individuals to whom the personal data relates), the information provided to the individuals prior to processing their personal data, the personal data breaches which may have to be notified to the national data protection authorities and data subjects, the measures to be taken when engaging processors, and obligations relating to the security and confidentiality of the personal data. EEA countries may also impose additional requirements in relation to the processing of health, genetic and biometric data through their national legislation.

In addition, the GDPR imposes specific restrictions on the transfer of personal data to countries outside of the EEA that are not considered by the European Commission ("EC") to provide an adequate level of data protection. Appropriate safeguards are required to enable such transfers. Among the appropriate safeguards that can be used, the data exporter may use the standard contractual clauses ("SCCs"). When relying on the appropriate safeguards, data exporters, with the assistance of the data importers, are also required to conduct a transfer risk assessment to verify if anything in the law and/or practices of the third country may impinge on the effectiveness of the safeguards in the context of the transfer at stake and, if so, to identify and adopt supplementary measures that are necessary to bring the level of protection of the data transferred to the EU standard of essential equivalence. Where no supplementary measure is suitable, the data exporter should avoid, suspend or terminate the transfer. With regard to the transfer of data from the EEA to the United States, on July 10, 2023, the EC adopted its adequacy decision for the EU-US Data Privacy Framework. On the basis of the new adequacy decision, personal data can flow from the EEA to U.S. companies participating in the framework.

With regard to the transfer of data from the EEA to the UK, based on the EC's adequacy decision of June 28, 2021 and subsequent renewals, personal data may continue to flow freely from the EEA to the UK on the basis that the UK is deemed to provide an adequate level of data protection until December 27, 2031. The adequacy decisions will automatically expire, unless renewed.

With respect to transfers from the UK to other countries, these transfers are also subject to specific transfer rules under the UK regime. These UK international transfer rules broadly mirror the EU GDPR rules.

On February 2, 2022, the UK Secretary of State laid before the UK Parliament the international data transfer agreement ("IDTA") and the international data transfer addendum to the EC's standard contractual clauses for international data transfers ("UK Addendum") and a document setting out transitional provisions. The IDTA and UK Addendum came into force on March 21, 2022 and are the primary UK-approved mechanisms for putting in place appropriate safeguards for UK restricted transfers, subject to transitional arrangements for legacy SCCs. Regarding transfers from the UK to the EEA, the UK Information Commissioner's Office ("ICO") guidance indicates that organizations do not need new arrangements. With regard to the transfer of personal data from the UK to the United States, the UK government has adopted an adequacy decision for the UK Extension to the EU-US Data Privacy Framework, the UK-US Data Bridge, which came into force on October 12, 2023. The UK-US Data Bridge recognizes the United States as offering an adequate level of data protection where the recipient is a U.S. organization certified to the EU-US Data Privacy Framework and participating in the UK Extension to the EU-US Data Privacy Framework.

Failure to comply with the requirements of the GDPR or UK GDPR and the related national data protection laws of the EEA countries may result in significant monetary fines for noncompliance of up to €20 million or £17.5 million (as applicable), 4% of the total worldwide annual turnover (for higher-tier infringements). This is enforced by ICO and is entirely separate from fines under EU GDPR. In addition, violations of national laws can trigger additional, administrative penalties, investigations, corrective orders, temporary or definitive bans, and, in some jurisdictions, and a number of criminal offenses for organizations and, in certain cases, their directors and officers, as well as civil liability claims from individuals whose personal data was processed.

Data protection authorities from the different EEA countries may still implement certain variations, enforce the GDPR and national data protection laws differently, and introduce additional national regulations and guidelines, which adds to the complexity of processing personal data in the EEA.

Furthermore, there are specific requirements relating to processing health data from clinical trials, including public disclosure obligations provided in the EU Clinical Trials Regulation No. 536/2014 ("CTR"), the EMA disclosure initiatives and voluntary commitments by industry. Failure to comply with these obligations could lead to government enforcement actions and significant penalties against us, harm to our reputation, and adversely impact our business and operating results.

Drug and Biologic Development Process

Regardless of where they are conducted, all clinical trials included in applications for marketing authorization ("MA") for human medicines in the EU/EEA must have been carried out in accordance with EU regulations. This means that clinical trials conducted in the EU/EEA have to comply with EU clinical trial legislation but also that clinical trials conducted outside the EU/EEA have to comply with ethical principles equivalent to those set out in

the EEA, including adhering to international good clinical practice and the Declaration of Helsinki. The conduct of clinical trials in the EU is governed by the CTR, which entered into force on January 31, 2022. The CTR replaced the Clinical Trials Directive 2001/20/EC, ("Clinical Trials Directive") and introduced a complete overhaul of the existing regulation of clinical trials for medicinal products in the EU.

Under the CTR, a sponsor is able to submit a single application for approval of a clinical trial through a centralized EU clinical trials portal (the "CTIS"). One national regulatory authority (the reporting EU member state proposed by the applicant) will take the lead in validating and evaluating the application consult and coordinate with the other concerned EU Member States. If an application is rejected, it may be amended and resubmitted through the EU clinical trials portal. If an approval is issued, the sponsor may start the clinical trial in all concerned EU Member States. However, a concerned EU member state may in limited circumstances declare an "opt-out" from an approval and prevent the clinical trial from being conducted in such member state. The CTR also aims to streamline and simplify the rules on safety reporting, and introduces enhanced transparency requirements such as mandatory submission of a summary of the clinical trial results to the EU database, including a layperson's summary. Since January 31, 2023, submission of initial clinical trial applications via CTIS is mandatory and CTIS serves as the single entry point for submission of clinical trial-related information and data. As of January 31, 2025, all ongoing trials approved under the former Clinical Trials Directive need to comply with the CTR and have to be transitioned to CTIS.

Under the CTR, national laws, regulations, and the applicable GCP and Good Laboratory Practice standards must also be respected during the conduct of the trials, including the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use guidelines on Good Clinical Practice and the ethical principles that have their origin in the Declaration of Helsinki. Under the current regime all suspected unexpected serious adverse reactions to the investigated drug that occur during the clinical trial must be reported to the National Competent Authority and to the Ethics Committees of the EU member state where they occur.

During the development of a medicinal product, the EMA and national regulators within the EU provide the opportunity for dialogue and guidance on the development program. At the EMA level, this is usually done in the form of scientific advice, which is given by the Committee for Medicinal Products for Human Use ("CHMP") on the recommendation of the Scientific Advice Working Party. A fee is incurred with each scientific advice procedure, but is significantly reduced for designated orphan medicines. Advice from the EMA is typically provided based on questions concerning, for example, quality (CMC testing), nonclinical testing and clinical studies, and pharmacovigilance plans and risk-management programs. Advice is not legally binding with regard to any future MAA of the product concerned.

Drug Marketing Authorization

In the EEA, after completion of all required clinical testing, pharmaceutical products may only be placed on the market after obtaining an MA. To obtain an MA of a drug under EU regulatory systems, an applicant can submit an MAA through, amongst others, a centralized or decentralized procedure.

To be used or sold in the UK, a drug must have an effective MA granted by the MHRA under the Human Medicines Regulations 2012 (SI 2012/1916), as amended. MA applications are submitted electronically via the MHRA Submissions Portal. Under the MHRA's national assessment procedure, the MHRA generally aims to reach a decision within 210 "clock-on" days, excluding any "clock-stops" while the applicant prepares responses to MHRA questions.

On August 30, 2023, the MHRA published detailed guidance on its recently announced new International Recognition Procedure ("IRP") for MAAs. The IRP applies since January 1, 2024 and replaces existing EU reliance procedures to apply for authorizations from seven international regulators (*e.g.,* Health Canada, Swiss Medic, FDA, EMA, among others). The IRP allows medicinal products approved in other jurisdictions that meet certain criteria to undergo a fast-tracked MHRA review to obtain and/or update a MA in the UK. Applicants can submit initial MAAs to the IRP but the procedure can also be used throughout the lifecycle of a product for post-authorization procedures including line extensions, variations and renewals.

Centralized Authorization Procedure

The centralized procedure provides for the grant of a single MA that is issued by the EC following the scientific assessment of the application by the EMA that is valid for all EU Member States as well as in the three additional EEA Member States (Norway, Iceland and Liechtenstein). The centralized procedure is compulsory for specific medicinal products, including for medicines developed by means of certain biotechnological processes, products designated as orphan medicinal products, advanced therapy medicinal products (gene therapy, somatic cell therapy, or tissue engineered medicines) and medicinal products with a new active substance indicated for the treatment of certain diseases (HIV/AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune diseases and other immune dysfunctions, and viral diseases). For medicinal products containing a new active substance not yet authorized in the EEA before May 20, 2004 and indicated for the treatment of other diseases, medicinal products that constitute significant therapeutic, scientific or technical innovations or for which the grant of a MA through the centralized procedure would be in the interest of public health at EU level, an applicant may voluntarily submit an application for a MA through the centralized procedure.

Under the centralized procedure, the CHMP is responsible for conducting the initial assessment of a drug. The CHMP is also responsible for several post-authorization and maintenance activities, such as the assessment of modifications or extensions to an existing MA. Under the centralized procedure, the timeframe for the evaluation of an MAA by the EMA's CHMP is, in principle, 210 days from receipt of a valid MAA. However, this timeline excludes clock stops, when additional written or oral information is to be provided by the applicant in response to questions asked by the CHMP, so the overall process typically takes a year or more, unless the application is eligible for an accelerated assessment. Accelerated evaluation might be granted by the CHMP in exceptional cases, when a medicinal product is expected to be of a major public health interest, particularly from the point of view of therapeutic innovation. Upon request, the CHMP can reduce the time frame to 150 days if the applicant provides sufficient justification for an accelerated assessment. The CHMP will provide a positive opinion regarding the application only if it meets certain quality, safety and efficacy requirements. This opinion is then transmitted to the EC, which has the ultimate authority for granting MA within 67 days after receipt of the CHMP opinion.

Decentralized Authorization Procedure

Medicines that fall outside the mandatory scope of the centralized procedure have three routes to authorization:

(i) they can be authorized under the centralized procedure if they concern a significant therapeutic, scientific or technical innovation, or if their authorization would be in the interest of public health;

(ii) they can be authorized under a decentralized procedure where an applicant applies for simultaneous authorization in more than one EU member state; or

(iii) they can be authorized in an EU member state in accordance with that state's national procedures and then be authorized in other EU countries by a procedure whereby the countries concerned agree to recognize the validity of the original, national MA (mutual recognition procedure).

The decentralized procedure permits companies to file identical MA applications for a medicinal product to the competent authorities in various EU Member States simultaneously if such medicinal product has not received marketing approval in any EU Member State before. This procedure is available for pharmaceutical products not falling within the mandatory scope of the centralized procedure. The competent authority of a single EU Member State, the reference member state, is appointed to review the application and provide an assessment report. The competent authorities of the other EU Member States, the concerned member states, are subsequently required to grant a MA for their territories on the basis of this assessment. The only exception to this is where the competent authority of an EU Member State considers that there are concerns of potential serious risk to public health, the disputed points are subject to a dispute resolution mechanism and may eventually be referred to the EC, whose decision is binding for all EU Member States.

Risk Management Plan

All new MAAs must include a Risk Management Plan ("RMP") describing the risk management system that the company will put in place and documenting measures to prevent or minimize the risks associated with the product. RMPs are continually modified and updated throughout the lifetime of the medicine as new information becomes available. An updated RMP must be submitted: (i) at the request of EMA or a national competent authority, or (ii) whenever the risk-management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit-risk profile or as a result of an important pharmacovigilance or risk-minimization milestone being reached. The regulatory authorities may also impose specific obligations as a condition of the MA. Since October 20, 2023, all RMPs for centrally authorized products are published by the EMA, subject only to limited redactions.

MA Validity Period

MAs have an initial duration of five years. After these five years, the authorization may subsequently be renewed on the basis of a reevaluation of the risk-benefit balance. Once renewed, the MA is valid for an unlimited period unless the EC or the national competent authority decides, on justified grounds relating to pharmacovigilance, to proceed with only one additional five-year renewal. Applications for renewal must be made to the EMA at least nine months before the five-year period expires.

Any authorization which is not followed by the actual placing of the drug on the EU market (in case of centralized procedure) or on the market of the authorizing member state within three years after authorization ceases to be valid.

For the UK, the period of three years during which the drug has not been marketed in Great Britain will be restarted from the date of conversion to a Great Britain MA. Following Windsor Framework changes, which became effective January 1, 2025, European Commission Union authorizations are no longer valid in Northern Ireland and centrally authorized products are instead authorized by the MHRA under UK-wide marketing authorizations; existing licenses for product licensed by the MHRA that covers Great Britain only become geographically valid UK-wide while retaining their license number/prefix.

On the other hand, for the EU, in the case the drug has been marketed in the UK, the placing on the UK market before the end of the period starting when the UK left the EU on January 31, 2020 and ending on December 31, 2020 (the "Brexit Transition Period") will be taken into account. If, after the end of the Brexit Transition Period, the drug is not placed on any other market of the remaining member states of the EU, the three-year period will start running from the last date the drug was placed on the UK market before the end of the Brexit Transition Period.

Advanced Therapy Medicinal Products

In the EU, medicinal products, including advanced therapy medicinal products ("ATMPs") are subject to extensive pre-and post-market regulation by regulatory authorities at both the EU and national levels. ATMPs comprise gene therapy products, somatic cell therapy products and tissue engineered products, which are genes, cells or tissues that have undergone substantial manipulation and that are administered to human beings in order to cure, diagnose or prevent diseases or regenerate, repair or replace a human tissue. Pursuant to Regulation (EC) No 1394/2007, the CAT is responsible in conjunction with the CHMP for the evaluation of ATMPs. The CHMP and CAT are also responsible for providing guidelines on ATMPs. These guidelines provide additional guidance on the factors that the EMA will consider in relation to the development and evaluation of ATMPs and include, among other things, the preclinical studies required to characterize ATMPs. Although such guidelines are not legally binding, compliance with them is often necessary to gain and maintain approval for product candidates.

In addition to the mandatory RMP, the holder of a MA for an ATMP must put in place and maintain a system to ensure that each individual product and its starting and raw materials, including all substances coming into contact with the cells or tissues it may contain, can be traced through the sourcing, manufacturing, packaging, storage, transport and delivery to the relevant healthcare institution where the product is used.

Exceptional Circumstances/Conditional Approval

Similar to accelerated approval regulations in the United States, conditional MAs can be granted in the EU in exceptional circumstances. A conditional MA can be granted for medicinal products where, although comprehensive clinical data referring to the safety and efficacy of the medicinal product have not been supplied, a number of criteria are fulfilled: (i) the benefit/risk balance of the product is positive, (ii) it is likely that the applicant will be in a position to provide the comprehensive clinical data, (iii) unmet medical needs will be fulfilled by the grant of the MA and (iv) the benefit to public health 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. Once a conditional MA has been granted, the MA holder must fulfil specific obligations within defined timelines. A conditional MA is valid for one year and must be renewed annually, but it can be converted into a standard MA once the MA holder fulfils the obligations imposed and the complete data confirm that the medicine's benefits continue to outweigh its risks.

Data and Market Exclusivity

As in the United States, it may be possible to obtain a period of market and/or data exclusivity in the EU that would have the effect of postponing the entry into the marketplace of a competitor's generic, hybrid or biosimilar product (even if the pharmaceutical product has already received a MA) and prohibiting another applicant from relying on the MA holder's pharmacological, toxicological and clinical data in support of another MA for the purposes of submitting an application, obtaining MA or placing the product on the market. Innovative medicinal products, referred to as New Chemical Entities ("NCE"), approved in the EU qualify for eight years of data exclusivity and 10 years of marketing exclusivity.

An additional non-cumulative one-year period of marketing exclusivity is possible if during the data exclusivity period (the first eight years of the 10-year marketing exclusivity period), the MA holder obtains an authorization for one or more new therapeutic indications that are deemed to bring a significant clinical benefit compared to existing therapies.

The data exclusivity period begins on the date of the product's first MA in the EU. After eight years, a generic product application may be submitted, and generic companies may rely on the MA holder's data. However, a generic product cannot launch until two years later (or a total of 10 years after the first MA in the EU of the innovator product), or three years later (or a total of 11 years after the first MA in the EU of the innovator product) if the MA holder obtains MA for a new indication with significant clinical benefit within the eight-year data exclusivity period. Additionally, another noncumulative one-year period of data exclusivity can be added to the eight years of data exclusivity where an application is made for a new indication for a well-established substance, provided that significant pre-clinical or clinical studies were carried out in relation to the new indication. Another year of data exclusivity may be added to the eight years, where a change of classification of a pharmaceutical product has been authorized on the basis of significant pre-trial tests or clinical trials (when examining an application by another applicant for or holder of market authorization for a change of classification of the same substance the competent authority will not refer to the results of those tests or trials for one year after the initial change was authorized).

Products may not be granted data exclusivity since there is no guarantee that a product will be considered by the EU's regulatory authorities to include a NCE. Even if a compound is considered to be a NCE and the MA applicant is able to gain the prescribed period of data exclusivity, another company nevertheless could also market another version of the medicinal product if such company can complete a full MAA with their own complete database of pharmaceutical tests, preclinical studies and clinical trials and obtain MA of its product.

On April 26, 2023, the EC submitted a proposal for the reform of the European pharmaceutical legislation and negotiations are still ongoing. The timing for finalization of these negotiations and entry into force are unclear.

The current drafts envisage:

- a shortening of the periods of data exclusivity from eight to six years (with transferrable vouchers for an additional year of market protection as an incentive for the development of new antibiotics),
- earlier regulatory guidance and extension of market exclusivity for orphan medicines (depending on certain conditions),
- four-year data exclusivity for additional indications of existing products, and rules governing the availability of products (including shortage prevention plans and some supply obligations for manufacturers).

Orphan Designation and Exclusivity

The criteria for designating an orphan medicinal product in the EU are similar in principle to those in the United States. The EMA grants orphan drug designation if the medicinal product is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting no more than five in 10,000 persons in the EU (prevalence criterion). In addition, Orphan Drug Designation can be granted if, for economic reasons, the medicinal product would be unlikely to be developed without incentives and if there is no other satisfactory method approved in the EU of diagnosing, preventing, or treating the condition, or if such a method exists, the proposed medicinal product is a significant benefit to patients affected by the condition. An application for orphan drug designation (which is not a MA, as not all orphan-designated medicines reach the authorization application stage) must be submitted first before an application for MA of the medicinal product is submitted. The applicant will receive a fee reduction for the MAA if the orphan drug designation has been granted, but not if the designation is still pending at the time the MA is submitted, and sponsors must submit an annual report to EMA summarizing the status of development of the medicine. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process. Designated orphan medicines are eligible for conditional MA.

The EMA's Committee for Orphan Medicinal Products reassesses the orphan drug designation of a product in parallel with the review for a MA; for a product to benefit from market exclusivity it must maintain its orphan drug designation at the time of MA review by the EMA and approval by the EC. Additionally, any MA granted for an orphan medicinal product must only cover the therapeutic indication(s) that are covered by the orphan drug designation. Upon the grant of an MA, orphan drug designation provides up to ten years of market exclusivity in the orphan indication.

During the 10-year period of market exclusivity, with a limited number of exceptions, the regulatory authorities of the EU Member States and the EMA may not accept applications for MA, accept an application to extend an existing MA or grant a MA for other similar medicinal products for the same therapeutic indication. A similar medicinal product is defined as a medicinal product containing a similar active substance or substances as contained in a currently authorized orphan medicinal product, and which is intended for the same therapeutic indication. An orphan medicinal product can also obtain an additional two years of market exclusivity for an orphan-designated condition when the results of specific studies are reflected in the Summary of Product Characteristics ("SmPC") addressing the pediatric population and completed in accordance with a fully compliant Pediatric Investigation Plan ("PIP"). No extension to any supplementary protection certificate can be granted on the basis of pediatric studies for orphan indications.

The 10-year market exclusivity may 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 designation, *i.e.,* the condition prevalence or financial returns criteria under Article 3 of Regulation (EC) No. 141/2000 on orphan medicinal products. When the period of orphan market exclusivity for an indication ends, the orphan drug designation for that indication expires as well. Orphan exclusivity runs in parallel with normal rules on data exclusivity and market protection. Additionally, an MA may be granted to a similar medicinal product (orphan or not) for the same or overlapping indication subject to certain requirements.

In the UK, following the post-Brexit transition period, a system for incentivizing the development of orphan medicines was introduced. Overall, the requirements for orphan designation largely replicate the requirements in the EU and the benefit of market exclusivity has been retained. Products with an orphan designation in the EU can be considered for an orphan MA in Great Britain and, marketing authorizations granted for products that fulfil UK orphan criteria are valid UK-wide regardless of whether there is an EU orphan designation. The MHRA will review applications for orphan designation at the time of an MA, and will offer incentives, such as market exclusivity and full or partial refunds for MA fees to encourage the development of medicines in rare diseases. Separately, the MHRA has stated that it is considering updating its licensing framework for orphan medicines, with a draft framework expected by spring 2026.

Pediatric Development

In the EU, companies developing a new medicinal product are obligated to study their product in children and must therefore submit a PIP together with a request for agreement to the EMA. The EMA issues a decision on the PIP based on an opinion of the EMA's Pediatric Committee. Companies must conduct pediatric clinical trials in

accordance with the PIP approved by the EMA, unless a deferral (*e.g.,* until enough information to demonstrate its effectiveness and safety in adults is available) or waiver (*e.g.,* because the relevant disease or condition occurs only in adults) has been granted by the EMA. The MAA for the medicinal product must include the results of all pediatric clinical trials performed and details of all information collected in compliance with the approved PIP, unless a waiver or a deferral has been granted, in which case the pediatric clinical trials may be completed at a later date. Medicinal products that are granted a MA on the basis of the pediatric clinical trials conducted in accordance with the approved PIP are eligible for a six month extension of the protection under a supplementary protection certificate (if any is in effect at the time of approval) or, in the case of orphan medicinal products, a two year extension of the orphan market exclusivity. This pediatric reward is subject to specific conditions and is not automatically available when data in compliance with the approved PIP are developed and submitted. An approved PIP is also required when a MA holder wants to add a new indication, medicinal form or route of administration for a medicine that is already authorized and covered by intellectual property rights.

In the UK, the MHRA has published guidance on the procedures for UK PIPs which, where possible, mirror the submission format and requirements of the EU system. From January 1, 2025, EU pediatric requirements are addressed via Windsor Framework categorization: for Category 2 products, both UK and EU pediatric requirements apply, and an EU-agreed PIP must also be in place (unless waived).

PRIME Designation

In March 2016, the EMA launched an initiative to facilitate the 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 on the basis of compelling non-clinical data and tolerability data from initial clinical trials. 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 potentially accelerated MAA assessment once a dossier has been submitted. Importantly, once a candidate medicine has been selected for the PRIME scheme, a dedicated contact point and rapporteur from the CHMP or from CAT are appointed facilitating increased understanding of the product at EMA's Committee level. A kick-off meeting with the CHMP/CAT rapporteur initiates these relationships and includes a team of multidisciplinary experts to provide guidance on the overall development plan and regulatory strategy. PRIME eligibility does not change the standards for product approval, and there is no assurance that any such designation or eligibility will result in expedited review or approval.

Post-Approval Regulation

Similar to the United States, both MA holders and manufacturers of medicinal products are subject to comprehensive regulatory oversight by the EMA, the EC and/or the competent regulatory authorities of the EU Member States. This oversight applies both before and after grant of manufacturing licenses and MAs. It includes control of compliance with EU good manufacturing practices rules, manufacturing authorizations, pharmacovigilance rules and requirements governing advertising, promotion, sale, and distribution, recordkeeping, importing and exporting of medicinal products.

Failure by us or by any of our third-party partners, including suppliers, manufacturers and distributors to comply with EU laws and the related national laws of individual EU Member States governing the conduct of clinical trials, manufacturing approval, MA of medicinal products and marketing of such products, both before and after grant of MA, statutory health insurance, bribery and anti-corruption or other applicable regulatory requirements may result in administrative, civil or criminal penalties. These penalties could include delays or refusal to authorize the conduct of clinical trials or to grant MA, product withdrawals and recalls, product seizures, suspension, withdrawal or variation of the MA, total or partial suspension of production, distribution, manufacturing or clinical trials, operating restrictions, injunctions, suspension of licenses, fines and criminal penalties.

The holder of an MA for a medicinal product must also comply with EU pharmacovigilance legislation and its related regulations and guidelines, which entail many requirements for conducting pharmacovigilance, or the assessment and monitoring of the safety of medicinal products.

These pharmacovigilance rules can impose on holders of MAs the obligation to conduct a labor intensive collection of data regarding the risks and benefits of marketed medicinal products and to engage in ongoing assessments of those risks and benefits, including the possible requirement to conduct additional clinical studies or post-authorization safety studies to obtain further information on a medicine's safety, or to measure the effectiveness of risk-management measures, which may be time consuming and expensive and could impact our profitability. MA holders must establish and maintain a pharmacovigilance system and appoint an individual qualified person for pharmacovigilance, who is responsible for oversight of that system. Key obligations include expedited reporting of suspected serious adverse reactions and submission of Periodic Safety Update Reports ("PSURs") in relation to medicinal products for which they hold MAs. The EMA reviews PSURs for medicinal products authorized through the centralized procedure. If the EMA has concerns that the risk benefit profile of a product has varied, it can adopt an opinion advising that the existing MA for the product be suspended, withdrawn or varied. The agency can advise that the MA holder be obliged to conduct post-authorization Phase IV safety studies. If the EC agrees with the opinion, it can adopt a decision varying the existing MA. Failure by the MA holder to fulfill the obligations for which the EC's decision provides can undermine the ongoing validity of the MA.

More generally, non-compliance with pharmacovigilance obligations can lead to the variation, suspension or withdrawal of the MA for the product or imposition of financial penalties or other enforcement measures.

The manufacturing process for pharmaceutical products in the EU is highly regulated and regulators may shut down manufacturing facilities that they believe do not comply with regulations.

Manufacturing requires a manufacturing authorization, and the manufacturing authorization holder must comply with various requirements set out in the applicable EU laws, regulations and guidance, including Directive 2001/83/EC, Directive 2003/94/EC (repealed by Directive 2017/1572 on January 31, 2022), Regulation (EC) No 726/2004 and the European Commission Guidelines for Good Manufacturing Practice ("GMP"). These requirements include compliance with EU GMP standards when manufacturing pharmaceutical products and active pharmaceutical ingredients, including the manufacture of active pharmaceutical ingredients outside of the EU with the intention to import the active pharmaceutical ingredients into the EU. Amendments or replacements of at least Directive 2001/83/EC and Regulation (EC) No 726/2004 are part of the reform proposal for European pharmaceutical legislation. Similarly, the distribution of pharmaceutical products into and within the EU is subject to compliance with the applicable EU laws, regulations and guidelines, including the requirement to hold appropriate authorizations for distribution granted by the competent authorities of the EU Member States. The manufacturer or importer must have a qualified person who is responsible for certifying that each batch of product has been manufactured in accordance with GMP, before releasing the product for commercial distribution in the EU or for use in a clinical trial. Manufacturing facilities are subject to periodic inspections by the competent authorities for compliance with GMP.

On October 27, 2025, the Council of the European Union approved a framework for compulsory licensing of crisis-relevant products (including medicinal products) in crisis situations. While the proposal focuses on voluntary agreements with intellectual property rights holders, it includes rules on compulsory licensing as a measure of last resort upon activation/declaration of a crisis or emergency mode. The European Parliament has not yet voted on the proposal.

Sales and Marketing Regulations

The advertising and promotion of our products is also subject to EU laws concerning promotion of medicinal products, interactions with physicians, misleading and comparative advertising and unfair commercial practices. In addition, other national legislation of individual EU Member States may apply to the advertising and promotion of medicinal products and may differ from one country to another. These laws require that promotional materials and advertising in relation to medicinal products comply with the product's SmPC as approved by the competent regulatory authorities. The SmPC is the document that provides information to physicians concerning the safe and effective use of the medicinal product. It forms an intrinsic and integral part of the MA granted for the medicinal product. Promotion of a medicinal product that does not comply with the SmPC is considered to constitute off-label promotion. All advertising and promotional activities for the product must be consistent with the approved SmPC and therefore all off-label promotion is prohibited. Direct-to-consumer advertising of prescription-only medicines is also prohibited in the EU. Violations of the rules governing the promotion of

medicinal products in the EU could be penalized by administrative measures, fines and imprisonment. These laws may further limit or restrict the advertising and promotion of our products to the general public and may also impose limitations on its promotional activities with healthcare professionals. EU regulation with regards to dispensing, sale and purchase of medicines has generally been preserved in the UK following Brexit, through the Human Medicines Regulations. However, organizations wishing to sell medicines online need to register with the MHRA. Following Brexit, the requirements to display the common logo no longer apply to UK-based online sellers, except for those established in Northern Ireland.

Anti-Corruption Legislation

In the EU, interactions between pharmaceutical companies and physicians are also governed by strict laws, regulations, industry self-regulation codes of conduct and physicians' codes of professional conduct both at EU level and in the individual EU Member States. 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 EU. The provision of benefits or advantages to physicians is also governed by the national anti-bribery laws of the EU Member States. Violation of these laws could result in substantial fines and imprisonment.

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

In the UK, the pharmaceutical sector is recognized as being particularly vulnerable to corrupt practices, some of which fall within the scope of the Bribery Act 2010. Due to the Bribery Act 2010's far-reaching territorial application, the potential penalized act does not have to occur in the UK to become within its scope. If the act or omission does not take place in the UK, but the person's act or omission would constitute an offense if carried out there and the person has a close connection with the UK, an offense will still have been committed.

The Bribery Act 2010 is comprised of four offenses that cover (i) individuals, companies and partnerships that give, promise or offer bribes, (ii) individuals, companies and partnerships that request, agree to receive or accept bribes, (iii) individuals, companies and partnerships that bribe foreign public officials and (iv) companies and partnerships that fail to prevent persons acting on their behalf from paying bribes. The penalties imposed under the Bribery Act 2010 depend on the offence committed, harm and culpability and penalties range from unlimited fines to imprisonment for a maximum term of ten years and in some cases both.

Regulations in the UK and Other Markets

The UK formally left the EU on January 31, 2020 and EU laws now only apply to the UK in respect of Northern Ireland as laid out in the protocol on Ireland and Northern Ireland and as amended by the Windsor Framework sets out a long-term set of arrangements for the supply of medicines into Northern Ireland. The EU and the UK agreed on a trade and cooperation agreement, which includes provisions affecting the life sciences sector (including on customs and tariffs). There are some specific provisions concerning pharmaceuticals, including the mutual recognition of GMP, inspections of manufacturing facilities for medicinal products and GMP-issued documents. The TCA does not, however, contain wholesale mutual recognition of UK and EU pharmaceutical regulations and product standards.

The UK government has adopted the Medicines and Medical Devices Act 2021 (the "MMDA") to enable the UK's regulatory frameworks to be updated following the UK's departure from the EU. The MMDA introduces regulation-making, delegated powers covering the fields of human medicines, clinical trials of human medicines, veterinary medicines and medical devices. The MHRA has since been consulting on future regulations for medicines and medical devices in the UK.

For other countries outside of the EU, such as countries in Eastern Europe, Latin America or Asia, the requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. In all cases, again, the clinical trials must be conducted in accordance with GCP and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

If we fail to comply with applicable foreign regulatory requirements, we may be subject to, among other things, fines, suspension of clinical trials, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

Additional Regulation

In addition to the foregoing, local, state and federal laws, including in the United States and Israel, regarding such matters as safe working conditions, manufacturing practices, environmental protection, fire hazard control and hazardous substances, including the Occupational Safety and Health Act, the Resource Conservancy and Recovery Act and the Toxic Substances Control Act, affect our business. These and other laws govern our use, handling and disposal of various biological, chemical and radioactive substances used in, and wastes generated by, our operations. If our operations result in contamination of the environment or expose individuals to hazardous or biohazardous substances, we could be liable for damages, environmental remediation, and/or governmental fines. We believe that we are in material compliance with applicable environmental laws and occupational health and safety laws that continued compliance therewith will not have a material adverse effect on our business. We cannot predict, however, how changes in these laws may affect our future operations. We may incur significant costs to comply with such laws and regulations now or in the future.

Our Employees

As of February 1, 2026, we had 11 employees, two of whom served on a full-time basis. Of these employees, five are engaged in research and development. None of our employees is represented by a labor union or covered under a collective bargaining agreement. We consider our relationship with employees to be good.

Nine of our employees are engaged through our Services Agreement with Mstone. See "*Certain Relationships and Related Transactions, and Director Independence — Related Party Transactions — Mstone Partners Healthcare Limited*." While Mstone professionals will continue to support Polaryx on a consulting basis pursuant to the Services Agreement we signed in November 2021, promoting continuity and strategic alignment during the company's next phase of growth, our future success depends on our ability to attract, develop and retain key personnel. Our human resources objectives include, among other things, identifying, recruiting, retaining, incentivizing and integrating prospective employees. We also retain independent contractors as needed to support our organization's needs.

Item 1A. Risk Factors

An investment in our common stock involves a high degree of risk. You should carefully consider the following risks and uncertainties, together with all of the other information contained in this Annual Report, including our financial statements and related notes appearing elsewhere in this Annual Report, before deciding whether to invest in our common stock. The occurrence of one or more of the events or circumstances described in these risk factors, alone or in combination with other events or circumstances, may have a material adverse effect on our business, reputation, revenue, financial condition, results of operations and future prospects, in which event you could lose all or part of your investment. The risks and uncertainties described below are not intended to be exhaustive and are not the only ones we face. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also impair our business operations. Moreover, some of the factors, events and contingencies discussed below may have occurred in the past, but the disclosures below are not representations as to whether or not the factors, events or contingencies have occurred in the past, and instead reflect our beliefs and opinions as to the factors, events or contingencies that could materially and adversely affect us in the future. This Annual Report also contains forward-looking statements that involve

risks and uncertainties. See "Special Note Regarding Forward-Looking Statements." Our actual results could differ materially and adversely from those anticipated in these forward-looking statements as a result of certain factors, including those described below.

Risk Factor Summary

Below is a summary of the material risks to our business, our operations and an investment in our common stock. This summary does not address all of the risks that we face. Risks and uncertainties not presently known to us or that we presently deem less significant may also impair our business operations. Additional discussion of the risks summarized in this risk factor summary, and other risks that we face, can be found below and should be carefully considered, together with other information in this Annual Report in its entirety before making investment decisions regarding our common stock.

- We have a limited operating history and have no products approved for commercial sale, and our results may vary from quarter to quarter.
- We will require substantial additional capital to finance our operations in the future. If we are unable to raise such capital when needed, or on acceptable terms, we may be forced to delay, reduce or eliminate clinical trials, product development programs or future commercialization efforts.
- We have incurred significant losses since inception, expect to incur significant losses for the foreseeable future and may not be able to achieve or sustain profitability in the future. We have no products for sale, have not generated any product revenue and may never generate product revenue or become profitable.
- PLX-200 and our preclinical programs may fail in development or suffer delays that materially and adversely affect their commercial viability. If we or our current or future collaborators are unable to complete development of, or commercialize, our drug candidates, or experience significant delays in doing so, our business will be materially harmed.
- We are substantially dependent on the success of our most advanced drug candidate, PLX-200, and our clinical trials of PLX-200 may not be successful.
- Delays in developing our manufacturing capabilities or failure to achieve operating efficiencies from such capabilities may require us to devote additional resources and management time to manufacturing operations and may delay our product development timelines.
- In order to successfully implement our plans and strategies, we will need to grow the size of our organization and we may experience difficulties in managing this growth.
- The regulatory approval processes of the FDA and other comparable foreign regulatory authorities are lengthy, time-consuming and inherently unpredictable. If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals for our drug candidates, we will not be able to commercialize, or will be delayed in commercializing, such drug candidates, and our ability to generate revenue will be materially impaired.
- Our executive officers, directors and principal stockholders have the ability to control or significantly influence all matters submitted to our stockholders for approval.
- We previously identified a material weakness in our information technology general controls that has since been remediated. If we experience additional material weaknesses in the future or otherwise fail to maintain an effective system of internal controls in the future, we may not be able to accurately or timely report our financial condition or results of operations, which may adversely affect investor confidence in us and, as a result, the value of our common stock.

Risks Related to Our Limited Operating History, Financial Position and Capital Requirements

We have a limited operating history and have no products approved for commercial sale, and our results may vary from quarter to quarter. We have incurred net losses since our inception, we expect to incur significant and increasing operating losses and we may never be profitable.

We are a clinical-stage biotechnology company with limited operating history. Since our inception in 2014, we have incurred significant operating losses and have used substantially all of our resources to conduct research and development activities, preclinical studies and clinical trials of our most advanced drug candidates, conduct business planning, develop and maintain our intellectual property portfolio, hire personnel, raise capital, and provide general and administrative support for these activities. We have limited experience as a company in initiating, conducting or completing clinical trials. In part because of this lack of experience, we cannot be certain that our planned clinical trials will begin on time, meet our anticipated timelines for enrollment and data analysis, or be completed on time, if at all. In addition, we have not yet demonstrated our ability to successfully complete late-stage clinical trials, obtain regulatory or 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. Additionally, we expect our financial condition and operating results to continue to fluctuate significantly from period to period due to a variety of factors, many of which are beyond our control. Consequently, any predictions made about our future success or viability may not be as accurate as they could be if we had a longer operating history.

In addition, as our business grows, we may encounter unforeseen expenses, restrictions, difficulties, complications, delays and other known and unknown factors. We will need to transition at some point from a company with an early research and development focus to a company capable of supporting larger pivotal clinical trials and eventually commercial activities, including the manufacture of commercial scale product. We may not be successful in such a transition.

We will require substantial additional capital to finance our operations in the future. If we are unable to raise such capital when needed, or on acceptable terms, we may be forced to delay, reduce or eliminate clinical trials, product development programs or future commercialization efforts.

Developing biotechnology products is a long, time-consuming, expensive and uncertain process that takes years to complete. Since our inception, we have funded our operations primarily through private financings and have incurred significant recurring losses. As of December 31, 2025, we had an accumulated deficit of approximately $99.6 million. We expect our expenses to increase in connection with our ongoing activities, particularly as we progress our Phase 2 clinical trial of PLX-200, with the expectation that we may also initiate additional clinical trials in the future, and continue to research, develop and conduct preclinical studies of our other potential drug candidates.

In addition, if we obtain regulatory approval for any drug candidate for commercial sale, including PLX-200, we anticipate incurring significant commercialization expenses related to product manufacturing, marketing, sales and distribution activities to launch any such product. Our expenses could increase beyond expectations if we are required by the FDA or other regulatory agencies to perform preclinical studies or clinical trials in addition to those that we currently anticipate. Because the design and outcome of our current, planned and anticipated clinical trials are highly uncertain, we cannot reasonably estimate the actual amount of funding that will be necessary to successfully complete the development and commercialization of any drug candidate we develop. Our future capital requirements depend on many factors, including factors that are not within our control.

We expect to incur increased costs associated with operating as a public company, and we do not anticipate achieving any significant revenue in the near term given the development stage of our drug candidates. Accordingly, we will require substantial additional funding to continue our operations. Based on our current operating plan,

we believe that our existing cash, cash equivalents and short-term investments should be sufficient to fund our operations through at least the third quarter of 2026. This estimate is based on assumptions that may prove to be materially wrong, and we could deplete our available capital resources sooner than we currently expect. Our future capital requirements will depend on many factors, including:

- the timing and progress of preclinical and clinical development activities;
- the number and scope of preclinical and clinical programs we pursue to develop our pipeline;
- our ability to establish an acceptable safety profile with IND-enabling toxicology studies to enable clinical trials;
- successful patient enrollment in, and the initiation and completion of, larger and later-stage clinical trials;
- the number of subjects that participate in clinical trials and per subject trial costs;
- the number and extent of trials required for regulatory approval;
- the countries in which the trials are conducted;
- the length of time required to enroll eligible subjects in clinical trials;
- the drop-out and discontinuation rate of subjects;
- potential additional safety monitoring requested by regulatory agencies;
- the duration of subject participation in the trials and follow-up;
- the extent to which we encounter any serious adverse events in our clinical trials;
- the timing of receipt of regulatory approvals from applicable regulatory authorities, including those required to initiate clinical trials;
- the timing, receipt and terms of any marketing approvals and post-marketing approval commitments from applicable regulatory authorities;
- the extent to which we establish collaborations, strategic partnerships, or other strategic arrangements with third parties, if any, and the performance of any such third party;
- the scale up of our clinical and regulatory capabilities, including establishing our cGMP manufacturing capabilities to support expansion of our pipeline and future registration-enabling clinical trials, and obtaining cGMP material for clinical trials or potential commercial sales;
- hiring and retaining research, clinical, regulatory, manufacturing (including quality control and quality assurance) and administrative personnel;
- our arrangements with third-party contract development and manufacturing organizations ("CDMOs") and contract research organizations ("CROs");
- the outfitting and validation of our cGMP manufacturing facility;
- the impact of any business interruptions to our operations or to those of the third parties with whom we work; and
- obtaining, maintaining, defending and enforcing patent claims and other intellectual property rights.

We do not have any committed external sources of funds, and adequate additional financing may not be available to us on acceptable terms, or at all. We may be required to seek additional funds sooner than planned through public or private equity offerings, debt financings, collaborations and licensing arrangements or other sources. Such financing may dilute our stockholders or the failure to obtain such financing may restrict our operating activities. Any additional fundraising efforts may divert our management from their day-to-day activities,

which may adversely affect our business. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms may include liquidation or other preferences and anti-dilution protections that adversely affect your rights as a stockholder. Debt financing may result in imposition of debt covenants, increased fixed payment obligations or other restrictions that may affect our business. If we raise additional funds through upfront payments or milestone payments pursuant to future collaborations with third parties, we may have to relinquish valuable rights to product development programs, or grant licenses on terms that are not favorable to us. Additional capital may not be available in sufficient amounts or on reasonable terms, if at all. Our ability to raise additional capital may be adversely impacted by global macroeconomic conditions, including rising interest rates, escalating trade tensions and restrictions, including tariffs, geopolitical instability, changes in government regulations and significant volatility in the credit and financial markets in the United States and worldwide, particularly in the biotechnology and biopharmaceutical industries, over which we may have no or little control. Our failure to raise capital as and when needed or on acceptable terms would have a negative impact on our financial condition and our ability to pursue our business strategy, and we may have to delay, reduce the scope of, suspend or eliminate clinical trials, product development programs or future commercialization efforts.

We have incurred significant losses since inception, expect to incur significant losses for the foreseeable future and may not be able to achieve or sustain profitability in the future. We have no products for sale, have not generated any product revenue and may never generate product revenue or become profitable.

Investment in biotechnology product development is a highly speculative undertaking and entails substantial upfront expenditures and significant risks that any program will fail to demonstrate adequate efficacy or potency or an acceptable safety profile, gain regulatory approval and become commercially viable. We have no products approved for commercial sale, have not generated any revenue from product sales to date, and continue to incur significant research and development and other expenses related to our ongoing operations. We do not expect to generate product revenue unless or until we successfully complete clinical development and obtain regulatory approval of, and then successfully commercialize, at least one drug candidate. We may never succeed in these activities and, even if we do, we may never generate product revenue or revenues that are significant or large enough to achieve profitability. If we are unable to generate sufficient revenue through the sale of any approved products, we may be unable to continue operations without additional funding.

We have incurred significant net losses in each period since we commenced operations in 2014. We incurred net losses of approximately $9.0 million and $30.4 million for the years ended December 31, 2025 and 2024, respectively. As of December 31, 2025, we had an accumulated deficit of approximately $99.6 million. We expect to continue to incur significant losses for the foreseeable future. Our operating expenses and net losses may fluctuate significantly from quarter to quarter and year to year. We anticipate that our expenses will increase substantially if and as we:

- advance our existing and future programs through preclinical and clinical development, including expansion into additional indications;
- seek to identify additional programs and additional drug candidates;
- continue to develop our pipeline;
- maintain, expand, enforce, defend and protect our intellectual property portfolio;
- seek regulatory and marketing approvals for drug candidates;
- seek to identify, establish and maintain additional collaborations and license agreements, including those which may enhance the biodistribution and delivery of our drug candidates;
- ultimately establish a sales, marketing and distribution infrastructure to commercialize any products for which we may obtain marketing approval, either by ourselves or in collaboration with others;
- generate revenue from commercial sales of products for which we receive marketing approval;
- hire additional personnel, including research and development, clinical and commercial;

- add operational, financial and management information systems and personnel to support further expansion and operation as a public company;
- acquire or in-license products, intellectual property and technologies which may enhance our current technology; and
- establish commercial-scale cGMP capabilities through our own or third-party manufacturing facilities.

In addition, our expenses will increase if, among other things, we are required by the FDA or other regulatory authorities to perform trials or studies in addition to, or different than, those that we currently anticipate, there are any delays in completing our clinical trials or the development of any drug 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 drug candidates, we expect to incur substantial additional research and development and other expenditures to develop and market additional programs and/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.

Our failure to become profitable would decrease our value and could impair our ability to raise capital, maintain our research and development efforts, expand our business and/or continue our operations. A decline in our value could also cause you to lose all or part of your investment.

Risks Related to Discovery, Development and Commercialization

We face competition from entities that have developed or may develop programs for the diseases we plan to address with PLX-200 and other drug candidates in development.

The development and commercialization of biological products is highly competitive. If approved, PLX-200 or any other drug candidates we may develop will face significant competition and our failure to effectively compete may prevent us from achieving significant market penetration. We compete with a variety of multinational biopharmaceutical companies, specialized biotechnology companies and emerging biotechnology companies, as well as academic institutions, governmental agencies, and public and private research institutions, among others. Many of the companies with which we are currently competing or will compete against 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. Mergers and acquisitions in the pharmaceutical and biotechnology industry may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also 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, PLX-200 and any other drug candidates we may develop.

As described in "*Business — Competition*" in this Annual Report, our competitors have developed, are developing or may develop programs or clinical stage products competitive with PLX-200 or our other earlier stage drug candidates. Competitive therapeutic treatments include those that have already been approved and accepted by the medical community for NCL, Tay-Sachs and Sandhoff diseases, Krabbe disease and NPD type A and type B, any new treatments for such diseases. Our success will depend partially on our ability to develop and commercialize products that have a competitive safety, efficacy or potency, dosing and/or presentation profile. Our commercial opportunity and success will be reduced or eliminated if competing products are safer, more effective or potent, have a more attractive or less invasive dosing profile or presentation or are less expensive than any products we may develop, or if competitors develop competing products that enter the market more quickly than we are able to, if we are able to at all, and are able to gain market acceptance.

PLX-200 and our preclinical programs may fail in development or suffer delays that materially and adversely affect their commercial viability. If we or our current or future collaborators are unable to complete development of, or commercialize, our drug candidates, or experience significant delays in doing so, our business will be materially harmed.

We have no products on the market. Our lead drug candidate, PLX-200, is currently in clinical trial development while other programs are in early stages of preclinical development. As a result, we expect it will be many years before we commercialize our drug candidates and ultimately may not be successful in commercializing any of our drug candidates. Our ability to achieve and sustain profitability depends on obtaining regulatory approvals for, and successfully commercializing, our lead drug candidate, PLX-200, or other drug candidates, either alone or with third parties, and we cannot guarantee that we will ever obtain regulatory approval for any drug candidates we may develop.

We have limited experience as a company in conducting and managing the clinical trials necessary to obtain regulatory approvals, including approval by the FDA or comparable foreign regulatory authorities. We have not yet demonstrated our ability to obtain regulatory approvals, manufacture a commercial scale product or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful product commercialization. Before obtaining regulatory approval for the commercial distribution of drug candidates, we or an existing or future collaborator must conduct extensive preclinical tests and clinical trials to demonstrate the safety, purity and efficacy or potency in humans of such drug candidates.

Challenges may prevent our success with or increase the cost of current, planned or future clinical trials. We or our collaborators may experience delays in initiating or completing clinical trials, and also may experience unforeseen events during, or as a result of, any current or future clinical trials that could delay or prevent our ability to receive marketing approval or commercialize PLX-200 or any other drug candidates, including:

- regulators or institutional review boards ("IRBs"), the FDA or ethics committees may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we may experience delays in reaching, or may fail to reach, agreement on acceptable terms with prospective trial sites and prospective CROs, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- the observation of an actual or suspected unexpected serious adverse reaction, serious adverse events, or adverse events of special interest could result in a partial or complete clinical hold for an unpredictable length of time, delay or halt future enrollment, require increased staggering between patient dosing, require dose reductions that could adversely affect the anticipated efficacy or potency product profile, or require a program discontinuation;
- clinical trial sites may fail to meet enrollment targets, may deviate from trial protocol, or may experience patients dropping out of a trial;
- clinical trials of any drug candidates may fail to show safety or efficacy or potency, or produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional preclinical studies or clinical trials or we may decide to abandon product development programs;
- the number of subjects required for clinical trials of any of our drug candidates may be larger than we anticipate, especially if the effect size observed in future clinical data from a Phase 2 clinical trial is small or is difficult to ascertain relative to natural history as a comparator, or if regulatory authorities require completion of a sham-controlled clinical trial;
- enrollment in clinical trials may be slower than we anticipate or subjects may drop out of clinical trials or fail to return for post-treatment follow-up at a higher rate than we anticipate;
- our third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all, or may deviate from the clinical trial protocol or drop out of the trial, which may require that we add new clinical trial sites or investigators;

- we may elect to, or regulators, independent data and safety monitoring boards ("DSMBs"), IRBs or ethics committees may require that we or our investigators suspend or terminate clinical research or trials, or delay further recruitment, enrollment or dosing of subjects in clinical trials or specific trial sites, for various reasons, including noncompliance with regulatory requirements, internal processes or protocols of the relevant review body, a finding that the participants in our trials are being exposed to unacceptable health risks, or any other development that may impact the benefit-risk assessment of our drug candidates;
- the cost of clinical trials of any of our drug candidates may be greater than we anticipate;
- the quality of our drug candidates or other materials necessary to conduct clinical trials of our drug candidates may be inadequate to initiate or complete a given clinical trial;
- we may be unable to manufacture sufficient quantities at adequate scales of our drug candidates for use in clinical trials;
- reports from clinical testing of other therapies may raise safety, efficacy or potency concerns about our drug candidates;
- we may fail to establish an appropriate safety profile for a drug candidate based on clinical or preclinical data for such drug candidate and data emerging from other therapies in the same class as our drug candidates; and
- the FDA or other regulatory authorities may require us to submit additional data, such as long-term toxicology studies, or impose other requirements before permitting us to initiate a clinical trial.

If safety concerns develop with respect to our drug candidates or clinical trial designs, we may be delayed in our development plans as we may need to pause our enrollment in a clinical trial, revise our trial designs, investigate potential safety developments, or take other measures that may increase the amount of time and resources required to bring our drug candidates forward.

Commencing clinical trials in the United States is subject to acceptance by the FDA of an IND or, if commenced in other jurisdictions, acceptance by the comparable foreign regulatory agency of a similar application, as well as finalizing the trial design. In the event that the FDA or applicable foreign regulatory agency requires us to complete additional preclinical studies, or we are required to satisfy other regulatory requests prior to commencing clinical trials, the start of our clinical trials may be delayed. Even after we receive and incorporate guidance from these regulatory authorities, the FDA or other regulatory authorities could disagree that we have satisfied their requirements to commence any clinical trial or change their position on the acceptability of our trial design or the clinical endpoints selected, which may require us to complete additional preclinical studies or clinical trials, delay the enrollment of our clinical trials or impose stricter approval conditions than we currently expect. There are equivalent processes and risks applicable to clinical trial applications in other jurisdictions, including the United Kingdom ("UK"), Australia and the European Union ("EU").

We may not have the financial resources to continue development of, or to modify existing collaborations or enter into new collaborations for, a drug candidate if we experience any issues that delay or prevent regulatory approval of, or our ability to commercialize, PLX-200 or any other drug candidates we are developing or may develop in the future. We or our current or future collaborators' inability to complete development of, or commercialize, PLX-200 or any other drug candidates or significant delays in doing so, could have a material and adverse effect on our business, financial condition, results of operations and prospects.

We intend to identify and develop novel drug candidates, which makes it difficult to predict the time, cost and potential success of drug candidate development.

We have invested in early-stage research and development with the goal of identifying and developing additional drug candidates. Our future success may depend in part on the successful development of novel therapeutic approaches. However, while our preclinical research and clinical trials may initially show promise in identifying potential drug candidates, they may ultimately fail to yield drug candidates for a number of reasons. It is difficult for us to predict the time and cost of drug candidate development, and we cannot predict whether our approach will result in the identification, development, and regulatory approval of any drug candidates, or that other

drug candidates will not be considered better or more attractive. There can be no assurance that any development problems we experience in the future related to our current drug candidates or any of our research programs will not cause significant delays or unanticipated costs, or that such development problems can be solved. Research programs to identify new drug candidates require substantial technical, financial, and human resources. If we are unable to identify suitable drug candidates for preclinical and clinical development in a cost-effective manner, we may not be able to successfully implement our business strategy, and may have to delay, reduce the scope of, suspend or eliminate one or more of our current or future drug candidates, clinical trials or future commercialization efforts, which would negatively impact our financial condition.

The disorders we seek to treat have low prevalence and it may be difficult to identify and enroll patients with these disorders. If we experience delays or difficulties in the enrollment and/or maintenance of patients in clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented.

Successful and timely completion of clinical trials will require that we enroll and maintain a sufficient number of patients. Patient enrollment is affected by many factors, including the size and nature of the patient population and competition for patients with other trials. Genetic diseases generally, and especially the rare diseases for which some of our current drug candidates are targeted, have low incidence and prevalence. For example, we estimate there are roughly 7,700 patients in the United States, Europe and select regions of the rest of the world with NCL. Accordingly, it may be difficult for us to identify and timely recruit a sufficient number of eligible patients to conduct our clinical trials. Further, any natural history studies that we or our collaborators may conduct may fail to provide us with patients for our clinical trials because patients enrolled in the natural history studies may not be good candidates for our clinical trials, or may choose to not enroll in our clinical trials.

Trials may be subject to delays as a result of patient enrollment taking longer than anticipated or patient withdrawal. We may not be able to initiate or continue clinical trials for our drug 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, the Medicines and Healthcare products Regulatory Agency ("MHRA") in the UK, the Therapeutic Goods Association in Australia, the European Medicines Agency ("EMA") or other foreign regulatory authorities. We cannot predict how successful we will be at enrolling subjects in future clinical trials. Subject enrollment is affected by other factors including:

- the eligibility criteria for the trial in question;
- the timely diagnosis of disease to meet such eligibility criteria;
- the size of the patient population and process for identifying patients;
- the perceived risks and benefits of the drug candidate in the trial, especially by clinician experts and patient advocacy organizations;
- the availability of competing commercially available therapies and other competing therapeutic candidates' clinical trials;
- the willingness of caregivers to enroll their children in our clinical trials;
- the efforts to facilitate timely enrollment in clinical trials;
- potential disruptions caused by pandemics or other public health crises, including difficulties in initiating clinical sites, enrolling and retaining participants, diversion of healthcare resources away from clinical trials, travel or quarantine policies that may be implemented, and other factors;
- the patient referral practices of physicians;
- the ability to monitor patients adequately during and after treatment; and
- the proximity and availability of clinical trial sites for prospective patients.

Even if we are able to enroll a sufficient number of patients in our clinical trials, we may have difficulty maintaining enrollment of such patients. Our inability to enroll or maintain a sufficient number of patients would result in significant delays in completing clinical trials or receipt of marketing approvals and increased development costs, or may require us to abandon one or more clinical trials altogether.

We are substantially dependent on the success of our most advanced drug candidate, PLX-200, and our clinical trials of PLX-200 may not be successful.

Our future success is substantially dependent on our ability to timely obtain marketing approval for, and then successfully commercialize, our most advanced drug candidate, PLX-200. We are investing a majority of our efforts and financial resources into the research and development of this drug candidate, as we are currently advancing the development of a Phase 2 trial for PLX-200.

PLX-200 will require additional clinical development, evaluation of clinical, preclinical and manufacturing activities, marketing approval in multiple jurisdictions, substantial investment and significant marketing efforts before we generate revenues from product sales, if any. We are not permitted to market or promote this drug candidate, or any other drug candidates we may develop, before we receive marketing approval from the FDA and/or comparable foreign regulatory authorities, and we may never receive such marketing approvals.

In addition, because our other product candidates are based on similar modes of action, if PLX-200 encounters safety or efficacy problems, manufacturing or supply interruptions, developmental delays, regulatory issues or other problems, its development plans and business related to those other indications for PLX-200 as well as other product candidates could be significantly harmed.

The success of PLX-200 will depend on a variety of factors. We do not have complete control over many of these factors, including certain aspects of clinical development and the regulatory submission process, potential threats to our intellectual property rights and the manufacturing, marketing, distribution and sales efforts of any future collaborator. Accordingly, we cannot guarantee that we will ever be able to generate revenue through the sale of this drug candidate, even if approved. If we are not successful in commercializing PLX-200, or are significantly delayed in doing so, our business will be materially harmed.

Our programs are focused on the development of therapeutics for patients with rare, pediatric lysosomal storage disorders, which is a rapidly evolving area of science, and the approach we are taking to discover and develop drug candidates is novel and may never lead to approved or marketable products.

The discovery and development of therapeutics for patients with rare, pediatric lysosomal storage disorders is an emerging field, and the scientific discoveries that form the basis for our efforts to discover and develop drug candidates are relatively new. The scientific evidence to support the feasibility of developing drug candidates based on these discoveries is both preliminary and limited. Although we believe, based on our preclinical work, that our programs have the potential to be disease-modifying therapies, clinical results may not confirm this hypothesis or may only confirm it for certain alterations or certain indications. The patient populations for our drug candidates are limited to those with specific lysosomal storage disorders. We cannot be certain that the patient populations for each specific disease will be large enough to allow us to successfully obtain approval and commercialize our drug candidates and achieve profitability.

If we do not achieve our projected development goals in the timeframes we announce and expect, the commercialization of PLX-200 or any other drug candidates may be delayed and, as a result, our stock price may decline.

From time to time, we estimate the timing of the anticipated accomplishment of various scientific, clinical, regulatory and other product development goals, which we sometimes refer to as milestones. These milestones may include the commencement or completion of scientific studies and clinical trials and the submission of regulatory filings. From time to time, we may publicly announce the expected timing of some of these milestones. All of these milestones are and will be based on numerous assumptions. The actual timing of these milestones can vary dramatically compared to our estimates, in some cases for reasons beyond our control. If we do not meet these milestones as publicly announced, or at all, the commercialization of PLX-200 or any other drug candidates may be delayed or never achieved and, as a result, our stock price may decline.

Preclinical and clinical development involves a lengthy and expensive process that is subject to delays and uncertain outcomes, and results of earlier studies and trials may not be predictive of future clinical trial results. If our preclinical studies and clinical trials are not sufficient to support regulatory approval of any of our drug candidates, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development of such drug candidate.

Before obtaining marketing approval from regulatory authorities for the sale of any drug candidate, we must complete preclinical studies, which are a lengthy, time-consuming and expensive process with a high risk of failure. The length of time of such testing may vary substantially according to the type, complexity and novelty of the program, and often can be several years or more per program. Delays associated with programs for which we are conducting preclinical testing and studies may cause us to incur additional operating expenses. For example, we depend on the availability of non-human primates ("NHPs") to conduct certain preclinical studies that we are required to complete prior to submitting an IND and initiating clinical development. A sustained global shortage of NHPs available for biological product development could cause the cost of obtaining NHPs for our future preclinical studies to increase significantly and result in delays to our development timelines. However, after conducting preclinical studies, we must then conduct extensive clinical trials to demonstrate the safety, purity, and efficacy or potency of our drug candidate in humans. Our clinical trials may not be conducted as planned or completed on schedule, if at all. Furthermore, failure can occur at any time during the preclinical study or clinical trial process, and the outcome of preclinical studies and early-stage clinical trials may not be predictive of the success of later clinical trials.

Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their drug candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their drug candidates. In addition, we expect to rely on patients, caregivers and clinicians to provide feedback on measures, which are subjective and inherently difficult to evaluate. These measures can be influenced by factors outside of our control, and can vary widely from day to day for a particular patient, and from patient to patient or caregiver to caregiver and from site to site within a clinical trial.

We cannot be sure that the FDA or comparable foreign regulatory authorities will agree with our clinical development plan. If the FDA or any comparable regulatory authorities require us to conduct additional trials or enroll additional patients, our development timelines may be delayed, or we may not be able to pursue further development due to such delays.

We cannot be sure that submission of an IND application, amendment to an existing IND application, clinical trial application ("CTA") or similar application will result in the FDA or comparable foreign regulatory authorities, as applicable, allowing clinical trials to begin in a timely manner, if at all. Additionally, even if the FDA or comparable foreign regulatory authorities agree with the design and implementation of the clinical trials set forth in an IND, we cannot guarantee that the FDA or comparable foreign regulatory authorities will not change their requirements in the future. These considerations also apply to new clinical trials we may submit as amendments to existing INDs or to a new IND.

Moreover, even if these trials begin, issues may arise that could cause regulatory authorities to require us to suspend or terminate such clinical trials. Events that may prevent successful or timely initiation or completion of clinical trials include: inability to generate sufficient preclinical, toxicology or other *in vivo* or *in vitro* data to support the initiation or continuation of clinical trials; delays in reaching a consensus with regulatory authorities on study design or implementation of the clinical trials; delays or failure in obtaining regulatory authorization to commence a trial; delays in reaching agreement on acceptable terms with prospective CROs and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and clinical trial sites; delays in identifying, recruiting and training suitable clinical investigators; delays in obtaining required IRB approval at each clinical trial site; difficulties in patient enrollment in our clinical trials for a variety of reasons; delays related to safety concerns; delays in manufacturing, testing, releasing, validating or importing/exporting sufficient stable quantities of our drug candidates for use in clinical trials or the inability to do any of the foregoing; failure by our CROs, other third parties or us to adhere to clinical trial protocols; failure to perform in accordance with the FDA's or any other regulatory authority's good clinical practices ("GCPs") or applicable regulatory guidelines in other countries; changes to the clinical trial protocols; clinical sites deviating from trial protocol or dropping out of a trial; changes in regulatory requirements and guidance that require amending

or submitting new clinical protocols; selection of clinical endpoints that require prolonged periods of observation or analyses of resulting data; transfer of manufacturing processes to larger-scale facilities operated by a CDMO and delays or failure by our CDMOs or us to make any necessary changes to such manufacturing process and demonstrate comparability to materials used in earlier clinical phases; and third parties being unwilling or unable to satisfy their contractual obligations to us.

We could also encounter delays if a clinical trial is placed on clinical hold, suspended or terminated by us, the IRBs of the institutions in which such trials are being conducted, or the FDA, the competent authorities and/or ethics committees of the UK, Australia, EU Member States or other regulatory authorities, if a clinical trial is recommended for suspension or termination by the DSMB or equivalent body for such trial, or on account of changes to federal, state, or local laws. If we are required to conduct additional clinical trials or other testing of PLX-200 or any other drug candidates beyond those that we contemplate, if we are unable to successfully complete clinical trials of PLX-200 or any other drug candidates, if the results of such trials are not positive or are only moderately positive or if there are safety concerns, our business and results of operations may be adversely affected and we may incur significant additional costs.

In addition, even if we are able to successfully complete the clinical trial for PLX-200, we cannot guarantee that the FDA or foreign regulatory authorities will interpret the results as we do, and more trials could be required before we submit our drug candidates for approval. This is particularly true for clinical trials in very rare diseases where the very small patient population makes it difficult to conduct two traditional, adequate and well-controlled studies. In such cases, the FDA or comparable foreign regulatory authorities are often required or permitted to exercise flexibility in approving therapies for such diseases, but obtaining flexibility is uncertain and may never occur. Moreover, results acceptable to support approval in one jurisdiction may be deemed inadequate by another regulatory authority to support regulatory approval in the other jurisdiction. To the extent that the results of the trials are not satisfactory to the FDA or applicable regulatory authorities for support of a marketing application, we may be required to expend significant resources, which may not be available to us, to conduct additional trials in support of potential approval of our drug candidates.

Preliminary, "topline" or interim data from our preclinical studies and clinical trials that we announce or publish from time to time may change as more patient data becomes available and are subject to audit and verification procedures.

From time to time, we may publicly disclose preliminary, interim or topline data from our preclinical studies and clinical trials, which are based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data. We also make assumptions, estimations, calculations and conclusions as part of our analyses of these data without the opportunity to fully and carefully evaluate complete data. Preliminary, interim 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 previously disclosed. These preliminary, interim or topline data are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available or as patients from our clinical trials continue other treatments. Because of this potential for change, preliminary, interim and topline data should be viewed with caution until final data are available. Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular drug candidate, the approvability or commercialization of a particular drug candidate and our company in general. In addition, the information we choose to publicly disclose regarding a particular preclinical study or clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is material or otherwise appropriate information to include in our disclosure. If the preliminary, interim or topline data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, PLX-200 or any other drug candidate may be harmed, which could harm our business, operating results, prospects or financial condition. In addition, differences between preliminary, interim or topline data and final data could significantly harm our business prospects and may cause the trading price of our common stock to fluctuate significantly.

Our current or future clinical trials may reveal significant adverse events or undesirable side effects not seen in our preclinical studies and may result in a safety profile that could halt clinical development, inhibit regulatory approval or limit commercial potential or market acceptance of PLX-200 or any other drug candidates or result in potential product liability claims.

Results of our clinical trials could reveal a high and unacceptable severity and prevalence of side effects, adverse events or unexpected characteristics. If serious adverse events or other adverse events or other side effects are observed in any of our current or future clinical trials, we may have difficulty recruiting patients to such trials, patients may drop out of our trials, patients may be harmed, or we may be required to delay enrollment or abandon one or more cohorts of a trial or delay or abandon the trials or our development efforts of one or more drug candidates altogether, including PLX-200. We, the FDA, MHRA, or other applicable regulatory authorities, or an IRB, may require suspension of any clinical trials of PLX-200 or any other drug candidates at any time for various reasons, including a finding that subjects or patients in such trials are being exposed to unacceptable health risks or adverse side effects. Some potential products developed in the biotechnology industry that initially showed therapeutic promise in early-stage trials have later been found to cause side effects that prevented their further development. Even if the side effects do not preclude a drug candidate from obtaining or maintaining marketing approval, undesirable side effects may inhibit market acceptance of an approved product due to its tolerability versus other therapies. Treatment-emergent adverse events could also affect patient recruitment or the ability of enrolled subjects to complete our clinical trials or could result in potential product liability claims. Potential side effects associated with PLX-200 or any other drug candidates may not be appropriately recognized or managed by the treating medical staff, as toxicities resulting from PLX-200 or any other drug candidates may not be normally encountered in the general patient population and by medical personnel. Any of these occurrences could harm our business, financial condition, results of operations and prospects significantly.

In addition, even if we successfully advance PLX-200 or any other drug candidates through clinical trials, such trials will only include a limited number of patients and limited duration of follow up to such drug candidates. As a result, we cannot be assured that adverse effects of PLX-200 or any other drug candidates will not be uncovered when a significantly larger number of patients are exposed to such drug candidate after approval, or a significantly longer follow up post-dosing is obtained as part of regulators' recommendations for long-term follow up of clinical study subjects treated with gene therapy. Further, any clinical trials may not be sufficient to determine the effect and safety consequences of using our drug candidates over a multi-year period.

If any of the foregoing events occur or if PLX-200 or any other drug candidates prove to be unsafe, our entire pipeline could be affected, which would have a material adverse effect on our business, financial condition, results of operations and prospects.

We may expend our limited resources to pursue a particular drug candidate, such as PLX-200 and PLX-300, and fail to capitalize on candidates that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and managerial resources, we intend to focus our research and development efforts on certain selected drug candidates. For example, to date we have allocated significant resources to our most advanced drug candidates, PLX-200 and PLX-300. As a result, we may forgo or delay pursuit of opportunities with other potential candidates that may 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 for specific indications may not yield any commercially viable drug candidates. If we do not accurately evaluate the commercial potential or target market for a particular drug candidate, we may relinquish valuable rights to that 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 candidate.

Even if regulatory approval is obtained, PLX-200 or any other drug candidate may not achieve adequate market acceptance among clinicians, patients, healthcare third-party payors and others in the medical community necessary for commercial success and we may not generate any future revenue from the sale or licensing of such products.

Even if regulatory approval is obtained for PLX-200 or any other drug candidates, our drug candidates may not gain market acceptance among physicians, patients, healthcare payors or the medical community. We may not generate or sustain revenue from sales of the product due to factors such as whether the product can be sold at a competitive cost and whether it will otherwise be accepted in the market. There are multiple drug candidates in various stages of development for the treatment of NCL, Tay-Sachs and Sandhoff diseases, Krabbe disease and NPD type A and type B. Market participants with significant influence over acceptance of new treatments, such as clinicians and third-party payors, may not adopt a product with a target product profile such as that of PLX-200 or for its targeted indications, and we may not be able to convince the medical community and third-party payors to accept and use, or to provide favorable reimbursement for, any drug candidates developed by us or our existing or future collaborators. Market acceptance of PLX-200 or any other drug candidates will depend on many factors, including factors that are not within our control.

Sales of biological products also depend on the willingness of clinicians to prescribe the treatment. We cannot predict whether clinicians, clinicians' organizations, hospitals, other healthcare providers, government agencies or private insurers will determine that any of our approved products are safe, therapeutically effective or potent, cost effective or less burdensome as compared with competing treatments. If PLX-200 or any other drug candidate is approved but does not achieve an adequate level of acceptance by such parties, we may not generate or derive sufficient revenue from that product and may not become or remain profitable.

We have never commercialized a drug candidate and may lack the necessary expertise, personnel and resources to successfully commercialize a drug candidate on our own or together with suitable collaborators.

We have never commercialized a drug candidate and currently have no sales force, marketing or distribution capabilities. To achieve commercial success for a drug candidate, we may opt to license such drug candidate to others, in which case we may rely on the assistance and guidance of our collaborators on that license arrangement. For a drug candidate for which we retain commercialization rights and marketing approval, we will have to develop our own sales, marketing and supply organization or outsource these activities to a third party. Factors that may affect our ability to commercialize a drug candidate, if approved, on our own include recruiting and retaining adequate numbers of effective sales and marketing personnel, developing adequate educational and marketing programs to increase public acceptance of our approved drug candidate, ensuring regulatory compliance of our company, employees and third parties under applicable healthcare laws and other unforeseen costs associated with creating an independent sales and marketing organization. Developing a sales and marketing organization will be expensive and time-consuming and could delay the launch of a drug candidate upon approval. Moreover, we may not be able to build an effective sales and marketing organization. If we are unable to build our own distribution and marketing capabilities or to find suitable partners for the commercialization of an approved drug candidate, we may not generate revenues from them or be able to reach or sustain profitability.

We have never completed any late-stage clinical trials and may not be able to file an IND application or other applications for regulatory approval to commence additional clinical trials on the timelines we expect. Even if we are able to complete such trials, the FDA or comparable foreign regulatory authorities may not permit us to proceed or could suspend or terminate any such trial after it has been initiated.

We will need to successfully complete later-stage and pivotal clinical trials in order to obtain FDA or comparable foreign regulatory approval to market our drug candidates. Carrying out clinical trials and the submission of a successful IND or CTA is a complicated process. Our lack of experience with FDA submissions may slow our progress towards FDA approval. We have not yet completed a Phase 2 clinical trial and have limited experience as a company in preparing, submitting and prosecuting regulatory filings.

We intend to engage with the FDA and other comparable foreign regulators to determine the requirements to support initiation of a pivotal clinical trial. However, regulatory authorities may recommend changes to the study design for PLX-200, including the number and size of registrational clinical trials required to be conducted in that

program. In addition, regulatory authorities could require manufacturing changes or have us implement additional analytical processes prior to initiation of a future clinical trial. Consequently, we may be unable to successfully and efficiently execute and complete necessary clinical trials in a way that leads to regulatory submission and approval of our drug candidates or we may determine that the regulatory requirements for submission are too burdensome to support continued development of one or more of our drug candidates. Additionally, even if regulatory authorities agree with the design and implementation of the clinical trials set forth in a regulatory meeting, such regulatory authorities may change their requirements in the future. The FDA or comparable foreign regulatory authorities may require the analysis of data from trials assessing different doses of the drug candidate alone or in combination with other therapies to justify the selected dose prior to the initiation of large trials in a specific indication. Any delays or failure to initiate clinical trials or obtain regulatory approvals for our trials may prevent us from completing our clinical trials or commercializing our products on a timely basis, if at all. We are subject to similar risks related to the review and authorization of our protocols and amendments by comparable foreign regulatory authorities.

For our preclinical pipeline, if the IND-enabling studies support a decision to advance into clinical development, we would plan to submit an IND or CTA with a foreign regulatory authority. We may not be able to file the IND or CTA in accordance with our desired timelines for future drug candidates. For example, we may experience manufacturing delays or other delays with IND-enabling studies, including with suppliers, study sites, or third-party contractors and vendors on which we depend. Moreover, we cannot be sure that submission of an IND application will result in the FDA or comparable foreign regulatory authorities allowing further clinical trials to begin, or that, once begun, issues will not arise that lead us to suspend or terminate such clinical trials.

Development of combination therapies may present more or different challenges than development of monotherapies.

We plan to pursue development of our drug candidates in combination with one or more additional products or drug candidates. The development of combination therapies may be more complex than the development of monotherapies and generally requires that sponsors demonstrate the contribution of each drug candidate to the claimed effect and the safety and efficacy of the combination as a whole. Regulatory authority requirements for the development of combination therapies may make the design and conduct of clinical trials more complex and/or burdensome, requiring more clinical trial participants and additional time and cost to complete than we plan or anticipate. We also may not be able to meet the FDA's current or future approval standards required for combination therapies or combination products, if we decided to administer or package a combination therapy as a single drug product. For example, under the "combination rule", the FDA may not file or approve a fixed-dose combination product unless each component of a proposed drug product is shown to make a contribution to the claimed effects and the dosage of each component (amount, frequency, duration) is safe and effective for the intended population. To satisfy these requirements, the FDA typically requires a clinical factorial trial, designed to assess the effects attributable to each drug in the combination product. This is particularly true when the ingredients are directed at the same sign or symptom of the disease or condition. The FDA has accepted a variety of approaches to satisfy the combination rule but the FDA has stated that factorial studies may be unethical (*e.g.,* omitting a drug known to improve survival) or impractical (there may be too many components to conduct a factorial trial, meaning the trial cannot be conducted). The FDA has also stated that it may be possible to use other types of clinical and nonclinical data and mechanistic information available to demonstrate the contributions of the individual active ingredients to the effect of the combination. In addition, combination products may require dose selection for each agent in the combination, which may require more and/or larger groups of participants than single agents. Our clinical trial and research efforts may not satisfy regulators' expectations of adequate exploration of dose ranging required for drug approval. Moreover, the applicable requirements for approval of a combination therapy may differ from country to country.

In the event that one of our drug candidates were to fail to demonstrate sufficient safety and efficacy data or establish its contribution to the claimed effects of a combination therapy or if we are unable to meet the FDA's current or future approval standards required for combination therapies or combination products in a timely manner, we would need to identify and research alternative monotherapy or combination treatments, run additional trials to produce supportive data or modify existing clinical trial plans. In the event we are unable to do so or are unable to do so on commercially reasonable terms or we are unable to continue development of one or more of drug candidates, our business and prospects would be materially harmed.

Risks Related to Manufacturing

Gene therapies are novel, complex and difficult to manufacture. We could experience manufacturing problems that result in delays in the development or commercialization of our drug candidates or otherwise harm our business.

The manufacture of gene therapy products is technically complex and necessitates substantial expertise and capital investment. Production difficulties caused by unforeseen events may delay the availability of material for our clinical studies. We expect to rely on contract manufacturers for certain portions of our manufacturing needs for the foreseeable future, such as those related to research grade material for our early preclinical studies.

The manufacturers of biological and pharmaceutical products must comply with strictly enforced cGMP requirements, state and federal regulations, as well as foreign requirements when applicable. Any failure of us or our CDMOs to adhere to or document compliance with such regulatory requirements could lead to a delay or interruption in the availability of our program materials for clinical trials or enforcement action from the FDA, EMA or other foreign regulatory authorities. If we or our manufacturers were to fail to comply with the FDA, EMA or other regulatory authority, it could result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of drug candidates or products, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our drug candidates. Our potential future dependence upon others for the manufacture of our drug candidates may also adversely affect our future profit margins and our ability to commercialize any drug candidates that receive regulatory approval on a timely and competitive basis.

We and our contract manufacturers are subject to significant regulation with respect to manufacturing of our products. The third-party manufacturing facilities on which we rely and any manufacturing facility that we may have in the future may have limited capacity or fail to meet the applicable stringent regulatory requirements.

We currently have relationships with a limited number of suppliers for the raw materials required by the manufacturing processes of our drug candidates. We may need to contract with additional manufacturers to produce the preclinical, clinical and commercial supply and such supply will be more uncertain and subject to delays. In addition, each supplier may require licenses to manufacture certain components of the supply if such processes are not owned by the supplier or in the public domain and we may be unable to license such intellectual property rights on reasonable commercial terms or to transfer or sublicense the intellectual property rights we may have with respect to such activities.

All entities involved in the preparation of therapeutics for clinical trials or commercial sale, including our existing contract manufacturers for components of our drug candidates, are subject to extensive regulation. Components of a finished therapeutic product approved for commercial sale or used in late-stage clinical trials must be manufactured in accordance with cGMP. These regulations govern manufacturing processes and procedures (including recordkeeping) and the implementation and operation of quality systems to control and assure the quality of investigational products and products approved for sale. Poor control of production processes can lead to the introduction of adventitious agents or other contaminants, or to inadvertent changes in the properties or stability of our drug candidates that may not be detectable in final product testing. We or our contract manufacturers must supply all necessary documentation in support of a biologics license application ("BLA"), a new drug application ("NDA") or marketing authorization application ("MAA") on a timely basis. Our facilities and quality systems and the facilities and quality systems of some or all of our third-party contractors must pass a pre-approval inspection for compliance with the applicable regulations as a condition of regulatory approval of our current or future drug candidates. In addition, regulatory authorities may, at any time, audit or inspect a manufacturing facility involved with the preparation of our current or future drug candidates or the associated quality systems for compliance with the regulations applicable to the activities being conducted, and they could put a hold on one or more of our clinical trials if the facilities of our CDMOs do not pass such audit or inspections. If these facilities do not pass a pre-approval plant inspection, the FDA or other foreign regulatory agency approval of the products will not be granted.

Regulatory authorities also may, at any time following approval of a product for sale, inspect or audit our manufacturing facilities or those of our third-party contractors. If any such inspection or audit identifies a failure to comply with applicable regulations or if a violation of our product specifications or applicable regulations occurs

independent of such an inspection or audit, we or the relevant regulatory authority may require remedial measures that may be costly and/or time-consuming for us or a third party to implement, and that may include the temporary or permanent suspension of a clinical trial or commercial sales or the temporary or permanent closure of a facility. Any such remedial measures imposed upon us or third parties with whom we contract could harm our business. If we or any of our third-party manufacturers fail to maintain regulatory compliance, the FDA or other foreign regulatory agencies can impose regulatory sanctions including, among other things, refusal to approve a pending application for a new drug product or biologic product, or revocation of a pre-existing approval. As a result, our business, financial condition and results of operations may be harmed.

Additionally, if supply from one approved manufacturer is interrupted, there could be a significant disruption in commercial supply. An alternative manufacturer would need to be qualified through a BLA, NDA and/or MAA supplement, which could result in further delay. The regulatory agencies may also require additional studies if a new manufacturer is relied upon for commercial production. Switching manufacturers may involve substantial costs and is likely to result in a delay in our desired clinical and commercial timelines.

These factors could cause the delay of clinical trials, regulatory submissions, required approvals or commercialization of our drug candidates, cause us to incur higher costs and prevent us from commercializing our products successfully, if approved. Further, if our suppliers fail to meet contractual requirements, and we are unable to secure one or more replacement suppliers capable of production at a substantially equivalent cost, our clinical trials may be delayed or we could lose future potential revenue, if any.

We depend on third-party suppliers for materials used in the manufacture of our drug candidates, and the loss of these third-party suppliers or their inability to supply us with adequate materials could harm our business.

We rely on third-party suppliers for certain materials and components required for the production of our drug candidates. Our dependence on these third-party suppliers and the challenges we may face in obtaining adequate supplies of materials involve several risks, including limited control over pricing, availability and quality of supplies and delivery schedules. There is substantial demand and limited supply for certain of the raw materials used to manufacture small molecule therapy and gene therapy products. As a small company, our negotiation leverage is limited and we are likely to get lower priority than our larger competitors. We cannot be certain that our suppliers will continue to provide us with the quantities of raw materials that we require or satisfy our anticipated specifications and quality requirements. One or more of our suppliers is the sole source of certain materials used by us in our manufacturing process, and a disruption of the supply of those materials could also negatively impact our ability to manufacture clinical supply as we would have to suspend or revise our operations to accommodate for any disruption in the supply of those materials. Any supply interruption in limited or sole sourced raw materials could materially harm our ability to manufacture our drug candidates until a new source of supply, if any, could be identified and qualified. We may be unable to find a sufficient alternative supply channel in a reasonable time or on commercially reasonable terms. Any performance failure on the part of our suppliers could delay the development and potential commercialization of our drug candidates, including limiting supplies necessary for clinical trials and regulatory approvals, which would have a material adverse effect on our business.

Any contamination or interruption in our manufacturing process, shortages of raw materials or failure of our suppliers to deliver necessary components could result in delays in our clinical development or marketing schedules.

Given the nature of gene therapy manufacturing, there is a risk of contamination. Any contamination could adversely affect our ability to produce drug candidates on schedule and could, therefore, harm our results of operations and cause reputational damage. Some of the raw materials required in our manufacturing process are derived from biologic sources. Such raw materials are difficult to procure and may be subject to contamination or recall. A material shortage, contamination, recall or restriction on the use of biologically derived substances in the manufacture of our drug candidates could adversely impact or disrupt the commercial manufacturing or the production of clinical material, which could adversely affect our development timelines and our business, financial condition, results of operations and prospects.

We may not be able to successfully manufacture our drug candidates in sufficient quality and quantity, which would delay or prevent us from developing our drug candidates and commercializing resulting approved products, if any.

To date, we have manufactured PLX-200 in quantities and quality adequate for preclinical, toxicology and clinical studies. In order to conduct clinical trials for a drug candidate and for commercialization of the resulting product if that drug candidate is approved for sale, we will need to manufacture drug candidates in additional cGMP campaigns or in larger batch sizes. We may not be able to successfully repeat or increase the manufacturing capacity for any of our drug candidates in a timely or cost-effective manner or at all. Significant changes or scale-up of manufacturing may require additional validation studies and/or analytical comparability studies, which are costly and which regulatory authorities must review and approve. In addition, quality issues may arise during those changes or scale-up activities. If we are unable to successfully manufacture any of our drug candidates in sufficient quality and quantity, the development of that drug candidate and regulatory approval or commercial launch for any resulting products may be delayed or there may be a shortage in supply, which could significantly harm our business.

Changes in methods of drug candidate manufacturing or formulation may result in additional costs or delay.

As drug candidates proceed through preclinical studies to late-stage clinical trials towards potential approval and commercialization, it is common that various aspects of the development program, such as manufacturing methods and formulation, are altered along the way in an effort to optimize processes and product characteristics. Such changes carry the risk that they will not achieve our intended objectives. Any such changes could cause our drug candidates to perform differently and affect the results of planned clinical trials or other future clinical trials conducted with the materials manufactured using altered processes. Such changes may also require additional testing, FDA notification or approval from the FDA or foreign regulatory agencies. This could delay completion of clinical trials, require the conduct of bridging clinical trials or the repetition of one or more clinical trials, increase clinical trial costs, delay approval of our drug candidates and jeopardize our ability to commence sales and generate revenue. In addition, we may be required to make significant changes to our upstream and downstream processes across our pipeline, which could delay the development of our future drug candidates.

Risks Related to Our Reliance on Third Parties

We currently rely, and intend in the future to rely, on third parties to conduct a significant portion of our preclinical studies and existing clinical trials and potential future clinical trials for drug candidates, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials.

We have engaged CROs or other third parties to conduct preclinical and IND enabling studies and our clinical trials.

We expect to continue to rely on third parties, including CROs, medical institutions and clinical investigators, to conduct those clinical trials. Any of these third parties may terminate their engagements with us, some in the event of an uncured material breach and some at any time for convenience. If any of our relationships with these third parties terminate, we may not be able to timely enter into arrangements with alternative third parties or do so on commercially reasonable terms, if at all. Switching or adding CROs involves substantial cost and requires management time and focus. In addition, there is a natural transition period when a new CRO commences work. As a result, delays occur, which can materially impact our ability to meet our desired clinical development timelines. Though we intend to carefully manage our relationships with CROs, there can be no assurance that we will not encounter challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business and financial condition.

In addition, any third parties conducting our clinical trials will not be our employees, and except for remedies available to us under our agreements with such third parties, we cannot control whether or not such third parties devote sufficient time and resources to our clinical programs. If these third parties do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols, regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated, we may incur additional and unexpected costs related to such failures, and we may not be able to obtain regulatory approval

for or successfully commercialize our drug candidates. Consequently, our results of operations and the commercial prospects for our drug candidates would be harmed, our costs could increase substantially and our ability to generate revenue could be delayed significantly.

Further, while our reliance on these third parties for research and development activities will reduce our control over these activities, we will not be relieved of our responsibilities for ensuring that each of our studies and trials is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards. For example, we will 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 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. 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 we or any of our CROs or other third parties, including trial sites, fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA, MHRA, EMA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials complies with GCP regulations. In addition, our clinical trials must be conducted with products produced under cGMP conditions. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process.

In addition, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and receive compensation in connection with such services. Under certain circumstances, we may be required to report some of these relationships to the FDA. The FDA may conclude that a financial relationship between us and a principal investigator has created a conflict of interest or otherwise affected interpretation of the trial. The FDA 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 and may ultimately lead to the denial of marketing approval of PLX-200 or any other drug candidates.

We currently store drug product for clinical trial sites outside of the United States, and currently rely on and expect in the future to rely on third parties to distribute product supplies for our clinical trials, as well as to distribute supply for clinical trial sites outside of the United States. Any performance failure on the part of us or our distributors could result in an unexpected increase in costs to us, delay clinical development or marketing approval of our drug candidates or commercialization of our products, if approved, producing additional losses and depriving us of potential revenue.

Our operations and financial condition also may be negatively impacted as a result of any delays or increased costs arising from the trade restrictions, tariffs or other extraordinary taxes, and other foreign regulatory requirements affecting our collaborators. We currently rely to some degree on foreign CROs in the UK, and may need to rely on foreign CROs and CDMOs in the future. We or the foreign CROs or CDMOs we may work with may be subject to U.S. legislation, including the potential passing of an act similar to the previously proposed BIOSECURE Act, sanctions, trade restrictions, increased taxes or tariffs and other foreign regulatory requirements which could increase the cost or reduce the supply of certain material we use, delay the procurement or supply of such material or disrupt our supply chain for certain raw materials or medical devices necessary for our clinical trial. Neither we, nor our vendors contract with any of the entities that were named as "companies of concern" in the BIOSECURE Act. In April 2025, the United States government imposed significant tariffs on imports from China and other countries and may impose more restrictions on goods, including biologically derived substances, manufactured in or imported from China or impose other restrictions on companies' ability to work with Chinese biotechnology companies or other foreign counterparties. To the extent these or future tariffs are applicable to the material we may import from China and other countries or if we are not able to secure supply of our drug candidates as a result of applicable legislation, our business and financial condition could be adversely affected.

Risks Related to Our Business and Operations

In order to successfully implement our plans and strategies, we will need to grow the size of our organization and we may experience difficulties in managing this growth.

Over time, we expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of preclinical and clinical product development, technical operations, clinical operations, regulatory affairs, manufacturing and, potentially, sales, marketing and distribution. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial personnel and systems, expand our facilities and recruit and train additional qualified personnel. Due to our limited financial resources and the limited experience of our management team working together 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. The expansion of our operations may 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.

We are highly dependent on our key personnel and anticipate hiring new key personnel. If we are not successful in attracting and retaining highly qualified personnel, we may not be able to successfully implement our business strategy.

Our ability to compete in the highly competitive biotechnology and pharmaceutical industries depends upon our ability to attract and retain highly qualified managerial, scientific and medical personnel. We are highly dependent on our managerial, scientific and medical personnel, including our Chief Medical Officer, as well as other key members of our leadership team. Our executive officers may terminate their employment with us at any time. We do not maintain "key person" insurance for any of our executives or other employees. 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 personnel may be difficult and may take an extended period of time. Failure to attract and retain qualified personnel could materially and adversely affect our business, financial condition and results of operations. We could in the future have difficulty attracting and retaining experienced personnel and may be required to expend significant financial resources on our employee recruitment and retention efforts.

Our future growth may depend, in part, on our ability to operate in foreign markets, where we would be subject to additional regulatory burdens and other risks and uncertainties.

Our future growth may depend, in part, on our ability to develop and commercialize PLX-200 or other drug candidates in foreign markets for which we may rely on collaborations with third parties. We are not permitted to market or promote any drug candidates before we receive regulatory approval from the applicable foreign regulatory authority, and may never receive such regulatory approval for any drug candidates. To obtain separate regulatory approval in many other countries, we must comply with numerous and varying regulatory requirements of such countries regarding safety and efficacy and governing, among other things, clinical trials and commercial sales, pricing and distribution of PLX-200 or other drug candidates, and we cannot predict success in these jurisdictions. If we fail to comply with the regulatory requirements in international markets or to receive applicable marketing approvals, our target market will be reduced and our ability to realize the full market potential of PLX-200 or other drug candidates will be harmed and our business will be adversely affected. Moreover, even if we obtain approval of PLX-200 or other drug candidates and ultimately commercialize such drug candidates in foreign markets, we would be subject to the risks and uncertainties of operating in such foreign markets, including the burden of complying with complex and changing foreign regulatory, tax, accounting and legal requirements and reduced protection of intellectual property rights in some foreign countries.

Our employees, independent contractors, consultants, commercial collaborators, principal investigators, CROs, CDMOs, suppliers and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements.

We are exposed to the risk that our employees, independent contractors, consultants, commercial collaborators, principal investigators, CROs, CDMOs, suppliers and vendors acting for or on our behalf may engage in misconduct or other improper activities. It is not always possible to identify and deter misconduct by these parties 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 comply with these laws or regulations.

Our systems, or those of any of our CROs, manufacturers, other contractors, third-party service providers or consultants or potential future collaborators, may fail or suffer security or data privacy breaches or other unauthorized or improper access to, use of, or destruction of our proprietary or confidential data, employee data or personal data, which could result in additional costs, loss of revenue, significant liabilities, harm to our brand and material disruption of our operations.

Despite the implementation of security measures in an effort to protect systems that store our information, given the size and complexity of such systems and the increasing amounts of information maintained on our internal information technology systems and those of our third-party CROs, other contractors (including sites performing our clinical trials), third-party service providers and supply chain companies, consultants and other partners, these systems are potentially vulnerable to breakdown or other damage or interruption from service interruptions, system malfunction, natural disasters, terrorism, war, and telecommunication and electrical failures, as well as security breaches from inadvertent or intentional actions by our employees, contractors, consultants, business partners and/or other third parties, or from cyber-attacks by malicious third parties, which may compromise our system infrastructure or lead to the loss, destruction, alteration or dissemination of, or damage to, our data. From time to time, we are subject to business email compromise attack attempts. If a material system failure, accident or security breach were to occur and cause interruptions in our operations or the operations of third-party collaborators, service providers, contractors and consultants, it could result in a material disruption of our development programs and significant reputational, financial, legal, regulatory, business or operational harm.

Further, since we sponsor clinical trials, any breach that compromises patient data and identities causing a breach of privacy could have significant adverse consequences on our business. For example, the loss of clinical trial data from completed or future clinical trials could affect trust in us, negatively impacting our ability to recruit for future clinical trials, 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, destruction, unavailability, alteration or dissemination of, or damage to, our data or applications, or inappropriate disclosure of confidential proprietary information, or for it to be believed or reported that any of these occurred, we could incur liability and reputational damage and the development and commercialization of PLX-200 or other drug candidates could be delayed.

As our employees work remotely and use network connections, computers, and devices outside of our premises or network, including working at home, while in transit and in public locations, there are risks to our information technology systems and data. Additionally, business transactions (such as acquisitions or integrations) could expose us to additional cybersecurity risks and vulnerabilities, as our systems could be negatively affected by vulnerabilities present in acquired or integrated entities' systems and technologies.

While we have implemented security measures designed to protect against security incidents, there can be no assurance that these measures will be effective. We may be unable in the future to detect vulnerabilities in our information technology systems because such threats and techniques change frequently, are often sophisticated in nature, and may not be detected until after a security incident has occurred. Further, we may experience delays in developing and deploying remedial measures designed to address any such identified vulnerabilities. Applicable data privacy and security obligations may require us to notify relevant stakeholders, patients or other individuals, regulators or, in certain circumstances, the media of security incidents. Such disclosures are costly, and the disclosure or the failure to comply with such requirements could lead to adverse consequences, including damage to our reputation.

We rely on third-party service providers and technologies to operate critical business systems, including to process sensitive information in a variety of contexts. Our ability to monitor these third parties' information security practices is limited, and these third parties may not have adequate information security measures in place. If our third-party service providers experience a security incident or other interruption, we could experience adverse consequences as a result. While we may be entitled to damages if our third-party service providers fail to satisfy their privacy or security-related obligations to us, any award may be insufficient to cover our monetary, reputational

and other damages, or we may be unable to recover such award. In addition, supply chain attacks have increased in frequency and severity, and we cannot guarantee that third parties' infrastructure in our supply chain or our third-party partners' supply chains have not been and will not be compromised.

If we (or a third party upon whom we rely) experiences a security incident or is perceived to have experienced a security incident, we may experience adverse consequences, such as government enforcement actions (for example, investigations, fines, penalties, audits, and inspections); additional reporting requirements and/or oversight; restrictions on processing personal information (including sensitive data); litigation (including class claims); indemnification obligations; negative publicity; reputational harm; monetary fund diversions; interruptions in our operations (including availability of data); increased investigation and compliance costs; financial loss; and other similar harms. Security incidents and attendant consequences may cause our stakeholders (including investors and potential customers) to stop supporting our business, deter new customers from our products, deter patients from participating in clinical trials and negatively impact our ability to grow and operate our business.

Our contracts may not contain limitations of liability, and even where they do, there can be no assurance that limitations of liability in our contracts are sufficient to protect us from liabilities, damages, or claims related to our data privacy and security obligations. We cannot be sure that our insurance coverage will be adequate or sufficient to protect us from or to mitigate liabilities arising out of our privacy and security practices or from disruptions in, or failure or security breach of, our systems or third-party systems where information important to our business operations or commercial development is stored, or that such coverage will continue to be available on commercially reasonable terms or at all, or that such coverage will pay future claims.

We are subject to stringent and changing laws, regulations and standards, and contractual obligations relating to privacy, data protection, and data security. The actual or perceived failure to comply with such obligations could lead to government enforcement actions (which could include civil or criminal penalties), fines and sanctions, private litigation, injunctive restrictions on data processing and/or adverse publicity and could negatively affect our operating results and business.

We, and third parties with whom we work, are or may become subject to numerous domestic and foreign laws, regulations, and standards relating to privacy, data protection, and data security, the scope of which are changing, subject to differing applications and interpretations, and may be inconsistent among countries, or conflict with other rules. In addition, there is proposed legislation in the U.S. Congress that could restrict working with certain biotech providers who are deemed "companies of concern" which may impact the ability of certain third parties with whom we work to meet their performance obligations. We are or may become subject to the terms of contractual obligations related to privacy, data protection, and data security. Our obligations may also change or expand as our business grows. The actual or perceived failure by us or third parties related to us to comply with such laws, regulations and obligations could increase our compliance and operational costs, expose us to regulatory scrutiny, actions, fines and penalties, result in reputational harm, lead to a loss of customers, result in litigation and liability, subject us to injunctive restrictions on data processing, adversely impact our ability to appropriately manage third parties with whom we work and otherwise cause a material adverse effect on our business, financial condition, and results of operations. See "*Business — Government Regulation-Data Privacy and Security"* in this Annual Report for a more detailed description of the laws that may affect our ability to operate.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business.

We are 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 may involve the use of hazardous and flammable materials, including chemicals and biological and 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.

Our ability to utilize our net operating loss carryforwards and certain other tax attributes may be limited.

As of December 31, 2025 and 2024, the Company had a federal net operating loss ("NOL") carryforward of $18.7 million and $15.7 million, respectively. As of December 31, 2025 and 2024, the Company had state NOL carryforwards of $15.7 million and $15.7 million, respectively. Of the $18.7 million of federal NOL carryforwards as of December 31, 2025, $1.1 million begins to expire in 2034 and $17.6 million may be carried forward indefinitely. The state NOL carryforwards begin to expire in 2034. To the extent that our taxable income exceeds any current year operating losses, we plan to use our carryforwards to offset income that would otherwise be taxable. Also, for state income tax purposes, the extent to which states will conform to the federal laws is uncertain and there may be periods during which the use of NOL carryforwards are suspended or otherwise limited, which could accelerate or permanently increase state taxes owed. In addition, under Section 382 of the U.S. Internal Revenue Code of 1986, as amended (the "Code"), changes in our ownership may limit the amount of our NOL carryforwards and tax credit carryforwards that could be utilized annually to offset our future taxable income, if any. This limitation would generally apply in the event of a cumulative change in ownership of more than 50% (as measured by value) among a stockholder or one or more groups of stockholders who own at least 5% of our stock within a three-year period. We have not performed an analysis to determine whether there has been an ownership change pursuant to Section 382. Any such limitation may significantly reduce our ability to utilize our NOL carryforwards and tax credit carryforwards before they expire. Any such limitation, whether as the result of a public offering, private placements, sales of our common stock by our existing stockholders or additional sales of our common stock by us, could have a material adverse effect on our results of operations in future years.

We may be subject to adverse legislative or regulatory tax changes that could negatively impact our financial condition.

The rules dealing with U.S. federal, state and local income taxation are constantly under review by persons involved in the legislative process and by the Internal Revenue Service (the "IRS") and the U.S. Treasury Department. Changes to tax laws (which changes may have retroactive application) could adversely affect us or our stockholders. We assess the impact of various tax reform proposals and modifications to existing tax treaties in all jurisdictions where we have operations and employees to determine the potential effect on our business and any assumptions we make about our future taxable income. We cannot predict whether any specific proposals will be enacted, the terms of any such proposals or what effect, if any, such proposals would have on our business if they were to be enacted. For example, the United States recently enacted the Inflation Reduction Act of 2022, which implements, among other changes, a 1% excise tax on certain stock buybacks. In addition, beginning in 2022, the Tax Cuts and Jobs Act eliminated the option to deduct research and development expenditures and requires taxpayers to amortize them generally over five years. The U.S. Congress is considering legislation that would restore the current deductibility of research and development expenditures, however, there is no assurance that the provision will be repealed or otherwise modified. Such changes, among others, may adversely affect our effective tax rate, results of operation and general business condition.

For example, beginning in 2022, the Tax Cuts and Jobs Act eliminated the previously available option to immediately deduct research and development expenditures and instead requires taxpayers to amortize them generally over five years for research activities conducted in the United States and over 15 years for research activities conducted outside the United States. On July 4, 2025, the U.S. Congress enacted the One Big Beautiful Bill Act, which includes a provision restoring the immediate deductibility of domestic research and development expenditures. The impact of this newly enacted law on our tax position will depend on how the provision is implemented and interpreted by the IRS and other regulatory authorities. In addition, we have no assurance as to whether, when and how this provision may be subject to further amendment or repeal. Such changes, among others, may adversely affect our effective tax rate, results of operation and financial condition.

We may acquire businesses or products, or form strategic alliances, in the future, and may not realize the benefits of such acquisitions.

We may acquire additional businesses or products, form strategic alliances, or create joint ventures with third parties that we believe will complement or augment our existing business. If we acquire businesses with promising markets or technologies, we may not be able to realize the benefit of acquiring such businesses if we are unable to successfully integrate them with our existing operations and company culture. We may encounter numerous difficulties in developing, manufacturing and marketing any new drug candidates or products resulting from a

strategic alliance or acquisition that delay or prevent us from realizing their expected benefits or enhancing our business. There is no assurance that, following any such acquisition, we will achieve the synergies expected in order to justify the transaction, which could result in a material adverse effect on our business and prospects.

We maintain our cash at financial institutions, at times in balances that exceed federally-insured limits. The failure of financial institutions could adversely affect our ability to pay our operational expenses or make other payments.

Our cash held in non-interest-bearing and interest-bearing accounts at financial institutions can at times exceed the Federal Deposit Insurance Corporation ("FDIC") insurance limits. If such banking institutions were to fail, we could lose all or a portion of those amounts held in excess of such insurance limitations. For example, the FDIC took control of Silicon Valley Bank on March 10, 2023. The Federal Reserve subsequently announced that account holders would be made whole. However, the FDIC may not make all account holders whole in the event of future bank failures. In addition, even if account holders are ultimately made whole with respect to a future bank failure, account holders' access to their accounts and assets held in their accounts may be substantially delayed. Any material loss that we may experience in the future or inability for a material time period to access our cash and cash equivalents could have an adverse effect on our ability to pay our operational expenses or make other payments, which could adversely affect our business.

There is substantial doubt about our ability to continue as a going concern.

We have prepared cash flow forecasts which indicate that, based on our expected operating losses and negative cash flows, there is substantial doubt about our ability to continue as a going concern for the twelve months after the respective dates our financial statements for the years ended December 31, 2025 and 2024 were issued. As a result, management has included disclosures in Note 1 of the financial statements and our independent registered public accounting firm has included an explanatory paragraph in its report on our financial statements for the fiscal year ended December 31, 2025 with respect to this uncertainty. Our future viability as an ongoing business is dependent on our ability to generate cash from our operating activities and to raise additional capital to finance our operations.

There is no assurance that we will succeed in obtaining sufficient funding on terms acceptable to us to fund continuing operations, if at all. The perception that we might be unable to continue as a going concern may also make it more difficult to obtain financing for the continuation of our operations on terms that are favorable to us, or at all, and could result in the loss of confidence by investors and employees. Our financial statements do not include any adjustments that might result from the outcome of this uncertainty. If we are unable to continue as a going concern, we may have to liquidate our assets and may receive less than the value at which those assets are carried on our financial statements, and it is likely that our investors will lose all or a part of their investment.

We previously identified a material weakness in our information technology general controls that has since been remediated. If we experience additional material weaknesses in the future or otherwise fail to maintain an effective system of internal controls in the future, we may not be able to accurately or timely report our financial condition or results of operations, which may adversely affect investor confidence in us and, as a result, the value of our common stock.

We previously identified a material weakness in our information technology general controls that has since been remediated. A material weakness is a deficiency, or a combination of deficiencies, in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of our annual or interim financial statements will not be prevented or detected on a timely basis. In preparing the financial statements as of and for the year ended December 31, 2024, management has identified it had not fully maintained components of the COSO framework, a system for establishing internal controls, which constituted a material weakness. Specifically, the control deficiencies related to administrative users' access to the financial system which allows them to create, edit, review and post journal entries resulting in the lack of appropriate segregation of duties.

This material weakness did not result in any adjustments to the financial statements. In October 2025, we implemented remediation measures to limit administrative user access to the financial system. Specifically, we have removed the segregation of duties conflicts related to senior management by removing excess access to the financial system from those users.

We cannot assure you that the measures we have taken to date will be sufficient to avoid potential future material weaknesses. There could continue to be a reasonable possibility that a future material misstatement of our financial statements would not be prevented or detected on a timely basis.

If we identify new material weaknesses in our internal controls over financial reporting, if we are unable to comply with the requirements of Section 404 of the Sarbanes-Oxley Act in a timely manner, if we are unable to conclude that our internal controls over financial reporting are effective, or if our independent registered public accounting firm is unable to express an opinion as to the effectiveness of our internal controls over financial reporting when we are no longer an emerging growth company, investors may lose confidence in the accuracy and completeness of our financial reports and the market price of our common stock could be negatively affected. As a result of such failures, we could also become subject to investigations by the stock exchange on which our securities are listed, the SEC or other regulatory authorities, and become subject to litigation from investors and stockholders, which could harm our reputation and financial condition or divert financial and management resources from our regular business activities.

The dual roles of our directors who also serve in similar roles with Mstone could create a conflict of interest and will require careful monitoring by our independent directors.

We share some directors with Mstone which could create conflicts of interest between the two companies in the future. While we believe that the Service Agreement was negotiated by independent parties on both sides on arm's length terms, and the fiduciary duties of both parties were thereby satisfied, in the future situations may arise under the operation of both agreements that may create a conflict of interest. We will have to be diligent to ensure that any such situation is resolved by independent parties. In particular, the Service Agreement does not contain any provision restricting Mstone and its affiliates from pursuing opportunities which could potentially be of interest to us, and they are not required to notify us prior to pursuing such opportunities. Any conflict of interest or pursuit by Mstone of such a corporate opportunity could expose us to claims by our investors and/or creditors and could harm our results of operations.

Risks Related to Intellectual Property

Our ability to protect our patents and other proprietary rights is uncertain, exposing us to the possible loss of competitive advantage.

We rely and expect to continue to rely upon a combination of patents, trademarks, trade secret protection and confidentiality agreements to protect the intellectual property related to our drug candidates and technologies and to prevent third parties from unfairly competing with us. Our success depends in large part on our ability to obtain and maintain patent protection for platform technologies and our drug candidates and their uses, as well as the ability to operate without infringing on or violating the proprietary rights of others. As of January 12, 2026, our patent portfolio consists of six distinct patent application families protecting the compositions of matter and methods of treatment of our product candidates, and expect to continue to file patent applications in the United States and abroad related to discoveries and technologies that are important to our business. However, we may not be able to protect our intellectual property rights throughout the world and the legal systems in certain countries may not favor enforcement or protection of patents, trade secrets and other intellectual property. Filing, prosecuting and defending patents on drug candidates worldwide would be prohibitively expensive and our intellectual property rights in some foreign jurisdictions may be less extensive than those in the United States. As such, we do not have patents in all countries or all major markets and may not be able to obtain patents in all jurisdictions even if we apply for them. Competitors may operate in countries where we do not have patent protection and could then freely use our technologies and discoveries in such countries to the extent such technologies and discoveries are publicly known or disclosed in countries where patent protection has not been requested. In addition, competitors may be able to design around our patents to create technologies that directly compete with ours without infringing our intellectual property.

Our pending and future patent applications may not result in patents being issued. Any issued patents may not afford sufficient protection of our drug candidates or their intended uses against competitors, nor can there be any assurance that the patents issued will not be infringed, designed around, invalidated by third parties, or effectively prevent others from commercializing competitive technologies, products or drug candidates. Even if these patents are granted, they may be difficult to enforce. Further, any issued patents that may be licensed or owned covering our drug candidates could be narrowed or found invalid or unenforceable if challenged in court or before administrative

bodies in the United States or abroad, including the United States Patent and Trademark Office ("USPTO"). Further, if we encounter delays in any clinical trials or delays in obtaining regulatory approval, the period of time during which we could market drug candidates under patent protection would be reduced. Thus, the patents that we may own or license may not afford any meaningful competitive advantage.

In addition to seeking patents for some of our technology and drug candidates, we may also rely on trade secrets, including unpatented know-how, technology and other proprietary information, to maintain our competitive position. Any disclosure, either intentional or unintentional, by our employees, the employees of third parties with whom we share facilities or third-party consultants and vendors that we engage to perform researches, clinical trials or manufacturing activities, or misappropriation by third parties (such as through a cybersecurity breach) of our trade secrets or proprietary information could enable competitors to duplicate or surpass our technological achievements, thus eroding our competitive position in the market. In order to protect our proprietary technology and processes, we rely in part on confidentiality agreements with collaborators, employees, consultants, outside scientific collaborators and sponsored researchers and other advisors. These agreements may not effectively prevent disclosure of confidential information and may not provide an adequate remedy in the event of unauthorized disclosure of confidential information. We may need to share our proprietary information, including trade secrets, with future business partners, collaborators, contractors and others located in countries at heightened risk of theft of trade secrets, including through direct intrusion by private parties or foreign actors and those affiliated with or controlled by state actors. In addition, while we undertake efforts to protect our trade secrets and other confidential information from disclosure, others may independently discover trade secrets and proprietary information, and in such cases, we may not be able to assert any trade secret rights against such party. Costly and time-consuming litigation could be necessary to enforce and determine the scope of our proprietary rights and failure to obtain or maintain trade secret protection could adversely affect our competitive business position.

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

We may not be successful in obtaining or maintaining necessary rights to drug candidates through acquisitions and in-licenses.

Because our development programs require and may in the future require the use of proprietary rights held by third parties, the growth of our business may depend in part on our ability to acquire, in-license, or use these third-party proprietary rights. We may be unable to acquire or in-license any compositions, methods of use, processes or other third-party intellectual property rights from third parties that we identify as necessary for drug candidates. The licensing and acquisition of third-party intellectual property rights is a competitive area, and a number of more established companies may pursue strategies to license or acquire third-party intellectual property rights that we may consider attractive or necessary. These established companies may have a competitive advantage over us due to their size, capital 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. We also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on investment or at all. If we are unable to successfully obtain rights to required third-party intellectual property rights or maintain the existing intellectual property rights we have, we may have to abandon development of the relevant drug candidate, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

While we will normally seek to obtain the right to control prosecution, maintenance and enforcement of the patents relating to a drug candidate, there may be times when the filing and prosecution activities for patents and patent applications relating to a drug candidate are controlled by future licensors or collaboration partners. For example, we currently license several patent families from Rush University Medical Center ("Rush"). If Rush fails to prosecute, maintain and enforce such patents and patent applications in a manner consistent with the best interests of our business, including by payment of all applicable fees for patents covering a drug candidate, we could lose rights to the intellectual property or exclusivity with respect to those rights, our ability to develop and commercialize such candidates may be adversely affected and we may not be able to prevent competitors from making, using and selling competing products. In addition, even where we have the right to control patent prosecution of patents and patent applications which may be licensed to and from third parties, we may still be adversely affected or prejudiced by actions or inactions of licensees, future licensors and their counsel that took place prior to the date upon which we assumed control over patent prosecution.

Our future licensors may rely on third-party consultants or collaborators or on funds from third parties such that future licensors are not the sole and exclusive owners of the patents we in-license. If other third parties have ownership rights to future in-licensed patents, they may be able to license such patents to our competitors, and the 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.

It is possible that we may be unable to obtain licenses at a reasonable cost or on reasonable terms, if at all. Even if we are able to obtain a license, it may be non-exclusive, thereby giving competitors access to the same technologies licensed to us. In that event, we may be required to expend significant time and resources to redesign our technology, drug candidates, or the methods for manufacturing the same, 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 drug candidates, which could harm our business, financial condition, results of operations, and prospects significantly. We cannot provide any assurances that third-party patents do not exist which might be enforced against our current technology or manufacturing methods, our drug candidates, or future methods or drug candidates, resulting in either an injunction prohibiting manufacture or future sales, or, with respect to future sales, an obligation on our part to pay royalties and/or other forms of compensation to third parties, which could be significant.

Disputes may arise between us and our future licensors regarding intellectual property subject to a license agreement, including: the scope of rights granted under the license agreement and other interpretation-related issues; whether and to what extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement; our right to sublicense patents and other rights to third parties; our right to transfer or assign the license; the inventorship and ownership of inventions and know-how resulting from the joint creations or use of intellectual property by future licensors and us and/or our partners; and the priority date of an invention of patented technology.

Certain of our current drug candidates and research programs are licensed from or based upon licenses from a third party and are field limited to certain indications. If these license agreements are terminated or interpreted to narrow our rights, our ability to advance our current drug candidates or develop new drug candidates based on these technologies will be materially adversely affected.

We depend on, and will continue to depend on, our current licenses with Rush, as well as potentially on other strategic relationships with third parties, for the research, development, manufacturing and commercialization of our current drug candidates. If any of our licenses or relationships or any in-licenses on which our licenses are based are terminated or breached, we may:

- lose our rights to develop and market our current drug candidates;
- lose patent or trade secret protection for our current drug candidates;
- experience significant delays in the development or commercialization of our current drug candidates;
- not be able to obtain any other licenses on acceptable terms, if at all; or
- incur liability for damages.

Additionally, even if not terminated or breached, our intellectual property licenses or sublicenses may be subject to disagreements over contract interpretation, which could narrow the scope of our rights to the relevant intellectual property or technology or increase our financial or other obligations.

If we experience any of the foregoing, it could have a materially adverse effect on our business and could force us to cease operations.

If we fail to comply with our obligations in any agreements under which we may license intellectual property rights from third parties or otherwise experience disruptions to our business relationships with our licensors, we could lose license rights that are important to our business.

We are party to license agreements with Rush and may from time to time in the future be party to other license and collaboration agreements with third parties to advance our research or allow commercialization of current or future drug candidates. Such agreements may impose numerous obligations, such as development, diligence,

payment, commercialization, funding, milestone, royalty, sublicensing, insurance, patent prosecution, enforcement and other obligations on us and may require us to meet development timelines, or to exercise commercially reasonable efforts to develop and commercialize licensed products, in order to maintain the licenses. Despite our best efforts, our licensors might conclude that we have materially breached our license agreements and might therefore terminate the license agreements, thereby removing or limiting our ability to develop and commercialize products and technologies covered by these license agreements.

If these licenses are terminated for any reason, or if the underlying patents fail to provide the intended exclusivity, we could lose significant rights and our ability to commercialize our current or future drug candidates may be harmed, and competitors or other third parties would have the freedom to seek regulatory approval of, and to market, products identical to ours and we may be required to cease our development and commercialization of certain of our current or future drug candidates. Any of the foregoing could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects.

Disputes may also arise between us and our licensors regarding intellectual property subject to a license agreement, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- whether and the extent to which our technology and processes infringe, misappropriate or otherwise violate intellectual property rights of the licensor that is not subject to the licensing agreement;
- our right to sublicense patent and other rights to third parties under collaborative development relationships;
- our diligence obligations with respect to the use of the licensed technology in relation to the development and commercialization of our current or future drug candidates, and what activities satisfy those diligence obligations;
- the priority of invention of any patented technology; and
- the ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our current or future licensors and by us and our other partners.

In addition, the agreements under which we may license intellectual property or technology from third parties are likely to be 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 may license prevent or impair our ability to maintain future licensing arrangements on acceptable terms, we may be unable to successfully develop and commercialize the affected current or future drug candidates, which could have a material adverse effect on our business, financial conditions, results of operations and prospects.

We may be subject to patent infringement claims or may need to file claims to protect our intellectual property, which could result in substantial costs, liability and diversion of resources, and prevent or delay us from commercializing potential products.

Because the intellectual property landscape in the biotechnology industry is rapidly evolving and interdisciplinary, it is difficult to conclusively assess our freedom to operate and guarantee that we can operate without infringing on or violating third-party rights. If certain of our drug candidates are ultimately granted regulatory approval, patent rights held by third parties, if found to be valid and enforceable, could be alleged to render one or more of such drug candidates infringing. We cannot be certain that patents owned or licensed by us will not be challenged by others in the course of litigation. If a third party successfully brings a claim against us, we may be required to pay substantial damages, be forced to abandon any affected drug candidate and/or seek a license from the patent holder. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have a material adverse effect on our business.

Competitors may infringe or otherwise violate our patents, trademarks, copyrights or other intellectual property. To counter infringement or other violations, we may be required to file claims, which can be expensive and time-consuming. Any such claims could provoke these parties to assert counterclaims against us, including claims alleging that our intellectual property, methods or products infringes their patents or other intellectual property rights. In addition, in a patent infringement proceeding, a court or administrative body may decide that one or more of the patents we assert is invalid or unenforceable, in whole or in part, construe the patent's claims narrowly or refuse to prevent the other party from using the technology at issue on the grounds that our patents do not cover the technology. Similarly, if we assert trademark infringement claims, a court or administrative body may determine that the marks asserted are invalid or unenforceable or that the party against whom we have asserted trademark infringement has superior rights to the marks in question. In such a case, we could ultimately be forced to cease use of such marks. In any intellectual property litigation, even if we are successful, any award of monetary damages or other remedy received may not be commercially valuable.

Further, we may be required to protect our patents from procedures created to attack the validity of a patent at the USPTO. An adverse determination in any such submission or proceeding could reduce the scope or enforceability of, or invalidate, our patent rights, which could adversely affect our competitive position. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in U.S. federal courts necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action.

If we are required to defend intellectual property actions brought by third parties, or if we sue to protect our own intellectual property rights or otherwise to protect our proprietary information and to prevent its disclosure, or if we are involved in other litigation, whether as a plaintiff or defendant, and whether or not successful, we may incur substantial legal expenses and the attention of our management and key personnel may be diverted from business operations. Further, some of our competitors may be able to sustain the costs of complex intellectual property litigation more effectively than we can because they have substantially greater resources.

In addition, if our drug candidates are found to infringe the intellectual property rights of third parties, these third parties may assert infringement claims against our future licensees and other parties with whom we have business relationships and we may be required to indemnify those parties for any damages they suffer as a result of these claims, which may require us to initiate or defend protracted and costly litigation on behalf of licensees and other parties regardless of the merits of such claims. If any of these claims succeed, we may be forced to pay damages on behalf of those parties or may be required to obtain licenses for the products they use, and may not be able to obtain such licenses on terms acceptable to us, if at all.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation or other legal proceedings relating to our intellectual property rights, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation or other proceedings.

We may be subject to claims that we have wrongfully hired an employee from a competitor or that employees, consultants or independent contractors have wrongfully used or disclosed confidential information of third parties.

As is common in the biotechnology industry, in addition to employees, we engage consultants to assist in the development of our drug candidates. Many of these consultants, and many of our employees, were or may have been previously employed at, or may have previously provided or may be currently providing consulting services to, other biotechnology or pharmaceutical companies including our competitors or potential competitors. We could in the future be subject to claims that we or our employees or consultants working on our behalf have inadvertently or otherwise used or disclosed alleged trade secrets or other confidential information of former employers or competitors. Although we try to ensure that our employees and consultants do not use the intellectual property, proprietary information, know-how or trade secrets of others in their work for us, we may become subject to claims that we caused an employee to breach the terms of his or her non-competition or non-solicitation agreement, or that we or these individuals have, inadvertently or otherwise, used or disclosed the alleged trade secrets or other proprietary information of a former employer or competitor.

We may litigate to defend ourselves against these claims, and even if we are successful, litigation could result in substantial costs and could be a distraction to management. If our defenses to these claims fail, in addition to requiring us to pay monetary damages, a court could prohibit us from using technologies or features that are essential to our drug candidates, if such technologies or features are found to incorporate or be derived from the trade secrets or other proprietary information of the former employers. Moreover, any such litigation or the threat thereof may adversely affect our reputation, our ability to form strategic alliances or sublicense our rights to collaborators, engage with scientific advisors or hire employees or consultants, each of which would have an adverse effect on our business, operations and financial condition.

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 (the "Leahy-Smith Act"), could increase the uncertainties and costs surrounding the prosecution of our owned and any future in-licensed patent applications and the maintenance, enforcement or defense of our owned and any future in-licensed issued patents. The Leahy-Smith Act includes a number of significant changes to U.S. 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 along with 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 16, 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 16, 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, operations and prospects.

In addition, the patent positions of companies in the development and commercialization of biologics and pharmaceuticals are particularly uncertain. U.S. Supreme Court and U.S. Court of Appeals for the Federal Circuit rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations, including in the antibody arts. This combination of events has created uncertainty with respect to the validity and enforceability of patents once obtained. 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.

Geopolitical actions in the United States and in foreign countries could increase the uncertainties and costs surrounding the prosecution or maintenance of patent applications and the maintenance, enforcement or defense of issued patents. Accordingly, our competitive position may be impaired, and our business, financial condition, operations and prospects may be adversely affected.

In addition, a European Unified Patent Court ("UPC") came into force in June 2023. The UPC is a common patent court to hear patent infringement and revocation proceedings effective for member states of the EU. This could enable third parties to seek revocation of a European patent in a single proceeding at the UPC rather than through multiple proceedings in each of the jurisdictions in which the European patent is validated. We currently have two pending European applications, and if we obtain such patents and applications in the future, any such revocation and loss of patent protection could have a material adverse impact on our business and our ability to commercialize or license our technology and products. Moreover, the controlling laws and regulations of the UPC will develop over time, and may adversely affect our ability to enforce or defend the validity of any European patents obtained. We may decide to opt out from the UPC for any future European patent applications that we may file and any patents we may obtain. If certain formalities and requirements are not met, however, such European patents and patent applications could be challenged for non-compliance and brought under the jurisdiction of the UPC. We cannot be certain that future European patents and patent applications will avoid falling under the jurisdiction of the UPC, if we decide to opt out of the UPC.

Obtaining and maintaining patent protection depends on compliance with various procedural, document submissions, 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 fees, renewal fees, annuities fees and various other governmental fees on patents and/or patent applications are due to be paid to the USPTO and foreign patent agencies in several stages over the lifetime of the patent and/or patent application. The USPTO and various foreign governmental patent agencies also require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. 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, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. If we fail to maintain the patents and patent applications covering our drug candidates, our competitive position would be adversely affected.

We may not identify relevant third-party patents or may incorrectly interpret the relevance, scope or expiration of a third-party patent, which might adversely affect our ability to develop and market our products.

We cannot guarantee that any of our patent searches or analyses, including the identification of relevant patents, the scope of patent claims or the expiration of relevant patents, are complete or thorough, nor can we be certain that we have identified each and every third-party patent and pending application in the United States and abroad that is relevant to or necessary for the commercialization of our drug candidates in any jurisdiction. The scope of a patent claim is determined by an interpretation of the law, the written disclosure in a patent and the patent's prosecution history. Our interpretation of the relevance or the scope of a patent or a pending application may be incorrect. For example, we may incorrectly determine that our products are not covered by a third-party patent or may incorrectly predict whether a third party's pending application will issue with claims of relevant scope. Our determination of the expiration date of any patent in the United States or abroad that we consider relevant may be incorrect. Our failure to identify and correctly interpret relevant patents may negatively impact our ability to develop and market our products.

In addition, because some patent applications in the United States may be maintained in secrecy until the patents are issued, patent applications in the United States and many foreign jurisdictions are typically not published until 18 months after filing, and publications in the scientific literature often lag behind actual discoveries, we cannot be certain that others have not filed patent applications for technology covered by our pending applications or any future issued patents, or that we were the first to invent the technology. Our competitors may have filed, and may in the future file, patent applications covering our products or technology similar to ours. Any such patent application may have priority over our patent applications or patents, which could require us to obtain rights to issued patents covering such technologies.

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

We may be subject to claims that former employees, collaborators or other third parties have an interest in our patents or other intellectual property as an inventor or co-inventor. The failure to name the proper inventors on a patent application can result in the patents issuing thereon being unenforceable. Inventorship disputes may arise from conflicting views regarding the contributions of different individuals named as inventors, the effects of foreign laws where foreign nationals are involved in the development of the subject matter of the patent, conflicting obligations of third parties involved in developing our drug candidates or as a result of questions regarding co-ownership of potential joint inventions. Litigation may be necessary to resolve these and other claims challenging inventorship and/or ownership. Alternatively, or additionally, we may enter into agreements to clarify the scope of our rights in such intellectual property. If we 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, valuable intellectual property. Such an outcome could have a material adverse effect on our business. 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.

Our current or future licensors may have relied on third-party consultants or collaborators or on funds from third parties, such as the U.S. government or academic institutions, such that our licensors are not the sole and exclusive owners of the patents we in-licensed. If other third parties have ownership rights or other rights to our in-licensed patents, 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, operations, and prospects.

Patent terms may be inadequate to protect our competitive position on our drug 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 drug 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 drug candidates, patents protecting such drug candidates might expire before or shortly after such drug candidates are commercialized. As a result, our owned and future licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

Some intellectual property that we have in-licensed may have been discovered through government-funded programs and thus may be subject to federal regulations such as "march-in" rights, certain reporting requirements and a preference for U.S.-based companies. Compliance with such regulations may limit our exclusive rights, and limit our ability to contract with non-U.S. manufacturers.

Certain of the intellectual property rights we have licensed may have been generated through the use of U.S. government funding and may therefore be subject to certain federal regulations. As a result, the U.S. government may have certain rights to intellectual property embodied in our current or future drug candidates pursuant to the Bayh-Dole Act of 1980 (the "Bayh-Dole Act") and implementing regulations. These U.S. government rights in certain inventions developed under a government-funded program include a non-exclusive, non-transferable, irrevocable worldwide license to use inventions for any governmental purpose. In addition, the U.S. government has the right to require our or our licensors' to grant exclusive, partially exclusive, or non-exclusive licenses to any of these inventions to a third party if it determines that: (i) adequate steps have not been taken to commercialize the invention; (ii) government action is necessary to meet public health or safety needs; or (iii) government action is necessary to meet requirements for public use under federal regulations (also referred to as "march-in rights"). The U.S. government also has the right to take title to these inventions if we fail, or the applicable licensor, fails to disclose the invention to the government and fails to file an application to register the intellectual property within specified time limits. These time limits have recently been changed by regulation, and may change in the future. Intellectual property generated under a government-funded program is also subject to certain reporting requirements, compliance with which may require us or the applicable licensor to expend substantial resources. In addition, the U.S. government requires that any products embodying the subject invention or produced through the use of the subject invention be manufactured substantially in the United States. The manufacturing preference requirement can be waived if the owner of the intellectual property can show that reasonable but unsuccessful efforts have been made to grant licenses on similar terms to potential licensees that would be likely to manufacture substantially in the United States or that under the circumstances domestic manufacture is not commercially feasible. This preference for U.S. manufacturers may limit our ability to contract with non-U.S. product manufacturers for products covered by such intellectual property. To the extent any of our current or future intellectual property is generated through the use of U.S. government funding, the provisions of the Bayh-Dole Act may similarly apply.

Risks Related to Government Regulation

The regulatory approval processes of the FDA and other comparable foreign regulatory authorities are lengthy, time-consuming and inherently unpredictable. If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals for our drug candidates, or if we determine that we are not willing or able to complete the regulatory approval process given the resources required to do so, we will not be able to commercialize, or will be delayed in commercializing, such drug candidates, and our ability to generate revenue will be materially impaired.

The process of obtaining regulatory approvals, both in the United States and abroad, is unpredictable, expensive and typically takes many years following commencement of clinical trials, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the drug candidates involved. We cannot commercialize drug candidates in the United States without first obtaining regulatory approval from the FDA. In addition, we may determine that the resources required to complete the regulatory approval process are in excess of what we are able or willing to expend on a particular program.

Similarly, we cannot commercialize drug candidates outside of the United States without obtaining regulatory approval from comparable foreign regulatory authorities. Before obtaining regulatory approvals for the commercial sale of our drug candidates, including our most advanced drug candidate, PLX-200, we must demonstrate through lengthy, complex and expensive preclinical and clinical trials that such drug candidates are safe, pure and effective or potent for each targeted indication.

Securing regulatory approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the relevant regulatory authority. Further, a drug candidate may not be effective or potent, may be only moderately effective or potent or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude its obtaining marketing approval. The FDA and comparable foreign regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional preclinical, clinical or other data. A drug candidate could be delayed in receiving, or fail to receive, regulatory approval for many reasons, including: the FDA or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical trials; we may be unable to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that a drug candidate is safe, pure, and effective or potent for its proposed indication; the results of clinical trials may not meet the level of statistical significance required by the FDA or comparable foreign regulatory authorities for approval; serious and unexpected product-related side effects may be experienced by participants in our clinical trials or by individuals using drugs or biological products similar to a drug candidate; we may be unable to demonstrate that a candidate's clinical and other benefits outweigh its safety risks; the FDA or comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials; the data collected from clinical trials of a drug candidate may not be acceptable or sufficient to support the submission of a BLA, NDA or other submission or to obtain regulatory approval in the United States or elsewhere, and we may be required to conduct additional clinical trials; the FDA or the applicable foreign regulatory authority may disagree regarding the formulation, labeling and/or the specifications of a drug candidate; the FDA or comparable foreign regulatory authorities may fail to approve the manufacturing processes or facilities of third-party manufacturers with which we contract for clinical and commercial supplies; and the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

Of the large number of products in development, only a small percentage successfully complete the FDA or foreign regulatory approval processes and are commercialized. The lengthy approval process as well as the unpredictability of future clinical trial results may result in us failing to obtain regulatory approval to market PLX-200 or other drug candidates, which would significantly harm our business, results of operations and prospects.

If we were to obtain approval, regulatory authorities may approve any such drug candidate for fewer or more limited indications than we request, including failing to approve the most commercially promising indications, may grant approval contingent on the performance of costly post-marketing clinical trials, or may approve a drug candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that drug candidate. If we are not able to obtain, or if there are delays in obtaining,

required regulatory approvals for a drug candidate, we will not be able to commercialize, or will be delayed in commercializing, such drug candidate and our ability to generate revenue may be materially impaired. In addition, the FDA and foreign regulatory authorities may undergo leadership changes, change their policies, issue additional regulations or revise existing regulations, or take other actions, such as those implemented by the recently established Department of Government Efficiency, which may impact our clinical development plans or prevent or delay approval of our drug candidates under development on a timely basis. Such policy or regulatory changes could impose additional requirements upon us that could delay our ability to obtain approvals and increase the costs of compliance. Additionally, changes in the leadership of the FDA and other federal agencies under President Trump's administration (the "Trump Administration") may also lead to new policies and changes in the regulations and operations of the FDA, which may impact our clinical development plans.

Because gene therapy is novel and the regulatory landscape that governs any drug candidates we may develop is rigorous, complex, uncertain and subject to change, we cannot predict the time and cost of obtaining regulatory approval, if received at all, for any drug candidates we may develop.

The regulatory requirements that will govern any novel gene therapy drug candidates we develop are not entirely clear and are subject to change. Within the broader genetic medicine field, very few therapeutic products have received marketing authorization from the FDA or 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 overlap in those responsible for review and 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"), as part of its reorganization of the Office of Tissues and Advanced Therapies, to consolidate the review of gene therapy and related products. In addition, the Cellular, Tissue and Gene Therapies Advisory Committee advises CBER on its review.

Our drug candidates will need to meet safety, purity and efficacy or potency standards applicable to any new biologic under the regulatory framework administered by the FDA. In addition to FDA oversight and oversight by IRBs under guidelines promulgated by the National Institutes of Health ("NIH") 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 research utilizing recombinant or synthetic nucleic acid molecules at that institution. The IBC assesses the safety of the research and identifies any potential risk to public health or the environment. While the NIH guidelines are not mandatory unless the research in question is being conducted at or sponsored by institutions receiving NIH funding of recombinant or synthetic nucleic acid molecule research, many companies and other institutions not otherwise subject to the NIH guidelines voluntarily follow them. 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 EU. The EMA's Committee for Advanced Therapies ("CAT") is responsible for assessing the quality, safety, and efficacy of advanced-therapy medicinal products. Advanced-therapy medicinal products include gene therapy medicines, somatic-cell therapy medicines and tissue-engineered medicines. 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 EU, the development and evaluation of a gene therapy product must be considered in the context of the relevant EU guidelines. The EMA may issue new guidelines concerning the development and marketing authorization for gene therapy 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 drug candidate we may develop, but that remains uncertain at this point.

Adverse developments in preclinical studies or clinical trials conducted by others in the field of gene therapy and gene regulation products may cause the FDA, the EMA, and other regulatory authorities to revise the requirements for approval of any drug candidates we may develop or limit the use of products utilizing gene regulation technologies, either of which could harm our business. In addition, the clinical trial requirements of the FDA, the EMA, and other regulatory authorities and the criteria these regulators use to determine the safety, purity and efficacy or potency of a drug candidate vary substantially according to the type, complexity, novelty, and intended use and market of the potential products. Because of this complexity, the regulatory approval process for drug candidates such as those being developed by us can be more expensive and take longer than for other,

better known, or more extensively studied pharmaceutical or other drug candidates. Further, we are developing novel potential treatments for diseases in which, in some cases, there is little clinical experience with potential new endpoints and methodologies, heightened risk that the FDA, the EMA or other regulatory authorities may not consider the clinical trial endpoints to provide clinically meaningful results, and the resulting clinical data and results may be more difficult to analyze. In addition, we may not be able to identify or develop appropriate animal disease models to enable or support planned clinical development. Any natural history studies that we may conduct or rely upon in our clinical development may not be accepted by the FDA, EMA or other regulatory authorities. Regulatory agencies administering existing or future regulations or legislation may not allow production and marketing of products utilizing gene regulation technology in a timely manner or under technically or commercially feasible conditions. In addition, regulatory action or private litigation could result in expenses, delays, or other impediments to our research programs or the commercialization of resulting products. Further, approvals by one regulatory agency may not be indicative of what other regulatory agencies may require for approval.

The regulatory review committees and advisory groups described above and the new guidelines they promulgate may lengthen the regulatory review process, require us to perform additional preclinical studies or clinical trials, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of these treatment candidates, or lead to significant post-approval limitations or restrictions. As we advance our research programs and develop future drug candidates, we will be required to consult with these regulatory and advisory groups and to comply with applicable guidelines. If we fail to do so, we may be required to delay or discontinue development of any drug candidates we identify and develop. These additional processes may result in a review and approval process that is longer than we otherwise would have expected. Delays as a result of an increased or lengthier regulatory approval process or further restrictions on the development of our drug candidates can be costly and could negatively impact our ability to complete clinical trials and commercialize our current and future drug candidates in a timely manner, if at all.

Disruptions at the FDA and other government agencies and regulatory authorities could negatively affect the review of our regulatory submissions or impact our ability to access the public markets, which could negatively impact our business.

The ability of the FDA and other regulatory authorities to review and approve regulatory submissions can be affected by a variety of factors, including statutory, regulatory and policy changes, inadequate government budget funding levels or a reduction in the FDA's workforce and its ability to hire and retain key personnel, disruptions caused by government shutdowns and public health crises. There have been mass layoffs of federal government employees since the start of the Trump Administration in January 2025, the full impact of which is unclear at this time. Average review times at the agency have fluctuated as a result. In addition, government funding of 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, the Trump Administration has made and is expected to continue to make changes in the leadership of various U.S. federal regulatory agencies and changes to U.S. federal government policy that have led to, in some cases, legal challenges and uncertainty around the funding, functioning and policy priorities of the U.S. federal regulatory agencies, including the FDA.

We are unable to predict the extent to which the current U.S. federal administration may impose or seek to impose leadership or policy changes at the U.S. federal regulatory agencies responsible for regulating our business or changes to rules and policies impacting our operations. It is unclear how these executive actions or other potential actions by the Trump Administration or other parts of the federal government will impact the FDA or other regulatory authorities that oversee our business. Government proposals to reduce or eliminate budgetary deficits or limit federal agency personnel may include reduced allocations to the FDA and other related government agencies. These budgetary pressures may reduce the FDA's ability to perform its responsibilities, potentially affecting our ability to progress development of our drug candidates or obtain regulatory approval for our drug candidates and could result in delays in our clinical trial timelines. Disruptions at the FDA and other agencies or comparable foreign regulatory authorities may also slow the time necessary for the review and approval of CTAs or MAAs, which would adversely affect our business. If a significant reduction in the FDA's workforce occurs, the FDA's budget is significantly reduced or a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions or take other actions critical to the development, manufacturing or marketing of our most advanced drug candidate, PLX-200, or other drug candidates, if approved, which could have a material adverse effect on our business.

If a prolonged government shutdown occurs, or if global health concerns prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews, or other regulatory activities, it could significantly impact the ability of the FDA or other regulatory authorities 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.

We may not be able to meet requirements for the chemistry, manufacturing and control of our drug candidates.

In order to receive approval of our products by the FDA and comparable foreign regulatory authorities, we must show that we and our contract manufacturing partners are able to characterize, control and manufacture our biological products safely and in accordance with regulatory requirements. This includes manufacturing the drug substance, developing an acceptable formulation, performing tests to adequately characterize the formulated product, documenting a repeatable manufacturing process, and demonstrating that our biological products meet stability requirements. Meeting these chemistry, manufacturing and control ("CMC") requirements is a complex task that requires specialized expertise. If we are not able to meet the CMC requirements, we may not be successful in getting our products approved.

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

We plan to conduct clinical trials outside the United States, including in the UK, Germany and Asia or other foreign jurisdictions. In cases where data from clinical trials conducted outside the United States are intended to serve as the sole basis for marketing approval in the United States, the FDA will generally not approve the application on the basis of foreign data alone unless (i) the data are applicable to the United States population and United States medical practice; (ii) the trials were performed by clinical investigators of recognized competence and (iii) the data may be considered valid without the need for an on-site inspection by the FDA or, if the FDA considers such an inspection to be necessary, the FDA is able to validate the data through an on-site inspection or other appropriate means. Additionally, the FDA's clinical trial requirements, including sufficient size of patient populations and statistical powering, must be met. 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 similar foreign regulatory authority will accept data from trials conducted outside of the United States or the applicable jurisdiction. If the FDA or any similar foreign regulatory authority does not accept such data, it would result in the need for additional trials, which would be costly and time-consuming and delay aspects of our business plan, and which may result in our drug candidates not receiving approval or clearance for commercialization in the applicable jurisdiction. Even if the FDA accepts such data, it could require us to modify our planned clinical trials to receive clearance to initiate such trials in the United States or to continue such trials once initiated.

Other risks inherent in conducting international clinical trials include: foreign regulatory requirements, differences in healthcare services, and differences in cultural customs that could restrict or limit our ability to conduct our clinical trials; administrative burdens of conducting clinical trials under multiple sets of foreign regulations; foreign exchange fluctuations; diminished protection of intellectual property in some countries; and political and economic risks relevant to foreign countries.

Our drug candidates for which we intend to seek approval as biologics may face competition sooner than anticipated.

The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, 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-licensed reference biological product. Under the BPCIA, an application for a highly similar or "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 its product.

Our investigational biological products, if approved, could be considered reference products entitled to 12-year exclusivity. However, there is a risk that this exclusivity could be shortened due to congressional action or otherwise, or that the FDA will not consider a drug candidate to be reference products for competing products, potentially creating the opportunity for 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. Moreover, the extent to which a biosimilar, once approved, will be substituted for any 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.

Even if we receive regulatory approval of PLX-200 or other drug candidates, we will be subject to extensive ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our drug candidates.

Any regulatory approvals that we may receive for PLX-200 or other drug candidates will require the submission of reports to regulatory authorities and surveillance to monitor the safety, purity and efficacy or potency of such drug candidates, may contain significant limitations related to use restrictions for specified age groups, warnings, precautions or contraindications, and may include burdensome post-approval study or risk management requirements. For example, the FDA may require a risk evaluation and mitigation strategy in order to approve a drug candidate, which could entail requirements for a medication guide, physician training and communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. In addition, if the FDA or comparable foreign regulatory authorities approve a drug candidate, the products and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, purity, efficacy or potency, recordkeeping, labeling, storage, approval, advertising, promotion, sale, distribution, import and export will be subject to comprehensive regulation by the FDA and other regulatory agencies in the United States and by comparable foreign regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as on-going compliance with current cGMPs and GCPs for any clinical trials that we conduct following approval. In addition, manufacturers of drug products and their facilities are subject to continual review and periodic, unannounced inspections by the FDA and other regulatory authorities for compliance with cGMPs.

If we or a regulatory authority discovers previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facilities where the product is manufactured, a regulatory authority may impose restrictions on that product, the manufacturing facility or us, including requiring recall or withdrawal of the product from the market or suspension of manufacturing, requiring the addition of labeling statements, such as a "black box" warning or a contraindication, requiring creation of a medication guide outlining the risk of such side effects for distribution to patients, withdrawal or suspension of existing approvals or licenses, refusal to approve pending applications or supplements, restrictions on our ability to conduct clinical trials, including full or partial clinical holds on ongoing or planned trials, restrictions on the manufacturing process, warning or untitled letters, civil and criminal penalties, injunctions, product seizures, detentions or import bans, voluntary or mandatory publicity requirements and imposition of restrictions on operations, including costly new manufacturing requirements. The occurrence of any event or penalty described above may inhibit our ability to commercialize PLX-200 or other drug candidates and generate revenue and could require us to expend significant time and resources in response and could generate negative publicity.

We may face difficulties from healthcare legislative reform measures.

Existing regulatory policies may change, and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of PLX-200 or other drug candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability. See "*Business — Government*

Regulation — Healthcare Reform" in this Annual Report for a more detailed description of healthcare reforms measures that may prevent us from being able to generate revenue, attain profitability, or commercialize drug candidates.

Our business operations and current and future arrangements with investigators, healthcare professionals, consultants, third-party payors, patient organizations and customers will be subject to applicable healthcare regulatory laws, which could expose us to penalties.

Our business operations and current and future arrangements with investigators, healthcare professionals, consultants, third-party payors, patient organizations and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations. These laws may constrain the business or financial arrangements and relationships through which we conduct our operations, including how we research, market, sell and distribute our drug candidates, if approved. See "*Business — Government Regulation — Other Healthcare Laws and Compliance Requirements*" in this Annual Report for a more detailed description of the laws that may affect our ability to operate.

Ensuring that our internal operations and future business arrangements with third parties comply with applicable healthcare laws and regulations will involve substantial costs. If our operations are found to be in violation of any of these laws or any other governmental laws and regulations that may apply to us, we may be subject to significant penalties, including civil, criminal and administrative penalties, damages, fines, exclusion from government-funded healthcare programs, integrity oversight and reporting obligations to resolve allegations of non-compliance, disgorgement, individual imprisonment, contractual damages, reputational harm, diminished profits and the curtailment or restructuring of our operations. Further, defending against any such actions can be costly and 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.

Even if we are able to commercialize PLX-200 or other drug candidates, due to unfavorable pricing regulations and/or third-party coverage and reimbursement policies, we may not be able to offer such products at competitive prices which would seriously harm our business.

We intend to seek approval to market PLX-200 and other drug candidates in both the United States and in selected foreign jurisdictions. If we obtain approval in one or more foreign jurisdictions for such drug candidates, we will be subject to rules and regulations in those jurisdictions. Our ability to successfully commercialize any drug candidates that we may develop will depend in part on the extent to which reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers and other organizations. Government authorities and other third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. Government authorities and other third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. These entities may create preferential access policies for a competitor's product, including a branded or generic/biosimilar product, over our products in an attempt to reduce their costs, which may reduce our commercial opportunity. Additionally, if any of our drug candidates are approved and we are found to have improperly promoted off-label uses of those programs, we may become subject to significant liability, which would materially adversely affect our business and financial condition. See "*Business — Government Regulation — Coverage and Reimbursement" and "— Regulation in the European Union*" in this Annual Report for a more detailed description of the government regulations and third-party payor practices that may affect our ability to commercialize drug candidates.

We are subject to U.S. and certain foreign export and import controls, sanctions, embargoes, anti-corruption laws, and anti-money laundering laws and regulations. We can face criminal liability and other serious consequences for violations, which can harm our business.

We are subject to export control and import laws and regulations, including the U.S. Export Administration Regulations, U.S. Customs regulations, various economic and trade sanctions regulations administered by the U.S. Treasury Department's Office of Foreign Assets Controls, the U.S. Foreign Corrupt Practices Act of 1977, as amended, the U.S. domestic bribery statute contained in 18 U.S.C. § 201, the U.S. Travel Act, the USA PATRIOT Act, and other state and national anti-bribery and anti-money laundering laws in the countries in which we conduct

activities. In addition, the U.S. Congress is currently contemplating legislation that could have the impact of limiting the ability of us and certain of our vendors to work with certain designated biotech companies from China and other nations.

Anti-corruption laws are interpreted broadly and prohibit companies and their employees, agents, contractors, and other collaborators from authorizing, promising, offering, or providing, directly or indirectly, improper payments or anything else of value to or from recipients in the public or private sector. We may engage third parties to sell products outside the United States, to conduct clinical trials, and/or to obtain necessary permits, licenses, patent registrations, and other regulatory approvals. We have direct or indirect interactions with officials and employees of government agencies or government-affiliated hospitals, universities, and other organizations. We can be held liable for the corrupt or other illegal activities of our employees, agents, contractors, and other collaborators, even if we do not explicitly authorize or have actual knowledge of such activities. Any violations of the laws and regulations described above may result in substantial civil and criminal fines and penalties, imprisonment, the loss of export or import privileges, debarment, tax reassessments, breach of contract and fraud litigation, reputational harm, and other consequences.

Governments outside the United States may impose strict price controls, which may adversely affect our revenue, if any.

In some countries, particularly member states of the EU, the pricing of prescription drugs is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after receipt of marketing approval for a therapeutic. In addition, there can be considerable pressure by governments and other stakeholders on prices and reimbursement levels, including as part of cost containment measures. 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 distribution, or arbitrage between low-priced and high-priced member states, can further reduce prices. To obtain coverage and reimbursement or pricing approvals in some countries, we or current or future collaborators of ours may be required to conduct a clinical trial or other studies that compare the cost-effectiveness of a product to other available therapies in order to obtain or maintain reimbursement or pricing approval. Publication of discounts by third-party payors or authorities may lead to further pressure on the prices or reimbursement levels within the country of publication and other countries. If reimbursement of any product approved for marketing is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business, financial condition, results of operations or prospects could be materially and adversely affected. Brexit could lead to legal uncertainty and potentially divergent national laws and regulations, including those related to the pricing of prescription pharmaceuticals, as the UK determines which EU laws to replicate or replace. If the UK were to significantly alter its regulations affecting the pricing of prescription pharmaceuticals, we could face significant new costs.

While we have received Fast Track designation for PLX-200 for the treatment of Juvenile Neuronal Ceroid Lipofuscinosis, such designation may not lead to a faster development or regulatory review or approval process.

The FDA may designate a product for Fast Track review if it is intended, whether alone or in combination with one or more other products, for the treatment of a serious or life-threatening disease or condition, and it demonstrates the potential to address unmet medical needs for such a disease or condition. 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. We have received Fast Track designation in the United States for PLX-200 for the treatment of CLN3 and we may seek additional designations for one or more of our other drug candidates that could expedite review and approval by the FDA.

Designation of a product for Fast Track review is within the discretion of the FDA. The receipt of Fast Track designation for a drug candidate is not a guarantee that there will be faster development or a faster or more streamlined regulatory review or approval process compared to products considered for approval under conventional FDA procedures. Fast Track designation does not assure ultimate approval by the FDA. In addition, the FDA may later decide that the drug candidates no longer meet the conditions to qualify for such programs, and we may not receive the benefits of such program for PLX-200, or decide that the time period for FDA review or approval

will not be shortened. Additionally, changes in the leadership of the FDA and other actions taken by the Trump Administration, including mass layoffs within the federal government, may impose constraints on the FDA's ability to engage in activities in the normal course and may result in reductions to the FDA's budget, employees and operations, which may lead to slower response times and longer review periods, potentially affecting our ability to progress development of our drug candidates or obtain regulatory approval for our drug candidates.

We may seek certain designations for our drug candidates, including Breakthrough Therapy and Priority Review designations by the FDA, however, even if we receive such designations, there is no guarantee that they would lead to faster development or regulatory review timelines or increase the likelihood of marketing approval for such drug candidate.

We may seek to have one or more of our products designated as a Breakthrough Therapy, which is defined as a product that is intended, alone or in combination with one or more other products, to treat a serious or life threatening disease or condition where preliminary clinical evidence indicates that the product 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 products 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.

We may seek a regenerative medicine advanced therapy ("RMAT") designation or a priority review designation for one or more of our drug candidates. If the FDA determines that a drug candidate qualifies as an RMAT, that is intended to treat, reverse, or cure a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the product has the potential to address unmet medical needs for such a disease or condition, the FDA may grant participation in the RMAT program for that drug candidate. If the FDA determines that a drug candidate offers a treatment for a serious condition, and if approved, would provide a significant improvement in safety or effectiveness where no adequate therapy exists, the FDA may designate the drug candidate for priority review. 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 ten months.

As with the Fast Track designation, these designations are within the discretion of the FDA. Even if we believe that one or more of our drug candidates meets the criteria for these designations, the FDA may not agree and instead may determine to not make such a designation. Even if one or more of our drug candidates qualifies for either or both of these designations, the FDA may later decide that such drug candidate no longer meets the conditions for those designations, and we may not receive the benefits of the designation for that drug candidate. If a drug candidate is awarded one or both designations by the FDA, it may not result in a faster or more streamlined regulatory review or approval process compared to products considered for approval under conventional FDA procedures, and it does not assure ultimate marketing approval of such drug candidate by the FDA.

We have received orphan drug designation for PLX-200, PLX-300 and PLX-100 and we may seek orphan drug designation for certain future drug candidates, but we may be unable to obtain such designations or to maintain the benefits associated with orphan drug designation, including market exclusivity, which may cause our revenue, if any, to be reduced.

We have received orphan drug designation from the FDA for PLX-200 for the treatment of all 13 subtypes of NCLs, Tay-Sachs and Sandhoff diseases, and Krabbe disease, PLX-300 for the treatment of Tay-Sachs and Sandhoff diseases, Krabbe disease, and NPD type A and type B, and PLX-100 for the treatment of CLN2. Although we may seek orphan product designation for some or all of our other drug candidates, we may never receive such designations. Under the Orphan Drug Act, the FDA may designate a drug or biological product as an orphan drug if it is intended to treat a rare disease or condition, defined as a patient population of fewer than 200,000 in the United States, or a patient population greater than 200,000 in the United States where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the United States. Orphan drug designation must be requested before submitting a BLA or NDA. In the EU, the EMA's Committee for Orphan Medicinal Products grants orphan drug designation to promote the development of products that are intended for the diagnosis, prevention, or treatment of a life-threatening or chronically debilitating condition affecting not more than five in 10,000 persons in the EU. Additionally, designation

is granted for products intended for the diagnosis, prevention, or treatment of a life-threatening, seriously debilitating or serious and chronic condition when, without incentives, it is unlikely that sales of the drug in the EU would be sufficient to justify the necessary investment in developing the drug or biological product or where there is no satisfactory method of diagnosis, prevention, or treatment, or, if such a method exists, the medicine must be of significant benefit to those affected by the condition.

In the United States, orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages, and application fee waivers. After the FDA grants orphan drug designation, the generic identity of the drug and its potential orphan use are disclosed publicly by the FDA.

In addition, if a product receives the first FDA approval for the indication for which it has orphan designation, the product is entitled to orphan drug exclusivity, which means the FDA may not approve any other application to market the same drug for the same indication for a period of seven years, except in limited circumstances, such as a showing of clinical superiority over the product with orphan exclusivity or where the manufacturer is unable to assure sufficient product quantity for the orphan patient population. Exclusive marketing rights in the United States may also be unavailable if we or our collaborators seek approval for an indication broader than the orphan designated indication and may be lost if the FDA later determines that the request for designation was materially defective. In the EU, orphan drug designation entitles a party to financial incentives such as reduction of fees or fee waivers and ten years of market exclusivity following drug or biological product approval. This period may be reduced to six years if the orphan drug designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity.

Even with an orphan drug designation for our current and potential future drug candidates, we may not be the first to obtain marketing approval for any particular orphan indication due to the uncertainties associated with developing pharmaceutical products. Further, even if we obtain orphan drug exclusivity for an existing or future drug candidate, that exclusivity may not effectively protect the product from competition because different drugs with different active moieties still can be approved for the same condition even with an orphan drug designation. Even after an orphan drug is approved, the FDA can subsequently approve the same drug with the same active moiety for the same condition if the FDA concludes that the later drug is clinically superior in that it is safer, more effective, or makes a major contribution to patient care. Orphan drug designation neither shortens the development time or regulatory review time of a drug or biologic nor gives the drug or biologic any advantage in the regulatory review or approval process.

We have received Rare Pediatric Disease designation by the FDA for PLX-300 for the treatment of GM2 gangliosidosis, Krabbe disease, and NPD type A and type B. However, Rare Pediatric Disease designation for any of our drug candidates does not guarantee that the BLA or NDA for the product will qualify for a priority review voucher upon approval, and it does not lead to a faster development or regulatory review process, or increase the likelihood that our drug candidates will receive marketing approval.

Under the Rare Pediatric Disease Priority Review Voucher program, upon the approval of a qualifying BLA for the treatment of a rare pediatric disease, the sponsor of such an application would be eligible for a rare pediatric disease priority review voucher that can be used to obtain priority review for a subsequent BLA or NDA. If a drug candidate is designated before December 20, 2024, it is eligible to receive a voucher if it is approved before September 30, 2026. While we have obtained Rare Pediatric Disease designation for PLX-300 for the treatment of GM2 gangliosidosis, Krabbe disease, and NPD type A and type B, it is unlikely that this drug candidate will be approved by September 30, 2026. If approval is not obtained by then, we would not be in a position to obtain a priority review voucher, unless Congress further reauthorizes the program beyond the current sunset dates, which require that a product designated as being for a rare pediatric disease be approved by September 30, 2026. Additionally, designation of a biological product for a rare pediatric disease does not guarantee that a BLA or NDA will meet the eligibility criteria for a rare pediatric disease priority review voucher at the time the application is approved. Finally, a Rare Pediatric Disease designation does not lead to faster development or regulatory review of the product or increase the likelihood that it will receive marketing approval.

Where appropriate, we plan to pursue approval from the FDA through the use of accelerated approval pathways. If we are unable to obtain such approval, we may be required to conduct additional preclinical studies or clinical trials beyond those that we contemplate, which could increase the expense of obtaining, and delay the receipt of, necessary marketing approvals. Even if we receive accelerated approval from the FDA, if our confirmatory trials do not verify clinical benefit, or if we do not comply with rigorous post-marketing requirements, the FDA may seek to withdraw accelerated approval.

Where appropriate, we plan to pursue accelerated development strategies in areas of medical need for PLX-200. We may seek an accelerated approval pathway for one or more of our product candidates from the FDA, including PLX-200 for the treatment of CLN2 and CLN3. Under the accelerated approval provisions in the Federal Food, Drug, and Cosmetic Act, and the FDA's implementing regulations, the FDA may grant accelerated approval to a product candidate designed to treat a serious or life-threatening disease or condition upon a determination that the product candidate has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on an intermediate clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. The FDA considers a clinical benefit to be a positive therapeutic effect that is clinically meaningful in the context of a given disease, such as irreversible morbidity or mortality. For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign, or other measure that is thought to predict clinical benefit, but is not itself a measure of clinical benefit. An intermediate clinical endpoint is a clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit. The accelerated approval pathway may be used in cases in which the advantage of a new drug over available therapy may not be a direct therapeutic advantage, but is a clinically important improvement from a patient and public health perspective. If granted, accelerated approval is usually contingent on the sponsor's agreement to conduct, in a diligent manner, additional post-approval confirmatory studies to verify and describe the drug's clinical benefit. If such post-approval studies fail to confirm the drug's clinical benefit, the FDA may withdraw its approval of the drug.

With passage of the Food and Drug Omnibus Reform Act ("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 a sponsor of a product granted accelerated approval to submit progress reports on its post-approval studies to the FDA every six months (until the study is completed), and use expedited procedures to withdraw accelerated approval of an NDA after the confirmatory trial fails to verify the product's clinical benefit. Further, FDORA requires the FDA to publish on its website the rationale for why a post-approval study is not appropriate or necessary whenever it decides not to require such a study upon granting accelerated approval.

Prior to seeking accelerated approval, we plan to seek feedback from the FDA, and will otherwise evaluate our ability to seek and receive such accelerated approval. There can be no assurance that after our evaluation of the feedback and other factors 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 subsequent feedback from the 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 decides to submit an application for accelerated approval or any other form of expedited development, review or approval, there can be no assurance that such submission or application will be accepted or that any expedited development, review or approval will be granted on a timely basis, or at all. The FDA could also require us to conduct further studies prior to considering our application or granting approval of any type. A failure to obtain accelerated approval or any other form of expedited development, review or approval for our product candidates would result in a longer time period to commercialization of such product candidates, could increase the cost of development of such product candidate and could harm our competitive position in the marketplace.

General Risk Factors

Our estimates of market opportunity and forecasts of market growth may prove to be inaccurate, and even if the markets in which we compete achieve the forecasted growth, our business may not grow at similar rates, or at all.

Our market opportunity estimates and growth forecasts are subject to significant uncertainty and are based on assumptions and estimates which may not prove to be accurate. Our estimates and forecasts relating to size and expected growth of our target market may prove to be inaccurate. Even if the markets in which we compete meet our size estimates and growth forecasts, our business may not grow at similar rates, or at all. Our growth is subject to many factors, including our success in implementing our business strategy, which is subject to many risks and uncertainties.

Our revenue will be dependent, in part, upon the size of the markets in the territories for which we gain regulatory approval, the accepted price for the product, the ability to obtain coverage and reimbursement and whether we own the commercial rights for that territory. If the number of our addressable patients is not as significant as we estimate, the indication approved by regulatory authorities is narrower than we expect or the treatment population is narrowed by competition, physician choice or treatment guidelines, we may not generate significant revenue from sales of such products, even if approved.

We may become exposed to costly and damaging liability claims, either when testing a drug candidate in the clinical or at the commercial stage, and our product liability insurance may not cover all damages from such claims.

We are exposed to potential product liability and professional indemnity risks that are inherent in the research, development, manufacturing, marketing, and use of pharmaceutical products. While we currently have no products that have been approved for commercial sale, the current and future use of a drug candidate in clinical trials, and the sale of any approved products in the future, may expose us to liability claims. These claims may be made by patients that use the product, healthcare providers, pharmaceutical companies, or others selling such product. Any claims against us, regardless of their merit, could be difficult and costly to defend and could materially and adversely affect the market for our products or any prospects for commercialization of our products. It is possible that our liabilities could exceed our insurance coverage or that in the future we may not be able to maintain insurance coverage at a reasonable cost or obtain insurance coverage that will be adequate to satisfy any liability that may arise. If a successful 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.

Litigation costs and the outcome of litigation could have a material adverse effect on our business.

From time to time we may be subject to litigation claims through the ordinary course of our business operations regarding, but not limited to, employment matters, security of patient and employee personal information, contractual relations with collaborators and intellectual property rights. Litigation to defend ourselves against claims by third parties, or to enforce any rights that we may have against third parties, may continue to be necessary, which could result in substantial costs and diversion of our resources, causing a material adverse effect on our business, financial condition, results of operations or cash flows.

Our business could be adversely affected by economic downturns, inflation, fluctuating interest rates, natural disasters, public health crises, political crises, geopolitical events, or other macroeconomic conditions, which could have a material and adverse effect on our results of operations and financial condition.

The global economy, including credit and financial markets, has experienced and may experience in the future extreme volatility and disruptions, including, among other things, diminished liquidity and credit availability, declines in consumer confidence, declines in economic growth, supply chain shortages, new or increased tariffs and other barriers to trade, especially in light of recent executive orders made by the Trump Administration, trade and other international disputes, increases in inflation rates, fluctuating interest rates, slower growth or recession, tighter credit, volatility in financial markets, high unemployment, labor availability constraints, public health crises, significant natural disasters, including as a result of climate change, changes to fiscal and monetary policy or

government budget dynamics (particularly in the pharmaceutical and biotechnology areas), political and military conflict, and uncertainty about economic stability. In recent months, the United States has announced tariffs on imports from most countries, including significant tariffs on imports from China. Historically, tariffs have led to increased trade and political tensions. In response to tariffs, other countries have implemented retaliatory tariffs on U.S. goods. Political tensions as a result of trade policies could reduce trade volume, investment, technological exchange and other economic activities between major international economies, resulting in a material adverse effect on global economic conditions and the stability of global financial markets. There is substantial uncertainty about the duration of existing tariffs and whether additional tariffs may be imposed, modified or suspended. Fluctuating interest rates, coupled with reduced government spending and volatility in financial markets, may increase economic uncertainty and affect consumer spending. Similarly, the ongoing military conflict between Russia and Ukraine and in the Middle East, and rising tensions with China have created extreme volatility in the global capital markets and may have further global economic consequences, including disruptions of the global supply chain. Any such volatility and disruptions may adversely affect our business or the third parties on whom we rely. If the equity and credit markets deteriorate, including as a result of economic or political uncertainty, political unrest or war, it may make any necessary debt or equity financing more costly, more dilutive, or more difficult to obtain in a timely manner or on favorable terms, if at all. Increased inflation rates can adversely affect us by increasing our costs, including materials, operational, labor and employee benefit costs.

We may in the future experience disruptions as a result of such macroeconomic conditions, including delays or difficulties in initiating or expanding clinical trials and manufacturing sufficient quantities of materials. Any one or a combination of these events could have a material and adverse effect on our results of operations and financial condition.

Geopolitical events and global economic conditions may also affect the ability of the FDA and other regulatory authorities to perform routine functions. If such concerns prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews or other regulatory activities, it could significantly impact the ability of the FDA or other regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

Risks Related to Ownership of Our Common Stock

We will incur additional costs and increased demands upon management as a result of complying with the laws and regulations affecting public companies. We will be subject to financial reporting and other requirements for which our accounting and other management systems and resources may not be adequately prepared.

We will incur significant legal, accounting and other expenses as a public company that may not be reflected in our historical financial statements, which reflect our operation as a private company. Some of these additional expenses include costs associated with public company reporting obligations under the Exchange Act. Our management team consists of our executive officers prior to the merger. These executive officers and other personnel will need to devote substantial time to complying with public company reporting requirements and compliance with applicable laws and regulations to ensure that we comply with all of these requirements. Any changes we make to comply with these obligations may not be sufficient to allow us to satisfy our obligations as a public company on a timely basis, or at all. These reporting requirements, rules and regulations, coupled with the increase in potential litigation exposure associated with being a public company, could also make it more difficult for us to attract and retain qualified persons to serve on the board of directors or on board committees or to serve as executive officers, or to obtain certain types of insurance, including directors' and officers' insurance, on acceptable terms.

Pursuant to Section 404 of the Sarbanes-Oxley Act, we will be required to furnish a report by our management on our internal control over financial reporting, including an attestation report on internal control over financial reporting issued by our independent registered public accounting firm, beginning with the first full year after we become a public company. However, while we remain an emerging growth company, 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 of the Sarbanes-Oxley Act, we will be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. We will need to continue to dedicate internal resources, potentially engage outside consultants, 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 neither we, nor our independent registered public accounting firm will be able to conclude within the prescribed time frame that our internal control over financial reporting is effective as required by Section 404 of the Sarbanes-Oxley Act. This could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements. We could also become subject to investigations by the SEC or other regulatory authorities, which could require additional financial and management resources.

As a public company, we will also be required to maintain disclosure controls and procedures. Disclosure controls and procedures means our controls and other procedures that are designed to ensure that information required to be disclosed by us in the reports that we file or submit under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the rules and forms of the SEC. We do not expect that our disclosure controls and procedures or our internal control over financial reporting will prevent or detect all errors and all fraud. We believe a control system, no matter how well-designed and operated, can provide only reasonable, not absolute, assurance that the control system's objectives will be met. Due to the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that misstatements due to error or fraud will not occur or that all control issues and instances of fraud, if any, have been detected. The design of any system of controls is based in part on certain assumptions about the likelihood of future events, and any design may not succeed in achieving its stated goals under all potential future conditions. Over time, controls may become inadequate because of changes in conditions or deterioration in the degree of compliance with policies or procedures. Accordingly, because of the inherent limitations in our control system, misstatements due to error or fraud may occur and not be detected.

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," as defined in the JOBS Act. For as long as we continue to be an emerging growth company, we may take advantage of certain exemptions and relief from various reporting requirements that are applicable to other public companies that are not emerging growth companies, including (i) not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act, (ii) having the option of delaying the adoption of certain new or revised financial accounting standards, (iii) reduced disclosure obligations regarding executive compensation in this Annual Report and our periodic reports and proxy statements and (iv) exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved. We may take advantage of these exemptions until such time that we are no longer an emerging growth company. Accordingly, the information contained herein may be different than the information you receive from other public companies in which you hold stock. Further, pursuant to Section 107 of the JOBS Act, we have elected to take advantage of the extended transition period for complying with new or revised accounting standards until those standards would otherwise apply to private companies. As a result, our operating results and financial statements may not be comparable to the operating results and financial statements of other companies who have adopted the new or revised accounting standards.

We will remain an emerging growth company until the earliest of (i) the last day of the fiscal year following the fifth anniversary of our listing, (ii) the last day of the fiscal year in which we have total annual gross revenue of at least $1.235 billion, (iii) the last day of the fiscal year in which we are deemed to be a "large accelerated filer" as defined in Rule 12b-2 under the Exchange Act, which would occur if the market value of our common stock held by non-affiliates was $700.0 million or more as of the last business day of the second fiscal quarter of such year or (iv) the date on which we have issued more than $1.0 billion in non-convertible debt securities during the prior three-year period.

We are also a "smaller reporting company" as defined in the Exchange Act. We may continue to be a smaller reporting company even after we are no longer an emerging growth company. We may take advantage of certain of the scaled disclosures available to smaller reporting companies until the fiscal year following the determination that our voting and non-voting common stock held by non-affiliates is $250 million or more measured on the last business day of our second fiscal quarter, or our annual revenues are less than $100 million during the most recently completed fiscal year and our voting and non-voting common stock held by non-affiliates is $700 million or more measured on the last business day of our second fiscal quarter.

It is possible that some investors will find our common stock less attractive as a result of the foregoing, which may result in a less active trading market for our common stock and higher volatility in our stock price.

Our amended and restated articles of incorporation ("articles of incorporation") and amended and restated bylaws ("bylaws") could make an acquisition of the Company more difficult and may prevent attempts by our stockholders to replace or remove management.

Provisions in our articles of incorporation and bylaws may discourage, delay or prevent a merger, acquisition or other change in control of the Company that stockholders may consider favorable, including transactions in which our common stockholders might otherwise receive a premium price 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 will be responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove current management by making it more difficult for stockholders to replace members of our board of directors.

Our governing documents provide that, unless we consent in writing to the selection of an alternative forum, certain designated courts will be the sole and exclusive forum, and provide for a limited waiver of trial by jury, for certain legal actions between us and our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers, employees or agents.

Our governing documents provide that, unless we consent in writing to an alternative forum, the Eighth Judicial District Court of Clark County, Nevada (or, if such state court lacks jurisdiction, then any other state or federal district court located in the State of Nevada), shall be the sole and exclusive forum for any action, suit, proceeding or claim (i) brought in the name or right or on behalf of the Company, (ii) for or based upon a breach of any fiduciary duty owed by any director, officer, employee or agent of the Company in such capacity, (iii) arising pursuant to, or to interpret, apply, enforce or determine the validity of, any provision of NRS Title 7 (including without limitation NRS Chapters 78 and 92A), our articles of incorporation or bylaws, or as to which the NRS confers jurisdiction on the courts of the State of Nevada, or (iv) asserting a claim governed by the internal affairs doctrine, which for purposes of this risk factor refers to herein as the "Nevada Forum Provision." Our governing documents further provide that, unless we consent in writing to an alternative forum, the federal district courts of the United States of America located in the State of Nevada will be the sole and exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act, which for purposes of this risk factor refers to herein as the "Federal Forum Provision." Neither the Nevada Forum Provision nor the Federal Forum Provision will apply to any causes of action arising under the Exchange Act. In addition, any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock will be deemed to have notice of and consented to the foregoing Nevada Forum Provision and Federal Forum Provision; *provided*, however, that stockholders cannot and will not be deemed to have waived our compliance with the U.S. federal securities laws and the rules and regulations thereunder.

Our governing documents provide that, to the fullest extent not inconsistent with any applicable U.S. federal laws, any and all "internal actions" (as defined in NRS 78.046) must be tried in a court of competent jurisdiction (subject to the exclusive forum provisions in our articles of incorporation) before the presiding judge as the trier of fact and not before a jury. Pursuant to NRS 78.046, such requirement will conclusively operate as a waiver of the right to trial by jury by each party to any such internal action, but not to the extent any such waiver would be inconsistent with or prohibited under the federal securities laws (including the Securities Act and the Exchange Act) and the rules and regulations thereunder, which for purposes of this risk factor refers to herein as the "Jury Trial Waiver Provision."

The Nevada Forum Provision and the Federal Forum Provision may impose additional litigation costs on our stockholders in pursuing any such claims, particularly if such stockholders do not reside in or near the State of Nevada. Additionally, these forum selection clauses and the Jury Trial Waiver Provision may limit our stockholders' ability to bring a claim in a judicial forum that they find favorable or in a trial by jury for disputes with us or our directors, officers or employees, which may discourage such lawsuits against us and our directors, officers and employees even though an action, if successful, might benefit our stockholders.

Our executive officers, directors and principal stockholders have the ability to control or significantly influence all matters submitted to our stockholders for approval.

Our executive officers, directors and principal stockholders beneficially own a significant percentage of our outstanding common 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 stockholders, if they choose to act together, would control or significantly influence the election of directors and approval of any merger, consolidation or sale of all or substantially all of our assets. This concentration of voting power could delay or prevent our acquisition on terms that other stockholders may desire.

We may be exposed to increased litigation, including stockholder litigation, which could have an adverse effect on our business and operations.

We may be exposed to increased litigation from stockholders, suppliers and other third parties, which may have an adverse impact on our business and results of operations or may cause disruptions to our operations. In the past, stockholders have initiated class action lawsuits against biotechnology companies following periods of volatility in the market prices of these companies' stock, and we may also be subject to threats of litigation based on our recent merger activity. Such litigation, if instituted against us, could cause us to incur substantial costs and divert management's attention and resources, which could have a material adverse effect on our business, financial condition and results of operations.

If equity research analysts do not publish research or reports, or publish unfavorable research or reports, about us, our business or our market, our stock price and trading volume could decline.

The trading market for our common stock will be influenced by the research and reports that equity research analysts publish about us and our business. Equity research analysts may elect to not provide research coverage of our common stock, and such lack of research coverage may adversely affect the market price of our common stock. If we do have equity research analyst coverage, we will not have any control over the analysts or the content and opinions included in their reports. The price of our common stock could decline if one or more equity research analysts downgrade our stock or issue other unfavorable commentary or research. If one or more equity research analysts ceases coverage of us or fails to publish reports on us regularly, demand for our common stock could decrease, which in turn could cause our stock price or trading volume to decline.

The price of our stock may be volatile, and you could lose all or part of your investment.

The trading price of our common stock has fluctuated, and is likely to continue to fluctuate substantially in response to various factors, some of which are beyond our control, including the factors discussed in this "*Risk Factors*" section and elsewhere in this Annual Report. The realization of any of these factors could have a dramatic and adverse impact on the market price of our common stock.

In addition, the stock market in general, and the market for biotechnology and biopharmaceutical companies in particular, have historically been particularly volatile and experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance. If the market price of our common stock does not exceed the price at which you purchase your shares, you may not realize any return on your investment in us and may lose some or all of your investment. In the past, securities class action litigation has often been instituted against companies following periods of volatility in the market price of a company's securities. This type of litigation, if instituted, could result in substantial costs and a diversion of management's attention and resources, which would materially adversely affect our business, financial condition and results of operation.

Our common stock has historically been thinly traded, and you may be unable to sell at or near ask prices or at all if you need to sell or liquidate a substantial number of shares at one time.

Although our common stock is listed on Nasdaq, our common stock has historically been traded at relatively low volumes. As a result, the number of persons interested in purchasing our common stock at or near bid prices at any given time may be relatively small. This situation is attributable to a number of factors, including that we are currently a small company which is still relatively unknown to securities analysts, stock brokers, institutional

investors and others in the investment community that generate or influence sales volume, and that even if we came to the attention of such persons, they tend to be risk-averse and reluctant to follow an unproven company such as ours or purchase or recommend the purchase of our shares until such time as we become more seasoned and viable. As a consequence, there may be periods of several days or more when trading activity in our shares is minimal, as compared to a seasoned issuer which has a large and steady volume of trading activity that will generally support continuous sales without an adverse effect on share price. We cannot provide any assurance that a broader or more active public trading market for our common stock will develop or be sustained, or that trading levels will be sustained.

Item 1B. Unresolved Staff Comments.

None.

Item 1C. Cybersecurity

Cybersecurity is an important aspect of our business operations, and we take steps to protect our systems, data, and the information of our clients and stakeholders. We consider cybersecurity, along with other significant risks that we face, within our overall enterprise risk management framework. Below is an overview of our cybersecurity risk management and the measures we have in place:

- ***Governance and Oversight:*** Our Board and senior management are actively involved in overseeing our cybersecurity policies and practices and managing those responsible for coordinating and implementing cybersecurity initiatives across the organization.
- ***Risk Assessment and Management:*** We conduct risk assessments to identify potential cybersecurity threats and vulnerabilities. This includes evaluating the likelihood and potential impact of various threats, such as data breaches, malware attacks, and insider threats. Based on these risk assessments, we develop and implement risk management strategies to mitigate identified risks.
- ***Information Security Policies and Procedures:*** We have established information security policies and procedures that govern the use, protection, and handling of sensitive information. These policies cover areas such as access controls, password management, incident response, and employee training.
- ***Network and Infrastructure Security:*** We employ a range of technical measures designed to secure our network and infrastructure, including firewalls, intrusion detection and prevention systems, and vulnerability assessments.
- ***Employee Training and Awareness:*** We provide cybersecurity training to employees to raise awareness of the latest threats and best practices for protecting sensitive information. This includes training on how to recognize phishing attempts, handling secure data, and reporting security incidents.
- ***Third-Party Risk Management:*** We assess the cybersecurity practices of our significant third-party vendors and service providers, including conducting due diligence on vendors before engaging their services and monitoring their compliance with our security requirements.
- ***Compliance and Rereporting:*** We seek to comply with all applicable laws and regulations related to cybersecurity, including data protection and privacy laws.

While we believe that our current cybersecurity measures are adequate, we understand that the cybersecurity landscape is constantly evolving, and we remain vigilant in monitoring and working to adapt our practices to address emerging threats. We seek to maintain the confidentiality, integrity, and availability of our systems and data and to protect the interests of our clients and stakeholders. Since the beginning of the last fiscal year, we have not identified risks from known cybersecurity threats, including as a result of any previous cybersecurity incidents, that have materially affected, or are reasonably likely to material affect, us. To mitigate potential financial consequences of any future cybersecurity incidents, we carry cyber-attack insurance.

Item 2. Properties.

Our corporate headquarters are located in Paramus, New Jersey, where we lease office space under a month-to-month lease. We believe that our existing facility is adequate to meet our current needs, and that suitable additional alternative spaces will be available in the future on commercially reasonable terms should we seek to negotiate new leases or evaluate additional or alternate space for our operations.

Item 3. Legal Proceedings.

We are not party to any material legal proceedings at this time. From time to time, we may become involved in various legal proceedings that arise in the ordinary course of our business. Regardless of outcome, litigation can have an adverse impact on us due to defense and settlement costs, diversion of management resources, negative publicity, reputational harm and other factors, and there can be no assurances that favorable outcomes will be obtained.

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 trades on The Nasdaq Capital Market under the symbol "PLYX". Trading of our common stock commenced on February 2, 2026 in connection with our direct listing public offering. Prior to that time, there was no established public trading market for our common stock.

Holders

As of February 1, 2026, we had approximately 329 holders of record of our common stock. This number does not include beneficial owners whose shares were held in street name.

Dividend Policy

We have never declared or paid dividends or made other distributions on our common stock. We currently intend to retain all available funds and any future earnings to fund the development, commercialization and growth of our business, and therefore we do not anticipate declaring or paying any dividends or making other distributions on our common stock in the foreseeable future. Any future determination as to the declaration and payment of dividends or other distributions, if any, will be at the discretion of our Board. Any such determination will also depend upon our business prospects, operating results, financial condition, capital requirements, general business conditions and other factors that our Board may deem relevant. Our future ability to pay dividends or make other distributions on our common stock may also be limited by the terms of any future debt securities or credit facility.

Recent Sales of Unregistered Securities

The following sets forth information regarding all unregistered securities we issued during the year ended December 31, 2025.

Issuances of Capital Stock

In January 2025, we issued 213,201 shares of our common stock at a purchase price per share of $1.17 to an existing investor for aggregate consideration of $250 thousand in cash.

In January 2025, we issued an aggregate of 3,704,307 shares of common stock to Rush and Mstone in return for an exclusive gene therapy patent license. Of the total share issuance, 277,823 shares were issued to Rush and 3,246,484 shares were issued to Mstone.

In July 2025 and through August 29, 2025, we issued 1,802,749 shares of common stock to investors at a price per share of $1.72 for aggregate consideration of $3.1 million.

In September 2025, the Company issued an aggregate of 158,020 shares of common stock to investors at a price per share of $2.55. These amounts consist of 143,756 shares issued at $2.80 per share, further reduced by an additional 14,264 bonus shares issued in connection with this offering for aggregate consideration of $383 thousand.

In October 2025 through November 3, 2025, the Company issued an aggregate of 313,449 shares of common stock to investors at a price per share of $2.58. These amounts consist of 290,376 shares issued at $2.80 per share, further reduced by an additional 23,073 incremental bonus shares issued in connection with these offerings for aggregate consideration of $802 thousand.

The offers, sales, and issuances of the securities listed in this Item 5 under the subheading "*Issuances of Capital Stock*" were deemed to be exempt from registration under the Securities Act in reliance on Section 4(a)(2) of the Securities Act or Rule 506 of Regulation D promulgated thereunder as transactions by an issuer not involving a public offering, or Section 3(a)(9) of the Securities Act, involving an exchange of securities exchanged by the issuer with its existing security holders exclusively where no commission or other remuneration is paid or given directly or indirectly for soliciting such exchange. The recipients of securities in each of these transactions acquired the securities for

investment only and not with a view to or for sale in connection with any distribution thereof, and appropriate legends were affixed to the securities issued in these transactions. Each of the recipients of securities in these transactions was an accredited investor within the meaning of Rule 501 of Regulation D under the Securities Act.

Grants of Restricted Stock Units

During the year ended December 31, 2025, we granted restricted stock units covering an aggregate of 2,092,757 shares of our common stock to employees, directors, and non-employee service providers.

None of the foregoing transactions involved any underwriters, underwriting discounts or commissions, or any public offering. The offers, sales and issuances of the securities listed in this Item 5 under the subheading "*Grants of Restricted Stock Units*" were deemed to be exempt from registration under the Securities Act in reliance on Rule 701 promulgated under the Securities Act as offers and sales of securities pursuant to certain compensatory benefit plans and contracts relating to compensation in compliance with Rule 701 or Rule 175.

Issuer Purchases of Equity Securities

None.

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 in conjunction with the financial statements and related notes thereto and other financial information included elsewhere in this Annual Report. The following discussion contains forward-looking statements that reflect our current plans, estimates and beliefs. Our historical results are not necessarily indicative of the results that may be expected for any period in the future. Our actual results and the timing of events could differ materially from those discussed in the forward-looking statements. Factors that could cause or contribute to these differences include those discussed below and elsewhere in this Annual Report, particularly in the section titled "Risk Factors." Please also see the section titled "Special Note Regarding Forward-Looking Statements."

Overview

We are a clinical-stage biotechnology company committed to the discovery, development, and commercialization of novel, disease-modifying therapies for rare, pediatric LSDs. Our therapeutic philosophy is centered on delivering safe, effective, and patient-friendly treatments that address the underlying pathophysiology of these catastrophic diseases and their significant unmet need. Our multi-modal approach integrates small molecule therapies, including a combination therapy, and a gene therapy, positioning us to potentially address both the genetic and downstream pathological features of LSDs. Our small molecule product candidates share target indications as well as similar mechanisms that have been demonstrated to address lysosomal dysfunction, neuroinflammation, and neuronal loss in our validated animal models that closely mimic human clinical phenotypes. Our most advanced product candidate, PLX-200, targets several LSDs and we intend to launch a Phase 2 proof-of-concept basket trial which may enhance PLX-200's potential to become the standard of care across multiple LSDs.

Our product candidate pipeline includes:

- PLX-200, our most advanced, clinical-stage product candidate, is an oral, repurposed small molecule.
- PLX-300 is a novel, oral small molecule therapy in IND application-enabling studies in treatment of lysosomal storage disorders.
- PLX-100 is a preclinical stage orally administrable combination therapy comprised of our PPARα agonist, PLX-200, and vitamin A, a retinoid X receptor alpha ("RXRα") agonist. PLX-100 is being developed for the treatment of LSDs.
- PLX-400 is a preclinical stage novel gene therapy in treatment of lysosomal storage disorders.

We focus our clinical development program on specific LSDs that are typically treated by symptom and palliative care and, with the exception of CLN2, lack approved disease-modifying therapies. We have accumulated an expansive base of preclinical data and knowledge on CLN2 and CLN3, Sandhoff disease, and NPD type A and type B. Our drug candidates have been validated in gold standard preclinical animal models. With similar broad disease pathology shared across multiple LSDs in terms of substrate accumulation, neuroinflammation and neuronal loss, we believe our small molecule drug candidates have the potential to demonstrate high therapeutic potential in other targeted indications. Our development program of focus includes NCLs, Krabbe disease, Tay-Sachs and Sandhoff Diseases, and NPD types A and B.

We are advancing PLX-200, our most advanced product candidate, through a Phase 2 proof-of-concept basket trial which we refer to as SOTERIA (PLX-200-600). We expect to initiate this trial in the second half of 2026. SOTERIA is an open-label, multi-indication, master study for the treatment of certain LSDs which we believe represent approximately one quarter of the LSD population, including CLN2, CLN3, Krabbe disease, and Sandhoff disease. We held a pre-IND submission meeting in April 2025. We submitted an IND application to the FDA for the SOTERIA trial in August 2025 and received a safe to proceed letter in October 2025. Data readouts from SOTERIA are expected to provide guidance and a clear pathway for each of the four indications towards potentially registrable trials. Further, with the precedent approval of Brineura, a drug approved to treat CLN2 on the basis of a single-arm, natural history comparator, open-label trial, we believe there may be an opportunity in CLN2 and CLN3 for PLX-200 to seek accelerated approval from the FDA based on precedent approval for a third-party drug with a similar trial design. Should PLX-200 evidence overwhelming efficacy from the CLN2 and CLN3 cohorts in the SOTERIA trial, we believe there may be a case to seek accelerated approval. Products studied for their safety and effectiveness in treating serious or life-threatening diseases or conditions may receive accelerated approval upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. As a condition of accelerated approval, the FDA will generally require the sponsor to perform adequate and well-controlled post-marketing clinical studies to verify and describe the anticipated effect on irreversible morbidity or mortality or other clinical benefit. The precedent case of cerliponase alfa, a drug approved by FDA in treatment of CLN2, provides a benchmark for accelerated approval based on results generated from an open-label, single arm trial comparing to natural history data studying Batten disease. SOTERIA's current trial design for the CLN2 and CLN3 cohorts share the same open-label, single-arm design using natural history.

PLX-200 has already received authorization under two separate IND applications to initiate potentially single pivotal trials in CLN2 and CLN3, the most prevalent subtypes of NCLs. The IND for CLN2 was filed in December 2019 by Polaryx, with CRO support from Premier Research. A Study May Proceed letter was received in January 2020. The IND for CLN3 was filed in March 2020 by Polaryx, with CRO support from Premier Research. A Study May Proceed letter was received in April 2020.

Since our inception in August 2014, we have devoted substantially all of our resources to raising capital, organizing and staffing our company, business and scientific planning, conducting discovery and research activities, acquiring product programs, establishing and protecting our intellectual property portfolio, developing and progressing our pipeline, establishing arrangements with third parties for the manufacture of our programs and component materials, and providing general and administrative support for these operations. We do not have any product candidates approved for sale and have not generated any revenue from product sales. Since our inception through the date of this Annual Report, we have funded our operations primarily through the issuance of $21.7 million of common stock and preferred stock.

We have incurred significant operating losses since inception and expect to incur losses in the future as we continue our research and development activities. Our ability to generate product revenue sufficient to achieve profitability will depend heavily on the successful development and eventual commercialization of any product candidates we may develop. We incurred net losses of approximately $9.0 million and $30.4 million for the years ended December 31, 2025 and 2024, respectively. As of December 31, 2025, we had an accumulated deficit of approximately $99.6 million.

We expect to continue to incur significantly increased expenses for the foreseeable future if and as we:

- advance the development of our lead product candidates through clinical development, and, if approved by the FDA, commercialization;
- advance our preclinical development programs into clinical development;
- incur manufacturing costs to supply our product candidates;
- seek regulatory approvals for any of our product candidates that successfully complete clinical trials;
- increase our research and development activities to identify and develop new product candidates;
- hire additional personnel;
- expand our operational, financial and management systems;
- meet the requirements and demands of operating as a public company;
- invest in further development to protect and expand our intellectual property;
- ultimately establish a sales, marketing, medical affairs and distribution infrastructure to commercialize any product candidates for which we may obtain marketing approval and intend to commercialize; and
- expand our manufacturing and develop our commercialization efforts.

Due to the numerous risks and uncertainties associated with biopharmaceutical product development and the economic and developmental uncertainty, we may be unable to accurately predict the timing or magnitude of all expenses. Our ability to ultimately generate revenue to achieve profitability will depend heavily on the development, approval, and subsequent commercialization of our product candidates. If we fail to become profitable or are unable to sustain profitability on a continuing basis, then we may be unable to continue our operations at planned levels and be forced to reduce or terminate our operations.

As a result, we will need substantial additional funding to support our long-term continuing operations and pursue our growth strategy. Until such time as we can generate significant revenue from product sales, if ever, we expect to finance our operations through the sale of equity, debt financings or other capital sources, which may include collaborations with other companies or other strategic transactions. We may not be able to raise additional funds or enter into such other agreements or arrangements when needed on favorable terms, or at all. If we fail to raise capital or enter into such agreements as and when needed, we will have to significantly delay, reduce or eliminate the development and commercialization of one or more of our product candidates or delay our pursuit of potential in-licenses or acquisitions.

As of December 31, 2025, we had cash and cash equivalents of approximately $5.1 million. Based on our current operating plan, we estimate that our existing cash and cash equivalents as of the date of this Annual Report, will be sufficient to enable us to fund our operating expenses and capital expenditure requirements through the third quarter of 2026. We have based this estimate on assumptions that may prove to be wrong, and we could exhaust our available capital resources sooner than we expect.

Financial Overview

Revenue

To date, we have not generated any revenue from product sales and do not expect to generate any revenue from the sale of products in the foreseeable future. If our development efforts for any of our product candidates are successful and result in regulatory approval, we may generate revenue in the future from product sales. We cannot predict if, when or to what extent we will generate revenue from the commercialization and sale of any of our product candidates. We may never succeed in obtaining regulatory approval for any of our product candidates.

Operating Expenses

Our operating expenses consist of (i) research and development expenses and (ii) general and administrative expenses.

Research and Development Expenses

Research and development expenses consist of costs associated with the preclinical and clinical development of our product candidates, which include:

- personnel-related expenses, including salaries and benefits for employees engaged in research and development functions;
- expenses incurred in connection with the clinical development and regulatory approval of our product candidates, including under agreements with third parties, such as consultants, contractors and CROs; and
- other expenses related to research and development.

We expense research and development costs as incurred. Advance payments that we make for goods or services to be received in the future for use in research and development activities are recorded as prepaid expenses. The prepaid amounts are expensed as the benefits are consumed.

Research and development activities are central to our business model. We expect that our research and development expenses will increase substantially for the foreseeable future in connection with our planned clinical development activities.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries and other related costs, including stock-based compensation and benefits for our personnel and advisors. General and administrative expenses also include legal fees relating to intellectual property and corporate matters, professional fees for accounting, auditing, tax and consulting services, insurance costs, travel, direct and allocated facility related expenses and other operating costs.

We anticipate that our general and administrative expenses will increase substantially for the foreseeable future as we increase our administrative headcount to operate as a public company and as we advance our product candidates through clinical development. We also will incur additional expenses as a result of operating as a public company, including expenses related to compliance with the rules and regulations of the SEC and the Nasdaq listing rules, additional insurance expenses, investor relations activities and other administrative and professional services. In addition, if we obtain regulatory approval for any of our product candidates, we expect to incur expenses associated with building a sales and marketing team if we choose to commercialize such product candidates on our own.

Other Expense — Direct Listing Offering Costs

Other expense — direct listing offering costs primarily consists of costs related to the direct listing public offering completed on February 2, 2026 (the "Direct Listing"), including legal, accounting, and other expenses.

Other Expense — Recapitalization of Common Stock

Other expense — recapitalization of common stock primarily consists of shares of common stock issued to certain existing stockholders to enable them to substantially align with the implied value of our Company as of that date determined by our Board.

Statements of Operations

Results of Operations

Comparison of the Years Ended December 31, 2025 and 2024

The following table summarizes our statements of operations for the periods presented.

	Year Ended December 31,		
	2025	2024	$ Change
		(in thousands)	
Operating expenses:			
Research and development expenses	$ 6,266	$ 2,811	$ 3,455
General and administrative expenses	1,555	1,541	14
Total operating expenses	7,821	4,352	3,469
Operating loss	(7,821)	(4,352)	(3,469)
Other expense – direct listing offering costs	(1,164)	—	(1,164)
Other expense – recapitalization of common stock	—	(26,004)	26,004
Net loss and comprehensive loss	$ (8,985)	$ (30,356)	$ 21,371

Research and development expenses

Research and development expenses increased by $3.5 million to $6.3 million for the year ended December 31, 2025, as compared to $2.8 million for the year ended December 31, 2024, primarily due to consulting expenses, expenses incurred under two statements of work pursuant to the Rush MSA, CRO services, and stock-based compensation expenses. Research and development expenses were substantially related to PLX-200. Stock-based compensation increased by $2.6 million primarily related to the issuance of 3,704,307 shares of common stock to two existing stockholders in return for an exclusive gene therapy patent license totaling $4.3 million, partially offset by $1.7 million related to Mstone as compensation for advisory services. Of the total 3,704,307 shares issued, 277,823 shares were issued to Rush and 3,426,484 shares were issued to Mstone. Consulting expenses increased by $267 thousand related to the support and business development-related services from Mstone. Expenses incurred under two statements of work pursuant to the Rush MSA increased by $133 thousand. CRO formulation services increased by $248 thousand and CRO toxicology services increased by $88 thousand.

General and administrative expenses

General and administrative expenses increased by $14 thousand to $1.5 million for the year ended December 31, 2025, as compared to $1.5 million for the year ended December 31, 2024, primarily due to decreased stock-based compensation, offset by increased audit and consulting expenses. Stock-based compensation decreased by $285 thousand, primarily due to the conclusion in June 2024 of Mstone's advisory services provided pursuant to the Letter Agreement, offset by increase in stock-based compensation, primarily due to shares issued to a financial advisor for advisory services that began in October 2024. This was offset by an increase in audit fees of $147 thousand and consulting services from Mstone of $97 thousand.

Other expense — direct listing offering costs

Other expense — direct listing offering costs was $1.2 million for the year ended December 31, 2025, as compared to zero for the year ended December 31, 2024 due to legal, accounting, and advisory expenses related to the preparation of the direct listing offering.

Other expense — recapitalization of common stock

Other expense — recapitalization of common stock was zero for the year ended December 31, 2025, as compared to $26.0 million for the year ended December 31, 2024, due to shares of common stock issued to certain stockholders in February 2024 to enable them to be substantially aligned with the implied value of Polaryx as of that date as determined by our Board.

Income taxes

The effective income tax rate was 0.0% for all periods. Currently, we have recorded a full valuation allowance against our net deferred tax assets.

Liquidity and Capital Resources

Since our inception, we have incurred significant operating losses. We expect to incur significant expenses and operating losses for the foreseeable future as we advance the clinical development of our programs. From our inception through the date of this Annual Report, we have funded our operations primarily with proceeds from the sales of our equity securities totaling $21.7 million. As of December 31, 2025, we have no outstanding debt.

The following table presents the Company's cash and cash equivalents as of December 31, 2025 and December 31, 2024:

	December 31, 2025	December 31, 2024
Cash and cash equivalents	$ 5,143	$ 4,621

Cash Flows

The following table presents cash provided by (used in) operating and financing activities during the years ended December 31, 2025 and 2024:

	Year Ended December 31,	
	2025	2024
	(in thousands)	
Net cash flows (used in) operating activities	$ (3,944)	$ (2,573)
Net cash flows provided by financing activities	4,466	7,192
Net change in cash and cash equivalents	$ 522	$ 4,619

Operating Activities

Net cash used in operating activities was $3.9 million for the year ended December 31, 2025 and was primarily due to a net loss of $9.0 million, offset by working capital increases of $316 thousand and stock-based compensation of $4.7 million.

Financing Activities

Net cash provided by financing activities was $4.5 million for the year ended December 31, 2025 and was primarily due to proceeds from issuance of common stock of $4.5 million partially offset by payments related to issuance of common stock of $27 thousand.

Future Funding Requirements

We do not have any products approved for sale, and we have never generated any revenue from product sales. We do not expect to generate any meaningful revenue unless and until we obtain regulatory approval of and commercialize any of our current or future product candidates and we do not know when, or if, that will occur. We expect to continue to incur significant losses for the foreseeable future, and we expect the losses to increase as we continue the development of, and seek regulatory approvals for, our current and future product candidates, and begin to commercialize any approved products. We are subject to all the risks typically related to the development of new product candidates, and we may encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may adversely affect our business. Moreover, we expect to incur additional costs associated with operating as a public company.

The financial statements have been prepared as though we will continue as a going concern, which contemplates the realization of assets and satisfaction of liabilities in the normal course of business. We have incurred operating losses and negative cash flows from operations since inception. As of December 31, 2025, we had an accumulated deficit of approximately $99.6 million. Management expects to continue to incur operating losses and negative cash flows.

We will need to raise additional capital to continue to fund our operations. We believe we will be able to obtain additional capital through equity financings or other arrangements to fund operations; however, there can be no assurance that such additional financing, if available, can be obtained on acceptable terms. If we are unable to obtain such additional financing, future operations would need to be scaled back or discontinued.

We believe that our existing capital will enable us to fund our operations through the third quarter of 2026. We may need to raise additional capital in connection with our cash needs for capital expenditures and working capital beyond the third quarter of 2026. We have based the foregoing estimate on assumptions that may prove to be incorrect, and we could use our capital resources sooner than we expect.

Our future funding requirements will depend on many factors, including, but not limited to:

- the initiation, progress, timeline, cost and results of our clinical trials for our product candidates;
- the initiation, progress, timeline, cost and results of additional research and preclinical studies related to pipeline development and other research programs we initiate in the future;
- the cost and timing of manufacturing activities, including our planned manufacturing scale-up activities associated with our product candidates and other programs as we advance them through preclinical and clinical development through commercialization;
- the potential expansion of our current development programs to seek new indications;
- the outcome, timing and cost of meeting regulatory requirements established by the FDA and other comparable foreign regulatory authorities;
- the cost of filing, prosecuting, defending and enforcing patent claims and other intellectual property rights, in-licensed or otherwise;
- the effect of competing technological and market developments;
- the payment of licensing fees, potential royalty payments and potential milestone payments;
- the cost of general operating expenses;
- the cost of establishing sales, marketing and distribution capabilities for any product candidates for which we may receive regulatory approval in regions where we choose to commercialize our products on our own; and
- the costs of operating as a public company.

Further, our operating plan may change, and we may need additional funds to meet operational needs and capital requirements for clinical trials and other research and development expenditures.

If we need to raise additional capital to fund our operations, funding may not be available to us on acceptable terms, or at all. If we are unable to obtain adequate financing when needed, we may have to delay, reduce the scope of or suspend one or more of our preclinical studies, clinical trials, research and development programs or commercialization efforts. We may seek to raise any necessary additional capital through a combination of public or private equity offerings, debt financings, collaborations and other licensing arrangements. If we raise additional capital through debt financing, we may be subject to covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise additional capital through marketing and distribution arrangements or other collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish certain valuable rights to our product candidates, technologies, future revenue streams or research programs or grant licenses on terms that may not be favorable to us.

Contractual Obligations and Other Commitments

As of December 31, 2025, we had no non-cancellable commitments for purchase of clinical materials, contract manufacturing, maintenance and committed funding which we expect to pay within one year.

Off-Balance Sheet Arrangements

During the periods presented, we did not have, nor do we currently have, any off-balance sheet arrangements or holdings in any variable interest entities.

Critical Accounting Policies and Estimates

Our management's discussion and analysis of our financial condition and results of operations is based on our financial statements, which we have prepared in accordance with accounting principles generally accepted in the United States. The preparation of financial statements in conformity with accounting principles generally accepted in the United States ("U.S. GAAP") requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and related disclosures of contingent assets and liabilities at the date of the financial statements as well as the reported amounts of revenues and expenses during the reporting period. Estimates are based on several factors including the facts and circumstances available at the time the estimates are made, historical experience, risk of loss, general economic conditions and trends and the assessment of the probable future outcome. Subjective and significant estimates include, but are not limited to, research and development accruals as well as stock-based compensation expense. Actual results could differ from those estimates. Estimates and assumptions are reviewed periodically and the effects of changes, if any, are reflected in the statements of operations in the period that they are determined.

We believe that the accounting policies described below involve a significant degree of judgment and complexity. Accordingly, we believe these are the most critical to aid in fully understanding and evaluating our financial condition and results of operations. For further information, refer to Note 2 "Summary of Significant Accounting Policies" to our financial statements included elsewhere in this Annual Report.

Research and Development Expenses and Accruals

All research and development expenses are charged to operations as incurred. Research and development expenses primarily consist of costs associated with the preclinical and clinical development of the Company's product candidates, including the following:

- external research and development expenses incurred under arrangements with third parties, such as CROs and other vendors and CMOs to produce drug substance and drug product; and
- employee-related expenses, including salaries and benefits.

As part of the process of preparing our financial statements, we are required to estimate our accrued expenses. This process involves reviewing quotations and contracts, identifying services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced. Most of our service providers invoice monthly in arrears for services performed or when contractual milestones are met. Estimates of accrued expenses as of each balance sheet date in our financial statements are based on facts and circumstances known at that time. We periodically confirm the accuracy of estimates with the service providers and adjust if necessary. The significant estimates in accrued research and development expenses are related to expenses incurred with respect to CROs, contract manufacturing organizations ("CMOs") and other vendors in connection with research and development and manufacturing activities.

We base our expenses related to CROs and CMOs on estimates of the services received and efforts expended pursuant to quotations and contracts with such vendors that conduct research and development and manufacturing activities on our behalf. 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 vendors will exceed the level of services provided and result in a prepayment of the applicable research and development or manufacturing expense. In accruing service fees, we estimate the time 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 estimates, the accrual or prepaid expense is adjusted accordingly. Although estimates are not expected

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 could result in amounts that are too high or too low in any particular period. There have been no material changes in estimates for the periods presented.

Stock-Based Compensation Expense and Common Stock Valuations

We recognize compensation costs related to stock-based awards to employees and non-employees based on the estimated fair value of the awards on the date of grant and it is recognized as an expense over the requisite service period. For grants containing performance-based vesting provisions, the grant-date fair value of the milestone-based stock-based payment awards is recognized as compensation expense once it is probable that the condition will be achieved. We account for actual forfeitures in the period the forfeitures occur.

We will continue to use judgment in evaluating the assumptions utilized for our stock-based compensation expense calculations on a prospective basis. Such assumptions involve inherent uncertainties and the application of significant judgment. As a result, if factors or expected outcomes change and we use significantly different assumptions or estimates, our stock-based compensation expenses could be materially different.

The calculation of the fair value of awards requires an estimate of the Company's equity value. As the Company historically has been a privately held company with no trading history for its common stock to date, the estimated fair value of the Company's common stock has been approved by the Board, with input from management, valuations by third-party specialists, as well as upon the price per share from recent stock issuances to certain investors at that time. To determine the fair value, management considered the price per share from recent stock issuances to certain investors at that time, most recently available third-party valuations of its common stock and an assessment of additional objective and subjective factors that it believed were relevant and which may have changed from the date of the most recent valuation through the date of the grant. Additional factors include, among others, the nature and history of the Company's business; the Company's stage of development and commercialization; external market conditions; valuations of the Company's industry peers; and the likelihood of achieving a liquidity event, such as an initial public offering or sale of the Company. These third-party valuations are performed in accordance with the guidance outlined in the American Institute of Certified Public Accountants' Accounting and Valuation Guide, Valuation of Privately-Held-Company Equity Securities Issued as Compensation. The third-party common stock valuations are prepared using the market approach (guideline public company method) to estimate the Company's enterprise value.

Recent Accounting Pronouncements

See Note 2 "Summary of Significant Accounting Policies" to our financial statements included elsewhere in this Annual Report for a discussion of accounting pronouncements recently issued but not yet adopted and their potential impact to our financial statements.

Emerging Growth Company Status and Smaller Reporting Company Status

We are an emerging growth company, as defined in Section 2(a) of the Securities Act of 1933, as amended (the "Securities Act"), as modified by the JOBS Act, and we may take advantage of certain exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies, including relief from the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002 (as amended, the "Sarbanes-Oxley Act"), less extensive disclosure obligations regarding executive compensation in our registration statements, periodic reports and proxy statements, exemptions from the requirements to hold a nonbinding advisory vote on executive compensation, and exemptions from stockholder approval of any golden parachute payments not previously approved. We may also elect to take advantage of other reduced reporting requirements in future filings. As a result, our stockholders may not have access to certain information that they may deem important and the information that we provide to our stockholders may be different than, and not comparable to, information presented by other public reporting companies. We could remain an emerging growth company until the earlier of (i) the last day of the year following the fifth anniversary of our listing, (ii) the last day of the year in which we have total annual gross revenue of at least $1.235 billion, (iii) the last day of the year in which we are deemed to be a "large accelerated filer" as defined in Rule 12b-2 under the Securities Exchange Act of 1934, as amended (the "Exchange Act"), which would occur if the market value of our common stock and non-voting

common stock held by non-affiliates exceeded $700.0 million as of the last business day of the second fiscal quarter of such year or (iv) the date on which we have issued more than $1.0 billion in non-convertible debt securities during the prior three-year period.

In addition, the JOBS Act also provides that an emerging growth company may take advantage of the extended transition period provided in the Securities Act for complying with new or revised accounting standards. An emerging growth company may therefore delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have elected to avail ourselves of this exemption and, as a result, will not be subject to the same implementation timing for new or revised accounting standards as are required of other public companies that are not emerging growth companies, which may make comparison of our financial information to those of other public companies more difficult.

We are also a "smaller reporting company," meaning that the market value of our common stock and non-voting common stock held by non-affiliates is less than $700.0 million and our annual revenue is less than $100.0 million during the most recently completed fiscal year. We may continue to be a smaller reporting company as long as (i) the market value of our common stock and non-voting common stock held by non-affiliates is less than $250.0 million or (ii) our annual revenue is less than $100.0 million during the most recently completed fiscal year and the market value of our common stock and non-voting common stock held by non-affiliates is less than $700.0 million. If we are a smaller reporting company at the time we cease to be an emerging growth company, we may continue to rely on exemptions from certain disclosure requirements that are available to smaller reporting companies. Specifically, as a smaller reporting company we may choose to present only the two most recent fiscal years of audited financial statements in our Annual Report on Form 10-K and, similar to emerging growth companies, smaller reporting companies have reduced disclosure obligations regarding executive compensation.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk

We are a smaller reporting company, as defined in Rule 12b-2 of the Securities Exchange Act of 1934, as amended, for this reporting period and are not required to provide the information required under this Item.

Item 8. Financial Statements and Supplementary Data

Polaryx Therapeutics, Inc.

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Report of Independent Registered Public Accounting Firm

Board of Directors and Stockholders
Polaryx Therapeutics, Inc.

Opinion on the financial statements

We have audited the accompanying balance sheets of Polaryx Therapeutics, Inc. (a Nevada corporation) (the "Company") as of December 31, 2025 and 2024, the related statements of operations and comprehensive loss, changes in stockholders' equity, and cash flows for each of the two years in the period ended December 31, 2025, and the related notes (collectively referred to as the "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2025 and 2024, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2025, in conformity with accounting principles generally accepted in the United States of America.

Going concern

The accompanying 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 incurred net losses of $9.0 million and $30.4 million and used cash in operating activities of $3.9 million and $2.6 million, during the years ended December 31, 2025 and December 31, 2024, respectively 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 financial statements do not include any adjustments that might result from the outcome of this uncertainty. Our opinion is not modified with respect to this matter.

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/ GRANT THORNTON LLP

We have served as the Company's auditor since 2024.

Edison, New Jersey
March 23, 2026

POLARYX THERAPEUTICS, INC.
BALANCE SHEETS
(In thousands, except per share and share amounts)

	As of	
	December 31, 2025	**December 31, 2024**
Assets		
Current assets:		
Cash and cash equivalents	$ 5,143	$ 4,621
Prepaid expenses	—	380
Other current assets	27	—
Total current assets	5,170	5,001
Total assets	$ 5,170	$ 5,001
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 470	$ 72
Due to related party	91	130
Accrued expenses – related party	23	—
Accrued expenses and other current liabilities	21	87
Total current liabilities	605	289
Total liabilities	605	289
Commitments and contingencies (Note 9)		
Stockholders' equity:		
Preferred stock: $0.0001 par value, 40,000,000 shares authorized; 0 and 0 shares issued and outstanding at December 31, 2025 and 2024, respectively	—	—
Common stock: $0.0001 par value; 560,000,000 shares authorized; 47,343,297 and 41,151,571 shares issued and outstanding at December 31, 2025 and 2024, respectively	5	4
Additional paid-in capital	104,195	95,358
Accumulated deficit	(99,635)	(90,650)
Total stockholders' equity	4,565	4,712
Total liabilities and stockholders' equity	$ 5,170	$ 5,001

The accompanying notes are an integral part of these financial statements.

POLARYX THERAPEUTICS, INC.
STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS
(In thousands, except per share and share amounts)

	Year Ended December 31,	
	2025	**2024**
Operating expenses:		
Research and development expenses	$ 6,266	$ 2,811
General and administrative expenses	1,555	1,541
Total operating expenses	7,821	4,352
Operating loss	(7,821)	(4,352)
Other expense – direct listing offering costs	(1,164)	—
Other expense – recapitalization of common stock	—	(26,004)
Net loss and comprehensive loss	$ (8,985)	$ (30,356)
Net loss per share – basic and diluted	$ (0.20)	$ (0.89)
Weighted average common shares outstanding – basic and diluted	45,422,581	34,200,660

The accompanying notes are an integral part of these financial statements.

POLARYX THERAPEUTICS, INC.
STATEMENTS OF CHANGES IN STOCKHOLDERS' EQUITY
(In thousands, except share amounts)

	Preferred Stock		Common Stock		Additional Paid-In Capital	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount	Shares	Amount			
Balances at December 31, 2023	736,215	$ —	11,203,435	$ 1	$ 61,570	$ (60,294)	$ 1,277
Issuance of common stock	—	—	7,039,460	1	7,786	—	7,787
Issuance of common stock recapitalization	—	—	22,172,461	2	26,002	—	26,004
Conversion of preferred stock	(736,215)	—	736,215	—	—	—	—
Net loss	—	—	—	—	—	(30,356)	(30,356)
Balances at December 31, 2024	—	$ —	41,151,571	$ 4	$ 95,358	$ (90,650)	$ 4,712

	Preferred Stock		Common Stock		Additional Paid-In Capital	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount	Shares	Amount			
Balances at December 31, 2024	—	$ —	41,151,571	$ 4	$ 95,358	$ (90,650)	$ 4,712
Issuance of common stock	—	—	6,191,726	1	8,837	—	8,838
Net loss	—	—	—	—	—	(8,985)	(8,985)
Balances at December 31, 2025	—	$ —	47,343,297	$ 5	$ 104,195	$ (99,635)	$ 4,565

The accompanying notes are an integral part of these financial statements.

POLARYX THERAPEUTICS, INC.
STATEMENTS OF CASH FLOWS
(In thousands)

	Year Ended December 31,	
	2025	**2024**
Cash flows from operating activities		
Net loss	$ (8,985)	$ (30,356)
Adjustments to reconcile net loss to net cash flows used in operating activities:		
Stock-based compensation	4,725	2,400
Other expense – recapitalization of common stock	—	26,004
Changes in assets and liabilities which provided (used) cash:		
Accounts payable	398	(401)
Due to related party	(39)	(220
Accrued expenses – related party	23	—
Accrued expenses and other current liabilities	(66)	—
Net cash flows used in operating activities	(3,944)	(2,573)
Cash flows from financing activities		
Proceeds from short-term debt – related party	—	65
Repayment of short-term debt – related party	—	(193)
Payments related to issuance of common stock	(27)	—
Proceeds from issuance of common stock	4,493	7,320
Net cash flows provided by financing activities	4,466	7,192
Net increase (decrease) in cash and cash equivalents	522	4,619
Cash and cash equivalents, beginning	4,621	2
Cash and cash equivalents, ending	$ 5,143	$ 4,621

The accompanying notes are an integral part of these financial statements.

1. Nature of the Business and Basis of Presentation

Polaryx Therapeutics, Inc. (the "Company") is a clinical-stage biotechnology company committed to the discovery, development, and commercialization of novel, disease-modifying therapies for rare, pediatric lysosomal storage disorders. On October 24, 2025, the Company completed the redomestication to convert into a Nevada corporation from a Wyoming corporation.

Basis of Presentation

The accompanying financial statements have been prepared in accordance with accounting principles generally accepted in the United States ("U.S. GAAP"). There is no difference between net loss and comprehensive loss in these financial statements.

Reverse Stock Split

Effective on January 12, 2026, the Company effected a 1-for-4 reverse stock split of its then-outstanding common stock. All share and per share amounts have been adjusted on a retroactive basis to reflect the effect of the reverse stock split. The shares of Common Stock retain a par value of $0.0001 per share.

Liquidity and Going Concern

The Company has no products approved for sale and has sustained recurring net losses and negative cash flows from operations since inception. For the years ended December 31, 2025 and 2024, the Company had a net loss of $9.0 million and $30.4 million, respectively, and used cash in operating activities of $3.9 million and $2.6 million, respectively. As of December 31, 2025, the Company had working capital of $4.6 million. Achieving profitability is dependent upon the successful development, approval, and commercialization of the Company's product candidates and achieving a level of revenue adequate to support the Company's cost structure. Management intends to fund future operations through additional financings, which could include private and/or public debt offerings and equity offerings. In addition, the Company may seek additional capital through arrangements with strategic partners or from other sources. There can be no assurances, however, that additional funding will be available on terms acceptable to the Company, or at all.

There can be no assurance that the Company's research and development projects will be successful, that products developed will obtain necessary regulatory approval, or that any approved product will be commercially viable. Further, there is no assurance that profitable operations will ever be achieved, and if achieved, could be sustained on a continuing basis. The Company is subject to certain risks associated with any clinical stage pharmaceutical company that has substantial expenditures for research and development. These matters, along with the conditions described above, raise substantial doubt about the Company's ability to continue as a going concern for a period of twelve months from the date these financial statements were available to be issued.

The financial statements have been prepared assuming the Company will continue to operate as a going concern, which contemplates the realization of assets and the settlement of liabilities in the normal course of business. The financial statements do not include adjustments to reflect the possible effects on the recoverability and classification of assets or the amounts and classification of liabilities that may result from the outcome of the uncertainty related to the Company's ability to continue as a going concern.

Risks and Uncertainties

The Company is subject to risks and uncertainties common to early-stage companies in the biopharmaceutical industry including, but not limited to, development by competitors of new technological innovations, dependence on key personnel, protection of proprietary technology, compliance with governmental regulations, dependency on key suppliers (including for certain active pharmaceutical ingredients) and the ability to secure additional capital to fund operations. Product candidates currently under development will require extensive preclinical and clinical testing and regulatory approval prior to commercialization. These efforts will require significant amounts of additional capital, adequate personnel, infrastructure and extensive compliance and reporting capabilities. Even if the Company's drug development efforts are successful, it is uncertain when, if ever, the Company will realize significant revenue from product sales.

2. Summary of Significant Accounting Policies

Cash and Cash Equivalents

Cash and cash equivalents consist principally of cash held in commercial bank accounts and money market funds. The Company considers all highly liquid investments with maturities of three months or less at the date of acquisition to be cash equivalents.

Concentration of Credit Risk

Financial investments that potentially subject the Company to concentrations of credit risk consist of cash and cash equivalents. The Company places its cash and cash equivalents with high credit quality U.S. financial institutions. At various times throughout the period, the Company's cash deposits with any one financial institution may exceed the amount insured by the Federal Deposit Insurance Corporation. Generally, these deposits may be redeemed upon demand and, therefore, bear minimal risk. The Company has not experienced any losses of such amounts and management believes it is not exposed to any significant credit risk on its cash and cash equivalents.

Use of Estimates

The preparation of financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and related disclosures of contingent assets and liabilities at the date of the financial statements as well as the reported amounts of expenses during the reporting period. Estimates are based on several factors, including the facts and circumstances available at the time the estimates are made, historical experience, risk of loss, general economic conditions and trends and the assessment of the probable future outcome. Actual results could differ from those estimates and changes in estimates may occur. Estimates and assumptions are reviewed periodically and the effects of changes, if any, are reflected in the statements of operations and comprehensive loss in the period that they are determined. The most significant matters involving management's estimates include accrued research and development expenses, and stock-based compensation expense.

Property and Equipment, Net

Property and equipment are stated at cost, less accumulated depreciation and amortization. Expenditures for repairs and maintenance are expensed as incurred. Depreciation and amortization are (or will be) computed using the straight-line method over the estimated useful lives of the assets as follows:

	Estimated Useful Life
Computer equipment	3 years
Office equipment	5 years
Lab equipment	5 years
Leasehold improvements	Shorter of remaining life of lease or useful life

There were no property and equipment, net as of December 31, 2025 and 2024.

Impairment of Long-Lived Assets

The Company regularly reviews the carrying values and estimated lives of its long-lived assets, including property and equipment, to determine whether indicators of impairment exist that warrant adjustments to carrying values or estimated useful lives. The determinants used for this evaluation include management's estimate of the asset's ability to generate positive income from operations and positive cash flow in future periods as well as the strategic significance of the assets to the Company's business objective. Should an impairment occur, the impairment loss would be measured based on the excess of the carrying amount over the asset's fair value. No impairment charge was recorded during the years ended December 31, 2025 or 2024. There were no long-lived assets as of December 31, 2025 and 2024.

2. Summary of Significant Accounting Policies (cont.)

Leases

The Company has adopted the Financial Accounting Standards Board ("FASB") Accounting Standard Update ("ASU") No. 2016-02, *Leases (Topic 842),* as subsequently amended. This is a comprehensive new standard that amends various aspects of existing accounting guidance for leases, including the recognition of a right-of-use asset and a lease liability on the balance sheet and disclosing key information about leasing arrangements.

Per FASB Accounting Standards Codification ("ASC") Topic 842, the leases standard requires lessees to record a right-of-use asset and a lease liability for all leases other than those that, at lease commencement, have a lease term of 12 months or less. A reporting entity can elect an accounting policy by class of underlying asset not to record such short-term leases on the balance sheet. A reporting entity may be able to establish reasonable capitalization thresholds below which assets and liabilities related to a lease are not recognized. For the years ended December 31, 2025 and 2024, office rent expense was $4 thousand and $4 thousand, respectively. Based on the standard above, the Company has concluded this is a short-term lease and under the capitalization threshold. As such, these amounts are recorded in general and administrative expenses on the statements of operations and comprehensive loss, and a right-of-use asset and lease liability are not recognized on the balance sheets.

Fair Value Measurements

FASB ASC Topic 820, *Fair Value Measurements and Disclosures*, defines fair value, establishes a framework for measuring fair value, and expands disclosures about fair value measurements. Fair value is to be determined based on the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants. In determining fair value, the Company used various valuation approaches. A fair value hierarchy has been established for inputs used in measuring fair value that maximizes the use of observable inputs and minimizes the use of unobservable inputs by requiring that the most observable inputs be used when available. Observable inputs are those that market participants would use in pricing the asset or liability based on market data obtained from sources independent of the Company. Unobservable inputs reflect the Company's assumption about the inputs that market participants would use in pricing the asset or liability developed based on the best information available in the circumstances.

The fair value hierarchy is categorized into three levels, based on the inputs, as follows:

- Level 1 — Valuations based on quoted prices for identical instruments in active markets. Since valuations are based on quoted prices that are readily and regularly available in an active market, valuation of these instruments does not entail a significant degree of judgment.
- Level 2 — Valuations based on observable inputs other than quoted prices included in Level 1, such as quoted prices for either similar instruments in active markets, identical or similar instruments in markets that are not active, or model-derived valuations whose inputs or significant value drivers are observable or can be corroborated by observable market data.
- Level 3 — Valuations based on inputs that are unobservable. These valuations require significant judgment.

The Company's Level 1 assets consist of cash and cash equivalents in the accompanying balance sheets. In addition, the value of prepaid expenses, accounts payable, and accrued expenses approximate fair value due to the short-term nature of these assets and liabilities. Related party liabilities are not presumed to be at fair value. As of December 31, 2025 and 2024, the Company did not have any assets or liabilities measured at fair value classified as Level 2 or Level 3.

2. Summary of Significant Accounting Policies (cont.)

Accrued/Prepaid Research and Development Expenses

As part of the process of preparing its financial statements, the Company is required to estimate its accrued expenses. This process involves reviewing quotations and contracts, identifying services that have been performed on the Company's behalf and estimating the level of service performed and the associated cost incurred for the service when the Company has not yet been invoiced. Most of the Company's service providers invoice monthly in arrears for services performed or when contractual milestones are met. Estimates of accrued expenses as of each balance sheet date in the financial statements are based on facts and circumstances known at that time. The Company periodically confirms the accuracy of estimates with the service providers and adjusts if necessary. The significant estimates in accrued research and development expenses are related to expenses incurred with respect to contract research organizations ("CROs"), contract manufacturing organizations ("CMOs") and other vendors in connection with research and development and manufacturing activities.

The Company bases its expenses related to CROs and CMOs on estimates of the services received and efforts expended pursuant to quotations and contracts with such vendors that conduct research and development and manufacturing activities on the Company's behalf. 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 vendors will exceed the level of services provided and result in a prepayment of the applicable research and development or manufacturing expense. In accruing service fees, the Company estimates the time 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 estimates, the accrual or prepaid expense is adjusted accordingly. Although estimates are not expected to be materially different from amounts actually incurred, the Company's understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and could result in amounts that are too high or too low in any particular period. There have been no material changes in estimates for the periods presented.

Research and Development Expenses

Research and development expenses primarily consist of costs associated with the preclinical and clinical development of the Company's product candidates, including the following:

- external research and development expenses incurred under arrangements with third parties, such as CROs and other vendors and CMOs to produce drug substance and drug product;
- estimated research and development consulting costs related to the Mstone Partners Healthcare Limited ("Mstone") Services Agreement ("Service Agreement"); and
- employee-related expenses, including salaries and benefits.

All research and development expenses are charged to operations as incurred in accordance with FASB ASC Topic 730, *Research and Development*.

Prepaid Expenses

Advance payments made for goods or services to be received in the future for use in research and development activities are recorded as prepaid expenses until the service has been performed or the goods have been received. The prepaid amounts are expensed as the benefits are consumed. Prepaid expenses are substantially comprised of research and development related activities.

Stock-Based Compensation Expense

The Company follows the provisions of FASB ASC Topic 718, *Compensation — Stock Compensation*, which requires the measurement and recognition of compensation expense for all stock-based payment awards made to employees and non-employee directors, including employee stock options. Stock-based compensation expense is

2. Summary of Significant Accounting Policies (cont.)

based on the grant-date fair value estimated in accordance with the provisions of ASC Topic 718 and is recognized as an expense over the requisite service period. For grants containing performance-based vesting provisions, the grant-date fair value of milestone-based stock-based payment awards is recognized as compensation expense once it is probable that the condition will be achieved. The Company accounts for actual forfeitures in the period the forfeitures occur.

The Company complies with ASU 2018-07, *Improvements to Nonemployee Share-Based Payment Accounting*, which supersedes ASC 505-50 and expands the scope of ASC 718 to include all share-based payments arrangements related to the acquisition of goods and services from both employees and non-employees. The measurement date for non-employee awards is the date of grant. Compensation expense for nonemployees is recognized, without changes to the fair value of the equity classified award, over the requisite service period, which is the vesting period of the respective award.

Collaborative Arrangements

The Company analyzes its licensing and collaborative arrangements to assess whether such arrangements involve joint operating activities performed by parties that are both active participants in the activities and exposed to significant risks and rewards, and therefore are within the scope of FASB ASC Topic 808, *Collaborative Arrangements*. For licensing and collaborative arrangements that contain multiple elements, the Company determines which units of account are deemed to be within the scope of ASC Topic 808 and which units of account are more reflective of a vendor-customer relationship and therefore are within the scope of ASC Topic 606. For units of account that are accounted for pursuant to ASC Topic 808, an appropriate recognition method is determined and applied consistently, either by analogy to appropriate accounting literature or by applying a reasonable accounting policy election.

For licensing and collaborative arrangements that are within the scope of ASC Topic 808, the Company evaluates the income statement classification for presentation of amounts due to or owed from other participants associated with multiple units of account in a collaborative arrangement based on the nature of each activity. Payments or reimbursements that are the result of a collaborative relationship instead of a customer relationship, such as co-development and co-commercialization activities, are recorded as increases or decreases to research and development expenses or general and administrative expenses, as appropriate. Milestone payments are considered contingent liabilities and are recognized when the Company deems the milestone event to be probable.

Segment Information

Operating segments are defined as components of a company about which separate financial information is available that is evaluated regularly by the chief operating decision maker ("CODM"), or decision-making group, in deciding how to allocate resources and assess performance. The Company determined its operating segment after considering the Company's organizational structure and the information regularly reviewed and evaluated by the Company's CODM. The Company has determined that its CODM is its Chief Executive Officer. The CODM reviews financial information on an aggregate basis for the purposes of allocating resources and evaluating financial performance. On the basis of these factors, the Company determined that it operates and manages its business as one operating segment.

Income Taxes

FASB ASC Topic 740, *Income Taxes*, sets forth standards for financial presentation and disclosure of income tax liabilities and expense. The Company accounts for income taxes under the asset and liability method, which requires the recognition of deferred tax assets and liabilities for the expected future tax consequences of events that have been included in the financial statements. Under this method, the Company determines deferred tax assets and liabilities on the basis of the differences between the financial statement and tax bases of assets

2. Summary of Significant Accounting Policies (cont.)

and liabilities by using enacted tax rates in effect for the year in which the differences are expected to reverse. The effect of a change in tax rates on deferred tax assets and liabilities is recognized in income in the period that includes the enactment date.

The Company recognizes deferred tax assets to the extent that it believes that these assets are more likely than not to be realized. In making such a determination, the Company considers all available positive and negative evidence, including future reversals of existing taxable temporary differences, projected future taxable income, tax-planning strategies, and results of recent operations. If the Company determines that it would be able to realize its deferred tax assets in the future in excess of their net recorded amount, the Company would make an adjustment to the deferred tax asset valuation allowance, which would reduce the provision for income taxes.

The Company records uncertain tax positions in accordance with ASC Topic 740 on the basis of a two-step process in which (1) the Company determines whether it is more likely than not that the tax positions will be sustained on the basis of the technical merits of the position and (2) for those tax positions that meet the more-likely-than-not recognition threshold, the Company recognizes the largest amount of tax benefit that is more than 50% likely to be realized upon ultimate settlement with the related tax authority.

The Company recognizes interest and penalties related to unrecognized tax benefits on the income tax expense line in the accompanying statements of operations and comprehensive loss. As of December 31, 2025 and 2024, there were no accrued interest or penalties recorded on the balance sheets.

The Company recognizes deferred tax assets to the extent that it believes that these assets are more likely than not to be realized. In making such a determination, the Company considers all available positive and negative evidence, including future reversals of existing taxable temporary differences, projected future taxable income, tax-planning strategies, and results of recent operations. If the Company determines that it would be able to realize its deferred tax assets in the future in excess of their net recorded amount, the Company would make an adjustment to the deferred tax asset valuation allowance, which would reduce the provision for income taxes.

Recent Accounting Pronouncements Not Yet Adopted

In November 2024, the FASB issued ASU 2024-03, *Disaggregation of Income Statement Expenses*, which requires disaggregated disclosure of income statement expenses for public business entities. In January 2025, the FASB issued ASU 2025-01, *Expense Disaggregation Disclosures (Subtopic 220-40): Clarifying the Effective Date,* which provides changes to the disclosure requirements and provides a delayed implementation timeline to give issuers additional time to prepare for the impacts of adoption. ASU 2025-01 is effective for the Company prospectively for all annual periods beginning after December 15, 2026, and interim periods within fiscal years beginning after December 15, 2027. Early adoption is permitted. The Company is currently evaluating the impact of this standard.

In December 2023, the FASB issued ASU No. 2023-09, Income Taxes (Topic 740): *Improvements to Income Tax Disclosures*, which focuses on the rate reconciliation and income taxes paid. ASU No. 2023-09 requires a public business entity ("PBE") to disclose, on an annual basis, a tabular rate reconciliation using both percentages and currency amounts, broken out into specified categories with certain reconciling items further broken out by nature and jurisdiction to the extent those items exceed a specified threshold. In addition, all entities are required to disclose income taxes paid, net of refunds received disaggregated by federal, state/local, and foreign and by jurisdiction if the amount is at least 5% of total income tax payments, net of refunds received. For PBEs, the new standard is effective for annual periods beginning after December 15, 2024, with early adoption permitted. For entities other than PBEs, the requirements will be effective for annual periods beginning after December 15, 2025. An entity may apply the amendments in this ASU prospectively by providing the revised disclosures for the period ending December 31, 2025 and continuing to provide the pre-ASU disclosures for the prior periods, or may apply the amendments retrospectively by providing the revised disclosures for all period presented. The Company is an emerging growth company and has elected to use the extended transition period for complying with new or revised accounting standards.

3. Accrued Expenses

The following table presents the components of accrued expenses as of December 31, 2025 and 2024:

	December 31,	
	2025	2024
	(In thousands)	
Accrued research and development expenses	$ —	$ 86
Accrued employee-related expenses	21	1
Accrued expenses	$ 21	$ 87

4. Stockholders' Equity (Deficit)

As of December 31, 2025, the Company's articles of incorporation provided for the authorization of the following classes of stock:

- 40,000,000 shares of preferred stock, par value $0.0001 ("Preferred Stock"); and
- 560,000,000 shares of common stock, par value $0.0001 ("Common Stock").

Preferred Stock

On June 30, 2024, all 736,215 remaining shares of Preferred Stock were converted to shares of Common Stock at a conversion ratio of one-to-one.

Holders of Preferred Stock are entitled to one vote per share, to receive dividends (on and if declared by the Board of Directors of the Company (the "Board")) and, upon liquidation or dissolution, to receive all assets available for distribution to stockholders, before any rights, preferences and privileges of any outstanding shares of Common Stock with respect to dividends and in connection with liquidation, winding up and dissolution of the Company. The holders of Preferred Stock have no preemptive or other subscription rights.

Common Stock

In February 2024, the Company issued 22,172,461 shares of Common Stock to certain existing stockholders to enable them to be substantially aligned with the implied value of the Company as of the date determined by the Board. The Company had an aggregate of 11,939,650 shares of common stock and preferred stock outstanding immediately before this transaction, and all current investors participated in this transaction. All shares issued in this transaction were Common Stock. The transaction was conducted at the discretion of the Board and was not based on any investors' pre-existing contractual right to receive additional shares or anti-dilution protection. In connection with the transaction, the Company recorded $26.0 million as other expense — recapitalization of common stock in the statements of operations and comprehensive loss.

In October 2024, the Company and Maxim Group LLC (the "Advisor") entered into an engagement letter (the "Engagement Letter"), pursuant to which the Company issued 796,937 shares of Common Stock to the Advisor, which represents 2.0% of the Common Stock outstanding on a fully diluted basis as of October 18, 2024, the execution date of the Engagement Letter, at an aggregate price of $467 thousand, for advisory services (see Note 5).

In January 2025, the Company issued an aggregate of 3,704,307 shares of Common Stock to two existing shareholders in return for an exclusive gene therapy patent license. Of the total share issuance, 277,823 shares were issued to Rush University Medical Center ("Rush") and 3,426,484 shares were issued to Mstone. In connection with the transaction, the Company recorded $4.3 million as research and development expenses in the statements of operations and comprehensive loss for year ended December 31, 2025 as there is no alternative future use in accordance with ASC 730-10. In January 2025, the Company also issued 213,201 shares of our common stock at a purchase price per share of $1.17 to an existing investor for aggregate consideration of $250 thousand in cash.

4. Stockholders' Equity (Deficit) (cont.)

In July 2025 and through August 29, 2025, the Company issued 1,802,749 shares of Common Stock to investors at a price per share of $1.72. Pursuant to these subscription agreements, there is an embedded derivative feature in which the number of subscribed shares shall increase by 15% if the Company's common stock is not listed for trading on a national securities exchange by the second anniversary after issuance. This feature was not bifurcated as it met the scope exception per ASC 815-10-15-74a since the contract was classified as equity and does not require cash settlement.

On September 3, 2025, the Company filed a Form C with the Securities Exchange Commission to raise up to $5.0 million at a price per share of $2.80. During the year ended December 31, 2025, the Company issued an aggregate of 17,200 shares at $2.62 per share pursuant to this Form C.

In September 2025, the Company issued an aggregate of 158,020 shares of Common Stock to investors at a price per share of $2.55. These amounts consist of 143,756 shares issued at $2.80 per share, further reduced by an additional 14,264 incremental shares ("bonus shares") issued in connection with our listing. To incentivize investment into the Company, the bonus shares were issued to certain shareholders based on the amount and timing of their investments. All of these shares were recorded at par value to Common Stock with any excess recorded as additional paid-in capital.

In October 2025 through November 3, 2025, the Company issued an aggregate of 313,449 shares of Common Stock, including 17,200 shares pursuant to Form C to investors at a price per share of $2.58. These amounts consist of 290,376 shares issued at $2.80 per share, further reduced by an additional 23,073 incremental bonus shares issued in connection with these offerings. To incentivize investment into the Company, the bonus shares were issued to certain shareholders based on the amount and timing of their investments. All of these shares were recorded at par value to Common Stock with any excess recorded as additional paid-in capital.

Holders of Common Stock are entitled to one vote per share, to receive dividends (on and if declared by the Board) and, upon liquidation or dissolution, to receive all assets available for distribution to stockholders, subordinate to the rights, preferences and privileges of any outstanding shares of Preferred Stock with respect to dividends and in connection with liquidation, winding up and dissolution of the Company. The holders of Common Stock have no preemptive or other subscription rights.

As of December 31, 2025 and 2024, no cash dividends have been declared or paid.

5. Stock-Based Compensation

In November 2021, the Company and Mstone entered a Service Agreement, pursuant to which Mstone provides certain support and business development-related services to the Company. In order to preserve capital for operating and clinical development expenses, in May 2023, the Company and Mstone entered into a Letter Agreement, pursuant to which the Company issued 1,250,000 shares of Common Stock (the "Share Obligation") with an aggregate grant fair value of $5.6 million to Mstone as compensation for advisory services. The grant date fair value per share was determined based upon the most recently available third-party valuation of Common Stock. The shares were fully vested upon issuance and were issued in exchange for a 50% fee reduction for one year of advisory services to be provided from June 2023 through June 2024. The Company determined that this issuance of vested shares in return for future service met the criteria for capitalization as a prepaid expense and was amortized on a straight-line basis. For the year ended December 31, 2025, total stock-based compensation expense under this agreement was zero due to the expiration of the Letter Agreement in June 2024. For the year ended December 31, 2024, total stock-based compensation expense under this agreement was $2.3 million, of which $1.7 million was recorded as research and development expense and $578 thousand was recorded as general and administrative expense.

The Company and the Advisor entered into the Engagement Letter on October 18, 2024. The Company agreed to issue 796,937 shares of the Company's Common Stock, of which 50% was fully vested upon issuance, with an aggregate grant date fair value of $467 thousand to the Advisor as compensation for advisory services.

5. Stock-Based Compensation (cont.)

The remaining 50% is vested contingent upon a public listing of the Company. The grant date fair value per share was determined based upon the price per share from recent stock issuances to certain investors at that time. The Company determined that this issuance of vested shares in return for future service met the criteria for capitalization as a prepaid expense and was amortized on a straight-line basis over 13 months. For the years ended December 31, 2025 and 2024, total stock-based compensation expense under this agreement was $380 thousand and $87 thousand recorded as general and administrative expense, respectively.

2022 Equity Incentive Plan

In March 2022, the Board approved the Company's 2022 Equity Incentive Plan (the "Incentive Plan"). The Incentive Plan provides for the grant of options, stock appreciation rights, restricted stock units, restricted stock, and other stock-based awards and for Incentive Bonuses, which may be paid in cash, shares of Common Stock, or a combination thereof. The aggregate number of shares of Common Stock issuable under the Incentive Plan initially is 1,590,573 shares, plus a 4% annual increase on January 1 of each year beginning in 2023 and ending on January 1, 2032, subject to Board approval (the "Share Pool"). In October 2024, the Board increased the Share Pool to 6.3 million shares of Common Stock. As of December 31, 2025, there were 2,063,861 shares available to be issued pursuant to the Incentive Plan. In advance of the direct listing offering, the Company adopted the Polaryx Therapeutics, Inc. 2025 Equity Incentive Plan (the "2025 Plan") in December 2025. Upon adoption of the 2025 Plan, no further awards will be granted under the Incentive Plan.

2025 Equity Incentive Plan

In December 2025, the Company adopted the 2025 Plan. The purpose of the 2025 Plan is to promote and closely align the interests of our employees, officers, non-employee directors, and other service providers and our stockholders by providing stock-based compensation and other performance-based compensation. The objectives of the 2025 Plan are to attract and retain the best available personnel for positions of substantial responsibility and to motivate participants to optimize our profitability and growth through incentives that are consistent with our goals and that link the personal interests of participants to those of our stockholders. The 2025 Plan allows for the grant of stock options, both incentive stock options and "non-qualified" stock options; stock appreciation rights ("SARs"), alone or in conjunction with other awards; restricted stock and RSUs; incentive bonuses, which may be paid in cash, stock, or a combination thereof; and other stock-based awards. We refer to these collectively herein as "Awards."

Stock Subject to 2025 Plan

The form of 2025 Plan approved in December 2025 provided that the maximum number of shares of common stock that may be issued under the 2025 Plan will not exceed 1,500,000 shares (the "Share Pool"); however, the Share Pool will be increased on January 1 of each calendar year beginning in 2026 by a number of shares equal to 5% of the outstanding shares of common stock on the immediately preceding December 31 (or such lesser amount as approved by the Administrator). As such, the Share Pool was increased by 2,367,158 shares on January 1, 2026. The Share Pool is subject to certain adjustments in the event of a change in our capitalization and was adjusted to reflect the Reverse Stock Split. Following the Reverse Stock Split and taking into account the increase to the Share Pool on January 1, 2026, the Share Pool is 3,867,158 shares. Shares of common stock issued under the 2025 Plan may be either authorized and unissued shares or previously issued shares acquired by us. On termination or expiration of an Award under the 2025 Plan, in whole or in part, the number of shares of common stock subject to such Award but not issued thereunder or that are otherwise forfeited back to the Company will again become available for grant under the 2025 Plan. Additionally, shares retained or withheld in payment of any exercise price, purchase price, or tax withholding obligation of an Award will again become available for grant under the 2025 Plan.

Fair Value Inputs

The calculation of the fair value of awards requires an estimate of the Company's equity value. As the Company historically has been a privately held company with no trading history for its Common Stock to date, the estimated fair value of the Company's Common Stock has been determined by management and approved by

5. Stock-Based Compensation (cont.)

the Board. To determine the fair value, management considered the price per share from recent stock issuances to certain investors at that time and an assessment of additional objective and subjective factors that it believed were relevant and which may have changed from the date of the most recent valuation through the date of the grant. Additional factors include, among others, the nature and history of the Company's business; the Company's stage of development and commercialization; external market conditions; valuations of the Company's industry peers; and the likelihood of achieving a liquidity event, such as an initial public offering or sale of the Company.

Restricted Stock Units

As of December 31, 2025, there were 4,186,139 restricted stock units outstanding. Pursuant to the amendment as executed on July 31, 2025, these restricted stock units vest over time but are only deliverable upon a change in control of the Company that occurs within seven years following the applicable date of grant. Vesting of the restricted stock units is contingent upon the recipient's services to the Company through three or four installments on the first three or four anniversaries of the vesting commencement date. The change in control requirement represents a performance condition that is recognized when it is probable, and therefore no compensation expense will be recorded, nor inclusion of the shares within the basic and diluted net income (loss) per share calculations, until the occurrence of a change in control of the Company.

The Company measures restricted stock compensation costs based on the stock price at the grant date less forfeitures as incurred.

The following table presents a summary of our restricted stock activity for the years ended December 31, 2025 and 2024:

	Number of Awards	Weighted Average Grant date Fair Value (per share)
Non-vested at December 31, 2023	955,953	
Granted	1,825,000	$ 1.78
Vested	—	
Forfeited or exercised[(1)]	(110,346)	
Non-vested at December 31, 2024	2,670,607	
Granted	2,092,757	$ 1.85
Vested	—	
Forfeited or exercised	(577,225)	
Non-vested at December 31, 2025	4,186,139	

(1) Forfeitures for the year ended December 31, 2024 were revised to reflect immaterial changes for certain terminated employees. There was no impact to any recorded amounts in the financial statements.

As of December 31, 2025, there was $7.6 million of total unrecognized compensation cost related to restricted stock units that will be recognized over a remaining weighted average service period of 2.9 years and upon a change in control of the Company. In connection with the amendment executed on July 31, 2025, the transaction was treated as a type IV modification (improbable to improbable) in accordance with ASC 718. As such, the Company calculated a new grant date fair value for the amended restricted stock units. The unrecognized compensation expense associated with these restricted stock units reflects the new grant date fair value as of the modification date. The fair value was equal to price per share from recent stock issuances to certain investors at that time which was $1.78 per share.

5. Stock-Based Compensation (cont.)

The Company recognized a total of $4.7 million stock-based compensation related to the Incentive Plan and shares issued to Mstone, Rush and Maxim Group LLC, of which $4.3 million and $380 thousand are included within research and development expenses and general and administrative expenses, respectively, in the statement of operations and comprehensive loss for the year ended December 31, 2025. The Company recognized a total of $2.4 million stock-based compensation related to the Incentive Plan and shares issued to Mstone and Maxim Group LLC, of which $1.7 million and $665 thousand are included within research and development expenses and general and administrative expenses, respectively, in the statement of operations and comprehensive loss for the year ended December 31, 2024.

6. Segment Information

The Company has one reportable segment: lysosomal storage disorders. The lysosomal storage disorders segment consists of the Company's costs associated with the preclinical and clinical development of the Company's product candidates. The Company currently is in the clinical stage and manages its business activities on an aggregate basis.

The accounting policies of the lysosomal storage disorders segment are consistent with those described in Note 2, *Summary of Significant Accounting Policies*, and the measure of segment assets is reported on the balance sheets as total assets. The Company's CODM is the chief executive officer. The CODM assesses performance of the lysosomal storage disorders segment using operating expenses as reported in the statements of operations and comprehensive loss. Operating expenses is assessed by the CODM to make decisions on how to allocate resources, such as determining additional costs for preclinical and clinical development of the Company's product candidates.

The following table summarized significant segment expenses for the years ended December 31, 2025 and 2024:

	Lysosomal Storage Disorders Segment	
	Year Ended December 31,	
	2025	2024
	(In thousands)	
Research and development expenses (excluding stock compensation)	$ (1,922)	$ (1,077)
General and administrative expenses (excluding stock compensation)	(1,174)	(875)
Stock-based compensation	(4,725)	(2,400)
Recapitalization of common stock	—	(26,004)
Other expense – direct listing offering costs.	(1,164)	—
Net loss	$ (8,985)	$ (30,356)

7. Net Loss Per Share

Basic net loss per share is computed using the weighted-average number of shares of Common Stock outstanding during the period. Diluted net loss per unit is computed using the weighted-average number of shares of Common Stock and, if dilutive, Common Stock equivalents outstanding during the period.

7. Net Loss Per Share (cont.)

The following table presents the calculation of basic and diluted net loss per share:

	Year Ended December 31,	
	2025	2024
	(In thousands, except unit amounts and per unit data)	
Net loss per share		
Numerator		
Net loss	$ (8,985)	$ (30,356)
Numerator for basic and diluted net loss per share	$ (8,985)	$ (3,779)
Denominator		
Weighted average common shares outstanding	45,422,581	34,200,660
Denominator for basic and diluted net loss per share	45,422,581	34,200,660
Net loss per share:		
Basic and diluted	$ (0.20)	$ (0.89)

The following potentially dilutive securities were excluded from the calculation of diluted net loss per share due to their anti-dilutive effect:

	Year Ended December 31,	
	2025	2024
Performance-based awards	398,469	398,469
Non-vested restricted stock units	4,186,139	2,584,072
Total potentially dilutive securities	4,584,608	2,982,541

8. Income Taxes

Income (loss) before provision for income taxes consisted of the following:

	December 31,	
	2025	2024
	(In thousands)	
Domestic	$ (8,985)	$ (30,356)
Foreign	—	—
Loss before provision for income taxes	$ (8,985)	$ (30,356)

A reconciliation of the Company's statutory income tax rate to the Company's effective income tax rate is as follows:

	December 31,	
	2025	2024
Income at US statutory rate	21.00%	21.00%
State taxes, net of federal benefit	0.00%	(0.19)%
Direct listing offering costs	(2.72)%	0.00%
Recapitalization of common stock	0.00%	(17.99)%
Tax credits	0.35%	0.02%
Valuation allowance	(18.63)%	(2.84)%
	0.00%	0.00%

8. Income Taxes (cont.)

The net deferred income tax asset balance related to the following:

	December 31,	
	2025	2024
	(In thousands)	
Net operating loss carryforwards	$ 4,742	$ 4,096
Gene therapy patent license	852	—
Credits	50	19
Capitalized research and development	998	1,217
Total deferred tax assets	6,642	5,332
Valuation allowance	(6,392)	(4,865)
Net deferred tax assets	$ 250	$ 467
Deferred tax liabilities		
Accruals and other	(250)	(467)
Net deferred tax liabilities	(250)	(467)
Net deferred tax assets (liabilities)	$ —	$ —

As of December 31, 2025 and 2024, the Company had a federal net operating loss ("NOL") carryforward of $18.7 million and $15.7 million, respectively. As of December 31, 2025 and 2024, the Company had state NOL carryforwards of $15.7 million and $15.7 million, respectively. Of the $18.7 million of federal NOL carryforwards as of December 31, 2025, $1.1 million begins to expire in 2034 and $17.6 million may be carried forward indefinitely. The state NOL carryforwards begin to expire in 2034.

As of December 31, 2025, the Company also had federal tax credits of $50 thousand, which begin to expire in 2042.

Future realization of the tax benefits of existing temporary differences and NOL carryforwards ultimately depends on the existence of sufficient taxable income within the carryforward period. As of December 31, 2025 and 2024, the Company performed an evaluation to determine whether a valuation allowance was needed. The Company considered all available evidence, both positive and negative, which included the results of operations for the current and preceding years. The Company determined that it was not possible to reasonably quantify future taxable income and determined that it is more likely than not that all of the deferred tax assets will not be realized. Accordingly, the Company maintained a full valuation allowance as of December 31, 2025 and 2024. The Company's valuation allowance increased for the year ended December 31, 2025 by $1.5 million due primarily to the generation of net operating losses.

Under Internal Revenue Code Section 382 ("Section 382"), if a corporation undergoes an "ownership change," the corporation's ability to use its pre-change NOL carryforwards and other pre-change tax attributes to offset its post-change income may be limited. We have not completed a study to assess whether an "ownership change" has occurred or whether there have been multiple ownership changes since we became a "loss corporation" as defined in Section 382. Future changes in our stock ownership, which may be outside of our control, may trigger an "ownership change." In addition, future equity offerings or acquisitions that have equity as a component of the purchase price could result in an "ownership change." If an "ownership change" has occurred or does occur in the future, utilization of the NOL carryforwards or other tax attributes may be limited, which could potentially result in increased future tax liability to us.

The calculation of the Company's tax liabilities involves dealing with uncertainties in the application of complex tax laws and regulations for both federal taxes and the many states in which we operate or do business in. ASC 740 states that a tax benefit from an uncertain tax position may be recognized when it is more likely than not that the position will be sustained upon examination, including resolutions of any related appeals or litigation processes, on the basis of the technical merits.

8. Income Taxes (cont.)

The Company records uncertain tax positions as liabilities in accordance with ASC 740 and adjusts these liabilities when its judgment changes as a result of the evaluation of new information not previously available. Because of the complexity of some of these uncertainties, the ultimate resolution may result in a payment that is materially different from the Company's current estimate of the unrecognized tax benefit liabilities. These differences will be reflected as increases or decreases to income tax expense in the period in which new information is available. As of December 31, 2025 and 2024, no uncertain tax positions have been recorded in the financial statements.

The Company files tax returns as prescribed by the tax laws of the jurisdictions in which it operates. In the normal course of business, the Company is subject to examination by federal and state jurisdictions, where applicable. There are currently no pending tax examinations. The Company's tax years are still open under statute from December 31, 2022 to the present. The resolution of tax matters is not expected to have a material effect on the Company's financial statements.

9. Commitments and Contingencies

License Agreements

On April 8, 2016, the Company entered into a license agreement with the Rush University Medical Center ("Rush") pursuant to which Rush granted the Company an exclusive license, with sublicensing rights, for the use of an invention/drug, made in the course of research at Rush, in the treatment of lysosomal storage diseases. Under this agreement, the Company is responsible for obtaining and maintaining all regulatory approvals for the drug, as well as for all clinical trials and commercialization activities relating to the drug. As part of the agreement, the Company agreed to issue 882,353 shares as a partial consideration for all the rights and licenses granted to the Company as specified in the license agreement. Upon execution of the agreement, the Company paid a license upfront fee of $70 thousand. Additional milestone-based payments are due upon completion of the Investigational New Drug filing of $50 thousand, which was paid in 2020, and $100 thousand due upon U.S. Food and Drug Administration approval of the product. Further, the Company must pay Rush royalties for the life of the patent of 3.5% on net sales.

The licenses agreement was further amended in July 2019, September 2019, and December 2021 for definition changes. There were no change to the milestone payments or terms of the agreement.

In January 2025, the Company issued 277,823 shares of common stock to Rush in return for an exclusive gene therapy patent license. Pursuant to the agreement with Rush (the "2022 Rush License Agreement"), the Company is obligated to pay Rush (i) up to $75 thousand upon the achievement of specific milestones for an orphan indication, (ii) up to $650 thousand upon the achievement of specific milestones for a non-orphan indication, and (iii) an annual royalty equal to 1.75% of net sales. In the event we sublicense the rights under the 2022 Rush License Agreement, we are also obligated to pay Rush (i) an annual royalty equal to 1.75% of such sublicensee's net sales and (ii) 7.5% of all non-royalty considerations we receive from such sublicensee (see Note 4).

Master Services Agreement with Rush University Medical Center

In June 2016, the Company entered into a Master Services Agreement with Rush (the "Rush MSA"), pursuant to which Rush provides services regarding the development and regulatory approval process for products currently under development by us, under statements of work for such services agreed to by the parties from time to time (see Note 10).

Contingencies

The Company is not presently a party to any matters such that the ultimate resolution will have a material effect on the Company's results of operations, financial condition, or cash flows.

10. Related Parties

Mstone is a controlling shareholder of the Company. During the year ended December 31, 2025 and 2024, Mstone provided consulting services to the Company pursuant to the terms of the Service Agreement and the total expenses incurred for the years ended December 31, 2025 and 2024 were $1.6 million and $1.2 million, respectively. For the year ended December 31, 2025, of the $1.6 million incurred, $1.2 million was recorded as research and development expense and approximately $400 thousand was recorded as general and administrative expense. For the year ended December 31, 2024, of the $1.2 million incurred, approximately $900 thousand was recorded as research and development expense and approximately $300 thousand was recorded as general and administrative expense. Consulting fees paid to Mstone for the years ended December 31, 2025 and 2024 were $1.6 million and $1.4 million, respectively. As of December 31, 2025 and 2024, there was $91 thousand and $130 thousand due to Mstone, respectively, which is recorded in due to related party in the balance sheet.

In February 2024, the Company issued 22,172,461 shares of Common Stock to certain existing stockholders, of which Mstone received 15,819,504 shares, to enable them to be substantially aligned with the implied value of the Company as of the date determined by the Board (See Note 4).

In November 2021, the Company and Mstone entered a Service Agreement, pursuant to which Mstone provides certain support and business development-related services to the Company. In order to preserve capital for operating and clinical development expenses, in May 2023, the Company and Mstone entered into a Letter Agreement, pursuant to which the Company issued 1,250,000 shares of Common Stock (the "Share Obligation") with an aggregate grant fair value of $5.6 million to Mstone as compensation for advisory services. For the year ended December 31, 2025, total stock-based compensation expense under this agreement was zero due to the expiration of the Letter Agreement in June 2024. For the year ended December 31, 2024, total stock-based compensation expense under this agreement was $2.3 million, of which $1.7 million was recorded as research and development expense and $578 thousand was recorded as general and administrative expense (See Note 5).

In January 2025, the Company entered into a Share Placement Agreement with Rush and Mstone, pursuant to which the Company issued 277,823 shares to Rush and 3,426,484 shares to Mstone at a price per share of $1.17 in exchange for an exclusive gene therapy patent license (See Note 4 and Note 9).

In April 2025, the Company paid $109 thousand under two statements of work pursuant to the Rush MSA. Total expenses incurred for the years ended December 31, 2025 and 2024 were $133 thousand and zero, respectively, which is recorded in research and development in the statement of operations and comprehensive loss. As of December 31, 2025 and 2024, there was $23 thousand and zero due to Rush, respectively, which is recorded in accrued expenses — related party in the balance sheet.

11. Subsequent Events

The Company has evaluated all events subsequent to December 31, 2025 through March 23, 2026, which represents the date these financial statements were available to be issued. The Company is not aware of any subsequent event that would require recognition or disclosure in the financial statements other than those described below.

On January 29, 2026, the SEC declared the Company's previously filed Form S-1 effective to begin trading on The Nasdaq Capital Market ("Nasdaq"). The Company's common stock was approved for listing on Nasdaq under the symbol "PLYX". The Company's common stock began trading on Nasdaq on February 2, 2026.

On March 23, 2026, the Company amended the Service Agreement with Mstone to be a fixed amount of $90 thousand per month beginning January 1, 2026.

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 Principal Executive Officer and our Principal Financial Officer, evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2025. Based on the foregoing evaluation, our Principal Executive Officer and Principal Financial Officer concluded that our disclosure controls and procedures were effective at a reasonable assurance level as of December 31, 2025. The term "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under 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 us in the reports we file or submit under the Exchange Act is accumulated and communicated to our management, including our Principal Executive Officer and Principal Financial Officer, 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.

Internal Control over Financial Reporting

This Annual Report does not include a report of management's assessment regarding internal control over financial reporting or an attestation report of our independent registered public accounting firm due to a transition period established by the rules of the SEC for newly public companies. Additionally, for as long as we remain an "emerging growth company" as defined in Section 2(a) of the Securities Act, as modified by the Jumpstart Our Business Startups Act of 2012, we intend to take advantage of the exemption permitting us not to comply with the requirement that our independent registered public accounting firm provide an attestation on the effectiveness of our internal control over financial reporting.

Changes in Internal Control over Financial Reporting

There were no changes in our internal control over financial reporting during the quarter ended December 31, 2025 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting, except for the following change.

In October 2025, we implemented remediation measures to limit administrative user access to the financial system. Specifically, we have removed the segregation of duties conflicts related to senior management by removing excess access to the financial system from those users.

Item 9B. Other Information.

Trading Plans

During the quarter ended December 31, 2025, no director or Section 16 officer adopted or terminated any Rule 10b5-1 trading arrangements or non-Rule 10b5-1 trading arrangements (in each case, as defined in Item 408(a) of Regulation S-K).

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections.

Not applicable.

PART III

Item 10. Directors, Executive Officers and Corporate Governance

Executive Officers and Directors

The following table sets forth the names, ages as of February 1, 2026, and positions of the individuals who serve as directors and executive officers of Polaryx Therapeutics, Inc.

NAME	AGE	POSITION(S)
Executive Officers:		
Alex Yang, J.D., LL.M.	56	Chief Executive Officer and Chair of the Board
Lisa L. Bollinger, M.D.	61	Chief Medical Officer
G. Michael Landis, CPA	59	Chief Financial Officer and Director
Andrew O	53	Chief Investment Officer
Non-Employee Directors:		
Mitchel Berger, M.D.[(1)(2)(3)]	73	Director
Francis A. Braun III, CPA[(1)]	65	Director
Charles Ryan, J.D., Ph.D.[(1)(2)(3)]	61	Director

(1) Member of the audit committee.
(2) Member of the compensation committee.
(3) Member of the nominating and corporate governance committee.

Executive Officers

Alex Yang, J.D., LL.M. has served as Chair of our Board since June 2021 and Chief Executive Officer since March 2023.

In 2016, Mr. Yang founded Mstone, a biotech incubation and investment platform where he serves as Chief Executive Officer. Since founding Mstone, Mr. Yang has held senior executive and board leadership roles in a number of biopharmaceutical, medical device, and healthcare services companies operating across the United States, Hong Kong, South Korea, and Singapore, including Mstone portfolio companies such as Forest Hills Partners Hong Kong Limited, Dr. KuDos Lab Limited, Humeryx Pharmaceutical Limited, and Epygenix Therapeutics, Inc. At Epygenix, as Chief Executive Officer and Chair of the board of directors, he led the sale of the company to Harmony Biosciences Holdings, Inc. (Nasdaq: HRMY).

Prior to establishing Mstone, Mr. Yang worked on fund formation, cross-border transactions, and private equity investments across a wide range of industries. Mr. Yang served as Managing Partner at the Hong Kong office of Kim & Chang, one of Asia's largest law firms, and as a Partner at Ernst & Young LLP's Hong Kong office, where he led the regional financial services practice encompassing banking, capital markets, asset management, and insurance. He previously held roles at Morgan Stanley's Hong Kong office in its Private Equity division, including holding positions at its investment and risk committees. At Morgan Stanley, he also worked on private equity funds in buyouts, growth capital, real estate and special situations across many industries in Asia. He also worked in the international tax and consulting divisions of Coopers & Lybrand and Ernst & Young LLP in New York.

Mr. Yang holds both a J.D. and an LL.M. from New York University School of Law and is admitted to the New York State Bar. He earned his B.A. in Economics from Binghamton University.

We believe Mr. Yang is qualified to serve on our Board because of his more than 25 years of global experience in law, finance, and strategic leadership across the biotechnology, healthcare, and investment sectors.

Lisa L. Bollinger, M.D. has served as our Chief Medical Officer since October 2025.

Dr. Bollinger is a board-certified pediatrician. Since June 2024, Dr. Bollinger also serves as Chief Executive Officer and President of Bollinger Regulatory Consulting (BRC), LLC, a consultancy firm specializing in regulatory affairs, due diligence, and pediatric drug development. Prior to joining Polaryx, from April 2021 to May 2024,

Dr. Bollinger served as Vice President, Regulatory Affairs, Global Regulatory Affairs and Clinical Safety (GRACS) at Merck & Co., Inc (NYSE: MRK), a global biopharmaceutical company, where she led the general medicine therapeutic area in regulatory affairs. From August 2018 to March 2021, Dr. Bollinger served as Vice President, Global Patient Safety & Pediatrics, and Labeling, Global Regulatory Affairs & Safety (GRAAS), Research and Development at Amgen Inc. (Nasdaq: AMGN), a global biopharmaceutical company. Earlier in her career, Dr. Bollinger held other executive roles at Amgen Inc. and the FDA, where she was Associate Director, Office of New Drugs, Center for Drug Evaluation and Research. Dr. Bollinger currently serves on the board of Apogee Therapeutics, Inc. (Nasdaq: APGE).

Dr. Bollinger earned her M.D. from the Uniformed Services University of the Health Sciences F. Edward Hebert School of Medicine and a B.S. in Physiology from the University of California, Davis. She completed her residency in pediatrics at the University of California Davis Medical Center.

G. Michael Landis, CPA has served as a member of our Board since August 2025 and as our Chief Financial Officer since June 2024. As of November 1, 2025, Mr. Landis transitioned to a full-time basis as our Chief Financial Officer. Mr. Landis is an accomplished financial executive with an over 25-year track record of public company expertise, capital market transactions, investor relations, and financial reporting. Prior to joining Polaryx, Mr. Landis served as Chief Financial Officer at Epygenix Therapeutics, Inc., a late-stage clinical biopharmaceutical company, from March 2022 until the company's acquisition in April 2024. At Epygenix, his responsibilities included leading all corporate finance and accounting functions as well as participating in activities related to the company's sale. From June 2021 to December 2021 Mr. Landis served as Chief Financial Officer at Avisa Diagnostics Inc. (CSE: AVBT), a medical device company, where he led strategic and tactical finance initiatives and was involved with investor relations and capital-raising activities. Earlier in his career, from 2009 to 2020, Mr. Landis served as Principal Accounting Officer and Treasurer at Lannett Company Inc., a pharmaceutical company, where he led acquisitions and related financing activities. Prior to joining Lannett, Mr. Landis was actively involved in the initial public offering process in previous financial leadership roles at companies, including Akrion Inc. and AlliedBarton Security Services, LLC. Mr. Landis began his career working in public accounting at Deloitte & Touche and Ernst & Young LLP.

Mr. Landis holds a B.A. in Accounting from Franklin & Marshall College and is a Certified Public Accountant (CPA).

Andrew O has served as our Chief Investment Officer since January 2022 and served as a member of our Board from March 2023 to January 2026. Mr. O is an accomplished leader with over 25 years of experience in asset management and global finance. As Polaryx's Chief Investment Officer, Mr. O builds on a career spanning traditional fund management and fundamentally driven hedge fund strategies. Mr. O joined Mstone, a biotech incubation and investment platform, in January 2022. Since joining Mstone, Mr. O has served in Head of Investor Relations and Business Development and Chief Investment Officer roles involved in corporate development and capital raising activities at various Mstone portfolio companies, including Epygenix Therapeutics, Inc., Forest Hills Partners Hong Kong Limited, Liberyx Therapeutics Limited, Humeryx Pharmaceutical, and Dr. KuDos Lab, in addition to his work for Polaryx. Prior to joining Polaryx, Mr. O served as a Managing Director and Senior Portfolio Manager at Manulife Investment Management (Hong Kong) Limited from January 2013 to January 2022, where his responsibilities included management of various equity portfolios with mandates to invest in non-Japan Asia companies across sectors and market capitalizations. Earlier in his career, Mr. O served in senior investment positions at leading institutions, such as Horizon Asset International (HK) Limited and FrontPoint Partners LP (Morgan Stanley Investment Management), and worked at Goldman Sachs & Co. and the International Finance Corporation, the World Bank's private investment arm.

Mr. O graduated from the University of Pennsylvania with a B.A. and undertook Master's-level studies at Yonsei University's Graduate School of International Studies.

Non-Employee Directors

Mitchel Berger, M.D. has served as a member of our Board since January 2026. Dr. Berger is the Director of the Brain Tumor Center at the University of California, San Francisco (UCSF), a position he has held since 1997, and serves as the Principal Investigator of the UCSF Brain Tumor Center's Specialized Program of Research Excellence (SPORE) in neuro-oncology, funded by the National Cancer Institute. From 1997 to 2020, Dr. Berger

served as the Chair of UCSF's Department of Neurological Surgery. During his career, Dr. Berger has served as President of the American Association of Neurological Surgeons, President of the Society of Neuro-Oncology, and President of the American Academy of Neurological Surgery. He has also been a director of the American Board of Neurological Surgery, a member of the board of directors of the American Association of Neurological Surgeons, a member of the National Football League's Head, Neck and Spine Committee, and a member of the Blue Ribbon Panel for the National Cancer Moonshot Initiative.

Dr. Berger earned his M.D. from the University of Miami School of Medicine. He completed his internship, residency, and advanced postdoctoral fellowship training at UCSF. He holds a B.A. from Harvard College.

We believe Dr. Berger is qualified to serve on our Board because of his extensive scientific and research experience and strong leadership background in the fields of medicine and academia.

Francis A. Braun III, CPA has served as a member of our Board since January 2026. Mr. Braun has served as a senior advisor to Stout Risius Ross, LLC, a global advisory firm, since April 2024, and a member of the advisory council of CrossCountry Consulting LLC, an advisory firm, since February 2024. Mr. Braun has served as a consultant to Kohlberg Kravis Roberts & Co. L.P., a global investment firm, from July 2024 to June 2025. Mr. Braun serves as a director of SHF Holdings, Inc. (Nasdaq: SHFS), a fintech company, since May 2025 and is the chairman of SHF Holdings' audit committee. He is also a director of Crown Bank, a New Jersey full-service commercial bank, since October 2024 and is the chairman of Crown Bank's audit committee. Mr. Braun served as a director of Elite Express Holdings, Inc. from August 2025 to October 2025. From December 2016 to July 2023, Mr. Braun served as a Partner at Grant Thorton LLP, a global audit, tax and advisory firm, where his experience included serving clients across the life science, technology, industrial manufacturing and service industries. Earlier in his career, Mr. Braun served as a Partner at Deloitte & Touche LLP from May 2002 to November 2016 and an employee and Partner at Arthur Andersen LLP from 1983 to 2002.

Mr. Braun holds a B.S. in Accounting from Rider University and is a Certified Public Accountant in New Jersey (CPA).

We believe Mr. Braun is qualified to serve on our Board because of his extensive financial and accounting background and experience working with life sciences companies.

Charles Ryan, J.D., Ph.D. has served as a member of our Board since January 2026. Dr. Ryan currently serves as President of Quince Therapeutics, Inc. (Nasdaq: QNCX), a late-stage biotechnology company, and Chief Executive Officer of their subsidiary company, Quince Therapeutics S.p.A, positions he has held since September 2023. Prior to joining Quince, Dr. Ryan served as a life sciences consultant from November 2022 to September 2023 working with a start-up company to identify a regulatory path for a novel device. Dr. Ryan served as President, Chief Executive Officer and Chairman of the Board of Travecta Therapeutics, Pte Ltd., a biopharmaceutical company, from May 2021 to October 2022, and Chief Executive Officer and Director of Neurotrope, Inc. (Nasdaq: NTRP), a biopharmaceutical company, from December 2017 to December 2020 and President and Chief Executive Officer of Orthobond Corporation from October 2016 to February 2018. Earlier in his career, Dr. Ryan served as Senior Vice President and Chief Intellectual Property Counsel at Forest Laboratories (now AbbVie) for more than ten years. Mr. Ryan previously served on the board of directors of Applied DNA Sciences, Inc. (Nasdaq: APDN) from August 2011 to November 2019 and BioRestorative Therapies, Inc. (Nasdaq: BRTX) from April 2015 to January 2020.

Dr. Ryan holds a J.D. from Western New England University, a Ph.D. in Oral Biology and Pathology from the State University of New York at Stony Brook, and a B.A. in Chemistry from The College of Wooster. He is a member of the New York State Bar and is a patent practitioner of the U.S. Patent and Trademark Office.

We believe Dr. Ryan is qualified to serve on our Board because of his extensive experience in the biotechnology sector, including leadership of several biotechnology companies, and his background in intellectual property law.

Family Relationships

There are no family relationships among any of our directors or executive officers.

Code of Business Conduct and Ethics

Our Board has adopted a Code of Business Conduct and Ethics that establishes the standards of ethical conduct applicable to all our directors, officers and employees. The full text of our Code of Business Conduct and Ethics is posted on our website at *www.polaryx.com*. It addresses, among other matters, compliance with laws and policies, conflicts of interest, corporate opportunities, regulatory reporting, external communications, confidentiality requirements, insider trading, proper use of assets and how to report compliance concerns. We intend to disclose any amendments to the Code of Business Conduct and Ethics, or any waivers of its requirements, on our website to the extent required by applicable rules. The Audit Committee is responsible for applying and interpreting our Code of Business Conduct and Ethics in situations where questions are presented to it. Information contained on, or that can be accessed through, our website is not incorporated by reference into this Annual Report, and you should not consider information on our website to be part of this Annual Report.

Insider Trading Policy

We have adopted insider trading policies and procedures governing the purchase, sale and other transactions in Company securities by our directors, officers and employees, and other covered persons, as well as the Company itself, that we believe are reasonably designed to promote compliance with insider trading laws, rules and regulations, and Nasdaq listing rules, as applicable. As part of these policies and procedures, we prohibit our directors, officers, employees and consultants from engaging in (a) short-term trading; (b) short sales; (c) transactions involving publicly traded options or other derivatives, such as trading in puts or calls with respect to Company securities; and (d) hedging or monetization transactions.

Audit Committee and Audit Committee Financial Expert

The members of our Audit Committee are Mitchel Berger, M.D., Francis A. Braun III, CPA and Charles Ryan, J.D., Ph.D., each of whom qualifies as an independent director for audit committee purposes, as defined under the rules of the SEC and the applicable Nasdaq listing rules and has sufficient knowledge in financial and auditing matters to serve on the Audit Committee. Francis A. Braun III, CPA chairs the Audit Committee. In addition, our Board determined that Francis A. Braun III, CPA and Charles Ryan, J.D., Ph.D. are each an "audit committee financial expert" as defined under the rules of the SEC.

Item 11. Executive Compensation

Overview

This section provides an overview of the material components of our executive compensation program each for the following named executive officers (collectively, our "NEOs") during the fiscal year ended December 31, 2025.

Name	Title
Alex Yang	Chief Executive Officer
Lisa Bollinger	Chief Medical Officer[(1)]
G. Michael Landis	Chief Financial Officer[(2)]

(1) Dr. Bollinger became a full-time employee as of October 15, 2025 and was appointed Chief Medical Officer on October 15, 2025.

(2) Mr. Landis became a full-time employee as of November 1, 2025.

During 2024, we did not employ any of our NEOs. Other than grants of restricted stock units ("RSUs") as described below, we do not have any agreements with our NEOs regarding their compensation or otherwise determine compensation earned by, or paid to, them.

Mstone provides services that would otherwise be provided by employees and has historically employed and compensated the Company's executive officers, including Mr. Yang and prior to November 2025, Mr. Landis, directly. Mstone determines the salaries, bonuses and other benefits earned by, or paid to, Mr. Yang (or Mr. Landis prior to November 2025). Our consulting agreement with Mstone does not require Mr. Yang (or Mr. Landis prior to November 2025) to dedicate a specific amount of time to fulfilling their obligations or specify an amount or percentage of the amounts we pay to Mstone that must be allocated to compensating Mr. Yang (or Mr. Landis prior to November 2025). While Mr. Yang may, in his capacity as Chief Executive Officer of Mstone, have played a role in Mstone's process for determining the compensation earned by, or paid to, Mr. Landis by Mstone prior to November 2025, our Board is not involved or consulted with regarding this process.

Summary Compensation Table

The following table provides information regarding all plan and non-plan compensation awarded to, earned by or paid to each of our NEOs for the fiscal years ended December 31, 2025 and December 31, 2024.

Name and Principal Position	Year	Salary ($)	Stock Awards ($)[1]	Total ($)
Alex Yang	2025	—	$ 792,000	$ 792,000
Chief Executive Officer	2024	—	$ 580,000	$ 580,000
Lisa Bollinger	2025	$ 62,500	$ 420,000	$ 482,500
Chief Medical Officer				
G. Michael Landis	2025	$ 46,667	$ 264,000	$ 310,667
Chief Financial Officer	2024	—	$ 87,000	$ 87,000

(1) Amounts reported in this column represent the aggregate grant date fair value of RSUs granted to our NEOs, as computed in accordance with FASB ASC Topic 718 based on the fair market value of our common stock on the applicable date of grant.

Narrative Disclosure to Summary Compensation Table

Offer Letters

Dr. Bollinger and Mr. Landis have each entered into an offer letter with us in connection with their commencement of full-time employment with us. Pursuant to the offer letters, Dr. Bollinger receives a base salary of $300,000 with a target annual bonus of 20% of base salary, and Mr. Landis receives a base salary of $280,000 with a target annual bonus of 20% of base salary. Mr. Landis is also eligible to receive a medical benefits stipend of $3,500 per month.

Long-Term Incentive Compensation

We have historically provided long-term incentive compensation to our NEOs through grants of RSUs under the Polaryx Therapeutics, Inc. 2022 Equity Incentive Plan (the "2022 Plan"). The 2022 Plan was adopted by our Board and approved by our stockholders in March 2022 and permitted the grant of stock options, stock appreciation rights, restricted stock, RSUs, incentive bonuses and other stock-based awards. All outstanding awards under the 2022 Plan remain outstanding and continue to be subject to their existing terms; however, no further awards will be granted under the 2022 Plan. On September 1, 2025, Mr. Yang was granted 1,800,000 RSUs and Mr. Landis was granted 600,000 RSUs, and on November 15, 2025, Dr. Bollinger was granted 600,000 RSUs (in each case, which amounts do not give effect to the Reverse Stock Split). The RSUs granted to our NEOs in 2025 vest in approximately equal increments on each of the first four anniversaries of the applicable date of grant, subject to the NEO's continued service through each vesting date, but are not deliverable until the later of (i) the consummation of a change in control within seven years of the applicable date of grant and (ii) the applicable vesting date.

In the event of an NEO's termination without cause or resignation for good reason, in each case, within three months prior to or within 12 months following a change in control, all RSUs will become fully vested. In addition, in the event of an NEO's death or disability, all RSUs will become fully vested and will be deliverable, regardless of whether or not a change in control has occurred.

Outstanding Equity Awards at December 31, 2025

The following table presents information regarding outstanding RSUs held by our NEOs as of December 31, 2025. The amounts set forth in the following table do not give effect to the Reverse Stock Split.

		Stock Awards	
Name	Grant Date	Equity Incentive Plan Awards: Number of Unearned Shares, Units or Other Rights That Have Not Vested (#)	Equity Incentive Plan Awards: Market or Payout Value of Unearned Shares, Units or Other Rights That Have Not Vested ($)[1]
Alex Yang	9/1/2025	1,800,000[2]	$ 4,689,000
	11/1/2024	2,000,000[3]	$ 5,210,000
	3/1/2023	1,800,000[4]	$ 4,689,000
Lisa Bollinger	11/15/2025	600,000[2]	$ 1,563,000
G. Michael Landis.	9/1/2025	600,000[2]	$ 1,563,000
	11/1/2024	300,000[3]	$ 781,500

(1) The market value was determined by multiplying the number of shares by $2.605, the fair market value of our common stock as of December 31, 2025 (without giving effect to the Reverse Split).

(2) These RSUs vest as to 25% on each of the first four anniversaries on the grant date, subject to the NEO's continued service through each vesting date, but are not deliverable unless and until we consummate a change in control within seven years of the grant date.

(3) These RSUs vested as to 34% on November 1, 2025 and will vest as to 33% on each of November 1, 2026 and November 1, 2027, subject to the NEO's continued service through each vesting date, but are not deliverable unless and until we consummate a change in control within seven years of the grant date.

(4) These RSUs vested as to 34% on March 1, 2024 and as to 33% on March 1, 2025 and will vest as to the remaining 33% on March 1, 2026, subject to the NEO's continued service through each vesting date, but are not deliverable unless and until we consummate a change in control within seven years of the grant date.

2025 Equity Incentive Plan

In December 2025, we adopted the Polaryx Therapeutics, Inc. 2025 Equity Incentive Plan (the "2025 Plan"). The purpose of the 2025 Plan is to promote and closely align the interests of our employees, officers, non-employee directors, and other service providers and our stockholders by providing stock-based compensation and other performance-based compensation. The objectives of the 2025 Plan are to attract and retain the best available personnel for positions of substantial responsibility and to motivate participants to optimize our profitability and growth through incentives that are consistent with our goals and that link the personal interests of participants to those of our stockholders. The 2025 Plan allows for the grant of stock options, both incentive stock options and "non-qualified" stock options; stock appreciation rights ("SARs"), alone or in conjunction with other awards; restricted stock and RSUs; incentive bonuses, which may be paid in cash, stock, or a combination thereof; and other stock-based awards. We refer to these collectively herein as "Awards."

The following description of the 2025 Plan is not intended to be complete and is qualified in its entirety by reference to the complete text of the 2025 Plan, a copy of which is filed as an exhibit to this Annual Report. Please read the 2025 Plan in its entirety.

Administration

The 2025 Plan is administered by our Board or a committee thereof designated by our Board to administer the 2025 Plan, which we refer to herein as the "Administrator." The Administrator has broad authority, subject to the provisions of the 2025 Plan, to administer and interpret the 2025 Plan and Awards granted thereunder. All decisions and actions of the Administrator will be final.

Stock Subject to 2025 Plan

The form of 2025 Plan approved in December 2025 provided that the maximum number of shares of common stock that may be issued under the 2025 Plan will not exceed 1,500,000 shares (the "Share Pool"); however, the Share Pool will be increased on January 1 of each calendar year beginning in 2026 by a number of shares equal to 5% of the outstanding shares of common stock on the immediately preceding December 31 (or such lesser amount as approved by the Administrator). As such, the Share Pool was increased by 2,367,158 shares on January 1, 2026. The Share Pool is subject to certain adjustments in the event of a change in our capitalization and was adjusted to reflect the Reverse Stock Split. Following the Reverse Stock Split and taking into account the increase to the Share Pool on January 1, 2026, the Share Pool is 3,867,158 shares. Shares of common stock issued under the 2025 Plan may be either authorized and unissued shares or previously issued shares acquired by us. On termination or expiration of an Award under the 2025 Plan, in whole or in part, the number of shares of common stock subject to such Award but not issued thereunder or that are otherwise forfeited back to the Company will again become available for grant under the 2025 Plan. Additionally, shares retained or withheld in payment of any exercise price, purchase price, or tax withholding obligation of an Award will again become available for grant under the 2025 Plan.

Eligibility

Current or prospective employees, officers, non-employee directors, and other service providers of the Company and its affiliates will be eligible to participate in the 2025 Plan.

Types of Awards

Stock Options. Stock options granted under the 2025 Plan may be granted as incentive stock options or non-qualified stock options, in either case with a term not to exceed 10 years. Subject to the express provisions of the 2025 Plan, stock options generally may be exercised over such period, in installments or otherwise, as the Administrator may determine. The exercise price for any stock option granted may not generally be less than the fair market value of the common stock subject to that option on the grant date. The exercise price may be paid in cash or such other method as determined by the Administrator, including an irrevocable commitment by a broker to pay over such amount from a sale of the shares issuable under an option, the delivery of previously owned shares, or withholding of shares deliverable upon exercise.

Stock Appreciation Rights. SARs may be granted alone or in conjunction with all or part of a stock option. Upon exercising a SAR, the participant is entitled to receive the amount by which the fair market value of the common stock at the time of exercise exceeds the exercise price of the SAR. This amount is payable in common stock, cash, restricted stock, or a combination thereof, at the Administrator's discretion. The exercise price for any SARs may not generally be less than the fair market value of the common stock subject to the SAR on the grant date.

Restricted Stock and RSUs. Awards of restricted stock consist of shares of stock that are transferred to the participant subject to restrictions that may result in forfeiture if specified conditions are not satisfied. RSUs result in the transfer of shares of cash or stock to the participant only after specified conditions are satisfied. The Administrator will determine the restrictions and conditions applicable to each award of restricted stock or RSUs, which may include performance vesting conditions.

Incentive Bonuses. Each incentive bonus will confer upon the participant the opportunity to earn a future payment tied to the level of achievement with respect to one or more performance criteria established for a specified performance period. The Administrator will establish the performance criteria and level of achievement versus these criteria that will determine the threshold, target, and maximum amount payable under an incentive bonus, which criteria may be based on financial performance and/or personal performance evaluations. Payment of the amount due under an incentive bonus may be made in cash or shares, as determined by the Administrator.

Other Stock-Based Awards. Other stock-based awards are Awards denominated in or payable in, valued in whole or in part by reference to, or otherwise based on or related to, the value of stock.

Performance Criteria

The Administrator may specify certain performance criteria which must be satisfied before Awards will be granted or will vest. The performance goals may vary from participant to participant, group to group, and period to period.

Transferability

Awards generally may not be sold, transferred for value, pledged, assigned, or otherwise alienated or hypothecated by a participant other than by will or the laws of descent and distribution, and each stock option or SAR may be exercisable only by the participant during his or her lifetime.

Clawback

Awards will be subject to recoupment in accordance with any clawback policy that we adopt, including any clawback policy required under Rule 10D-1 of the Exchange Act.

Amendment and Termination

Our Board has the right to amend, alter, suspend, or terminate the 2025 Plan at any time, provided certain enumerated material amendments may not be made without stockholder approval. No amendment or alteration to the 2025 Plan or an Award or Award agreement will be made that would materially impair the rights of the holder, without such holder's consent; however, no consent will be required if the Administrator determines in its sole discretion and prior to the date of any change in control that such amendment or alteration either is required or advisable in order for us, the 2025 Plan, or such Award to satisfy any law or regulation or to meet the requirements of or avoid adverse financial accounting consequences under any accounting standard, or is not reasonably likely to significantly diminish the benefits provided under such Award, or that any such diminishment has been adequately compensated. The 2025 Plan was adopted by our Board and approved by our stockholders in December 2025 and will automatically terminate as to the grant of future awards, unless earlier terminated by our Board, on December 23, 2035.

DIRECTOR COMPENSATION

2025 Director Compensation

During 2025, no members of our Board received compensation paid for their service as members of our Board; however, members of our Board who also served as executive officers during 2025 received compensation in the form of RSUs for their service as executive officers of the Company. Accordingly, on September 1, 2025, Mr. O was granted 700,000 RSUs and Dr. Ronald B. Moss, our former Chief Medical Officer, was granted 400,000 RSUs (in each case, which amounts do not give effect to the Reverse Stock Split), subject to the same terms and conditions as the RSUs granted to our NEOs, as described above under "*Executive Compensation — Narrative Disclosure to Summary Compensation Table — Long-Term Incentive Compensation*."

The following table provides information regarding all compensation awarded to, earned by or paid to each of our directors other than Messrs. Yang and Landis for the fiscal year ended December 31, 2025. The compensation of Messrs. Yang and Landis are described above under "*Executive Compensation*."

Name	Stock Awards ($)[1]	Total ($)
Ronald B. Moss	$ 176,000	$ 176,000
Andrew O	$ 308,000	$ 308,000

(1) Amounts reported in this column represent the aggregate grant date fair value of RSUs granted to our directors, as computed in accordance with FASB ASC Topic 718 based on the fair market value of our common stock on the applicable date of grant. As of December 31, 2025, Dr. Moss held no outstanding RSUs and Mr. O held 608,228 vested and 1,277,500 unvested RSUs, in each case, that are not deliverable unless and until we consummate a change in control within seven years of the grant date. These amounts do not give effect to the Reverse Stock Split.

Director Compensation Policy

Members of our Board who are not our employees or officers are eligible to receive compensation for their service on our Board in accordance with the director compensation policy approved by our Board, which became effective in connection with the Direct Listing. The director compensation policy provides for the following annual cash retainers:

Annual Cash Retainer	$	40,000
Audit Committee Retainers:		
Chair	$	15,000
Non-Chair Member	$	7,500
Compensation Committee Retainers:		
Chair	$	10,000
Non-Chair Member	$	5,000
Nominating and Corporate Governance Committee Retainers:		
Chair	$	8,000
Non-Chair Member	$	4,000

Each eligible director will also be eligible to receive grants of RSUs.

In addition, all non-employee directors are reimbursed their reasonable travel expenses incurred in attending board and committee meetings.

Compensation Committee Interlocks and Insider Participation

None of the members of our Compensation Committee has at any time been one of our officers or employees since our inception. None of our executive officers currently serves, or in the past fiscal year has served, as a member of the board of directors or compensation committee of any entity that has one or more executive officers serving on our Board or Compensation Committee.

Item 12. Security Ownership of Certain beneficial Owners and Management and Related Stockholder Matters

Security Ownership of Certain Beneficial Owners and Management

The following table sets forth certain information with respect to the beneficial ownership of our common stock as of February 1, 2026 for:

- each person or group of affiliated persons known by us to be the beneficial owner of more than 5% of our common stock;
- each of our directors and named executive officers; and
- all of our directors and named executive officers as a group.

We have based percentage of beneficial ownership for the following table on 47,343,297 shares of common stock outstanding as of February 1, 2026. In addition, in accordance with the rules of the SEC, beneficial ownership includes voting or investment power with respect to securities issuable within 60 days of February 1, 2026. As such, shares of common stock issuable pursuant to options, warrants and restricted stock units that may be exercised or settled within 60 days of February 1, 2026 are deemed to be outstanding for purposes of computing the percentage of the class beneficially owned by the person holding such securities but are not deemed to be outstanding for purposes of computing the percentage of the class beneficially owned by any other person.

Except as otherwise indicated in the footnotes to the table set forth below, all persons listed have sole voting power and investment power, except to the extent that authority is shared by spouses under applicable law, and record and beneficial ownership of their common stock. Unless otherwise indicated, the business address of each of the individuals and entities named below is c/o Polaryx Therapeutics, Inc., South Tower, 140 E Ridgewood Avenue, Suite 415, Paramus, New Jersey 07652.

Name of Beneficial Owner	Common Stock		Percentage of Total Voting Power
	Number	%	
Executive Officers and Directors			
G. Michael Landis, CPA	358	*	*
Lisa L. Bollinger, M.D.	358	*	*
Andrew O	376	*	*
Mitchel Berger, M.D.	—	—	—
Francis A. Braun III, CPA	—	—	—
Charles Ryan, J.D., Ph.D.	—	—	—
Alex Yang, J.D, LL.M.[1]	22,744,796	48.04%	48.04%
All executive officers and directors as a group (persons)	22,745,888	48.05%	48.05%
5% Stockholders			
Entities Affiliated with Mstone[1]	22,744,796	48.04%	48.04%
Rush University Medical Center[2]	3,807,236	8.04%	8.04%
Entities Affiliated with Gershon Koh[3]	5,527,102	11.68%	11.68%
Young Poong Pharmaceutical Co., Ltd.[4]	2,480,629	5.24%	5.24%

* Represents beneficial ownership of less than 1%.

(1) Consists of 22,452,954 shares held by Mstone Partners Healthcare Limited, 183,560 shares held by MBstone Biotech Flagship Limited ("MBstone") and 108,282 shares held by Mstone Pediaorphan Singapore I Pte. Limited ("Mstone Singapore"). The address of Mstone, MBstone and Mstone Singapore is 7/F, 80 Gloucester Road, Wanchai, Hong Kong. Alex Keun Mo Yang is the founder and Chief Executive Officer of Mstone, the Chief Executive Officer of MBstone and the Chief Executive Officer of Mstone Singapore. Mr. Yang has voting power over the securities held by Mstone, MBstone and Mstone Singapore. Mr. Yang disclaims beneficial ownership over any securities owned by Mstone, MBstone and Mstone Singapore, except to the extent of his pecuniary interest.

(2) Consists of 3,807,236 shares held by Rush University Medical Center. The address of Rush is 1653 West Congress Parkway, Chicago, IL, 60612. Alex Wiggins is the Chief Investment Officer of Rush and has dispositive power over the securities held by Rush. Mr. Wiggins disclaims beneficial ownership over any securities owned by Rush, except to the extent of his pecuniary interest.

(3) Consists of 1,500,000 shares held by Gernavia Capital Pte Ltd ("Gernavia"), 1,705,606 shares held by Gershon Koh, and 2,321,496 shares held by Proioxis Ventures Pte Ltd ("Proioxis"). The address of Gervania is 11 North Buona Vista Drive, Level 8, The Metropolis, Singapore 138589. The address of Gershon Koh is 11 Holland Link, #01-50, Singapore 275764. The address of Proioxis is Level 39, Marina Bay Financial Centre Tower 2, 10 Marina Blvd, Singapore 018983. Mr. Koh is the Chief Executive Officer of Gervania and Proioxis. Mr. Koh has voting power over the securities held by Gernavia and Proioxis. Mr. Koh disclaims beneficial ownership over any securities owned by Gernavia and Proioxis, except to the extent of his pecuniary interest.

(4) Consists of 2,480,629 shares held by Young Poong Pharmaceutical Co., Ltd. ("YPP"). The address of YPP is 333, Hambangmoe-ro, Namdong-gu, Incheon, Republic of Korea. Kim Jae Hoon is the owner and Chief Executive Officer of YPP and has dispositive power over the securities held by YPP. Mr. Kim disclaims beneficial ownership over any securities owned by YPP except to the extent of his pecuniary interest.

Securities Authorized for Issuance Under Equity Compensation Plans

The following table provides information as of December 31, 2025 with respect to the shares of our common stock that may be issued under our existing equity compensation plans.

Plan Category	Number of Securities to be Issued Upon Exercise of Outstanding Options, Warrants and Rights	Weighted average Exercise Price of Outstanding Options, Warrants and Rights[1]	Number of Securities Remaining Available for Future Issuance Under Equity Compensation Plans (Excluding Securities Reflected in the First Column)
Equity compensation plans approved by stockholders[2]	—	$ —	1,500,000
Equity compensation plans not approved by stockholders	—	—	—
Total	—	$ —	1,500,000

(1) The weighted-average exercise price does not take into account shares issuable upon vesting of any outstanding restricted stock units and restricted stock awards, which have no exercise price.

(2) Includes our 2025 Plan. Excludes 2,367,158 shares that were added to our 2025 Plan on January 1, 2026 pursuant to the evergreen provisions thereunder that provide for automatic annual increases on January 1 of each year during the term of the respective plan equal to 5% of our outstanding shares as of the preceding December 31 (or such lesser amount as approved by the plan administrator).

Item 13. Certain Relationships and Related Transactions, and Director Independence

The following is a summary of transactions or series of transactions since January 1, 2024, or any currently proposed transactions or series of transactions, to which we were, or will be, a party, in which:

- the amount involved exceeded, or will exceed, the lesser of $120,000 and 1% of our total assets; and
- any of our directors, executive officers, or to our knowledge, beneficial owners of 5% or more of our capital stock, or any member of the immediate family of, or entities affiliated with, any of the foregoing persons, had, or will have, a direct or indirect material interest.

Related Party Transactions

License Agreements

In April 2016, we entered into the 2016 Rush License Agreement with Rush pursuant to which Rush granted us an exclusive license, with sublicensing rights, for the use of an invention/drug, made in the course of research at Rush, in the treatment of lysosomal storage diseases. Under the 2016 Rush License Agreement, we are responsible for obtaining and maintaining all regulatory approvals for the drug, as well as for all clinical trials and commercialization activities relating to the drug. As part of the License Agreement, we issued 882,353 shares in April 2016 as a partial consideration for all the rights and licenses granted to us as specified in the License Agreement. Upon execution of the agreement, we paid a license upfront fee of $70 thousand. In May 2020, we paid a milestone-based payments of $50 thousand upon completion of the IND filing. An additional milestone-based payment of $100 thousand will be due upon FDA approval of the product. Further, we must pay Rush royalties for the life of the patent of 3.5% on net sales.

In January 2025, we issued 277,823 shares of common stock to Rush in return for an exclusive gene therapy patent license (see Gene Therapy Patent License below).

Master Services Agreement with Rush University Medical Center

In June 2016, the Company entered into a Master Services Agreement with Rush (the "Rush MSA"), pursuant to which Rush provides services regarding the development and regulatory approval process for products currently under development by us, under statements of work for such services agreed to by the parties from time to time.

In April 2025, the Company paid $109 thousand under two statements of work pursuant to the Rush MSA. Total expenses incurred for the years ended December 31, 2025 and 2024 were $133 thousand and zero, respectively, which is recorded in research and development in the statement of operations and comprehensive loss. As of December 31, 2025 and 2024, there was $23 thousand and zero due to Rush, respectively, which is recorded in accrued expenses — related party in the balance sheet.

Mstone Partners Healthcare Limited

We are party to a number of agreements with Mstone. Mr. Alex Yang is the Chairman of our Board and our Chief Executive Officer and also the Chief Executive Officer of Mstone, which is a beneficial owner of 5% or more of our capital stock. Mr. Yang and the Company were party to a consulting agreement effective June 1, 2021, pursuant to which Mr. Yang provided consulting services. The consulting agreement was terminated effective on June 30, 2023. During the year ended December 31, 2022, the Company paid Mr. Yang an advance for services to be performed in 2023 of $75 thousand. As of December 31, 2024 and 2023, the Company did not have amounts due to Mr. Yang under the consulting agreement. Mr. Yang is also the controlling stockholder of MBstone. During the year ended December 31, 2022, we issued 35,758 shares of preferred stock at an aggregate price of $607 thousand to MBstone. In June 2024, all preferred stock was converted to common stock at a conversion ratio of one-to-one.

In November 2021, we entered into the Services Agreement ("Service Agreement") with Mstone, pursuant to which Mstone provides certain support and business development-related services to us. During the year ended December 31, 2025 and 2024, Mstone provided consulting services to the Company pursuant to the terms of the Service Agreement and the total expenses incurred for the years ended December 31, 2025 and 2024 were $1.6 million and $1.2 million, respectively. Consulting fees paid to Mstone for the years ended December 31, 2025 and 2024 were $1.6 million and $1.4 million, respectively. As of December 31, 2025 and 2024, there was $91 thousand and $130 thousand due to Mstone, respectively, which is recorded in due to related party in the balance sheet.

In May 2023, we entered into a Letter Agreement with Mstone (the "Letter Agreement"), pursuant to which we agreed to issue 1,250,000 shares of common stock with an aggregate grant fair value of $5.6 million to Mstone as compensation for advisory services. The shares were fully vested upon issuance and were issued in exchange for a 50% fee reduction for one year of advisory services to be provided from June 2023 through June 2024.

In February 2024, we issued 22,172,461 shares of common stock to certain existing stockholders to enable them to be substantially aligned with the implied value of the Company as of that date as determined by the Board, of which Mstone received 15,819,504 shares.

In December 2024, we issued 1,705,606 shares of our common stock at a purchase price per share of $1.17 to Proioxis Ventures Pte Ltd, which is a beneficial owner of 5% or more of our capital stock, for an aggregate consideration of $2.0 million in cash.

In March 2026, we amended the Service Agreement with Mstone to be a fixed amount of $90 thousand per month beginning January 1, 2026.

Related Party Financing Arrangements

Mstone has a direct controlling ownership interest in Forest Hills. Mr. Alex Yang, our Chief Executive Officer, is also the Chief Executive Officer of Forest Hills. In November 2023, we entered into a loan agreement with Forest Hills for $200 thousand with an interest rate of 5% per annum. The loan matured on November 1, 2024. In February 2024, we received an additional $65 thousand under the loan with Forest Hills. The total loan balance of $193 thousand was fully repaid on May 22, 2024.

Gene Therapy Patent License

In January 2025, we issued an aggregate of 3,704,307 shares of common stock to Rush and Mstone in return for an exclusive gene therapy patent license. Of the total share issuance, 277,823 shares were issued to Rush and 3,426,484 shares were issued to Mstone.

Indemnification Agreements

In connection with the Direct Listing, we agreed to enter into agreements to indemnify our directors and executive officers. These agreements require us to, among other things, indemnify these individuals for certain expenses (including attorneys' fees), judgments, fines and settlement amounts reasonably incurred by such person in any action or proceeding, including any action by or in our right, on account of any services undertaken by such person on behalf of our company or that person's status as a director or officer or otherwise, as applicable, to the maximum extent allowed under the NRS.

Related Party Transaction Policy

We have adopted a related party transaction policy that sets forth our procedures for the identification, review, consideration and approval or ratification of related person transactions. For purposes of our policy only, a related person transaction is a transaction, arrangement or relationship, or any series of similar transactions, arrangements or relationships, in which we and any related person are, were or will be participants in which the amount involved exceeds $100,000. A related person is any executive officer, director or beneficial owner of more than 5% of any class of our voting securities, including any of their immediate family members and any entity owned or controlled by such persons. Transactions involving compensation for services provided to us as an employee or director, among other limited exceptions, are deemed to have standing pre-approval by the Audit Committee but may be specifically reviewed if appropriate in light of the facts and circumstances.

Under the policy, if a transaction has been identified as a related party transaction, including any transaction that was not a related party transaction when originally consummated or any transaction that was not initially identified as a related party transaction prior to consummation, our management must present information regarding the related party transaction to our Audit Committee for review, consideration and approval or ratification. The presentation must include a description of, among other matters, the material facts, the interests, direct and indirect, of the related persons, the benefits to us of the transaction and whether the transaction is on terms that are comparable to the terms available to or from, as the case may be, an unrelated third party or to or from employees generally. Under the policy, we will collect information that we deem reasonably necessary from each director, executive officer and, to the extent feasible, significant stockholder to enable us to identify any existing or potential related party transactions and to effectuate the terms of the policy. In addition, under our Code of Business Conduct and Ethics, our employees and directors have an affirmative responsibility to disclose any transaction or relationship that reasonably could be expected to give rise to a conflict of interest. In considering related party transactions, our Audit Committee will take into account the relevant available facts and circumstances including, but not limited to:

- the risks, costs and benefits to us;
- the impact on a director's independence in the event that the related person is a director, immediate family member of a director or an entity with which a director is affiliated;
- the availability of other sources for comparable services or products; and
- the terms available to or from, as the case may be, unrelated third parties or to or from employees generally.

The policy requires that, in determining whether to approve, ratify or reject a related party transaction, our Audit Committee must consider, in light of known circumstances, whether the transaction is in, or is not inconsistent with, our best interests and those of our stockholders, as our Audit Committee determines in the good faith exercise of its discretion.

The transactions described above were consummated prior to our adoption of the formal, written policy described above, and, accordingly, the foregoing policies and procedures were not followed with respect to these transactions.

Director Independence

Our Board has reviewed the independence of all directors in light of each director's (or any family member's, if applicable) affiliations with the Company and members of management, as well as significant holdings of our securities. The Board used the definition of independence from Nasdaq listing standards to assess independence of our directors.

Nasdaq rules have objective tests and a subjective test for determining who is an "independent director." The subjective test states that an independent director must be a person who lacks a relationship that, in the opinion of the Board, would interfere with the exercise of independent judgment in carrying out the responsibilities of a director. The Board did not establish categorical standards or guidelines to make these subjective determinations, but considered all relevant facts and circumstances. Subject to specified exceptions, each member of a listed company's audit, compensation and nominating committees must be independent, and audit and compensation committee members must satisfy additional independence criteria. After considering the foregoing factors, our Board determined that Mitchel Berger, M.D., Francis A. Braun III, CPA and Charles Ryan, J.D., Ph.D. qualify as "independent directors" as defined by Nasdaq rules. G. Michael Landis, CPA and Alex Yang, J.D., LL.M. are not deemed to be independent under Nasdaq rules by virtue of their respective roles as Chief Financial Officer and Chief Executive Officer of the Company.

Item 14. Principal Accountant Fees and Services

Grant Thornton LLP ("Grant Thornton") has served as our independent auditor since 2024. The following table summarizes the audit fees billed and expected to be billed by Grant Thornton for the indicated fiscal years and the fees billed by Grant Thornton for all other services rendered during the indicated fiscal years.

	Year Ended December 31,	
	2025	2024
Audit Fees[1]	$ 459,290	$ 126,087
Audit-Related Fees[2]	—	—
Tax Fees[3]	—	—
All Other Fees[4]	—	—
Total Fees	$ 459,290	$ 126,087

(1) Consists of aggregate fees for professional services provided in connection with the annual audit of our consolidated financial statements, the review of our quarterly condensed consolidated financial statements and comfort letters, consents and review of documents filed with the SEC.
(2) Consists of fees for assurance and related services associated with consultations on matters directly related to the audit.
(3) Consists of fees for tax compliance, advice and tax services.
(4) Consists of fees for all other services.

Pre-Approval Policies and Procedures

Our Audit Committee has adopted procedures requiring the pre-approval of all audit and non-audit services performed by our independent auditor in order to assure that these services do not impair the auditor's independence. These procedures generally approve the performance of specific services subject to a cost limit for all such services. This general approval is reviewed, and if necessary modified, at least annually. Management must obtain the specific prior approval of the committee for each engagement of our auditor to perform other audit-related or non-audit services. The committee does not delegate its responsibility to pre-approve services performed by our auditor to any member of management. The committee has delegated authority to the committee chair to pre-approve audit and non-audit services to be provided to us by our auditor provided that the fees for such services do not exceed $100,000. Any pre-approval of services by the committee chair pursuant to this delegated authority must be reported to the committee at its next regularly scheduled meeting.

PART IV

Item 15. Exhibits

1. *Financial Statements*: For a list of the financial statements included herein, see the Index to the Financial Statements of this Annual Report, which is incorporated into this Item by reference.

2. *Financial Statement Schedules:* Financial statement schedules have been omitted because they are either not required or not applicable or the information is included in the consolidated financial statements or the notes thereto.

Exhibit No.	Description
3.1	Amended and Restated Articles of Incorporation of the registrant (filed with the SEC as Exhibit 3.3 to the Company's Form S-1/A filed on January 14, 2026)
3.2	Amended and Restated Bylaws of the registrant (filed with the SEC as Exhibit 3.4 to the Company's Form S-1/A filed on January 14, 2026)
4.1	Reference is made to Exhibits 3.1 and 3.2
4.2*	Description of the Company's Securities
10.1	Polaryx Therapeutics, Inc. 2022 Equity Incentive Plan (filed with the SEC as Exhibit 10.1 to the Company's Form S-1 filed on November 21, 2025)
10.2	Form of Grant Notice for Restricted Stock Unit Award and Standard Terms and Conditions for Restricted Stock Units under the Polaryx Therapeutics, Inc. 2022 Equity Incentive Plan (filed with the SEC as Exhibit 10.2 to the Company's Form S-1 filed on November 21, 2025)
10.3	Offer Letter by and between Polaryx Therapeutics, Inc. and G. Michael Landis (filed with the SEC as Exhibit 10.3 to the Company's Form S-1 filed on November 21, 2025)
10.4	Offer Letter by and between Polaryx Therapeutics, Inc. and Lisa L. Bollinger (filed with the SEC as Exhibit 10.4 to the Company's Form S-1 filed on November 21, 2025)
10.5#	Form of Polaryx Therapeutics, Inc. 2025 Equity Incentive Plan (filed with the SEC as Exhibit 10.5 to the Company's Form S-1 filed on November 21, 2025)
10.6	License Agreement, dated April 6, 2016, between Rush University Medical Center and Polaryx Therapeutics, Inc. (filed with the SEC as Exhibit 10.6 to the Company's Form S-1 filed on November 21, 2025)
10.7	License Agreement, dated May 26, 2022, between Rush University Medical Center and Somaryx Therapeutics Limited (filed with the SEC as Exhibit 10.7 to the Company's Form S-1 filed on November 21, 2025)
10.8	Novation Agreement, dated January 9, 2025, between Rush University Medical Center, Somaryx Therapeutics Limited and Polaryx Therapeutics, Inc. (filed with the SEC as Exhibit 10.8 to the Company's Form S-1 filed on November 21, 2025)
10.9	Master Services Agreement, dated June 24, 2016, between Rush University Medical Center and Polaryx Therapeutics, Inc. (filed with the SEC as Exhibit 10.9 to the Company's Form S-1 filed on November 21, 2025)
10.10	Consultancy Agreement, dated November 30, 2021, between Mstone Partners Healthcare Limited and Polaryx Therapeutics, Inc. (filed with the SEC as Exhibit 10.10 to the Company's Form S-1 filed on November 21, 2025)
10.11	Addendum to Consultancy Agreement, dated June 1, 2023, by and between Mstone Partners Healthcare Limited and Polaryx Therapeutics, Inc. (filed with the SEC as Exhibit 10.11 to the Company's Form S-1 filed on November 21, 2025)
10.12	Letter Agreement, dated May 31, 2023, by and between Mstone Partners Healthcare Limited and Polaryx Therapeutics, Inc. (filed with the SEC as Exhibit 10.12 to the Company's Form S-1 filed on November 21, 2025)
10.13*	Addendum #2 to Consultancy Agreement, dated March 23, 2026, by and between Mstone Partners Healthcare Limited and Polaryx Therapeutics, Inc.
10.14#	Form of Indemnification Agreement (filed with the SEC as Exhibit 10.13 to the Company's Form S-1 filed on January 27, 2025)
19.1*	Insider Trading Policy
24.1*	Power of Attorney

Exhibit No.	Description
31.1*	Certification of the principal executive officer pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934
31.2*	Certification of the principal financial officer pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934
32.1(1)	Certification of the principal executive officer and principal financial officer pursuant to 18 U.S.C. Section 1350 and Rule 13a-14(b) under the Securities Exchange Act of 1934
97.1*	Incentive Compensation Clawback Policy
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
101.LAB*	Inline XBRL Taxonomy Extension Label Linkbase Document
101.PRE*	Inline XBRL Taxonomy Extension Presentation Linkbase Document
104*	Cover Page Interactive Data File (embedded within the Inline XBRL document)

* Filed herewith.

\# Indicates management contract or compensatory plan or arrangement.

(1) Furnished herewith and not to be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the Exchange Act) or otherwise subject to the liability of such section, and not to be deemed incorporated by reference into any filing under the Securities Act of 1933, as amended, or the Exchange Act.

Item 16. Form 10-K Summary.

None.

SIGNATURES

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

Polaryx Therapeutics, Inc.

Date: March 23, 2026

By: /s/ Alex Yang
Alex Yang
Chief Executive Officer
(Principal Executive Officer)

Date: March 23, 2026

By: /s/ G. Michael Landis
G. Michael Landis
Chief Financial Officer
(Principal Financial and Accounting Officer)

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Alex Yang and G. Michael Landis, and each of them, as his true and lawful attorneys-in-fact and agents, with full power of substitution and resubstitution for him and in his name, place, and stead, in any and all capacities, to sign any and all amendments to this Annual Report on Form 10-K, and to file the same, with exhibits thereto and other documents in connection therewith, with the SEC, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done therewith, as fully to all intents and purposes as he or she might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents, and any of them or their substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

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

Signature	Title	Date
/s/ Alex Yang Alex Yang	Chief Executive Officer, Director (*Principal Executive Officer*)	March 23, 2026
/s/ G. Michael Landis G. Michael Landis	Chief Financial Officer, Director (*Principal Financial and Accounting Officer*)	March 23, 2026
/s/ Mitchel Berger Mitchel Berger	Director	March 23, 2026
/s/ Francis A. Braun III Francis A. Braun III	Director	March 23, 2026
/s/ Charles Ryan Charles Ryan	Director	March 23, 2026