Prothena Corporation plc

Directors' Report and Consolidated Financial Statements

For the Year Ended 31 December 2024

Registered number: 518146

Prothena Corporation plc

Directors’ Report and Financial Statements

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Prothena Corporation plc

Directors' Report

For the year ended 31 December 2024

The directors present their annual report and audited financial statements for Prothena Corporation plc ("Prothena" or "the Company") and its subsidiary undertakings (collectively "the group") for the year ended December 31, 2024. The consolidated financial statements can be found from pages 62 to 96.

The directors have elected to prepare the Consolidated Financial Statements in accordance with Section 279 of the Companies Act 2014, which provides that a true and fair view of the assets and liabilities, financial position and profit or loss of a company and its subsidiary undertakings may be given by preparing its group financial statements in accordance with U.S. accounting standards ("US GAAP"), as defined by Section 279(1) of the Companies Act 2014, to the extent that the use of those standards in the preparation of the financial statements does not contravene any provision of Part 6 of the Companies Act 2014.

PRINCIPAL ACTIVITIES

Prothena Corporation plc ("Prothena" or the "Company") is a late-stage clinical biotechnology company with expertise in protein dysregulation and a pipeline of investigational therapeutics with the potential to change the course of devastating neurodegenerative and rare peripheral amyloid diseases.

Fueled by our deep scientific expertise built over decades of research, we are advancing a pipeline of therapeutic candidates for a number of indications and novel targets for which our ability to integrate scientific insights around neurological dysfunction and the biology of misfolded proteins can be leveraged. Our wholly-owned programs include birtamimab for the potential treatment of AL amyloidosis, and a portfolio of programs for the potential treatment of Alzheimer's disease including PRX012, which targets amyloid beta (Aβ), and PRX123, a novel dual Aβ-tau vaccine. Our partnered programs include prasinezumab for the potential treatment of Parkinson's disease and other related synucleinopathies that targets alpha-synuclein in collaboration with Roche. In addition, we have partnered BMS-986446 (formerly PRX005) for the potential treatment of Alzheimer's disease that targets tau and PRX019 for the potential treatment of neurodegenerative diseases with an undisclosed target in two separate license agreements with Bristol Myers Squibb (BMS). We are also entitled to certain potential milestone payments pursuant to our share purchase agreement with Novo Nordisk pertaining to our ATTR amyloidosis business (inclusive of coramitug, formerly PRX004).

We were formed on September 26, 2012, under the laws of Ireland and re-registered as an Irish public limited company on October 25, 2012. Our ordinary shares began trading on The Nasdaq Global Market under the symbol "PRTA" on December 21, 2012, and currently trade on The Nasdaq Global Select Market.

BASIS OF PREPARATION

The accompanying consolidated financial statements include the accounts of Prothena Corporation plc and our subsidiary undertakings.

PRINCIPAL RISKS AND UNCERTAINTIES

You should carefully consider the risks described below, together with all of the other information included in this Directors' Report in considering our business and prospects. Set forth below and elsewhere in this report and in other documents we file with the U.S. Securities and Exchange Commission (the "SEC") are descriptions of certain risks, uncertainties, and other factors that could cause our actual results to differ materially from those anticipated. If any of the following risks, other unknown risks, or risks that we think are immaterial occur, our business, financial condition, results of operations, cash flows, or growth prospects could be adversely impacted, in which case, the market price of our ordinary shares could decline, and you may lose all or part of your investment in our ordinary shares. Additional risks and uncertainties not presently known to us or that we currently deem immaterial also may impair our business operations.

Risks Relating to Our Financial Position, Our Need for Additional Capital, and Our Business

We anticipate that we will incur losses for the foreseeable future and we may never sustain profitability.

We may not generate the cash that is necessary to finance our operations in the foreseeable future. We incurred net losses of $122.3 million, $147.0 million and $116.9 million for the years ended December 31, 2024, 2023, and 2022, respectively. As of December 31, 2024, we had an accumulated deficit of $1.1 billion. We expect to continue to incur substantial losses for the foreseeable future as we:

- support the Phase 3 AFFIRM-AL clinical trial for birtamimab, the Phase 1 clinical trials for PRX012, the Phase 1 clinical trial for PRX019, and potential additional clinical trials for these and other programs, including PRX123;
- develop and possibly commercialize our drug candidates, including birtamimab, PRX012, and PRX123;
- undertake nonclinical development of other drug candidates and initiate clinical trials, if supported by nonclinical data;
- pursue our early stage research and seek to identify additional drug candidates; and
- potentially acquire rights from third parties to drug candidates or technologies through licenses, acquisitions, or other means.

We must generate significant revenue to achieve and maintain profitability. Even if we succeed in discovering, developing, and commercializing one or more drug candidates, we may not be able to generate sufficient revenue and we may never be able to achieve or sustain profitability.

We will require additional capital to fund our operations, and if we are unable to obtain such capital, we will be unable to successfully develop and commercialize drug candidates.

As of December 31, 2024, we had cash and cash equivalents of $471.4 million. The majority of such cash is held in accounts at U.S. banking institutions that we believe are of high quality. Cash held in depository accounts may exceed the $250,000 Federal Deposit Insurance Corporation 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. Although we believe, based on our current business plans, that our existing cash and cash equivalents will be sufficient to meet our obligations for at least the next twelve months, we anticipate that we will require additional capital in order to continue the research and development, and eventual commercialization, of our drug candidates. Our future capital requirements will depend on many factors that are currently unknown to us, including, without limitation:

- the timing of progress, results, and costs of our clinical trials, including the Phase 3 clinical trial for birtamimab, the Phase 2 clinical trial for prasinezumab being conducted by Roche, the Phase 2b clinical trial for prasinezumab being conducted by Roche, the Phase 2 clinical trial for coramitug (formerly PRX004) being conducted by Novo Nordisk, the Phase 2 clinical trial for BMS-986446 being conducted by BMS, the Phase 1 clinical trials for PRX012, and the Phase 1 clinical trial for PRX019;
- the timing, initiation, progress, results, and costs of these and our other research, development, and possible commercialization activities;
- the results of our research, nonclinical studies, and clinical trials;
- the costs of manufacturing our drug candidates for clinical development as well as for future commercialization needs;
- if and when appropriate, the costs of preparing for commercialization of our drug candidates;
- the costs of preparing, filing, and prosecuting patent applications, and maintaining, enforcing, and defending intellectual property-related claims;

- our ability to establish strategic collaborations, licensing, or other arrangements;
- the timing, receipt, and amount of any capital investments, cost-sharing contributions or reimbursements, milestone payments, or royalties that we might receive under current or potential future collaborations;
- the costs to satisfy our obligations under current and potential future collaborations; and
- the timing, receipt, and amount of revenues or royalties, if any, from any approved drug candidates.

We have based our expectations relating to liquidity and capital resources on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. Because of the numerous risks and uncertainties associated with the development and commercialization of our drug candidates, we are unable to estimate the amounts of increased capital outlays and operating expenses associated with completing the development and commercialization of our current drug candidates.

In the pharmaceutical industry, the research and development process is lengthy and involves a high degree of risk and uncertainty. This process is conducted in various stages and, during each stage, there is substantial risk that drug candidates in our research and development pipeline will experience difficulties, delays or failures. This makes it difficult to estimate the total costs to complete our clinical trials and to estimate anticipated completion dates with any degree of accuracy, which raises concerns that attempts to quantify costs and provide estimates of timing may be misleading by implying a greater degree of certainty than actually exists.

In order to develop and obtain regulatory approval for our drug candidates we will need to raise substantial additional funds. We expect to raise any such additional funds through public or private equity or debt financings, collaborative agreements with corporate partners, or other arrangements. Our ability to raise additional capital, including our ability to secure new collaborations, may also be adversely impacted by global economic conditions, including any disruptions to, and volatility in, the credit and financial markets in the United States and worldwide, geopolitical turmoil, and the ongoing conflict in Israel and any potential escalation or geographic expansion of such conflict, which could heighten other risks identified in this report. We cannot assure that additional funds will be available when we need them on terms that are acceptable to us or at all. If we raise additional funds by issuing equity securities, including pursuant to our Amended Distribution Agreement (as may be further amended from time to time, and as discussed below), substantial dilution to existing shareholders would result. If we raise additional funds by incurring debt financing, the terms of the debt may involve significant cash payment obligations as well as covenants and specific financial ratios that may restrict our ability to operate our business. We may be required to relinquish rights to our technologies or drug candidates or grant licenses on terms that are not favorable to us in order to raise additional funds through strategic alliances, joint ventures, or licensing arrangements.

If adequate funds are not available on a timely basis, we may be required to:

- terminate or delay clinical trials or other development activities for one or more of our drug candidates;
- delay arrangements for activities that may be necessary to commercialize our drug candidates;
- curtail or eliminate our drug research and development programs that are designed to identify new drug candidates; or
- cease operations.

In addition, if we do not meet our payment obligations to third parties as they come due, we may be subject to litigation claims. Even if we are successful in defending against these claims, litigation could result in substantial costs and distract management and may have unfavorable results that could further adversely impact our financial condition.

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

We are highly dependent on key personnel, including Dr. Gene G. Kinney, our President and Chief Executive Officer. There can be no assurance that we will be able to retain Dr. Kinney or any of our key personnel. The loss of the services of Dr. Kinney or any other person on whom we are highly dependent might impede the achievement of our research, development, and commercial objectives. We do not carry "key person" insurance covering any members of our senior management.

Attracting and retaining qualified scientific and other personnel are critical to our growth and future success. Competition for qualified personnel in our industry is intense. We may not be able to attract and retain these personnel on acceptable terms given that competition. Additionally, we may not be able to integrate and motivate qualified personnel to enable them to succeed in their positions. Failure to attract, integrate, retain, and motivate qualified personnel could have a material adverse effect on our business, financial condition, results of operations, and/or growth prospects.

Our collaborators, prospective collaborators, and suppliers may need assurances that our financial resources and stability on a stand-alone basis are sufficient to satisfy their requirements for doing or continuing to do business with us.

Some of our collaborators, prospective collaborators, and suppliers may need assurances that our financial resources and stability on a stand-alone basis are sufficient to satisfy their requirements for doing or continuing to do business with us. If our collaborators, prospective collaborators or suppliers are not satisfied with our financial resources and stability, it could have a material adverse effect on our ability to develop our drug candidates, enter into licenses or other agreements and on our business, financial condition or results of operations.

The agreements we entered into with Elan involve conflicts of interest and therefore may have materially disadvantageous terms to us.

We entered into certain agreements with Elan in connection with our separation from Elan, which set forth the main terms of the separation and provided a framework for our initial relationship with Elan. These agreements may have terms that are materially disadvantageous to us or are otherwise not as favorable as those that might be negotiated between unaffiliated third parties. In December 2013, Elan was acquired by Perrigo Company plc ("Perrigo"), and in February 2014 Perrigo caused Elan to sell all of its shares of Prothena in an underwritten offering. As a result of the acquisition of Elan by Perrigo and the subsequent sale of all of its shares of Prothena, Perrigo may be less willing to collaborate with us in connection with the agreements to which we and Elan are a party and other matters.

We have been, and may in the future be, adversely affected by business disruptions beyond our control, including outbreaks of epidemic, pandemic, or contagious disease, geopolitical turmoil, earthquakes or other natural disasters, and adverse weather events, including as a result of climate change.

The operational and financial impact of a business disruption beyond our control, such as a public health crisis, geopolitical turmoil, or an adverse weather event has, and could, adversely affect our business in the following ways:

- As we have seen with the outbreak of the COVID-19 pandemic, outbreaks of epidemic, pandemic, or contagious disease or other public health emergencies have historically and may in the future disrupt our operations, including clinical trials, research and nonclinical studies, the manufacture or shipment of both drug substance and finished drug product for drug candidates for preclinical testing and clinical trials, and access to stable credit and financial markets in the United States and worldwide. For example, the Phase 3 clinical trial for birtamimab and the Phase 2 clinical trial for prasinezumab conducted by Roche were disrupted by the COVID-19 pandemic as a result of (i) the inability or unwillingness of study participants, site investigators or other study personnel to travel to clinical trial sites or otherwise follow study protocols and (ii) the diversion of healthcare resources away from the conduct of clinical trials.

- Geographic regions where we operate may be affected by war, terrorism, or political instability, and our operations may be vulnerable to disruption, including disturbances to the credit and financial markets (in such region or worldwide), or to services generally, including healthcare services. For example, the Phase 3 clinical trial for birtamimab has clinical trial sites located globally, including in Israel and Eastern Europe, and operations at such clinical trial sites may be disrupted by ongoing conflicts and/or new conflicts, which could result in (i) the inability or

unwillingness of study participants, site investigators or other study personnel to travel to such clinical trial sites or otherwise follow study protocols, (ii) the diversion of healthcare resources away from the conduct of clinical trials, or (iii) the complete or partial cessation of operations at such clinical trial sites.

- Our key research facility and a significant portion of our operations are in the San Francisco Bay Area of Northern California, which in the past has experienced severe earthquakes. If an earthquake, other natural disaster, or similar event were to occur and prevent us from using all or a significant portion of those operations or local critical infrastructure, or that otherwise disrupts our operations, it could be difficult or impossible for us to continue our business for a substantial period of time. We have disaster recovery and business continuity plans, but they may prove to be inadequate in the event of a natural disaster or similar event. We may incur substantial expenses if our disaster recovery and business continuity plans prove to be inadequate. We do not carry earthquake insurance. Furthermore, third parties upon which we are materially dependent upon, including our clinical trial sites, may be vulnerable to natural disasters or similar events.

- Climate change could have an impact on longer-term natural weather trends. Extreme weather events that are linked to rising temperatures, changing global weather patterns, sea, land and air temperatures, as well as sea levels, rain and snow could result in increased occurrence and severity of adverse weather events.

Any one or more of these force majeure events could have a material adverse effect on our liquidity, results of operations, financial condition or business, including the progress of, and timelines for, our nonclinical and clinical development programs, and may create safety challenges for our employees and safe occupancy of our job sites, financial market volatility and significant macroeconomic uncertainty in global markets. Furthermore, any governmental or business actions, or any actions taken by individuals in response to any such events (including mandatory quarantines, travel restrictions, delay in operations of the U.S. FDA and comparable foreign regulatory agency, and interruptions to healthcare services), may divert healthcare resources away from the conduct of clinical trials and development programs.

We may experience breaches or similar disruptions of our information technology systems or data.

Our business is increasingly dependent on critical, complex, and interdependent information technology systems to support business processes as well as internal and external communications. Despite the implementation of security measures, our internal computer systems, and those of our current and any future CROs and other contractors, consultants, and collaborators, have been subject to and remain vulnerable to damage from cyberattacks, "phishing" attacks, ransomware, computer viruses, unauthorized access, natural disasters, terrorism, war, and telecommunication or electrical failures. Attacks upon information technology systems are increasing in their frequency, levels of persistence, sophistication, and intensity, and are being conducted by sophisticated and organized groups and individuals with a wide range of motives and expertise. As a result of the COVID-19 pandemic, we may also face increased cybersecurity risks due to our reliance on internet technology and the number of our employees who are working remotely, which may create additional opportunities for cybercriminals to exploit vulnerabilities. Furthermore, because the techniques used to obtain unauthorized access to or to sabotage systems change frequently and often are not recognized until launched against a target, we may be unable to anticipate these techniques or implement adequate preventative measures. We may also experience security breaches that may remain undetected for an extended period. Any breakdown, malicious intrusion, or computer virus could result in the impairment of key business processes or breach of data security, which could result in a material disruption of our development programs and cause interruptions in our business operations, whether due to a loss of our trade secrets or other intellectual property or lead to unauthorized disclosure of personal data of our employees, third parties with which we do business, clinical trial participants, or others. For example, the loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. In addition, such a breach may require notification to governmental agencies, the media, or individuals pursuant to applicable data privacy and security law and regulations. Such an event could have an adverse effect on our business, financial condition, or results of operations.

Changes in and failures to comply with U.S. and foreign privacy and data protection laws, regulations, and standards may adversely affect our business, operations, and financial performance.

We and our partners are subject to certain federal, state, and foreign data privacy and security laws and regulations. The legislative and regulatory landscape for privacy and data protection continues to evolve, and there has been an increasing focus

on privacy and data protection issues, which may affect our business and may increase our compliance costs and exposure to liability. In the United States, numerous federal and state laws and regulations, including state security breach notification laws, federal and state health information privacy laws (including U.S. Health Insurance Portability and Accountability Act of 1996 ("HIPAA"), as amended by the Health Information Technology for Economic and Clinical Health Act, and regulations promulgated thereunder), and federal and state consumer protection laws (including Section 5 of the Federal Trade Commission Act), govern the collection, use, disclosure, and protection of personal information. Each of these laws is subject to varying interpretations by courts and government agencies, creating complex compliance issues. State privacy laws in particular are evolving, with more than a dozen new state privacy laws passed in recent years, along with additional health privacy specific laws. These laws may further increase our compliance obligations, and potential legal privacy risks. For example, Washington recently passed the My Health My Data Act, which has a broader scope than HIPAA and includes a private right of action. In addition, we may obtain health information from third parties, including research institutions from which we obtain clinical trial data, that are subject to privacy and security requirements under HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, and the regulations promulgated thereunder. Depending on the facts and circumstances, we could be subject to significant penalties if we obtain, use or disclose individually identifiable health information in a manner that is not authorized or permitted by HIPAA.

Compliance with these and any other applicable privacy and data security laws and regulations is a rigorous and time-intensive process, and we may be required to substantially amend existing procedures and policies or put in place additional procedures and policies to ensure compliance with privacy and data protection rules and requirements. These changes could adversely impact our business by increasing operational and compliance costs or impact business practices. Further, there is a risk that the amended policies and procedures will not be implemented correctly or that individuals within the business will not be fully compliant with the new procedures. If we fail to comply with any such laws or regulations, we may face significant litigation, government investigations, fines and penalties as well as reputational damage which could adversely affect our business, operations, financial condition and prospects. Furthermore, the laws are not consistent, and compliance in the event of a widespread data breach is costly. In addition, states are constantly adopting new laws or amending existing laws, requiring attention to frequently changing regulatory requirements. For example, the California Consumer Privacy Act (the "CCPA") went into effect January 1, 2020. The CCPA, among other things, imposes new data privacy obligations on covered companies and provides expanded privacy rights to California residents, including the right to access, delete, and opt out of certain disclosures of their information. The CCPA provides for civil penalties for violations, as well as a private right of action with statutory damages for certain data breaches, which may increase the frequency and likelihood of data breach litigation. Although the law includes limited exceptions for health-related information, including clinical trial data, such exceptions may not apply to all of our operations and processing activities. Further, the California Privacy Rights Act (the "CPRA") imposes additional data protection obligations on covered businesses, including additional consumer rights processes, limitations on data uses, audit requirements for higher risk data, and opt outs for certain uses of sensitive data. It also creates a California data protection agency authorized to issue substantive regulations and could result in increased privacy and information security enforcement. The majority of the provisions went into effect on January 1, 2023, and additional compliance investment and potential business process changes may be required. Although the CCPA currently exempts certain health-related information, including clinical trial data, the CCPA and the amendments under the CPRA may increase our compliance costs and potential liability.

Multiple states have followed California to legislate comprehensive privacy laws with data privacy rights. For example, Virginia passed the Virginia Consumer Data Protection Act, which went into effect on January 1, 2023, and affords consumers similar rights to the CCPA, along with additional rights, such as the right to opt-out of processing for profiling and targeted advertising purposes. Additionally, the Colorado Privacy Act and Connecticut Personal Data Privacy and Online Monitoring Act went into effect on July 1, 2023. While these new laws generally include exemptions for HIPAA-covered and clinical trial data, they impact the overall privacy landscape. Several other states have followed suit and passed similar legislation which will go into effect in the coming years. Further, additional privacy laws that are similar in nature have been proposed in other states and at the federal level and, if passed, such laws may have potentially conflicting requirements that would make compliance challenging.

We are also or may become subject to rapidly evolving data protection laws, rules, and regulations in foreign jurisdictions. For example, in the European Union ("EU"), the EU General Data Protection Regulation (the "EU GDPR") governs the collection of, and other processing activities involving, personal data (i.e., data which identifies an individual or from which an individual is identifiable), including clinical trial data, and grants individuals various data protection rights (e.g.,

the right to the erasure of personal data). The EU GDPR imposes a number of obligations on companies, including inter alia: (i) accountability and transparency requirements, and enhanced requirements for obtaining valid consent; (ii) obligation to consider data protection when any new products or services are developed, and to limit the amount of personal data processed; and (iii) obligations to implement appropriate technical and organizational measures to safeguard personal data and to report certain personal data breaches to: (x) the data protection supervisory authority without undue delay (and no later than 72 hours, where feasible) after becoming aware of the personal data breach, unless the personal data breach is unlikely to result in a risk to the data subjects' rights and freedoms; and (y) affected data subjects where the personal data breach is likely to result in a high risk to their rights and freedoms. In addition, the EU GDPR prohibits the transfer of personal data from the European Economic Area ("EEA") to jurisdictions that the European Commission does not recognize as having "adequate" data protection laws unless a data transfer mechanism has been put in place or a derogation under the EU GDPR can be relied on. In July 2020, the Court of Justice of the EU limited how organizations could lawfully transfer personal data from the EEA to the United States by invalidating the EU-US Privacy Shield Framework for purposes of international transfers and imposing further restrictions on the use of standard contractual clauses ("EU SCCs") including, a requirement for companies to carry out a transfer privacy impact assessment ("TIA"), which, among other things, assesses the laws governing access to personal data in the recipient country and considers whether supplementary measures that provide privacy protections additional to those provided under the EU SCCs will need to be implemented to ensure an "essentially equivalent" level of data protection to that afforded in the EEA. On July 31, 2023, the European Commission adopted its Final Implementing Decision granting the United States adequacy ("Adequacy Decision"), for EU-U.S. transfers of personal data for entities self-certified to the EU-U.S. Data Privacy Framework ("DPF"). Entities relying on EU SCCs for transfers to the United States are also able to rely on the analysis in the Adequacy Decision as support for their TIA regarding the equivalence of U.S. national security safeguards and redress. The EU GDPR imposes substantial fines for breaches and violations (up to the greater of €20 million or 4% of the noncompliant company's total annual global turnover). The EU GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with data protection supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the EU GDPR.

The EU GDPR has been implemented (as implemented, the "UK GDPR") in the United Kingdom ("UK"). The UK GDPR sits alongside the UK Data Protection Act 2018 which implements certain derogations in the EU GDPR into UK law. Under the UK GDPR, companies not established in the UK but which process personal data in relation to the offering of goods or services to individuals in the UK, or the monitoring of their behavior will be subject to the UK GDPR – the requirements of which are (at this time) largely aligned with those under the EU GDPR and as such, may lead to similar compliance and operational costs with potential fines up to the greater of £17.5 million or 4% of the noncompliant company's total annual global turnover. The UK GDPR also imposes similar restrictions on international transfers of personal data from the UK to jurisdictions that the UK Government does not consider "adequate". The UK's Information Commissioner's Office published: (i) its own form of EU SCCs, known as the International Data Transfer Agreement for transfers to outside the UK; (ii) a "UK addendum" to the new EU SCCs which amends the relevant provisions of such clauses to work in a UK context; and (iii) its own version of the TIA (although entities may choose to adopt either the EU or UK-style TIA). Further, on September 21, 2023, the UK Secretary of State for Science, Innovation and Technology established a UK-U.S. data bridge (i.e., a UK equivalent of the Adequacy Decision) and adopted UK regulations to implement the UK-U.S. data bridge ("UK Adequacy Regulations"). Personal data may now be transferred from the UK under the UK-U.S. data bridge through the UK extension to the DPF to organizations self-certified under the UK extension to the DPF. The above-described changes may lead to additional costs and increase our overall risk exposure.

Compliance with U.S. and foreign data privacy and security laws, rules, and regulations have required us, and may require us in the future, to take on more onerous obligations in our contracts, require us to engage in costly compliance exercises, restrict our ability to collect, use and disclose data, or in some cases, impact our or our partners' or suppliers' ability to operate in certain jurisdictions. Each of these constantly evolving laws can be subject to varying interpretations. If we fail to comply with any such laws, rules, or regulations, we may face government investigations and/or enforcement actions, fines, civil or criminal penalties, private litigation, or adverse publicity that could adversely affect our business, financial condition, and results of operations.

Risks Related to the Discovery, Development, and Regulatory Approval of Drug Candidates

Our success is largely dependent on the success of our research and development programs. Our drug candidates are in various stages of development and we may not be able to successfully discover, develop, obtain regulatory approval for, or commercialize any drug candidates.

The success of our business depends substantially upon our ability to discover, develop, obtain regulatory approval for and commercialize our drug candidates successfully. Our research and development programs are prone to the significant and likely risks of failure inherent in drug development, which can result from the failure of the drug candidate to be sufficiently effective, the safety profile of the drug candidate, a clinical trial that is not sufficiently enrolled or powered or adequately designed to detect a drug effect, or other reasons. We intend to continue to invest most of our time and financial resources in our research and development programs.

There is no assurance that the results of the Phase 3 clinical trial for birtamimab, the Phase 2 clinical trial for prasinezumab, the Phase 2b clinical trial for prasinezumab, the Phase 2 clinical trial for coramitug, the Phase 2 clinical trial for BMS-986446, the Phase 1 clinical trials for PRX012, and the Phase 1 clinical trial for PRX019 will support further development of these drug candidates. In addition, we currently do not, and may never, have any other drug candidates in clinical trials, and we have not identified drug candidates for many of our research programs.

Before obtaining regulatory approvals for the commercial sale of any drug candidate for a target indication, we must demonstrate with substantial evidence gathered in adequate and well-controlled clinical trials that the drug candidate is safe and effective for use for that target indication. In the U.S., this must be done to the satisfaction of the FDA; in the EU, this must be done to the satisfaction of the European Medicines Agency (the "EMA"); and in other countries this must be done to the satisfaction of comparable regulatory authorities.

Satisfaction of these and other regulatory requirements is costly, time consuming, uncertain, and subject to unanticipated delays. Despite our efforts, our drug candidates may not:

- offer improvement over existing treatment options;
- be proven safe and effective in clinical trials; or
- meet applicable regulatory standards.

Positive results in nonclinical studies of a drug candidate may not be predictive of similar results in humans during clinical trials, and promising results from early clinical trials of a drug candidate may not be replicated in later clinical trials. Interim results of a clinical trial do not necessarily predict final results. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials even after achieving promising results in early-stage development. Accordingly, the results from completed nonclinical studies and early clinical trials for our drug candidates may not be predictive of the results we may obtain in later stage studies or trials. Our nonclinical studies or clinical trials may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional nonclinical studies or clinical trials, or to discontinue clinical trials altogether.

Furthermore, we have not marketed, distributed, or sold any products. Our success will, in addition to the factors discussed above, depend on the successful commercialization of any drug candidates that obtain regulatory approval. Successful commercialization may require:

- obtaining and maintaining commercial manufacturing arrangements with third-party manufacturers;
- developing the marketing and sales capabilities, internal and/or in collaboration with pharmaceutical companies or contract sales organizations, to market and sell any approved drug; and
- acceptance of any approved drug in the medical community and by patients and third-party payers.

Many of these factors are beyond our control. We do not expect any of our drug candidates to be commercially available for several years and some or all may never become commercially available. Accordingly, we may never generate revenues through the sale of products.

We have entered into collaborations with Roche and BMS and may enter into additional collaborations in the future, and we might not realize the anticipated benefits of such collaborations.

Research, development, commercialization and/or strategic collaborations, including those that we have with Roche and BMS, are subject to numerous risks, which include the following:

- collaborators may have significant control or discretion in determining the efforts and resources that they will apply to a collaboration, and might not commit sufficient efforts and resources or might misapply those efforts and resources;
- we may have limited influence or control over the approaches to research, development, and/or commercialization of products candidates in the territories in which our collaboration partners lead research, development, and/or commercialization;
- collaborators might not pursue research, development, and/or commercialization of collaboration drug candidates or might elect not to continue or renew research, development, and/or commercialization programs based on nonclinical and/or clinical trial results, changes in their strategic focus due to the acquisition of competing products, availability of funding, or other factors, such as a business combination that diverts resources or creates competing priorities;
- collaborators might delay, provide insufficient resources to, or modify or stop research or clinical development for collaboration drug candidates or require a new formulation of a drug candidate for clinical testing;
- collaborators could develop or acquire products outside of the collaboration that compete directly or indirectly with our drug candidates or require a new formulation of a drug candidate for nonclinical and/or clinical testing;
- collaborators with sales, marketing, and distribution rights to one or more drug candidates might not commit sufficient resources to sales, marketing, and distribution or might otherwise fail to successfully commercialize those drug candidates;
- collaborators might not properly maintain or defend our intellectual property rights or might use our intellectual property improperly or in a way that jeopardizes our intellectual property or exposes us to potential liability;
- collaboration activities might result in the collaborator having intellectual property covering our activities or drug candidates, which could limit our rights or ability to research, develop, and/or commercialize our drug candidates;
- collaborators might not be in compliance with laws applicable to their activities under the collaboration, which could impact the collaboration or us;
- disputes might arise between us and a collaborator that could cause a delay or termination of the collaboration or result in costly litigation that diverts management attention and resources; and
- collaborations might be terminated, which could result in a need for additional capital to pursue further research, development, and/or commercialization of our drug candidates.

In addition, funding provided by a collaborator might not be sufficient to advance drug candidates under the collaboration.

If a collaborator terminates a collaboration or a program under a collaboration, including by failing to exercise a license or other option under the collaboration, whether because we fail to meet a milestone or otherwise, any potential revenue from the collaboration would be significantly reduced or eliminated. In addition, we will likely need to either secure other funding to advance research, development, and/or commercialization of the relevant drug candidate or abandon that program, the

development of the relevant drug candidate could be significantly delayed, and our cash expenditures could increase significantly if we are to continue research, development, and/or commercialization of the relevant drug candidates.

Any one or more of these risks, if realized, could reduce or eliminate future revenue from drug candidates under our collaborations, and could have a material adverse effect on our business, financial condition, results of operations, and/or growth prospects.

If clinical trials of our drug candidates are prolonged, delayed, suspended, or terminated, we may be unable to commercialize our drug candidates on a timely basis, if at all, which would require us to incur additional costs and delay or prevent our receipt of any revenue from potential product sales.

We cannot predict whether we, or our partners (as applicable), will encounter problems with the Phase 3 clinical trial for birtamimab, the Phase 2 clinical trial for prasinezumab, the Phase 2b clinical trial for prasinezumab, the Phase 2 clinical trial for coramitug, the Phase 2 clinical trial for BMS-986446, the Phase 1 clinical trials for PRX012, the Phase 1 clinical trial for PRX019, or any other future clinical trials that will cause us or any regulatory authority to delay, suspend or terminate those clinical trials or delay the analysis of data derived from them. A number of events, including any of the following, could delay the completion of our ongoing or planned clinical trials and negatively impact our ability to obtain regulatory approval for, and to market and sell, a particular drug candidate:

- conditions imposed on us by the FDA, the EMA, or other comparable regulatory authorities regarding the scope or design of our clinical trials;
- delays in obtaining, or our inability to obtain, required approvals from institutional review boards ("IRBs") or other reviewing entities at clinical sites selected for participation in our clinical trials;
- insufficient supply or deficient quality of our drug candidates or other materials necessary to conduct our clinical trials;
- delays in obtaining regulatory authority authorization for the conduct of our clinical trials;
- lower than anticipated enrollment and/or retention rate of subjects in our clinical trials, which can be impacted by a number of factors, including size of patient population, design of trial protocol, trial length, eligibility criteria, perceived risks and benefits of the drug candidate, patient proximity to trial sites, patient referral practices of physicians, availability of other treatments for the relevant disease, and competition from other clinical trials;
- slower than expected rates of events in trials with a primary endpoint that is event-based;
- serious and unexpected drug-related side effects experienced by subjects in clinical trials; or
- failure of our third-party contractors and collaborators to meet their contractual obligations to us or otherwise meet their development or other objectives in a timely manner.

Further, conducting clinical trials in foreign countries, as we do and may continue do for our drug candidates, presents potential additional risks for our clinical trials. These risks include the failure in foreign countries to adhere to clinical protocol as a result of differences in regional or local healthcare services or customs, obtaining clinical data and/or clinical samples from sites in such foreign countries, managing additional administrative burdens associated with foreign regulatory requirements, as well as political and economic risks relevant to such foreign countries.

We are dependent upon Roche with respect to further development of prasinezumab. Under the terms of our collaboration with Roche, Roche is responsible for that further development, including the conduct of the ongoing Phase 2 and Phase 2b clinical trials and any future clinical trial of that drug candidate.

We are dependent upon Novo Nordisk with respect to further development of coramitug, including the Phase 2 clinical trial and any future clinical trial of that drug candidate.

We are dependent upon BMS with respect to further development of BMS-986446, including the Phase 2 clinical trial and any future clinical trial of that drug candidate.

Clinical trials may also be delayed or terminated as a result of ambiguous or negative data or results. In addition, a clinical trial may be delayed, suspended or terminated by us, the FDA, the EMA or other comparable regulatory authorities, the IRBs for the sites where the IRBs are overseeing a trial, or the safety oversight committee overseeing the clinical trial at issue due to a number of factors, including:

- failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols;
- inspection of the clinical trial operations or trial sites by the FDA, the EMA, or other regulatory authorities resulting in the imposition of a clinical hold on or imposition of additional conditions for the conduct of the trial;
- interpretation of data by the FDA, the EMA, or other regulatory authorities;
- requirement by the FDA, the EMA, or other regulatory authorities to perform additional studies;
- failure to achieve primary or secondary endpoints or other failure to demonstrate efficacy or adequate safety;
- unforeseen safety issues; or
- lack of adequate funding to continue the clinical trial.

Additionally, changes in regulatory requirements and guidance may occur and we may need to amend clinical trial protocols to reflect these changes. Amendments may require us to resubmit our clinical trial protocols to regulatory authorities and IRBs for reexamination, which may impact the cost, timing, or successful completion of a clinical trial. For example, the FDA may modify or enhance clinical trial requirements which could affect enrollment and retention of patients. Such effects on recruitment and retention of patients may hinder or delay a clinical trial, which could increase costs and delay clinical programs.

We do not know whether our clinical trials will be conducted as planned, will need to be restructured, or will be completed on schedule, if at all. Delays in our clinical trials will result in increased development costs for our drug candidates. In addition, if we experience delays in the completion of, or if we terminate, any of our clinical trials, the commercial prospects for our drug candidates may be delayed or harmed and our ability to generate product revenues will be delayed or jeopardized. Furthermore, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of a drug candidate.

The regulatory approval processes of the FDA, the EMA, and other comparable regulatory authorities are lengthy, time consuming, and inherently unpredictable, and if we are ultimately unable to obtain regulatory approval for our drug candidates, our business will be substantially harmed.

The time required to obtain approval by the FDA, the EMA, and other comparable regulatory authorities is inherently unpredictable but typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the substantial discretion of the regulatory authorities. In addition, approval policies, regulations, or the type and amount of clinical data necessary to gain approval may change during the course of a drug candidate's clinical development and may vary among jurisdictions. We have not obtained regulatory approval for any drug candidate, and it is possible that none of our existing drug candidates or any drug candidates we may seek to develop in the future will ever obtain regulatory approval.

Our drug candidates could fail to receive regulatory approval for many reasons, including the following:

- the FDA, the EMA, or comparable regulatory authorities may disagree with the design, implementation, or conduct of our clinical trials;

- we may be unable to demonstrate to the satisfaction of the FDA, the EMA, or comparable regulatory authorities that a drug candidate is safe and effective for its proposed indication;

- the results of clinical trials may not meet the level of statistical significance required by the FDA, the EMA, or comparable regulatory authorities for approval;

- we may be unable to demonstrate that a drug candidate's clinical and other benefits outweigh its safety risks;

- the FDA, the EMA, or comparable regulatory authorities may disagree with our interpretation of data from nonclinical studies or clinical trials;

- the data collected from clinical trials of our drug candidates may not be sufficient to support the submission of an NDA or a BLA to the FDA, a Marketing Authorization Application ("MAA") to the EMA, or similar applications to comparable regulatory authorities;

- the FDA, the EMA, or comparable regulatory authorities may fail to approve the manufacturing processes or facilities of third-party manufacturers with which we contract for clinical and commercial supplies; or

- the approval policies or regulations of the FDA, the EMA, or comparable regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

This lengthy approval process as well as the unpredictability of future clinical trial results may result in our failing to obtain regulatory approval to market our drug candidates, which would significantly harm our business, results of operations, and/or growth prospects.

In addition, even if we were to obtain approval, regulatory authorities may approve any of our drug candidates for fewer or more limited indications than we request, 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. Any of the foregoing scenarios could materially harm the commercial prospects for our drug candidates.

The FDA or other comparable foreign regulatory authorities may not accept data from trials conducted in locations outside of their jurisdiction.

We are and may choose to conduct international clinical trials in the future. The acceptance of study data by the FDA or other comparable foreign regulatory authority from clinical trials conducted outside of their respective jurisdictions may be subject to certain conditions. In cases where data from foreign clinical trials are intended to serve as the basis for marketing approval in the United States, the FDA will generally not approve the application on the basis of foreign data alone unless (1) the data are applicable to the United States population and United States medical practice; (2) the trials are performed by clinical investigators of recognized competence; and (3) the data may be considered valid without the need for an on-site inspection by the FDA, or if the FDA considers such an inspection to be necessary, the FDA is able to validate the data through an on-site inspection or other appropriate means. 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 other comparable foreign regulatory authority will accept data from trials conducted outside of its applicable jurisdiction. If the FDA or any other comparable 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 product candidates not receiving approval for commercialization in the applicable jurisdiction.

Even if our drug candidates receive regulatory approval in one country or jurisdiction, we may never receive approval or commercialize our products in other countries or jurisdictions.

In order to market drug candidates in a particular country or jurisdiction, we must establish and comply with numerous and varying regulatory requirements of that country or jurisdiction, including with respect to safety and efficacy. Approval procedures vary among countries and can involve additional product testing and additional administrative review periods. The

time required to obtain approval in other countries might differ from that required to obtain, for example, FDA approval in the U.S. or EMA approval in the EU. The regulatory approval process in other countries may include all of the risks detailed above regarding FDA approval in the U.S. and EMA approval in the EU as well as other risks. Regulatory approval in one country or jurisdiction does not ensure regulatory approval in another country or jurisdiction, but a failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory process in others. Failure to obtain regulatory approval in one country or jurisdiction or any delay or setback in obtaining such approval would impair our ability to develop other markets for that drug candidate.

Although we have obtained agreement with the FDA on a special protocol assessment ("SPA") with regard to our Phase 3 AFFIRM-AL clinical trial of birtamimab, a SPA does not guarantee approval of birtamimab or any other particular outcome from regulatory review.

On January 27, 2021, the FDA agreed to a SPA for our Phase 3 AFFIRM-AL clinical trial of birtamimab. The FDA's SPA process is designed to facilitate the FDA's review and approval of drugs by allowing the FDA to evaluate proposed critical design features of certain clinical trials that are intended to form the primary basis for determining a drug candidate's efficacy and safety. Upon specific request by a clinical trial sponsor, the FDA will evaluate the study protocol and statistical analysis plan and respond to a sponsor's questions regarding protocol design and scientific and regulatory requirements. FDA aims to complete SPA reviews within 45 days of receipt of the request. The FDA ultimately assesses whether specific elements of the protocol design for the trial, such as entry criteria, endpoints, size, duration, and planned analyses, are acceptable to support an application for regulatory approval of the drug candidate with respect to the effectiveness of and safety for the indication studied. All agreements and disagreements between the FDA and the sponsor regarding a SPA must be clearly documented in a SPA letter or the minutes of a meeting between the sponsor and the FDA.

Although the FDA has agreed to the SPA for our Phase 3 AFFIRM-AL clinical trial with respect to the primary endpoint and certain other aspects of the clinical trial, a SPA agreement does not guarantee approval of a drug candidate. The FDA may limit the scope of its agreement to a SPA agreement to certain, specific aspects of the clinical trial design. Even if the FDA agrees to the design, execution, and analysis proposed in a protocol reviewed under the SPA process, the FDA may revoke or alter its agreement in certain circumstances. In particular, a SPA agreement is not binding on the FDA if public health concerns emerge that were unrecognized at the time of the SPA agreement, other new scientific concerns regarding product safety or efficacy arise, the sponsor fails to comply with the agreed upon study protocol, or the relevant data, assumptions, or information provided by the sponsor in a request for the SPA change or are found to be false or to omit relevant facts. In addition, even after a SPA agreement is finalized, the SPA agreement may be modified, and such modification will be deemed binding on the FDA review division, except under the circumstances described above, if the FDA and the sponsor agree in writing to the modification of the study protocol and/or statistical analysis plan. Generally, such modification is intended to improve the study. The FDA retains significant latitude and discretion in interpreting the terms of the SPA agreement and the data and results from any study that is the subject of the SPA agreement.

Moreover, if the FDA revokes or alters its agreement under the SPA, or interprets the data collected from the clinical trial differently than the sponsor, the FDA may not deem the data sufficient to support an application for regulatory approval.

Both before and after marketing approval, our drug candidates are subject to ongoing regulatory requirements and continued regulatory review, and if we fail to comply with these continuing requirements, we could be subject to a variety of sanctions and the sale of any approved products could be suspended.

Both before and after regulatory approval to market a particular drug candidate, adverse event reporting, manufacturing, labeling, packaging, storage, distribution, advertising, promotion, record keeping, and reporting related to the product are subject to extensive, ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, as well as continued compliance with current good manufacturing practice ("cGMP") requirements and current good clinical practice ("cGCP") requirements for any clinical trials that we conduct. Any regulatory approvals that we receive for our drug candidates may also be subject to limitations on the approved indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase 4 clinical trials, and surveillance to monitor the safety and efficacy of the drug candidate. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or not previously observed in clinical trials, or problems with our third-party manufacturers or manufacturing processes, or failure

to comply with the regulatory requirements of the FDA, the EMA, or other comparable regulatory authorities could subject us to administrative or judicially imposed sanctions, including:

- restrictions on the marketing of our products or their manufacturing processes;
- warning letters;
- civil or criminal penalties;
- fines;
- injunctions;
- product seizures or detentions;
- import or export bans;
- voluntary or mandatory product recalls and related publicity requirements;
- suspension or withdrawal of regulatory approvals;
- total or partial suspension of production; and
- refusal to approve pending applications for marketing approval of new products or supplements to approved applications.

The policies of the FDA, the EMA, or other comparable regulatory authority may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our drug candidates. 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, which would adversely affect our business, prospects and ability to achieve or sustain profitability.

If side effects are identified during the time our drug candidates are in development, or, if they are approved by applicable regulatory authorities, after they are on the market, we may choose to or be required to perform lengthy additional clinical trials, discontinue development of the affected drug candidate, change the labeling of any such products, or withdraw any such products from the market, any of which would hinder or preclude our ability to generate revenues.

Undesirable side effects caused by our drug candidates could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA, the EMA, or other comparable regulatory authorities. Drug-related side effects could affect patient recruitment or the ability of enrolled patients to complete a trial or result in potential product liability claims. Any of these occurrences may harm our business, financial condition and prospects significantly. Even if any of our drug candidates receives marketing approval, as greater numbers of patients use a drug following its approval, an increase in the incidence or severity of side effects or the incidence of other post-approval problems that were not seen or anticipated during pre-approval clinical trials could result in a number of potentially significant negative consequences, including:

- regulatory authorities may withdraw their approval of the product;
- regulatory authorities may require the addition of labeling statements, such as contraindications, warnings, or precautions; or impose additional safety monitoring or reporting requirements;
- we may be required to change the way the product is administered, or to conduct additional clinical trials;
- we could be sued and held liable for harm caused to patients; and

- our reputation may suffer.

Any of these events could substantially increase the costs and expenses of developing, commercializing and marketing any such drug candidates or could harm or prevent sales of any approved products.

We deal with hazardous materials and must comply with environmental laws and regulations which can be expensive and restrict how we do business.

Some of our research and development activities involve the controlled storage, use, and disposal of hazardous materials. We are subject to U.S. federal, state, local, and other countries' and jurisdictions' laws and regulations governing the use, manufacture, storage, handling, and disposal of these hazardous materials. Although we believe that our safety procedures for the handling and disposing of these materials comply with the standards prescribed by these laws and regulations, we cannot eliminate the risk of accidental contamination or injury from these materials. In the event of an accident, state or federal authorities may curtail our use of these materials, and we could be liable for any civil damages that result, which may exceed our financial resources and may seriously harm our business. Because we believe that our laboratory and materials handling policies and practices sufficiently mitigate the likelihood of materials liability or third-party claims, we currently carry no insurance covering such claims. An accident could damage, or force us to shut down, our operations.

Risks Related to the Commercialization of Our Drug Candidates

Even if any of our drug candidates receives regulatory approval, if such approved product does not achieve broad market acceptance, the revenues that we generate from sales of the product will be limited.

Even if any drug candidates we may develop or acquire in the future obtain regulatory approval, they may not gain broad market acceptance among physicians, healthcare payers, patients and the medical community. The degree of market acceptance for any approved drug candidate will depend on a number of factors, including:

- the indication and label for the product and the timing of introduction of competitive products;
- demonstration of clinical safety and efficacy compared to other products;
- prevalence, frequency, and severity of adverse side effects;
- availability of coverage and adequate reimbursement from managed care plans and other third-party payers;
- convenience and ease of administration;
- cost-effectiveness;
- other potential advantages of alternative treatment methods; and
- the effectiveness of marketing and distribution support of the product.

Consequently, even if we discover, develop, and commercialize a product, the product may fail to achieve broad market acceptance and we may not be able to generate significant revenue from the product.

The success of prasinezumab in the United States, if approved, will be dependent upon the strength and performance of our collaboration with Roche. If we fail to maintain our existing collaboration with Roche, such termination would likely have a material adverse effect on our ability to develop and commercialize prasinezumab and our business. Furthermore, in May 2021, we opted out of profit and loss sharing with Roche for prasinezumab in Parkinson's disease; however if we opt out of profit and loss sharing for any other Licensed Products and/or indications, our revenues from such other Licensed Products and/or indications will be reduced.

Directors' Report *(continued)*

The success of sales of prasinezumab in the U.S. will be dependent on the ability of Roche to successfully develop in collaboration with us, and launch and commercialize prasinezumab, if approved by the FDA, pursuant to the License Agreement we entered into in December 2013. Our collaboration with Roche is complex, particularly with respect to future U.S. commercialization of prasinezumab, with respect to financial provisions, allocations of responsibilities, cost estimates, and the respective rights of the parties in decision making. Accordingly, significant aspects of the development and commercialization of prasinezumab require Roche to execute its responsibilities under the arrangement, or require Roche's agreement or approval, prior to implementation, which could cause significant delays that may materially impact the potential success of prasinezumab in the U.S. In addition, Roche may under some circumstances independently develop products that compete with prasinezumab, or Roche may decide to not commit sufficient resources to the development, commercialization, marketing and distribution of prasinezumab. If we are not able to collaborate effectively with Roche on plans and efforts to develop and commercialize prasinezumab, our business could be materially adversely affected.

Furthermore, the terms of the License Agreement provide that Roche has the ability to terminate such arrangement for any reason after the first anniversary of the License Agreement at any time upon 90 days' notice (if prior to first commercial sale) or 180 days' notice (if after first commercial sale). For example, even if prasinezumab was approved by the FDA, Roche may determine that the outcomes of clinical trials made prasinezumab a less attractive commercial product and terminate our collaboration. If the License Agreement is terminated, our business and our ability to generate revenue from sales of prasinezumab could be substantially harmed as we will be required to develop, commercialize, and build our own sales and marketing organization, or enter into another strategic collaboration in order to develop and commercialize prasinezumab in the U.S. Such efforts may not be successful and, even if successful, would require substantial time and resources to carry out.

The manner in which Roche launches prasinezumab, if approved by the FDA, including the timing of launch and potential pricing, will have a significant impact on the ultimate success of prasinezumab in the U.S., and the success of the overall commercial arrangement with Roche. If launch of commercial sales of prasinezumab in the U.S. by Roche is delayed or prevented, our revenue will suffer and our stock price may decline. Further, if launch and resulting sales by Roche are not deemed successful, our business would be harmed and our stock price may decline. Any lesser effort by Roche in its prasinezumab sales and marketing efforts may result in lower revenue and thus lower profits with respect to the U.S. The outcome of Roche's commercialization efforts in the U.S. could also have a negative effect on investors' perception of potential sales of prasinezumab outside of the U.S., which could also cause a decline in our stock price.

In May 2021, we opted out of profit and loss sharing with Roche for prasinezumab in Parkinson's disease. However, pursuant to the License Agreement, we are responsible for 30% of all development and commercialization costs for any future Licensed Products and/or indications (other than Parkinson's disease with prasinezumab) that we opt to co-develop, in each case unless we elect to opt out of profit and loss sharing. If we elect to opt out of profit and loss sharing, we will instead receive sales milestones and royalties, and our revenue, if any, from such other Licensed Products and/or indications will be reduced.

Our right to co-develop Licensed Products and/or indications under the License Agreement (other than Parkinson's disease with prasinezumab for which we have opted out of co-development) will terminate if we commence certain studies for a competitive product that treats Parkinson's disease or other indications that we opted to co-develop. In addition, our right to co-promote prasinezumab and other Licensed Products will terminate if we commence a Phase 3 study for a competitive product that treats Parkinson's disease.

Moreover, under the terms of the License Agreement, we rely on Roche to provide us estimates of their costs, revenue, and revenue adjustments and royalties, which estimates we use in preparing our quarterly and annual financial reports. If the underlying assumptions on which Roche's estimates were based prove to be incorrect, actual results or revised estimates supplied by Roche that are materially different from the original estimates could require us to adjust the estimates included in our reported financial results. If material, these adjustments could require us to restate previously reported financial results, which could have a negative effect on our stock price.

Our ability to receive any significant revenue from prasinezumab will be dependent on Roche's efforts and may result in lower levels of income than if we marketed or developed our drug candidates entirely on our own. Roche may not fulfill its obligations or carry out marketing activities for prasinezumab as diligently as we would like. We could also become involved in disputes with Roche, which could lead to delays in or termination of development or commercialization activities and time-consuming and expensive litigation or arbitration. If Roche terminates or breaches the License Agreement, or otherwise decides

not to complete its obligations in a timely manner, the chances of successfully developing, commercializing, or marketing prasinezumab would be materially and adversely affected.

Outside of the United States, we are solely dependent on the efforts and commitments of Roche, either directly or through third parties, to further develop and, if prasinezumab is approved by applicable regulatory authorities, commercialize prasinezumab. If Roche's efforts are unsuccessful, our ability to generate future product sales from prasinezumab outside the United States would be significantly reduced.

Under our License Agreement, outside of the U.S., Roche has responsibility for developing and commercializing prasinezumab and any future Licensed Products targeting α-synuclein. As a consequence, any progress and commercial success outside of the U.S. is dependent solely on Roche's efforts and commitment to the program. For example, Roche may delay, reduce, or terminate development efforts relating to prasinezumab outside of the U.S., or under some circumstances independently develop products that compete with prasinezumab, or decide not to commit sufficient resources to the commercialization, marketing, and distribution of prasinezumab.

In the event that Roche does not diligently develop and commercialize prasinezumab, the License Agreement provides us the right to terminate the License Agreement in connection with a material breach uncured for 90 days after notice thereof. However, our ability to enforce the provisions of the License Agreement so as to obtain meaningful recourse within a reasonable timeframe is uncertain. Further, any decision to pursue available remedies including termination would impact the potential success of prasinezumab, including inside the U.S., and we may choose not to terminate as we may not be able to find another partner and any new collaboration likely will not provide comparable financial terms to those in our arrangement with Roche. In the event of our termination, this may require us to develop and commercialize prasinezumab on our own, which is likely to result in significant additional expense and delay. Significant changes in Roche's business strategy, resource commitment and the willingness or ability of Roche to complete its obligations under our arrangement could materially affect the potential success of the drug candidate. Furthermore, if Roche does not successfully develop and commercialize prasinezumab outside of the U.S., our potential to generate future revenue outside of the U.S. would be significantly reduced.

If we are unable to establish sales and marketing capabilities or enter into agreements with third parties to market and sell approved products, we may be unable to generate product revenue.

We do not currently have a fully-scaled organization for the sales, marketing, and distribution of pharmaceutical products. In order to market any products that may be approved by the FDA, the EMA, or other comparable regulatory authorities, we must build our sales, marketing, managerial, and other non-technical capabilities or make arrangements with third parties to perform these services.

We have entered into the License Agreement with Roche for the development of prasinezumab and may develop our own sales force and marketing infrastructure to co-promote prasinezumab in the U.S. for the treatment of Parkinson's disease and any future Licensed Products approved for Parkinson's disease in the U.S. If we exercise our co-promotion option and are unable to develop our own sales force and marketing infrastructure to effectively commercialize prasinezumab or other Licensed Products, our ability to generate additional revenue from potential sales of prasinezumab or such products in the U.S. may be harmed. In addition, our right to co-promote prasinezumab and other Licensed Products will terminate if we commence a Phase 3 study for a competitive product that treats Parkinson's disease.

For any other products that may be approved, if we are unable to establish adequate sales, marketing, and distribution capabilities, whether independently or with third parties, we may not be able to generate product revenue and may not become profitable.

If government and third-party payers fail to provide coverage and adequate reimbursement rates for any of our drug candidates that receive regulatory approval, our revenue and prospects for profitability will be harmed.

In both U.S. and non-U.S. markets, our sales of any future products will depend in part upon the availability of reimbursement from third-party payers. Such third-party payers include government health programs such as Medicare and Medicaid, managed care providers, private health insurers, and other organizations. There is significant uncertainty related to the third-party coverage and reimbursement of newly approved drugs. Coverage and reimbursement may not be available for

any drug that we or our collaborators commercialize and, even if these are available, the level of reimbursement may not be satisfactory. Third-party payers often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies. Third-party payers are also increasingly attempting to contain healthcare costs by demanding price discounts or rebates limiting both coverage and the amounts that they will pay for new drugs, and, as a result, they may not cover or provide adequate payment for our drug candidates. We might need to conduct post-marketing studies in order to demonstrate the cost-effectiveness of any future products to such payers' satisfaction. Such studies might require us to commit a significant amount of management time and financial and other resources. Our future products might not ultimately be considered cost-effective. Adequate third-party reimbursement might not be available to enable us to maintain price levels sufficient to realize an appropriate return on investment in product development. If coverage and adequate reimbursement are not available or reimbursement is available only to limited levels, we or our collaborators may not be able to successfully commercialize any drug candidates for which marketing approval is obtained.

Additionally, pursuant to the Medicaid Drug Rebate Statute, we will be required to participate in the Medicaid Drug Rebate Program in order for federal payment to be available for our products under Medicaid and Medicare Part B. Under the Medicaid Drug Rebate Program, we will be required to, among other things, pay a rebate to each state Medicaid program for quantities of our products utilized on an outpatient basis (with some exceptions) that are dispensed to Medicaid beneficiaries and paid for by a state Medicaid program. Medicaid Drug Rebate Program rebates are calculated using a statutory formula, state-reported utilization data, and pricing data that are calculated and reported by us on a monthly and quarterly basis to the Centers for Medicare and Medicaid Services ("CMS"). These data include the average manufacturer price and, in the case of single source and innovator multiple source products, the best price for each drug.

The regulations that govern marketing approvals, pricing, coverage, and reimbursement for new drugs vary widely from country to country. Current and future legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or licensing approval is granted. In some countries, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we or our collaborators might obtain marketing approval for a drug in a particular country, but then be subject to price regulations that delay commercial launch of the drug, possibly for lengthy time periods, and negatively impact our ability to generate revenue from the sale of the drug in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more drug candidates, even if our drug candidates obtain marketing approval.

U.S. and other governments continue to propose and pass legislation designed to reduce the cost of healthcare. In the U.S., we expect that there will continue to be federal and state proposals to implement similar governmental controls. In addition, recent changes in the Medicare program and increasing emphasis on managed care in the U.S. will continue to put pressure on pharmaceutical product pricing. For example, in 2010, the U.S. Patient Protection and Affordable Care Act, as amended by the U.S. Health Care and Education Reconciliation Act (collectively, the "ACA"), was enacted. The ACA substantially changed the way healthcare is financed by both governmental and private insurers and significantly affects the pharmaceutical industry. Among the provisions of the ACA of importance to the pharmaceutical industry are the following:

- an annual, nondeductible fee on any entity that manufactures or imports certain branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs;

- an increase in the minimum rebates a manufacturer must pay under the U.S. Medicaid Drug Rebate Program to 23.1% and 13.0% of the average manufacturer price for branded and generic drugs, respectively;

- expansion of healthcare fraud and abuse laws, including the U.S. False Claims Act ("FCA") and the U.S. Anti-Kickback Statute, new government investigative powers and enhanced penalties for non-compliance;

- extension of manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;

- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals and by adding new mandatory eligibility categories for certain individuals with

income at or below 133% of the federal poverty level, thereby potentially increasing a manufacturer's Medicaid rebate liability;

- a licensure framework for follow-on biologic products;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- implementation of the federal Physician Payments Sunshine Act, which requires pharmaceutical manufacturers, among others, to annually track and report all payments and other transfers of value they make to certain healthcare providers, as well as physician ownership held in the company;
- a requirement for manufacturers and distributors to annually report drug samples that they provide to physicians; and
- establishment of the Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

In addition, other legislative changes have been proposed and adopted since the ACA was enacted. These changes include aggregate reductions to Medicare payments to providers of 2% per fiscal year, which went into effect in 2013 and will stay in effect through the first six months of the FY 2032 sequestration order, unless additional congressional action is taken, with the exception of a temporary suspension from May 1, 2020, through March 31, 2022, and a subsequent 1% cut in Medicare payments in effect from March 31, 2022 to July 1, 2022, due to the COVID-19 pandemic. In 2013, the U.S. American Taxpayer Relief Act of 2012, among other things, further reduced Medicare payments to several types of providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other healthcare funding, which could have a material adverse effect on customers for our drugs, if approved, and, accordingly, our financial operations.

Since its enactment, there have been judicial, executive, and Congressional challenges to certain aspects of the ACA. While Congress has not passed comprehensive repeal legislation, two bills affecting the implementation of certain taxes under the ACA have been signed into law, including the repeal, effective January 1, 2019, of the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate." On June 17, 2021, the U.S. Supreme Court dismissed the most recent judicial challenge to the ACA brought by several states who argued that, without the individual mandate, the entire ACA was unconstitutional. The Supreme Court's dismissal of the lawsuit did not specifically rule on the constitutionality of the ACA.

Moreover, President Biden signed into law the Inflation Reduction Act (IRA) on August 16, 2022, which allows Medicare to: beginning in 2026, establish a "maximum fair price" for a fixed number of pharmaceutical and biological products covered under Medicare Parts B and D following a price negotiation process with CMS; and, beginning in 2023, penalize drug companies that raise prices for products covered under Medicare Parts B and D faster than inflation, among other reforms. CMS has also taken steps to implement the IRA, including: on October 2, 2024, releasing final guidance outlining the process for the second round of price negotiations for products subject to the "maximum fair price" provision; on December 20, 2024, releasing a list of 64 Medicare Part B products that had an adjusted coinsurance rate based on the inflationary rebate provisions of the IRA for the time period of January 1, 2025 to March 31, 2025; and on January 17, 2025, releasing a list of fifteen additional drugs covered under Medicare Part D subject to price negotiations during 2025. It is unclear how future regulatory actions to implement the IRA, as well as the outcome of pending litigation against the IRA brought against the Department of Health and Human Services (HHS), the Secretary of HHS, CMS, and the CMS Administrator challenging the constitutionality and administrative implementation of the IRA's drug price negotiation provisions, may affect our products and future profitability.

Additionally, on October 14, 2022, President Biden issued an Executive Order on Lowering Prescription Drug Costs for Americans, which instructed the Secretary of HHS to consider whether to select for testing by the CMS Innovation Center new health care payment and delivery models that would lower drug costs and promote access to innovative drug therapies for beneficiaries enrolled in the Medicare and Medicaid programs. On February 14, 2023, HHS issued a report in response to the October 14, 2022 Executive Order, which, among other things, selects three potential drug affordability and accessibility models to be tested by the CMS Innovation Center. Specifically, the report addresses: (1) a model that would allow Part D

Sponsors to establish a "high-value drug list" setting the maximum co-payment amount for certain common generic drugs at $2.00; (2) a Medicaid-focused model that would establish a partnership between CMS, manufacturers, and state Medicaid agencies that would result in multi-state outcomes-based agreements or certain cell and gene therapy drugs; and (3) a model that would adjust Medicare Part B payment amounts for Accelerated Approval Program drugs to advance the developments of novel treatments.

We expect that other healthcare reform measures that may be adopted in the future may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any approved drug. Legislation and regulations affecting the pricing of pharmaceuticals might change before our drug candidates are approved for marketing. Any reduction in reimbursement from Medicare or other government healthcare programs may result in a similar reduction in payments from private payers. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our drugs.

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

The markets for our drug candidates are subject to intense competition. If we are unable to compete effectively, our drug candidates may be rendered noncompetitive or obsolete.

The research, development, and commercialization of new drugs is highly competitive. We will face competition with respect to all drug candidates we may develop or commercialize in the future from pharmaceutical and biotechnology companies worldwide. The key factors affecting the success of any approved product will be its indication, label, efficacy, safety profile, drug interactions, method of administration, pricing, coverage, reimbursement, and level of promotional activity relative to those of competing drugs.

Furthermore, many large pharmaceutical and biotechnology companies, academic institutions, governmental agencies, and other public and private research organizations are pursuing the development of novel drugs that target the same indications we are targeting with our research and development program. We face, and expect to continue to face, intense and increasing competition as new products enter the market and advanced technologies become available. Many of our competitors have:

- significantly greater financial, technical and human resources than we have and may be better equipped to discover, develop, manufacture, and commercialize drug candidates;
- more extensive experience in nonclinical testing and clinical trials, obtaining regulatory approvals, and manufacturing and marketing pharmaceutical products;
- drug candidates that have been approved or are in late-stage clinical development; and/or
- collaborative arrangements in our target markets with leading companies and research institutions.

Competitive products may render our research and development program obsolete or noncompetitive before we can recover the expenses of developing and commercializing our drug candidates. Furthermore, the development of new treatment methods and/or the widespread adoption or increased utilization of any vaccine or development of other products or treatments for the diseases we are targeting could render any of our drug candidates noncompetitive, obsolete or uneconomical. If we successfully develop and obtain approval for a drug candidate, we will face competition based on the safety and effectiveness of the approved product, the timing of its entry into the market in relation to competitive products in development, the availability and cost of supply, marketing and sales capabilities, coverage, reimbursement, price, patent position and other factors. Even if we successfully develop drug candidates but those drug candidates do not achieve and maintain market acceptance, our business will not be successful.

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

Our current drug candidates are regulated by the FDA as biologic products and we intend to seek approval for these products pursuant to the BLA pathway. The U.S. Biologics Price Competition and Innovation Act of 2009 (the "BPCIA") created an abbreviated pathway for the approval of biosimilar and interchangeable biologic products. The abbreviated regulatory pathway establishes legal authority for the FDA to review and approve biosimilar biologics, including the possible designation of a biosimilar as "interchangeable" based on its similarity to an existing brand product.

Under the BPCIA, an application for a biosimilar product cannot be submitted to the FDA until four years following the date that the reference product was first licensed by the FDA, and cannot be approved by the FDA until 12 years after the original branded product was approved under a BLA. The BPCIA also created certain exclusivity periods for biosimilars approved as interchangeable products. However, during the 12-year period of reference product exclusivity, another company may obtain FDA licensure and market a competing version of the reference product if the FDA approves a full de novo BLA, not an abbreviated BLA for a biosimilar product, 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 law is complex and is still being interpreted and implemented by the FDA. Any processes adopted by the FDA to implement the BPCIA could have a material adverse effect on the future commercial prospects for our biologic products. In addition, there has been discussion of whether Congress should 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 implementation of the BPCIA is subject to significant uncertainty.

We believe that any of our drug candidates approved as a biologic product under a BLA should qualify for the 12-year period of 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 our drug candidates to be reference products for competing products, potentially creating the opportunity for generic competition sooner than anticipated. Moreover, the extent to which a biosimilar, once approved, will be substituted for any one of our reference products in a way that is similar to traditional generic substitution for non-biologic products is not yet clear, and will depend on a number of marketplace and regulatory factors that are still developing.

We may be unable to maintain the benefits associated with Orphan Drug Designation, including the potential for supplemental market exclusivity.

Birtamimab has been granted Orphan Drug Designation by both the FDA and EMA for the treatment of AL amyloidosis. In addition, we may seek Orphan Drug Designation for one or more of our current or future drug candidates. Regulatory authorities in some jurisdictions, including the United States and Europe, may designate drug products for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may grant orphan designation to a drug product intended to treat a rare disease or condition, defined as a disease or condition with a patient population of fewer than 200,000 in the United States. 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 user-fee waivers. Orphan Drug Designation does not convey any advantage in, or shorten the duration of, the regulatory review and licensure process.

If a drug product that has Orphan Drug Designation subsequently receives the first FDA approval or licensure for a particular active ingredient for the disease for which it has such designation, the drug product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications, including an NDA or BLA, to market the same drug product for the same indication for seven years, except in limited circumstances such as a showing of clinical superiority to the product with orphan drug exclusivity or if the FDA finds that the holder of the orphan drug exclusivity has not shown that it can assure the availability of sufficient quantities of the orphan drug to meet the needs of patients with the disease or condition for which the biological product was designated. As a result, even if one of our drug candidates receives orphan exclusivity, the FDA can still approve or license other drug products that have a different active ingredient for use in treating the same indication or disease. Further, the FDA can waive orphan exclusivity if we are unable to manufacture sufficient supply of our drug product.

A Fast Track designation by the FDA, even if granted for current or future drug candidates, may not lead to a faster development or regulatory review, licensure process and does not increase the likelihood that our drug candidates will receive marketing licensure.

Birtamimab, for the treatment of AL amyloidosis, and PRX012 and PRX123, each for the treatment of Alzheimer's disease, have each been granted Fast Track Designation by the FDA. In addition, we may seek Fast Track designation for one or more of our future drug candidates. If a drug candidate is intended for the treatment of a serious condition and demonstrates the potential to address an unmet medical need for this condition, the sponsor may apply for FDA Fast Track designation for a particular indication. We may seek Fast Track designation for our drug candidates, but there is no assurance that the FDA will grant this status to any of our drug candidates. The FDA has broad discretion whether or not to grant Fast Track designation, and even if we consider a particular drug candidate to be eligible for this designation, there is no assurance that it will be granted by the FDA. Even if we do receive Fast Track designation, we may not experience a faster review or approval compared to other, non-expedited FDA procedures, and receiving a Fast Track designation does not provide assurance of ultimate FDA approval. In addition, the FDA may withdraw Fast Track designation if it believes that the designation is no longer supported by data from our applicable clinical development program. Marketing applications filed by sponsors of products granted Fast Track designation may qualify for priority review under FDA policies and procedures, but Fast Track designation does not assure any such review or ultimate marketing approval by the FDA.

We are subject to healthcare and other laws and regulations, including anti-bribery, anti-kickback, fraud and abuse, false claims, and physician payment transparency laws and regulations, which could expose us to criminal, civil and/or administrative sanctions and penalties; exclusion from governmental healthcare programs or reimbursements; contractual damages; and reputational harm.

Our operations and activities are directly, or indirectly through our service providers and collaborators, subject to numerous healthcare and other laws and regulations, including, without limitation, those relating to anti-bribery, anti-kickback, fraud and abuse, false claims, physician payment transparency, and health information privacy and security, in the U.S., the EU, and other countries and jurisdictions in which we conduct our business. These laws include:

- the U.S. federal Anti-Kickback Statute, an intent-based federal criminal statute which prohibits, among other things, persons and entities from knowingly and willfully soliciting, receiving, offering, providing, or paying remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, lease, order or arrangement for, or recommendation of an item or service for which payment may be made, in whole or in part, by a federal healthcare program, such as the Medicare and Medicaid programs. 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 term remuneration has been interpreted broadly to include anything of value. Further, courts have found that if any "one purpose" of an arrangement involving remuneration is to induce referrals of federal healthcare program business, the federal Anti-Kickback Statute has been violated. The federal Anti-Kickback Statute applies to arrangements between pharmaceutical manufacturers on the one hand and individuals, such as prescribers, patients, purchasers, and formulary managers on the other hand, including, for example, consulting/speaking arrangements, discount and rebate offers, grants, charitable contributions, and patient support offerings, among others. Although there are several statutory exceptions and regulatory safe harbors to the federal Anti-Kickback Statute that protect certain common industry activities from prosecution, these exceptions and safe harbors are narrowly drawn. Arrangements that do not fully satisfy all elements of an available exception or safe harbor are evaluated based on the specific facts and circumstances and are typically subject to increased scrutiny;

- U.S. federal false claims laws, including the civil FCA, which impose criminal and civil penalties, including civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, claims for payment or approval from Medicare, Medicaid, or other third-party payers that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government. In addition, the ACA specified that any claims submitted as a result of a violation of the federal Anti-Kickback Statute constitute false claims and are subject to enforcement under the federal False Claims Act. Violations of the FCA may be subject to significant civil fines and penalties for each false claim, currently ranging from $13,946-$27,894 per false claim, treble damages, and potential exclusion from participation in federal healthcare programs;

- HIPAA, which imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program and making false statements in connection with the delivery of or payment for healthcare benefits, items or services. Similar to the U.S. federal Anti-Kickback Statute, 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 U.S. federal Physician Payments Sunshine Act, which 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, among others, to track and report annually to CMS information related to "payments or other transfers of value" made to U.S.-licensed physicians (defined to include doctors, dentists, optometrists, podiatrists and licensed chiropractors), physician assistants, nurse practitioners, clinical nurse specialists, certified registered nurse anesthetists, anesthesiology assistants, certified nurse midwives, and teaching hospitals; as well as tracking and reporting of ownership and investment interests held by the U.S.-licensed physicians (as defined by statute) and their immediate family members;

- analogous state laws and regulations that may apply to sales or marketing arrangements and claims for healthcare items or services reimbursed by non-governmental third-party payers, including private insurers, that may be broader in scope than their federal equivalents; state laws and regulations that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government or otherwise restrict payments that may be made to healthcare providers; state laws and regulations that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or require the disclosure of marketing expenditures and other pricing information; and

- similar and other laws and regulations in the U.S. (federal, state and local), in the EU (including member countries), and other countries and jurisdictions.

Ensuring our compliance with applicable laws and regulations involves substantial costs, and it is possible that governmental authorities or third parties will assert that our business practices fail to comply with these laws and regulations. If our actions are found to be in violation of any laws and regulations, we may be subject to significant civil, criminal, and administrative damages, penalties, and fines, as well as exclusion from participation in government healthcare programs, curtailment or restructuring of our operations, and reputational harm, any of which could have a material adverse effect on our business, financial condition, or results of operations.

If a successful product liability or clinical trial claim or series of claims is brought against us for uninsured liabilities or in excess of insured liabilities, we could incur substantial liability.

The use of our drug candidates in clinical trials and the sale of any products for which we obtain marketing approval will expose us to the risk of product liability and clinical trial liability claims. Product liability claims might be brought against us by consumers, healthcare providers, or others selling or otherwise coming into contact with our products. Clinical trial liability claims may be filed against us for damages suffered by clinical trial subjects or their families. If we cannot successfully defend ourselves against product liability claims, we could incur substantial liabilities. In addition, regardless of merit or eventual outcome, product liability claims may result in:

- decreased demand for any approved drug candidates;

- impairment of our business reputation;

- withdrawal of clinical trial participants;

- costs of related litigation;

- distraction of management's attention;

- substantial monetary awards to patients or other claimants;

- loss of revenues; and
- the inability to successfully commercialize any approved drug candidates.

We currently have clinical trial liability insurance coverage for all of our clinical trials. However, our insurance coverage may not be sufficient to reimburse us for any expenses or losses we may suffer. Moreover, insurance coverage is becoming increasingly expensive, and, in the future, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. If and when we obtain marketing approval for any of our drug candidates, we intend to expand our insurance coverage to include the sale of commercial products; however, we may be unable to obtain this product liability insurance on commercially reasonable terms. On occasion, large judgments have been awarded in class action lawsuits based on drugs that had unanticipated side effects. A successful product liability claim or series of claims brought against us could cause our ordinary share price to decline and, if judgments exceed our insurance coverage, could decrease our cash and adversely affect our business.

Risks Related to Our Dependence on Third Parties

We rely on third parties to conduct our clinical trials, and those third parties may not perform satisfactorily, including failing to meet established deadlines for the completion of any such clinical trials.

We do not have the ability to independently conduct clinical trials for our drug candidates, and we rely on third parties, such as consultants, contract research organizations, medical institutions, and clinical investigators to assist us with these activities. Our reliance on these third parties for clinical development activities results in reduced control over these activities. Furthermore, these third parties may also have relationships with other entities, some of which may be our competitors. Although we have and will enter into agreements with these third parties, we will be responsible for confirming that our clinical trials are conducted in accordance with their general investigational plans and protocols. Moreover, the FDA, the EMA, and other comparable regulatory authorities require us to comply with regulations and standards, commonly referred to as cGCPs, for conducting, recording, and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the trial participants are adequately protected. Our reliance on third parties does not relieve us of these responsibilities and requirements. If we or any of our third-party contractors fail to comply with applicable cGCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA, the EMA, or other comparable 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 cGCP regulations. In addition, our clinical trials must be conducted with product produced under cGMPs. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process. Requirements regarding clinical trial data may evolve, and any such changes to data requirements may cause the FDA or comparable foreign regulatory authorities to disagree with data from preclinical studies or clinical trials, and to require further studies.

To date, we believe our consultants, contract research organizations, and other third parties with which we are working have generally performed satisfactorily; however, if these third parties do not successfully carry out their contractual duties, meet expected deadlines, or comply with applicable regulations, we have been, and may be, required to replace them. Although we believe that there are a number of other third-party contractors we could engage to continue these activities, we may not be able to enter into arrangements with alternative third-party contractors or to do so on commercially reasonable terms, which may result in a delay of our planned clinical trials. Accordingly, we may be delayed in obtaining regulatory approvals for our drug candidates and may be delayed in our efforts to successfully develop our drug candidates.

In addition, our third-party contractors are not our employees, and except for remedies available to us under our agreements with such third-party contractors, we cannot control whether or not they devote sufficient time and resources to our ongoing clinical and nonclinical programs. If third-party contractors 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 and we may not be able to obtain regulatory approval for or successfully commercialize our drug candidates. As a result, our results of operations and the commercial prospects for our drug candidates would be harmed, our costs could increase and our ability to generate revenues could be delayed.

If we do not establish additional strategic collaborations, we may have to alter our research, development, and/or commercialization plans.

Research, development, and potential commercialization of our drug candidates will require substantial additional cash to fund expenses. Our strategy includes potentially collaborating with additional leading pharmaceutical and biotechnology companies to assist us in furthering research, development, and/or potential commercialization of some of our drug candidates in some or all geographies. It may be difficult to enter into one or more of such collaborations in the future. We face significant competition in seeking appropriate collaborators and these collaborations are complex and time-consuming to negotiate and document. We may not be able to negotiate collaborations on acceptable terms, or at all, in which case we may have to curtail the development of a particular drug candidate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we will need to obtain additional capital, which may not be available to us on acceptable terms, or at all. If we do not have sufficient funds, we will not be able to bring our drug candidates to market and generate product revenue.

We have no manufacturing capacity and depend on third-party manufacturers to supply us with nonclinical and clinical trial supplies of all of our drug candidates, and we will depend on third-party manufacturers to supply us with any drug product for commercial sale if we obtain marketing approval from the FDA, the EMA, or any other comparable regulatory authority for any of our drug candidates.

We do not own or operate facilities for the manufacture, packaging, labeling, storage, testing, or distribution of nonclinical or clinical supplies of any of our drug candidates. We instead contract with and rely on third parties to manufacture, package, label, store, test, and distribute nonclinical and clinical supplies of our drug candidates, and we plan to continue to do so for the foreseeable future. We also rely on third-party consultants to assist us with managing these third parties and with our manufacturing strategy. Certain of these third parties have failed to perform these activities for us and any of these third parties may fail to perform these activities for us in the future, which could cause nonclinical or clinical development of our drug candidates to be delayed, which could have an adverse effect on our business, financial condition, results of operations, and/or growth prospects.

If the FDA, the EMA, or any other comparable regulatory authority approves any of our drug candidates for commercial sale, we expect to continue to rely, at least initially, on third parties to manufacture, package, label, store, test, and distribute commercial supplies of such approved drug product. Significant scale-up of manufacturing may require additional comparability validation studies, which the FDA, the EMA, or other comparable regulatory authorities must review and approve. Our third-party manufacturers might not be able to successfully establish such comparability or increase their manufacturing capacity in a timely or economic manner, or at all. If our third-party manufacturers are unable to successfully establish comparability or increase their manufacturing capacity for any drug product, and we are unable to timely establish our own manufacturing capabilities, the commercial launch of that drug candidate could be delayed or there could be a shortage in supply, which could have an adverse effect on our business, financial condition, results of operations, and/or growth prospects.

Our third-party manufacturers' facilities could be damaged by fire, power interruption, information system failure, natural disaster or other similar event, which could cause a delay or shortage in supplies of our drug candidates, which could have an adverse effect on our business, financial condition, results of operations, and/or growth prospects.

Our drug candidates require, and any future drug product will require, precise, high quality manufacturing, packaging, labeling, storage, and testing that meet stringent cGMP, other regulatory requirements and other standards. Our third-party manufacturers are subject to ongoing periodic and unannounced inspections by the FDA, the EMA, and other comparable regulatory authorities to ensure compliance with these cGMPs, other regulatory requirements and other standards. We do not have control over, and are dependent upon, our third-party manufacturers' compliance with these cGMPs, regulations and standards. Any failure by a third-party manufacturer to comply with these cGMPs, regulations or standards or that compromises the safety of any of our drug candidates or any drug product could cause a delay or suspension of production of nonclinical or clinical supplies of our drug candidates or commercial supplies of drug product, cause a delay or suspension of nonclinical or clinical development, product approval and/or commercialization of our drug candidates or drug product, result in seizure or recall of clinical or commercial supplies, result in fines and civil penalties, result in liability for any patient injury or death or

otherwise increase our costs, any of which could have an adverse effect on our business, financial condition, results of operations, and/or growth prospects. If a third-party manufacturer cannot or fails to perform its contractual commitments, does not have sufficient capacity to meet our nonclinical, clinical or eventual commercial requirements or fails to meet cGMPs, regulations or other standards, we have been, and may be, required to replace it or qualify an additional third-party manufacturer. Although we believe there are a number of potential alternative manufacturers, the number of manufacturers with the necessary manufacturing and regulatory expertise and facilities to manufacture biologics like our antibodies is limited. In addition, we have incurred, and could incur, significant additional costs and delays in identifying and qualifying any new third-party manufacturer, due to the technology transfer to such new manufacturer and because the FDA, the EMA, and other comparable regulatory authorities must approve any new manufacturer prior to manufacturing our drug candidates. Such approval would require successful technology transfer, comparability and other testing and compliance inspections. Transferring manufacturing to a new manufacturer could therefore interrupt supply, delay our clinical trials and any commercial launch, and/or increase our costs for our drug candidates, any of which could have an adverse effect on our business, financial condition, results of operations, and/or growth prospects.

Rentschler Biopharma SE ("Rentschler") and Catalent Indiana, LLC ("Catalent Indiana") are our third-party manufacturers of clinical supplies of birtamimab. We are dependent on Rentschler and Catalent Indiana to manufacture these clinical supplies.

Catalent Pharma Solutions, LLC ("Catalent Pharma") and Sharp Sterile Manufacturing, LLC ("Sharp Sterile") are our third-party manufacturers of clinical supplies of our drug candidate PRX012. We are dependent on Catalent Pharma and Sharp Sterile to manufacture these clinical supplies.

Lonza Ltd ("Lonza") is our third-party manufacturer of clinical supplies of our drug candidate PRX019. We are dependent on Lonza to manufacture these clinical supplies.

We are dependent on Roche, and its third-party manufacturers if applicable, to manufacture clinical supplies of prasinezumab.

We are dependent on Novo Nordisk, and its third-party manufacturers if applicable, to manufacture clinical supplies of coramitug.

We are dependent on BMS, and its third-party manufacturers if applicable, to manufacture clinical supplies of BMS-986446.

In July 2021, the Company sold the equity interests of a subsidiary that owns and has exclusive licenses to intellectual property rights and other assets pertaining to the investigational humanized monoclonal antibody known as coramitug (formerly PRX004), and we might not realize the anticipated benefits of such transaction.

On July 8, 2021, the Company, together with its wholly owned subsidiary, Prothena Biosciences Limited ("PBL"), entered into a Share Purchase Agreement with Novo Nordisk and NNRE (together with Novo Nordisk, "Buyer"), pursuant to which PBL sold and transferred to NNRE, all issued and outstanding ordinary shares of Neotope Neuroscience Limited, a wholly owned subsidiary of PBL, for an aggregate purchase price of up to $1.23 billion. The aggregate purchase price consists of an upfront payment of $60 million in cash, subject to customary purchase price adjustments, and an aggregate of $1.17 billion in cash, payable on Buyer's achievement of certain development, commercialization and net sales-based milestones. On November 21, 2022, we earned a $40 million milestone payment. There can be no assurance that such remaining milestones will be met. If we do not receive additional milestone payments as a result of the transaction in anticipated amounts or at all, we may need to seek additional sources of capital to pursue further research, development, and/or commercialization of our drug candidates, and this could have a material adverse effect on our business, financial condition, results of operations, and/or growth prospects.

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

We rely on third-party suppliers for the raw materials 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 raw materials involve several risks, including limited control over pricing, availability, quality, and delivery schedules. We cannot be certain that our suppliers will continue to provide us with the quantities of these raw materials that we require or satisfy our anticipated specifications and quality requirements. Any supply interruption in limited or sole sourced raw materials could materially harm our ability to manufacture our products until a new source of supply, if any, could be identified and qualified. Although we believe there are currently several other suppliers of these raw materials, 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.

Risks Related to Our Intellectual Property

If we are unable to adequately protect or enforce the intellectual property relating to our drug candidates our ability to successfully commercialize our drug candidates will be harmed.

Our success depends in part on our ability to obtain patent protection both in the U.S. and in other countries for our drug candidates. Our ability to protect our drug candidates from unauthorized or infringing use by third parties depends in substantial part on our ability to obtain and maintain valid and enforceable patents. Due to evolving legal standards relating to the patentability, validity and enforceability of patents covering pharmaceutical inventions and the scope of claims made under these patents, our ability to obtain, maintain and enforce patents is uncertain and involves complex legal, factual and scientific questions. Accordingly, rights under any issued patents may not provide us with sufficient protection for our drug candidates or provide sufficient protection to afford us a commercial advantage against competitive products or processes. Additionally, our ability to obtain patent protection for our drug candidates also depends on our collaborators, partners, contractors, and employees involved in the generation of intellectual property to carry out their contractual duties, including those to assign or license relevant intellectual property rights developed on our behalf to us.

In addition, the strength of patents in the biotechnology and pharmaceutical field can be uncertain, and evaluating the scope of such patents involves complex legal, factual, and scientific analyses and has in recent years been the subject of much litigation, resulting in court decisions, including Supreme Court decisions, which have increased uncertainties as to the ability to enforce patent rights in the future. We cannot guarantee that any patents will issue from any pending or future patent applications owned by or licensed to us or our affiliates. In addition, the coverage claimed in a patent application can be significantly reduced before the patent is issued, and its scope can be reinterpreted after issuance. Consequently, we may not obtain or maintain adequate patent protection for any of our programs and product candidates. Even if patents have issued or will issue, we cannot guarantee that the claims of these patents are or will be valid or enforceable or will provide us with any significant protection against competitive products or otherwise be commercially valuable to us. Patent applications in the U.S. are maintained in confidence for up to 18 months after their filing. In some cases, however, patent applications remain confidential in the U.S. Patent and Trademark Office (the "USPTO") for the entire time prior to issuance as a U.S. patent. Similarly, publication of discoveries in the scientific or patent literature often lags behind actual discoveries. Consequently, we cannot be certain that we or our licensors or co-owners were the first to invent, or the first to file patent applications on, our drug candidates or their use as drugs. In the event that a third party has also filed a U.S. patent application relating to our drug candidates or a similar invention, we may have to participate in interference or derivation proceedings declared by the USPTO to determine priority of invention in the U.S. The costs of these proceedings could be substantial and it is possible that our efforts would be unsuccessful, resulting in a loss of our U.S. patent position. Furthermore, we may not have identified all U.S. and non-U.S. patents or published applications that affect our business either by blocking our ability to commercialize our drugs or by covering similar technologies. Composition-of-matter patents on the biological or chemical active pharmaceutical ingredient are generally considered to be the strongest form of intellectual property protection for pharmaceutical products, as such patents provide protection without regard to any method of use. We cannot be certain that the claims in our patent applications covering composition-of-matter of our drug candidates will be considered patentable by the USPTO and courts in the U.S. or by the patent offices and courts in other countries, nor can we be certain that the claims in our issued composition-of-matter patents will not be found invalid or unenforceable if challenged. Method-of-use patents protect the use of a product

for the specified method. This type of patent does not prevent a competitor from making and marketing a product that is identical to our product for an indication that is outside the scope of the patented method. Moreover, even if competitors do not actively promote their product for our targeted indications, physicians may prescribe these products "off-label." Although off-label prescriptions may infringe or contribute to the infringement of method-of-use patents, the practice is common and such infringement is difficult to prevent or prosecute.

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, which may negatively impact our ability to market our products. 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, which may negatively impact our ability to develop and market our drug candidates. Our failure to identify and correctly interpret relevant patents may negatively impact our ability to develop and market our products.

We may be subject to a third-party preissuance submission of prior art to the USPTO and foreign patent agencies, or become involved in opposition, derivation, reexamination, *inter partes* review, post-grant review, or other patent office proceedings or litigation, in the U.S. or elsewhere, challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could result in loss of exclusivity or in patent claims being narrowed, invalidated, or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and products. In addition, given the amount of time required for the development, testing and regulatory review of new drug candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. Any failure to obtain or maintain patent protection with respect to our drug candidates could have a material adverse effect on our business, financial condition, results of operations, and/or growth prospects.

Changes in U.S. patent law could diminish the value of patents in general, thereby impairing our ability to protect our products.

As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involves both technological and legal complexity and is costly, time-consuming, and inherently uncertain. Changes in either the patent laws or interpretation of the patent laws in the United States could increase the uncertainties and costs, and may diminish our ability to protect our inventions, obtain, maintain, and enforce our intellectual property rights and, more generally, could affect the value of our intellectual property or narrow the scope of our owned and licensed patents. Recent patent reform legislation in the United States and other countries, including the Leahy-Smith America Invents Act, or the Leahy-Smith Act, signed into law on September 16, 2011, could increase those uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents. The Leahy-Smith Act includes a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications are prosecuted, redefine prior art and provide more efficient and cost-effective avenues for competitors to challenge the validity of patents. These include allowing third-party submission of prior art to the USPTO during patent prosecution and additional procedures to attack the validity of a patent by USPTO administered post-grant proceedings, including post-grant review, *inter partes* review, and derivation proceedings. After March 2013, under the Leahy-Smith Act, the United States transitioned to a first inventor to file system in which, assuming that the other statutory requirements 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. A third party that files a patent application in the USPTO after March 2013, but before we file an application covering the same invention, could therefore be awarded a patent covering an invention of ours even if we had made the invention before it was made by such third party. This will require us to be cognizant going forward of the time from invention to filing of a patent application. Since patent applications in the United States and most other countries are confidential for a period of time after filing or until issuance, we cannot be certain that we or our licensors were the first to either (i) file any patent application related to our drug candidates and other proprietary technologies we may develop or (ii) invent any of the inventions claimed in our or our licensor's patents or

patent applications. Even where we have a valid and enforceable patent, we may not be able to exclude others from practicing the claimed invention where the other party can show that they used the invention in commerce before our filing date or the other party benefits from a compulsory license. However, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business, financial condition, results of operations, and/or growth prospects.

Recent U.S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents once obtained. Depending on decisions by Congress, the federal courts, the USPTO and the relevant law-making bodies in other countries, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future. We cannot predict how future decisions by Congress, the federal courts or the USPTO may impact the value of our patents.

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

Periodic maintenance fees on any issued patent are due to be paid to the USPTO and foreign patent agencies in several stages over the lifetime of the patent. The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment, and other similar provisions during the patent application process. Although an inadvertent lapse, including due to the effect of geopolitical conflict on us or our patent maintenance vendors, 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. Noncompliance events that could result in abandonment or lapse of a patent or patent application or invalidity of an issued patent include failure to respond to official actions within prescribed time limits, non-payment of fees, failure to properly legalize and submit formal documents, and failure to submit certain prior art. In any such event, our competitors might be able to enter the market, which would have a material adverse effect on our business.

The lives of our patents may not be sufficient to effectively protect our products and business.

Patents have a limited lifespan. In the United States, if all maintenance fees are paid timely, the natural expiration of a patent is generally 20 years after its first effective filing date. Although various extensions may be available, the life of a patent, and the protection it affords, is limited. Given the amount of time required for the development, testing, and regulatory review of new drug candidates, patents protecting such candidates might expire before or shortly after such drug candidates are commercialized. Even if patents covering our drug candidates are obtained, once a patent covering a drug candidate has expired, we may be open to competition, including biosimilar or generic medications. As a result, our patent portfolio may not provide us with sufficient rights to exclude others from commercializing drug candidates similar or identical to ours. Our patents issued as of December 31, 2024, are anticipated to expire on dates ranging from 2025 to 2042, subject to any patent extensions that may be available for such patents. If patents are issued on our patent applications pending as of December 31, 2024, the resulting patents are projected to expire on dates ranging from 2025 to 2045. In addition, although upon issuance in the United States a patent's life can be increased based on certain delays caused by the USPTO, this increase can be reduced or eliminated based on certain delays caused by the patent applicant during patent prosecution. A patent term extension based on regulatory delay may be available in the United States. However, only a single patent can be extended for each first regulatory review period for a product, and any patent can be extended only once, for a single product. Moreover, the scope of protection during the period of the patent term extension does not extend to the full scope of the claim, but instead only to the scope of the product as approved. Laws governing analogous patent term extensions in foreign jurisdictions vary widely, as do laws governing the ability to obtain multiple patents from a single patent family. Additionally, we may not receive an extension if we fail to exercise due diligence during the testing phase or regulatory review process, apply within applicable deadlines, fail to apply prior to expiration of relevant patents or otherwise fail to satisfy applicable requirements. If we are unable to obtain patent term extension or restoration, or the term of any such extension is less than we request, the period during which we will have the right to exclusively market our product will be shortened and our competitors may obtain approval of competing products following our patent expiration and may take advantage of our investment in development and clinical trials by referencing our

clinical and preclinical data to launch their product earlier than might otherwise be the case, and our revenue could be reduced, possibly materially. If we do not have sufficient patent life to protect our products, our business and results of operations will be adversely affected.

We may be 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. For example, we may have inventorship disputes arise from conflicting obligations of consultants or others who are involved in developing our drug candidates. Alternatively, or additionally, we may enter into agreements to clarify the scope of our rights in such intellectual property. Litigation may be necessary to defend against these and other claims challenging inventorship. 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.

We or our licensors may have relied on third-party consultants or collaborators or on funds from third parties, such as the U.S. government, such that we or 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 patents, including 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, results of operations, and prospects.

In addition, while it is our policy to require our employees and contractors who may be involved in the conception or development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who, in fact, conceives or develops intellectual property that we regard as our own. The assignment of intellectual property rights may not be self-executing, or the assignment agreements have been, and may be, breached, and we have been, and may be, forced to bring claims against third parties, or defend claims that they may bring against us, to determine the ownership of what we regard as our intellectual property. We may not have adequate remedies for any breach of our assignment agreements or related claims. Such claims related to the ownership of what we regard as our intellectual property could have a material adverse effect on our business, financial condition, results of operations, and/or growth prospects.

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

Patents are of national or regional effect, and filing, prosecuting, maintaining, and defending patents on drug candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can have a different scope and strength than do those in the United States. In addition, the laws of some foreign countries, particularly certain developing countries, do not currently, or may not in the future, protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and further, may export otherwise infringing products to territories where we have patent protection, but enforcement rights are not as strong as those in the United States. These products may compete with our products and our patents or other intellectual property rights may not be effective or adequate to prevent them from competing.

We license patent rights from third-party owners. Such licenses may be subject to early termination if we fail to comply with our obligations in our licenses with third parties, which could result in the loss of rights or technology that are material to our business.

We are a party to licenses that give us rights to third-party intellectual property or technology that is necessary or useful for our business, and we may enter into additional licenses in the future. Under these license agreements we are obligated to pay the licensor fees, which may include annual license fees, milestone payments, royalties, a percentage of revenues associated with the licensed technology and a percentage of sublicensing revenue. In addition, under certain of such agreements, we are required to diligently pursue the development of products using the licensed technology. If we fail to comply with these obligations, including due to our use of the intellectual property licensed to us in an unauthorized manner, and fail to cure our breach within a specified period of time, the licensor may have the right to terminate the applicable license, in which event we could lose valuable rights and technology that are material to our business, harming our ability to develop, manufacture, and/or commercialize our platform or drug candidates.

In addition, the agreements under which we license intellectual property or technology to or from third parties are complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology or increase what we believe to be our financial or other obligations under the relevant agreement, either of which could have a material adverse effect on our business, financial condition, results of operations, and/or growth prospects. Moreover, if disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on commercially acceptable terms, we may be unable to successfully develop and commercialize the affected drug candidates. Our business also would suffer if any current or future licensors fail to abide by the terms of the license, if the licensors fail to enforce licensed patents against infringing third parties, if the licensed patents or other rights are found to be invalid or unenforceable, or if we are unable to enter into necessary licenses on acceptable terms. Moreover, our licensors may own or control intellectual property that has not been licensed to us and, as a result, we may be subject to claims, regardless of their merit, that we are infringing or otherwise violating the licensor's rights.

In addition, while we cannot currently determine the amount of the royalty obligations we would be required to pay on sales of future products, if any, the amounts may be significant. The amount of our future royalty obligations will depend on the technology and intellectual property we use in products that we successfully develop and commercialize, if any. Therefore, even if we successfully develop and commercialize products, we may be unable to achieve or maintain profitability.

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 research programs or drug candidates and our business, financial condition, results of operations, and/or growth prospects could suffer.

Licensing of intellectual property is of critical importance to our business and involves complex legal, business and scientific issues and is complicated by the rapid pace of scientific discovery in our industry. Disputes may also arise between us and our licensors regarding intellectual property subject to a license agreement, including those relating to:

- 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 on intellectual property of the licensor that is not subject to the license agreement;
- our right to sublicense patent and other rights to third parties under collaborative development relationships;
- whether we are complying with our diligence obligations with respect to the use of the licensed technology in relation to our development and commercialization of our drug candidates, and what activities satisfy those diligence obligations;
- the priority of invention of patented technology;
- the amount and timing of payments owed under license agreements; and

- the allocation of ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and by us and our partners.

If disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, we may be unable to successfully develop and commercialize the affected drug candidates. We are generally also subject to all of the same risks with respect to protection of intellectual property that we license as we are for intellectual property that we own, which are described below. If we or our licensors fail to adequately protect this intellectual property, our ability to commercialize our products could suffer.

We depend, in part, on our licensors to file, prosecute, maintain, defend, and enforce patents and patent applications that are material to our business.

If the licensor retains control of prosecution of the patents and patent applications licensed to us, we may have limited or no control over the manner in which the licensor chooses to prosecute or maintain its patents and patent applications and have limited or no right to continue to prosecute any patents or patent applications that the licensor elects to abandon. If our licensors or any future licensees having rights to file, prosecute, maintain, and defend our patent rights fail to conduct these activities for patents or patent applications covering any of our drug candidates, including due to the impact of geopolitical conflict on our licensors' business operations, our ability to develop and commercialize those drug candidates may be adversely affected and we may not be able to prevent competitors from making, using, or selling competing products. We cannot be certain that such activities by our licensors have been or will be conducted in compliance with applicable laws and regulations or will result in valid and enforceable patents or other intellectual property rights. Pursuant to the terms of the license agreements with some of our licensors, the licensors may have the right to control enforcement of our licensed patents or defense of any claims asserting the invalidity of these patents and, even if we are permitted to pursue such enforcement or defense, we cannot ensure the cooperation of our licensors. We cannot be certain that our licensors will allocate sufficient resources or prioritize their or our enforcement of such patents or defense of such claims to protect our interests in the licensed patents. Even if we are not a party to these legal actions, an adverse outcome could harm our business because it might prevent us from continuing to license intellectual property that we may need to operate our business. In addition, even when we have the right to control patent prosecution of licensed patents and patent applications, enforcement of licensed patents, or defense of claims asserting the invalidity of those patents, we may still be adversely affected or prejudiced by actions or inactions of our licensors and their counsel that took place prior to or after our assuming control. In the event we breach any of our obligations related to such prosecution, we may incur significant liability to our licensing partners.

We may wish to form collaborations in the future with respect to our drug candidates, but may not be able to do so or to realize the potential benefits of such transactions, which may cause us to alter or delay our development and commercialization plans.

Our drug candidates may also require specific components to work effectively and efficiently, and rights to those components may be held by others. We may be unable to in-license any compositions, methods of use, processes or other third-party intellectual property rights from third parties that we identify. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, which would harm our business. If we fail to obtain licenses to necessary third-party intellectual property rights, we may need to cease use of the compositions or methods covered by such third-party intellectual property rights and may need to seek to develop alternative approaches that do not infringe on such intellectual property rights which may entail additional costs and development delays, even if we were able to develop such alternatives, which may not be feasible. Even if we are able to obtain a license, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. In that event, we may be required to expend significant time and resources to develop or license replacement technology. Any delays in entering into new collaborations or strategic partnership agreements related to our drug candidates could delay the development and commercialization of our drug candidates in certain geographies, which could harm our business prospects, financial condition, and results of operations.

The licensing and acquisition of third-party intellectual property rights is a competitive practice, and companies that may be more established, or have greater resources than we do, may also be pursuing strategies to license or acquire third-party intellectual property rights that we may consider necessary or attractive in order to commercialize our drug candidates. More established companies may have a competitive advantage over us due to their larger size and cash resources or greater clinical development and commercialization capabilities. There can be no assurance that we will be able to successfully complete such

negotiations and ultimately acquire the rights to the intellectual property surrounding the additional drug candidates that we may seek to acquire.

Moreover, some of our owned and in-licensed patents or patent applications or future patents are or may be co-owned with third parties. If we are unable to obtain an exclusive license to any such third-party co-owners' interest in such patents or patent applications, such co-owners may be able to license their rights to other third parties, including our competitors, and our competitors could market competing products and technology. In addition, we may need the cooperation of any such co-owners of our patents in order to enforce such patents against third parties, and such cooperation may not be provided to us. Furthermore, our owned and in-licensed patents may be subject to a reservation of rights by one or more third parties. Any of the foregoing could have a material adverse effect on our competitive position, business, financial conditions, results of operations and prospects.

Litigation regarding patents, patent applications, and other proprietary rights may be expensive and time consuming. If we are involved in such litigation, it could cause delays in bringing drug candidates to market and harm our ability to operate.

Our success will depend in part on our ability to operate without infringing the proprietary rights of third parties. Although we are not currently aware of any litigation or other proceedings or third-party claims of intellectual property infringement related to our drug candidates, the pharmaceutical industry is characterized by extensive litigation regarding patents and other intellectual property rights, as well as administrative proceedings for challenging patents, including interference, derivation, *inter partes* review, post-grant review, and reexamination proceedings before the USPTO, or oppositions and other comparable proceedings in foreign jurisdictions, as well as administrative proceedings for challenging patents, including interference, derivation, *inter partes* review, post-grant review, and reexamination proceedings before the USPTO, or oppositions and other comparable proceedings in foreign jurisdictions. Other parties may hold or obtain patents in the future and allege that the use of our technologies infringes these patent claims or that we are employing their proprietary technology without authorization. Furthermore, patent reform and changes to patent laws add uncertainty to the possibility of challenge to our patents in the future. We cannot assure you that our drug candidates and other proprietary technologies we may develop will not infringe existing or future patents owned by third parties.

In addition, third parties may challenge our existing or future patents. Competitors may also infringe our patents or other intellectual property or the intellectual property of our licensors. To cease such infringement or unauthorized use, we may be required to file patent infringement claims, which can be expensive and time-consuming and divert the time and attention of our management and scientific personnel. Proceedings involving our patents or patent applications or those of others could result in adverse decisions regarding:

- the patentability of our inventions relating to our drug candidates; and/or
- the enforceability, validity or scope of protection offered by our patents relating to our drug candidates; and/or
- findings that our drug candidates, products, or activities infringe third-party patents or other intellectual property rights.

Litigation or other legal proceedings relating to intellectual property claims, with or without merit, is unpredictable and generally expensive and time consuming and, even if resolved in our favor, is likely to divert significant resources from our core business including distracting our technical and management personnel from their normal responsibilities. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and more mature and developed intellectual property portfolios. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace.

Third parties asserting their patent or other intellectual property rights against us may seek and obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize our drug candidates or force us to cease some of our business operations. Defense of these claims, regardless of their merit, would involve substantial litigation

expense and would be a substantial diversion of management and other employee resources from our business, cause development delays, and may impact our reputation. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business.

In the event we are able to establish third-party infringement of our patents, the court may decide not to grant an injunction against further infringing activity and instead award only monetary damages, which may or may not be an adequate remedy. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our ordinary shares.

If we are unable to avoid infringing the patent rights of others, we may be required to seek a license, defend an infringement action, or challenge the validity of the patents in court. Patent litigation is costly and time consuming. We may not have sufficient resources to bring these actions to a successful conclusion. In addition, if we do not obtain a license, develop or obtain non-infringing technology, fail to defend an infringement action successfully, or have infringed patents declared invalid, we may:

- incur substantial monetary damages, including treble damages and attorneys' fees for willful infringement;
- obtain one or more licenses from third parties and potentially pay royalties;
- redesign our infringing products, which may be impossible on a cost-effective basis or require substantial time and monetary expenditure;
- encounter significant delays in bringing our drug candidates to market; and/or
- be precluded from participating in the manufacture, use, or sale of our drug candidates or methods of treatment requiring licenses.

In that event, we would be unable to further develop and commercialize our drug candidates, which could harm our business significantly.

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

Our current or future trademarks or trade names may be challenged, infringed, circumvented, declared generic or descriptive, or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names or may be forced to stop using these names, which we need for name recognition by potential partners or customers in our markets of interest. During trademark registration proceedings, we may receive rejections of our applications by the USPTO or in other foreign jurisdictions. Although we would be given an opportunity to respond to those rejections, we may be unable to overcome such rejections. In addition, in the USPTO and in comparable agencies in many foreign jurisdictions, third parties are given an opportunity to oppose pending trademark applications and to seek to cancel registered trademarks. Opposition or cancellation proceedings may be filed against our trademarks, and our trademarks may not survive such proceedings. If we are unable to establish name recognition based on our trademarks and trade names, we may not be able to compete effectively and our business may be adversely affected. We may license our trademarks and trade names to third parties, such as distributors. Though these license agreements may provide guidelines for how our trademarks and trade names may be used, a breach of these agreements or misuse of our trademarks and tradenames by our licensees may jeopardize our rights in or diminish the goodwill associated with our trademarks and trade names.

Moreover, any name we have proposed to use with our drug candidate in the United States must be approved by the FDA, regardless of whether we have registered it, or applied to register it, as a trademark. Similar requirements exist in Europe. The FDA typically conducts a review of proposed product names, including an evaluation of potential for confusion with other product names. If the FDA (or an equivalent administrative body in a foreign jurisdiction) objects to any of our proposed

proprietary product names, it may be required to expend significant additional resources in an effort to identify a suitable substitute name that would qualify under applicable trademark laws, not infringe the existing rights of third parties and be acceptable to the FDA. Furthermore, in many countries, owning and maintaining a trademark registration may not provide an adequate defense against a subsequent infringement claim asserted by the owner of a senior trademark. At times, competitors or other third parties may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of other registered trademarks or trademarks that incorporate variations of our registered or unregistered trademarks or trade names. If we assert trademark infringement claims, a court may determine that the marks we have 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 this case, we could ultimately be forced to cease use of such trademarks.

We may be unable to adequately prevent disclosure of trade secrets and other proprietary information.

We rely on trade secrets to protect our proprietary technologies, especially where we do not believe patent protection is appropriate or obtainable; however, trade secrets are difficult to protect. We rely in part on confidentiality agreements with our employees, consultants, outside scientific collaborators, sponsored researchers, and other advisors to protect our trade secrets and other proprietary information. 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. Any disclosure, either intentional or unintentional, by our employees, the employees of third parties with whom we share our facilities or third-party consultants and vendors that we engage to perform research, 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 our market. In addition, others may independently discover our trade secrets and proprietary information, and we would have no right to prevent them from using that technology or information to compete with us. 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. Furthermore, the laws of some foreign countries do not protect proprietary rights to the same extent or in the same manner as the laws of the United States. As a result, we may encounter significant problems in protecting and defending our intellectual property both in the United States and abroad. If we are unable to prevent unauthorized material disclosure of our intellectual property to third parties, or misappropriation of our intellectual property by third parties, we will not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business, operating results, and financial condition.

We may be subject to claims that our employees, collaborators, partners, contractors, or advisors have wrongfully used or disclosed alleged trade secrets of third parties.

Many of our employees were previously employed at universities, Elan or Elan subsidiaries, or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Likewise, our collaborators, partners, contractors, and advisors may have in the past, or may currently, work with or for universities, or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees do not use the proprietary information or know-how of third parties is not disclosed to us or used in their work for us, we may be subject to claims that we or our employees, collaborators, partners, contractors, or advisors have used or disclosed intellectual property, including trade secrets or other proprietary information, of third parties. Litigation may be necessary to defend against these claims. Even if we are successful in defending against these claims, litigation could result in substantial cost and be a distraction to our management and employees. 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, be derived from, or benefited from the knowledge of the trade secrets or other proprietary information of third parties. 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, results of operations and financial condition. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.

Intellectual property rights do not necessarily address all potential threats to our competitive advantage.

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

- others may be able to make drug candidates that are similar to ours but that are not covered by the claims of the patents that we own or have exclusively licensed;
- we or our licensors or future collaborators might not have been the first to make the inventions covered by the issued patent or pending patent application that we own or have exclusively licensed;
- we or our licensors or future collaborators might not have been the first to file patent applications covering certain of our inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights;
- it is possible that our pending patent applications will not lead to issued patents;
- issued patents that we own or have exclusively licensed may be held invalid or unenforceable, as a result of legal challenges by our competitors;
- our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we may not develop additional proprietary technologies that are patentable;
- we cannot predict the scope of protection of any patent issuing based on our patent applications, including whether the patent applications that we own or in-license will result in issued patents with claims that cover our drug candidates or uses thereof in the United States or in other foreign countries;
- the claims of any patent issuing based on our patent applications may not provide protection against competitors or any competitive advantages, or may be challenged by third parties;
- if enforced, a court may not hold that our patents are valid, enforceable and infringed;
- we may need to initiate litigation or administrative proceedings to enforce and/or defend our patent rights which will be costly whether we win or lose;
- we may choose not to file a patent in order to maintain certain trade secrets or know-how, and a third party may subsequently file a patent covering such intellectual property;
- we may fail to adequately protect and police our trademarks and trade secrets; and
- the patents of others may have an adverse effect on our business, including if others obtain patents claiming subject matter similar to or improving that covered by our patents and patent applications.

Should any of these events occur, they could significantly harm our business, results of operations, and prospects.

Risks Related to Our Ordinary Shares

The market price of our ordinary shares may fluctuate widely.

Our ordinary shares commenced trading on the Nasdaq Global Market on December 21, 2012 and currently trade on the Nasdaq Global Select Market. We cannot predict the prices at which our ordinary shares may trade. The market price of our ordinary shares may fluctuate widely, depending upon many factors, some of which may be beyond our control, including:

- our ability to obtain financing as needed;
- progress in and results from our ongoing or future nonclinical research and clinical trials;
- the execution of our agreements with third parties, including with Roche, BMS, and Novo Nordisk;
- failure or delays in advancing our nonclinical drug candidates or other drug candidates we may develop in the future into clinical trials;
- results of clinical trials conducted by others, including on drugs that would compete with our drug candidates;
- issues in manufacturing our drug candidates;
- regulatory developments or enforcement in the U.S. and other countries;
- developments or disputes concerning patents or other proprietary rights;
- introduction of technological innovations or new commercial products by our competitors;
- changes in estimates or recommendations by securities analysts, if any, who cover our company;
- public concern over our drug candidates;
- litigation;
- future sales of our ordinary shares by us or by existing shareholders;
- general market conditions;
- changes in the structure of healthcare payment systems;
- failure of any of our drug candidates, if approved, to achieve commercial success;
- economic and other external factors or other disasters or crises;
- period-to-period fluctuations in our financial results;
- overall fluctuations in U.S. equity markets;
- our quarterly or annual results, or those of other companies in our industry;
- announcements by us or our competitors of significant acquisitions or dispositions;
- the operating and ordinary share price performance of other comparable companies;
- investor perception of our company and the drug development industry;

- natural or environmental disasters that investors believe may affect us;
- changes in tax laws or regulations applicable to our business or the interpretations of those tax laws and regulations by taxing authorities; or
- fluctuations in the budgets of federal, state and local governmental entities around the world.

These and other external factors may cause the market price and demand for our ordinary shares to fluctuate substantially, which may limit or prevent investors from readily selling their ordinary shares and may otherwise negatively affect the liquidity of our ordinary shares. In particular, stock markets in general have experienced volatility that has often been unrelated to the operating performance of a particular company. These broad market fluctuations may adversely affect the trading price of our ordinary shares. Some companies that experienced volatility in the trading price of their stock have been the subject of securities class action litigation. If any of our shareholders brought a lawsuit against us, we could incur substantial costs defending the lawsuit. Such a lawsuit could also divert the time and attention of our management.

Your percentage ownership in Prothena may be diluted in the future.

As with any publicly traded company, your percentage ownership in us may be diluted in the future because of equity issuances for acquisitions, capital raising transactions (including the sale of ordinary shares pursuant to our Amended Distribution Agreement, as may be further amended from time to time, and as discussed below), or otherwise. We may need to raise additional capital in the future. If we are able to raise additional capital, we may issue equity or convertible debt instruments, which may severely dilute your ownership interest in us. In addition, we intend to continue to grant option awards to our directors, officers and employees, which would dilute your ownership stake in us. As of December 31, 2024, the number of ordinary shares available for issuance pursuant to outstanding and future equity awards under our equity plans was 15,332,174.

If we are unable to maintain effective internal controls, our business could be adversely affected.

We are subject to the reporting and other obligations under the U.S. Securities Exchange Act of 1934, as amended, including the requirements of Section 404 of the U.S. Sarbanes-Oxley Act, which require annual management assessments of the effectiveness of our internal control over financial reporting. In addition, under Section 404(b) of the U.S. Sarbanes-Oxley Act, if we are either an "accelerated filer" or "large accelerated filer," our independent registered public accounting firm must attest to the effectiveness of our internal control over financial reporting. The rules governing the standards that must be met for management to assess our internal control over financial reporting are complex and require significant documentation, testing and possible remediation to meet the detailed standards under the rules. During the course of its testing, our management may identify material weaknesses or deficiencies which may not be remedied in time to meet the deadline imposed by the Sarbanes-Oxley Act. These reporting and other obligations place significant demands on our management and administrative and operational resources, including accounting resources.

Our management is responsible for establishing and maintaining adequate internal control over financial reporting. Our internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of our financial statements for external purposes in accordance with accounting principles generally accepted in the U.S. During the course of our review and testing of our internal controls, we have identified, and may identify in the future, deficiencies and may be unable to remediate them before we must provide the required reports. Furthermore, if we have a material weakness in our internal controls over financial reporting, we may not detect errors on a timely basis and our consolidated financial statements may be materially misstated. We, or our independent registered public accounting firm (if required), may not be able to conclude on an ongoing basis that we have effective internal control over financial reporting, which could harm our operating results, cause investors to lose confidence in our reported financial information and cause the trading price of our stock to fall.

We cannot provide assurance that a material weakness will not occur in the future, or that we will be able to conclude on an ongoing basis that we have effective internal controls over financial reporting in accordance with Section 404 and the related rules and regulations of the SEC when required. A material weakness in internal control over financial reporting 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 a company's annual or interim consolidated financial statements will not be prevented or detected on a timely basis by the company's internal controls. If we cannot in the future favorably assess, or our independent registered public accounting firm (if required), is unable to provide an unqualified attestation report on, the effectiveness of our internal controls over financial reporting, investor confidence in the reliability of our financial reports may be adversely affected, which could have a material adverse effect on our share price. In addition, any failure to report our financial results on an accurate and timely basis could result in sanctions, lawsuits, delisting of our shares from the Nasdaq Global Select Market or other adverse consequences that would have an adverse effect on our business, financial position and results of operations.

If we were treated as a passive foreign investment company for U.S. federal income tax purposes, it could result in adverse U.S. federal income tax consequences to United States holders of our ordinary shares.

Significant potential adverse U.S. federal income tax implications generally apply to U.S. investors owning shares of a passive foreign investment company ("PFIC"), directly or indirectly. In general, we would be a PFIC for a taxable year if either (i) 75% or more of our income constitutes passive income, or (ii) 50% or more of our assets produce passive income or are held for the production of passive income. Changes in the composition of our active or passive income, passive assets or changes in our fair market value may cause us to become a PFIC. A separate determination must be made each taxable year as to whether we are a PFIC (after the close of each taxable year).

We do not believe we were a PFIC for U.S. federal income tax purposes for our taxable year ended December 31, 2024. However, the application of the PFIC rules is subject to uncertainties in a number of respects, and we cannot assure that the U.S. Internal Revenue Service (the "IRS") will not take a contrary position. We also cannot assure that we will not be a PFIC for U.S. federal income tax purposes for the current taxable year or any future taxable year.

We may not be able to successfully maintain our tax rates, which could adversely affect our business and financial condition, results of operations and growth prospects.

We are incorporated in Ireland and maintain subsidiaries or offices in Ireland and the U.S. We are able to achieve a low average tax rate through the performance of certain functions and ownership of certain assets in tax-efficient jurisdictions, together with intra-group service agreements. However, changes in tax laws or interpretations thereof in any of these jurisdictions could adversely affect our ability to do so in the future. Taxing authorities, such as the IRS and the Irish Revenue Commissioners ("Irish Revenue"), actively audit and otherwise challenge these types of arrangements, and have done so in our industry. We are subject to reviews and audits by the IRS, Irish Revenue and other taxing authorities from time to time, and the IRS, Irish Revenue or other taxing authorities may challenge our structure and inter-group arrangements. The Company's U.S. subsidiaries are currently under examination by the IRS for the tax year 2021. Responding to or defending against challenges from taxing authorities may be expensive and time consuming, and may divert management's time and focus away from operating our business. We cannot predict whether and when taxing authorities will conduct an audit, challenge our tax structure or the cost involved in responding to any such audit or challenge. If we are unsuccessful, we may be required to pay taxes for prior periods, interest, fines or penalties, and may be obligated to pay increased taxes in the future, all of which could have an adverse effect on our business, financial condition, results of operations, and/or growth prospects. In addition to the impact of changes in tax laws, our provision for income tax can be materially impacted, for example, by the geographical mix of our profits and losses, changes in our business, such as internal restructuring and acquisitions, changes and accounting guidance and other regulatory, legislative or judicial developments changes in tax rates, tax audit determinations, changes in our uncertain tax positions, changes in our intent and capacity to permanently reinvest foreign earnings, changes to our transfer pricing practices, tax deductions attributed to equity compensation and changes in our need for a valuation allowance for deferred tax assets.

Future changes to the tax laws relating to multinational corporations could adversely affect us.

Under current law, we are treated as a foreign corporation for U.S. federal tax purposes. However, changes to the U.S. Internal Revenue Code, U.S. Treasury Regulations or other IRS guidance thereunder could adversely affect our status as a foreign corporation or otherwise affect our effective tax rate. For example, in 2017 the United States enacted tax reform that contained significant changes to corporate taxation, including a provision that requires capitalization and amortization of research and development costs over five years for tax years beginning after December 31, 2021. In addition, the Irish Government, Irish Revenue, U.S. Congress, the IRS, the Organization for Economic Co-operation and Development

("OECD"), and other governments and agencies in jurisdictions where we do business have recently focused on issues related to the taxation of multinational corporations, including the OECD's Global Anti-Base Erosion Model Rules (Pillar Two), which apply a 15% global minimum tax rate on a jurisdiction-by-jurisdiction basis to groups with turnover of not less than €750 million in at least two of the four prior fiscal years. Pillar Two has been implemented into Irish law with effect for periods beginning on or after December 31, 2023. As a result of Pillar Two or other policy changes, whether at national or supranational level, the tax laws in Ireland, the U.S., and other countries in which we do business could change on a prospective or retroactive basis, and any such changes could have an adverse effect on our business, financial condition, results of operations, and/or growth prospects.

Irish law differs from the laws in effect in the United States and may afford less protection to holders of our ordinary shares.

It may not be possible to enforce court judgments obtained in the U.S. against us in Ireland based on the civil liability provisions of the U.S. federal or state securities laws. In addition, there is uncertainty as to whether the courts of Ireland would recognize or enforce judgments of U.S. courts obtained against us or our directors or officers based on the civil liabilities provisions of the U.S. federal or state securities laws or hear actions against us or those persons based on those laws. We have been advised that the U.S. currently does not have a ratified treaty providing for the reciprocal recognition and enforcement of judgments in civil and commercial matters with Ireland. Therefore, a final judgment for the payment of money rendered by any U.S. federal or state court based on civil liability, whether or not based solely on federal or state securities laws, would not automatically be enforceable in Ireland.

As an Irish incorporated company, we are governed by the Irish Companies Act 2014, as amended (the "Companies Act"), which differs in some material respects from laws generally applicable to U.S. corporations and shareholders, including, among others, differences relating to interested director and officer transactions and shareholder lawsuits. Likewise, the duties of directors and officers of an Irish company generally are owed to the company only. Shareholders of Irish companies generally do not have a personal right of action against directors or officers of the company and may exercise such rights of action on behalf of the company only in limited circumstances. Accordingly, holders of our ordinary shares may have more difficulty protecting their interests than would holders of securities of a corporation incorporated in a jurisdiction of the U.S.

The operation of the Irish Takeover Rules may affect the ability of certain parties to acquire our ordinary shares.

Under the Irish Takeover Panel Act, 1997, Takeover Rules, 2022 (the "Irish Takeover Rules"), if an acquisition of ordinary shares were to increase the aggregate holding of the acquirer and its concert parties to ordinary shares that represent 30% or more of the voting rights of the company, the acquirer and, in certain circumstances, its concert parties would be required (except with the consent of the Irish Takeover Panel) to make an offer for the outstanding ordinary shares at a price not less than the highest price paid for the ordinary shares by the acquirer or its concert parties during the previous 12 months. This requirement would also be triggered by an acquisition of ordinary shares by a person holding (together with its concert parties) ordinary shares that represent between 30% and 50% of the voting rights in the company if the effect of such acquisition were to increase that person's percentage of the voting rights by 0.05% within a 12 month period. Under the Irish Takeover Rules, certain separate concert parties are presumed to be acting in concert. Our board of directors and their relevant family members, related trusts and "controlled companies" are presumed to be acting in concert with any corporate shareholder who holds 20% or more of our shares. The application of these presumptions may result in restrictions upon the ability of any of the concert parties and/or members of our board of directors to acquire more of our securities, including under the terms of any executive incentive arrangements. In the future, we may consult with the Irish Takeover Panel with respect to the application of this presumption and the restrictions on the ability to acquire further securities, although we are unable to provide any assurance as to whether the Irish Takeover Panel will overrule this presumption. Accordingly, the application of the Irish Takeover Rules may restrict the ability of certain of our shareholders and directors to acquire our ordinary shares.

Irish law differs from the laws in effect in the United States with respect to defending unwanted takeover proposals and may give our board of directors less ability to control negotiations with hostile offerors.

We are subject to the Irish Takeover Rules, pursuant to which our Board is not permitted to take any action that might frustrate an offer for our ordinary shares once our Board has received an approach that may lead to an offer or has reason to believe that such an offer is or may be imminent, subject to certain exceptions. Potentially frustrating actions such as (i) the issue of ordinary shares, options or convertible securities, (ii) material acquisitions or disposals, (iii) entering into contracts

other than in the ordinary course of business, or (iv) any action, other than seeking alternative offers, which may result in frustration of an offer, are prohibited during the course of an offer or at any earlier time during which our Board has reason to believe an offer is or may be imminent. These provisions may give our Board less ability to control negotiations with hostile offerors and protect the interests of holders of ordinary shares than would be the case for a corporation incorporated in a jurisdiction of the U.S.

Irish law requires that our shareholders renew every five years the authority of our Board of Directors to issue shares and to do so for cash without applying the statutory pre-emption right, and if our shareholders do not renew these authorizations by May 17, 2027 (or any renewal is subject to limitations), our ability to raise additional capital to fund our operations would be limited.

As an Irish incorporated company, we are governed by the Companies Act. The Companies Act requires that every five years our shareholders renew the separate authorities of our Board to (a) allot and issue shares, and (b) opt out of the statutory pre-emption right that otherwise applies to share issuances for cash (which pre-emption right would require that shares issued for cash be offered to our existing shareholders on a pro rata basis before the shares may be issued to new shareholders). At our shareholders' annual general meeting held on May 17, 2022, our shareholders authorized our Board to issue ordinary shares up to the amount of our authorized share capital, and to opt out of the statutory pre-emption right for such issuances. Under Irish law, these authorizations will expire on May 17, 2027, five years after our shareholders last renewed these authorizations. Irish law requires that our shareholders renew the authority for our Board to issue ordinary shares by a resolution approved by not less than 50% of the votes cast at a general meeting of our shareholders. Irish law requires that our shareholders renew the authority of our Board to opt out of the statutory pre-emption right in share issuances for cash by a resolution approved by not less than 75% of the votes cast at a general meeting of our shareholders. If these authorizations are not renewed before May 17, 2027, or are renewed with limitations, our Board would be limited in its ability to issue shares, which would limit our ability to raise additional capital to fund our operations, including the research, development and potential commercialization of our drug candidates.

Transfers of our ordinary shares may be subject to Irish stamp duty.

Irish stamp duty may be payable in respect of transfers of our ordinary shares (currently at the rate of 1% of the price paid or the market value of the shares acquired, if greater).

Under the Irish Stamp Duties Consolidation Act, 1999 (the "Stamp Duties Act"), a transfer of our ordinary shares from a seller who holds shares through The Depository Trust Company ("DTC") to a buyer who holds the acquired shares through DTC will not be subject to Irish stamp duty. Shareholders may also transfer their shares into or out of DTC without giving rise to Irish stamp duty provided that there is no change in the beneficial ownership of such shares and the transfer into or out of DTC is not effected in contemplation of a subsequent sale of such shares to a third party; in order to benefit from this exemption from Irish stamp duty, the seller must confirm to us that there is no change in the ultimate beneficial ownership of the shares as a result of the transfer and there is no agreement for the sale of the shares by the beneficial owner to a third party being contemplated.

A transfer of our ordinary shares (i) by a seller who holds shares outside of DTC to any buyer, or (ii) by a seller who holds the shares through DTC to a buyer who holds the acquired shares outside of DTC, may be subject to Irish stamp duty. Payment of any Irish stamp duty is generally a legal obligation of the transferee.

Any Irish stamp duty payable on transfers of our ordinary shares could adversely affect the price of those shares.

We do not anticipate paying cash dividends, and accordingly, shareholders must rely on ordinary share appreciation for any return on their investment.

We anticipate losing money for the foreseeable future and, even if we do turn a profit, we do not anticipate declaring or paying any cash dividends for the foreseeable future. Therefore, the success of an investment in our ordinary shares will depend upon appreciation in their value and in order to receive any income or realize a return on your investment, you will need to sell your Prothena ordinary shares. There can be no assurance that our ordinary shares will maintain their price or appreciate in value.

Dividends paid by us may be subject to Irish dividend withholding tax.

Although we do not currently anticipate paying cash dividends, if we were to do so in the future, an Irish dividend withholding tax (currently at a rate of 25%) may arise. A number of exemptions from Irish dividend withholding tax exist such that shareholders resident in the U.S. and shareholders resident in other countries that have entered into a double taxation treaty with Ireland may be entitled to exemptions from Irish dividend withholding tax subject to the completion of certain dividend withholding tax declaration forms.

Shareholders entitled to an exemption from Irish dividend withholding tax on any dividends received from us will not be subject to Irish income tax in respect of those dividends, unless they have some connection with Ireland other than their shareholding (for example, they are resident in Ireland). Non-Irish resident shareholders who receive dividends subject to Irish dividend withholding tax will generally have no further liability to Irish income tax on those dividends.

Prothena ordinary shares received by means of a gift or inheritance could be subject to Irish capital acquisitions tax.

Irish capital acquisitions tax ("CAT") could apply to a gift or inheritance of our ordinary shares irrespective of the place of residence, ordinary residence or domicile of the parties. This is because our ordinary shares will be regarded as property situated in Ireland. The person who receives the gift or inheritance has primary liability for CAT. Gifts and inheritances passing between spouses are exempt from CAT. It is recommended that each shareholder consult his or her own tax advisor as to the tax consequences of holding our ordinary shares or receiving dividends from us.

REVIEW OF BUSINESS PERFORMANCE

Overview

Our clinical research and development pipeline includes six therapeutic antibody programs currently in clinical development: birtamimab for the potential treatment of AL amyloidosis; prasinezumab, in collaboration with Roche, for the potential treatment of Parkinson's disease and other related synucleinopathies; coramitug, which is being developed by Novo Nordisk, for the potential treatment of ATTR amyloidosis; PRX012 for the potential treatment of Alzheimer's disease; and BMS-986446 and PRX019, in collaboration with BMS, for the potential treatment of Alzheimer's disease and neurodegenerative diseases respectively.

In addition to our clinical development pipeline, we have recently received clearance by the FDA for an investigational new drug (IND) application for PRX123. PRX123 is our Alzheimer's disease vaccine program and was also granted Fast Track designation from the FDA. We also have a number of discovery- and late-preclinical-stage programs targeting proteins implicated in neurological diseases.

While we are modality agnostic, we have deep expertise in antibody targeting and have developed a diverse pipeline that includes antibody as well as small molecule and vaccine approaches. We believe a diverse portfolio positions us to make an impact on a broad spectrum of diseases and we may also pursue opportunities in other modalities such as gene and cell therapies.

2024 Performance Highlights. Highlights of the Company's performance during 2024 include the following:

- ***We Made Significant Advances in our Neurodegenerative Diseases Portfolio.***
  - PRX012, a wholly-owned potential best-in-class, next-generation subcutaneous antibody for the treatment of Alzheimer's disease (AD) that targets a key epitope at the N-terminus of amyloid beta (Aβ) with high binding potency. In 2024, Prothena continued enrollment in our ongoing ASCENT clinical trials (reaching approximately 260 patients) and presented posters at the Alzheimer's Association International Conference (AAIC) and the Clinical Trials on Alzheimer's Disease conference (CTAD) highlighting the clinical trial design of the Phase 1 ASCENT clinical trials.
  - BMS-986446 (formerly PRX005), a potential best-in-class antibody for the treatment of AD that specifically targets a key epitope within the microtubule binding region (MTBR) of tau, a protein implicated in the causal pathophysiology of AD. BMS-986446 is part of the global neuroscience research and development collaboration with Bristol Myers

Squibb (BMS). In 2024, BMS continued to enroll the ongoing Phase 2 TargetTau-1 clinical trial in approximately 475 patients with early Alzheimer's disease and presented the design of the ongoing Phase 2 TargetTau-1 clinical trial in a poster presentation at AAIC and an oral encore presentation at CTAD.

- Prasinezumab, a potential first-in-class antibody, for the treatment for Parkinson's disease (PD), that is designed to target key epitopes within the C-terminus of alpha-synuclein and is the focus of the worldwide collaboration with Roche. In 2024, Roche reported results from the Phase 2b PADOVA clinical trial in patients with early-stage Parkinson's disease missed the primary endpoint but showed a numerical delay in motor progression and positive trends on multiple secondary and exploratory endpoints suggesting possible clinical benefit. Roche announced that they will continue to evaluate the data and work together with health authorities to determine next steps.
- PRX019, a potential treatment of neurodegenerative diseases with an undisclosed target, is part of the global neuroscience research and development collaboration with BMS. In 2024, Bristol Myers Squibb obtained the exclusive global license for PRX019 for $80 million; and Prothena initiated a Phase 1 first-in-human clinical trial to evaluate the safety, tolerability, immunogenicity, and pharmaco-kinetics of single ascending and multiple doses in healthy adults.

- ***We Made Significant Advances in our Rare Peripheral Amyloid Diseases Portfolio.***
  - Birtamimab, a wholly-owned potential best-in-class amyloid depleter antibody for the treatment of AL amyloidosis designed to directly neutralize soluble toxic light chain aggregates and promote clearance of amyloid that causes organ dysfunction and failure. In 2024, Prothena published Birtamimab's mechanism of action and pharmacological characteristics in Leukemia & Lymphoma and presented Longitudinal Health-Related Quality of Life data (SF-36v2) across domains from the VITAL Phase 3 clinical trial at the International Society of Amyloidosis. We continued the confirmatory Phase 3 AFFIRM-AL clinical trial (NCT04973137) in patients with Mayo Stage IV AL amyloidosis under a Special Protocol Assessment (SPA) agreement with the FDA with a primary endpoint of all cause mortality (time-to-event) at a significance level of 0.10.
  - Coramitug (formerly PRX004), a potential first-in-class amyloid depleter antibody for the treatment of ATTR cardiomyopathy designed to deplete the pathogenic, non-native forms of the transthyretin (TTR) protein and is being developed by Novo Nordisk as part of their up to $1.2 billion acquisition of our ATTR amyloidosis business and pipeline. In 2024, Phase 1 clinical trial results for coramitug in patients with ATTR amyloidosis was published in Amyloid, the official journal of the International Society of Amyloidosis, and Novo Nordisk continued the ongoing Phase 2 signal-detection clinical trial in patients with ATTR-CM.

- ***We Carefully Managed our Cash Balance.***
  - During fiscal year 2024, we carefully managed our capital. While progressing all of our development programs described above, our cash used in operating and investing activities was $150.3 million, which was in-line with our guidance range of $148 to $160 million. We finished fiscal year 2024 with $472.2 million in cash, cash equivalents, and restricted cash, including cash used in operating and financing activities, which exceeded our guidance of $468 million, providing a solid financial foundation for continuing to advance the Company's discovery and clinical programs.

Results of Operations

Comparison of Years Ended December 31, 2024 and 2023

Revenue

	Year Ended December 31,		Change	
	2024	2023	$	%
	(Dollars in thousands)			
Collaboration revenue	$ 135,107	$ 91,320	$ 43,787	48 %
Revenue from license and intellectual property	50	50	—	— %
Total revenue	$ 135,157	$ 91,370	$ 43,787	48 %

Directors' Report *(continued)*

Total revenue was $135.2 million and $91.4 million for the years ended December 31, 2024, and 2023, respectively.

Collaboration revenue from BMS increased $43.8 million for the year ended December 31, 2024, compared to the year ended December 31, 2023. Collaboration revenue from BMS for 2024 included recognition of $110.1 million from the PRX019 Global License Agreement and related development services and $25.0 million was related to BMS's material rights for the US Rights and Global Rights for the TDP-43 Collaboration Target that expired unexercised as a result of the expiration of the research term of the Collaboration Agreement. Collaboration revenue from BMS for 2023 included recognition of $91.3 million from the Tau Global License Agreement and related development services. See Note 6, "Significant Agreements" to the Consolidated Financial Statements regarding the Collaboration Agreement with BMS for more information.

License and intellectual property revenue for the year ended December 31, 2024 was $50,000 compared to $50,000 for the year ended December 31, 2023. See Note 6, "Significant Agreements" to the Consolidated Financial Statements regarding the Novo Nordisk Share Purchase Agreement for more information.

Assuming no significant change in our business, we expect our 2025 revenue to decline over the prior year as our 2024 revenue was primarily comprised of nonrecurring revenue.

Operating Expenses

	Year Ended December 31,		Change	
	2024	2023	$	%
	(Dollars in thousands)			
Research and development	$ 222,519	$ 220,571	$ 1,948	1 %
General and administrative	67,199	61,835	5,364	9 %
Total operating expenses	$ 289,718	$ 282,406	$ 7,312	3 %

Total operating expenses consist of R&D expenses, general and administrative ("G&A") expenses. Our operating expenses were $289.7 million and $282.4 million for the years ended December 31, 2024, and 2023, respectively.

Our research activities are aimed at developing new drug products. Our development activities involve the translation of our research into potential new drugs. Our R&D expenses primarily consist of personnel costs and related expenses, including share-based compensation and external costs associated with clinical activities and drug development related to our drug programs, including birtamimab, BMS-986446 (PRX005), PRX012, PRX123, PRX019 and preclinical activities related to our discovery programs.

Our G&A expenses primarily consist of personnel costs and related expenses, including share-based compensation and consulting expenses.

Research and Development Expenses

Our R&D expense increased by $1.9 million for the year ended December 31, 2024, compared to the prior year. The increase for the year ended December 31, 2024, was primarily due to higher clinical trial expenses primarily related to the PRX012 and birtamimab programs, higher personnel expenses; offset in part by lower manufacturing expense and lower other R&D expenses.

The following table sets forth the R&D expenses for our major programs (specifically, any active program with successful first dosing in a Phase 1 clinical trial), which were birtamimab, prasinezumab, coramitug, BMS-986446 (PRX005), PRX012, PRX019 and other R&D expenses for the years ended December 31, 2024, and 2023 (in thousands):

	Year Ended December 31,	
	2024	2023
Birtamimab (NEOD001)	$ 85,649	$ 68,831
Prasinezumab (PRX002/RG7935)	49	34
Coramitug (NNC6019/PRX004)[1]	4	91
BMS-986446 (PRX005)	264	10,063
PRX012	116,359	102,767
PRX019[2]	5,035	7,703
Other R&D[3]	15,159	31,082
Total research and development	$ 222,519	$ 220,571

(1) *On July 8, 2021, we sold shares of one of our wholly-owned subsidiaries to Novo Nordisk. In connection with the transaction, Novo Nordisk acquired our ATTR amyloidosis business, including the clinical stage antibody coramitug (PRX004). Expenses incurred relate to certain close out activities and transition services provided to Novo Nordisk.*

(2) *R&D costs include the costs incurred from the date when PRX019 was separately tracked in preclinical development.*

(3) *Other R&D is comprised primarily of preclinical development and discovery programs that have not progressed to first patient dosing in a Phase 1 clinical trial and close out costs for programs that we are no longer advancing.*

General and Administrative Expenses

Our G&A expenses increased by $5.4 million, for the year ended December 31, 2024, compared to the prior year primarily due to higher personnel expense.

Other Income (Expense)

	Year Ended December 31,		Change	
	2024	2023	$	%
	(Dollars in thousands)			
Interest income	$ 25,816	$ 31,014	$ (5,198)	(17)%
Other income (expense), net	(185)	(458)	273	(60)%
Total other income (expense), net	$ 25,631	$ 30,556	$ (4,925)	(16)%

Interest income decreased by $5.2 million for the year ended December 31, 2024, compared to the prior year, primarily due to lower interest income from our cash and money market accounts resulting from lower interest rates and lower cash and money market balances.

Other income (expense), net for the year ended December 31, 2024, was primarily foreign exchange losses from transactions with vendors denominated in euros.

Provision for (benefit from) Income Taxes

	Year Ended December 31,		Change	
	2024	2023	$	%
	(Dollars in thousands)			
Benefit from income taxes	$ (6,620)	$ (13,452)	$ 6,832	(51)%

The benefit from income taxes decreased by $6.8 million for the year ended December 31, 2024, compared to the same period in the prior year. The decline in benefit from income taxes for the year ended December 31, 2024, compared to the prior year, was primarily due to a lower increase in deferred tax assets related to Section 174 R&D Capitalization.

The tax provisions for all periods presented primarily reflect U.S. federal taxes associated with recurring profits attributable to intercompany services that our U.S. subsidiary performs for the Company. No tax benefit has been recorded related to tax losses recognized in Ireland and any deferred tax assets for those losses are offset by a valuation allowance.

Comparison of the years ended December 31, 2023 and 2022

Refer to "Review of Business Performance" in our 2023 Directors Report and Consolidated Financial Statements for a discussion of the business performance for the year ended December 31, 2023 compared to the year ended December 31, 2022.

FINANCIAL RISK MANAGEMENT

We are exposed to market risks in the ordinary course of our business including the effect of changes in foreign currency exchange rates and interest rates. Market risk represents the risk of loss that may impact our financial position due to adverse changes in financial market prices and rates.

Foreign Currency Risk

Our business is primarily conducted in U.S. dollars except for our agreements with contract manufacturers for drug supplies which are primarily denominated in euros. We recorded losses on foreign currency exchange rate differences of approximately $185,000, $458,000 and $397,000 during the years ended December 31, 2024, 2023 and 2022, respectively. If we increase our business activities that require the use of foreign currencies, we may be exposed to losses if the euro and other such currencies strengthen against the U.S. dollar.

Interest Rate Risk

Our exposure to interest rate risk is limited to our cash equivalents, which consist of accounts maintained in money market funds. We have assessed that there is no material exposure to interest rate risk given the nature of money market funds. In general, money market funds are not subject to interest rate risk because the interest paid on such funds fluctuates with the prevailing interest rate. Accordingly, our interest income fluctuates with short-term market conditions.

In the future, we anticipate that our exposure to interest rate risk will primarily be related to our investment portfolio. We may invest any surplus funds in accordance with a policy approved by our board of directors which will specify the categories, allocations, and ratings of securities we may consider for investment. The primary objectives of our investment policy are to preserve principal and maintain proper liquidity to meet our operating requirements. Our investment policy also specifies credit quality standards for our investments and limits the amount of credit exposure to any single issue, issuer or type of investment.

Credit Risk

Financial instruments that potentially subject us to concentration of credit risk consist of cash and cash equivalents and accounts receivable. We place our cash and cash equivalents with high credit quality financial institutions and pursuant to our investment policy, we limit the amount of credit exposure with any one financial institution. Deposits held with banks have exceeded, and will continue to exceed, federally insured limits on such deposits. We are exposed to credit risk in the event of a

default by the financial institutions holding our cash and cash equivalents. We have not experienced any losses on our deposits of cash and cash equivalents. Our credit risk exposure is up to the extent recorded on the Company's Consolidated Balance Sheets.

Liquidity Risk

As of December 31, 2024, we had $471.4 million in cash and cash equivalents. Based on our current business plans, we believe that our existing cash and cash equivalents at December 31, 2024 are sufficient to meet our obligations for at least the next twelve months. To operate beyond such period, or if we elect to increase our spending on research and development programs significantly above current long-term plans or enter into potential licenses and/or other acquisitions of complementary technologies, products or companies, we may need additional capital. Additionally, in order to develop and obtain regulatory approval for our potential products we will need to raise substantial additional capital. We expect to continue to finance future capital needs that exceed our existing cash and cash equivalents, payments pursuant to our agreements with Roche, BMS, and Novo Nordisk, and, to the extent necessary, other collaboration agreements with corporate partners, or other arrangements, and through proceeds from public or private equity or debt financings, and loans, including pursuant to the Amended Distribution Agreement (See Note 7, "Shareholders' Equity" to the Consolidated Financial Statements for more information). We cannot assume that such additional financings will be available on acceptable terms, if at all, and such financings may only be available on terms dilutive to our shareholders.

In managing our liquidity needs in Ireland, we do not rely on unrepatriated earnings as a source of funds. As of December 31, 2024, $265.3 million of our outstanding cash and cash equivalents related to U.S. operations are considered permanently reinvested. We do not intend to repatriate these funds. However, if these funds were repatriated back to Ireland, we would incur a withholding tax from the dividend distribution.

The adequacy of our cash resources depends on many assumptions, including assumptions with respect to our expenses. These assumptions may prove to be wrong, and we could use our available capital resources sooner than we currently expect. Because of the numerous risks and uncertainties associated with the development and commercialization of our product candidates, we are unable to estimate the amounts of increased capital outlays and operating expenses associated with completing the development of our product candidates. Our future capital requirements will depend on numerous factors, including, without limitation, the timing of initiation, progress, results and costs of our clinical trials; the results of our research and nonclinical studies; the costs of clinical manufacturing and of establishing commercial manufacturing arrangements; the costs of preparing, filing and prosecuting patent applications and maintaining, enforcing and defending intellectual property-related claims; the costs and timing of capital asset purchases; our ability to establish research collaborations, strategic collaborations, licensing or other arrangements; the costs to satisfy our obligations under current and potential future collaborations; the costs of any in-licensing transactions; and the timing, receipt, and amount of revenues or royalties, if any, from any approved drug candidates.

Our cash and cash equivalents may also be potentially supplemented in the future by proceeds from our collaboration partners BMS (formerly Celgene), Roche and milestone payments from Novo Nordisk. Pursuant to the Collaboration Agreement with Roche, we are eligible to receive payments for commercial and regulatory milestones and royalties on net sales of Collaboration Products. See Note 6, "Significant Agreements" to our Consolidated Financial Statements regarding the Roche License Agreement for more information. Pursuant to the Collaboration Agreement with BMS, we are eligible to receive payments for commercial and regulatory milestones and royalties on net sales of Collaboration Products. See Note 6, "Significant Agreements" to our Consolidated Financial Statements regarding the Collaboration Agreement with BMS for more information. Pursuant to the share purchase agreement with Novo Nordisk, we are eligible to receive development and sales milestone payments. See Note 6, "Significant Agreements" to our Consolidated Financial Statements regarding the Novo Nordisk Share Purchase Agreement for more information.

ACCOUNTING RECORDS

The directors believe that they have complied with the requirement of Sections 281 to 285 of the Companies Act 2014 with regard to adequate accounting records by engaging the services of a fellow group undertaking which employs accounting personnel with appropriate expertise and by providing adequate resources to the financial function. The accounting records of the Company are located at the offices of its wholly owned subsidiary Prothena Biosciences Inc, in Brisbane, California, U.S.

Directors' Report *(continued)*

Such accounting records as are required to be kept at a place within Ireland, under Section 283(2) of the Companies Act 2014, are located at the Company's office in Dublin, Ireland.

RELEVANT AUDIT INFORMATION

The directors believe that they have taken all steps necessary to make themselves aware of any relevant audit information and have established that the group's statutory auditor is aware of that information. In so far as they are aware, there is no relevant audit information of which the group's statutory auditor is unaware.

AUDIT COMMITTEE

The Company's Board of Directors ("the Board") has an Audit Committee. The Audit Committee's primary purposes are to oversee our corporate accounting and financial reporting processes and the audits and reviews of our financial statements, as well as our legal and ethical compliance activities. Among other matters, the Audit Committee is responsible for the appointment, compensation, retention, and oversight of our independent registered public accounting firm (the "auditor"); reviewing and confirming the auditor's independence; periodically reviewing the adequacy and effectiveness of the Company's internal control over financial reporting; reviewing with the management and the auditor the audited and reviewed financial statements to be included in the Company's annual and quarterly reports, respectively, filed with the SEC. The Audit Committee also reviews the Company's major risk exposures — including cybersecurity risks — and steps to control them, and reviews the Company's policies, programs, and systems intended to ensure compliance with applicable laws and ethical standards.

The current members of our Audit Committee are Ms. Cobb, Mr. Collier, and Mr. Cooke. Mr. Cooke serves as chair of the Committee. Each member of the Committee is an "independent director" and meets the heightened independence requirements and also meets the financial literacy requirements under Nasdaq rules. Our Board has determined that Mr. Cooke is an "audit committee financial expert" as defined under SEC rules and each has the requisite additional financial sophistication required under Nasdaq rules. The Audit Committee operates under a written charter, a copy of which is available on our website at *https://ir.prothena.com/corporate-governance*.

DIRECTORS' COMPLIANCE STATEMENT

The directors acknowledge that they are responsible for securing compliance by the Company with its relevant obligations, as defined in the Companies Act 2014 (the "Relevant Obligations").

The directors confirm that they have drawn up a statement setting out the Company's policies that, in the directors' opinion, are appropriate to the Company respecting compliance by the Company with its Relevant Obligations.

The directors further confirm that the Company has put in place appropriate arrangements or structures that are, in the directors' opinion, designed to secure material compliance with the Company's relevant obligations and that they have conducted a review of these arrangements or structures during the financial year to which this report relates.

DIRECTORS, SECRETARIES AND THEIR INTEREST

The directors and secretaries who held office at December 31, 2024 had no interests other than those shown below in the shares of the Company.

The Company had nine directors serving on its Board of Directors at December 31, 2024. The following table sets forth information regarding interest in shares and share options held by each of the directors and secretary who held office at December 31, 2024.

Directors' Report *(continued)*

Name	December 31, 2024		2023	
	Shares	Options	Shares	Options
Daniel G. Welch (appointed 21 February 2024)	—	147,000	—	—
Paula K. Cobb	—	112,500	—	97,500
Richard T. Collier	1,219	131,554	1,219	116,554
Shane M. Cooke	—	131,554	—	116,554
William H. Dunn, Jr.	—	45,000	—	30,000
Lars G. Ekman	243	131,544	243	116,544
Helen S. Kim	—	60,000	—	45,000
Gene G. Kinney	12,793	2,421,700	12,793	2,114,700
Dennis J. Selkoe	4,208	100,044	4,208	85,044
Secretary				
Michael J. Malecek	—	434,000	—	349,000
Yvonne M. Tchrakian	—	31,450	—	25,200

The Company's Constitution requires that at least one-third (which, if not a round number, is rounded to the number which is nearest to and less than one-third) of the directors (excluding any director who wishes to retire and does not wish to offer themselves for re-appointment, and any director appointed by the Board to fill a vacancy since the last annual general meeting) must stand for election at each annual general meeting of shareholders, and that directors must stand for election no later than the third annual general meeting subsequent to their election or appointment to the Board. Generally, vacancies on the Board may be filled only by ordinary resolution of the Company's shareholders or the affirmative vote of a majority of the remaining directors. A director appointed by the Board to fill a vacancy will serve until the subsequent annual general meeting and must stand for election at that time.

As of the date of this Directors' Report, we have nine directors serving on our Board. Our Board currently is divided into the following groups:

- Paula K. Cobb and Lars G. Ekman, whose current terms will expire at the Annual Meeting;
- Helen S. Kim, Gene G. Kinney, and Dennis J. Selkoe, whose current terms will expire no later than the annual general meeting of shareholders to be held in 2026; and
- Richard T. Collier, Shane M. Cooke, William H. Dunn, Jr., and Daniel G. Welch, whose current terms will expire no later than the annual general meeting of shareholders to be held in 2027.

Ms. Cobb, Dr. Ekman, and Dr. Kinney have been nominated by the Board to stand for election. Each of Ms. Cobb, Dr. Ekman, and Dr. Kinney were previously elected to the Board by our shareholders. The Board nominated Dr. Kinney to stand for election even though his three-year term does not expire until 2026 because the Company's Constitution requires that one-third of the directors (excluding any director who wishes to retire and does not wish to offer themselves for re-appointment, and any director appointed by the Board to fill a vacancy since the last annual general meeting) stand for election at each annual general meeting and that a director longest in office since being appointed or last elected must be nominated to complete such slate of directors. If elected by our shareholders at the Annual Meeting, Ms. Cobb, Dr. Ekman, and Dr. Kinney will each hold office from the date of their election until no later than the third subsequent annual general meeting of shareholders (i.e., in 2028), or until their earlier death, resignation, or removal.

In order to be elected as a director, each nominee must receive the affirmative vote of a majority of the votes cast in person or by proxy at the Annual Meeting; if a director nominee does not receive this majority vote, such nominee will not be elected to the Board. In the event that any nominee becomes unavailable for election as a result of an unexpected occurrence, the proxy holders may vote your shares for the election of any substitute nominee whom the Board proposes.

ACQUISITION OF COMPANY'S OWN SHARES

The Company or a nominee of the Company does not hold any shares or interest in shares in the Company.

Directors' Report *(continued)*

POLITICAL AND CHARITABLE CONTRIBUTION

During the year, the group and the Company did not make any donations disclosable in accordance with Section 26(1) of The Electoral Act, 1997 (as amended).

POST BALANCE SHEET EVENTS

No important events affecting the Company have taken place since the end of the financial year.

DIVIDENDS

The group recorded a loss of $122.3 million for the year ended December 31, 2024 (2023: loss of $147.0 million). The consolidated results of the group are set out on page 63 of the financial statements. The directors do not recommend the payment of a dividend.

SIGNIFICANT SHAREHOLDINGS

Ordinary Shares

As of December 31, 2024, the Company had 100,000,000 ordinary shares authorized for issuance with a par value of $0.01 per ordinary share and 53,826,982 ordinary shares issued and outstanding. Each ordinary share is entitled to one vote and, on a pro rata basis, to dividends when declared and the remaining assets of the Company in the event of a winding up. As of December 31, 2024, 15,332,174 ordinary shares are reserved for issuance pursuant to outstanding and future equity awards under the Company's equity incentive plans.

Euro Deferred Shares

As of December 31, 2024, the Company had 10,000 Euro Deferred Shares authorized for issuance with a nominal value of €22 per share. No Euro Deferred Shares are outstanding at December 31, 2024. The rights and restrictions attaching to the Euro Deferred Shares rank *pari passu* with the ordinary shares and are treated as a single class in all respects.

December 2022 Offering

In December 2022, the Company completed an underwritten public offering of an aggregate of 3,250,000 of its ordinary shares at a public offering price of $56.50 per ordinary share. The Company received aggregate net proceeds of approximately $172.4 million, after deducting the underwriting discount and offering costs.

In January 2023, the Company issued an additional 395,096 ordinary shares resulting from the underwriters' partial exercise of their 30-day option to purchase up to an additional 487,500 ordinary shares of as part of the December 2022 underwritten public offering. The Company received approximately $20.9 million proceeds from the exercise, net of underwriting discount but before deducting any offering costs.

At-the-Market Offerings

In December 2021, the Company entered into an Equity Distribution Agreement (the "December 2021 Distribution Agreement"), pursuant to which the Company could issue and sell, from time to time, the Company's ordinary shares. In connection with entering into the December 2021 Distribution Agreement, on December 23, 2021, the Company filed with the SEC a prospectus supplement relating to the offer, issuance and sale of up to $250.0 million of the Company's ordinary shares (the "December 2021 Prospectus") pursuant to the December 2021 Distribution Agreement.

For the years ended December 31, 2023, and 2022 the Company sold and issued 42,361 and 911,228 ordinary shares, respectively, pursuant to the December 2021 Distribution Agreement under the December 2021 Prospectus. For the years ended December 31, 2023, and 2022, total gross proceeds were approximately $3.2 million and $53.1 million, respectively, before deducting underwriting discounts, commissions, and other offering expenses payable by the Company of $0.1 million and $1.7 million, respectively.

Directors' Report *(continued)*

The December 2021 Prospectus was no longer effective as of March 23, 2024. As of March 23, 2024, the Company had sold and issued 953,589 ordinary shares pursuant to the December 2021 Distribution Agreement under the December 2021 Prospectus for total gross proceeds of approximately $56.3 million before deducting underwriting discounts, commissions, and other offering expenses paid by the Company of $1.8 million.

In February 2024, the Company amended the Equity Distribution Agreement that it entered into in December 2021 (the "Amended Distribution Agreement"), pursuant to which the Company may issue and sell, from time to time, the Company's ordinary shares. In connection with amending the Amended Distribution Agreement, on February 22, 2024, the Company filed with the SEC a prospectus relating to the offer, issuance, and sale of up to $250.0 million of the Company's ordinary shares (the "February 2024 Prospectus") pursuant to the Amended Distribution Agreement. For the year ended December 31, 2024, the Company sold and issued no ordinary shares pursuant to the Amended Distribution Agreement under the February 2024 Prospectus.

The issuance and sale of the Company's ordinary shares pursuant to the December 2021 Distribution Agreement and the Amended Distribution Agreement is deemed an "at-the-market" offering and is registered under the Securities Act of 1933, as amended.

The following table presents information as to the beneficial ownership of our ordinary shares as of March 3, 2025 for each person, or group of affiliated persons, known by us to beneficially own more than 5% of our ordinary shares.

Percentage ownership of our ordinary shares in the table is based on 53,826,982 ordinary shares issued and outstanding on March 3, 2025, the Company's Record Date for its 2025 Proxy Statement.

Name and Address of Beneficial Owner	Total Shares Deemed Beneficially Owned	Percent of Outstanding Shares
5% Shareholders:		
Entities Associated with EcoR1 Capital, LLC 357 Tehama Street, #3 San Francisco, California 94103, USA	11,584,280	21.5%
Entities Associated with Fidelity Investments 245 Summer Street Boston, Massachusetts 02210, USA	8,049,796	15.0%
William P. Scully 771 Manatee Cove Vero Beach, Florida 32963, USA	5,558,290	10.3%
Wellington Management Company LLP c/o Wellington Management Company LLP 280 Congress Street, Boston Massachusetts 02210, USA	5,130,876	9.5%
Todd W. Fennell 979 Beachland Boulevard Vero Beach, Florida 32963, USA	4,645,147	8.6%
T. Rowe Price Associates, Inc. 100 E Pratt Street Baltimore, Maryland, 21202, USA	3,822,434	7.1%
BlackRock, Inc. 55 East 52nd Street New York, New York 10055, USA	3,770,650	7.0%

Directors' Report *(continued)*

SUBSIDIARY UNDERTAKINGS

The Company's subsidiaries at December 31, 2024 are Prothena Biosciences Limited (formerly known as Neotope Biosciences Limited), Othair Prothena Limited, Prothena Pharma Limited, and Prothena Platform Technologies Limited which are located in Ireland, and Prothena Biosciences Inc and Prothena Finance Inc which are located in the U.S.

PROPERTIES

Our corporate registered address and office is in Dublin, Ireland and our U.S. operations are in Brisbane, California.

In Dublin, Ireland, we occupy approximately 920 square feet of office spaces under two leases which expire on July 31, 2025.

In Brisbane, California, we occupy approximately 31,157 square feet of office and laboratory space under a sublease with Arcus Biosciences, Inc. which expires on September 30, 2028, unless terminated earlier.

We believe that our facilities are sufficient to meet our current needs.

EMPLOYEES

As of December 31, 2024, we had 163 employees, of whom 116 were engaged in research and development activities and the remainder were working in general and administrative areas. The vast majority of these employees are in the U.S.

To attract and retain qualified employees, we offer a total rewards package consisting of base salary and cash target bonus, a comprehensive benefit and wellness package, and equity compensation for every employee. An objective of our equity incentive program has been, and continues to be, to align the interests of equity incentive plan participants with those of our shareholders. We benchmark and survey the market to ensure we maintain competitive compensation and benefits programs for our employees.

GOING CONCERN

These Consolidated and Parent Company Financial Statements have been prepared on a going concern basis. On the basis of its current cash resources and its business plan for 2025 and 2026 the directors believe that the Group and Parent Company have adequate resources to continue in operational existence for at least the next 12 months and that it is appropriate to continue to adopt the going concern basis in preparing the financial statements. These financial statements do not include any adjustments that would result from the going concern basis of preparation being inappropriate.

AUDITOR

Pursuant to Section 383(2) of the Companies Act 2014, the Company's auditor, KPMG, Chartered Accountants, will continue in office.

On behalf of the board:

/s/ Gene G. Kinney	/s/ Shane M. Cooke	
Gene G. Kinney	Shane M. Cooke	March 20, 2025
Director	*Director*	

Prothena Corporation plc

Statement of Directors' Responsibilities in respect of the annual report and the financial statements

The directors are responsible for preparing the annual report and financial statements in accordance with applicable law and regulations.

Company law requires the directors to prepare Group and Parent Company financial statements for each financial year. Under that law the directors have elected to prepare the Group financial statements in accordance with US Generally Accepted Accounting Principles ('US GAAP'). The directors have elected to prepare the Company financial statements in accordance with IFRS as adopted by the European Union applicable law. Under company law the directors must not approve the Group and Company financial statements unless they are satisfied that they give a true and fair view of the assets, liabilities and financial position of the Group and Parent Company and of the Group's profit or loss for the period then ended.

The directors are responsible for keeping adequate accounting records which disclose with reasonable accuracy at any time the assets, liabilities, financial position of the Group and Parent Company and the profit and loss of the Group and which enable them to ensure that the financial statements are prepared in accordance with the applicable accounting framework and comply with the provision of the Companies Act 2014. The directors are also responsible for taking all reasonable steps to ensure such records are kept by its subsidiaries which enable them to ensure that the financial statements of the Group comply with the provisions of the Companies Act 2014. They are responsible for such internal controls as they determine is necessary to enable the preparation of financial statements that are free from material misstatement, whether due to fraud or error, and have a general responsibility for safeguarding the assets of the Parent Company and the Group, and hence for taking reasonable steps for the prevention and detection of fraud and other irregularities. The directors are also responsible for preparing a directors' report that complies with the requirements of the Companies Act 2014.

In preparing the Group and Parent Company financial statements, the directors are required to:

- select suitable accounting policies and then apply them consistently;
- make judgments and estimates that are reasonable and prudent;
- state whether applicable Accounting Standards have been followed, subject to any material departures disclosed and explained in the financial statements;
- assess the Group and Parent Company's ability to continue as a going concern, disclosing, as applicable, matters related to going concern; and
- use the going concern basis of accounting unless as regards the Group, liquidation is imminent and as regards the Parent Company, they either intend to liquidate the Parent Company or to cease operations, or have no realistic alternative but to do so.

The directors are responsible for the maintenance and integrity of the Financial Statements included on the Company's website. Legislation in Ireland governing the preparation and dissemination of financial statements may differ from legislation in other jurisdictions.

On behalf of the board:

/s/ Gene G. Kinney	/s/ Shane M. Cooke	
Gene G. Kinney	Shane M. Cooke	March 20, 2025
Director	*Director*	

Independent Auditor's Report to the Members of Prothena Corporation plc

Report on the audit of the financial statements

Opinion

We have audited the financial statements of Prothena Corporation plc ('the Parent Company') and its consolidated undertakings ('the Group') for the year ended December 31, 2024 set out on pages 62 to 105, which comprise the Consolidated and Parent Company Balance Sheets, the Consolidated Profit and Loss Account, the Consolidated and Parent Company Statements of Shareholders' Equity, the Consolidated and Parent Company Statements of Cash Flows and related notes, including the summary of significant accounting policies set out in note 2.

The financial reporting framework that has been applied in their preparation is Irish law and US Generally Accepted Accounting Principles ("US GAAP") and as regards the Parent Company financial statements, Irish law and International Financial Reporting Standards ("IFRS") as adopted by the European Union.

In our opinion:

- The Group financial statements give a true and fair view, in accordance with US GAAP, of the assets, liabilities and financial position of the Group as at December 31, 2024 and of the Group's loss for the year then ended;
- the Parent Company balance sheet gives a true and fair view, in accordance with IFRS as adopted by the European Union, of the assets, liabilities and financial position of the Parent Company as at December31, 2024;
- the Group financial statements have been properly prepared in accordance with US GAAP, as permitted by the Companies Act 2014;
- the Parent Company financial statements have been properly prepared in accordance with IFRS as adopted by the European Union, as applied in accordance with the provisions of the Companies Act 2014; and
- the Group and Company financial statements have been properly prepared in accordance with the requirements of the Companies Act 2014.

Basis for opinion

We conducted our audit in accordance with International Standards on Auditing (Ireland) (ISAs (Ireland)) and applicable law. Our responsibilities under those standards are further described in the Auditor's Responsibilities for the audit of the financial statements section of our report. We have fulfilled our ethical responsibilities under, and we remained independent of the Group in accordance with ethical requirements that are relevant to our audit of financial statements in Ireland, including the Ethical Standard issued by the Irish Auditing and Accounting Supervisory Authority (IAASA), as applied to listed entities.

We believe that the audit evidence we have obtained is sufficient and appropriate to provide a basis for our opinion.

Report on the audit of the financial statements *(continued)*

Conclusions relating to going concern

In auditing the financial statements, we have concluded that the directors' use of the going concern basis of accounting in the preparation of the financial statements is appropriate. Our evaluation of the directors' assessment of the Group's and Parent Company's ability to continue to adopt the going concern basis of accounting included:

- considering the Group's and Parent Company's cash position as of December 31, 2024;
- analysing the scenario cashflow projections prepared by management and considering the reasonableness of the underlying assumptions.

Based on the work we have performed, we have not identified any material uncertainties relating to events or conditions that, individually or collectively, may cast significant doubt on the Group or the Parent Company's ability to continue as a going concern for a period of at least twelve months from the date when the financial statements are authorised for issue.

Our responsibilities and the responsibilities of the directors with respect to going concern are described in the relevant sections of this report.

Detecting irregularities including fraud

We identified the areas of laws and regulations that could reasonably be expected to have a material effect on the financial statements and risks of material misstatement due to fraud, using our understanding of the entity's industry, regulatory environment and other external factors and inquiry with the directors. In addition, our risk assessment procedures included:

- Inquiring with the directors as to the Group's policies and procedures regarding compliance with laws and regulations, identifying, evaluating and accounting for litigation and claims, as well as whether they have knowledge of non-compliance or instances of litigation or claims.
- Inquiring of directors as to the Group's policies and procedures to prevent and detect fraud, as well as whether they have knowledge of any actual, suspected or alleged fraud.
- Inquiring of directors and the audit committee, regarding their assessment of the risk that the financial statements may be materially misstated due to irregularities, including fraud.
- Inspecting the Group's regulatory and legal correspondence.
- Reading Board and audit committee meeting minutes.
- Performing planning analytical procedures to identify any usual or unexpected relationships.

We discussed identified laws and regulations, fraud risk factors and the need to remain alert among the audit team.

Firstly, the Group is subject to laws and regulations that directly affect the financial statements including companies and financial reporting legislation. We assessed the extent of compliance with these laws and regulations as part of our procedures on the related financial statement items, including assessing the financial statement disclosures and agreeing them to supporting documentation when necessary.

Report on the audit of the financial statements *(continued)*

Detecting irregularities including fraud *(continued)*

Secondly, the Group is subject to many other laws and regulations where the consequences of non-compliance could have a material effect on amounts or disclosures in the financial statements, for instance through the imposition of fines or litigation. We identified the following areas as those most likely to have such an effect: health and safety, anti-bribery, employment law, environmental law, regulatory capital and liquidity.

Auditing standards limit the required audit procedures to identify non-compliance with these non-direct laws and regulations to inquiry of the directors and inspection of regulatory and legal correspondence, if any. These limited procedures did not identify actual or suspected non-compliance..

We assessed events or conditions that could indicate an incentive or pressure to commit fraud or provide an opportunity to commit fraud. As required by auditing standards, we performed procedures to address the risk of management override of controls. On this audit we do not believe there is a fraud risk related to revenue recognition. We did not identify any additional fraud risks.

In response to the fraud risks, we also performed procedures including:

- Identifying journal entries to test based on risk criteria and comparing the identified entries to supporting documentation.
- Assessing significant accounting estimates for bias.

As the Group is regulated, our assessment of risks involved obtaining an understanding of the legal and regulatory framework that the Group operates and gaining an understanding of the control environment including the entity's procedures for complying with regulatory requirements.

Owing to the inherent limitations of an audit there is an unavoidable risk that we may not have detected some material misstatements in the financial statements, even though we have properly planned and performed our audit in accordance with auditing standards. For example, the further removed non-compliance with laws and regulations (irregularities) is from the events and transactions reflected in the financial statements, the less likely the inherently limited procedures required by auditing standards would identify it.

In addition, as with any audit, there remains a higher risk of non-detection of irregularities, as these may involve collusion, forgery, intentional omissions, misrepresentations, or the override of internal controls. We are not responsible for preventing non-compliance and cannot be expected to detect non-compliance with all laws and regulations.

Key audit matters: our assessment of risks of material misstatement

Key audit matters are those matters that, in our professional judgement, were of most significance in the audit of the financial statements and include the most significant assessed risks of material misstatement (whether or not due to fraud) identified by us, including those which had the greatest effect on: the overall audit strategy; the allocation of resources in the audit; and directing the efforts of the engagement team. These matters were addressed in the context of our audit of the financial statements as a whole, and in forming our opinion thereon, and we do not provide a separate opinion on these matters.

Report on the audit of the financial statements *(continued)*

Key audit matters: our assessment of risks of material misstatement *(continued)*

In arriving at our audit opinion above, the key audit matters were as follows (unchanged from 2023).

Group key audit matters

Evaluation of Accrued Research and Development Costs $13.4m (2023: $14.7m)

Refer to note 2 on page 67 (significant accounting policies)

The key audit matter	How the matter was addressed in our audit
As discussed in Notes 2 and 4 to the consolidated financial statements, research and development costs are expensed by the Company as incurred. As of December 31, 2024, the Company recognised accrued research and development costs of $13.4 million and prepaid research and development expenses of $12.0 million. Costs for certain development activities, such as clinical trials, are recognised based on an evaluation of the progress to completion of specific tasks using data such as patient enrollment, clinical site activations, or information provided to the Company by its vendors, including contract research organisations, on their actual costs incurred. Expense accruals related to clinical trials are recognised based on the Company's estimate of the degree of completion of the events specified in the specific clinical study or trial contract. Payments for these activities are based on the terms of the individual arrangements, which may differ from the pattern of costs incurred, and are reflected in the consolidated financial statements as prepaid or accrued research and development. We identified the evaluation of certain prepaid and accrued research and development costs relating to contract research organisations and investigative sites as a key audit matter. Complex and subjective auditor judgment was involved in evaluating the estimated degree of completion of the events specified in the specific clinical study or trial contract used to determine certain prepaid and accrued research and development costs due to the nature and extent of evidence available. For the reasons outlined above the engagement team determine this matter to be a key audit matter.	Our audit procedures included: • We evaluated the design and tested the operating effectiveness of certain internal controls related to prepaid and accrued research and development costs. This included a control related to the estimated degree of completion of the events specified in the specific clinical study or trial contract. • For a sample of certain prepaid and accrued research and development costs, we agreed the amount, duration and any key terms to the underlying contract. • We examined underlying documentation and third-party evidence from contract research organisations and compared them to the significant inputs used in developing the estimated degree of completion of the events specified in the specific clinical study or trial contract. • In addition, we inquired of the individuals who are responsible for monitoring and tracking the status of the clinical trials to understand the degree of completion of the reported activities. Based on evidence obtained, we found that the judgements made by management were supported by reasonable assumptions. The significant judgement made by the engagement team was in evaluating the estimated degree of completion of the events specified in the specific clinical study or trial contract used to determine certain prepaid and accrued research and development costs due to the nature and extent of evidence available.

Report on the audit of the financial statements *(continued)*

Key audit matters: our assessment of risks of material misstatement *(continued)*

Parent Company key audit matters

Financial Assets $745.5 million (2023: $826.0 million)

Refer to note 1 on page 100 (significant accounting policies) and 3 on page 101 (financial disclosures)

The key audit matter	How the matter was addressed in our audit
The carrying amount of the Parent Company's Financial Assets represents 91.31% (2023: 70.19%) of the Parent Company's total assets. At December 31, 2024, the carrying value of Financial Assets was $745.5 million. There is a risk in respect of the carrying value of these Financial Assets if the market capitalisation not sufficient to support the balance sheet value. For the reasons outlined above the engagement team determine this matter to be a key audit matter.	Our audit procedures included: • We compared the carrying value of Financial Assets in the Parent Company's Balance Sheet to the net assets of the subsidiary financial statements. • We compared the carrying value of Financial Assets to the market capitalisation of the Parent Company at December 31, 2024. Based on evidence obtained, we found management's assessment of the carrying value of Financial Assets undertakings to be appropriate. There was no significant judgement associated with the testing performed.

Our application of materiality and an overview of the scope of our audit

Materiality for the Group financial statements and Parent Company financial statements as a whole was set at $14.00m (2023: $13.70m) and $14.00m (2023: $13.70m) respectively, determined with reference to benchmarks of total Group operating expenses and Parent Company total assets (of which it represents 4.83% (2023: 4.85%) and 1.71% (2023: 1.16%)) respectively.

We consider total expenses and total assets to be the most appropriate benchmark for the Group financial statements and the Parent Company Financial Statements respectively, having considered the loss making nature of the Group, the holding company activities of the Parent Company and the focus for users of the financial statements.

In applying our judgement in determining the most appropriate benchmark, the factors, which had the most significant impact were:

- the elements of the financial statements
- the items on which the attention of the users of the particular entity's financial statements tends to be focused and the industry and economic environment in which the entity operates, and
- the entity's ownership structure and the way it is financed.

Report on the audit of the financial statements *(continued)*

Our application of materiality and an overview of the scope of our audit *(continued)*

Performance materiality for the Group financial statements and Parent Company financial statements as a whole was set at $10.5m (2023: $10.275m) and $10.5m (2023: $10.275m) respectively, determined with reference to benchmarks of total expenses for the Group and total assets for the Parent Company (of which it represents 3.6% (2023: 3.6%) and 1.29% (2023: 0.87%)) respectively. We applied this percentage in our determination of performance materiality based on the level of identified control deficiencies during the prior period.

We reported to the Audit Committee any corrected or uncorrected identified misstatements exceeding $0.7m (2023: $0.51m), in addition to other identified misstatements that warranted reporting on qualitative grounds. Our audit was undertaken to the materiality and performance materiality level specified above and we applied materiality to assist us determine what risks were significant risks and the procedures to be performed.

As part of establishing the overall Group audit strategy and plan, we conducted risk assessment procedures and we have determined for the purpose of the Group Audit that the entire Group is considered to be one component. We tailored the scope of our audit to ensure that we performed sufficient audit procedures to be able to give an opinion on the financial statements as a whole.

Our audit was conducted over the consolidated results of the Group as a whole and our audit team included team members from the US office. We liaised extensively with the US team members in order to assess the audit risk and strategy and work undertaken. Video and telephone conference meetings were held in which the US team communicated their findings to the wider audit team.

Other Information

The directors are responsible for the other information presented in the Annual Report together with the financial statements. The other information comprises the information included in the directors' report. The financial statements and our auditor's report thereon do not comprise part of the other information. Our opinion on the financial statements does not cover the other information and, accordingly, we do not express an audit opinion or, except as explicitly stated below, any form of assurance conclusion thereon.

Our responsibility is to read the other information and, in doing so, consider whether, based on our financial statements audit work, the information therein is materially misstated or inconsistent with the financial statements or our audit knowledge. Based solely on that work we have not identified material misstatements in the other information.

Based solely on our work on the other information, we report that:

- we have not identified material misstatements in the directors' report;
- in our opinion, the information given in the directors' report is consistent with the financial statements;
- in our opinion, the directors' report has been prepared in accordance with the Companies Act 2014.

Report on the audit of the financial statements *(continued)*

Our application of materiality and an overview of the scope of our audit *(continued)*

Our opinions on other matters prescribed by the Companies Act 2014 are unmodified

We have obtained all the information and explanations which we consider necessary for the purposes of our audit.

In our opinion the accounting records of the Group and Parent Company were sufficient to permit the financial statements to be readily and properly audited and the financial statements are in agreement with the accounting records. We have nothing to report in this regard.

We have nothing to report on other matters on which we are required to report by exception

The Companies Act 2014 requires us to report to you if, in our opinion, the disclosures of directors' remuneration and transactions required by sections 305 to 312 of the Act are not made.

Respective responsibilities and restrictions on use

Directors' responsibilities

As explained more fully in the directors' responsibilities statement set out on page 53, the directors are responsible for: the preparation of the financial statements including being satisfied that they give a true and fair view; such internal control as they determine is necessary to enable the preparation of financial statements that are free from material misstatement, whether due to fraud or error; assessing the Group and Parent Company's ability to continue as a going concern, disclosing, as applicable, matters related to going concern; and using the going concern basis of accounting unless they either intend to liquidate the Group or the Parent Company or to cease operations, or have no realistic alternative but to do so.

Auditor's responsibilities for the audit of the financial statements

Our objectives are to obtain reasonable assurance about whether the financial statements as a whole are free from material misstatement, whether due to fraud or error, and to issue an auditor's report that includes our opinion. Reasonable assurance is a high level of assurance but is not a guarantee that an audit conducted in accordance with ISAs (Ireland) will always detect a material misstatement when it exists. Misstatements can arise from fraud or error and are considered material if, individually or in the aggregate, they could reasonably be expected to influence the economic decisions of users taken on the basis of these financial statements.

A fuller description of our responsibilities is provided on IAASA's website at https://iaasa.ie/publications/description-of-the-auditors-responsibilities-for-the-audit-of-the-financial-statements/.

Report on the audit of the financial statements *(continued)*

The purpose of our audit work and to whom we owe our responsibilities

Our report is made solely to the Parent Company's members, as a body, in accordance with Section 391 of the Companies Act 2014. Our audit work has been undertaken so that we might state to the Parent Company's members those matters we are required to state to them in an auditor's report and for no other purpose. To the fullest extent permitted by law, we do not accept or assume responsibility to anyone other than the Parent Company and the Parent Company's members, as a body, for our audit work, for this report, or for the opinions we have formed.

Stephen J. King
for and on behalf of
KPMG
Chartered Accountants, Statutory Audit Firm
1 Stokes Place
St. Stephen's Green
Dublin 2
Ireland

21 March 2025

Prothena Corporation plc

Consolidated Balance Sheets

As of 31 December 2024 and 2023
(in thousands, except number of shares and par value)

	Notes	2024 $	2023 $
Assets			
Fixed Assets			
Tangible fixed assets	4	3,081	3,836
Operating lease right-of-use assets	5	10,708	12,162
Current assets			
Debtors	4	61,931	61,554
Cash at bank and in-hand		471,388	618,830
Total assets		547,108	696,382
Liabilities			
Capital and reserves			
Euro deferred shares, €22 nominal value:		—	—
Authorized shares — 10,000 at December 31, 2024 and 2023			
Issued and outstanding shares — none at December 31, 2024 and 2023			
Ordinary shares, $0.01 par value:		538	537
Authorized shares — 100,000,000 at December 31, 2024 and 2023			
Issued and outstanding shares — 53,826,982 and 53,682,117 at December 31, 2024 and 2023, respectively			
Share premium		1,319,704	1,317,798
Other reserves		291,157	245,193
Profit and loss account		(1,124,473)	(1,002,163)
Total shareholders' equity		486,926	561,365
Creditors			
Creditors	4	60,182	135,017
Total creditors		60,182	135,017
Total equity and liabilities		547,108	696,382

See accompanying Notes to Consolidated Financial Statements.

/s/ Gene G. Kinney
Gene G. Kinney
Director

/s/ Shane M. Cooke
Shane M. Cooke
Director

March 20, 2025

Prothena Corporation plc

Consolidated Profit and Loss Account

For the Years Ended 31 December 2024, 2023 and 2022
(in thousands, except per share data)

	2024	2023	2022
	$	$	$
Collaboration revenue	135,107	91,320	13,855
Revenue from license and intellectual property	50	50	40,050
Total revenue	135,157	91,370	53,905
Cost of revenue	—	—	—
Gross Profit	135,157	91,370	53,905
Research and development costs	222,519	220,571	135,562
General and administrative expenses	67,199	61,835	49,900
Operating loss	(154,561)	(191,036)	(131,557)
Interest income	25,816	31,014	6,349
Other expense, net	(185)	(458)	(397)
Loss on ordinary activities before taxation	(128,930)	(160,480)	(125,605)
Taxation benefit	(6,620)	(13,452)	(8,656)
Loss for the financial year	(122,310)	(147,028)	(116,949)
Basic and diluted net loss per ordinary share	(2.27)	(2.76)	(2.47)
Shares used to compute basic and diluted net loss per ordinary share	53,772	53,216	47,369

See accompanying Notes to Consolidated Financial Statements.

/s/ Gene G. Kinney
Gene G. Kinney
Director

/s/ Shane M. Cooke
Shane M. Cooke
Director

March 20, 2025

Prothena Corporation plc

Consolidated Statements of Cash Flows

For the Years Ended 31 December 2024, 2023 and 2022
(in thousands)

	2024	2023	2022
	$	$	$
Operating activities			
Net loss	(122,310)	(147,028)	(116,949)
Adjustments to reconcile net loss to cash used in operating activities:			
Depreciation and amortization	893	928	744
Share-based compensation	45,964	40,914	31,322
Deferred income taxes	(9,346)	(15,689)	(11,133)
Reduction in the carrying amount of right-of-use assets	2,692	7,484	5,997
Loss on disposal of fixed assets	—	15	1
Changes in operating assets and liabilities:			
Accounts receivable	5,159	(5,159)	—
Prepaid expenses and other assets	2,539	(2,537)	(10,809)
Deferred revenue	(55,107)	(29,330)	(13,855)
Accounts payable, accruals and other liabilities	(18,298)	22,855	11,865
Operating lease liabilities	(2,236)	(6,359)	(6,004)
Net cash used in operating activities	(150,050)	(133,906)	(108,821)
Investing activities			
Purchases of property and equipment	(298)	(2,810)	(464)
Proceeds from disposal of fixed assets	—	37	—
Net cash used in investing activities	(298)	(2,773)	(464)
Financing activities			
Proceeds from issuance of ordinary shares in public offering, net	—	20,689	172,583
Proceeds from issuance of ordinary shares in at-the market offering, net	(353)	2,894	51,033
Proceeds from issuance of ordinary shares upon exercise of stock options	1,907	21,520	17,841
Net cash provided by financing activities	1,554	45,103	241,457
Net increase (decrease) in cash, cash equivalents and restricted cash	(148,794)	(91,576)	132,172
Cash, cash equivalents and restricted cash, beginning of the year	621,042	712,618	580,446
Cash, cash equivalents and restricted cash, end of the year	472,248	621,042	712,618

	2024	2023	2022
	$	$	$
Supplemental disclosures of cash flow information			
Cash paid for income taxes, net	3,172	1,554	2,659
Supplemental disclosures of non-cash investing and financing activities			
Receivable from option exercises	—	—	62
Acquisition of property and equipment included in accounts payable and accrued liabilities	75	237	—
Right-of-use assets obtained in exchange for lease obligations	217	3,810	151
Reclassification of prepaid lease payments to right-of-use assets upon lease commencement	—	7,763	—
At-the market offering costs included in accounts payable and accrued liabilities	—	6	13
Public offering costs included in accounts payable and accrued liabilities	—	—	220

Prothena Corporation plc

Consolidated Statements of Cash Flows

For the Years Ended 31 December 2024, 2023 and 2022
(in thousands)

See accompanying Notes to Consolidated Financial Statements.

The following table provides a reconciliation of cash, cash equivalents and restricted cash reported within the statement of financial position that sum to the total of the same such amounts shown in the Consolidated Statements of Cash Flows.

	2024	2023	2022
	$	$	$
Cash and cash equivalents	471,388	618,830	710,406
Restricted cash, current	—	1,352	—
Restricted cash, non-current	860	860	2,212
Total cash, cash equivalents and restricted cash, end of the year	472,248	621,042	712,618

Prothena Corporation plc

Consolidated Statements of Shareholders' Equity

For the Years Ended 31 December 2024, 2023 and 2022

(in thousands, except share data)

	Ordinary Shares		Share Premium	Other Reserves	Profit and Loss Account	Total Shareholders' Equity
	Number	Share Capital				
		$	$	$	$	$
Balances at December 31, 2021	**46,660,294**	**466**	**1,030,774**	**172,957**	**(738,155)**	**466,042**
Share-based compensation	—	—	—	31,322	—	31,322
Issuance of ordinary shares upon exercise of stock options	1,282,086	14	17,876	—	—	17,890
Issuance of ordinary shares in public offering, net of offering costs	3,250,000	32	172,331	—	—	172,363
Issuance of ordinary shares under the at-the-market offering program	911,228	9	51,396	—	—	51,405
Share issue costs - at-the-market offering program	—	—	—	—	(31)	(31)
Net loss	—	—	—	—	(116,949)	(116,949)
Balances at December 31, 2022	**52,103,608**	**521**	**1,272,377**	**204,279**	**(855,135)**	**622,042**
Share-based compensation	—	—	—	40,914	—	40,914
Issuance of ordinary shares upon exercise of stock options	1,135,302	12	21,445	—	—	21,457
Issuance of ordinary shares upon vesting of restricted stock units	5,750	—	—	—	—	—
Issuance of ordinary shares in public offering, net of offering costs	395,096	4	20,905	—	—	20,909
Issuance of ordinary shares under the at-the-market offering program, net of offering costs	42,361	—	3,071	—	—	3,071
Net loss	—	—	—	—	(147,028)	(147,028)
Balances at December 31, 2023	**53,682,117**	**537**	**1,317,798**	**245,193**	**(1,002,163)**	**561,365**
Share-based compensation	—	—	—	45,964	—	45,964
Issuance of ordinary shares upon exercise of stock options	125,615	1	1,906	—	—	1,907
Issuance of ordinary shares upon vesting of restricted stock units	19,250	—	—	—	—	—
Net loss	—	—	—	—	(122,310)	(122,310)
Balances at December 31, 2024	**53,826,982**	**538**	**1,319,704**	**291,157**	**(1,124,473)**	**486,926**

See accompanying Notes to Consolidated Financial Statements.

Prothena Corporation plc

Notes

forming part of the Consolidated Financial Statements

1. Organization

Description of Business

Prothena Corporation plc ("Prothena" or the "Company") is a late-stage clinical biotechnology company with expertise in protein dysregulation and a pipeline of investigational therapeutics with the potential to change the course of devastating neurodegenerative and rare peripheral amyloid diseases.

Fueled by its deep scientific expertise built over decades of research, the Company is advancing a pipeline of therapeutic candidates for a number of indications and novel targets for which its ability to integrate scientific insights around neurological dysfunction and the biology of misfolded proteins can be leveraged. The Company's wholly-owned programs include birtamimab for the potential treatment of AL amyloidosis, and a portfolio of programs for the potential treatment of Alzheimer's disease including PRX012, which targets amyloid beta (Aβ), and PRX123, a novel dual Aβ-tau vaccine. The Company's partnered programs include prasinezumab for the potential treatment of Parkinson's disease and other related synucleinopathies that targets alpha-synuclein in collaboration with Roche. In addition, we have partnered BMS-986446 (formerly PRX005) for the potential treatment of Alzheimer's disease that targets tau and PRX019 for the potential treatment of neurodegenerative diseases with an undisclosed target in two separate license agreements with Bristol Myers Squibb ("BMS"). The Company is also entitled to certain potential milestone payments pursuant to the Company's share purchase agreement with Novo Nordisk pertaining to the Company's ATTR amyloidosis business (inclusive of coramitug, formerly PRX004).

The Company was formed on September 26, 2012, under the laws of Ireland and re-registered as an Irish public limited company on October 25, 2012. The Company's ordinary shares began trading on The Nasdaq Global Market under the symbol "PRTA" on December 21, 2012, and currently trade on The Nasdaq Global Select Market.

Liquidity and Business Risks

As of December 31, 2024, the Company had an accumulated deficit of $1.1 billion and cash and cash equivalents of $471.4 million.

Based on the Company's business plans, management believes that the Company's cash and cash equivalents at December 31, 2024, are sufficient to meet its obligations for at least the next twelve months. To operate beyond such period, or if the Company elects to increase its spending on research and development programs significantly above current long-term plans or enters into potential licenses and/or other acquisitions of complementary technologies, products or companies, the Company may need additional capital. Additionally, in order to develop and obtain regulatory approval for our potential products the Company will need to raise substantial additional capital. The Company expects to continue to finance future capital needs that exceed its existing cash and cash equivalents from payments pursuant to its agreements with Roche, BMS, and Novo Nordisk, and, to the extent necessary, other collaborative agreements with corporate partners, or other arrangements, and through proceeds from public or private equity or debt financings, and loans including pursuant to the Amended Distribution Agreement (See Note 7, "Shareholders' Equity" for more information). The Company cannot assume that such additional financings will be available on acceptable terms, if at all, and such financings may only be available on terms dilutive to its shareholders.

2. Summary of Significant Accounting Policies

Basis of Preparation and Presentation of Financial Information

The directors have elected to prepare the Consolidated Financial Statements in accordance with Section 279 of the Companies Act 2014, which provides that a true and fair view of assets and liabilities, financial position and profit or loss of a company and its subsidiary undertakings may be given by preparing its group financial statements in accordance with U.S. GAAP, to the extent that the use of U.S. GAAP in the preparation of the financial statements does not contravene any provision of Part 6 of the Companies Act 2014.

The Consolidated Financial Statements are prepared in accordance with Irish Company Law, to present to the shareholders of Prothena Corporation plc and file with the Companies Registration Office in Ireland. Accordingly, these Consolidated Financial Statements include disclosures required by the Companies Act 2014 of Ireland in addition to those required under U.S. GAAP. The Consolidated Financial Statements and the majority of the information in the Notes thereto have been reconciled to our Annual Report on Form 10-K for the fiscal year ended December 31, 2024 filed with the U.S. Securities and Exchange Commission on February 27, 2025.

The Consolidated Financial Statements of Prothena Corporation plc are presented in U.S. dollars, which is the functional currency of the Company and its consolidated subsidiaries. These Consolidated Financial Statements include the accounts of the Company and its consolidated subsidiaries. All intercompany balances and transactions have been eliminated in consolidation.

Going Concern

These Consolidated and Parent Company Financial Statements have been prepared on a going concern basis. On the basis of its current cash resources and its business plan for 2025 and 2026 the directors believe that the Group and Parent Company have adequate resources to continue in operational existence for at least 12 months from the date of approval of these financial statements and that it is appropriate to continue to adopt the going concern basis in preparing the financial statements. These financial statements do not include any adjustments that would result from the going concern basis of preparation being inappropriate.

Use of Estimates

The preparation of the Consolidated Financial Statements in conformity with U.S. GAAP requires the Company to make judgments, estimates and assumptions that affect the reported amounts of assets, liabilities, revenues and expenses, and related disclosures. On an ongoing basis, management evaluates its estimates, including critical accounting policies or estimates related to revenue recognition and research and development expenses. The Company bases its estimates on historical experience and on various other market specific and other relevant assumptions that management believes to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Because of the uncertainties inherent in such estimates, actual results may differ materially from these estimates.

Significant Accounting Policies

Cash, Cash Equivalents, and Restricted Cash

The Company considers all highly liquid investments held at financial institutions, such as commercial paper, money market funds, and other money market securities with original maturities of three months or less at date of purchase to be cash equivalents.

Cash accounts that are restricted to withdrawal or usage are presented as restricted cash. As of December 31, 2024, the Company had $0.9 million of restricted cash held by a bank in certificates of deposit as collateral to standby letters of credit under certain operating leases. See Note 5, "Commitments and Contingencies" for additional information regarding the Company’s operating leases.

Accounts Receivable

The accounts receivable balance on the Consolidated Balance Sheets represents amounts receivable from the Company's collaboration partners. The Company monitors the financial performance and creditworthiness of customers so that it can properly assess and respond to changes in their credit profiles. The Company makes judgments as to its ability to collect outstanding receivables and provides an allowance for credit losses against the trade account receivables, when appropriate.

Tangible Fixed Assets, net

Tangible fixed assets, net are stated at cost less accumulated depreciation and amortization. Depreciation and amortization is computed using the straight-line method over the estimated useful lives of the related assets. Maintenance and repairs are charged to expense as incurred, and leasehold improvements where the Company is deemed the accounting owner are capitalized. When assets are retired or otherwise disposed of, the cost and accumulated depreciation are removed from the balance sheet and any resulting gain or loss is reflected in operations in the period realized. Depreciation and amortization periods for the Company's property and equipment are as follows:

Asset	Estimated Useful Life
Machinery and equipment	4-7 years
Leasehold improvements	Shorter of expected useful life or lease term
Purchased computer software	4 years

Impairment of Long-lived Assets

The Company periodically evaluates its property and equipment and right-of-use assets for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable or the estimated useful life is no longer appropriate. If such events or changes in circumstances arise, the Company compares the carrying amount of the asset to the estimated undiscounted future cash flows expected to be generated by the asset. If the carrying amount of the long-lived asset is not recoverable on an undiscounted cash flow basis, an impairment charge is recognized to the extent that the carrying amount exceeds its fair value. The Company determines fair value using the income approach based on the present value of expected future cash flows. The Company's cash flow assumptions consider historical and forecasted revenue and operating costs and other relevant factors.

There were no impairment charges recorded during the years ended December 31, 2024, 2023 and 2022. See Note 4, "Composition of Certain Balance Sheet Items" for discussion on disposals.

Leases

The Company leases both real property and certain equipment for use in its operations. A determination is made as to whether an arrangement is a lease at inception. If so, the Company evaluates the lease agreement to determine whether the lease is an operating or finance lease using the criteria in ASC 842. The Company does not recognize right-of-use assets and lease liabilities that arise from short-term leases for any class of underlying assets.

When lease agreements also require the Company to make additional payments for taxes, insurance and other operating expenses incurred during the lease period, such payments are expensed as incurred. See Note 5, "Commitments and Contingencies," which provides additional details on the Company's current lease arrangements. As of December 31, 2024 and 2023, the Company had no financing leases.

Operating leases are included in the operating lease right-of-use ("ROU") assets, lease liability, current and lease liability, non-current in the Company's Consolidated Balance Sheets. Operating lease ROU assets represent the Company's right to use an underlying asset for the lease term and lease liabilities represent the Company's obligation to make lease payments arising from the lease. Operating lease ROU assets and liabilities are recognized at the lease commencement date based on the present value of all lease payments over the lease term. In determining the present value of lease payments, the Company uses its incremental borrowing rate based on information available at the lease commencement date. The operating lease ROU assets also include any lease prepayments made and exclude lease incentives such as rent abatements and/or concessions and rent holidays. The Company does not assume renewals in its determination of the lease term unless the renewals are deemed by management to be reasonably certain at lease inception. Tenant improvements made by the Company as a lessee in which they are deemed to be owned by the lessor are viewed as lease prepayments by the Company and included in the operating lease ROU assets upon commencement of the lease prior to which they are recorded as prepaid assets. Lease expense for operating leases is recognized on a straight-line basis over the expected lease term as an operating expense. For lease agreements that include lease and non-lease components, such components are generally accounted for separately.

Revenue Recognition

The Company's collaboration revenue includes revenue recognized under the Company's Collaboration Agreement with BMS as well as revenue recognized for milestone payments and reimbursements under the Company's License Agreement with Roche. The Company's license and intellectual property revenue includes revenue from Novo Nordisk for the sale of intellectual property and related rights to the Company's ATTR amyloidosis business and pipeline and milestones payments.

The Company analyzes its collaboration arrangements to assess whether they are financing arrangements within the scope of ASC 730 or as a collaboration arrangement pursuant to ASC 808, or whether such arrangements are reflective of a vendor-customer relationship and therefore within the scope of Topic 606. As of December 31, 2024, the Company has not had any arrangements outside the scope of Topic 606. The following describes the Company's accounting treatment pursuant to Topic 606:

License, Option and Collaboration Revenue

The terms of license, option and collaboration agreements entered into typically include payment of one or more of the following: non-refundable, up-front license fees; option exercise fees; development, regulatory and commercial milestone payments; payments for manufacturing supply and research and development services and royalties on net sales of licensed products.

In determining the appropriate amount of revenue to be recognized as the Company fulfills its obligations under each of its agreements, the Company performs the following steps: (i) identification of the promised goods or services in the contract; (ii) determination of whether the promised goods or services are performance obligations including whether they are distinct in the context of the contract; (iii) measurement of the transaction price, including the constraint on variable consideration; (iv) allocation of the transaction price to the performance obligations based on estimated selling prices; and (v) recognition of revenue when (or as) the Company satisfies each performance obligation.

Amounts received prior to satisfying the revenue recognition criteria are recorded as contract liabilities recorded as deferred revenue in the Company's Consolidated Balance Sheets.

At contract inception, for contracts that contain multiple performance obligations, such as the Company's Collaboration Agreement with BMS and the License Agreement with Roche, the Company accounts for the individual performance obligations separately if they are distinct. Factors considered in the determination of whether the license performance obligations are distinct included, among other things, the research and development capabilities of each of BMS and Roche and their respective sublicense rights, and for the remaining performance obligations the fact that they are not proprietary and can be and have been provided by other vendors. The transaction price is allocated to the separate performance obligation on a relative standalone selling price basis.

Revenue is recognized only when the Company satisfies an identified performance obligation by transferring a promised good or service to a customer (in the Company's case, BMS and Roche). An asset is transferred when, or as, the customer obtains control of that asset, which for a service is considered to be as the services are received and used. The Company recognizes revenue over time by measuring the progress toward complete satisfaction of the relevant performance obligation using an appropriate input or output method based on the nature of the service promised to the customer.

Milestone Revenue

The Company generally classifies each of its milestones into one of three categories: (i) clinical milestones; (ii) regulatory and development milestones; and (iii) commercial milestones. Clinical milestones are typically achieved when a product candidate advances into or completes a defined phase of clinical research. For example, a milestone payment may be due to the Company upon the initiation of a clinical trial for a new indication. Regulatory and development milestones are typically achieved upon acceptance of the submission for marketing approval of a product candidate or upon approval to market the product candidate by the FDA or other regulatory authorities. For example, a milestone payment may be due to the Company upon submission for marketing approval of a product candidate by the FDA. Commercial milestones are typically

achieved when an approved product reaches certain defined levels of net royalty sales by the licensee of a specified amount within a specified period.

At the inception of each arrangement that includes developmental, regulatory or commercial milestone payments, the Company evaluates whether achieving the milestones is considered probable and estimate the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the value of the associated milestone (such as a regulatory submission by the Company) is included in the transaction price. Milestone payments that are not within the control of the Company, such as approvals from regulators or where attainment of the specified event is dependent on the development activities of a third party, are not considered probable of being achieved until those approvals are received or the specified event occurs. The Company considers such milestone payments as variable consideration with constraint and therefore recognizes the revenue from such milestone payments as collaboration revenue at point in time when the Company can conclude it is probable that a significant revenue reversal will not occur in future periods.

Taxes, Shipping and Handling

The Company excludes from the measurement of the transaction price all taxes assessed by a governmental authority that are both imposed on and concurrent with a specific revenue-producing transaction and collected by the Company from a customer (e.g., sales, use, value added, some excise taxes). In addition, the Company accounts for shipping and handling as activities that are performed after its customers obtain control of the goods as activities to fulfill our performance obligation to transfer the goods.

Research and Development

Research and development costs are expensed as incurred. Such costs include, but are not limited to, salaries and benefits, share-based compensation, costs related to preclinical and clinical trial activities including fees paid to clinical research organizations and investigative sites, costs related to drug development and manufacturing prior to regulatory approval for commercial sale, and consulting fees.

There can be judgment involved in measuring the research and development expenses to be recognized in a particular period. The level of judgment varies based on the nature of the services being performed and the underlying support obtained. The Company recognizes costs for certain development activities, such as clinical trials, based on an evaluation of the progress to completion of specific tasks using data such as patient enrollment, clinical site activations, or information provided to the Company by our vendors on their actual costs incurred. For certain clinical trials, expense is recorded based on information obtained from vendors as an intermediary to those performing the underlying services, such as contract research organizations. These estimates are inherently more judgmental because the quality and availability of the underlying data may vary. The Company recognizes costs for contract manufacturing based on evaluation of the progress to completion of specific tasks. The objective of the Company's accrual policy is to match the recording of the expenses in the Consolidated Financial Statements to the actual services the Company has received and efforts expended by our vendors. As such, expense accruals related to clinical trials and contract manufacturing are recognized based on the Company's estimate of the degree of completion of the events specified in the specific clinical study or trial contract or drug development and manufacturing contract, respectively. The Company does not make significant estimates where costs incurred are supported by invoices or reports of costs incurred are obtained from a vendor that is directly performing the underlying services, such as a consultant or contract manufacturing organization. Payments for these activities are based on the terms of the individual arrangements, which may differ from the pattern of costs incurred, and are reflected in the Consolidated Financial Statements as prepaid or accrued research and development. Amounts due may be fixed fee, fee for service, and may include upfront payments, monthly payments, and payments upon the completion of milestones or receipt of deliverables. Nonrefundable advance payments for goods and services that will be used or received in future research and development activities are deferred and recognized as expense in the period in which the related goods are delivered or services are performed.

The Company has acquired and may continue to acquire the rights to develop and commercialize new drug candidates from third parties. The upfront payments to acquire license, product or rights, as well as any future milestone payments, are immediately recognized as research and development expense provided that the drug has not achieved regulatory approval for marketing and, absent obtaining such approval, has no alternative future use.

Share-based Compensation

The Company's share-based compensation programs include options for the purchase of shares and restricted share units (RSUs). Such awards may be granted to employees, directors, and non-employee service providers.

The Company measures compensation expense for all share-based awards at the grant date based on the fair value measurement of the award. Share-based compensation expense is recognized on a straight-line basis over the requisite service period, which is generally the vesting period, for each award. The fair value of RSUs is based on the closing market price of the Company's ordinary shares on the date of grant. To determine the fair value of options for the purchase of shares, the Company uses the Black-Scholes option-pricing model. The determination of fair value using the Black-Scholes option-pricing model is affected by the Company's share price as well as assumptions regarding a number of complex and subjective variables. Judgment is required in determining the assumptions used in these models which include the risk-free interest rate, expected term, expected volatility and expected dividend yield. The Company uses its historical volatility for the Company's shares to estimate expected volatility. The simplified method has been used to estimate the expected term of all options in previous years. Beginning January 1, 2023, expected term is estimated based on historical experience.

Share-based compensation expense recognized in the Consolidated Statements of Operations is based on awards expected to vest and therefore the amount of expense has been reduced for estimated forfeitures which are based on historical experience. Share-based compensation expense is adjusted in subsequent periods for actual forfeitures.

The Company records any excess tax benefits or tax shortfalls from its equity awards in its Consolidated Statements of Operations in the reporting periods in which options for the purchase of shares are exercised or RSUs vest.

Income Taxes

The Company files its own U.S. and foreign income tax returns and income taxes are presented in the Consolidated Financial Statements using the asset and liability method prescribed by the accounting guidance for income taxes. Deferred tax assets ("DTAs") and liabilities are determined based on the difference between the financial statement and tax basis of assets and liabilities using the enacted tax rates projected to be in effect for the year in which the differences are expected to reverse. Net deferred tax assets are recorded to the extent the Company believes that these assets will more likely than not be realized. In making such determination, all available positive and negative evidence is considered, including scheduled reversals of deferred tax liabilities, recent cumulative earnings/losses by taxing jurisdiction, projected future taxable income, tax planning strategies and recent financial operations. Actual operating results in future years could differ from our current assumptions, judgments and estimates.

The Company's significant tax jurisdictions are Ireland and the United States. Estimates are required in determining the Company's provision for income taxes. Some of these estimates are based on management's interpretations of jurisdiction-specific tax laws or regulations. Various internal and external factors may have favorable or unfavorable effects on the future effective income tax rate of the business. These factors include, but are not limited to, changes in tax laws, regulations and/or rates, changing interpretations of existing tax laws or regulations, changes in estimates of prior years' items, past and future levels of R&D spending, the impact of accounting for share-based compensation, and changes in overall levels of income before taxes.

The Company did not recognize certain tax benefits from uncertain tax positions within the provision for income taxes. The tax benefit from an uncertain tax position is recognized only if it is more likely than not the tax position will be sustained on examination by the taxing authorities, based on the technical merits of the position. The tax benefits recognized in the financial statements from such positions are then measured based on the largest benefit that has a greater than 50% likelihood of being realized upon settlement. Changes in recognition or measurement are reflected in the period in which the change in judgment occurs. Interest and penalties related to unrecognized tax benefits are accounted for in income tax expense.

Net Income (Loss) per Ordinary Share

Basic net income (loss) per ordinary share is calculated by dividing net income (loss) by the weighted-average number of ordinary shares outstanding during the period. Diluted net income per ordinary share is computed based on the treasury stock

method by dividing net income by the weighted-average number of ordinary shares outstanding, plus potentially dilutive ordinary equivalent shares outstanding. However, where there is a net loss, no adjustment is made for potentially issuable ordinary shares because their effect would be anti-dilutive and therefore diluted net loss per share is equal to basic net loss per share.

Net loss per ordinary share was determined as follows (in thousands, except per share amounts):

	Year Ended December 31,		
	2024	2023	2022
Numerator:			
Net loss	$ (122,310)	$ (147,028)	$ (116,949)
Denominator:			
Weighted-average ordinary shares outstanding used in per share calculations	53,772	53,216	47,369
Net loss per share:			
Basic and diluted net loss per ordinary share	$ (2.27)	$ (2.76)	$ (2.47)

The equivalent ordinary shares not included in diluted net income (loss) per share because their effect would be anti-dilutive are as follows (in thousands):

	Year Ended December 31,		
	2024	2023	2022
Stock options to purchase ordinary shares	11,107	9,866	9,480
Restricted Stock Units (RSU)	6	25	23
Total	11,113	9,891	9,503

Comprehensive Loss

Comprehensive income (loss) is comprised of net income (loss) and other comprehensive income (loss). The Company has no components of other comprehensive income (loss). Therefore, net income (loss) equals comprehensive income (loss) for all periods presented and, accordingly, the Consolidated Statements of Comprehensive Income (Loss) is not presented in a separate statement.

Concentration of Risks

Financial instruments that potentially subject the Company to concentration of credit risk consist of cash and cash equivalents and accounts receivable. The Company places its cash equivalents with high credit quality financial institutions and, by policy, limits the amount of credit exposure with any one financial institution. Deposits held with banks have exceeded, and will continue to exceed, federally insured limits. The Company is exposed to credit risk in the event of a default by the financial institutions holding its cash and cash equivalents. The Company has not experienced any losses on its deposits of cash and cash equivalents and its credit risk exposure is up to the extent recorded on the Company's Consolidated Balance Sheet.

The Company’s business is primarily conducted in U.S. dollars except for its agreements with contract manufacturers for drug supplies which are primarily denominated in euros. The Company recorded losses on foreign currency exchange rate differences of approximately $185,000, $458,000 and $397,000 during the years ended December 31, 2024, 2023 and 2022, respectively. If the Company increases its business activities that require the use of foreign currencies, it may be exposed to losses if the euro and other such currencies continue to strengthen against the U.S. dollar.

As of December 31, 2024, and 2023, $3.1 million and $3.8 million, respectively, of the Company’s property and equipment, net were held in the U.S. and a nominal amount were in Ireland.

The Company does not own or operate facilities for the manufacture, packaging, labeling, storage, testing or distribution of nonclinical or clinical supplies of any of its drug candidates. The Company instead contracts with and relies on third-parties to manufacture, package, label, store, test and distribute all preclinical development and clinical supplies of our drug candidates, and it plans to continue to do so for the foreseeable future. The Company also relies on third-party consultants to assist in managing these third-parties and assist with its manufacturing strategy.

Recently Issued Accounting Pronouncements Not Yet Adopted

On November 4, 2024, the Financial Accounting Standards Board ("FASB") issued Accounting Standards Update (ASU) 2024-03, Income Statement — Reporting Comprehensive Income — Expense Disaggregation Disclosures, which requires public business entities to disclose, on an annual and interim basis, disaggregated information about certain income statement line items in a tabular format in the notes to the financial statements. This guidance will be effective for the Company's annual period ending December 31, 2027, and interim periods beginning January 1, 2028. Early adoption is permitted. Entities may apply the guidance prospectively or retrospectively. The Company is currently evaluating the impact of this new standard on its financial statement disclosures.

On March 6, 2024, the SEC issued final rule, "The Enhancement and Standardization of Climate-Related Disclosures for Investors", which requires registrants to disclose material climate-related risks, including descriptions of board oversight and risk management activities, the material impacts of these risks on a registrants strategy, business model and outlook and any material climate-related targets or goals. The rule requires these climate-related information to be disclosed in registration statements and annual reports. Registrants will also need to quantify certain effects of severe weather events and other natural conditions in a note to their audited financial statements. In addition, accelerated and large accelerated filers will need to disclose Scope 1 and Scope 2 greenhouse gas (GHG) emissions, if material, which will be subject to third-party assurance. The Company would be required to comply with the rule in fiscal year beginning January 1, 2025 for all disclosures other than the compliance with quantitative and qualitative disclosure requirements of material expenditures and material impacts on financial estimates that directly result from (1) activities to mitigate or adapt to the climate-related risks, (2) targets or goals and (3) transition plans will be required beginning fiscal year 2026. The Company's other compliance dates are the following: 1) Scope 1 and Scope 2 GHG emissions - fiscal year beginning January 1, 2026; Limited assurance - fiscal year beginning January 1, 2029; Reasonable assurance - fiscal year beginning January 1, 2033; and Electronic tagging - fiscal year beginning January 1, 2026. The Company is currently evaluating the impact of the new standard on its consolidated financial statements and related disclosures. On April 4, 2024, the Securities and Exchange Commission (SEC) voluntarily stayed implementation of its recently adopted Climate Disclosure Rules.

In December 2023, the FASB issued ASU 2023-09, Improvements to Income Tax Disclosures, which requires public business entities to disclose a tabular reconciliation using both percentages and amounts, broken out into specific categories with certain reconciling items at or above 5% of the expected tax further broken out by nature and/or jurisdiction. The guidance also requires all entities to disclose income taxes paid, net of refunds, disaggregated by federal (national), state and foreign taxes for annual periods and to disaggregate the information by jurisdiction based on a quantitative threshold. All entities are required to apply the guidance prospectively, with the option to apply it retrospectively. The guidance will be effective for the Company's annual period ending December 31, 2025. Early adoption is permitted. The Company is currently evaluating the impact of the new standard on its income tax disclosures.

Recently Adopted Accounting Pronouncement - Segment Reporting

On November 27, 2023, FASB issued Accounting Standards Update 2023-07 ("ASU 2023-07"), Segment Reporting - Improvements to Reportable Segment Disclosures, which requires public entities to provide disclosures on significant segment expenses that are regularly provided to the chief operating decision maker ("CODM") and included within each reported measure of segment profit or loss and other segment items on an annual and interim basis. The guidance also requires public entities to provide all disclosures about reportable segment's profit or loss and assets in interim periods that are currently required annually. Public entities with a single reportable segment have to provide all disclosures required by Accounting Standards Codification (ASC) 280, Segment Reporting including the significant segment expense disclosures. The guidance is applied retrospectively to all periods presented in financial statements and is effective for fiscal years beginning after December 15, 2023, and for interim periods beginning after December 15, 2024. Early adoption is permitted. The Company adopted ASU 2023-07 during its fiscal year ended December 31, 2024. For the purpose of the adoption of ASU 2023-07, the Company

performed an evaluation of financial information regularly reviewed by the Company's CODM for purposes of evaluating performance, allocating resources, setting incentive compensation targets, and planning and forecasting future periods. Financial information provided to and used by the CODM is consistent with the Company's consolidated GAAP financial statements including its Consolidated Statements of Operations that includes the Company's consolidated profit and loss.

Segment Information

The Company currently manages its operations as a single segment focused on the discovery and development of novel therapies to treat diseases caused by protein dysregulation. A single management team reports to the chief operating decision maker who comprehensively manages the entire business. All clinical programs are included in one operating segment because the majority of the Company's clinical programs have similar economic and other characteristics, including the nature of the clinical programs and production processes, and regulatory environment.

Consistent with the Company's operational structure, the chief executive officer, as the CODM, manages and allocates resources at the global corporate level using consolidated, single-segment GAAP financial statement reported profit and loss and consolidated budget and forecast information for purpose of evaluating performance, allocating resources, setting incentive targets, and planning and forecasting future periods. Managing and allocating resources at the global corporate level enables the CODM to assess both the overall level of resources available and how to best deploy these resources across functions, therapeutic areas and research and development projects in line with our overarching long-term corporate-wide strategic goals, rather than on a clinical program basis. The Company is not organized by market and is managed and operated as one business. As a single reportable segment entity the determined measure of profit or loss is the Company's consolidated net income (loss). Consolidated asset information for the Company's single-segment is presented in the Company's consolidated Balance Sheet.

The following table sets forth significant research and development ("R&D") expenses by program as regularly provided to the CODM (in thousands):

	Year Ended December 31,		
	2024	**2023**	**2022**
Birtamimab (NEOD001)	$ 85,649	$ 68,831	$ 49,312
BMS-986446 (PRX005)	264	10,063	14,444
PRX012	116,359	102,767	41,990
PRX019	5,035	7,703	9,117
Other R&D	15,212	31,207	20,699
Total research and development	$ 222,519	$ 220,571	$ 135,562

3. Fair Value Measurements

The Company measures certain financial assets and liabilities at fair value on a recurring basis, including cash equivalents. Fair value is an exit price, representing the amount that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants. As such, fair value is a market-based measurement that should be determined based on assumptions that market participants would use in pricing an asset or a liability. A three-tier fair value hierarchy is established as a basis for considering such assumptions and for inputs used in the valuation methodologies in measuring fair value:

Level 1 — inputs are quoted prices (unadjusted) for identical assets or liabilities in active markets.

Level 2 — inputs are other than quoted prices included in Level 1 that are observable for the asset or liability, either directly or indirectly.

Level 3 — inputs are unobservable inputs that are supported by little or no market activities, which would require the Company to develop its own assumptions.

The fair value hierarchy also requires an entity to maximize the use of observable inputs and minimize the use of unobservable inputs when measuring fair value. The carrying amounts reflected in the Consolidated Balance Sheets for cash equivalents, prepaid expenses and other current assets, accounts receivable, accounts payable and accrued liabilities, approximate their fair value due to their short-term nature.

Based on the fair value hierarchy, the Company classifies its cash equivalents within Level 1. This is because the Company values its cash equivalents using quoted market prices. The Company's Level 1 securities consisted of $440.3 million and $589.9 million in money market funds included in cash and cash equivalents at December 31, 2024, and 2023, respectively.

4. Composition of Certain Balance Sheet Items

Tangible Fixed Assets

Tangible fixed assets consisted of the following (in thousands):

	Machinery and Equipment $	Leasehold Improvements $	Purchased Computer Software $	Total $
Cost:				
At January 1, 2024	9,019	—	2,232	11,251
Additions at cost	118	10,641	20	10,779
Disposals	—	(10,641)	—	(10,641)
At December 31, 2024	9,137	—	2,252	11,389
Accumulated Depreciation:				
At January 1, 2024	(6,129)	—	(1,286)	(7,415)
Charged during the year	(645)	—	(248)	(893)
Disposals	—	—	—	—
At December 31, 2024	(6,774)	—	(1,534)	(8,308)
Net Book Amount:				
At December 31, 2024	2,363	—	718	3,081
At December 31, 2023	2,890	—	946	3,836

Depreciation expense was $0.9 million, $0.9 million, and $0.7 million for the years ended December 31, 2024, 2023 and 2022, respectively.

Debtors

Debtors consisted of the following at December 31 (in thousands):

	2024	2023
	$	$
Amount falling due within one year:		
Accounts receivable	—	5,159
Prepaid expenses and other current assets	14,024	15,293
	14,024	20,452
Amount falling due after more than one year:		
Deferred tax assets, non-current	43,239	33,893
Other non-current assets	4,668	7,209
	47,907	41,102
Total debtors	61,931	61,554

Creditors

Creditors consisted of the following at December 31 (in thousands):

	2024	2023
	$	$
Amount falling due within one year:		
Trade creditors	21,198	40,115
Income tax	—	339
Lease liability, current	2,610	1,114
Deferred Revenue, current	8,850	—
Other short-term creditors	15,843	15,323
	48,501	56,891
Amount falling due after more than one year:		
Deferred revenue, non-current	3,448	67,405
Lease liability, non-current	8,233	10,721
Other long-term creditors	—	—
	11,681	78,126
Total creditors	60,182	135,017

Other short-term creditors include $0.9 million and $0.9 million of social insurance payable as of December 31, 2024 and 2023, respectively.

5. Commitments and Contingencies

Lease Commitments

As of December 31, 2024, the Company currently has four leases relating to its facilities in the United States and Dublin, Ireland.

South San Francisco Facility

The Company had a noncancelable operating sublease (the "SSF Lease") covering 128,751 square feet of office and laboratory space in South San Francisco, California, U.S. (the "SSF Facility"), which expired on December 31, 2023.

Total operating lease cost was nil, $6.3 million and $6.3 million for the years ended December 31, 2024, 2023 and 2022, respectively. Total cash paid against the operating lease liability was nil, $6.5 million, and $6.3 million for the years ended December 31, 2024, 2023 and 2022, respectively. The Company obtained a standby letter of credit which could be drawn down by the sublandlord in the event the Company failed to fully and faithfully perform all of its obligations under the SSF Lease and to compensate the sublandlord for all losses and damages the sublandlord may have suffered as a result of the occurrence of any default on the part of Company not cured within the applicable cure period. This standby letter of credit was collateralized by a certificate of deposit of the same amount which was classified as restricted cash as of December 31, 2023. The remaining standby letter of credit amount of $1.4 million was released to the Company in May 2024.

Sub-Sublease of South San Francisco Facility

The Company had a Sub-Sublease Agreement (the "Sub-Sublease") with Assembly Biosciences, Inc. covering approximately 46,641 square feet of office and laboratory space of the SSF Facility. The Sub-Sublease expired on December 15, 2023, in connection with the expiration of the SSF Lease. The Sub-Sublease was considered an operating lease under ASC 842. For the years ended December 31, 2024, 2023 and 2022, the Company recorded nil, $2.8 million, and $2.9 million respectively, of sub-lease rental income as an offset to its operating expenses.

Dublin

In June 2021, the Company entered into a lease agreement for office space in Dublin, Ireland, which commenced in August 2021 and had an initial term of one year. In addition, the Company entered into a lease agreement for additional office space in Dublin, Ireland, which commenced in August 2023 and had an initial term of one year. Both leases have an automatic renewal clause, pursuant to which each agreement will be extended automatically for successive periods equal to their current terms, unless each agreement is cancelled by the Company. In April 2024, the Company renewed both leases, each for another one year term with termination dates in July 2025.

Brisbane Facility

On October 28, 2022, the Company entered into a noncancelable operating sublease (the "Brisbane Sublease") to sublease approximately 31,157 square feet of office and laboratory space located in Brisbane, California (the "Brisbane Facility") with Arcus Biosciences, Inc., (the "Sublandlord"). The Brisbane Sublease became effective on October 28, 2022. The Brisbane Sublease provides that the Company's obligation to pay rent commenced on July 1, 2023, which is subject to abatement for the first six months following such date, with the exception of the seventh rent payment that was due upon execution of the Brisbane Sublease. The Company is obligated to make lease payments totaling approximately $14.9 million over the lease term, which expires on September 30, 2028, unless terminated earlier. The Brisbane Sublease further provides that the Company is obligated to pay the Sublandlord certain costs, including taxes and operating expenses. The Company has the option to extend the sublease by providing written notice at least nine months prior to the expiration of the sublease term. As of December 31, 2024, the Brisbane Sublease has a remaining lease term of 3.8 years.

The Brisbane Sublease is considered an operating lease and the accounting lease commencement date was on July 31, 2023 when the Company gained control over the Brisbane Facility. The Company recorded a right-of-use asset of approximately $11.4 million and lease liability of approximately $3.6 million relating to the Brisbane Sublease on the lease commencement date. The discount rate used to determine the lease liability was 5.76%. The initial measurement of the right-of-use asset for the Brisbane Sublease includes the tenant improvement added by the Company wherein the lessor was deemed the accounting owner.

The Company was entitled to an improvement allowance of up to $9.3 million, to be used for costs incurred by the Company to construct certain improvements to the Brisbane Facility and to prepare for the Company's occupancy of the Brisbane Facility. As of December 31, 2024, all of the $9.3 million improvement allowance has been received from the Sublandlord and the Company is obligated to fund construction costs incurred in excess of the improvement allowance.

Total operating lease cost for the Brisbane Sublease was $3.2 million and $1.3 million for the year ended December 31, 2024 and 2023, respectively. Total cash paid against the operating lease liability was $2.7 million and $0.4 million for the year ended December 31, 2024 and 2023, respectively.

In conjunction with the Brisbane Sublease, the Company obtained a standby letter of credit in the initial amount of $0.9 million, which may be drawn down by the Sublandlord in the event the Company fails to fully and faithfully perform all of its obligations under the Brisbane Sublease and to compensate the Sublandlord for all losses and damages the Sublandlord may suffer as a result of the occurrence of any default on the part of the Company not cured within the applicable cure period. As of December 31, 2024, none of the standby letter of credit amount of $0.9 million has been used.

The following table sets out a maturity analysis of payments under the Company's operating leases, including a reconciliation to the lease liabilities recognized in the Consolidated Balance Sheets as of December 31, 2024 (in thousands):

	Operating Leases
Year Ended December 31,	**$**
2025	3,179
2026	3,158
2027	3,269
2028	2,523
Thereafter	—
Total	12,129
Less: Present value adjustment	(1,286)
Total lease liability	10,843
Less: Lease liability, current	(2,610)
Lease liability, non-current	8,233

Indemnity Obligations

The Company has entered into indemnification agreements with its current and former directors and officers and certain key employees. These agreements contain provisions that may require the Company, among other things, to indemnify such persons against certain liabilities that may arise because of their status or service and advance their expenses incurred as a result of any indemnifiable proceedings brought against them. The obligations of the Company pursuant to the indemnification agreements continue during such time as the indemnified person serves the Company and continues thereafter until such time as a claim can be brought. The maximum potential amount of future payments the Company could be required to make under these indemnification agreements is unlimited; however, the Company has a director and officer liability insurance policy that limits its exposure and enables the Company to recover a portion of any future amounts paid. As a result of its insurance policy coverage, the Company believes the estimated fair value of these indemnification agreements is minimal. Accordingly, the Company had no liabilities recorded for these agreements as of December 31, 2024, and 2023.

Other Commitments

In the normal course of business, the Company enters into various firm purchase commitments primarily related to research and development activities. As of December 31, 2024, the Company had non-cancelable purchase commitments to suppliers for $12.7 million of which $1.8 million is included in current liabilities, and contractual obligations under license agreements of $0.3 million of which nil is included in current liabilities. The following is a summary of the Company's non-cancelable purchase commitments and contractual obligations as of December 31, 2024 (in thousands):

	Total	2025	2026	2027	2028	Thereafter
Purchase Obligations [1]	$ 12,729	$ 12,633	$ 96	$ —	$ —	$ —
Contractual obligations under license agreements	274	64	60	60	45	45
Total	$ 13,003	$ 12,697	$ 156	$ 60	$ 45	$ 45

[(1)] *Purchase obligations consist of non-cancelable purchase commitments to suppliers and contract research organizations.*

Legal Proceedings

We are not currently a party to any material legal proceedings. We may at times be party to ordinary routine litigation incidental to our business. When appropriate in management's estimation, we may record reserves in our financial statements for pending legal proceedings.

6. Significant Agreements

Roche License Agreement

In December 2013, the Company through its wholly owned subsidiary Prothena Biosciences Limited and Prothena Biosciences Inc entered into a License, Development, and Commercialization Agreement (the "License Agreement") with F. Hoffmann-La Roche Ltd. and Hoffmann-La Roche Inc. (together, "Roche") to develop and commercialize certain antibodies that target α-synuclein, including prasinezumab, which are referred to collectively as "Licensed Products." Upon the effectiveness of the License Agreement in January 2014, the Company granted to Roche an exclusive, worldwide license to develop, make, have made, use, sell, offer to sell, import and export the Licensed Products. The Company retained certain rights to conduct development of the Licensed Products and an option to co-promote prasinezumab in the U.S. During the term of the License Agreement, the Company and Roche will work exclusively with each other to research and develop antibody products targeting alpha-synuclein (or α-synuclein) potentially including incorporation of Roche's proprietary Brain Shuttle™ technology to potentially increase delivery of therapeutic antibodies to the brain. The License Agreement provided for Roche making an upfront payment to the Company of $30.0 million, which was received in February 2014; making a clinical milestone payment of $15.0 million upon initiation of the Phase 1 clinical trial for prasinezumab, which was received in May 2014; making a clinical milestone payment of $30.0 million upon dosing of the first patient in the Phase 2 clinical trial for prasinezumab, which was achieved in June 2017; and making a clinical milestone payment of $60.0 million upon dosing of the first patient in the global Phase 2b PADOVA study for prasinezumab, which was achieved in May 2021.

For prasinezumab, Roche is obligated to pay:

- up to $290.0 million upon the achievement of development, regulatory, and various first commercial sales milestones;
- up to $155.0 million upon achievement of U.S. commercial sales milestones;
- up to $175.0 million upon achievement of ex-U.S. commercial sales milestones; and
- tiered, high single-digit to high double-digit royalties in the teens based on U.S. and ex-U.S. annual net sales, subject to certain adjustments, with respect to the applicable Licensed Product.

Roche bore 100% of the cost of conducting the research collaboration under the License Agreement during the research term, which expired December 31, 2017. In May 2021, the Company exercised its rights under the terms of License Agreement to receive potential U.S. commercial sales milestone and royalties, in lieu of a U.S. profit and loss share for prasinezumab in Parkinson's disease. Thus, in the U.S., through May 28, 2021, the parties shared all development costs, all of which were allocated 70% to Roche and 30% to the Company, for prasinezumab in the Parkinson's disease indication. If the Company opts in to participate in co-development and co-funding for any other Licensed Products and/or indications, the parties will share all development and commercialization costs, as well as profits, all of which will be allocated 70% to Roche and 30% to the Company.

The Company initiated a Phase 1 clinical trial for prasinezumab in 2014. Following the Phase 1 clinical trial, Roche became primarily responsible for developing, obtaining and maintaining regulatory approval for and commercializing Licensed Products. Roche also became responsible for the clinical and commercial manufacture and supply of Licensed Products.

In addition, the Company has an option under the License Agreement to co-promote prasinezumab in the U.S. in the Parkinson's disease indication. If the Company exercises such option, it may also elect to co-promote additional Licensed Products in the U.S. approved for Parkinson's disease. Outside the U.S., Roche will have responsibility for developing and commercializing the Licensed Products. Roche bears all costs that are specifically related to obtaining or maintaining regulatory approval outside the U.S. and will pay the Company a variable royalty based on annual net sales of the Licensed Products outside the U.S.

The License Agreement continues on a country-by-country basis until the expiration of all payment obligations under the License Agreement. The License Agreement may also be terminated (i) by Roche at will after the first anniversary of the effective date of the License Agreement, either in its entirety or on a Licensed Product-by-Licensed Product basis, upon 90 days' prior written notice to the Company prior to first commercial sale and 180 days' prior written notice to Prothena after first commercial sale, (ii) by either party, either in its entirety or on a Licensed Product-by-Licensed Product or region-by-region basis, upon written notice in connection with a material breach uncured 90 days after initial written notice, and (iii) by either party, in its entirety, upon insolvency of the other party. The License Agreement may be terminated by either party on a patent-by-patent and country-by-country basis if the other party challenges a given patent in a given country. The Company's rights to co-develop Licensed Products under the License Agreement will terminate if the Company commences certain studies for certain types of competitive products. The Company's rights to co-promote Licensed Products under the License Agreement will terminate if the Company commences a Phase 3 study for such competitive products.

The License Agreement cannot be assigned by either party without the prior written consent of the other party, except to an affiliate of such party or in the event of a merger or acquisition of such party, subject to certain conditions. The License Agreement also includes customary provisions regarding, among other things, confidentiality, intellectual property ownership, patent prosecution, enforcement and defense, representations and warranties, indemnification, insurance, and arbitration and dispute resolution.

Performance Obligations

As of December 31, 2024, and December 31, 2023, there were no remaining performance obligations under the License Agreement since the obligations related to research and development activities were only for the Phase 1 clinical trial and the remaining obligations were delivered or performed.

Milestone Accounting

Under the License Agreement, the Company is eligible to receive certain milestone payments upon the achievement of development, regulatory and various first commercial sales milestones. Milestone payments are evaluated under ASC Topic 606. Factors considered in this determination included scientific and regulatory risk that must be overcome to achieve each milestone, the level of effort and investment required to achieve the milestone, and the monetary value attributed to the milestone. Accordingly, the Company estimates payments in the transaction price based on the most likely approach, which considers the single most likely amount in a range of possible amounts related to the achievement of these milestones. Additionally, milestone payments are included in the transaction price only when the Company can conclude it is probable that a significant revenue reversal will not occur in future periods when the milestone is achieved.

The Company excludes the milestone payments and royalties in the initial transaction price calculation because such payments are considered to be variable considerations with constraint. Such milestone payments and royalties will be recognized as revenue once the Company can conclude it is probable that a significant revenue reversal will not occur in future periods.

The clinical and regulatory milestones under the License Agreement after the point at which the Company could opt out are considered to be variable considerations with constraint due to the fact that active participation in the development activities that generate the milestones is not required under the License Agreement, and the Company can opt out of these activities. There are no refunds or claw-back provisions and the milestones are uncertain of occurrence even after the Company has opted out. Based on this determination, these milestones will be recognized when the Company can conclude it is probable that a significant revenue reversal will not occur in future periods.

Collaboration Agreement with Bristol Myers Squibb

Overview

On March 20, 2018, the Company, through its wholly owned subsidiary Prothena Biosciences Limited ("PBL"), entered into a Master Collaboration Agreement (the "Collaboration Agreement") with Celgene Switzerland LLC ("Celgene"), a subsidiary of Celgene Corporation (which was acquired by Bristol Myers Squibb ("BMS") in November 2019), pursuant to which Prothena granted to Celgene a right to elect in its sole discretion to exclusively license rights both in the U.S. (the "US Rights") and on a global basis (the "Global Rights"), with respect to the Company's programs to develop and commercialize antibodies targeting tau, TDP-43 and an undisclosed target (the "Collaboration Targets").

The Collaboration Agreement provided for Celgene making an upfront payment to the Company of $100.0 million, plus future potential license exercise payments and regulatory and commercial milestones for each program under the Collaboration Agreement, as well as royalties on net sales of any resulting marketed products. In connection with the Collaboration Agreement, the Company and Celgene entered into a Share Subscription Agreement on March 20, 2018, under which Celgene subscribed to 1,174,536 of the Company's ordinary shares for a price of $42.57 per share, for a total of approximately $50.0 million.

BMS US and Global Rights and Licenses

On a program-by-program basis, beginning on the effective date of the Collaboration Agreement and ending on the date that the IND Option term expires for such program (which generally occurs sixty days after the date on which the Company delivers to BMS the first complete data package for an IND that was filed for a lead candidate from the relevant program), BMS may elect in its sole discretion to exercise its US Rights to receive an exclusive license to develop, manufacture and commercialize antibodies targeting the applicable Collaboration Target in the U.S. (the "US License"). If BMS exercises its US Rights for a collaboration program, it is obligated to pay the Company an exercise fee of approximately $80.0 million per program. Thereafter, following the first to occur of (a) completion by the Company, in its discretion and at its cost, of Phase 1 clinical trials for such program or (b) BMS' election to assume responsibility to complete such Phase 1 clinical trials (at its cost), BMS would have the sole right to develop, manufacture and commercialize antibody products targeting the relevant Collaboration Target for such program (the "Collaboration Products") in the U.S.

On a program-by-program basis, following completion of a Phase 1 clinical trial for a collaboration program for which BMS has previously exercised its US Rights, BMS may elect in its sole discretion to exercise its Global Rights with respect to such collaboration program to receive a worldwide, exclusive license to develop, manufacture and commercialize antibodies targeting the applicable Collaboration Target (the "Global License"). If BMS exercises its Global Rights, BMS would be obligated to pay the Company an additional exercise fee of $55.0 million for such collaboration program. The Global Rights would then replace the US Rights for that collaboration program, and BMS would have decision making authority over developing, obtaining and maintaining regulatory approval for, manufacturing and commercializing the Collaboration Products worldwide.

After BMS' exercise of Global Rights for a collaboration program, the Company is eligible to receive up to $562.5 million in regulatory and commercial milestones per program. Following an exercise by BMS of either US Rights or Global Rights for such collaboration program, the Company will also be eligible to receive tiered royalties on net sales of Collaboration Products ranging from high single digit to high teen percentages, on a weighted average basis depending on the achievement of certain net sales thresholds. Such exercise fees, milestones and royalty payments are subject to certain reductions as specified in the Collaboration Agreement, the agreement for US Rights and the agreement for Global Rights.

BMS will continue to pay royalties on a Collaboration Product-by-Collaboration Product and country-by-country basis, until the latest of (i) expiration of certain patents covering the Collaboration Product, (ii) expiration of all regulatory exclusivity for the Collaboration Product, and (iii) an agreed period of time after the first commercial sale of the Collaboration Product in the applicable country (the "Royalty Term").

Term and Termination

The term of the Collaboration Agreement expired on May 24, 2024.

The term of any US License or Global License would continue on a Licensed Product-by-Licensed Product and country-by-country basis until the expiration of all Royalty Terms under such agreement.

Performance Obligations

The Company assessed the Collaboration Agreement and concluded that it represented a contract with a customer within the scope of ASC 606. Per ASC 606, a performance obligation is defined as a promise to transfer a good or service or a series of distinct goods or services. At inception of the Collaboration Agreement, the Company is not obligated to transfer any US License or Global License to BMS unless BMS exercises its US Rights or Global Rights, respectively, and the Company is not obligated to perform development activities under the development plan during preclinical and Phase 1 clinical trials including the regulatory filing of the IND.

The discovery, preclinical and clinical development activities performed by the Company are to be performed at the Company's discretion and are not promised goods or services and therefore are not considered performance obligations under ASC 606, unless and until the Company agrees to perform the Phase 1 clinical trials (after the IND option exercise) that are determined to be performance obligations at the time the option is exercised. Per the terms of the Collaboration Agreement, the Company may conduct discovery activities to characterize, identify and generate antibodies to become collaboration candidates that target such Collaboration Target, and thereafter may pre-clinically develop collaboration candidates to identify lead candidates that target such Collaboration Target and file an IND with the U.S. Food and Drug Administration (the "FDA") for a Phase 1 clinical trial for such lead candidates. In the event the Company agrees to be involved in a Phase 1 clinical trial, the Company will further evaluate whether any such promise represents a performance obligation at the time the option is exercised. If it is concluded that the Company has obligated itself to an additional performance obligation besides the license granted at IND option exercise, then the effects of the changes in the arrangement will be evaluated under the modification guidance of ASC 606.

The Company is not obligated to perform manufacturing activities. Per the terms of the Collaboration Agreement, to the extent that the Company, at its discretion, conducts a program, the Company shall be responsible for the manufacture of collaboration candidates and collaboration products for use in such program, as well as the associated costs. Delivery of manufactured compound (clinical product supply) is not deemed a performance obligation under ASC 606 as the Company is not obligated to transfer supply of collaboration product to BMS unless BMS exercises its right to participate in the Phase 1 development.

Compensation for the Company's provision of inventory supply, to the extent requested by BMS would be paid to the Company by BMS at a reasonable stand-alone selling price for such supply. Given that (i) there is substantial uncertainty about the development of the programs, (ii) the pricing for the inventory is at its standalone selling price and (iii) the manufacturing services require the entity to transfer additional goods or services that are incremental to the goods and services provided prior to the resolution of the contingency, the Company's supply of product is not a material right. Therefore, the inventory supply is not considered a performance obligation unless and until, requested by BMS.

In addition to the grant of the Global License after BMS exercises the Global Rights for a program, BMS is entitled to receive certain ancillary development services from the Company, such as ongoing clinical trial support upon request by BMS, transition supply, if requested by BMS, and regulatory support for coordination of pharmacovigilance matters.

The Company evaluated the potential obligations to transfer the US Licenses and Global Licenses and performance of the ancillary development services subsequent to exercise of the US Rights and Global Rights, if the options are exercised by BMS, under ASC 606-10-55-42 and 55-43 to determine whether the US Rights or the Global Rights provided BMS a "material right" and concluded that BMS' options to exercise its US Rights and Global Rights represented "material rights" to BMS that it would not have received without entering into the Collaboration Agreement.

At inception of the Collaboration Agreement, there were a total of six options, including US Rights and Global Rights to acquire a US License and a Global License, respectively, and rights to request certain development services (following exercise of the US Rights and Global Rights, respectively) for each of the three programs. None of which were remaining as of May 24, 2024. The deferred revenue balance as of December 31, 2024 of $12.3 million is related to the outstanding PRX019 Phase 1 Clinical Trial Obligation ("PRX019 Phase 1 Clinical Trial Obligation").

US License Agreement for the Tau/BMS-986446 Collaboration Target

BMS exercised its US Rights for the tau/BMS-986446 (formerly PRX005) Collaboration Target and on July 30, 2021, PBL entered into a U.S. License Agreement granting BMS an exclusive license to develop, manufacture and commercialize tau Collaboration Products in the United States targeting tau (the "Tau US License Agreement"). The Company received an associated option exercise fee of $80.0 million.

The Tau US License Agreement included the following distinct performance obligations: (1) the delivery of the US License for tau/BMS-986446 Collaboration Target ("Tau US License Obligation"); and (2) the Company's obligation to provide development activities under the development plan during any Phase 1 clinical trials (the "Tau US Development Services Obligation"). Revenue allocated to the Tau US License Obligation was recognized when the Company satisfied its obligation at a point in time, while the revenue allocated to the Tau US Development Services Obligation was recognized over time using an input-based model. All performance obligations have been delivered.

Global License Agreement for the Tau/BMS-986446 Collaboration Target

Subsequently, BMS exercised its Global Rights for the tau/BMS-986446 Collaboration Target and on July 5, 2023, PBL entered into a Global License Agreement granting BMS an exclusive license to develop, manufacture and commercialize tau Collaboration Products globally for any and all uses or purposes with respect to any human or animal disease, disorder or condition (the "Tau Global License Agreement"). The Tau Global License Agreement supersedes and replaces the Tau US License Agreement in its entirety. The Company received an associated option exercise fee of $55.0 million in August 2023 and it is eligible to receive regulatory and sales milestones up to $562.5 million upon achievement of certain events, including regulatory approval of a tau Collaboration Product, and on BMS achieving certain annual, worldwide net sales thresholds. The Company also is eligible to receive tiered royalties on net sales of tau Collaboration Products, ranging from high single digit to high teen percentages, on a weighted average basis depending on the achievement of certain net sales thresholds.

The Company's distinct performance obligation under the Tau Global License Agreement was limited to the delivery of the Global License for tau/BMS-986446 Collaboration Target ("Tau Global License Obligation"). Revenue allocated to the Tau Global License Obligation was recognized by the Company at the time that the license was delivered in July 2023.

Global License Agreement for the undisclosed/PRX019 Collaboration Target

On May 24, 2024, PBL entered into a Global License Agreement granting BMS an exclusive license to develop, manufacture and commercialize Collaboration Products targeting an undisclosed target (including PRX019) globally for any and all uses or purposes with respect to any human or animal disease, disorder or condition (the "PRX019 Global License Agreement"). The Company received an associated option exercise fee of $80.0 million in June 2024 and is eligible to receive further development and regulatory milestones of up to $242.5 million upon achievement of certain development and regulatory milestones, including regulatory approval, of a Collaboration Product, and up to $375.0 million upon BMS achieving certain annual, worldwide net sales thresholds. The Company also is eligible to receive tiered royalties on annual, worldwide net sales of Collaboration Products, ranging from high single digit to high teen percentages, on a weighted average basis depending on the achievement of certain net sales thresholds. Such milestones and royalty payments (i) could be reduced in the case where BMS is successful in developing a modified version of PRX019 that achieves certain specified improved metrics, and (ii) are subject to certain reductions as specified in the PRX019 Global License Agreement.

The PRX019 Global License Agreement included the following distinct performance obligations: (1) the delivery of the Global License for the undisclosed Collaboration Target ("PRX019 Global License Obligation"); and (2) the Company's obligation to run a Phase 1 clinical trial for PRX019. Pursuant to the terms of the PRX019 Global License Agreement, BMS may elect to assume responsibility for completing such Phase 1 clinical trial (at its cost). Revenue allocated to the PRX019

Global License Obligation was recognized when the Company satisfied its obligation at a point in time, while the revenue allocated to the PRX019 Phase 1 Clinical Trial Obligation is recognized over time using an input-based model.

Transaction Price

At inception of the Collaboration Agreement, the Company did not transfer any goods or services to BMS that were material. Accordingly, the Company concluded that the initial transaction price would be recognized as a contract liability and would be deferred until the Company transfers control of goods or services to BMS (which would be when BMS exercises the US Right or Global Right and receives control of the US License or Global License for at least one of the programs), or when the IND Option term expires if BMS had not yet exercised the US Right, or when the Phase 1 Option term expires if BMS had not yet exercised the Global Right, or at the termination of the Collaboration Agreement, whichever occurs first. At such point that the Company transfers control of goods or services to BMS, or when the option expires, the Company would recognize revenue as a continuation of the original contract. Under this approach, the Company would treat the consideration allocated to the material right as an addition to the consideration for the goods or services underlying the contract option.

At inception of the Collaboration Agreement, the Company estimated the standalone selling price for each performance obligation (i.e., the US Rights and Global Rights by program). The estimate of standalone selling price for the US Rights and Global Rights by program was based on the adjusted market assessment approach using a discounted cash flow model. The key assumptions used in the discounted cash flow model included the market opportunity for commercialization of each program in the U.S. or globally depending on the license, the probability of successfully developing and commercializing a given program target, the estimated remaining development costs for the respective program, the estimated time to commercialization of the drug for that program, and a discount rate.

The initial transaction price under the Collaboration Agreement, pursuant to ASC 606, was $110.2 million, including the $100.0 million upfront payment and $10.2 million premium on the ordinary shares purchased under the SSA. The Company allocated the initial transaction price across the US Rights and Global Rights for each program in a range of approximately $15-$25 million and $10-$18 million, respectively.

The Company did not include the option fees in the initial transaction price because such fees are contingent on the options to the US Rights and the Global Rights being exercised. Upon the exercise of the US Rights and the Global Rights for a program, the Company would have the obligation to deliver the US License and Global License and provide certain ancillary development services if requested by BMS, subsequent to its exercise of the US Rights and Global Rights, respectively, for such program. The Company would include the option fees in the transaction price at the point in time a material right is exercised and the Company transfers control of the goods and services to BMS. In addition, the Company did not include in the initial transaction price certain clinical and regulatory milestone payments since they relate to licenses for which BMS had not yet exercised its option to obtain and these variable considerations are constrained due to the likelihood of a significant revenue reversal.

Upon entering into the Tau Global License Agreement, the Company granted BMS a Global License for the tau/BMS-986446 Collaboration Target, which transferred control of such underlying Global License to BMS. Following execution of the Tau Global License Agreement, BMS paid the Company a $55.0 million option exercise fee. Under the continuation of the original contract method, the Company computed the relative sales price after the Company transferred control of the Global License for tau/BMS-986446. The Company used the original allocated consideration for the Global Right for tau/BMS-986446 of $17.9 million (computed at the inception of the contract) plus the $55.0 million option exercise fee to arrive at the total transaction price of approximately $72.9 million. Given that the Company's distinct performance obligation under the Tau Global License Agreement was limited to the Tau Global License Obligation no further allocation was required.

Upon entering into the PRX019 Global License Agreement, the Company granted BMS a Global License for the undisclosed/PRX019 Collaboration Target, which transferred control of such underlying Global License to BMS. Following execution of the PRX019 Global License Agreement, BMS paid the Company an $80.0 million option exercise fee. As the original contract contemplated a US and Global payment for $80.0 million and $55.0 million, respectively, and a new payment structure and only one license was agreed to, accordingly, the payment was accounted for under modification accounting. The Company concluded that the modification would be accounted for on a prospective basis as a termination of the existing contract and creation of a new contract. The Company computed the relative sales price for the identified remaining

performance obligations consisting of the Global License for PRX019 and the PRX019 Phase 1 Clinical Trial Obligation. The transaction price consisted of the original allocated consideration for the US Right for PRX019 of $24.9 million, and original allocated consideration for the Global Right for PRX019 of $17.4 million (both computed at the inception of the Collaboration Agreement) plus the $80.0 million option exercise fee to arrive at the total transaction price of approximately $122.4 million. This total transaction price was allocated using the relative sales price method between the PRX019 Global License Obligation and the PRX019 Phase 1 Clinical Trial Obligation.

The best estimate of selling price for the Global License for PRX019 was based on a discounted cash flow model. The key assumptions used in the discounted cash flow model used to determine the best estimate of selling price for the license included the market opportunity for commercialization of PRX019, the probability of successfully developing/commercializing PRX019, the remaining development costs for PRX019, and the estimated time to commercialization of PRX019 using a discount rate of 13%. Based on the relative selling price method, the amount that the Company allocated to the performance obligations was as follows: $106.3 million to the license to be recognized concurrent with the delivery of the license; and $16.1 million as development services for the Phase 1 clinical trial to be recognized based on input-based model over the service period.

Significant Payment Terms

The upfront payment of $100.0 million was received in April 2018, while all option fees and milestone payments are due within 30 days after the achievement of the relevant milestone by BMS or receipt by BMS of an invoice for such an amount from the Company.

The Collaboration Agreement does not have a significant financing component since a substantial amount of consideration promised by BMS to the Company is variable and the amount of such variable consideration varies based upon the occurrence or non-occurrence of future events that are not within the control of either BMS or the Company. Variable considerations related to clinical and regulatory milestone payments and option fees are constrained due to the likelihood of a significant revenue reversal.

Revenue and Expense Recognition

Collaboration revenue from BMS was $135.1 million, $91.3 million and $13.9 million for the year ended December 31, 2024, 2023 and 2022, respectively. For the year ended December 31, 2024, collaboration revenue included recognition of $110.1 million for the transfer of the PRX019 Global License and partial performance of the PRX019 Phase 1 Clinical Trial Obligation. In addition, the material rights for the US Rights and Global Rights for the TDP-43 Collaboration Target of $14.6 million and $10.4 million, respectively, expired unexercised on May 24, 2024 as a result of the expiration of the research term of the Collaboration Agreement. Accordingly, $25.0 million of deferred revenue was recognized as revenue on May 24, 2024.

Collaboration revenue for the year ended December 31, 2023 included recognition of $72.9 million for the Tau Global License Obligation ($55.0 million tau global option exercise fee and $17.9 million of deferred revenue recognized for the Global Right for the tau Collaboration Product), $4.7 million under a supply agreement with BMS and the remainder was primarily recognized for Tau US Development Services Obligation. Collaboration revenue for the year ended December 31, 2022, included recognition of $13.9 million for Tau US Development Services Obligation.

As of December 31, 2024, the aggregate amount of the transaction price allocated to the performance obligations that are unsatisfied was $12.3 million. The Company had nil and $5.2 million accounts receivable from BMS at December 31, 2024, and December 31, 2023, respectively.

Deferred Revenue

The deferred revenue balance at the beginning of the fiscal year was $67.4 million and the $80.0 million global exercise fee was added during 2024. During the year ended December 31, 2024, $110.1 million of deferred revenue was recognized as collaboration revenue related to the PRX019 Phase 1 Clinical Trial Obligation performed, and $25.0 million was recognized for TDP-43 Collaboration Target which expired unexercised. As of December 31, 2024, the total deferred revenue balance of $12.3 million relates to outstanding performance obligations related to the PRX019 Phase 1 Clinical Trial Obligation of which $8.9

million, and $3.4 million remained in current and non-current deferred revenue, respectively. The deferred revenue balance will be recognized as revenue over the remaining service period.

Milestone and Royalties Accounting

Under the Tau Global License Agreement, the Company is eligible to receive milestone payments of up to $187.5 million upon the achievement of certain specified regulatory milestones and milestone payments of up $375.0 million upon the achievement of certain specified commercial sale milestones. Under the PRX019 Global License Agreement, the Company is eligible to receive milestone payments of up to $242.5 million upon the achievement of certain specified development and regulatory milestones and milestone payments of up $375.0 million upon the achievement of certain specified commercial sale milestones. Milestone payments are evaluated under ASC Topic 606. Factors considered in this determination included scientific and regulatory risk that must be overcome to achieve each milestone, the level of effort and investment required to achieve the milestone, and the monetary value attributed to the milestone. Accordingly, the Company estimates payments in the transaction price based on the most likely approach, which considers the single most likely amount in a range of possible amounts related to the achievement of these milestones. Additionally, milestone payments are included in the transaction price only when the Company can conclude it is probable that a significant revenue reversal will not occur in future periods.

The Company excluded the milestone payments and royalties in the initial transaction price because such payments are considered to be variable considerations with constraint. Such milestone payments and royalties will be recognized as revenue at a point in time when the Company can conclude it is probable that a significant revenue reversal will not occur in future periods.

The Company did not achieve any clinical and regulatory milestones under the Collaboration Agreement during the years ended December 31, 2024, 2023 and 2022, respectively.

Novo Nordisk Share Purchase Agreement

On July 8, 2021, the Company together with its wholly owned subsidiary, PBL, entered into a definitive share purchase agreement with Novo Nordisk A/S and Novo Nordisk Region Europe A/S (each an unrelated party). Under the terms of such agreement, Novo Nordisk acquired PBL's wholly-owned subsidiary, Neotope Neuroscience Limited ("NNL") and gained full worldwide rights to the intellectual property and related rights to the Company's ATTR amyloidosis business and pipeline. Upon consummation of the transaction, NNL ceased to be a related party of PBL. The aggregate purchase price consisted of an upfront payment of $60.0 million in cash, subject to customary purchase price adjustments.

Should Novo Nordisk achieve certain stages of development or commercialization for products or product candidates containing coramitug (formerly PRX004) or a derivative thereof in ATTR amyloidosis, PBL is entitled to receive certain milestone payments based on specified development and commercial milestones. The development and commercialization milestone payments will be discounted if the milestone events are achieved with respect to other indications. Should Novo Nordisk achieve specified thresholds of worldwide, annual net sales of the milestone products, regardless of indication, PBL will also be entitled to receive specified one-time net sales milestone payments. All milestone payments attributable to an achieved milestone will be paid to PBL, subject to Novo Nordisk's offset right for indemnity claims or unpaid amounts in respect of any purchase price adjustment.

The upfront payment of $60.0 million was accounted for as revenue in 2021. In addition to the upfront payment, Novo Nordisk agreed to pay for certain out of pocket expenses under the Transition Services Agreement, which netted to $0.7 million after closing adjustments related to the sale of the ATTR amyloidosis business and pipeline.

Contingent Consideration/Milestone Accounting

In December 2022, the Company received a $40.0 million development milestone payment related to the continued advancement of coramitug in a Phase 2 clinical trial for the treatment of ATTR cardiomyopathy. This amount was accounted for as revenue from license and intellectual property in 2022.

The Company is eligible to receive additional development and sales milestone payments from Novo Nordisk totaling up to $1.13 billion upon achievement of certain specified development and commercial sales milestones under the share purchase agreement.

The Company excluded the milestone payments in the initial transaction price because such payments are considered to be variable considerations with constraint. Such milestone payments will be recognized as revenue at a point in time when the Company can conclude it is probable that a significant revenue reversal will not occur in future periods.

Revenue Recognition

Total revenue recognized related to the transaction during the years ended December 31, 2024, 2023 and 2022 was nil, nil and $40.0 million, respectively. The Company had no accounts receivable from Novo Nordisk as of December 31, 2024, and 2023, respectively.

7. Shareholders' Equity

Ordinary Shares

As of December 31, 2024, the Company had 100,000,000 ordinary shares authorized for issuance with a par value of $0.01 per ordinary share and 53,826,982 ordinary shares issued and outstanding. Each ordinary share is entitled to one vote and, on a pro rata basis, to dividends when declared and the remaining assets of the Company in the event of a winding up. As of December 31, 2024, 15,332,174 ordinary shares are reserved for issuance pursuant to outstanding and future equity awards under the Company's equity incentive plans.

Euro Deferred Shares

As of December 31, 2024, the Company had 10,000 Euro Deferred Shares authorized for issuance with a nominal value of €22 per share. No Euro Deferred Shares are outstanding at December 31, 2024. The rights and restrictions attaching to the Euro Deferred Shares rank *pari passu* with the ordinary shares and are treated as a single class in all respects.

December 2022 Offering

In December 2022, the Company completed an underwritten public offering of an aggregate of 3,250,000 of its ordinary shares at a public offering price of $56.50 per ordinary share. The Company received aggregate net proceeds of approximately $172.4 million, after deducting the underwriting discount and offering costs.

In January 2023, the Company issued an additional 395,096 ordinary shares resulting from the underwriters' partial exercise of their 30-day option to purchase up to an additional 487,500 ordinary shares of as part of the December 2022 underwritten public offering. The Company received approximately $20.9 million proceeds from the exercise, net of underwriting discount but before deducting any offering costs.

At-the-Market Offerings

In December 2021, the Company entered into an Equity Distribution Agreement (the "December 2021 Distribution Agreement"), pursuant to which the Company could issue and sell, from time to time, the Company's ordinary shares. In connection with entering into the December 2021 Distribution Agreement, on December 23, 2021, the Company filed with the SEC a prospectus supplement relating to the offer, issuance and sale of up to $250.0 million of the Company's ordinary shares (the "December 2021 Prospectus") pursuant to the December 2021 Distribution Agreement.

For the years ended December 31, 2023, and 2022 the Company sold and issued 42,361 and 911,228 ordinary shares, respectively, pursuant to the December 2021 Distribution Agreement under the December 2021 Prospectus. For the years ended December 31, 2023, and 2022, total gross proceeds were approximately $3.2 million and $53.1 million, respectively, before deducting underwriting discounts, commissions, and other offering expenses payable by the Company of $0.1 million and $1.7 million, respectively.

The December 2021 Prospectus was no longer effective as of March 23, 2024. As of March 23, 2024, the Company had sold and issued 953,589 ordinary shares pursuant to the December 2021 Distribution Agreement under the December 2021 Prospectus for total gross proceeds of approximately $56.3 million before deducting underwriting discounts, commissions, and other offering expenses paid by the Company of $1.8 million.

In February 2024, the Company amended the Equity Distribution Agreement that it entered into in December 2021 (the "Amended Distribution Agreement"), pursuant to which the Company may issue and sell, from time to time, the Company's ordinary shares. In connection with amending the Amended Distribution Agreement, on February 22, 2024, the Company filed with the SEC a prospectus relating to the offer, issuance, and sale of up to $250.0 million of the Company's ordinary shares (the "February 2024 Prospectus") pursuant to the Amended Distribution Agreement. For the year ended December 31, 2024, the Company sold and issued no ordinary shares pursuant to the Amended Distribution Agreement under the February 2024 Prospectus.

The issuance and sale of the Company's ordinary shares pursuant to the December 2021 Distribution Agreement and the Amended Distribution Agreement is deemed an "at-the-market" offering and is registered under the Securities Act of 1933, as amended.

8. Share-Based Compensation

Equity Incentive Plans

The Company's equity incentive plans, the 2018 Long Term Incentive Plan, as amended (the "2018 LTIP"), 2020 Employment Inducement Incentive Plan, as amended (the "2020 EIIP"), and previously, the Amended and Restated 2012 Long Term Incentive Plan (the "2012 LTIP"), reserve ordinary shares for the issuance of stock options, stock appreciation rights, restricted shares, RSUs, performance bonus awards, performance share units awards, dividend equivalents and other share or cash-based awards to eligible individuals. Options granted under each of the 2018 LTIP, 2020 EIIP, and 2012 LTIP expire no later than ten years from the date of grant.

In May 2024, the Company's shareholders approved an amendment to the 2018 LTIP to increase the number of ordinary shares available for issuance under the 2018 LTIP by 2,000,000 ordinary shares. As of December 31, 2024, the number of ordinary shares authorized under the 2018 LTIP was 16,620,433. Upon adoption of the 2018 LTIP, no new awards are permitted under the 2012 LTIP.

As of December 31, 2024, the number of ordinary shares authorized under the 2020 EIIP was 1,485,000 and 341,584 ordinary shares remained available for future awards under the 2020 EIIP. The Company's Board of Directors has adopted a series of amendments to increase the ordinary shares available for issuance under the 2020 EIIP and it reserves the right to both amend the 2020 EIIP to increase the number of ordinary shares available and make additional awards to key new hires.

The Company's option awards generally vest over four years, while RSUs vest over two years. As of December 31, 2024, 4,218,801 ordinary shares remained available for grant under its equity plans.

Share-based Compensation Expense

Share-based compensation expense recorded in these Consolidated Financial Statements for the years ended December 31, 2024, 2023 and 2022, was based on awards granted under the 2012 LTIP, the 2018 LTIP, and the 2020 EIIP. The estimated forfeiture rate as of December 31, 2024 was 7%. Changes in our estimates and assumptions relating to forfeitures may cause us to realize changes in stock-based compensation expense in the future.

The amount of unearned share-based compensation related to unvested stock options at December 31, 2024, is $74.5 million. The weighted-average period over which this unearned share-based compensation is expected to be recognized is 2.54 years.

The following table summarizes share-based compensation expense for the periods presented (in thousands):

	Year Ended December 31,		
	2024	2023	2022
Research and development	$ 20,931	$ 19,211	$ 14,805
General and administrative	25,033	21,703	16,517
Total share-based compensation expense	$ 45,964	$ 40,914	$ 31,322

The Company recognized tax benefits from share-based awards of $8.3 million, $7.2 million, and $5.8 million, for the years ended December 31, 2024, 2023 and 2022, respectively.

The fair value of the options granted to employees and non-employee directors during the years ended December 31, 2024, 2023 and 2022 was estimated as of the grant date using the Black-Scholes option-pricing model using the key assumptions listed in the following table.

	Year Ended December 31,		
	2024	2023	2022
Expected volatility*	74.5% - 78.6%	76.4% - 90.1%	82.1% - 86.0%
Risk-free interest rate*	3.5% - 4.7%	3.5% - 4.8%	1.5% - 4.2%
Expected dividend yield	—%	—%	—%
Expected life (in years)*	4.6 - 5.7	4.4 - 5.4	6.0 - 6.0
Weighted average grant date fair value	$18.69	$37.32	$23.43

**The presentation of the expected volatility, risk-free interest rate, and expected life for 2023 and 2022 has been revised to present as range of values to conform to the current year presentation.*

The fair value of employee stock options is amortized on a straight-line basis over the requisite service period for each award. Each of the inputs discussed above is subjective and generally requires management judgment to determine.

The following table summarizes the Company's stock option activity during the year ended December 31, 2024:

	Options	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (years)	Aggregate Intrinsic Value (in thousands)
Outstanding at December 31, 2023	9,866,337	$ 29.06	6.60	$ 118,447
Granted	2,288,450	28.69		
Exercised	(125,615)	15.19		
Forfeited	(524,505)	36.44		
Expired	(397,294)	31.70		
Outstanding at December 31, 2024	11,107,373	$ 28.70	6.16	$ 3,401
Vested and expected to vest at December 31, 2024	10,827,212	$ 28.52	6.09	$ 3,401
Exercisable at December 31, 2024	7,546,069	$ 25.17	4.99	$ 3,397

The total intrinsic value of options exercised was $1.3 million, $52.1 million, and $49.2 million during the years ended December 31, 2024, 2023 and 2022, respectively, determined as of the date of exercise.

The following table summarizes the activity and related information for RSUs during the year ended December 31, 2024:

	Number of Units	Weighted Average Grant-Date Fair Value	Weighted Average Remaining Contractual Term (years)	Aggregate Intrinsic Value (in thousands)
Unvested at December 31, 2023	25,250	$ 58.01	1.09	$ 918
Units Granted	—	—		
Units Vested	(19,250)	59.95		
Units Forfeited	—	—		
Unvested at December 31, 2024	6,000	$ 51.80	0.71	$ 83
Unvested and expected to vest at December 31, 2024	5,699	$ 52.06	0.71	$ 79

The fair value of RSUs was determined on the date of grant based on the market price of the Company's ordinary shares as of that date. The fair value of the RSUs is recognized as an expense on a straight-line basis over the vesting period of each RSU. Upon the vesting of the RSUs, a portion of the shares vested are sold by the employee to satisfy employee withholding tax requirements (sell-to-cover). As of December 31, 2024, total compensation cost not yet recognized related to unvested RSUs was $0.1 million, which is expected to be recognized over a weighted-average period of 0.71 years. RSUs settle into ordinary shares upon vesting.

9. Income Taxes

The Company files its U.S. and Irish income tax returns and income taxes are presented in the Consolidated Financial Statements using the asset and liability method prescribed by the accounting guidance for income taxes.

Income (loss) before provision for income taxes by country for each of the fiscal periods presented is summarized as follows (in thousands):

	Year Ended December 31,		
	2024	2023	2022
Ireland	$ (129,602)	$ (153,920)	$ (119,571)
U.S.	672	(6,560)	(6,034)
Loss before provision for income taxes	$ (128,930)	$ (160,480)	$ (125,605)

Components of the provision for income taxes for each of the fiscal periods presented consisted of the following (in thousands):

	Year Ended December 31,		
	2024	2023	2022
Current:			
U.S. Federal	$ 2,676	$ 2,200	$ 2,422
U.S. State	50	37	55
Ireland	—	—	—
Total current provision	$ 2,726	$ 2,237	$ 2,477
Deferred:			
U.S. Federal	$ (9,298)	$ (15,647)	$ (11,039)
U.S. State	(48)	(42)	(94)
Ireland	—	—	—
Total deferred benefit	$ (9,346)	$ (15,689)	$ (11,133)
Benefit from income taxes	$ (6,620)	$ (13,452)	$ (8,656)

The Company recorded a net tax shortfall (windfall) from stock option exercises of $1.0 million, $(3.5) million, and $(3.2) million for the years ended December 31, 2024, 2023 and 2022 respectively, all of which were recorded as part of its income tax provision in the Consolidated Statements of Operations.

The provision for income taxes differs from the statutory tax rate of 12.5% applicable to Ireland primarily due to Irish net operating losses for which a tax provision benefit is not recognized, U.S. income taxed at different rates, adjustments to deferred tax assets for the deductibility of stock compensation and capitalization of research and development costs. Following is a reconciliation between income taxes computed at the Irish statutory tax rate and the provision for income taxes for each of the fiscal periods presented (in thousands):

	Year Ended December 31,		
	2024	2023	2022
Taxes at the Irish statutory tax rate of 12.5%	$ (16,116)	$ (20,060)	$ (15,700)
Income tax at rates other than applicable statutory rate	(5,594)	(7,072)	(2,338)
Change in valuation allowance	18,760	22,406	22,681
Share-based payments	7,533	615	518
Tax credits	(8,769)	(9,382)	(8,949)
Income not subject to tax	(2,560)	—	(5,000)
Other	126	41	132
Benefit from income taxes	$ (6,620)	$ (13,452)	$ (8,656)

Deferred income taxes reflect the net tax effect of temporary differences between the carrying amount of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes.

Significant components of the Company's net deferred tax assets as of December 31, 2024, and 2023 are as follows (in thousands):

	December 31, 2024	December 31, 2023
Deferred tax assets:		
Net operating loss carryforwards	$ 171,191	$ 156,046
Tax credits	23,968	23,728
Lease liabilities	2,424	2,686
Accruals and other	1,521	1,887
Capitalized R&D	33,951	25,067
Share-based compensation	11,810	9,364
Gross deferred tax assets	244,865	218,778
Valuation allowance	(198,869)	(181,713)
Net deferred tax assets	45,996	37,065
Deferred tax liability:		
Operating lease right-of-use assets	(2,393)	(2,706)
Fixed Assets	(364)	(466)
Net deferred tax assets	$ 43,239	$ 33,893

The Company's deferred tax assets ("DTA") are composed primarily of its Irish subsidiaries' net operating loss carryforwards, state net operating loss carryforwards available to reduce future taxable income of the Company's U.S. subsidiaries, federal and California tax credit carryforwards, share-based compensation, capitalized R&D, and other temporary differences. The Company maintains a valuation allowance against certain U.S. federal and state and Irish deferred tax assets. Each reporting period, the Company evaluates the need for a valuation allowance on its deferred tax assets by jurisdiction.

For the year ended December 31, 2024, the Company recorded an increase in DTA of $9.3 million, primarily due to Section 174 R&D Capitalization requirements of $8.9 million. For the year ended December 31, 2023, the Company recorded an increase in DTA of $15.7 million, primarily due to Section 174 R&D Capitalization requirements of $14.5 million, which became effective in 2022.

Recognition of deferred tax assets is appropriate when realization of such assets is more likely than not. Based upon the weight of available evidence, especially the uncertainties surrounding the realization of deferred tax assets through future taxable income, the Company believes it is not yet more likely than not that certain deferred tax assets will be fully realizable. Accordingly, the Company has provided a valuation allowance of $198.9 million against its deferred tax assets as of December 31, 2024, primarily in relation to deferred tax assets arising from Irish net operating losses and Federal and California tax credits. The deferred tax assets recognized net of the valuation allowance, $43.2 million as of December 31, 2024, consisted predominantly of U.S. federal temporary differences. Due to expected future U.S. operating income, the Company expects to realize such deferred tax assets. The net increase of $17.2 million in the valuation allowance during the year ended December 31, 2024, was primarily due to Irish net operating losses.

As of December 31, 2024, certain of the Company's Irish entities had trading loss carryovers of $1.2 billion and non-trading loss carryovers of $20.9 million, each of which can be carried forward indefinitely. Trading losses are available against income from the same trade/trades while non-trading losses (excess management expenses) are available against future investment income in the company in which they arise. In addition, as of December 31, 2024, the Company had state net operating loss carryforwards of approximately $128.9 million, which are available to reduce future taxable income, if any, for the Company's U.S. subsidiary. If not utilized, the state net operating loss carryforward begins expiring in 2032.

The Company also has federal and California research and development credit carryforwards of $17.3 million and $22.1 million, respectively, at December 31, 2024. The Tax Reform Act of 1986 and similar California legislation impose substantial

restrictions on the utilization of net operating losses and tax credit carryforwards in the event that there is a change in ownership as provided by Section 382 of the Internal Revenue Code and similar state provisions. Such a limitation could result in the expiration of the net operating loss carryforwards and tax credits before utilization, which could result in increased future tax liabilities. The federal research and development credit carryforwards will expire starting in 2042 if not utilized. The California tax credits can be carried forward indefinitely.

Cumulative unremitted earnings of the Company's U.S. subsidiaries total approximately $247.4 million at December 31, 2024. The Company's U.S. subsidiaries' cash balances at December 31, 2024, are committed for its working capital needs and are considered to be indefinitely invested. As such, no provision for income tax has been recognized on undistributed earnings of the Company's U.S. subsidiaries. The determination of a hypothetical unrecognized deferred tax liability as of December 31, 2024 is not practicable because of the complexity and variety of assumptions necessary to compute the tax.

A reconciliation of the beginning and ending amounts of unrecognized tax benefits is as follows (in thousands):

	2024	2023
Gross Unrecognized Tax Benefits at January 1	$ 13,354	$ 11,564
Additions for tax positions taken in the current year	2,201	2,355
Additions for tax positions taken in the prior year	—	—
Reductions for tax positions taken in the prior year	(128)	(565)
Gross Unrecognized Tax Benefits at December 31	$ 15,427	$ 13,354

If recognized, none of the Company's unrecognized tax benefits as of December 31, 2024, would reduce its annual effective tax rate, primarily due to corresponding adjustments to its deferred tax valuation allowance. As of December 31, 2024, the Company has not recorded a liability for potential interest or penalties. The Company also does not expect its unrecognized tax benefits to change significantly over the next 12 months.

The Company is subject to reviews and audits by the U.S. Internal Revenue Service ("IRS"), the Irish Revenue Commissioners, and other taxing authorities from time to time. The Company's U.S. subsidiaries are currently under examination by the IRS for tax year 2021. The Company periodically reviews its uncertain tax positions. The Company's assessment is based on many factors, including any ongoing IRS audits. For the year ended December 31, 2024, the Company's assessment did not result in a material change in unrecognized tax benefits. The tax years 2013 to 2024 remain subject to examination by the U.S taxing authorities and the tax years 2019 to 2024 remain subject to examination by the Irish taxing authorities as of December 31, 2024.

10. Employee Retirement Plan

In the U.S., the Company provides a qualified retirement plan under section 401(k) of the Internal Revenue Code (the "IRC") under which participants may contribute up to 100% of their eligible compensation, subject to maximum deferral limits specified by the IRC. In addition, the Company contributes 3% of each participating employee's eligible compensation, subject to limits specified by the IRC, on a quarterly basis. Further, the Company may make an annual discretionary matching and/or profit-sharing contribution as determined solely by the Company. The Company recorded total expense for matching contributions in the U.S. of $1.9 million, $1.7 million and $1.3 million for the years ended December 31, 2024, 2023 and 2022, respectively.

In Ireland, the Company operates a defined contribution plan in which it contributes up to 7.5% of an employee's eligible earnings. The Company recorded total expense for employer contribution in Ireland of $181,000, $152,000, and $133,000 in the years ended December 31, 2024, 2023 and 2022, respectively.

11. Employees

The average number of persons employed by the Company during the years ended December 31, 2024 and 2023 was 169 and 154, respectively. The employees were grouped in the following categories:

	2024	2023
Research and development	122	112
General and administrative	47	42
Total employees	169	154

The aggregate payroll costs for the years ended December 31, 2024 and 2023 (in thousands) were as follows:

	2024 $	2023 $
Wages and salaries	44,232	40,280
Social welfare costs	6,481	6,556
Share based compensation expense	45,842	40,884
Pension and post retirement expense	2,052	1,849
Other:		
Principally employee benefits	10,539	10,579
Total employee costs	109,146	100,148

12. Director Remuneration

The following table sets forth information concerning the directors' emoluments for the years ended December 31, 2024 and 2023(in thousands):

	2024 $	2023 $
Emoluments: Non-Executive Director		
Gains on the exercise of certain share options	—	2,227
Fees for services as non-executive director	630	596
Emoluments: Executive Director		
Gains on the exercise of certain share options	—	1,975
Other emoluments - executive director	1,047	990
Contributions to pension schemes [(1)]	16	15
Total	1,693	5,803

[(1)] *Company contributions under the Company's tax-qualified 401(k) defined contribution plan*

13. Auditor's Remuneration

The following table sets forth fees paid (in thousands) to KPMG LLP (including its affiliate KPMG Ireland) for services provided to the Company during the years ended December 31, 2024 and 2023 (in thousands). All fees described below were approved by the Audit Committee.

	2024	2023
	$	$
Audit Fees[1]	1,437	1,366
Audit-Related Fees	—	—
Tax Fees[2]	173	97
All Other Fees	—	—
Total Fees	1,610	1,463

(1) *Consists of fees and out-of-pocket expenses for services rendered (a) for the audits of our annual financial statements, reviews of our quarterly financial statements, and audits of our Irish statutory financial statements, and (b) for the reviews of our registration statements, including the provision of comfort letters and consents. These amounts include fees paid to KPMG Ireland for the statutory audit of Prothena Corporation plc's Consolidated Financial Statements of $187,575 and $183,000 for fiscal year 2024 and 2023, respectively.*

(2) *Consists of fees and out-of-pocket expenses incurred in connection with international tax compliance and tax consultation services. These amounts include fees paid to KPMG Ireland for statutory tax compliance services for Prothena Corporation plc's Consolidated Financial Statements of $90,107 and $65,741 for fiscal year 2024 and 2023, respectively, and $82,764 and $31,474 for tax advisory services for fiscal year 2024 and 2023, respectively.*

14. Approval of the Financial Statements

The financial statements were approved by the directors on March 20, 2025.

Prothena Corporation plc

Parent Company Balance Sheet

As of 31 December 2024 and 2023
(in thousands, except par value)

	Notes	2024 $	2023 $
Assets			
Fixed assets			
Financial assets	*Note 3*	745,504	825,956
Current assets			
Debtors	*Note 4*	703	944
Cash at bank and in-hand		70,160	349,839
Total assets		816,367	1,176,739
Liabilities			
Capital and reserves			
Euro deferred shares, €22 nominal value:		—	—
Authorized shares — 10,000 at December 31, 2024 and 2023			
Issued and outstanding shares — none at December 31, 2024 and 2023			
Ordinary shares, $0.01 par value:		538	537
Authorized shares — 100,000,000 at December 31, 2024 and 2023			
Issued and outstanding shares — 53,826,982 and 53,682,117 at December 31, 2024 and 2023, respectively			
Share premium		479,746	477,840
Other reserves		286,288	240,324
Profit and loss account		49,317	457,563
Total shareholders' equity		815,889	1,176,264
Creditors			
Creditors	*Note 4*	478	475
Total creditors		478	475
Total equity and liabilities		816,367	1,176,739

See accompanying notes to the Parent Company Financial Statements.

/s/ Gene G. Kinney
Gene G. Kinney
Director

/s/ Shane M. Cooke
Shane M. Cooke
Director

March 20, 2025

Prothena Corporation plc

Parent Company Statement of Cash Flows

For the Years Ended 31 December 2024 and 2023

(in thousands)

	2024	2023
	$	$
Cash flows from operating activities:		
Net income (loss)	(408,246)	16,403
Adjustments to reconcile net income to cash used in operating activities:		
Share-based compensation	4,570	4,904
Interest income	(20,143)	(12,615)
Loss on impairment of financial assets	426,989	—
Changes in operating assets and liabilities:		
Other assets	519	(120)
Accounts payable, accruals and other liabilities	10	74
Net cash provided by operating activities	3,699	8,646
Cash flows from investing activities:		
Investments in subsidiaries	—	—
Return of investment in subsidiary	—	—
Net cash used in investing activities	—	—
Cash flows from financing activities:		
Loans to group undertakings	(285,000)	—
Proceeds from issuance of ordinary shares in public offering, net	—	20,689
Proceeds from issuance of ordinary shares in at-the market offering, net	(353)	2,894
Proceeds from issuance of ordinary shares upon exercise of stock options	1,975	25,204
Net cash provided by (used in) financing activities	(283,378)	48,787
Net increase (decrease) in cash and cash equivalents	(279,679)	57,433
Cash and cash equivalents at beginning of year	349,839	292,406
Cash and cash equivalents at end of year	70,160	349,839
Supplemental disclosures of non-cash investing and financing activities:		
Receivable from stock option exercises	—	68
Provision for impairment of financial assets	426,989	—
At-the market offering costs included in accounts payable and accrued liabilities	—	6
Difference between face amount of loans to subsidiary and its fair value included as investment in subsidiary	38,329	—

See accompanying notes to the Parent Company Financial Statements.

Prothena Corporation plc

Parent Company Statement of Shareholders' Equity

For the Years Ended 31 December 2024 and 2023
(in thousands)

	Ordinary Shares					
	Number	Share Capital	Share Premium	Other Reserves	Profit and Loss Account	Total Shareholders' Equity
		$	$	$	$	$
Balance at 31 December 2022	**52,103,608**	**521**	**432,419**	**199,410**	**441,160**	**1,073,510**
Share-based compensation				40,914		40,914
Issuance of ordinary shares upon exercise of stock options	1,135,302	12	21,445	—	—	21,457
Issuance of ordinary shares upon vesting of restricted stock units	5,750	—	—	—	—	—
Issuance of ordinary shares in public offering, net of offering costs	395,096	4	20,905	—	—	20,909
Issuance of ordinary shares under the at-the-market offering program	42,361	—	3,071	—	—	3,071
Share issue costs - at-the-market offering program	—	—	—	—	—	—
Net Income	—	—	—	—	16,403	16,403
Balance at 31 December 2023	**53,682,117**	**537**	**477,840**	**240,324**	**457,563**	**1,176,264**
Share-based compensation				45,964		45,964
Issuance of ordinary shares upon exercise of stock options	125,615	1	1,906	—	—	1,907
Issuance of ordinary shares upon vesting of restricted stock units	19,250	—	—	—	—	—
Net loss	—	—	—	—	(408,246)	(408,246)
Balance at 31 December 2024	**53,826,982**	**538**	**479,746**	**286,288**	**49,317**	**815,889**

See accompanying notes to the Parent Company Financial Statements.

Attributable income (loss) of the company

The income (loss) attributable to shareholders dealt with in the financial statements of the Company for the period ended 31 December 2024 was $(408.2) million (2023: $16.4 million). A separate profit and loss account is not presented in these financial statements as the Company has availed of the exemption provided by Section 304 of the Companies Act 2014.

Prothena Corporation plc

Notes

Forming part of the Parent Company Financial Statements

1. Summary of Significant Accounting Policies

Basis of Preparation

The directors have elected to prepare the Parent Company Financial Statements in accordance with Section 279 of the Companies Act 2014, which provides that a true and fair view of the assets and liabilities, financial position and profit or loss of a company and its subsidiary undertakings may be given by preparing its financial statements in accordance with U.S. accounting standards ("US GAAP") through December 31, 2023, as defined by Section 279(1) of the Companies Act 2014, to the extent that the use of those standards in the preparation of the financial statements does not contravene any provision of Part 6 of the Companies Act 2014. For 2024, the financial statements were prepared under Irish company law and IFRS as adopted by European Union. Management after careful consideration have not identified any material differences in the conversion.

Functional Currency

Items included in the balance sheet are measured using the currency of the primary economic environment in which the Company operates (the "functional currency"). The balance sheet is presented in U.S. dollars, which is the Company's functional currency. Transactions in foreign currencies are recorded at the rate ruling at the date of the transaction. The resulting monetary assets and liabilities are translated at the balance sheet rate with the resulting gains or losses reflected in the profit and loss account.

Profit and Loss Account

In accordance with Section 304 of the Companies Act 2014, the Company has availed of the exemption from presenting the individual profit and loss account. The net income (loss) for the years ended 31 December 2024 and 2023 was $(408.2) million and $16.4 million, respectively.

Financial Assets

The Company's original investment in subsidiary was recorded at cost, which equaled fair value on 20 December 2012 (the day immediately preceding the effective date of the separation and distribution referred to in Note 3 below), based on the Company's market capitalization at that time. This initial valuation is the Company's cost basis for its initial investment in its subsidiaries. Subsequent investments in subsidiaries are recorded at cost at the time of such investments. The investment is tested for impairment if circumstances or indicators suggest that impairment may exist and in any case, on an annual basis impairments are recognized directly in the profit and loss account.

Cash and Cash Equivalents

The Company considers all highly liquid investments held at financial institutions, such as commercial paper, money market funds, and other money market securities with original maturities of three months or less at date of purchase to be cash equivalents.

Taxation

Current tax is provided on the Company's taxable profits, at amounts expected to be paid, using the tax rates and laws that have been enacted or substantially enacted by the balance sheet date.

Deferred tax is accounted for in respect of all timing differences that have originated but not reversed at the balance sheet date. Provision is made at the tax rates that are expected to apply in the periods in which the timing differences are expected to reverse. Timing differences arise from the inclusion of items in income and expenditure in tax computations in periods different from those in which they are included in the financial statements.

A deferred tax asset is only recognized when it is more likely than not the asset will be recoverable in the foreseeable future out of suitable taxable profits from which the underlying timing differences can be recovered.

2. History and Description of the Company

The Company was incorporated in Ireland as a private limited company under the name "Neotope Corporation Limited" on 26 September 2012. On 25 October 2012, the Company re-registered as a public limited company and changed the name of the Company to "Neotope Corporation plc". On 1 November 2012, the Company's shareholders resolved to change the name of the Company to "Prothena Corporation plc", and this was approved by the Irish Registrar of Companies on 7 November 2012.

The Company's ordinary shares commenced trading on The Nasdaq Global Market under the symbol "PRTA" on 21 December 2012 and currently trade on The Nasdaq Global Select Market.

3. Financial Fixed Assets

Financial fixed assets consisted of the following at 31 December (in thousands):

	2024	2023
	$	$
Investment in subsidiaries	598,633	518,910
Amounts due from group undertakings	573,860	307,046
	1,172,493	825,956
Less: Provision for impairment of financial assets	(426,989)	—
	745,504	825,956

Loan Agreement with Prothena Biosciences Limited (PBL)

On 20 May 2015, the Company entered into a facility agreement which provides up to $60.0 million of loans to PBL. Loans drawn down under this facility are interest free and mature on 31 December 2022. On 8 June 2020, the Company entered into an amendment to increase the credit line by $110.0 million, and extended the maturity date for the loans drawn under this facility to 31 December 2024. This loan facility was further amended on 21 May 2021 to increase the credit line by $160.0 million.

On 18 Oct 2022, this loan facility was amended to increase the credit line by $20.0 million and extend the maturity date for the loans drawn under this facility to 31 December 2026.

This loan facility was further amended on 16 May 2023 to increase the credit line by $250.0 million, and on 2 October, 2024, this loan facility was further amended to increase the credit line by $60.0 million.

At 31 December 2024, the total amount drawn down and outstanding on this facility was $631.6 million (2023: $346.6 million) and the fair value of this loan as at 31 December 2024 $573.9 million (2023: $307.0 million).

At 31 December 2024, the provision for impairment of financial assets was $(427.0) million (2023: nil) which represents the difference between the market capitalization of the company as of 31 December 2024 and the carrying value of its financial assets.

Notes

Forming part of the Parent Company Financial Statements (continued)

Financial Fixed Assets (continued)

Investment in Subsidiaries

Investment in subsidiaries are as follows for the years ended 31 December (in thousands):

	2024 $	2023 $
Beginning cost	518,910	482,900
Fair value of loan to subsidiary	38,329	—
Capital contribution from substantial modification of loans to subsidiary	—	—
Share-based compensation for Prothena subsidiaries	41,394	36,010
Ending cost	598,633	518,910

The principal activity of Prothena Corporation plc is an investment holding company. Prothena Corporation plc is the 100% parent of Prothena Biosciences Limited (“PBL”). PBL is the 100% parent of Prothena Biosciences Inc (“PBI”), Othair Prothena Limited (“OPL”), Prothena Pharma Limited (“PPL”) and Prothena Platform Technologies Limited (”PPTL”), and from 2019 through a portion of 2021, PBL was a 100% parent of Neotope Neuroscience Limited (“NNL”). PBI is the 100% parent of Prothena Finance Inc (“PFI”). PBL, OPL, PPL, PPTL and NNL were incorporated in Ireland while PBI and PFI were incorporated in the United States. The principal activity of each remaining subsidiary is set out in the column entitled “Nature of Business” in the chart below.

In 2012, the Company acquired 100% of the ordinary share capital of PBL. The Company’s investment in PBL was recorded at fair value of $100,829,000 on 20 December 2012 (date of the separation and distribution) based on the market price of the Prothena Corporation plc ordinary shares at the time of the separation and distribution. This initial valuation became the Company’s cost basis in PBL.

In 2015 and 2016, respectively, the Company entered into Deeds of Capital Contribution (the "Deeds") with its subsidiary PBL. Under the terms of the Deeds, the Company made irrevocable, non-refundable and unconditional shareholder contributions to PBL in the amounts of $92.0 million and $45.0 million, respectively. Such contributions did not create a debt against PBL and were made without the issuance of shares to the Company by PBL.

In July, 2021, the Company together with PBL, entered into a definitive share purchase agreement with Novo Nordisk A/S and Novo Nordisk Region Europe A/S (each an unrelated party). Under the terms of such agreement, Novo Nordisk acquired PBL’s wholly-owned subsidiary NNL and gained full worldwide rights to the intellectual property and related rights to the Company’s ATTR amyloidosis business and pipeline. Upon consummation of the transaction, NNL ceased to be a related party of PBL.

Notes

Forming part of the Parent Company Financial Statements (continued)

At 31 December 2024, the following are the Company's subsidiary undertakings:

Company	Parent Company	Nature of Business	Class of Shares	Shares Held by Parent	Consideration Paid	Interest at	Registered Office
Prothena Biosciences Limited	Prothena Corporation plc	Late-stage clinical biotechnology company with focus on research and development on therapeutics for neurodegenerative diseases and peripheral amyloid.	Ordinary shares, par value $1.00 per share	100,811,000	$237.9M	100%	77 Sir John Rogerson's Quay, Block C Grand Canal Docklands Dublin 2, D02 VK60, Ireland
Prothena Biosciences Inc	Prothena Biosciences Limited	Clinical biotechnology company with focus on research and development on therapeutics for neurodegenerative diseases and peripheral amyloid.	Common Stock, par value $0.01 per share	100	$100	100%	1800 Sierra Point Parkway, Brisbane, CA 94005, U.S.A.
Othair Prothena Limited	Prothena Biosciences Limited	Clinical biotechnology company with focus on research and development in neurodegenerative diseases including Abeta.	Ordinary shares, par value $1.00 per share	100	$100	100%	77 Sir John Rogerson's Quay, Block C Grand Canal Docklands Dublin 2, D02 VK 60, Ireland
Prothena Pharma Limited	Prothena Biosciences Limited	Commercialization of pharmaceutical products	Ordinary shares, par value $1.00 per share	100	$100	100%	77 Sir John Rogerson's Quay, Block C Grand Canal Docklands Dublin 2, D02 VK 60, Ireland
Prothena Finance Inc	Prothena Biosciences Inc	Treasury and cash management services	Common Stock, par value $0.01 per share	70	$70.0M	100%	160 Greentree Drive, Suite 101, Dover, Delaware, 19904, Kent County, DE
Prothena Platform Technologies Limited	Prothena Biosciences Limited	Acquisition, development, exploitation and sale of intellectual property	Common Stock, par value $0.01 per share	100	$100	100%	77 Sir John Rogerson’s Quay, Block C, Grand Canal Docklands, Dublin 2, D02 VK60, Ireland

Notes

Forming part of the Parent Company Financial Statements (continued)

4. Debtors and Creditors

Debtors

Debtors consisted of the following at 31 December (in thousands):

	2024	2023
	$	$
Amount falling due within one year:		
Amounts owed by group undertakings[(1)]	—	68
Prepaid expenses and other current assets	351	355
	351	423
Amount falling due after more than one year:		
Other non-current assets	352	521
Total debtors	703	944

[(1)] *Amounts owed by other group undertakings are unsecured and repayable on demand.*

Creditors

Creditors consisted of the following at 31 December (in thousands):

	2024	2023
	$	$
Amount falling due within one year:		
Trade creditors	278	307
Amounts due to group undertakings	24	36
Accrued liabilities	176	132
Total creditors	478	475

5. Shareholders' Equity

Pursuant to sections 84 and 85 of the Companies Act of 2014 and pursuant to the special resolution of the members of the Company passed on 18 May 2021, that the Company's capital be reduced by reducing the amount standing credited to the Company's share premium account by $850.0 million such that the reserve resulting from the reduction share be treated as profits available for distribution as defined by section 117 of the Companies Act of 2014. This was approved by the High Court on 14 December 2021.

6. Employees

The Company had no employees as of 31 December 2024 and 2023.

Notes

Forming part of the Parent Company Financial Statements (continued)

7. Auditor's Remuneration

The following table sets forth fees (in thousands) to KPMG Ireland for services provided to the Company during the years ended 31 December 2024 and 2023:

	2024 $	2023 $
Audit fees [1]	13	12
Tax fees [2]	32	19
Total fees	45	31

[1] *Consists of fees to KPMG in Ireland for the statutory audit of Prothena Corporation plc.*

[2] *Consists of fees and out-of-pocket expenses to KPMG in Ireland for tax consultation and compliance services. These amounts include fees for corporate tax compliance for Prothena Corporation plc of 13,953 and 9,824 for fiscal year 2024 and 2023, respectively, and fees for tax advisory services of 11,700 and 5,787 for fiscal year 2024 and 2023, respectively.*

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