Table of Contents

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

FORM 20-F

(Mark One)

☐ **REGISTRATION STATEMENT PURSUANT TO SECTION 12(b) OR (g) OF THE SECURITIES EXCHANGE ACT OF 1934**

OR

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

For the fiscal year ended December 31, 2024

OR

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

OR

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

Date of event requiring this shell company report

For the transition period from _____ to _____ .

Commission file number: 001-40010

Pharvaris N.V.

(Exact name of Registrant as specified in its charter)

The Netherlands
(Jurisdiction of incorporation or organization)

Emmy Noetherweg 2
2333 BK Leiden
The Netherlands
+31 (0)71 2036 410
(Address of principal executive offices)

Berndt Modig,
Chief Executive Officer
Tel: +31 (0)71 2036 410
Emmy Noetherweg 2, 2333 BK Leiden, the Netherlands
(Name, Telephone, E-mail and/or Facsimile number and Address of Company Contact Person)

Copies to:

Sophia Hudson, P.C.
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Kirkland & Ellis LLP
601 Lexington Avenue
New York, NY 10022 Phone: (212) 446-4750
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Securities registered or to be registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Ordinary shares, par value €0.12 per share	**PHVS**	**The NASDAQ Global Select Market**

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

Securities for which there is a reporting obligation pursuant to Section 15(d) of the Act:
None

Indicate the number of outstanding shares of each of the issuer's classes of capital or common stock as of the close of the period covered by the annual report.

The number of outstanding common shares as of December 31, 2024 was 54,379,491.

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

If this report is an annual or transition report, indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934. Yes ☐ No ☒

Note – Checking the box above will not relieve any registrant required to file reports pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934 from their obligations under those Sections.

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

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

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

Large Accelerated Filer ☒	Accelerated Filer ☐	Non-accelerated Filer ☐
		Emerging growth company ☐

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

† The term "new or revised financial accounting standard" refers to any update issued by the Financial Accounting Standards Board to its Accounting Standards Codification after April 5, 2012.

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

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

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

Indicate by check mark which basis of accounting the registrant has used to prepare the financial statements included in this filing:

U.S. GAAP ☐	International Financial Reporting Standards as issued by the International Accounting Standards Board ☒	Other ☐

If "Other" has been checked in response to the previous question, indicate by check mark which financial statement item the registrant has elected to follow. ☐ Item 17 ☐ Item 18

If this is an annual report, indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes ☐ No ☒

Pharvaris N.V.

TABLE OF CONTENTS

Table of Contents

Unless otherwise indicated or the context otherwise requires, all references in this Annual Report on Form 20-F, or this Annual Report, to "Pharvaris N.V.," "Pharvaris," the "Company," "we," "our," "ours," "us" or similar terms refer to Pharvaris N.V. and its subsidiaries.

Presentation of Financial and Other Information

We report under IFRS Accounting Standards, or IFRS, as issued by the International Accounting Standards Board, or the IASB. None of the consolidated financial statements in this Annual Report were prepared in accordance with generally accepted accounting principles in the United States, or United States Generally Accepted Accounting Principles, or U.S. GAAP. We present our consolidated financial statements in euros and in accordance with IFRS, as issued by the IASB. We have made rounding adjustments to some of the figures included in this Annual Report. Accordingly, numerical figures shown as totals in some tables may not be an arithmetic aggregation of the figures that preceded them.

Unless otherwise indicated, all references in this Annual Report to "€," "euro," "EUR" or "cents" are to the currency introduced at the start of the third stage of the European Economic and Monetary Union pursuant to the treaty establishing the European Community, as amended. All references to "$," "US$" or "U.S. dollars" are to the lawful currency of the United States.

In connection with our initial public offering in the first quarter of 2021, we converted the legal form of our company under Dutch law from a private company with limited liability (*besloten vennootschap met beperkte aansprakelijkheid*) to a public company with limited liability (*naamloze vennootschap*) and changed our name from Pharvaris B.V. to Pharvaris N.V.

Market and Industry Data

The information in this Annual Report that has been sourced from third parties has been accurately reproduced and, as far as we are aware and able to ascertain from the information published by that third-party, no facts have been omitted that would render the reproduced information inaccurate or misleading. Industry publications generally state that their information is obtained from sources they believe reliable but that the accuracy and completeness of such information is not guaranteed and that the projections they contain are based on a number of significant assumptions. We are not aware of any exhaustive industry or market reports that cover or address our specific markets.

Trademarks

All trademarks, trade names and service marks appearing in this Annual Report are the property of their respective owners. Solely for convenience, the trademarks and trade names in this Annual Report are referred to without the symbols ® and ™, but such references should not be construed as any indication that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto. We do not intend to use or display other companies' trademarks or trade names to imply a relationship with, or endorsement or sponsorship of us by, any other companies.

CAUTIONARY STATEMENT REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report contains certain statements that are or may be forward-looking statements with respect to us, our industry and our business that involve substantial risks and uncertainties. All statements other than statements of historical fact contained in this Annual Report, including statements regarding our future financial condition, results of operations and/or business achievements, including, without limitation, statements containing the words "believe," "anticipate," "expect," "estimate," "may," "could," "should," "would," "will," "intend" and similar expressions are forward-looking statements. We have based these forward-looking statements largely on our current expectations and projections about future events and trends that we believe may affect our financial condition, results of operations, business strategy and financial needs. Such forward-looking statements involve unknown risks, uncertainties and other factors which may cause our actual results, financial condition, performance or achievements, or industry results, to be materially different from any future results, performance or achievements expressed or implied by such forward-looking statements. Factors that might cause such a difference include, but are not limited to:

- uncertainty in the outcome of our interactions with regulatory authorities, including the U.S. Food and Drug Administration or FDA, with respect to clinical trials in the U.S. and our ability to resolve any issues to the satisfaction of the FDA or any regulatory agency in a timely manner;
- the expected timing, progress, or success of our clinical development programs, especially for IR (immediate-release deucrictibant capsules) and XR (extended-release deucrictibant tablets), which are in late-stage global clinical trials;
- our ability to replicate the efficacy and safety demonstrated in the RAPIDe-1 and CHAPTER-1 Phase 2 study in ongoing and future nonclinical studies and clinical trials;
- risks arising from epidemic diseases which may adversely impact our business, nonclinical studies and clinical trials, the outcome and timing of regulatory approvals and the value of our ordinary shares;
- the timing, costs and other limitations involved in obtaining regulatory approval for our product candidates IR and XR or any other product candidate that we may develop in the future;
- our ability to market, commercialize and achieve market acceptance for our product candidates IR and XR or any of our other product candidates that we may develop in the future, if approved;
- our ability to establish commercial capabilities or enter into agreements with third parties to market, sell and distribute our product candidates;
- our dependence on third parties to perform critical activities related to the research, nonclinical safety and toxicology studies, development and manufacturing of our product candidates;
- disruptions at the FDA and other government agencies;
- the expense, time and uncertainty involved in the development and consistent manufacturing and supply of our product candidates, some or all of which may never reach the regulatory approval stage;
- our ability to raise capital when needed and on acceptable terms;
- our ability to enter into any new licensing agreements or to maintain any licensing agreements with respect to our product candidates;
- our reliance on collaboration partners and licensees, whose actions we cannot control;
- the willingness of private insurers and other payors to provide reimbursement for our products;
- regulatory developments in the United States, the European Union and other jurisdictions;
- the outcome and timing of price negotiations with governmental authorities;
- our ability to compete in the pharmaceutical industry, including with respect to existing therapies, emerging potentially competitive therapies and with competitive generic products;
- our ability to protect our intellectual property and know-how and operate our business without infringing the intellectual property rights or regulatory exclusivity of others;
- side effects or adverse events associated with the use of our product candidates;
- our ability to defend against costly and damaging liability claims resulting from the testing of our product candidates in the clinic or, if, approved, any commercial sales;
- the loss of any of our key personnel;
- our estimates of market sizes and anticipated uses of our product candidates;
- our estimates of future performance;
- our estimates regarding anticipated operating losses, future revenues, expenses, capital requirements and our needs for additional financing;

- our ability to comply with existing or future laws and regulations in a cost-efficient manner;
- our ability to manage negative consequences from changes in applicable laws and regulations, including tax laws;
- our ability to maintain an effective system of internal control over financial reporting;
- our expectations regarding the time during which we will be a foreign private issuer; and
- changes and uncertainty in general market, political and economic conditions, including as a result of inflation and the conflict between Russia and Ukraine and the Hamas attack against Israel and the ensuing war.

You should refer to the "ITEM 3. KEY INFORMATION—D. Risk factors." section of this Annual Report for a discussion of important factors that may cause our actual results to differ materially from those expressed or implied by our forward-looking statements. As a result of these factors, we cannot assure you that the forward-looking statements in this Annual Report will prove to be accurate. Furthermore, if our forward-looking statements prove to be inaccurate, the inaccuracy may be material. In light of the significant uncertainties in these forward-looking statements, you should not regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified time frame or at all. We undertake no obligation to publicly update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law. The Private Securities Litigation Reform Act of 1995 and Section 27A of the Securities Act do not protect any forward-looking statements that we make in connection with this Annual Report.

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

You should read this Annual Report and the documents that we reference in this Annual Report and have filed as exhibits to the Annual Report, completely and with the understanding that our actual future results may be materially different from what we expect. We qualify all of our forward-looking statements by these cautionary statements.

ENFORCEABILITY OF JUDGMENTS

We are organized and existing under the laws of the Netherlands. As such, under Dutch private international law, the rights and obligations of our shareholders vis-à-vis the Company originating from Dutch corporate law and our articles of association, as well as the civil liability of our officers (*functionarissen*) (including our directors and executive officers) are governed in certain respects by the laws of the Netherlands.

We are not a resident of the United States and our officers may also not all be residents of the United States. As a result, depending on the subject matter of the action brought against us and/or our officers, United States courts may not have jurisdiction. If a Dutch court has jurisdiction with respect to such action, that court will apply Dutch procedural law and Dutch private international law to determine the law applicable to that action. Depending on the subject matter of the relevant action, a competent Dutch court may apply another law than the laws of the United States.

Also, service of process against non-residents of the United States can in principle (absent, for example, a valid choice of domicile) not be effected in the United States.

Furthermore, most of our assets are located outside the United States. On the date of this Annual Report, (i) there is no treaty in force between the United States and the Netherlands for the reciprocal recognition and enforcement of judgments, other than arbitration awards, in civil and commercial matters and (ii) both the Hague Convention on Choice of Court Agreements (2005) and the Hague Judgments Convention (2019) have entered into force for the Netherlands, but have not entered into force for the United States. Consequently, a judgment rendered by a court in the United States will not automatically be recognized and enforced by the competent Dutch courts. However, if a person has obtained a judgment rendered by a court in the United States that is enforceable under the laws of the United States and files a claim with the competent Dutch court, the Dutch court will in principle give binding effect to that United States judgment if (i) the jurisdiction of the United States court was based on a ground of jurisdiction that is generally acceptable according to international standards, (ii) the judgment by the United States court was rendered in legal proceedings that comply with the Dutch standards of proper administration of justice including sufficient safeguards (*behoorlijke rechtspleging*), (iii) binding effect of such United States judgment is not contrary to Dutch public order (*openbare orde*) and (iv) the judgment by the United States court is not incompatible with a decision rendered between the same parties by a Dutch court, or with a previous decision rendered between the same parties by a foreign court in a dispute that concerns the same subject and is based on the same cause, provided that the previous decision qualifies for recognition in the Netherlands. Even if such a United States judgment is given binding effect, a claim based thereon may, however, still be rejected if the United States judgment is not or no longer formally enforceable. Moreover, if the United States judgment is not final (for instance when appeal is possible or pending) a competent Dutch court may postpone recognition until the United States judgment will

have become final, refuse recognition under the understanding that recognition can be asked again once the United States judgment will have become final, or impose as a condition for recognition that security is posted.

A competent Dutch court may deny the recognition and enforcement of punitive damages or other awards. Moreover, a competent Dutch court may reduce the amount of damages granted by a United States court and recognize damages only to the extent that they are necessary to compensate actual losses or damages. Finally, there may be specific other instances, including pursuant to anti-boycott rules and regulations, where Dutch law prohibits the recognition and enforcement of a United States judgment. United States investors may not be able, or experience difficulty, to enforce a judgment obtained in a United States court against us or our officers.

PART I

ITEM 1. IDENTITY OF DIRECTORS, SENIOR MANAGEMENT AND ADVISERS

A. Directors and senior management

Not applicable.

B. Advisers

Not applicable.

C. Auditors

Not applicable.

ITEM 2. OFFER STATISTICS AND EXPECTED TIMETABLE

A. Offer statistics

Not applicable.

B. Method and expected timetable

Not applicable.

ITEM 3. KEY INFORMATION

A. Reserved

B. Capitalization and indebtedness

Not applicable.

C. Reasons for the offer and use of proceeds

Not applicable.

D. Risk factors

You should carefully consider the risks and uncertainties described below and the other information in this Annual Report before making an investment in our ordinary shares. Our business, financial condition or results of operations could be materially and adversely affected if any of these risks occur, and as a result, the market price of our ordinary shares could decline, and you could lose all or part of your investment. This Annual Report also contains forward-looking statements that involve risks and uncertainties. See "Cautionary Statement Regarding Forward-Looking Statements." Our actual results could differ materially and adversely from those anticipated in these forward-looking statements as a result of certain factors.

Summary Risk Factors

- We have a limited operating history, have generated no revenues to date and have incurred significant losses since our inception. We expect to incur losses over the next several years, will not generate revenues until we are able to commercialize our products and may never achieve profitability, while our net losses are expected to fluctuate significantly.
- If we are unable to raise capital when needed or on acceptable terms, we may need to delay, reduce or terminate our product development programs and may be unable to continue as a going concern and could ultimately go into insolvency.
- Our business and operations may be adversely affected by a variety of events outside our control, including, but not limited to, outbreaks of infectious diseases and geopolitical instability such as the conflict between Russia and Ukraine and the Hamas attack against Israel and the ensuing war.
- We are heavily dependent on the success of our product candidates: (i) extended-release ("XR") tablet formulation of deucrictibant (previously referred to as PHVS719) and (ii) immediate-release ("IR") capsule formulation of deucrictibant (previously referred to as PHVS416), which are in late-stage development. We have released topline data from our RAPIDe-1 study demonstrating efficacy in our Phase 2 clinical trial for treatment of HAE attacks on demand using deucrictibant IR and topline data from our CHAPTER-1 study demonstrating efficacy in our Phase 2 clinical trial of deucrictibant XR of HAE attacks. We cannot give any assurance that either product candidate, or any other compounds in development, will successfully complete

clinical trials, receive regulatory approval, be commercialized, or be differentiated in the market. If we are unable to successfully commercialize our product candidates, or experience significant delays in doing so, our business, financial condition, results of operations and prospects would be materially adversely affected.

- We may experience setbacks in our clinical trials, including delays in commencing, conducting or completing our clinical trials. Moreover, we have established proof-of-concept for deucrictibant in Phase 2 trials for both treatment and prophylaxis of HAE attacks. We have designed and advanced our future clinical development program based on these results as well as modelling of our results from those trials with additional in vitro and in vivo data and comparisons to published results for other currently available products from different trials. We may not be able to replicate these results or analyses in future clinical trials that assess the endpoints required to obtain regulatory approval or we may have inconclusive or negative results. Any setbacks in our clinical development program could have a material adverse effect on our business, financial condition, results of operations and prospects.
- Clinical trials of our product candidates may not uncover all possible adverse effects that patients may experience.
- There can be no assurance that we will be able to obtain or, if obtained, maintain orphan drug status.
- If we fail to maintain effective internal control over financial reporting, we may not be able to accurately report our financial results or prevent fraud, and as a result, shareholders could lose confidence in our financial and other public reporting, which would harm our business and the trading price of our ordinary shares.
- We and our partners may be subject to new legislation, regulatory proposals and healthcare payor initiatives that may increase our costs of compliance and adversely affect our or our partners' ability to market our products, obtain collaborators and raise capital.
- Manufacturing issues may arise that could increase product and regulatory approval costs or delay commercialization of our products.
- The market opportunities for our product candidates may also be smaller than currently anticipated, lowering our potential revenue.
- If our product candidates achieve marketing approval, we expect that they will be priced at a significant premium over competitive generic products. This may make it difficult for us to achieve our business strategy of using our product candidates in combination with existing therapies or replacing existing therapies with our product candidates.
- Governments and/or pricing authorities, especially in the European Union, often impose strict price and access controls, which may adversely affect our future profitability.
- The insurance coverage and reimbursement status of newly approved products is uncertain. Failure to obtain or maintain adequate coverage and reimbursement for new or current products could limit our ability to market those products and decrease our ability to generate revenue.
- We may become exposed to costly and damaging liability claims, either when testing our product candidates in the clinic or after commercialization; and our product liability insurance may not cover all damages from such claims.
- If third parties on which we depend to conduct our clinical trials do not perform as contractually required, fail to satisfy regulatory or legal requirements or miss expected deadlines, our development program could be delayed with materially adverse effects on our business, financial condition, results of operations and prospects.
- We are dependent on the services of our management and other clinical and scientific personnel, and if we are not able to retain these individuals or recruit additional management or clinical and scientific personnel, our business will suffer.
- We are heavily dependent on third-party service providers to perform critical activities related to the research, development and manufacturing of our product candidates. If these third-party service providers fail to perform, our development program could be delayed with materially adverse effects on our business, financial condition, results of operations and prospects.
- If we are unable to obtain and maintain patent or trade secret protection for any products or product candidates we develop and for our technology, or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize products and technology similar or identical to ours, and our ability to successfully commercialize any product candidates or technology we may develop may be adversely affected. Our competitors may seek or may have already obtained patents that will limit, interfere with or eliminate our ability to make, use, sell, import or otherwise exploit our product candidates, processes or other technologies.
- If we fail to make required payments under the terms of the agreement with BRAIN Biotech AG, or BRAIN (as successor in interest to AnalytiCon Discovery GmbH), pursuant to which we acquired certain of our core intellectual property, BRAIN may exercise remedies that would materially and adversely affect our business and results of operations.
- The market price of our ordinary shares is likely to be highly volatile.
- We do not currently intend to pay dividends on our securities and, consequently, your ability to achieve a return on your investment will depend on appreciation in the price of our ordinary shares.
- We may be a passive foreign investment company, or a PFIC, which could result in adverse U.S. federal income tax consequences to U.S. investors.

Risks Related to Our Financial Position

We have a limited operating history, have generated no revenues to date and have incurred significant losses since our inception. We expect to incur losses over the next several years, will not generate revenues until we are able to commercialize our products and may never achieve profitability, while our net losses are expected to fluctuate significantly.

We are a clinical-stage biopharmaceutical company with a limited operating history upon which you can evaluate our business and prospects. Since inception, we have incurred significant operating losses and have generated no revenues as we focused on our discovery efforts and developing our product candidates. We expect that it will be several years, if ever, before we have a product candidate ready for commercialization. To date, we have financed our operations primarily through sales of equity. We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. We anticipate that our expenses will increase substantially if and as we:

- continue clinical development of our current product candidates;
- seek to identify additional product candidates and initiate clinical trials for such additional product candidates;
- acquire or in-license other products and technologies or enter into collaboration arrangements with regards to product discovery;
- seek marketing approvals for our product candidates that successfully complete clinical trials;
- establish a sales, commercialization and distribution infrastructure to commercialize any products for which we may obtain marketing approval;
- maintain, expand and protect our intellectual property portfolio;
- hire additional personnel;
- add operational, financial and management information systems and personnel, including personnel to support our product development and planned future commercialization efforts; and
- continue to incur increased costs as a result of operating as a public company.

To become and remain profitable, we must develop and eventually commercialize a product or products with significant market potential. This will require us to be successful in a range of challenging activities, including completing clinical trials of our product candidates, obtaining marketing approval for these product candidates and manufacturing, commercializing and selling those products for which we may obtain marketing approval. We may never succeed in these activities and, even if we do, we may never generate revenues that are significant or large enough to achieve profitability. If we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease the value of our business and could impair our ability to raise capital, maintain our discovery and nonclinical development efforts, expand our business or continue our operations and may require us to raise additional capital that may dilute the ownership interest of shareholders. A decline in the value of our business could also cause shareholders to lose all or part of their investment.

We will need substantial additional funding to continue our operations. If we are unable to raise capital when needed or on acceptable terms, we may need to delay, reduce or terminate our product development programs and may be unable to continue as a going concern and could ultimately go into insolvency.

We expect our expenses to increase in parallel with our ongoing activities, particularly as we continue our discovery and nonclinical development to identify new clinical candidates and initiate clinical trials of, and seek marketing approval for, our product candidates. In addition, if we obtain marketing approval for any of our product candidates, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution. Because the outcome of any clinical trial or preclinical study is highly uncertain, we cannot reasonably estimate the actual amounts necessary to successfully complete the development and commercialization of our product candidates. If we do not have sufficient cash and cash equivalents to fund the completion of the research, nonclinical studies and clinical development of our programs, we will be required to seek a significant amount of additional funds by raising additional equity, convertible financing or non-dilutive financing such as debt financing arrangements, strategic transactions or other means. We may also delay, reduce the scope of, eliminate or divest clinical programs, partner with others or divest one or more of our activities and consider other cost reduction initiatives, such as withholding initiation or expansion of clinical trials or research and slowing down patient recruitment of clinical trials. We may also be required to sell or license to others, technologies or clinical product candidates or programs that we would prefer to develop and commercialize ourselves. In the event we are not able to generate sufficient funds from these measures, we may be unable to continue as a going concern, our business, financial condition and/or results of operations could be materially and adversely affected and we may ultimately go into insolvency.

In addition, even if we believe we have sufficient funds for our current or future operating plans, we may seek additional capital if market conditions are favorable or if we have specific strategic considerations. Our future funding requirements will depend on many factors, including:

- the progress and cost of our discovery and nonclinical development;
- the progress and cost of our clinical trials, including payments of patient cost, clinical investigator cost and payments to Contract Research Organizations ("CROs") that are assisting with our sponsored clinical trials, and other research and development activities;
- the cost and timing of obtaining regulatory approval to commence further clinical trials;
- the costs associated with any future investigator-sponsored clinical trials;
- the cost of filing, prosecuting, defending and enforcing any patent applications, claims, patents and other intellectual property rights;
- the cost and timing of obtaining sufficient quantities of our product candidates for clinical trials by establishing our contracted and/or own production capacities;
- the costs and expenditures associated with process optimizations and nonclinical and clinical manufacturing;
- the cost and timing to develop suitable formulations and manufacture final product;
- the terms and timing of any collaborative, licensing and other arrangements that we may establish;
- the cost of acquiring or licensing additional products or technologies, if any;
- the cost of preparing for launch and commercialization of our product candidates; and
- the cost of operating as a public company in the United States.

There can be no assurance that funding will be available in a timely manner, on favorable terms, or at all, or that such funds, if raised, would be sufficient to enable us to continue to implement our long-term business strategy. Also, general conditions in the global economy, including market volatility or other factors, could adversely impact our ability to access capital as and when needed. If we are unable to obtain sufficient funding in a timely manner or on commercially acceptable terms, we may have to delay, reduce the scope of, eliminate or divest clinical programs, partner with others or divest one or more of our activities, and consider other cost reduction initiatives, such as downsizing our operations, withholding initiation or expansion of clinical trials or research, and slowing down patient recruitment of clinical trials. In the event we are not able to generate sufficient funds, we may be unable to continue as a going concern and our business, financial condition and/or results of operations could be materially and adversely affected and could reduce the price of our ordinary shares and we may ultimately go into insolvency. In addition, any perceived or actual inability by us to finance our clinical development program and other business activities, including as a result of required milestone and royalty payments to third parties, may cause the market price of our ordinary shares to decline.

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

We have and may continue to seek additional funding through a combination of equity offerings, debt financings, collaborations and/or licensing arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms may include liquidation or other preferences that adversely affect your rights as a holder of our ordinary shares. The incurrence of indebtedness and/or the issuance of certain equity securities could result in increased fixed payment obligations and could also result in certain additional restrictive covenants, such as limitations on our ability to incur additional debt and/or issue additional equity, limitations on our ability to acquire or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. In addition, issuance of additional equity securities, or the possibility of such issuance, may cause the market price of our ordinary shares to decline. In the event that we enter into collaborations and/or licensing arrangements in order to raise capital, we may be required to accept unfavorable terms, including relinquishing or licensing to a third-party on unfavorable terms our rights to technologies or product candidates that we otherwise would seek to develop or commercialize ourselves or potentially reserve for future potential arrangements when we might be able to achieve more favorable terms. Additional funding may not be available to us on acceptable terms, or at all. If we are unable to obtain funding on a timely basis, we may be required to significantly curtail one or more of programs or cease operations altogether.

Exchange rate fluctuations could negatively affect our financial condition.

Our consolidated financial statements are presented in euros. We mainly operate via our Dutch and Swiss entities, but we also conduct business in the United States and the United Kingdom. Therefore, we have expenses denominated in U.S. dollars, Swiss Francs and British pound sterling in connection with, among other things, our sponsored clinical trials, purchase of drug product for our clinical trials, process development and the prosecution and maintenance of our intellectual property portfolio. As a result, our business and share price may be affected by fluctuations between the euro and the U.S. dollar, the euro and the Swiss franc and the British pound sterling, which may have a significant impact on our reported results of operations and cash flows from period to period.

If we fail to maintain effective internal control over financial reporting, we may not be able to accurately report our financial results or prevent fraud, and as a result, shareholders could lose confidence in our financial and other public reporting, which would harm our business and the trading price of our ordinary shares.

Effective internal controls over financial reporting are necessary for us to provide reliable financial reports and, together with adequate disclosure controls and procedures, are designed to prevent fraud. Section 404 of the Sarbanes-Oxley Act requires management of public companies to develop and implement internal control over financial reporting and to evaluate the effectiveness thereof. If we identify one or more material weaknesses in our internal control over financial reporting, we will not be able to assert that our internal controls and procedures are effective. A material weakness is a deficiency or a combination of deficiencies in internal control over financial reporting such that there is a reasonable possibility that a material misstatement of our financial statements will not be prevented or detected on a timely basis. In connection with the preparation of our annual financial statements through December 31, 2023, we identified material weaknesses in the design of our internal control over financial reporting, which our management concluded to have been remediated as of December 31, 2024.

We cannot assure you that material weaknesses will not be discovered in the future. If we do not remediate these issues or if we fail to design and operate effective internal controls in the future, it could result in material misstatements in our financial statements and potentially require us to restate our financial statements which may result in the trading value of our ordinary shares being materially and adversely affected.

Our management is required to assess the effectiveness of our internal controls over financial reporting on an annual basis pursuant to SOX 404(a). Now that we are no longer an “emerging growth company,” our independent registered public accounting firm is required to 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. Our management may not be able to effectively and timely implement controls and procedures that adequately respond to the increased regulatory compliance and reporting requirements that are applicable to us as a U.S. public company and an assessment of the effectiveness of our internal control over financial reporting by an independent registered public accounting firm in accordance with the provisions of Section 404 could detect additional significant deficiencies or material weaknesses that our management’s assessment might not. Undetected material weaknesses in our internal controls could lead to financial statement restatements and require us to incur the expense of remediation. Investors may lose confidence in the accuracy and completeness of our financial reports, which could cause the market price of our ordinary shares to decline and also restrict our future access to the capital markets.

We could be also subject to sanctions or investigations by Nasdaq, the SEC or other regulatory authorities.

We operate in many jurisdictions with highly complex and varied tax regimes. Changes in tax rules, new or revised legislation or the outcome of tax assessments and audits could cause a material adverse effect on our results.

We operate in different jurisdictions with highly complex and varied tax regimes. Changes in tax rules, new or revised legislation or the outcome of tax assessments and audits could have a material adverse effect on our results.

We are subject to taxation in the Netherlands, Switzerland, the United States, and other jurisdictions. Our future effective income tax rate may be variable and depend on changes in the level of operating results within various local jurisdictions and changes in the applicable taxation rates of these jurisdictions. If legislators, tax authorities, or government agencies in the jurisdictions in which we operate were to change applicable tax laws and regulations (for example, as a result of the various global, regional and local initiatives to reform the international tax framework, such as the base erosion and profit shifting project undertaken by the Organization for Economic Co-operation and Development and G20 Inclusive Framework and the two-pillar solution to address the tax challenges arising from the digitalization of the economy) or successfully challenge the manner in which our income taxes are currently recognized or calculated or the transfer pricing policies employed by us (including policies set forth in any advance pricing agreements entered into with any taxing authorities), our income tax expense could increase, which would adversely impact our cash flow and profitability.

In addition, tax benefits or benefits from net operating losses accumulated in prior years in some jurisdictions may not be available in the future due to changes in the local jurisdictions or credits on net operating losses no longer available due to either full utilization or expiration of the statute of limitations in such jurisdictions. As a result, our future effective tax rate could increase and/or our benefits from carrying forward net operating losses could affect our deferred tax assets in certain countries in the coming years. The ultimate realization of deferred tax assets is dependent upon, among other things, our ability to generate future taxable income that is sufficient to utilize in certain jurisdictions loss carry-forwards or tax credits before their expiration or our ability to implement prudent and feasible tax optimization strategies.

Furthermore, in many of the jurisdictions in which we operate, the tax laws and regulations are very complex and are open to different interpretations and application. The final determination of tax by means of an assessment or an audit could be materially different from our tax provisions and accruals and may negatively impact our financial results.

On December 20, 2021, the OECD published the Global Anti-Base Erosion Model Rules (the "GloBE Rules**"**), also known as Pillar II. The GloBE Rules aim to impose a global minimum tax of 15% on multinational enterprises with a revenue in excess of €750 million. On December 22, 2021, the European Commission published a legislative proposal for Pillar II (the "EU Pillar II Directive**"**). The EU Pillar II Directive is largely aligned with the GloBE Rules. Some deviations were introduced to ensure compliance with EU treaties.

On December 15, 2022, the Council of the European Union formally adopted the EU Pillar II Directive. The EU Pillar II Directive aims at consistently implementing among all 27 member states the GloBE Rules. EU Member States had *Income Taxes* to transpose the EU Pillar II Directive into their national laws and will have to apply the Pillar II measures in respect of the fiscal years beginning on or after December 31, 2023. The Netherlands have transposed the EU Pillar II Directive into its national legislation with effect from December 31, 2023, pursuant to the Dutch Minimum Tax Act 2024 (Wet minimumbelasting 2024).

We do not yet meet the revenue threshold for Pillar II of €750 million but (i) should this threshold be reduced or (ii) should our revenue increase, then the application of Pillar II could have a material adverse effect on our business, financial position and results of operations. We will continue to monitor the impact of Pillar II going forward.

Risks Related to the Development and Clinical Testing of Our Product Candidates

We have experienced, and may continue to experience, setbacks in our clinical trials, including as a result of the clinical holds which were lifted in June 2023 and January 2024. Moreover, we have established proof-of-concept for deucrictibant in Phase 2 trials for both treatment and prophylaxis of HAE attacks. We have designed and advanced our future clinical development program based on these results as well as modelling of our results from those trials with additional in vitro and in vivo data and comparisons to published results for other currently available products from different trials. We may not be able to replicate these results or analyses in future clinical trials that assess the endpoints required to obtain regulatory approval or we may have inconclusive or negative results. Any setbacks in our clinical development program could have a material adverse effect on our business, financial condition, results of operations and prospects.

Clinical trials are expensive and complex. Each trial can take many years to complete and have uncertain outcomes. Failure of a product can occur at any stage of the testing, including later phases of clinical trials despite having progressed through preclinical and nonclinical studies and early phase clinical trials, for a variety of reasons, such as changes in formulation of the product, differences in patient populations, changes in trial and manufacturing protocols and complexities of larger, multi-center trials, among others. The results from nonclinical studies or early phase clinical trials of a product candidate may not predict the results that will be obtained in later phase clinical trials of the product candidate. For example, we have established proof-of-concept for deucrictibant in Phase 2 trials for both treatment and prophylaxis of HAE attacks. We have designed and advanced our future clinical development program based on these results as well as modelling of our results from those trials with additional in vitro and in vivo data and comparisons to published results for other currently available products from different trials. We may not be able to replicate these results or analyses in future clinical trials that assess the endpoints required to obtain regulatory approval. We, the FDA or other applicable regulatory authorities may suspend or terminate clinical trials of a product candidate at any time for numerous reasons, including, but not limited to, a belief that subjects participating in such trials are being exposed to unacceptable health risks or adverse side effects, or other adverse experiences or findings. For instance, in August 2022, we announced that the FDA has placed clinical holds on our clinical trials of deucrictibant in the U.S. under two Investigational New Drug, or IND, applications for the treatment of HAE (on-demand and prophylactic) based on its review of nonclinical data. The clinical hold letters stated that the nonclinical observations were unlikely due to B2 receptor antagonism, the primary mechanism of action of our compound. However, the FDA requested that we conduct an additional long-term rodent toxicology study and update the investigator's brochure. Following review of data from a preplanned interim analysis of the ongoing 26-week nonclinical rodent study, the FDA lifted the clinical hold on the IND application for deucrictibant for the on-demand treatment of HAE in June 2023. In January 2024, the FDA lifted the clinical hold on the IND application for deucrictibant for the prophylactic treatment of HAE attacks following review of the full data set from the completed 26-week rodent toxicology study. While the clinical hold was lifted, there can be no assurance that we will not encounter similar challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition, results of operation and prospects.

Even if clinical trials are successful, before granting approval to any product candidate, regulatory authorities can request additional clinical trials, including with larger patient numbers, find deficiencies in the manufacturing processes or facilities upon which we rely and change their approval policies or regulations or their prior guidance to us during clinical development in a manner that renders our clinical data insufficient for approval. We have, and may continue to experience numerous setbacks during, or as a result of, the clinical trial process that could delay or prevent the commencement, conduct and completion of clinical trials or the commercialization of our current and any future programs, such as:

- delays in reaching a consensus with regulatory agencies on the design or implementation of our clinical trials, including with respect to our strategy for sharing Phase 1 and Phase 2 data between IR and XR programs and designs for improving the efficiency of our clinical development path;
- delays in obtaining regulatory approval or ethics committee approval to commence a clinical trial;
- delays in reaching agreement on acceptable terms with prospective contract research organizations, or CROs, and clinical trial sites;
- failure of CROs to adequately supervise investigators;
- failure to recruit sufficient investigators or recruit and enroll sufficient subjects for our clinical trials in a timely manner or at all, including due to (i) pandemics and (ii) geopolitical tensions;
- delay or failure in having subjects complete a trial or return for post-treatment follow-up, including due to (i) pandemics and (ii) geopolitical tensions;

- failure to obtain and maintain the required institutional review board, or IRB, or ethics committee approval at each clinical trial site;
- clinical sites or investigators deviating from trial protocol or dropping out of a trial;
- lack of adequate funding to continue a clinical trial;
- delays in sufficiently developing, characterizing or controlling a manufacturing process suitable for advanced clinical trials;
- clinical trials of our product candidates producing negative or inconclusive results, which may result in our deciding, or regulators requiring us, to conduct additional clinical trials or abandon product development programs; or
- failure of ourselves or any third-party manufacturers, contractors or suppliers to comply with regulatory requirements, maintain adequate quality controls, or be able to provide sufficient product supply to conduct and complete clinical trials of our product candidates.

Before commencing clinical trials, we are required to apply to country-level regulators before opening sites in their countries. If we are not able to timely receive their approval or enroll patients at sites in other countries, we may not be able to complete clinical trials on our anticipated timelines.

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

If we suffer any material delays, negative results or other setbacks in our clinical trials or nonclinical studies or if any of our clinical trials are put on clinical hold or terminated, we may incur increased costs or be unable to continue development of deucrictibant, including our product candidates IR and XR, which could have a material adverse effect on our business, financial condition, results of operations and prospects.

We are heavily dependent on the success of our product candidates deucrictibant IR and deucrictibant XR, which are in late-stage development. We have released topline data from our RAPIDe-1 study demonstrating efficacy in our Phase 2 clinical trial for treatment of HAE attacks on demand using deucrictibant immediate-release (IR) and topline data from our CHAPTER-1 study demonstrating efficacy in our Phase 2 clinical trial of deucrictibant for the prophylactic treatment of HAE attacks. We cannot give any assurance that either product candidate, or any other compounds in development, will successfully complete clinical trials, receive regulatory approval, be commercialized, or be differentiated in the market. If we are unable to successfully commercialize our product candidates, or experience significant delays in doing so, our business, financial condition, results of operations and prospects would be materially adversely affected.

We do not have any drugs that have received regulatory approval and may never be able to develop marketable products. We expect that a substantial portion of our efforts and expenses for the foreseeable future will be devoted to the clinical development of our product candidates, deucrictibant IR and deucrictibant XR, and as a result, our business currently depends heavily on the successful development, regulatory approval and commercialization of these product candidates. To date we have data from preclinical studies, Phase 1 clinical trials in healthy volunteers, and Phase 2 trials in people living with HAE of deucrictibant in both treatment and prophylaxis of HAE attacks. However, we have not conducted a head-to-head comparison of icatibant or any other drug candidate to deucrictibant in a clinical trial. We have compared the published data for icatibant to data from our Phase 1 clinical trial of deucrictibant and Phase 2 trial of IR (RAPIDe-1). Accordingly, the value of comparisons to icatibant in this Annual Report may be limited because they are not derived from a head-to-head trial, and they are from trials that were conducted under different protocols at different sites and at different times. Without head-to-head data, we will be unable to make comparative claims for our product candidates, if approved. Future clinical trials may not confirm our analyses to date. The development of IR and XR has been and will continue to be a time-consuming and costly process and may leave us with insufficient resources to advance other programs and product candidates. We cannot be certain that any deucrictibant-containing product candidate, including IR and XR, will receive regulatory approval or be successfully commercialized, even if we receive regulatory approval.

The research, testing, manufacturing, safety, efficacy, labeling, approval, sale, advertising promotion, commercialization and distribution of our product candidates are, and will remain, subject to comprehensive regulation by the FDA in the United States, the European Union and the European Medicines Agency or EMA in Europe and regulatory authorities in other countries, with regulations differing from country to country. We will not be permitted to market our drug candidates in the United States or Europe until we receive approval of a New Drug Application, or NDA, from the FDA or a marketing authorization, or MA, from the European Commission (based on the positive opinion of the EMA), respectively. We have not submitted any marketing authorization applications for any of our product candidates. NDAs and MAs must include extensive nonclinical and clinical data and supporting information to establish the drug candidate's safety and effectiveness for each desired indication. The nonclinical and clinical development of our product candidates is susceptible to the

risk of failure inherent at any stage of drug development, including failure to demonstrate efficacy or safety; the occurrence of adverse events that are severe or medically or commercially unacceptable; our or our partners' failure to comply with trial protocols, applicable regulatory requirements, and industry standards; or a determination by the FDA or any comparable foreign regulatory authority that a product candidate may not continue development or be approved in accordance with our development plans or at all. We cannot guarantee that any nonclinical studies and clinical trials will be conducted as planned or completed on schedule, if at all, or that the results of such trials will be sufficient to support regulatory approval for our product candidates. Failure to obtain regulatory approval for any of our product candidates IR and XR or any other product candidate in the United States, Europe or other jurisdictions will prevent us from commercializing and marketing these products in such jurisdictions.

Even if we were to successfully obtain approval from the FDA, EMA and comparable foreign regulatory authorities for our product candidates, any approval might contain significant limitations related to use restrictions for specified age groups, warnings, precautions or contraindications or may be subject to burdensome post-approval study or risk management requirements. We may also be limited in our ability to advertise, promote and/or market our product candidates in a way that successfully differentiates them in the market. For example, we may not be able to position our product as safer, more effective, more convenient or better for a patient's quality of life. Furthermore, we will still need to develop a commercial infrastructure, or otherwise develop relationships with collaborators to commercialize, establish a viable pricing structure and obtain coverage and adequate reimbursement from third-party payors, including government healthcare programs. If we, or our collaborators, are unable to successfully commercialize any product candidate, we may not be able to generate sufficient revenue to continue our business.

Our business and operations, including ongoing and planned clinical trials, may be adversely affected by a variety of events outside our control, including pandemics, epidemics or outbreaks of infectious diseases, and geopolitical instability, such as the conflict between Russia and Ukraine and the Hamas attack against Israel and the ensuing war.

A wide variety of events beyond our control, including natural or man-made disasters, power shortages, fires, extreme weather conditions, pandemics, epidemics or outbreaks of infectious diseases, political instability or other events could disrupt our business or operations or those of our development partners, manufacturers, regulators or other third parties with whom we conduct business now or in the future. These events may cause businesses and government agencies to be shut down, supply chains to be interrupted, slowed, or rendered inoperable, and individuals to become ill, quarantined, or otherwise unable to work and/or travel due to health reasons or governmental restrictions. The spread of variants of infectious diseases may interrupt, or delay, our clinical trial activities, regulatory reviews, manufacturing activities and supply chain. Infectious disease pandemics may delay enrollment in our clinical trials due to prioritization of hospital resources towards the outbreak or other factors, and some patients may be unwilling to enroll in our trials or be unable to comply with clinical trial protocols if quarantines impede patient movement or interrupt healthcare services, which would delay our ability to conduct clinical trials or release clinical trial results and could delay our ability to obtain regulatory approvals and commercialize our product candidates. In addition, even with our distributed operations, employee vaccinations and our observation of social distancing measures, there remains the possibility that key personnel may become ill or are otherwise unable to work, which could affect our operations.

Moreover, unforeseen global events, such as the armed conflict between Russia and Ukraine and the Hamas attack against Israel and the ensuing war, could adversely impact our business and operations. The invasion of Ukraine and the Hamas attack against Israel and the retaliatory measures that have been taken, or could be taken in the future, by the United States, NATO, and other countries have created global security concerns that could result in regional conflicts and also adversely affect our ability to conduct ongoing and future clinical trials of our product candidates. For example, our studies include a significant number of patients in Germany, Poland and Bulgaria, and we have a patient in Israel. A further escalation of the conflict in Ukraine and the Middle East may potentially impact our ability to complete our ongoing and planned clinical trials in these countries on a timely basis, or at all. Clinical trials in these countries could be suspended or terminated, and we may be prevented from obtaining data on patients already enrolled at affected sites. Our ability to conduct clinical trials in these regions may also become restricted under applicable sanctions laws, which may require us to identify alternative trial sites. Any of the foregoing could impede the execution of our clinical development plans, which could materially harm our business.

Disruptions at the FDA, European Medical Agency or EMA and other government agencies, including as a result of the new administration, funding shortages or global health concerns could hinder their ability to hire, retain or deploy key leadership and other personnel, or otherwise prevent new or modified products from being developed, cleared or approved or commercialized in a timely manner or at all, which could negatively impact our business.

The ability of the FDA, EMA and other comparable government agencies to review and clear or approve new products can be affected by a variety of factors, including government budget and funding levels, statutory, regulatory, and policy changes including policy changes coming from the new administration, ability to hire and retain key personnel and accept the payment of user fees, and other events that may otherwise affect their ability to perform routine functions. Government funding of government agencies that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable. Disruptions at the FDA, EMA and other agencies may also slow the time necessary for new drugs or modifications to cleared or approved drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. If a prolonged government shutdown occurs, or if global health concerns prevent the FDA, EMA or other regulatory authorities from conducting their regular inspections, reviews, or other regulatory activities, it could significantly impact the ability of the FDA, EMA or other regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

We may not be able to design and develop an extended-release formulation.

Our current strategy includes developing an extended-release formulation for the deucrictibant prophylactic indication (XR). To date, we have studied prospective extended-release formulation only in clinical studies in healthy volunteers. We are planning to conduct multiple dose study to assess the PK and safety of the final extended-release formulation. In future multiple dose studies, either in healthy volunteers or in HAE clinical studies, we may not observe the desired PK profile with the current or any extended-release formulation.

We have filed patent applications covering the specific formulation developed, as well as its use for the treatment of HAE. There can, however, be no assurance that such an extended-release formulation will be successfully developed in a timely manner, that adequate patent protection can be obtained or that any such formulation would provide us with a commercial advantage. If we are unable to develop this extended-release formulation on our own, we may need to in-license patented technology to do so. Many third parties have patents covering technologies and manufacturing processes needed to develop and make extended-release formulations and there can be no assurance that we would be able to obtain rights to such patents on attractive financial terms, if at all.

If we experience delays or difficulties in the enrollment of patients in clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented and expenses for development of our product candidates could increase.

We may not be able to initiate or continue clinical trials for our product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials to demonstrate safety and efficacy. We are currently entering late-stage clinical trials: we have completed Phase 2 trials in the on-demand and prophylactic settings which have provided critical data for dose selection for late phase clinical trials. We do not know whether planned or ongoing clinical trials will enroll subjects in a timely fashion, require redesign of essential trial elements or be completed on our projected schedule. In particular, because we are focused on patients with HAE, which is a rare disease, our ability to enroll eligible patients in trials may be limited or may result in slower enrollment than we anticipate. In addition, competitors have ongoing clinical trials for product candidates being studied for the same indications as our product candidates, and patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors' product candidates. Patient enrollment can also be affected by a number of other factors including:

- the eligibility criteria for the study in question;
- the perceived risks and benefits of the product candidate under study;
- the efforts to facilitate timely enrollment in clinical trials;
- the availability of existing or experimental treatments affecting our ability to recruit patients;
- the inability to identify and maintain a sufficient number of trial sites, many of which may already be engaged in other clinical trial programs, including some that may be for the same disease indication;
- the patient referral practices of physicians;
- the proximity and availability of clinical trial sites for prospective patients;
- any delays and difficulties in enrollment due to the spread of an infectious disease;
- ambiguous or negative interim results of our clinical trials, or results that are inconsistent with earlier results;
- feedback from the FDA, EMA and any comparable foreign regulatory authority, data safety monitoring boards, or a comparable foreign regulatory authority, or results from earlier stage or concurrent nonclinical studies and clinical trials, that might require modifications to the protocol;
- decisions by the FDA, EMA and any comparable foreign regulatory authority, or recommendations by data safety monitoring boards, to suspend or terminate clinical trials at any time for safety issues or for any other reason; and
- unacceptable risk-benefit profile, perceived or actual, or unforeseen safety issues or adverse effects.

Our inability to enroll a sufficient number of patients for our clinical trials would result in significant delays, may result in increased development costs for our product candidates, and could also require us to abandon one or more clinical trials altogether, any of which could cause a material adverse effect on our business, financial position and results of operations.

Clinical trials of our product candidates may not uncover all possible adverse effects that patients may experience.

Clinical trials are conducted in a limited sample of the patient population for the disease or condition under study; the actual patient population may have significantly more variability than the clinical trial subjects. In addition, clinical trials are, by design, limited with respect to the number of subjects, the duration of exposure to the product candidate, and by inclusion and exclusion criteria to a restricted composition of the overall patient population. As a result of such limitations, we cannot be sure that all side effects of our product candidates may be uncovered during our clinical trials or that a complete safety profile of our product candidates will be identified. Further, even larger clinical trials may not identify rare serious adverse effects, or the duration of such studies may not be of sufficient length to identify when those events may occur. There have been other products that have been approved by the regulatory authorities but for which safety concerns have been uncovered following approval. Such safety concerns have led to labeling changes, the imposition of other regulatory requirements (e.g., Risk Evaluation and Mitigation Strategy or REMs, or post-authorization safety studies, or PASS) or withdrawal of products from the market, and any of our product candidates may be subject to similar risks.

Although to date we have not seen evidence of significant safety concerns with our product candidates currently in clinical trials, patients treated with our products, if approved, may experience adverse reactions and it is possible that the FDA or other regulatory authorities may ask for additional safety data as a condition of, or in connection with, our efforts to obtain approval of our product candidates. If safety events occur or are identified after our product candidates reach the market, we may, or regulatory authorities may require us to amend the labeling of our products, institute a REMs or PASS, recall our products or even withdraw approval for our products.

Clinical development is a lengthy and expensive process with an uncertain outcome, and results of earlier studies and trials as well as data from any interim analysis of ongoing clinical trials may not be predictive of future trial results. Clinical failure can occur at any stage of clinical development.

Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. Although product candidates may demonstrate promising results in early clinical (human) trials and nonclinical (animal) studies, they may not prove to be safe or effective in subsequent clinical trials. For example, the results of animal studies may not accurately predict human experience. Likewise, early clinical trials may not be predictive of eventual safety or effectiveness results in larger-scale pivotal clinical trials. In this Annual Report we discuss the potency of deucrictibant as shown in preclinical, Phase 1 clinical trials, and Phase 2 clinical trials (RAPIDe-1 and CHAPTER-1). Potency as used in this Annual Report refers to the amount of drug required to produce a pharmacological effect of given intensity and is not a measure of therapeutic efficacy. We have released topline data from our RAPIDe-1 study demonstrating efficacy in our Phase 2 clinical trial for treatment of HAE attacks on demand using deucrictibant immediate-release (IR) and topline data from our CHAPTER-1 study demonstrating efficacy in our Phase 2 clinical trial of deucrictibant for the prophylactic treatment of HAE attacks. The results of preclinical studies and early and mid-stage clinical trials, as well as data from interim analysis of ongoing clinical trials, may not be predictive of the results of ongoing or future clinical trials.

In addition, the studies and trials of other products with similar mechanisms of action to our product candidates may not be predictive of our clinical trial results. There can be significant variability in safety and/or efficacy results between different trials of the same product candidate due to numerous factors, including changes in trial protocols, differences in composition of the patient populations, adherence to the dosing regimen and other trial protocols and the rate of dropout among clinical trial participants. Product candidates in later phase clinical trials may fail to show the desired safety and efficacy traits despite having progressed through nonclinical studies and earlier clinical trials. In addition to the safety and efficacy trials of any product candidate, clinical trial failures may result from a multitude of factors including flaws in trial design, dose selection, placebo effect and patient enrollment criteria. A number of companies in the pharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier trials, and it is possible that our product candidates will as well which may have an adverse effect on our business and the value of the ordinary shares.

We may not be able to conduct, or contract others to conduct, animal testing in the future, which could harm our research and development activities.

Certain laws and regulations relating to drug development require us to test our product candidates in pre- and nonclinical animals before initiating clinical trials involving humans. Pre- and nonclinical animal testing activities have been the subject of controversy and adverse publicity. Animal rights groups and other organizations and individuals have attempted to stop animal testing activities by pressing for legislation and regulation in these areas and by disrupting these activities through protests and other means. To the extent the activities of these groups are successful, our research and development activities may be interrupted or delayed.

Risks Related to Regulatory Approval of Our Clinical Development Programs and Our Product Candidates

Clinical development is subject to extensive regulation, which can be costly and time-consuming to comply with, and we may not obtain approvals for performing clinical trials or for marketing any of our product candidates.

We are not permitted to conduct clinical trials with or market any product candidate until we obtain authorization from the appropriate regulatory authorities. We must obtain authorization for conducting clinical trials with any product candidate and for marketing any product candidate from the appropriate regulatory authority of each jurisdiction in which we wish to perform clinical trials or market our product candidates.

Since the 1990s, many companies have tried but failed to discover oral B2 antagonists, as the bradykinin B2 receptor proved to be a difficult target for the development of orally available antagonists. Current treatment guidelines also recommend against the use of the traditionally used oral HAE medications, such as antifibrinolytics (tranexamic acid or epsilon aminocaproic acid), due to limited efficacy. As our product candidates are based on novel technologies, it is difficult to predict the time or costs associated with the regulatory approval process or be certain of our ability to successfully commence, conduct, and complete clinical development, or obtain the necessary regulatory and reimbursement approvals required for the commercialization of our product candidates IR and XR. As discussed under "—Risks Related to the Development and Clinical Testing of Our Product Candidates—We may experience setbacks in our clinical trials, including delays in commencing, conducting or completing our clinical trials, as well as inconclusive or negative results, all of which could have a material adverse effect on our business, financial condition, results of operations and prospects," we or our partners may experience any number of unfavorable outcomes during or as a result of nonclinical studies and clinical trials which could delay or prevent regulatory approval of our product candidates, or negatively impact our management's credibility, our value and our operating results.

We may invest substantial time and resources in preclinical and nonclinical studies, clinical trials, manufacturing and the preparation and submission of various regulatory applications without any assurance that we will obtain regulatory approval or recoup our investment.

The FDA and other regulatory authorities exercise substantial discretion with respect to the development and approval of drug product candidates. The number, size and design of nonclinical studies and clinical trials that will be required for regulatory approval will vary depending on the program, the primary indication and the specific regulations and guidance documents applicable to any particular program. The FDA and other regulatory authorities can delay, limit or deny (i) clinical trial development (e.g., placing a clinical trial under clinical hold) and (ii) approval of a program for many reasons, including:

- manufacturing related issues or concerns;
- concerns relating to the product candidate's safety or efficacy;
- concerns relating to the design, control or conduct of nonclinical studies and clinical trials including the use of placebo or active controls in blinded studies;
- negative or ambiguous results of any nonclinical study or clinical trial;
- concerns relating to the sufficiency of clinical trial results;
- the failure of more advanced clinical results to confirm positive results from preclinical studies or earlier clinical trials; or
- the development or observation of unexpected safety issues, adverse events or adverse side effects.

Should any of these or other factors affecting our development programs or product candidates occur, regulatory approval of our product candidates could be denied, delayed or have conditions placed upon it. Failure to obtain regulatory approval in a timely manner, in a limited manner or at all would have a material adverse effect on our business, financial condition, results of operations or prospects.

Additionally, effective as of January 31, 2020, the United Kingdom withdrew from the European Union, a process referred to as "Brexit". As a result of Brexit, commercializing our product candidates in the United Kingdom would require us to obtain separate marketing approvals from the Medicines and Healthcare products Regulatory Agency, or the MHRA, instead of single marketing approvals obtained from the European Commission which, in turn, are based on the positive opinion of the European Medicines Agency, or the EMA. With significant regulatory oversight shifted from the EMA to the MHRA, and the MHRA having limited capacities and resources, obtaining marketing approvals for our product candidates in the United Kingdom may take longer than it would take in the European Union. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, would prevent us from commercializing our product candidates in the United Kingdom and restrict our ability to generate revenue and achieve and sustain profitability. If any of these outcomes occur, we may be forced to restrict or delay efforts to seek regulatory approval in the United Kingdom for any of our product candidates, which could significantly and materially harm our business.

There can be no assurance that we will be able to maintain orphan drug status.

Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is intended to treat a rare disease or condition, defined as a patient population of fewer than 200,000 in the U.S., or a patient population greater than 200,000 in the U.S. where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the U.S. In the European Union, after a recommendation from the EMA's Committee for Orphan Medicinal Products, the European Commission grants orphan drug designation to promote the development of products that are intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition either affecting not more than five in 10,000 persons in the European Union or when, without incentives, it is unlikely that marketing of the medicine would generate sufficient returns to justify the investment needed for its development. Orphan drug exclusivity confers market exclusivity, subject to certain limitations, upon the first product to receive marketing approval by the relevant regulatory authority for the jurisdiction and entails the right to market exclusively the product for the specified indication, during a maximum of ten years for the European Union and during a period of seven years in the United States. The period of exclusivity in the European Union may be reduced to six years if, at the end of the fifth year, the product no longer meets the criteria for orphan drug designation if, among other things, it is established that the product is sufficiently profitable not to justify market exclusivity.

On March 18, 2022, the FDA granted orphan drug designation to PHA121 (deucrictibant), the active ingredient in our IR and XR product candidates for treatment of bradykinin-mediated angioedema. Even though we have obtained orphan drug exclusivity for deucrictibant in the U.S., an approval may be granted to other applicants of a similar product for the same indication if we are unable to supply sufficient quantities of the product, we consent to such an approval, or if the product of a second applicant is deemed to be clinically superior to our product. Changes to the current regulatory frameworks governing orphan drugs may also impact existing and future market exclusivities provided as a result of orphan drug designation. Even if we were to succeed in maintaining market exclusivity for products through orphan drug status, the orphan drug regulations would not preclude competitors from developing or marketing different products for the same indications to which our programs are directed, or from independently developing versions of our products for different indications. Further, we may lose orphan drug exclusivity if the FDA determines that the request for designation was materially defective. If we fail to obtain or maintain orphan exclusivity for deucrictibant or any future products, or if the commercial value of market exclusivity is diminished, our competitive position or financial and commercial prospects could be materially adversely affected.

If we fail to comply with ongoing regulatory obligations and restrictions following regulatory approval of any product candidate, regulatory authorities may take enforcement action against us, for example, any regulatory approval granted could be withdrawn or revoked and sale of any products could be suspended, or financial penalties could be imposed.

If any of our product candidates are approved for commercialization by the FDA or another regulatory authority, we would be subject to extensive regulatory requirements over, among other things, product manufacturing, testing, labeling, packaging, storage, advertising,

promotion, marketing, distribution, export, import, adverse event reporting and record keeping. These requirements include submissions of safety and other post-commercialization information and reports, drug establishment registration and drug listing requirements, current Good Manufacturing Practices, or cGMP, relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents. In addition, we would be subject to other requirements regarding the distribution of drug samples to physicians. We and our suppliers, Contract Development and Manufacturing Organization ("CDMOs") and contract testing laboratories would also be subject to inspection by the FDA or other regulatory authorities to determine compliance with these requirements. In addition, facilities in the European Union that manufacture any of our product candidates must be licensed by the relevant regulatory authorities. In the United States, there are also certain state requirements with respect to drug manufacturing and distribution with which we must comply.

The FDA, or other regulatory authorities, may also impose significant limitations on the use or marketing of our approved product candidates, which could reduce the potential market for any products. The FDA and other regulatory authorities closely regulate the post-approval advertising, promotion, and commercialization of drugs to ensure drugs are marketed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA imposes stringent restrictions on manufacturers' communications regarding use of their products and if we promote our products beyond their approved indications or in other ways that violate FDA requirements, we may be subject to enforcement action for, among other things, off-label promotion. In the EU, promotion of prescription-only drugs to the general public as well as off-label promotion are strictly prohibited and can result in significant fines and reputational damage. For the United States, alleged, or potential violations of the Federal Food, Drug, and Cosmetic Act relating to the promotion of prescription drugs may lead to investigations alleging violations of federal and state health care fraud and abuse laws, as well as state consumer protection laws. Advertising, promotion, and marketing activities may also give rise to litigation by competitors.

The FDA, or other regulatory authorities, may also impose requirements for costly post-commercialization studies or clinical trials and surveillance to monitor the safety or efficacy of an approved drug. Previously unknown problems with the drug may result in restrictions on the commercialization of the product and could include withdrawal of the drug from the market.

In addition, as discussed under "—Risks Related to the Development and Clinical Testing of Our Product Candidates—We and our partners may be subject to new legislation, regulation, regulatory proposals and healthcare payor initiatives that may increase our costs of compliance and adversely affect our or our partners' ability to market our products, obtain collaborators and raise capital," new statutory requirements or additional regulations or initiatives may be enacted. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability, which would adversely affect our business, prospects, financial condition and results of operations. Failure to comply with the requirements of the FDA and other applicable regulatory authorities may also subject us to administrative or judicially imposed sanctions, including civil and criminal penalties, injunctions, product seizure or recall, import bans, restrictions on the conduct of our operations, total or partial suspension of production and refusal to approve a pending NDA, and financial penalties. If we are subject to any of these sanctions, our competitive position or financial and commercial prospects could be materially adversely affected.

We and our partners may be subject to new legislation, regulation, regulatory proposals and healthcare payor initiatives that may increase our costs of compliance and adversely affect our or our partners' ability to market our products, obtain collaborators and raise capital.

In various jurisdictions, including the United States, there have been and continue to be a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of our product candidates, subject us to more stringent drug labeling and post- commercialization testing or restrict or regulate post-approval activities and affect our ability, or the ability of our future collaborators, to profitably sell any product candidates for which we obtain marketing approval.

Among policy makers and payors, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access. In the United States, there has been heightened governmental scrutiny recently over the manner in which drug manufacturers set prices for their marketed products. For instance, recently, President Biden signed into law the Inflation Reduction Act of 2022, or IRA, which included several measures intended to lower the cost of prescription drugs and limit out-of-pocket spending, including by requiring drug manufacturers to pay rebates to Medicare if they increase prices faster than inflation for drugs used by Medicare beneficiaries.

Further, in the United States, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, collectively, the ACA, enacted in 2010, has had a significant impact on the healthcare industry. The ACA increased federal oversight of private health insurance plans and included a number of provisions designed to reduce Medicare expenditures and the cost of health care generally, to reduce fraud and abuse, and to provide access to increased health coverage. Since its enactment there have been judicial, Presidential and Congressional challenges to certain aspects of the ACA, and we expect there will be additional challenges and amendments to the ACA. In addition, the Trump administration took several executive actions, including the issuance of a number of executive orders, that could impose significant burdens on, or otherwise materially delay, the FDA's ability to engage in routine regulatory and oversight activities such as implementing statutes through rulemaking, issuance of guidance, and review and approval of marketing applications. An under-staffed FDA could result in delays in the FDA's responsiveness or in its ability to review submissions or applications within the established Prescription Drug User Fee Act time frames, issue regulations or guidance, or implement or enforce regulatory requirements in a timely fashion or at all. In the coming years, legislative and regulatory changes could be made to governmental health programs that could significantly impact pharmaceutical companies and the success of our product candidates. As such, we cannot predict what effect the ACA or other healthcare reform initiatives that may be adopted in the future will have on our business.

In some countries outside the United States, the proposed pricing for a treatment must be approved before it may be lawfully marketed. In addition, in some markets, the pricing of prescription drugs is subject to government control and reimbursement which may in some cases be unavailable. The requirements governing drug pricing vary widely from country to country. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our product candidates that may be approved. Historically, pharmaceutical products launched in the European Union do not follow price structures of the United States and generally tend to have significantly lower prices.

We expect that market access constraints, pricing controls and discounting and other restrictions will become more acute as public and private payers continue to take aggressive steps to control their expenditures. These efforts and other healthcare reform measures that may be adopted in the future may result in more rigorous coverage criteria and additional downward pressure on the price that we receive for any approved product, and any reduction in reimbursement from any government program may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenues, attain profitability, or commercialize our product candidates, if approved.

We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action in the United States, the European Union or another jurisdiction, or the effect that any such future legislation or administrative action may have on our business.

Risks Related to Our Operations

Due to our limited resources and access to capital, we must prioritize development of certain programs and our decision to pursue these programs may prove to be unsuccessful as they may never receive regulatory approval or achieve profitability.

Because we have limited resources and access to capital to fund our operations, we must decide which product candidates to pursue and the amount of resources to allocate to each product candidate. As such, we are currently primarily focused on the development of IR and XR. These, and future decisions concerning the allocation of capabilities, infrastructure, management and financial resources towards particular programs or therapeutic areas may not lead to the development of viable commercial products and may divert resources from better opportunities. Similarly, these and future decisions to delay or terminate product development programs could cause us to miss valuable opportunities. If we make incorrect determinations regarding the market potential of our product candidates or misread trends in the pharmaceutical industry, our business, financial condition and results of operations could be materially adversely affected.

If we cannot manufacture our product candidates in sufficient amounts, with CDMOs or ourselves, at acceptable costs and on a timely basis, we may be unable to supply sufficient product candidates for nonclinical studies or clinical trials or to support commercialization of our product candidates, if approved.

We do not own or operate manufacturing facilities and have no plans to build our own clinical or commercial-scale manufacturing capabilities. We cannot ensure that our suppliers will remain in business, have sufficient capacity or supply to meet our needs, or that they will not be purchased by one of our competitors or another company that is not interested in continuing to work with us. If we cannot establish sufficient supply through alternative third-party CDMOs or in our own facilities should we develop these, our ability to conduct the planned and future clinical trials and our plans for commercialization would be materially adversely affected.

In addition, we currently rely on a small number of CDMOs for the production of certain of our product candidates and, as a result, face certain additional risks relating to our manufacturing operations. A single significant disruptive event at the manufacturing operations of one of our CDMOs can have a material adverse effect on our business, prospects, financial condition and results of operations. In addition, one of our CDMOs is located in the United Kingdom and we cannot rule out the possibility of delays in obtaining our product candidates as a result of changes in the governing regulatory framework, including import/export restrictions, due to Brexit. Business interruption insurance may not adequately compensate us for any losses that may occur, and we would have to bear the additional cost of any disruption. For instance, if we were to experience an unexpected loss of supply, or if our CDMOs are unable to meet our demand for our product candidates or their services, we could experience delays in our research and development activities, planned clinical trials or commercialization of approved products. Finding alternative CDMOs or suppliers of acceptable quality who can deliver appropriate volumes at acceptable cost may be challenging. Moreover, the long transition periods involved in the change of CDMOs and suppliers, if necessary, would significantly delay our clinical trials and the commercialization of our product candidates, if approved.

We will need to work with CDMOs that can meet all applicable FDA and other regulatory authority requirements on an ongoing basis. If the manufacturing process is changed during the course of product development, the FDA or other regulatory authorities could require us to repeat some or all previously conducted trials or conduct additional trials to obtain bridging data, which could delay or impede our ability to obtain marketing approval. If we or our CDMOs are unable to reliably produce and release our product candidates to specifications acceptable to the FDA or other regulatory authorities, we may not obtain or maintain the approvals we need to further develop, conduct clinical trials for, and commercialize such product candidates. Similarly, approval of our product candidates could be delayed or denied if the intended manufacturing site fails to pass the required preapproval inspection. Even if we obtain regulatory approval for any of our product candidates, there is no assurance that either we or our CDMOs will be able to manufacture the approved product to specifications acceptable to the FDA or other regulatory authorities, to produce it in sufficient quantities to meet the requirements for the potential launch of the product, or to meet potential future demand. Any of these challenges could delay completion of clinical trials, require clinical trials to obtain bridging data or the repetition of one or more clinical trials, increase clinical trial costs, delay approval of our product candidates, impair commercialization efforts, increase our cost of goods, and have a material adverse effect on our business, financial condition, results of operations and growth prospects.

We expect that development of our own manufacturing facilities could provide us with enhanced control of material supply for our product candidates for clinical trials and the commercial market. However, we have no experience as a company in developing and operating a manufacturing facility and may never be successful in developing our own manufacturing facility or capability should we decide to do so. In particular, if we do pursue the construction of our own manufacturing facilities, we may not complete construction in a timely manner, if at all. Such facilities would also need to be inspected and approved by the FDA and other regulatory agencies before these facilities can be used to manufacture our product candidates, which may subject us to unforeseen delays in our manufacturing efforts and additional regulatory inspections.

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

Manufacturing issues may arise that could increase product and regulatory approval costs or delay commercialization of our products.

As the manufacturing processes are scaled up, they may reveal manufacturing challenges or previously unknown impurities that could require resolution in order to proceed with our planned clinical trials and obtain regulatory approval for the commercial marketing of our products. In the future, we may identify manufacturing issues or impurities that could result in delays in the clinical program and regulatory approval for our products, increases in our operating expenses, or failure to obtain or maintain approval for our products. Our reliance on third-party manufacturers entails risks, including the following:

- the inability to meet our product specifications, including product formulation, and quality requirements consistently;
- a delay or inability to procure or expand sufficient manufacturing capacity;
- manufacturing and product quality issues, including those related to scale-up of manufacturing;
- a failure to comply with cGMP and similar quality standards;
- termination or nonrenewal of manufacturing agreements with third parties in a manner or at a time that is costly or damaging to us;
- operations of our third-party manufacturers or suppliers could be disrupted by conditions unrelated to our business or operations, including the bankruptcy of the manufacturer or supplier;
- carrier disruptions or increased costs that are beyond our control;
- the failure to deliver our products under specified storage conditions and in a timely manner; and
- the imposition of tariffs on our products in the future.

Any of these events could lead to delays in any clinical trial we may undertake, failure to obtain regulatory approval or impact our ability to successfully commercialize any product candidates. Some of these events could be the basis for FDA or other regulatory authorities' action, including injunction, recall, seizure, or total or partial suspension of production.

Our third-party manufacturers or suppliers may use potent chemical agents and hazardous materials, and any claims relating to improper handling, storage or disposal of these materials could be time-consuming or costly.

Our third-party manufacturers or suppliers may use hazardous materials, including chemicals and biological agents and compounds that could be dangerous to human health and the safety of the environment. The operations of our third-party manufacturers and suppliers also produce hazardous waste products. Various laws and regulations govern the use, generation, manufacture, storage, handling and disposal of these materials and wastes. Compliance with applicable environmental laws and regulations may be expensive, and current or future environmental laws and regulations may impair our product development efforts. In addition, we cannot eliminate the risk of accidental injury or contamination from these materials or waste, and we may be sued for any injury or contamination that results from our use or the use by third parties of these materials. In the event of contamination or injury, we could be held liable for damages or be penalized with fines in an amount exceeding our resources, and our clinical trials or regulatory approvals could be suspended.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations, which have tended to become more stringent over time. These current or future laws and regulations may impair our research, development or production efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions or liabilities, which could materially adversely affect our business, financial condition, results of operations and prospects.

Our activities rely heavily on sensitive and personal materials and information, an area which is highly regulated by privacy laws. Our failure to comply with such laws or to adequately secure the information we hold could result in significant liability or reputational harm and, in turn, a material adverse effect on our client base, member base and revenue. Further, if we are

unable to generate or maintain access to essential patient samples or data for our research and development and manufacturing activities for our programs, our business could be materially adversely affected.

As a result of our clinical development, we will have access to very sensitive data regarding the patients enrolled in our clinical trials, and our current and future product candidates will rely on the use of patient and donor data and material. This data will contain information that is personal in nature, and the maintenance of this data is subject to certain privacy-related laws, which impose administrative burdens, substantial costs and litigation risks upon us, such as the rules promulgated by the U.S. Department of Health and Human Services under the U.S.Health Insurance Portability and Accountability Act ("HIPAA"), and U.S. state privacy laws. These rules inter alia require that written authorizations from patients are obtained, and that policies, procedures and reasonable and appropriate security measures are implemented that protect individually identifiable health and other information we receive and to ensure that such information is used only as authorized by the patient. If the patient fails to execute an authorization or the authorization fails to contain all required provisions, then we will not be allowed access to the patient's information and our research efforts can be substantially delayed. Also, any violations of these rules by us could subject us to civil and criminal penalties and adverse publicity and could harm our ability to initiate and complete clinical trials.

In addition, there are significant international laws that protect data privacy which we must adhere to. For example, we are subject to the EU General Data Protection Regulation, or the GDPR (as implemented by countries in the EEA), which applies extra-territorially and imposes onerous requirements on controllers (e.g., sponsors) and processors (e.g., CROs, laboratories, third-party vendors) of EEA personal data, including, for example: (i) accountability, transparency and accuracy requirements, and enhanced requirements for obtaining valid consent (separate and apart from informed medical consent); (ii) adhering to the principles of 'privacy by design and by default' when developing new products or services; (iii) complying with data minimization obligations; (iv) obligations in relation to the rights of data subjects; (v) ensuring that all processors that process personal data on our behalf have adequate protections in place; and (vi) reporting of personal data breaches to the supervisory authority without undue delay (and no later than 72 hours). The GDPR also prohibits the international transfer of personal data from the EEA to countries outside of the EEA unless made to a country deemed to have adequate data privacy laws by the European Commission or where a data transfer mechanism with appropriate safeguards has been put in place, such as the standard contractual clauses, or SCCs, and supplementary measures that provide privacy protections additional to those provided under SCCs. Further, the GDPR provides that countries in the EEA may establish their own laws and regulations further restricting the processing of certain personal data, including genetic data, biometric data, and health data. After assessing the severity and frequency of the EEA personal data processing activities we engage in, we appointed an external data protection officer that has expert knowledge of data protection law and practices and assists us with monitoring internal compliance with the GDPR.

We have relatively limited experience with the relevant privacy and security policies, practices and regulations, and cannot assure that our policies and practices will be sufficient to protect us from liability or adverse publicity relating to the privacy and security of personal data. Privacy laws, rules and regulations also evolve frequently, and their scope may continually change, through new legislation, amendments to existing legislation and changes in enforcement, and may be inconsistent from one jurisdiction to another. The interpretation and application of consumer, health-related and data protection laws, especially with respect to genetic samples and data, in the United States, the European Union and elsewhere, are often uncertain, contradictory and in flux. As a result, implementation standards and enforcement practices are likely to remain uncertain for the foreseeable future, and we cannot determine the impact such future laws, regulations and standards may have on our business. We cannot provide assurance that current or future legislation will not prevent us from generating or maintaining personal data or that patients will consent to the use of their personal data (as necessary); either of these circumstances may prevent us from undertaking or publishing essential research and development, manufacturing and commercialization, which could have a material adverse effect on our business, results of operations, financial condition and prospects.

Complying with these various laws and regulations could cause us to incur substantial costs or require us to change our business practices, systems and compliance procedures in a manner adverse to our business. For example, failure to comply with the GDPR requirements could result in regulatory investigations, enforcement notices requiring us to stop or change the way we use personal data and/or fines of up to 20 million Euros or up to 4% of the total worldwide annual turnover of the preceding financial year, whichever is higher, as well as compensation claims for financial or non-financial loss by affected individuals, negative publicity, reputational harm and a potential loss of business and goodwill.

These laws, rules and regulations evolve frequently, and their scope may continually change, through new legislation, amendments to existing legislation and changes in enforcement, and may be inconsistent from one jurisdiction to another. The interpretation and application of consumer, health-related and data protection laws, especially with respect to genetic samples and data, in the United States, the European Union, or EU, and elsewhere, are often uncertain, contradictory and in flux. As a result, implementation standards and enforcement practices are likely to remain uncertain for the foreseeable future, and we cannot determine the impact such future laws, regulations and standards may have on our business. Our internal computer systems, or those used by our clinical investigators, contractors or consultants, may fail or suffer security breaches.

We are a party to certain agreements that contain liability or indemnification provisions under which we may claim damages from our counterparties and under which our counterparties may claim damages from us, including damages caused by product defects.

We are a party to certain agreements, including clinical trial agreements and licensing agreements which contain liability or indemnification provisions under which we or the counterparty may claim damages. In the event we need to claim damages from a counterparty, we may not receive payments covering our damages in full, either because the applicable provision is unenforceable for any reason or because the counterparty is unable to pay (due to insolvency or otherwise). Although in many cases we try to limit our liability,

such limitations may not be enforceable in certain jurisdictions or effective in the event that we need to pay damages and we nevertheless could become liable to make substantial payments. If we must make substantial liability payments under an agreement, this could have a material adverse effect on our business, results of operations, financial condition and prospects.

Risks Related to the Commercialization of Our Product Candidates

If we are unable to commercialize our product candidates IR and XR or any other product candidates that we may pursue, or experience significant delays in doing so, our business, financial condition, results of operations and prospects would be materially adversely affected.

We do not expect to generate product revenues in the foreseeable future. If our product candidates IR and XR or any other program that we may pursue fails, we will have to develop, acquire, or license new programs. Our product candidates, as well as any other programs we may pursue, could be unsuccessful if they:

- do not demonstrate acceptable safety or efficacy in nonclinical studies or clinical trials or otherwise do not meet applicable regulatory standards for approval;
- generate unacceptable adverse side effects;
- do not offer therapeutic or other improvements over existing or future products used to treat the same conditions;
- are not accepted in the medical community or by insurers, either public or private; or
- are not capable of being produced and delivered to patients in commercial quantities at acceptable costs.

The results of the research and trials to date cannot provide assurance that acceptable efficacy or safety will be shown upon completion of ongoing or planned clinical trials. Many products that show promise in proof-of-concept, Phase 1 and/or Phase 2 trials fail in later clinical trials or in a commercial setting. If we are unable to make our product candidates commercially available, or we experience significant delays in doing so, our business, financial condition, results of operations and prospects would be materially adversely affected.

The market opportunities for our product candidates may be smaller than currently anticipated, lowering our potential revenue.

The market opportunities for our product candidates may be smaller than currently anticipated, lowering our potential revenue. We make projections of both the number of people who have HAE, as well as the number of individuals within our target patient population who have the desire to switch to an oral therapy and the potential to benefit from treatment with our product candidates. These projections are derived from scientific literature and patient foundations but are highly contingent on a number of variables that are difficult to predict and may prove to be too high, resulting in a smaller population of patients who are interested in, and could benefit from, our product candidates than we currently anticipate which would result in lower potential revenue.

Moreover, if we are successful in developing both IR and XR, we cannot accurately predict the proportion of patients choosing prophylactic or on-demand only treatment regimens.

Use of our product candidates could be associated with side effects or adverse events.

As with all pharmaceutical products, use of our product candidates could be associated with side effects or adverse events, which can vary in severity and frequency. Side effects or adverse events associated with the use of our product candidates may be observed at any time, including in clinical trials or once a product is commercialized, and any such side effects or adverse events may negatively affect our ability to obtain regulatory approval or market our product candidates. Side effects or adverse events associated with the use of our product candidates could result in a label change, require us to perform additional studies or halt development or sale of these product candidates or expose us to product liability lawsuits, which will harm our business. We may be required by regulatory agencies to conduct additional nonclinical studies or clinical trials regarding the safety of our product candidates, which we have not planned or anticipated. For instance, we were required to conduct a 26-week rodent toxicology study to resolve the clinical holds placed by the FDA on clinical trials of deucrictibant in the U.S. We cannot provide any assurance that we will resolve any issues related to any product-related side effects or adverse events to the satisfaction of the FDA or any regulatory agency in a timely manner or ever, which could harm our business, prospects and financial condition.

If we are successful in commercializing our product candidates, the FDA and other comparable foreign regulatory authorities require that we analyze and report certain information about adverse events that our products may have caused or contributed to. The FDA and other foreign regulatory authorities impose strict requirements with respect to the analysis of such events and the manner and timing of our reporting of the information to the regulatory authorities. We may fail to comply with the requirements for assessing and reporting adverse events and if we fail to comply with these obligations, the FDA or other comparable foreign regulatory authorities could take action including the issuance of warning letters or other regulatory correspondence, criminal prosecution, the imposition of civil sanctions, seizure of our products, or delay in approval or clearance of future products.

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

Our product candidates may not be commercially successful. Even if any of our product candidates receive regulatory approval, they may not gain sufficient market acceptance among physicians, patients, healthcare payors or others in the medical community. The commercial success of any of our current or future product candidates will depend significantly on the broad adoption and use of the resulting product by physicians and patients for approved indications. The degree of market acceptance of any of our potential products as may receive marketing authorization will depend on a variety of factors, many of which are outside our control, including:

- demonstration of clinical efficacy and safety compared to other more established products;
- the limitation of our targeted patient population and other limitations or warnings contained in any approved labeling;
- acceptance of a new drug for the relevant indication by healthcare providers and their patients;
- the pricing and cost-effectiveness of our products, as well as the cost of treatment with our products in relation to alternative treatments and therapies;
- our ability to obtain and maintain sufficient third-party coverage and adequate reimbursement from government healthcare programs, private health insurers and other third-party payors;
- the willingness of patients to pay all, or a portion of, out-of-pocket costs associated with our products in the absence of sufficient third-party coverage and adequate reimbursement;
- any restrictions on the use of our products, and the prevalence and severity of any adverse effects;
- the timing of market introduction of our products as well as competitive drugs;
- the effectiveness of our or any of our potential future collaborators' sales and commercialization strategies; and
- unfavorable publicity relating to the product.

If any products that we may develop fail to achieve market acceptance, we may not be able to generate sufficient revenues. We may make substantial investments in clinical development, manufacturing, supply chain and commercialization without any assurance that we will be able to attain significant market share at a price that would enable us to recover our investments. If we are unable to do so, our business, financial condition, results of operations and prospects would be materially adversely affected.

We face substantial competition, which may result in others discovering, developing or commercializing competing products before or more successfully than we do.

The development and commercialization of new drug products is highly competitive. We face competition with respect to our current product candidates and will face competition with respect to any product candidates that we may seek to develop or commercialize in the future, from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide. As discussed under "ITEM 4. INFORMATION ON THE COMPANY—B. Business overview—Competition," there are several licensed therapies for HAE and we are aware of a number of HAE therapies in clinical development. Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop. In addition, our ability to compete may be affected in many cases by insurers or other third-party payors seeking to encourage the use of generic products. Generic products are expected to become available over the coming years, potentially creating pricing pressure. If our product candidates achieve marketing approval, we expect that they will be priced at a significant premium over competitive generic products. This may make it difficult for us to achieve our business strategy of using our product candidates in combination with existing therapies or replacing existing therapies with our product candidates. Competition may further increase as a result of advances in the commercial applicability of technologies and greater availability of capital for investment in these industries.

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

We may encounter difficulties in managing our growth and expanding our operations successfully.

If we advance our product candidates through clinical trials and regulatory approvals, we will need to expand our development, manufacturing, regulatory, commercialization and supply chain capabilities or contract with third parties to provide these capabilities for us. Our ability to realize our commercialization strategy and manage any growth will require us to continue to recruit and train additional

qualified personnel and make appropriate changes to our operational, financial and management controls. We may experience a delay in becoming aware of certain issues or information material to management decisions. The expansion of our operations, including potential expansion into global markets outside of the European Union and the United States, may lead to significant costs, new challenges and risks and may divert the attention of our management and our business development resources. Any inability to manage anticipated growth and expanding operations, including as a result of failing to realize our commercialization strategy for our product candidates IR and XR, could adversely affect our business, financial condition, results of operations or prospects.

Governments and/or pricing authorities, especially in the European Union, often impose strict price and access controls, which may adversely affect our future profitability.

In some markets, especially in the European Union, prescription drug pricing is subject to governmental/ pricing authority control which can vary by country and degree. In these countries, pricing negotiations with governmental/pricing authorities can take considerable time after the receipt of marketing approval for a product. If reimbursement of any future products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels or the pricing negotiation is considerably delayed, we may be unable to achieve or sustain profitability.

Drug pricing and other healthcare costs continue to be subject to intense political and societal pressures, which we anticipate will continue and escalate on a global basis. These pressures may result in harm to our business and reputation, cause the market price of our ordinary shares to decline or experience periods of volatility and adversely affect our results of operations and our ability to raise funds.

The insurance coverage and reimbursement status of newly approved products is uncertain. Failure to obtain or maintain adequate coverage and reimbursement for new or current products could limit our ability to market those products and decrease our ability to generate revenue.

The availability and extent of reimbursement by governmental and private payors is essential for most patients to be able to afford expensive treatments. Sales of our product candidates will depend substantially, both domestically and abroad, on the extent to which the costs of our product candidates will be paid by health maintenance, managed care, pharmacy benefit and similar healthcare management organizations, or reimbursed by government health administration authorities, private health coverage insurers and other third-party payors. If reimbursement is not available, or is available only to limited levels, we may not be able to successfully commercialize our product candidates. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish or maintain pricing sufficient to realize a sufficient return on our investment.

There is significant uncertainty related to the insurance coverage and reimbursement of newly approved products. In the United States, the principal decisions about reimbursement for new medicines are typically made by the CMS. CMS decides whether and to what extent a new medicine will be covered and reimbursed under Medicare. Private payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement rates. It is difficult to predict what CMS will decide with respect to reimbursement for fundamentally novel products such as ours, as there is no body of established practices and precedents for these new products.

Outside the United States, international operations are generally subject to extensive governmental price controls and other market regulations, and we believe the increasing emphasis on cost-containment initiatives in Europe, Canada, and other countries has and will continue to put pressure on the pricing and usage of our product candidates. In many countries, the prices of medical products are subject to varying price control mechanisms as part of national health systems. In general, the prices of medicines under such systems are substantially lower than in the United States. Other countries allow companies to fix their own prices for medicines but monitor and control company profits. Additional foreign price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our product candidates. Accordingly, in markets outside the United States, the reimbursement for our products may be reduced compared with the United States and may be insufficient to generate commercially reasonable revenues and profits.

Moreover, increasing efforts by governmental and third-party payors, in the United States and abroad, to cap or reduce healthcare costs may cause such organizations to limit both coverage and level of reimbursement for new products approved and, as a result, they may not cover or provide adequate payment for our product candidates. We expect to experience pricing pressures in connection with the sale of any of our product candidates, due to the trend toward managed healthcare, the increasing influence of health maintenance organizations and additional legislative changes.

The downward pressure on healthcare costs in general, particularly prescription drugs and surgical procedures and other treatments, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products into the healthcare market.

In addition, many private payors contract with commercial vendors who sell software that provide guidelines that attempt to limit utilization of, and therefore reimbursement for, certain products deemed to provide limited benefit to existing alternatives. Such organizations may set guidelines that limit reimbursement or utilization of our products.

We may become exposed to costly and damaging liability claims, either when testing our product candidates in the clinic or after commercialization; and our product liability insurance may not cover all damages from such claims.

We face an inherent risk of product liability as a result of the clinical testing of our product candidates and will face an even greater risk if we commercialize any products. For example, we may be sued if any product we develop allegedly causes injury or is found to be otherwise unsuitable during product testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of

defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability and a breach of warranties. Physicians and patients may not comply with any warnings that identify known potential adverse effects and patients who should not use our products. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to stop development or, if approved, limit commercialization of our product candidates. Even successful defenses would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in:

- delay or termination of clinical trials;
- injury to our reputation and negative publicity;
- withdrawal of clinical trial participants, patients or clinical investigators;
- initiation of investigations by regulators or ethics committees;
- costs to defend the related litigation;
- a diversion of management's time and our resources;
- substantial monetary awards to trial participants or patients;
- decreased demand for our product candidates;
- product recalls or withdrawals, or labeling, marketing or promotional restrictions;
- loss of revenues from product sales;
- the inability to commercialize any of our product candidates, if approved; and
- a decline in the price of our ordinary shares.

Any product liability insurance coverage we obtain may not fully cover potential liabilities that we may incur. Our insurance policies have various exclusions, and we may be subject to a product liability claim for which we have no coverage. The cost of any product liability litigation or other proceeding, even if resolved in our favor, could be substantial. We will have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts.

We will also need to increase our insurance coverage if we commercialize any product that receives marketing approval. Insurance coverage is becoming increasingly expensive. If we are unable to maintain sufficient insurance coverage at an acceptable cost or to otherwise protect against potential product liability claims, it could prevent or inhibit the development and commercial production and sale of our product candidates, which could harm our business, financial condition, results of operations and prospects.

If we are unable to establish commercial capabilities or enter into agreements with third parties to market, sell and distribute our product candidates, we may be unable to generate any revenues if and when our product candidates are approved.

If any of our product candidates receive marketing approval, we intend to market, sell and distribute them using our own commercial infrastructure. However, we have no experience in commercialization, selling and distributing pharmaceutical products or establishing a commercial organization. We may enter into collaborations with other entities to utilize their mature sales, marketing and distribution capabilities, but we may be unable to enter into commercialization agreements on favorable terms, if at all. If our future collaborative partners do not commit sufficient resources to commercialize our product candidates, if approved, or if we are unable to develop the necessary commercialization capabilities on our own, we will be unable to generate sufficient product revenues to sustain our business. Further, we may not have sufficient control or oversight over our future collaborative partners to ensure they sell and market our product candidates in compliance with all applicable law. In building our commercial infrastructure or commercializing our product candidates, if approved, we will be competing with other well-funded companies that currently have or are building extensive commercial operations. Without an internal team or the support of a third-party to perform commercial functions, we may be unable to successfully commercialize our product candidates, if approved, and/or compete successfully against these companies.

Risks Related to Our Reliance on Third Parties and Key Personnel

If third parties on which we depend to conduct our clinical trials do not perform as contractually required, fail to satisfy regulatory or legal requirements or miss expected deadlines, our development program could be delayed with materially adverse effects on our business, financial condition, results of operations and prospects.

We rely on CROs, independent clinical investigators, clinical data management organizations, consultants and other third-party firms to design, conduct, supervise and monitor clinical trials. We and these third parties are required to comply with extensive regulations, including good clinical practices, or GCP, which are enforced by the competent authorities of the member states of the European Economic Area, or EEA, the FDA and other comparable regulatory authorities; GCP are intended to ensure that the health, safety and rights of patients are protected in clinical development and clinical trials, and that trial data integrity is assured. In fact, as sponsor of the clinical trials, GCP compliance remains our responsibility. Regulatory authorities ensure compliance with these requirements through periodic inspections of trial sponsors, clinical investigators and trial sites. Our reliance on third parties that we do not control does not relieve us of these responsibilities and requirements. If we or any of these third parties fail to comply with applicable requirements, clinical trials may be put on "clinical hold," the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign

regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials comply with such requirements. In addition, our clinical trials must be conducted with products that are cGMP produced. Failure to comply with these regulations may result in a clinical hold or require us to repeat nonclinical studies and clinical trials, which would delay the regulatory approval process.

Third-party staff are not our employees and, except for remedies available to us under our agreements with such third parties, we cannot control whether or not they devote sufficient time and resources to our ongoing clinical and nonclinical programs and meet their quality and other requirements. If these third parties do not successfully carry out their contractual duties or obligations or meet expected deadlines or if the quality or accuracy of the product or 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 put on hold, extended, delayed or terminated and we may not be able to obtain regulatory approval for or successfully commercialize our product candidates. As a result, our operations and the commercial prospects for our product candidates in development would be harmed, our costs could increase and our ability to generate revenues could be delayed.

Because we have relied on third parties, our internal capacity to perform these functions is limited. Outsourcing these functions involves the risk that third parties may not perform to our standards, may not produce results in a timely manner or may fail to perform at all. In addition, the use of third-party service providers requires us to disclose our proprietary information to these parties, which could increase the risk that this information will be misappropriated. We currently have a small number of employees, which limits the internal resources we have available to identify and monitor our third-party providers. To the extent we are unable to identify and successfully manage the performance of third-party service providers in the future, our business may be adversely affected. Though we carefully manage the relationships with third parties, there can be no assurance that we will not encounter similar challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition, results of operation and prospects.

If we cannot contract with acceptable third parties on commercially reasonable terms, or at all, or if these third parties do not carry out their contractual duties, satisfy legal and regulatory requirements for the conduct of nonclinical studies or clinical trials or meet expected deadlines, our clinical development programs could be delayed and otherwise adversely affected. Any such event could have a material adverse effect on our business, financial condition, results of operations and prospects.

We are dependent on the services of our management and other clinical and scientific personnel, and if we are not able to retain these individuals or recruit additional management or clinical and scientific personnel, our business will suffer.

Our success depends in part on our continued ability to attract, retain and motivate highly qualified management, clinical and scientific personnel. We are highly dependent upon our senior management team as well as our senior scientists. The loss of services of any of these individuals could delay or prevent the successful development of our product candidates, initiation or completion of our planned clinical trials or the commercialization of our product candidates. Our industry has experienced a high rate of turnover of management, clinical and scientific personnel in recent years and despite our efforts to retain valuable employees, members of our management, scientific and development teams may terminate their employment with us. In addition, as we expand our operations, we may not be successful in maintaining our unique company culture and continuing to attract or retain qualified management and scientific and clinical personnel in the future due to the intense competition for qualified personnel among pharmaceutical, biotechnology and other businesses. Replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval of and commercialize products. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. If we do not have sufficient numbers of skilled employees to support our research, development, manufacturing, regulatory compliance or management functions, or if our employees lack the skills necessary for the development of our operations, we may need to retain consultants and advisers, if available on terms acceptable to us, if at all, who may have conflicts of interest or other commitments, such as consulting or advisory contracts with other organizations that may affect their ability to contribute to us. In addition, if we are not able to attract, integrate, retain and motivate sufficient scientific, technical and managerial personnel, we will be unable to advance our clinical programs or expand our business, which may have a material adverse effect on our business, financial condition, results of operations and prospects.

We are heavily dependent on third parties to perform critical activities related to the research, development and manufacturing of our product candidates. If these third parties fail or are unable to perform, our development programs and candidate products could be materially and adversely affected and our business and prospects will suffer.

We are heavily dependent on third parties to conduct certain key activities relating to the research, development and manufacturing of our product candidates. For example, we rely on third-party firms to conduct development, studies, and trials with respect to our candidate products and to manufacture and supply the material used in our studies and trials.

Our reliance on third parties may pose the following risks to us:

- third parties have significant discretion in determining the efforts and resources that they will apply to our development programs and product candidates;
- third parties could independently develop, supply, manufacture, commercialize or collaborate with additional third parties, products that compete directly or indirectly with our product candidates;

- third parties may not properly prosecute, maintain, enforce or defend our intellectual property rights or may use our proprietary information in a way that gives rise to actual or threatened litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation, or other intellectual property proceedings;
- disputes may arise with respect to ownership of any intellectual property developed pursuant to our collaborations and activities with third parties;
- disputes may arise between us and our third-party collaborators and service provider that cause the delay or termination of the development, manufacturing, supply or commercialization of our product candidate, or that result in costly litigation or arbitration that diverts management's attention and resources; and
- if a current or future third-party collaborator or service provider of ours were to be involved in a business combination, the continued pursuit and emphasis on our product development or commercialization program could be delayed, diminished or terminated.

As a result, if any third parties upon which we are dependent fail or are unable to perform, our development programs and candidate products could be materially adversely affected.

We may be unable to enter into or maintain strategic alliances or collaborations which could affect our ability to commercialize our product candidates, if approved.

We may seek strategic alliances or collaborations to further the clinical development and commercialization of certain of our product candidates as they would likely require expensive and time-consuming clinical trials. In seeking strategic partners, we face significant competition from other companies as well as public and private research institutions. There can be no assurance that we will be able to enter into or maintain strategic alliances on terms favorable to us, or at all. Potential partners may require royalty or milestone payments, rights to current or after-developed intellectual property, exclusivity rights, limitations on liabilities, indemnities or other provisions that are adverse to us. Potential partners may fail to diligently fund, develop or commercialize our product candidates. Any of the foregoing may have a material adverse effect on our business, financial condition, results of operations and prospects.

Risks Related to Our Intellectual Property

If we fail to make required payments pursuant to the agreements with BRAIN pursuant to which we acquired certain of our core intellectual property or are otherwise in material breach of such agreements (and fail to cure such breaches within a specified time period), BRAIN may exercise remedies pursuant to such agreements that would materially and adversely affect our business and results of operations.

Certain intellectual property that is core to our business has been invented by BRAIN and contractually assigned to us by BRAIN, with whom we continue to collaborate for the development of our product candidates. Under the BRAIN agreements, we owe milestone payments contingent on our achievement of certain clinical development and regulatory events, as well as royalties and milestone payments based on sales of such product candidates. If we fail to make such payments or are otherwise in material breach of certain agreements that we entered into with BRAIN (and fail to cure such breaches within a specified time period), and BRAIN exercises contractual remedies available to it under such agreements, then we may be required to grant BRAIN an exclusive license to the intellectual property that it assigned to us for use in all applications, including HAE. In addition, we could be prevented from competing with BRAIN until five years after the commercial launch of any product candidates containing a compound from the OB2RA Class. If we failed to make such payments and BRAIN were to exercise such remedies, we would not be able to continue our current development program or commercialize our product candidates and our business and results of operations would be materially and adversely affected. For a description of our arrangement with BRAIN, please see "ITEM 4. INFORMATION ON THE COMPANY—B. Business overview—License Agreement."

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

Our commercial success depends in significant part on obtaining and maintaining current and future patent protection, trade secrets and confidential know-how for our technologies, product candidates, the methods used to manufacture those product candidates and the methods for treating patients using those product candidates. We may not be able to file, prosecute, maintain, enforce, or license all necessary or desirable patents and patent applications at a reasonable cost or in a timely manner. Our failure to obtain, maintain or extend patent protection or to protect trade secrets or confidential know-how could materially adversely affect our ability to compete and to exclude others from copying our processes and technologies.

Obtaining and enforcing patents in the pharmaceutical industry involves both technological and legal complexity and is therefore costly, time consuming and subject to numerous risks and uncertainties. These risks and uncertainties include, but are not limited, to the following:

- the United States Patent and Trademark Office, or USPTO, and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent process, the

noncompliance with which can result in abandonment or lapse of a patent or patent application, and partial or complete loss of patent rights in the relevant jurisdiction;

- patent applications may not result in any patents being issued;
- patents may be challenged, invalidated, modified, revoked, circumvented, found to be unenforceable or otherwise may not provide any competitive advantage;
- our competitors, many of whom have substantially greater resources than we do and many of whom have made significant investments in competing technologies, may seek or may have already obtained patents that will limit, interfere with or block our ability to make, use and sell our product candidates;
- there may be significant pressure on the U.S. government and international governmental bodies to limit the scope of patent protection both inside and outside the United States for disease treatments that prove successful, as a matter of public policy regarding worldwide health concerns; and
- countries other than the United States may have patent laws less favorable to patentees than those upheld by U.S. courts, allowing foreign competitors a better opportunity to create, develop and market competing products.

If we or any third parties that develop or create any intellectual property for us are unable to secure necessary assignments or rights, including from investors, as applicable, then our rights to such intellectual property, and ultimately our ability to protect our candidate products, may be adversely affected.

It is also possible that we fail to identify patentable aspects of our research and development output in time to obtain patent protection. In addition, we may not be aware of all third-party intellectual property rights potentially relating to our product candidates and technology. We cannot guarantee that any of our or our licensors' patent searches or analyses, including but not limited to the identification of relevant patents, analysis of the scope of relevant patent claims or determination of 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 elsewhere that is relevant to or necessary for the development and commercialization of our product candidates in any jurisdiction. For example, publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot be certain that we were the first to make the inventions claimed in any licensed patents or pending patent applications (or claimed in any patents or patent applications that we may own in the future, if any), or that we were the first to file for patent protection of such inventions.

The duration and scope of any patents we are issued in the future (if any) or the patent rights of our licensors or collaborators may not be sufficient to effectively protect our product candidates and business.

The patent position of biopharmaceutical companies generally is highly uncertain, involves complex legal and factual questions, and has been the subject of much litigation in recent years. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Even if our current or future patent applications are issued as patents, they may not be issued with the scope of claims sought by us, or the scope of claims we or our licensors are seeking may not be sufficiently broad to protect our product candidates or provide us with any competitive advantage. Any patents that we may own in the future (if any) may be challenged or circumvented by third parties or may be narrowed or invalidated as a result of challenges by third parties. Consequently, we do not know whether our product candidates will be protectable by valid and enforceable patents.

Moreover, the coverage claimed in a patent application can be significantly reduced before the patent is issued, and its scope can be reinterpreted after issuance. Changes in or different interpretations of patent laws in the United States, Europe, and other jurisdictions may also permit others to use our discoveries or to develop and commercialize our technology and products without providing any compensation to us, or may limit the number of patents or claims we can obtain. The laws of some countries do not protect intellectual property rights to the same extent as U.S. and European laws and those countries may lack adequate rules and procedures for defending our intellectual property rights.

Our competitors and other third parties would be able to offer and sell products so long as they do not infringe any valid and enforceable patents or other proprietary rights that we or others, including our licensors, may have. The specific content of patents and patent applications that are necessary to support and interpret the scope of patent claims is highly uncertain due to the complex nature of the relevant legal, technical and factual issues. Such risks will increase if we or our licensors are not able to obtain additional patents protecting aspects of our product candidates and technology, such as product improvements, formulations, methods of production or novel uses of the relevant product candidates.

In addition, patents have a limited lifespan. For example, if renewal fees are paid in a timely manner, a European patent expires 20 years after its effective filing date. Similarly, if all maintenance fees are timely paid, a patent in the United States generally expires 20 years after its effective filing date. Depending upon the timing, duration and specifics of any FDA marketing approval of any product candidates we may develop in the United States, any patents we are issued in the future (if any) may qualify for a limited patent term extension if certain criteria are met (e.g., in case of significant delays during patent prosecution or during FDA approval for bringing a drug covered by a patent to market) under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Amendments. Specifically, the Hatch Waxman Amendments permit a patent extension term of up to five years as compensation for patent term lost during the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent may be extended and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended. However, in such an event we may not be granted an extension because of,

for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents, or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. In the European Union, an extension of the duration of protection for a pharmaceutical product on the basis of a supplementary protection certificate could be applied for after a valid market authorization is obtained and if the product is specifically covered by a basic patent in force. As a result, an additional term of protection could be obtained for the relevant product on top of the maximum lifespan of the patent. The term of the allowed extension varies, and in principle is at most five and a half years. Consequently, despite these general possibilities for obtaining a certain extension of the duration of protection based on a patent if certain criteria are met, the protection provided by a patent is limited in time.

Furthermore, given the amount of time required for the development, testing, and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. Even if additional patents covering our product candidates are obtained, the expiration of a patent may leave us more vulnerable to competition from biosimilar or generic alternatives, and our business, financial condition, results of operations and prospects could be materially harmed. As a result, our intellectual property may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours. Any of the foregoing could have a material adverse effect on our competitive position, business, financial conditions, results of operations and prospects.

Patents covering our technology and product candidates that may be issued (if any) could be found invalid or unenforceable if challenged in court or an issuing body.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and any patents we may own in the future (if any) may be challenged in the courts or patent offices in the United States and elsewhere. Such challenges may result in loss of exclusivity or in patent claims being narrowed, invalidated or held unenforceable which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and product candidates.

To the extent that we obtain any patents in the future, our patent protection in respect of our product candidates and technologies may be limited or lost if patents that may be issued to us or patents we use under the terms of exclusive commercial licenses were to be declared invalid, rendered unenforceable or narrowed in scope as a result of any re-examination, post grant review, inter partes review, interference proceedings, derivation proceedings, equivalent proceedings in other jurisdictions or judicial action. If one of our licensing partners or we initiate legal proceedings against a third-party to enforce a patent covering one of our product candidates or technologies, the defendant could counterclaim that the patent covering our product candidate is invalid or unenforceable. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, lack of patentable subject matter, lack of written description or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld information material to patentability from the relevant issuing body, or made a misleading statement, during prosecution. A challenge to patents could result in a ruling adverse to us that could invalidate or render unenforceable such patents or substantially reduce the scope of protection afforded by them. A court may also determine, retrospectively, that despite the issuance of the patent by the relevant issuing body, the corresponding patent application did not meet the statutory requirements. If a competitor or other third parties were to successfully challenge our patents (to the extent any are obtained), and claims in these patents were consequently narrowed, rendered unenforceable or invalidated, our ability to protect the related product candidate or technology from competition could be compromised. Such proceedings could result in the revocation or cancellation of or amendment to such patents in such a way that they no longer cover our product candidates. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which the patent examiner and we or our licensing partners were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity or unenforceability, we could lose at least part, and perhaps all, of the patent protection on one or more of our product candidates to the extent that any such patents are issued. Such a loss of patent protection could have a material adverse impact on our business.

We may not be able to protect or enforce our intellectual property rights in all jurisdictions.

Filing, prosecuting, and defending patents on product candidates in all countries throughout the world would be prohibitively expensive, and the laws of foreign countries may not protect our rights to the same extent as the laws of the United States or the European Union. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries, or from selling or importing products made using our inventions in and into the United States, the European Union or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and may export otherwise infringing products and these products may compete with our product candidates in jurisdictions where we do not have any issued patents.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. Patent laws vary by jurisdiction, and, accordingly, the degree of protection afforded to the same technology, if any, may differ depending on the jurisdiction. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents and other intellectual property protection, particularly those relating to biopharmaceuticals, which could make it difficult for us to stop the infringement of any patents we are issued in the future (if any) or commercialization of competing products in violation of our proprietary rights generally. Proceedings to enforce any patent rights we are issued in the future (if any) in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put such patents at risk of being invalidated or interpreted narrowly and could provoke third parties to assert claims against us. In such an event, we may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property and proprietary rights around the world may be inadequate to obtain a significant commercial advantage from the

intellectual property that we develop or license. Our inability to protect or enforce our intellectual property rights throughout the world could have a material adverse effect on our business, prospects, financial condition, results of operations and prospects.

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

Changes in patent law could diminish the value of patents in general, thereby impairing our ability to protect our product candidates.

To the extent that we are issued patents covering our product candidates (if any), changes in either patent laws or interpretations of patent laws in the United States, the European Union, Canada or other jurisdictions may diminish the value of our intellectual property or narrow the scope of our patent protection and could increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents (to the extent any such patents are issued).

For example, patent reform legislation in the United States, including the Leahy-Smith America Invents Act, or the America Invents Act, could increase those uncertainties and costs. The America Invents Act was signed into law on September 16, 2011, and many of the substantive changes became effective on March 16, 2013. The America Invents Act reforms United States patent law in part by changing the U.S. patent system from a “first to invent” system to a “first inventor to file” system in which, assuming that other requirements for patentability are met, the first inventor to file a patent application will be entitled to the patent on an invention regardless of whether a third-party was the first to invent the claimed invention. In addition, the America Invents Act expands the definition of prior art and develops a post-grant review system. This legislation changed United States patent law in a way that may weaken our ability to obtain patent protection in the United States for those applications filed after March 16, 2013.

Further, the America Invents Act created new procedures to challenge the validity of issued patents in the United States, including post grant review, *inter partes* review, and derivation proceedings, which some third parties have been using to cause the cancellation of selected or all claims of issued patents. These adversarial actions at the USPTO review patent claims without the presumption of validity afforded to U.S. patents in lawsuits in U.S. federal courts and use a lower burden of proof than used in litigation in U.S. federal courts. Therefore, it is generally considered easier for a competitor or third-party to have a U.S. patent invalidated in a USPTO post-grant review or *inter partes* review proceeding than invalidated in a litigation in a U.S. federal court. If any patents that we are issued in the future (if any) or our licensor’s patents are challenged by a third-party in such a USPTO proceeding, there is no guarantee that we or our licensors or collaborators will be successful in defending the patent, which would result in a loss of the challenged patent right to us.

In addition, the patent positions of companies in the development and commercialization of pharmaceuticals are particularly uncertain. Recent court rulings in cases such as *Association for Molecular Pathology v. Myriad Genetics, Inc., BRCA1-&BRCA2-Based Hereditary Cancer Test Patent Litigation, Mayo Collaborative Services v. Prometheus Laboratories, Inc., Promega Corp. v. Life Technologies Corp. and Abbvie Deutschland GmbH v. Janssen Biotech, Inc.* 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 future actions by the U.S. Congress, the U.S. courts, and 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 patents that we might obtain in the future. Any changes to patent law in the U.S. or other jurisdictions that impairs our ability to protect our deucrictibant and other product candidates that we may pursue could have a material adverse effect on our business, financial condition, results of operations and prospects.

Confidentiality agreements with employees and third parties may not prevent unauthorized disclosure of trade secrets and other proprietary information and may not provide an adequate remedy.

We consider proprietary trade secrets and confidential know-how and unpatented know-how to be important to our business. We rely on trade secrets and confidential know-how to protect our technology, especially where we do not believe that patent protection is appropriate or obtainable. However, trade secrets and confidential know-how are difficult to protect and some courts in the United States, the European Union and elsewhere are less willing or unwilling to protect trade secrets. We seek to protect our proprietary trade secrets and confidential know-how, in part, by entering into confidentiality agreements with our current and former employees, consultants, contractors, outside scientific collaborators and other advisers. However, we cannot guarantee that we have entered into such agreements with each party that may have or has had access to our trade secrets or confidential know-how or that such agreements will fully protect our proprietary trade secrets and confidential know-how. Our current or former employees, consultants, contractors, outside scientific collaborators and other advisers may have access to and unintentionally or willfully disclose our confidential information, including to competitors. Our confidentiality agreements may be breached by such individuals and we may not have adequate remedies for any breach. Enforcing a claim that a third-party obtained illegally and is using trade secrets and confidential know-how illegally is expensive and time consuming and the outcome is unpredictable. Failure to obtain or maintain trade secret and confidential know-how trade protection could adversely affect our competitive business position. Moreover, our competitors and other third parties may independently develop equivalent knowledge, methods and know-how and may even apply for patent protection in respect of the same. If successful in obtaining such patent

protection, our competitors could limit how we use our trade secrets and confidential know-how, which may have a material adverse effect on our business, financial condition, results of operations and prospects.

If we or our licensors infringe, misappropriate or otherwise violate intellectual property rights of third parties, we may face increased costs or we may be unable to commercialize our product candidates.

Our commercial success depends upon our ability to develop, manufacture, market, sell and distribute our product candidates and use our proprietary technologies without infringing, misappropriating or otherwise violating the proprietary rights and intellectual property of third parties. The biotechnology and pharmaceutical industries are characterized by extensive and complex litigation regarding patents and other intellectual property rights. There is a risk that third parties may allege that our employees, consultants, independent contractors or the licensors have wrongfully used or disclosed trade secrets and we infringed, are infringing, or will infringe the proprietary rights of third parties because patents and pending applications belonging to third parties exist in the European Union, the United States and elsewhere in the world in the areas in which our research is conducted. Because patent applications take several years to complete, there may be currently pending applications, unknown to us, which may later result in issued patents that cover the development production, manufacture, commercialization or use of our product candidates and technology. In addition, the development production, manufacture, commercialization or use of our product candidates may infringe existing patents of which we are not aware. Even if we believe such claims of infringement are without merit, a court of competent jurisdiction could hold that these third-party patents are valid, enforceable and infringed, which could materially and adversely affect our ability to commercialize our product candidates and technology. In order to successfully challenge the validity of any such U.S. patent in federal court, we would need to overcome a presumption of validity. As this burden is a high one requiring us to present clear and convincing evidence as to the invalidity of any such U.S. patent claim, there is no assurance that a court of competent jurisdiction would invalidate the claims of any such U.S. patent. Even if we are successful in defending against such claims, litigation could be time-consuming and result in substantial costs and be a distraction to management.

If we are found to infringe a third-party's valid and enforceable intellectual property rights, we could be required to:

- cease developing, manufacturing, selling or licensing the infringing product candidates or technology;
- obtain a license from such third-party to continue developing, manufacturing and marketing our product candidates and technologies, which may not be available on commercially reasonable terms or at all and even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors and other third parties access to the same technologies licensed to us, and it could require us to make substantial licensing and royalty payments or grant a cross license to our patents (to the extent any such patents are issued) to another patent holder;
- pay substantial damages for past infringement, including treble damages and attorneys' fees, if we are found to have willfully infringed a patent or other intellectual property right; or
- be required to redesign the formulation of a product such that it does not infringe, which may not be possible or could require substantial funds and time.

Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

We have received proprietary information and know-how from third parties. In addition, many of our employees were previously employed at other biotechnology or pharmaceutical companies. Although we try to ensure that our employees, consultants, and advisors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or these individuals have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such individual's current or former employer. We may be subject to ownership disputes in the future arising, for example, from conflicting obligations of consultants or others who are involved in developing our product candidates. We may also be subject to claims that former employees, consultants, advisors or other third parties have an ownership interest in our patents or other intellectual property. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel, which could have a material adverse effect on our business, financial condition, results of operations and prospects, and be a distraction to our management and employees.

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

To the extent that we are issued any patents covering our product candidates, competitors may infringe such patents or the patents of our licensing partners. However, we may not have the resources to reliably detect infringements of intellectual property rights, and even if we detect an infringement, we may not be able to trace the source of the infringement, or uphold our rights. We may need to resort to litigation to enforce our intellectual property rights, including any patents issued to us (if any) or our licensors. If a competitor or other third-party files a patent application claiming technology also invented by us, in order to protect our rights, we may have to participate in an expensive and time-consuming opposition proceeding before the European Patent Office, the USPTO or patent authorities or courts in other jurisdictions, with an uncertain outcome and which may have a material adverse effect on our business, financial condition, results of operations and prospects.

In addition, our success depends in part on avoiding the infringement of other parties' patents and other intellectual property rights as well as avoiding the breach of any licenses relating to our technologies and products. In the United States, patent applications filed in recent years are confidential for 18 months, while older applications are not published until the patent issues. As a result, avoiding patent infringement may be difficult and we may inadvertently infringe third-party patents or proprietary rights. Countering infringement or

unauthorized use claims or to defend against such claims and challenges can be expensive and time consuming. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our ordinary shares.

Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses and could distract our technical and management personnel from their normal responsibilities. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, commercialization 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 finance our business activities and to compete in the marketplace.

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

Periodic maintenance fees, renewal fees, annuity fees and various other government fees on patents and/or applications will be due to be paid to various patent agencies over the lifetime of our licensed patents and/or applications and any patent rights we may own in the future. Patent agencies also require compliance with several procedural fee payments and other similar provisions during the patent application process. In many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. There are situations, however, in which non-compliance 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. In such an event, we may not be able to prevent potential competitors from entering the market and this circumstance could have a material adverse effect on our business.

We may not be successful in obtaining necessary rights to any product candidates we may develop through acquisitions and licenses.

Many pharmaceutical companies, biotechnology companies, and academic institutions are competing with us and filing patent applications potentially relevant to our business. If patents issued to third parties contain valid claims that cover our product candidates or their manufacture or uses or assays relevant to our development plans, in order to avoid infringing these patents, we may be required or find it prudent to obtain licenses to these patents or to develop or obtain alternative technology. However, we may be unable to secure such licenses or otherwise acquire or license any compositions, methods of use, processes, or other intellectual property rights from third parties that we identify as necessary for product candidates we may develop. The licensing or acquisition of third-party intellectual property rights is a competitive area, and several more established companies may pursue strategies to license or acquire third-party intellectual property rights that we may consider attractive or necessary. These established companies may have a competitive advantage over us due to their size, capital resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment or at all. If we are unable to successfully obtain rights to required third-party intellectual property rights or maintain the existing intellectual property rights we have, we may have to abandon development of the relevant program or product candidate.

In addition, if a patent is issued to a third-party that covers our product candidates or their manufacture or uses or assays related to our technology or product candidates and we cannot obtain a license to such patent, then we may not be in a position to commercialize such technology or product candidates unless we develop non-infringing alternative or successfully pursue litigation to have that patent invalidated or enter into a licensing arrangement with the patent holder. Any such litigation would be time consuming and costly, and the outcome would not be guaranteed. We cannot be certain that we would be able to enter into a licensing agreement with the patent holder on commercially reasonable terms, if at all. In either case, our business prospects could be materially adversely affected.

Intellectual property rights do not necessarily address all potential risks 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 products that are similar to any product candidates we may develop or utilize similar technology but that are not covered by the claims of the patents that we license or may own in the future;
- we, or our license partners or current or future collaborators, might not have been the first to make the inventions covered by the issued patent (if any) or pending patent application that we license or may own in the future;
- we, or our license partners or current or future collaborators, might not have been the first to file patent applications covering certain of our or their inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our owned or licensed intellectual property rights;
- it is possible that patent applications that we currently, or may in the future, own or license will not lead to issued patents;
- the claims of patents or patent applications that we may own or license may, when issued, not cover our product candidates;

- issued patents (if any) to which we may hold rights may be held invalid or unenforceable, including as a result of legal challenges by our competitors;
- our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we may develop additional proprietary technologies that are not patentable;
- the patents of others may harm our business; and
- we may choose not to file a patent in order to maintain certain trade secrets or know-how, and a third-party may subsequently file a patent covering such intellectual property.

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

Risks Related to Our Business and Industry

Our relationships with health care professionals, institutional providers, principal investigators, consultants, customers and third-party payors are, and will continue to be, subject, directly and indirectly, to laws and regulations on health care fraud and abuse, false claims, commercialization expenditure tracking and disclosure, and health information privacy and security. If we are unable to comply, or have not fully complied, with such laws, we could face penalties, including, without limitation, civil, criminal, and administrative penalties, damages, fines, exclusion from government-funded health care programs and the curtailment or restructuring of our operations.

Although we do not currently have any products on the market, our business operations and activities may be directly or indirectly subject to various laws and regulations on health care fraud and abuse, false claims, commercialization expenditure tracking and disclosure, and health information privacy and security. If we obtain approval for any of our product candidates from the FDA or comparable other regulatory authorities and begin commercializing those products in geographies for which they have been approved, our potential exposure under such laws will increase significantly, and our costs associated with compliance with such laws are also likely to increase. These laws may impact, among other things, our current activities with principal investigators and research subjects, as well as proposed and future sales, marketing and education programs.

The laws that may affect our ability to operate include, but are not limited to:

- the federal Anti-Kickback Statute, which is an intent-based federal criminal statute that prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing any remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, lease, order, recommendation or arranging of, any item or service, for which payment may be made, in whole or in part, under a federal health care program such as Medicare and Medicaid;
- the federal civil False Claims Act, which imposes civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for, among other things, knowingly presenting, or causing to be presented, false or fraudulent claims for payment to a federal health care program or knowingly making using or causing to be made or used a false statement or record material to payment of a false claim or avoiding, decreasing or concealing an obligation to pay money to the federal government;
- the federal criminal statute on false statements relating to health care matters, which prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious, or fraudulent statements or representations in connection with the delivery of or payment for health care benefits, items or services;
- the federal criminal health care fraud statute, enacted as a part of the HIPAA, which imposes criminal and civil liability for executing, or attempting to execute, a scheme or artifice to defraud any health care benefit program or to obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any health care benefit program in connection with the delivery of or payment for healthcare benefits, items, or services;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 and their respective implementing regulations, which impose requirements on certain covered health care providers, health plans, and health care clearinghouses as well as their respective business associates that perform services for them that involve the use, or disclosure of individually identifiable health information, relating to the privacy, security and transmission of individually identifiable health information without appropriate authorization;
- certain U.S. state laws, as well as the General Data Protection Regulation, impose particular requirements regarding the processing of personal data especially when handling sensitive data, such as health information. Additionally, laws in all 50 U.S. states and the General Data Protection Regulation require in some circumstances businesses to notify relevant (Data Protection) Authorities and data subjects when a data breach has occurred;
- the federal Physician Payments Sunshine Act that requires “applicable manufacturers” of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the State Children’s Health Insurance Program, among others, to track and report annually to the Department of Health and Human Services (for disclosure to the public) information related to certain payments and other transfers of value to “covered recipients”, which includes U.S.-licensed physicians,

teaching hospitals and, for reports submitted on or after January 1, 2022, physician assistants, nurse practitioners, clinical nurse specialists, certified nurse anesthetists, and certified nurse midwives;

- federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers;
- the Foreign Corrupt Practices Act, or the FCPA, a U.S. law which regulates certain financial relationships with foreign government officials which could include, for example, certain medical professionals;
- analogous U.S. state law equivalents to the above federal laws, such as analogous state laws to the Anti-Kickback Statute and the False Claims Act, which may apply to items and services reimbursed by any third-party payor, including commercial insurers (i.e., so-called "all-payor anti-kickback laws");
- U.S. state laws regulating pharmaceutical manufacturer compliance programs, commercialization-related activities, drug price transparency disclosures, and other practices; and
- analogous foreign laws and regulations (for example, with respect to Dutch law, including but not limited to the anti-bribery, anti-corruption, anti-fraud and anti-forgery provisions).

The Affordable Care Act, among other things, amended the intent standard of the federal Anti-Kickback Statute and criminal health care fraud statutes to a stricter standard such that a person or entity no longer needs to have actual knowledge of this statute or specific intent to violate it. In addition, the Affordable Care Act codified case law that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal False Claims Act.

Efforts to ensure that our business arrangements will comply with applicable health care laws may involve substantial costs. It is possible that governmental and enforcement authorities will conclude that our business practices may not comply with current or future statutes, regulations, guidance or case law interpreting applicable fraud and abuse or other health care laws and regulations. If we are unable to comply, or have not fully complied, with such laws, we could face penalties, including, without limitation, civil, criminal, and administrative penalties, damages, fines, exclusion from government funded health care programs, such as Medicare and Medicaid, disgorgement, reputational harm, additional oversight and reporting obligations pursuant to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with applicable laws and regulations, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to market our products, if approved, and adversely impact our financial results. Although effective compliance programs can mitigate the risk of investigation and prosecution for violations of these laws and regulations, these risks cannot be entirely eliminated. Any action against us for an alleged or suspected violation could cause us to incur significant legal expenses and could divert our management's attention from the operation of our business, even if our defense is successful. If any of the physicians or other healthcare providers or entities with whom we expect to do business is found not to be in compliance with applicable laws, it may be costly to us in terms of money, time and resources, and they may be subject to criminal, civil or administrative sanctions, including exclusions from government-funded healthcare programs.

In addition, the regulatory approval and commercialization of any of our product candidates outside the United States will also likely subject us to foreign equivalents of the health care laws mentioned above, among other foreign laws.

Rapid technological change could make our product candidates or technologies obsolete.

Pharmaceutical technologies and products are subject to rapid and significant technological change. We expect our competitors and physicians will develop new technologies, protocols and products that may render our product candidates and drug formulation technologies uncompetitive or obsolete. The products, protocols and technologies of our competitors and physicians may be more effective than the products, product candidates and drug formulation technologies developed by us. As a result, our product candidates may become obsolete before we recover expenses incurred in connection with their development or realize revenues from any commercialized product. We are aware of other pharmaceutical companies that are developing competing technologies, which could render our product candidates obsolete, which would have a material adverse effect on our business, financial condition, results of operations and prospects.

Our business may become subject to economic, political, regulatory and other risks associated with international operations.

Our business is subject to risks associated with conducting business internationally. Many of our suppliers and collaborative and clinical trial relationships are located in different countries. Accordingly, our future results could be harmed by a variety of factors, including, but not limited to:

- economic weakness and uncertainty, including rising inflation and interest rates, or political instability in particular economies and markets;
- differing regulatory requirements for drug approvals in different jurisdictions;
- differing jurisdictions could present different issues for securing, maintaining and/or obtaining freedom to operate in such jurisdictions;
- potentially reduced protection for intellectual property rights;
- difficulties in compliance with laws and regulations;

- changes in regulations and customs, tariffs and trade barriers;
- changes in currency exchange rates of the euro and currency controls;
- changes in a specific country's or region's political or economic environment;
- trade protection measures, import or export licensing requirements or other restrictive actions by various governments;
- differing reimbursement regimes and price controls in certain markets;
- negative consequences from changes in tax laws;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- difficulties associated with staffing and managing international operations, including differing labor relations;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geopolitical actions, including war and terrorism, or natural disasters and weather-related events, including earthquakes, typhoons, floods and fires.

If we do not achieve our projected development goals in the timeframes we announce and expect, the commercialization of our products may be delayed and, as a result, our stock price may decline.

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

Risks Related to Legal Compliance Matters

Because we and our suppliers are subject to environmental, health and safety laws and regulations, we may become exposed to enforcement, liability and substantial expenses in connection with compliance or remediation activities which may adversely affect our business and financial condition.

Our operations, including our research, development, testing and manufacturing activities, are subject to numerous environmental, health and safety laws and regulations, and possible permit obligations. These laws and regulations, including any permit obligations, govern, among other things, the controlled use, storage, handling, release and disposal of, and the maintenance of a registry for, hazardous materials and biological materials (goods and substances), chemicals, biological materials and biotechnology. Our operations produce hazardous waste products. We contract with licensed third parties for the disposal of these materials, substances and waste. Apart from compliance with the applicable regulations, we may not be able to eliminate the risk of contamination or injury from these materials completely. In the event of contamination or injury resulting from any use of hazardous materials, we could be held liable for any resulting damages. We also could incur significant costs associated with civil, administrative and/or criminal fines and penalties for failure to comply with all of these laws, regulations, and associated compliance activities.

The third parties with whom we contract to manufacture our product candidates are also subject to these and other environmental, health and safety laws and regulations. Liabilities they incur pursuant to these laws and regulations or any violations thereof could result in significant costs, significant administrative, civil and/or criminal fines, measurements and/or sanctions, or in certain circumstances, an interruption in operations, any of which could adversely impact our business and financial condition, especially if we are unable to find an alternate supplier in a timely manner.

Regulatory and legislative bodies in the United States, Europe and elsewhere continue to focus on environmental policies relating to climate change, greenhouse gas emissions, carbon taxes and sustainable manufacturing, as well as human rights and equity matters, and disclosure regarding the foregoing, many of which policies may be ambiguous, inconsistent, dynamic or conflicting. We expect to experience increased restrictions, compliance costs, legal costs and expenses related to such new or changing legal or regulatory requirements, current and future environmental, health and/or safety compliance, remediation obligations and/or measurement obligations, in which case, our production and development efforts may be interrupted or delayed and our financial condition and results of operations may be materially adversely affected. Moreover, compliance with any such legal or regulatory requirements may require us to devote substantial time and attention to these matters. In addition, we could be subject to penalties or potential litigation if such laws and regulations are interpreted or applied in a manner inconsistent with our practices.

We, our employees, contractors, principal investigators, CROs, consultants, agents, vendors and collaboration partners may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could have a material adverse effect on our business.

We are exposed to the risk that we, our employees, contractors, principal investigators, CROs, consultants, agents, vendors and collaboration partners may engage in fraudulent conduct or other illegal activities. Misconduct by these parties could include intentional, reckless and negligent conduct or unauthorized activities that violate, among other things: (i) the legal requirements or other requirements of the FDA and comparable authorities, including those laws that require the reporting of true, complete and accurate information to such authorities; (ii) manufacturing standards; (iii) data privacy, security, fraud and abuse and other healthcare laws and regulations; or (iv) laws that require the reporting of true, complete and accurate financial information and data. In particular, our business activities may be subject to the FCPA and anti-bribery or anti–corruption laws, regulations or rules in other relevant countries for our activities, including the U.K. Bribery Act. The FCPA generally prohibits offering, promising, giving, or authorizing others to give anything of value, either directly or indirectly, to a non-U.S. government official in order to influence official action, or otherwise obtain or retain business. The FCPA also requires public companies to make and keep books and records that accurately and fairly reflect the transactions of the corporation and to devise and maintain an adequate system of internal accounting controls. Our business is heavily regulated and therefore involves significant interaction with public officials, including officials of non-U.S. governments. Additionally, in many other countries, the health care providers who prescribe pharmaceuticals are (directly or indirectly) employed by their government, and the purchasers of pharmaceuticals are government entities; therefore, our dealings with these prescribers and purchasers are subject to regulation under, but not limited to, the FCPA. Recently the SEC and Department of Justice have also increased their FCPA enforcement activities with respect to pharmaceutical companies.

Sales, commercialization and business arrangements in the healthcare industry are generally subject to extensive laws and regulations intended to prevent fraud, misconduct, bribery (e.g., kickbacks), self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Activities subject to these laws and regulations could also involve the improper use or misrepresentation of information obtained in the course of clinical trials or creating fraudulent data in our nonclinical studies or clinical trials, which could result in enforcement and/or sanctions and cause serious harm to our reputation.

Further, we are subject to trade and economic sanctions and embargoes on certain countries, persons, groups, entities, projects and/or activities, and export control regulations, applicable in the United States and other relevant countries for our activities.

There is no certainty that all of our employees, agents, contractors, principal investigators, CROs, consultants, vendors or (other) collaborators, or those of our affiliates, will comply with all applicable laws and regulations, particularly given the high level of complexity of these laws. It is not always possible to identify and deter misconduct by these parties and other third-parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions, claims or lawsuits stemming from a failure to comply with such laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could result, among others, in significant administrative, civil and criminal fines, disgorgement, and other sanctions, remedial measures or consequences, such as the closing down of our facilities, exclusion from participation in federal healthcare programs including Medicare and Medicaid, integrity and compliance oversight and reporting obligations, and prohibitions on the conduct of our business. Any such violations and consequences could materially damage our reputation, our brand, our international expansion efforts, our ability to attract and retain employees, and our business, prospects, operating results and financial condition.

Risks Related to Our Ordinary Shares and Our Status as a Public Company

An active trading market for our ordinary shares may not be sustainable. If an active trading market is not maintained, investors may not be able to resell their shares at or above the offering price and our ability to raise capital in the future may be impaired.

Although our ordinary shares are listed and being traded on Nasdaq, an active trading market for our shares may not be maintained. If an active market for our ordinary shares is not maintained, it may be difficult for you to sell shares you have purchased without depressing the market price for the shares or at all. An inactive trading market may also impair our ability to raise capital to continue to fund operations by selling shares and may impair our ability to acquire other companies or technologies by using our shares as consideration.

The ownership of our ordinary shares is concentrated, and your interests may conflict with the interests of our significant shareholders.

As of April 1, 2025, our significant shareholders beneficially owned ordinary shares representing approximately 56.41% of our outstanding ordinary shares. For more information regarding our significant shareholders, please see “ITEM 7. MAJOR SHAREHOLDERS AND RELATED PARTY TRANSACTIONS—A. Major Shareholders.”

These significant shareholders have in the past often taken a similar position and exercised influence over matters requiring the approval of our shareholders or our Board. They may act jointly or independently in the future and will continue to be able to exert significant influence over the outcome of matters requiring approval of our shareholders or our Board, including but not limited to the approval of significant transactions. Their interests may differ from the interests of other shareholders. Among other consequences, this concentration

of ownership may have the effect of delaying or preventing a change in control and might therefore negatively affect the market price of our ordinary shares.

We do not currently intend to pay dividends on our securities and, consequently, your ability to achieve a return on your investment will depend on appreciation in the price of our ordinary shares. In addition, any distribution of dividends must be in accordance with the rules and restrictions applying under Dutch law.

We have not declared or paid any cash dividends on our ordinary shares since our incorporation and do not currently intend to pay cash dividends on our ordinary shares in the foreseeable future. We expect to retain all earnings, if any, generated by our operations for the development and growth of our business. Therefore, you are not likely to receive any dividends on your ordinary shares for the foreseeable future and the success of an investment in our ordinary shares will depend upon any future appreciation in our value. Consequently, investors may need to sell all or part of their holdings of ordinary shares after price appreciation, which may never occur, as the only way to realize any future gains on their investment. There is no guarantee that our ordinary shares will appreciate in value or even maintain the price at which our shareholders have purchased our ordinary shares. Investors seeking cash dividends should not purchase ordinary shares.

Under Dutch law, we may only pay dividends and other distributions from our reserves to the extent our shareholders' equity (*eigen vermogen*) exceeds the sum of the paid-up and called-up share capital plus the reserves required to be maintained by Dutch law or our Articles of Association and (if it concerns a distribution of profits) after adoption of our statutory annual accounts by our general meeting from which it appears that such distribution is allowed. Subject to those restrictions, any future determination to pay dividends or other distributions from our reserves will be at the discretion of the Board and will depend upon a number of factors, including our results of operations, earnings, cash flow, financial condition, future prospects, contractual restrictions, capital investment requirements, restrictions imposed by applicable law and other factors considered relevant by the Board.

Under our Articles of Association, our Board may decide that all or part of our profits shown in our adopted statutory annual accounts will be added to our reserves. After such reservation of any such profits, any remaining profits will be at the disposal of the general meeting at the proposal of our Board for distribution on our ordinary shares, subject to the applicable restrictions of Dutch law. Our Board is permitted, subject to certain requirements and applicable restrictions of Dutch law, to declare interim dividends without the approval of the general meeting. Dividends and other distributions shall be made payable no later than a date determined by the Board. Claims to dividends and other distributions not made within five years from the date that such dividends or distributions became payable will lapse and any such amounts will be considered to have been forfeited to us (verjaring).

In addition, exchange rate fluctuations may affect the amount of euros that we are able to distribute, and the amount in U.S. dollars that our shareholders receive upon the payment of cash dividends or other distributions we declare and pay in euros, if any. These factors could harm the value of our ordinary shares, and, in turn, the U.S. dollar proceeds that holders receive from the sale of our ordinary shares.

We have broad discretion in the use of our cash on hand and may invest or spend it in ways with which you do not agree and in ways that may not yield a return on your investment.

As of December 31, 2024, we had €280.7 million in cash and cash equivalents. Our management has broad discretion in the use of such cash and could spend it in ways that do not improve our results of operations or enhance the value of our ordinary shares. You will not have the opportunity to influence our decisions on how to use our cash on hand. The failure by our management to apply these funds effectively could result in financial losses that could harm our business, cause the price of our ordinary shares to decline and delay the development of our product candidates. Pending its use, we may invest our cash on hand in a manner that does not produce income or that loses value.

A significant portion of our ordinary shares may be sold into the public market in the near future, which could cause the market price of our ordinary shares to drop significantly, even if our business is doing well.

The market price of our ordinary shares may decline as a result of sales of a large number of our ordinary shares in the market or the perception that these sales may occur. These sales, or the possibility that these sales may occur, also might make it more difficult for us to sell equity securities in the future at a time and at a price that we deem appropriate.

We had a total of 54,493,142 ordinary shares outstanding as of April 1, 2025. If our existing shareholders sell substantial amounts of ordinary shares in the public market, or the market perceives that such sales may occur, the market price of our ordinary shares and our ability to raise capital through an issue of equity securities in the future could be adversely affected.

We are not obligated to, and do not, comply with all best practice provisions of the Dutch Corporate Governance Code.

We are subject to the Dutch Corporate Governance Code, or the DCGC. The DCGC contains both principles and best practice provisions on corporate governance that regulate relations between the Board and the general meeting and matters in respect of financial reporting, auditors, disclosure, compliance and enforcement standards. The DCGC is based on a "comply or explain" principle. Accordingly, companies are required to disclose in their annual reports, filed in the Netherlands, whether they comply with the provisions of the DCGC. If they do not comply with those provisions (for example, because of a conflicting Nasdaq requirement), the company is required to give the reasons for such noncompliance. The DCGC applies to Dutch companies listed on a government-recognized stock exchange, whether in the Netherlands or elsewhere, including Nasdaq. We do not comply with all best practice provisions of the DCGC. This may affect your

rights as a shareholder, and you may not have the same level of protection as a shareholder in a Dutch company that fully complies with the DCGC.

As a foreign private issuer, we are permitted to adopt certain home country practices in relation to corporate governance matters that differ significantly from Nasdaq corporate governance listing standards. These practices may afford less protection to shareholders than they would enjoy if we complied fully with Nasdaq corporate governance listing standards.

We are a "foreign private issuer," as defined in the SEC's rules and regulations. The Nasdaq Listing Rules include certain accommodations in the corporate governance requirements that allow foreign private issuers to follow "home country" corporate governance practices in lieu of the otherwise applicable corporate governance standards of Nasdaq. The application of such exceptions requires that we disclose the Nasdaq Listing Rules that we do not follow and describe the Dutch corporate governance standards, including those as per the DCGC that we do follow in lieu of the relevant Nasdaq corporate governance standard. We intend to continue to follow Dutch corporate governance practices in lieu of the corporate governance requirements of Nasdaq in certain respects.

In accordance with Dutch law and generally accepted business practices, our Articles of Association do not provide quorum requirements generally applicable to general meetings of shareholders. To this extent, our practice varies from the requirement of Nasdaq Listing Rule 5620(c), which requires an issuer to provide in its bylaws for a generally applicable quorum, and that such quorum may not be less than one-third of the outstanding voting stock. Although we must provide shareholders with an agenda and other relevant documents for the general meeting of shareholders, Dutch law does not have a regulatory regime for the solicitation of proxies and the solicitation of proxies is not a generally accepted business practice in the Netherlands, thus our practice will vary from the requirement of Nasdaq Listing Rule 5620(b). As permitted by the listing requirements of Nasdaq, we have also opted out of the requirements of Nasdaq Listing Rule 5610, which requires an issuer to disclose within four business days any waiver of the code of conduct that has been granted to directors and officers. In addition, we have opted out of shareholder approval requirements, as included in the Nasdaq Listing Rules, for the issuance of securities in connection with certain events such as the acquisition of shares or assets of another company, the establishment of or amendments to equity-based compensation plans for employees, a change of control of us and certain private placements. To this extent, our practice varies from the requirements of Nasdaq Rule 5635, which generally requires an issuer to obtain shareholder approval for the issuance of securities in connection with such events. Accordingly, you may not have the same protections afforded to shareholders of companies that are subject to these Nasdaq requirements.

We are a foreign private issuer and, as a result, we are not subject to U.S. proxy rules and are subject to Exchange Act reporting obligations that, to some extent, are more lenient and less frequent than those of a U.S. domestic public company.

We report under the Exchange Act as a non-U.S. company with foreign private issuer status. Because we qualify as a foreign private issuer under the Exchange Act, we are exempt from certain provisions of the Exchange Act that are applicable to U.S. domestic public companies, including (i) the sections of the Exchange Act regulating the solicitation of proxies, consents or authorizations in respect of a security registered under the Exchange Act, (ii) the sections of the Exchange Act requiring insiders to file public reports of their stock ownership and trading activities and liability for insiders who profit from trades made in a short period of time and (iii) the rules under the Exchange Act requiring the filing with the SEC of annual reports on Form 10-Q containing unaudited financial and other specified information, or current reports on Form 8-K, upon the occurrence of specified significant events. In addition, foreign private issuers are not required to file their annual report on Form 20-F until four months after the end of each fiscal year, while U.S. domestic issuers that are non-accelerated filers are required to file their annual report on Form 10-K within 90 days after the end of each fiscal year. Foreign private issuers are also exempt from the Regulation Fair Disclosure, aimed at preventing issuers from making selective disclosures of material information. As a result of the above, you may not have the same protections afforded to shareholders of companies that are not foreign private issuers.

We may lose our foreign private issuer status in the future, which could result in significant additional cost and expense.

While we currently qualify as a foreign private issuer, the determination of foreign private issuer status is made annually on the last business day of an issuer's most recently completed second fiscal quarter. In the future, we would lose our foreign private issuer status if we fail to meet the requirements necessary to maintain our foreign private issuer status as of the relevant determination date. For example, if more than 50% of our securities are held by U.S. residents and more than 50% of either our directors or executive officers are residents or citizens of the United States, we could lose our foreign private issuer status.

The regulatory and compliance costs to us under U.S. securities laws as a U.S. domestic issuer may be significantly more than costs we incur as a foreign private issuer. If we are not a foreign private issuer, we will be required to file periodic reports and registration statements on U.S. domestic issuer forms with the SEC, which are more detailed and extensive in certain respects than the forms available to a foreign private issuer. We would be required under current SEC rules to prepare our financial statements in accordance with U.S. Generally Accepted Accounting Principles, or U.S. GAAP, rather than IFRS, as issued by IASB. Such conversion of our financial statements to U.S. GAAP would involve significant time and cost, and we would still be required to prepare financial statements in accordance with IFRS as adopted by the European Union as required by Dutch law. In addition, we may lose our ability to rely upon exemptions from certain corporate governance requirements on United States stock exchanges that are available to foreign private issuers such as the ones described above and exemptions from procedural requirements related to the solicitation of proxies.

The rights of shareholders in companies subject to Dutch corporate law differ in material respects from the rights of shareholders of corporations incorporated in the United States.

Our corporate affairs are governed by our Articles of Association, our internal rules and policies and by Dutch law. There can be no assurance that Dutch law will not change in the future or that it will serve to protect shareholders in a similar fashion afforded under corporate law principles in the United States, which could adversely affect the rights of our shareholders. The rights of shareholders and the responsibilities of members of our Board are in many ways different from the rights and obligations of shareholders and a board of directors in companies governed by the laws of United States jurisdictions. In particular, pursuant to Dutch law members of the Board are required to act in the interest of the Company and the sustainable success of its business, with an aim to creating long-term value, taking into account the interests of its employees, clients, shareholders and other stakeholders of the Company, in all cases with due observation of the principles of reasonableness and fairness. It is possible that some of these stakeholders will have interests that are different from, or in addition to, your interests as a shareholder.

Dutch corporate law and our Articles of Association contain or may contain provisions that may discourage, delay or prevent a takeover attempt, which could adversely affect the price of our ordinary shares.

Under Dutch law, various protective measures are possible and permissible within the boundaries set by Dutch law and Dutch case law.

In this respect, certain provisions of our Articles of Association may make it more difficult for a third party to acquire control of us or effect a change in the composition of our Board. These include:

- a provision that our directors can only be appointed on the basis of a binding nomination prepared by our Board, which can only be overruled by the general meeting by a resolution adopted by a two-thirds majority of the votes cast, representing more than half of our issued share capital (in which case the Board shall make a new nomination);
- a provision that our directors may only be dismissed by the general meeting by a two-thirds majority of the votes cast representing more than half of our issued share capital, unless the dismissal is proposed by our Board in which latter case a simple majority of the votes cast would be sufficient;
- a provision which allows the most recent (former) chairman of our Board or our most recent (former) chief executive officer to be charged with our management if all of our directors are absent or incapacitated; and
- requirements that certain matters, including an amendment of our Articles of Association, may only be resolved upon by our general meeting if proposed by our Board.

In addition, Dutch law allows for staggered multi-year terms of our directors, as a result of which only part of our directors may be subject to appointment or re-appointment in any given year.

Furthermore, in accordance with the DCGC, shareholders who have the right to put an item on the agenda for our general meeting or to request the convening of a general meeting shall not exercise such rights until after they have consulted our Board. If exercising such rights may result in a change in our strategy (for example, through the dismissal of one or more of our directors), our Board must be given the opportunity to invoke a reasonable period of up to 180 days to respond to the shareholders' intentions. If invoked, our Board must use such response period for further deliberation and constructive consultation, in any event with the shareholder(s) concerned and exploring alternatives. At the end of the response time, our Board shall report on this consultation and the exploration of alternatives to our general meeting. The response period may be invoked only once for any given general meeting and shall not apply (i) in respect of a matter for which either a response period or a statutory cooling-off period (as discussed below) has been previously invoked or (ii) in situations where a shareholder holds at least 75% of our issued share capital as a consequence of a successful public bid.

Dutch cooling-off period in face of shareholder activism or hostile take-over.

Our Board can invoke a cooling-off period of up to 250 days when shareholders, using their right to have items added to the agenda for a general meeting or their right to request a general meeting, propose an agenda item for our general meeting to dismiss, suspend or appoint one or more directors (or to amend any provision in the Articles of Association dealing with those matters) or when a public offer for our company is made or announced without our support, provided, in each case, that our board of directors believes that such proposal or offer materially conflicts with the interests of our company and its business. During a cooling-off period, our general meeting cannot dismiss, suspend or appoint directors (or amend the provisions in the Articles of Association dealing with those matters) except at the proposal of our Board.

During a cooling-off period, our Board must gather all relevant information necessary for a careful decision-making process and at least consult with shareholders representing 3% or more of our issued share capital at the time the cooling-off period was invoked, as well as with our Dutch works council (if we or, under certain circumstances, any of our subsidiaries would have one). Formal statements expressed by these stakeholders during such consultations must be published on our website to the extent these stakeholders have approved that publication. Ultimately one week following the last day of the cooling-off period, our Board must publish a report in respect of its policy and conduct of affairs during the cooling-off period on our website. This report must remain available at our office for inspection by shareholders and others with meeting rights under Dutch law and must be tabled for discussion at the next general meeting. Shareholders representing at least 3% of our issued share capital may request the Enterprise Chamber of the Amsterdam Court of Appeal, or the

Enterprise Chamber (*Ondernemingskamer*) for early termination of the cooling-off period. The Enterprise Chamber must rule in favor of the request if the shareholders can demonstrate that:

- our Board, in light of the circumstances at hand when the cooling-off period was invoked, could not reasonably have concluded that the relevant proposal or hostile offer constituted a material conflict with the interests of our company and its business;
- our Board cannot reasonably believe that a continuation of the cooling-off period would contribute to careful policy-making; or
- other defensive measures, having the same purpose, nature and scope as the cooling-off period, have been activated during the cooling-off period and have not since been terminated or suspended within a reasonable period at the relevant shareholders' request (i.e., no 'stacking' of defensive measures).

Shareholders may not be able to exercise preemptive rights and, as a result, may experience substantial dilution upon future issuances of ordinary shares or grants of rights to subscribe for shares.

In the event of an issuance of our ordinary shares or a grant of rights to subscribe for ordinary shares, subject to certain exceptions, each shareholder will have a pro rata preemptive right in proportion to the aggregate nominal value of the ordinary shares held by such holder. These preemptive rights may be restricted or excluded by a resolution of the general meeting or by another corporate body designated by the general meeting. Our Board is authorized for a period of five years after our conversion into a Dutch public company with limited liability (*naamloze vennootschap*) to issue shares or grant rights to subscribe for shares up to our authorized share capital from time to time and to limit or exclude preemptive rights in connection therewith. This could cause existing shareholders to experience substantial dilution of their interest in us.

U.S. investors may have difficulty enforcing civil liabilities against our company and directors and/or officers.

We are organized and existing under the laws of the Netherlands. As such, under Dutch private international law, the rights and obligations of our shareholders vis-à-vis the Company originating from Dutch corporate law and our articles of association, as well as the civil liability of our officers (functionarissen) (including our directors and executive officers) are governed in certain respects by the laws of the Netherlands.

We are not a resident of the United States, and our officers may also not all be residents of the United States. As a result, depending on the subject matter of the action brought against us and/or our officers, United States courts may not have jurisdiction. If a Dutch court has jurisdiction with respect to such action, that court will apply Dutch procedural law and Dutch private international law to determine the law applicable to that action. Depending on the subject matter of the relevant action, a competent Dutch court may apply another law than the laws of the United States.

Also, service of process against non-residents of the United States can in principle (absent, for example, a valid choice of domicile) not be effected in the United States.

Furthermore, most of our assets are located outside the United States. On the date of this Annual Report, (i) there is no treaty in force between the United States and the Netherlands for the reciprocal recognition and enforcement of judgments, other than arbitration awards, in civil and commercial matters and (ii) both the Hague Convention on Choice of Court Agreements (2005) and the Hague Judgments Convention (2019) have entered into force for the Netherlands, but have not entered into force for the United States. Consequently, a judgment rendered by a court in the United States will not automatically be recognized and enforced by the competent Dutch courts. However, if a person has obtained a judgment rendered by a court in the United States that is enforceable under the laws of the United States and files a claim with the competent Dutch court, the Dutch court will in principle give binding effect to that United States judgment if (i) the jurisdiction of the United States court was based on a ground of jurisdiction that is generally acceptable according to international standards, (ii) the judgment by the United States court was rendered in legal proceedings that comply with the Dutch standards of proper administration of justice including sufficient safeguards (behoorlijke rechtspleging), (iii) binding effect of such United States judgment is not contrary to Dutch public order (openbare orde) and (iv) the judgment by the United States court is not incompatible with a decision rendered between the same parties by a Dutch court, or with a previous decision rendered between the same parties by a foreign court in a dispute that concerns the same subject and is based on the same cause, provided that the previous decision qualifies for recognition in the Netherlands. Even if such a United States judgment is given binding effect, a claim based thereon may, however, still be rejected if the United States judgment is not or no longer formally enforceable. Moreover, if the United States judgment is not final (for instance when appeal is possible or pending) a competent Dutch court may postpone recognition until the United States judgment will have become final, refuse recognition under the understanding that recognition can be asked again once the United States judgment will have become final, or impose as a condition for recognition that security is posted.

A competent Dutch court may deny the recognition and enforcement of punitive damages or other awards. Moreover, a competent Dutch court may reduce the amount of damages granted by a United States court and recognize damages only to the extent that they are necessary to compensate actual losses or damages. Finally, there may be specific other instances, including pursuant to anti-boycott rules and regulations, where Dutch law prohibits the recognition and enforcement of a United States judgment. United States investors may not be able, or experience difficulty, to enforce a judgment obtained in a United States court against us or our officers.

Our articles of association designate specific courts as the exclusive forum for certain litigation that may be initiated by our shareholders, which could limit our shareholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Our Articles of Association provide for a federal forum selection provision stating that the sole and exclusive forum for any complaint asserting a cause of action arising under the Securities Act, to the fullest extent permitted by applicable law, shall be the U.S. federal district courts. In principle, our shareholders will be bound by this arrangement, provided, however, that our shareholders cannot and will not be deemed to have waived compliance with U.S. federal securities laws and the rules and regulations thereunder. Our federal forum selection provision may limit a shareholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or employees, which may discourage the filing of lawsuits against us or our directors, officers or employees, even though an action, if successful, might benefit our shareholders. In addition, while the Delaware Supreme Court ruled in March 2020 that federal forum selection provisions purporting to require claims under the Securities Act be brought in federal court are "facially valid" under Delaware law, there is uncertainty as to whether other courts, including the competent courts of the Netherlands and other courts within the United States, will enforce our federal forum selection provision. If our federal forum selection provision is found to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions and/or before other courts, which could adversely affect our results of operations and financial condition. Our federal forum provision may also impose additional litigation costs on our shareholders who assert that the provision is not enforceable or invalid. The competent courts of the Netherlands and the U.S. federal district courts may also reach different judgments or results than would other courts, including courts where a shareholder considering an action may be located or would otherwise choose to bring the action, and such judgments may be more or less favourable to us than our shareholders.

We may be a passive foreign investment company, or "PFIC," which could result in adverse U.S. federal income tax consequences to U.S. investors

Under the United States Internal Revenue Code of 1986, as amended, or the Code, we will be a PFIC for any taxable year in which, after the application of certain look-through rules with respect to subsidiaries, either (i) 75% or more of our gross income consists of "passive income," or (ii) 50% or more of the average quarterly value of our assets consists of assets that produce, or are held for the production of, "passive income." Passive income generally includes dividends, interest, certain non-active rents and royalties, and capital gains. Based on the nature of our business, our financial statements, our expectations about the nature and amount of our income, and our assets and activities, we do not believe we were a PFIC in 2024 and we do not expect to be a PFIC for our current taxable year or in the foreseeable future. In addition, we may, directly or indirectly, hold equity interests in other PFICs. Whether we or any of our subsidiaries will be a PFIC in 2025 or any future year is a factual determination that must be made annually at the close of each taxable year, and, thus, is subject to significant uncertainty; because a determination of whether a company is a PFIC must be made annually after the end of each taxable year and will depend on the composition of our income and assets and the market value of our assets from time to time, we cannot assure you that we will not be a PFIC for the current or any future taxable year. Accordingly, there can be no assurance that we will not be a PFIC in 2025 or any future taxable year.

If we are a PFIC for any taxable year during which a U.S. Holder (as defined in "Material United States and Dutch Income Tax Considerations—Material U.S. Federal Income Tax Considerations to U.S. Holders") holds our ordinary shares, we generally would continue to be treated as a PFIC with respect to that U.S. investor for all succeeding years during which the U.S. Holder holds our ordinary shares even if we ceased to meet the threshold requirements for PFIC status, unless certain exceptions apply. Such a U.S. Holder may be subject to adverse U.S. federal income tax consequences, including (i) the treatment of all or a portion of any gain on disposition as ordinary income, (ii) the application of a deferred interest charge on such gain and the receipt of certain dividends and (iii) compliance with certain reporting requirements. There is no assurance that we will provide information that will enable investors to make a qualified electing fund election, also known as a QEF Election, which could mitigate the adverse U.S. federal income tax consequences should we be classified as a PFIC.

Dutch and European insolvency laws are substantially different from U.S. insolvency laws and may offer our shareholders less protection than they would have under U.S. insolvency laws.

We are subject to Dutch insolvency laws in the event any insolvency proceedings are initiated against us, including, among other laws and regulations, Regulation (EU) 2015/848 of the European Parliament and of the Council of May 20, 2015 on insolvency proceedings. Should a court in another Member State of the European Union determine that our center of main interests, or COMI, is situated in that Member State, the courts in that Member State will in principle have jurisdiction over the insolvency proceedings initiated against us and the insolvency laws of that Member State will in principle apply to us, in accordance with and subject to such the aforementioned Regulation and the rules promulgated thereunder. Insolvency laws in the Netherlands or the relevant other Member State of the European Union, as applicable, may offer our shareholders less protection than they would have under U.S. insolvency laws and make it more difficult for our shareholders to recover the amount they could expect to recover in a liquidation under U.S. insolvency laws.

General Risk Factors

Our internal computer systems, or those used by our clinical investigators, contractors or consultants, may fail or suffer security breaches.

Despite the implementation of security measures, our internal computer systems and those of our contractors and consultants are vulnerable to damage from cyber-attacks or intrusions, including by computer hackers, foreign governments, foreign companies or competitors, or may be breached by employee error, malfeasance or other disruption. A breakdown, invasion, corruption, destruction or interruption of critical information technology systems could negatively impact operations. If our systems or those of our contractors or consultants are damaged, fail to function properly or otherwise become unavailable, we may incur substantial costs to repair or replace

them, and we may experience loss of critical data and interruptions or delays in our ability to perform critical functions, which could adversely affect our business, financial condition or results of operations. For example, the loss of clinical trial data from clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could be subject to significant fines, penalties or other liabilities and the development and commercialization of our product candidates could be delayed, which could have a material adverse effect on our business, results of operations, financial condition and prospects. Some of the federal, state and foreign government requirements also include obligations of companies to notify regulators and/or individuals of security breaches involving personally identifiable information, which could result from breaches experienced by us or by our vendors, contractors, or organizations with which we have formed strategic relationships. Even though we may have contractual protections with such vendors, contractors, or other organizations, notifications and follow-up actions related to a security breach could impact our reputation and cause us to incur significant costs. Any failure to prevent or mitigate security breaches or improper access to, use, disclosure or other misappropriation of our data or consumers' personal data could result in significant liability under state (e.g., state breach notification and privacy laws), federal (e.g., the Health Insurance Portability and Accountability Act of 1996 (HIPAA) and the Health Information Technology for Economic and Clinical Health Act (HITECH Act)) and international laws (e.g., the GDPR). For example, a breach impacting personal data which is subject to the GDPR could result in fines of up to 20 million Euros or up to 4% of the total worldwide annual turnover of the preceding financial year, whichever is higher, as well as compensation claims for financial or non-financial loss by affected individuals. To the extent that any disruption or security breach resulted in a loss of or damage to our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability, and the further development of our product candidates could be delayed. For example, the loss of or damage to clinical trial data, such as from completed or ongoing clinical trials, for any of our product candidates would likely result in delays in our marketing approval efforts and significantly increased costs in an effort to recover or reproduce the data.

We may engage in strategic transactions that could impact our liquidity, increase our expenses and present significant distractions to our management.

We may consider strategic transactions, such as acquisitions of companies, asset purchases and out-licensing or in-licensing of intellectual property, products or technologies. Any future transactions could increase our near and long-term expenditures, result in potentially dilutive issuances of our equity securities, including our ordinary shares, or the incurrence of debt, contingent liabilities, amortization expenses or acquired in process research and development expenses, any of which could affect our financial condition, liquidity and results of operations. Additional potential transactions that we may consider in the future include a variety of business arrangements, including spin-offs, strategic partnerships, joint ventures, restructurings, divestitures, business combinations and investments. These transactions may never be successful and may require significant time and attention of management. In addition, the integration of any business that we may acquire in the future may disrupt our existing business and may be a complex, risky and costly endeavor for which we may never realize the anticipated benefits. Accordingly, although there can be no assurance that we will undertake or successfully complete any transactions of the nature described above, any transactions that we do complete could have a material adverse effect on our business, results of operations, financial condition and prospects.

The trading price of our ordinary shares has been, and may in the future be, highly volatile, which could result in substantial losses for holders of our ordinary shares.

Our share price has been highly volatile. In addition, because of our relatively small public float our ordinary shares may be less liquid than the ordinary shares of companies with broader public ownership and trading of a relatively small volume of our ordinary shares may have a greater impact on the market price for our ordinary shares than would be the case if our public float were larger. The market price of our ordinary shares may fluctuate significantly in response to numerous factors, many of which are beyond our control, including, but not limited to:

- results and timing of clinical trials of our and our competitors' product candidates;
- failure of any of our product candidates, if approved, to achieve commercial success;
- competition from existing products or new products that may emerge;
- issues in manufacturing our product candidates or future approved products;
- public concern relating to the commercial value or safety of any of our product candidates;
- disputes or other developments related to proprietary rights, including patents, litigation matters, and our ability to obtain intellectual property protection for our technologies;
- failure to adequately protect our trade secrets;
- additions and departures of key personnel;
- our inability to raise additional capital or the terms on which we raise it;
- period-to-period fluctuations in our financial condition and results of operations, including the timing of receipt of any milestone or other payments under commercialization or licensing agreements;
- public health crises, illnesses, epidemics or pandemics;
- changes in market conditions for biopharmaceutical stocks;

- changes in general market and economic conditions; and
- other risk factors discussed in this section.

In addition, the stock market in general has experienced substantial price and volume fluctuations that have often been unrelated to or disproportionate to the operating performance of particular companies affected. These broad market and industry factors may materially harm the market price of our ordinary shares, regardless of our operating performance. As we operate in a single industry, we are especially vulnerable to these factors to the extent that they affect our industry or our product candidates, or to a lesser extent our markets. In the past, securities class action litigation has often been initiated against companies and their management following periods of volatility in their stock price. This type of litigation could result in substantial costs and divert our management's attention and resources and could also require us to make substantial payments to satisfy judgments or to settle litigation.

If securities or industry analysts do not publish research or publish inaccurate or unfavorable research about our business, the price of our ordinary shares and trading volume could decline.

The trading market for our ordinary shares depends in part on the research and reports that securities or industry analysts publish about us or our business. If no or few securities or industry analysts cover us, the trading price for our ordinary shares would likely be negatively impacted. If one or more of the analysts who cover us downgrades our ordinary shares or publishes incorrect or unfavorable research about our business, the price of our ordinary shares would likely decline. If one or more of these analysts ceases coverage of us or fails to publish reports on us regularly, or downgrades our ordinary shares, demand for our ordinary shares could decrease, which could cause the price of our ordinary shares or trading volume to decline.

The requirements of being a public company may strain our resources, divert management's attention and affect our ability to attract and retain qualified board members.

As a public company, we are subject to the reporting requirements of the Exchange Act, the Sarbanes-Oxley Act and any rules promulgated thereunder, as well as the rules of Nasdaq. The requirements of these rules and regulations increase our legal and financial compliance costs, make some activities more difficult, time-consuming or costly and increase demand on our systems and resources. We will also expect to incur significantly higher legal, accounting and other expenses if we cease to qualify as a foreign private issuer.

The Sarbanes-Oxley Act requires, among other things, that we maintain effective disclosure controls and procedures and internal controls for financial reporting. In order to maintain and, if required, improve our disclosure controls and procedures and internal control over financial reporting to meet this standard, significant resources and management oversight are required. We may need to hire additional accounting, finance and other personnel in connection with our continued efforts to comply with these requirements, and our management and other personnel will continue to devote a substantial amount of time towards maintaining compliance with these requirements. These rules and regulations can also make it more difficult for us to attract and retain qualified independent members of our board of directors. Additionally, these rules and regulations make it more difficult and more expensive for us to obtain director and officer liability insurance. We may be required to accept reduced coverage or incur substantially higher costs to obtain coverage. The increased costs of compliance with public company reporting requirements and our potential failure to satisfy these requirements can have a material adverse effect on our operations, business, financial condition or results of operations.

If our estimates or judgments relating to our critical accounting policies are based on assumptions that change or prove to be incorrect, our operating results could fall below the expectations of securities analysts and investors, resulting in a decline in the market price of our ordinary shares.

The preparation of financial statements in conformity with IFRS requires management to make estimates and assumptions that affect the amounts reported in our financial statements and accompanying notes. We base our estimates on historical experience and on various other assumptions that we believe to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets, liabilities, equity and expenses that are not readily apparent from other sources. It is possible that interpretation, industry practice and guidance may evolve over time. If our assumptions change or if actual circumstances differ from our assumptions, our operating results may be adversely affected and could fall below the expectations of securities analysts and investors, resulting in a decline in the market price of our ordinary shares.

Our disclosure controls and procedures may not prevent or detect all errors or acts of fraud.

We designed our disclosure controls and procedures to provide reasonable assurance that information we must disclose in reports we file or submit under the Exchange Act is accumulated and communicated to management, and recorded, processed, summarized and reported within the time periods specified in the rules and forms of the SEC. We believe that any disclosure controls and procedures, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. These inherent limitations include the realities that judgments in decision-making can be faulty, and that breakdowns can occur because of simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by an unauthorized override of the controls. Accordingly, because of the inherent limitations in our control system, misstatements due to error or fraud may occur and not be detected.

ITEM 4. INFORMATION ON THE COMPANY

A. History and development of the Company

We are a late-stage biopharmaceutical company focused on the development and commercialization of innovative therapies for rare diseases with significant unmet need, initially focused on angioedema and other bradykinin-mediated diseases. Our first molecule, deucrictibant (previously referred to as PHA121 or PHA-022121), is a novel, oral, small-molecule bradykinin B2 receptor antagonist under development for the prevention or treatment of attacks due to bradykinin-mediated angioedema, including hereditary angioedema (HAE) and acquired angioedema due to C1-inhibitor deficiency (AAE-C1INH). Deucrictibant has the potential to address unmet medical needs by improving upon the therapeutic profile of existing medicines and providing patients with quality of life and ease-of-administration that is superior to current standard-of-care. We believe deucrictibant has the potential to provide injectable-like efficacy and placebo-like tolerability with the convenience of an oral therapy for both the prophylactic and on-demand treatment of HAE attacks.

HAE is a rare and potentially life-threatening genetic condition with symptoms that include episodes of debilitating and often painful swelling in the hands, feet, face (lips and tongue), gastrointestinal tract, urogenital region, or airways. Attacks are unpredictable in frequency, location, timing, and severity, with multiple types of triggers. According to scientific publications, patients experience a median of 14 attacks per year, and half of patients experience a potentially life-threatening airway attack at least once in their lifetime. Airway attacks are particularly dangerous and can lead to asphyxiation. If left untreated, attacks can last multiple days and are commonly painful, leading to multiple sick days and even hospitalization. According to HAE International, as of October 2014, HAE affected from 1:30,000 to 1:80,000 individuals globally, or at least 7,000 patients in the U.S. and at least 15,000 patients in the EU.

AAE-C1INH is a rare disorder with an estimated prevalence of approximately 1:500,000 patients. The disease manifests with episodes of unpredictable swelling that occur as a result of inadequate control of the kallikrein/kinin system, resulting in excessive bradykinin formation. These episodes of swelling can be debilitating, painful, and even lethal, similar to HAE. However, AAE-C1INH results from underlying conditions such as lymphoproliferative disorders, plasma cell dyscrasias, or autoimmune disorders, and occurs either as a result of consumption of C1-inhibitor owing to activation of the classical complement pathway or as a result of neutralization by autoantibodies. There are no approved medicines available to treat or prevent AAE-C1INH.

Bradykinin-mediated vascular leakage and angioedema formation via activation of its bradykinin B2 receptor is involved in various types of angioedema (hereditary or acquired) with different underlying pathogenetic mechanisms. Bradykinin B2 receptor inhibition is a clinically validated mechanism for the treatment of HAE, as demonstrated by icatibant, which is a peptide bradykinin B2 receptor antagonist approved in Europe in 2008 and in the United States in 2011 (as FIRAZYR).

Deucrictibant is designed to block the interaction of bradykinin with the B2 receptors, rather than blocking an upstream signal in one of the bradykinin production cascades as other treatments; therefore, deucrictibant may prevent bradykinin aberrant signaling regardless the underlying pathway that produces bradykinin and may address a broader range of angioedema attacks than other available treatments.

Our legal and commercial name is Pharvaris N.V. In connection with our initial public offering in the first quarter of 2021, we converted the legal form of our company under Dutch law from a private company with limited liability (besloten vennootschap met beperkte aansprakelijkheid) to a public company with limited liability (naamloze vennootschap) and changed our name from Pharvaris B.V. to Pharvaris N.V. Pharvaris B.V. was incorporated on September 30, 2015, and is based in Leiden, the Netherlands. Our principal executive offices are located in Emmy Noetherweg 2, 2333 BK Leiden, the Netherlands, telephone: +31 (0)71 2036 410. Our agent for service of process in the United States is Chris Deon, who is registered at PO Box 121, Buckingham, PA 19407-4550, USA.

Our principal expenditures since inception have been our research and development expenses, as more fully described elsewhere in this Annual Report. To date, we have relied solely on the issuance of equity securities to finance our operations and internal growth. For more information, please see “ITEM 5. OPERATING AND FINANCIAL REVIEW AND PROSPECTS—B. Liquidity and Capital Resources.”

The SEC maintains an Internet website that contains reports and other information about issuers, like us, that file electronically with the SEC. The address of that website is www.sec.gov. Our website can be found at www.pharvaris.com. The information on our website is not incorporated by reference into this Annual Report, and you should not consider information contained on our website to be a part of this Annual Report.

B. Business Overview

Overview

Deucrictibant is a novel, highly potent inhibitor and selective oral small molecule bradykinin B2 receptor antagonist. Deucrictibant has been observed to be a potent inhibitor in vitro as assessed using human recombinant bradykinin B2 receptors (150 pM); ex vivo as studied against endogenous bradykinin B2 receptors in a human umbilical vein model (350 pM); and in vivo in the human bradykinin-challenge model (170 pM). Potency as used in this Annual Report refers to the amount of drug required to produce a pharmacological effect of given intensity and is not a measure of therapeutic efficacy. Deucrictibant demonstrated over 4000-fold selectivity for the bradykinin B2 receptor when compared to approximately 170 other molecular targets, including the bradykinin-B1-receptor. We designed deucrictibant as a new chemotype with properties compatible with oral delivery.

Deucrictibant may address unmet medical needs of people living with HAE by both preventing attacks from occurring, using an extended-release (XR) tablet formulation of deucrictibant (previously referred to as PHVS719), as well as treat the manifestations of HAE attacks, using an immediate-release (IR) capsule formulation of deucrictibant (previously referred to as PHVS416). The XR tablet formulation is designed to maintain therapeutic levels for at least 24 hours and to achieve a steady-state plasma concentration within 72 hours, supporting a once-daily dosing regimen. The IR capsule formulation is designed to rapidly reach therapeutic exposure in order to mitigate HAE attacks symptoms quickly and completely with a single oral dose.

In our Phase 1 clinical trials to-date, we have observed rapid exposure and predictable linear pharmacokinetics (PK) with and without food. In addition, we observed deucrictibant to be a potent antagonist of the bradykinin B2 receptor, in vitro and in vivo with healthy volunteers. We conducted a proof-of-concept clinical trial testing the effects of bradykinin in healthy volunteers in our bradykinin-challenge trial, where we evaluated the effect of deucrictibant on cardiovascular parameters affected by bradykinin such as blood pressure, heart rate and cardiac output in healthy volunteers. We evaluated the pharmacodynamic (PD) and PK of deucrictibant in a bradykinin-challenge model in healthy subjects and generated a PK/PD correlation model for deucrictibant. The bradykinin challenge was validated as a surrogate assessment for dose selection in the original development program for icatibant, as reviewed by the FDA and the EMA. The clinical dose of icatibant established with the bradykinin challenge has demonstrated successful treatment of HAE attacks in multiple randomized clinical trials and over 10 years of clinical experience. From the bradykinin challenge model, we were able to predict the duration of effect of a single oral dose of deucrictibant; the topline data from our deucrictibant Phase 2 RAPIDe-1 trial treating HAE attacks were consistent with the predictions of the bradykinin challenge in both onset of symptom relief and duration of effect (use of rescue medication).

In our Phase 2 placebo-controlled trial evaluating the efficacy and tolerability of deucrictibant IR capsules for the on-demand treatment of attacks in patients with HAE type 1 and 2 (RAPIDe-1), a statistically significant and clinical meaningful reduction of the patient-reported symptoms of HAE was observed for the attacks treated with all doses of deucrictibant (10, 20, 30 mg) compared to placebo-treated attacks. The study's primary endpoint—symptom relief at four hours after treatment with study drug—as well as all key secondary efficacy endpoints were met. Consistently with its pharmacokinetic profile, deucrictibant IR demonstrated rapid onset of action, symptom relief, and resolution of the manifestations of HAE attacks as well as sustained clinical effects, with consistent findings across outcome measures. In addition, deucrictibant IR substantially reduced the use of rescue medication compared to the placebo. Deucrictibant was generally well tolerated at all dose levels with three treatment-related adverse events (TRAEs) reported for one 30-mg-treated attack (2.8%) and one TRAE reported for one placebo-treated attack (1.9%); there were no treatment-related serious adverse events (SAEs), no treatment-related adverse events (AEs) of severe severity, and no AEs leading to treatment discontinuation. We commenced RAPIDe-1 in February 2021 and reported positive topline Phase 2 data in December 2022. We believe these positive Phase 2 data support further development of deucrictibant as a potential oral on-demand therapy for HAE attacks.

In our Phase 2 placebo-controlled trial evaluating the efficacy and the safety and tolerability of deucrictibant for long-term prophylaxis against angioedema attacks in HAE type 1 and 2 (CHAPTER-1), a statistically significant and clinical meaningful reduction in mean monthly attack rate was observed compared to placebo-treated attacks. The study's primary endpoint was met as 40 mg per day orally administered deucrictibant significantly reduced the mean monthly HAE attack rate by 84.5% compared to placebo. In the analysis of the secondary endpoints, deucrictibant demonstrated clinically meaningful improvement in the severity of attacks and a decrease in the number of attacks treated with on-demand medication. Participants on deucrictibant treatment experienced a meaningful improvement in their quality of life. Throughout 12 weeks of treatment in CHAPTER-1, both doses of deucrictibant were well-tolerated. There were no serious adverse events, no severe treatment-emergent adverse events, and no adverse events leading to treatment discontinuation. We commenced CHAPTER-1 in 2021 using twice-daily dosing of deucrictibant IR capsules as a proof-of-concept for once-daily deucrictibant XR tablets, and announced positive topline data in December 2023. We believe these positive Phase 2 data support further development of deucrictibant as a potential oral prophylactic therapy for HAE attacks.

In August 2022, the FDA placed a hold on the clinical trials of deucrictibant in the U.S. based on its review of nonclinical data. The FDA requested that Pharvaris conduct an additional long-term rodent toxicology study and update the Investigator's Brochure. Pharvaris participated in a Type A meeting with the FDA to discuss paths to address the on-demand and prophylactic holds and aligned on a protocol for a 26-week rodent toxicology study. Following review of data from a preplanned interim analysis of the ongoing 26-week nonclinical rodent study, the FDA lifted the clinical hold on the IND application for deucrictibant for the on-demand treatment of HAE in June 2023. In January 2024, the FDA lifted the clinical hold on the IND application for deucrictibant for the prophylactic treatment of HAE attacks following review of the full data set from the completed 26-week rodent toxicology study.

Additional trials are required by the FDA, EMA or other regulators even with positive data from RAPIDe-1 and CHAPTER-1.

In March 2024, we initiated a global, pivotal, randomized, double-blind-placebo-controlled Phase 3 study of orally administered deucrictibant IR capsule (20 mg) for the on-demand treatment of HAE attacks in adults and adolescents (12 years and older). We intend to enroll approximately 120 participants. The primary efficacy endpoint is time to onset of symptom relief, as measured by Patient Global Impression of Change (PGI-C) rating of at least "a little better" for two consecutive timepoints within 12 hours post-treatment. Other efficacy endpoints include time to End of Progression (EoP) in attack symptoms, substantial symptom relief, complete attack resolution and proportion of attacks achieving symptom resolution with one dose of deucrictibant as measured by Patient Global Impression of Severity (PGI-S) and by Angioedema Symptom Rating Scale (AMRA).

In December 2024, we initiated a global, pivotal, randomized, double-blind, placebo-controlled Phase 3 study of orally administered deucrictibant extended-release tablet for the prophylaxis against angioedema attacks in adults and adolescents (12 years and older) with HAE. The study aims to enroll approximately 81 participants with HAE and randomize them in a 2:1 ratio to receive deucrictibant XR tablet (40 mg/day), which is currently the intended commercial dosage, or placebo, once daily for 24 weeks. The primary endpoint of the study is

to evaluate the efficacy of deucrictibant compared to placebo for prophylaxis against angioedema attacks as measured by the time-normalized number of investigator-confirmed HAE attacks during the 24-week treatment period. Other objectives of the study include evaluating additional clinically relevant outcomes, deucrictibant's safety and tolerability, pharmacokinetics and its impact on health-related quality of life measures in the prophylactic setting.

In addition, we are also running open-label extension studies in both on-demand and prophylactic settings to collect long-term safety and efficacy data in HAE patients.

Global sales of treatments for HAE in 2022 are estimated at approximately $2.7 billion based on publicly available information and, according to public research reports, are forecast to grow at an approximately 9% compound annual growth rate to $4.3 billion through 2027. Current approved products treat acute HAE attacks in an on-demand setting or seek to prevent or reduce future HAE attacks in a prophylactic setting. Each of these products generally works in one of the following ways: inhibiting the bradykinin B2 receptor, replacing the deficiency in C1-INH activity, or inhibiting plasma kallikrein. Currently most standard-of-care therapies are administered by injection, which patients can find challenging despite their efficacy because these therapies often result in painful injection-site reactions (leading some patients to delay treatment and risk attacks), are time consuming to receive (as some need to be administered in a clinic), and are difficult to carry and/or store. The only orally available products have shown limitations in terms of efficacy compared to injectables and/or come with burdensome side effects for patients. We believe HAE patients need alternatives that better meet their objectives for ease of disease treatment, disease control, and improved quality of life. We anticipate that there will be strong interest in safe and effective, orally delivered, small-molecule treatments that can match or improve upon the efficacy profile of existing therapies.

Differentiation of deucrictibant

We believe that deucrictibant, as the molecule underlying both the IR capsule formulation and the XR tablet formulation, has the potential to be highly differentiated for both the on-demand and prophylactic settings with the key benefits below:

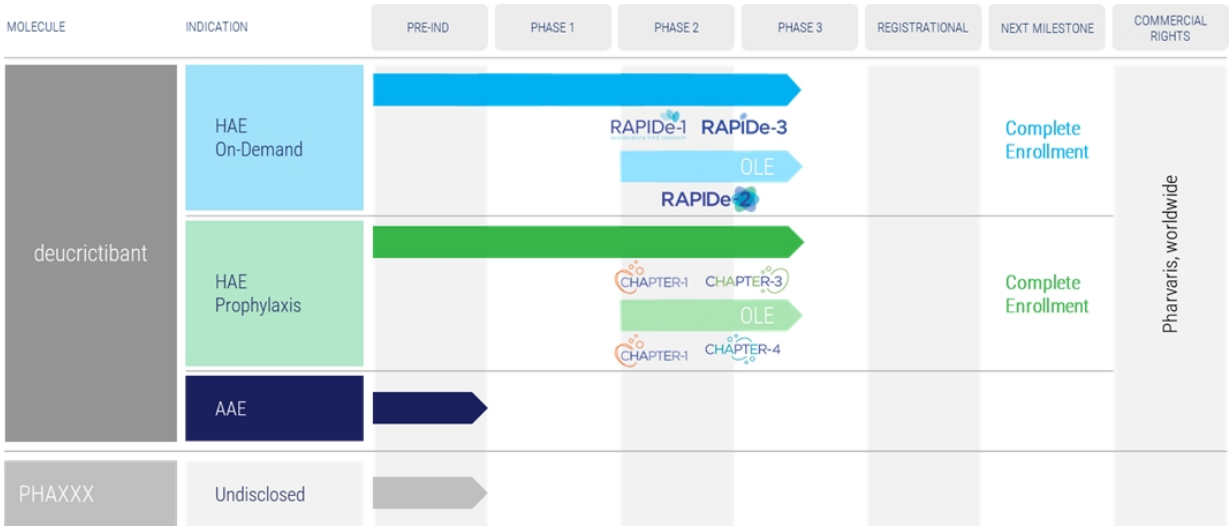
Deucrictibant IR capsule. We believe that deucrictibant IR capsules, an on-demand, rapid exposure softgel capsule, has the potential to be highly differentiated for patients suffering from acute HAE attacks with the following benefits:

Complete Symptom Resolution	• Clinically validated mechanism of bradykinin B2 receptor antagonism • Utilizing same *in vivo* surrogate assessment for dose selection as the development program for icatibant (validity confirmed in the RAPIDe-1 Phase 2 trial) • More potent inhibitor than icatibant • Longer half-life than icatibant
Rapid Onset of Activity	• Exposure exceeds the anticipated threshold therapeutic plasma level (EC_{85}) in 30 minutes, with or without food
Potential Reduced Treatment Burden / Enhanced Patient Convenience	• No injection needed • Convenient oral formulation removes barriers inherent in current injectable treatments to facilitate early treatment of acute HAE attacks and overall treatment of more attacks than currently reported • Capsule reduces treatment burden • Potential lowest dosage of any oral HAE on-demand treatment

Deucrictibant XR tablet. We believe that deucrictibant XR tablets, a prophylactic extended-release tablet designed to be as a daily oral therapy, has the potential to be highly differentiated for HAE patients with the following benefits:

Protection From Attacks	• Validated, proven mechanism to address all bradykinin, regardless of pathway
Ideal Release Profile for Prophylactic Use	• Exposure exceeds the anticipated threshold therapeutic plasma level (EC_{85}) from day one of treatment and reaches and maintains steady-state concentration within 72 hours. providing rapid attack protection • Appropriate pharmacokinetic profile with or without food
Potential Reduced Treatment Burden / Enhanced Patient Convenience	• Convenient oral daily dosing with extended-release tablet • Potential for once-a-day dosing • Potential lowest dosage of any oral HAE treatment; ease of administration • Well tolerated throughout therapeutic ranges as demonstrated by multiple clinical trials to-date • No injection needed

In addition to the differentiation of our individual products, having on-demand and prophylactic products with the same active ingredient enables patients to maintain a trusted active medicine when they change their dosing regimen and delivery mechanism moving from on-demand to prophylactic treatment (or back). This may be particularly valued by children or adolescents who typically begin therapy with on-demand only and gradually move to prophylaxis as attack frequency increases (commonly after puberty). To our knowledge, we are the only company that will offer this option to patients.



Expansion of the Portfolio

Our goal is to expand our portfolio with additional programs addressing other bradykinin-mediated diseases, building on our strategic strength and expertise in the bradykinin B2 receptor pathway. Our approach is to identify additional disease areas and indications with strong scientific rationale, high unmet medical need, a defined target population and significant differentiation potential. We are actively pursuing new synthesis, medicinal chemistry, and lead optimization to identify additional and/or follow-on product candidates. In collaboration and discussion with key opinion leaders, we are considering exploratory proof-of-concept studies to validate the potential of bradykinin B2 receptor antagonism in new indications that could include cardiovascular, allergy and immunology and others.

Our Strengths

Our company is built upon the following strengths:

- Broad strength and expertise in the bradykinin B2 receptor pathway. Members of the management team include an inventor of icatibant, the leadership team that developed FIRAZYR through European approval, and a key member from the TAKHZYRO development team;
- Deucrictibant is an orally available product candidate with a clinically validated mechanism of action that addresses serious unmet medical need in HAE;
- Deucrictibant has demonstrated physicochemical properties suitable to formulations as both an on-demand product candidate, via IR capsule formulation, and a distinct prophylactic product candidate, via XR tablet formulation;
- Deucrictibant, compared to icatibant, the currently approved bradykinin B2 receptor inhibitor, demonstrated higher preclinical potency in blocking bradykinin signaling at the bradykinin B2 receptor, and good oral bioavailability and a longer half-life in humans, which has resulted in longer duration of the bradykinin-blocking PD effect in humans;
- We wholly own intellectual property – including granted and pending patent applications – covering deucrictibant and additional molecules, formulations and use; Our scientific experience allows us to leverage deep insight and experience in the bradykinin B2 receptor pathway to expand our portfolio into other bradykinin-mediated angioedema and bradykinin-mediated diseases beyond angioedema; and
- Our deep market expertise across the different functional areas of the company through the hiring of research, clinical development, medical & commercial staff with a long history in HAE.

Our Strategy

Our strategy is to develop and commercialize therapies that are superior to currently available treatment options and improve patient quality of life and convenience. Our initial approach for HAE and potential expansions into other BK-mediated angioedema and diseases is based upon extensive patient, physician, and payer research to identify the key needs in the market. According to our analysis, oral therapy remains the highest unmet need for both on-demand and prophylactic use in HAE. Importantly, our research shows that patients are not willing to accept significantly reduced efficacy or safety with a switch to oral therapy. A therapy for HAE, whether for on-demand or prophylaxis, needs to offer strong efficacy, high tolerability & safety, and convenient administration. Our intention with the IR capsule formulation and the XR tablet formulation is to develop products for the on-demand and prophylactic setting that can meet all of these needs. We are not aware of any other therapies on the market or in development that are able to provide such a comprehensive value proposition across the spectrum for HAE.

The key elements of our strategy include:

- *Continue to advance deucrictibant through clinical development for on-demand treatment of HAE utilizing a rapid-onset formulation, known as deucrictibant immediate-release (IR) capsules.* We intend to develop and commercialize deucrictibant IR capsules as a fast-acting, orally available, potent inhibitor and selective on-demand treatment for HAE attacks. We are currently enrolling approximately 120 participants in RAPIDe-3, a global, pivotal Phase 3 clinical study of deucrictibant IR capsules for the on-demand treatment of HAE attacks in adults and adolescents.
- *Advance the development of deucrictibant for prophylactic treatment of HAE utilizing an extended-release formulation, known as deucrictibant extended-release (XR) tablets*. We intend to advance deucrictibant XR tablets through clinical development as an extended-release prophylactic treatment of HAE. We plan to leverage our clinical data and experience from the development of deucrictibant in the on-demand setting to expedite our efforts in the prophylactic setting. We are currently enrolling approximately 81 participants in CHAPTER-3, a global, pivotal Phase 3 clinical study of deucrictibant XR tablets for the prophylactic treatment of HAE attacks in adults and adolescents.
- *Expand the range of bradykinin-mediated angioedema indications to which deucrictibant can be applied.* In addition to Type 1 or Type 2 HAE, bradykinin is also an important mediator for other types of non-histaminergic angioedema, such as: hereditary angioedema with normal C1-INH and acquired angioedema (AAE) due to C1-INH deficiency (AAE-C1INH). Our first molecule, deucrictibant (previously referred to as PHA121 or PHA-022121), is a novel, oral, small-molecule bradykinin B2 receptor antagonist under development for the prevention or treatment of attacks due to bradykinin-mediated angioedema, including hereditary angioedema (HAE) and acquired angioedema due to C1-inhibitor deficiency (AAE-C1INH). Deucrictibant is designed to block the interaction of bradykinin with the B2 receptors, rather than blocking an upstream signal in one of the bradykinin production cascades as other treatments; therefore, deucrictibant may prevent bradykinin aberrant signaling regardless the underlying pathway that produces bradykinin and may address a broader range of angioedema attacks than other available treatments. Currently there are still no treatments approved for these angioedema patients who are unresponsive to conventional antihistamine/glucocorticoid treatment and have a high unmet medical need for effective therapies. Several clinical reports indicate that off-label use of icatibant has successfully treated acute attacks of these non-histaminergic angioedema patients, which provides a strong rationale to expand the development deucrictibant to address such a high unmet medical need.
- *Expand upon our expertise in the bradykinin B2 receptor pathway*. We intend to leverage the strategic strengths, insight, and deep experience of our team in the bradykinin B2 receptor pathway to identify additional disease areas and indications with strong scientific rationale, high unmet medical need, a defined target population and significant differentiation potential. As such,

we will seek to develop follow-on product candidates that serve additional bradykinin-mediated diseases beyond angioedema, such as cardiovascular, allergy and immunology, neurological disease or others.

- *Commercialize our product candidates.* We intend to retain economic and commercial ownership of our current product candidates. If approved, we expect to independently commercialize both deucrictibant XR and deucrictibant IR in the United States, Europe and certain other countries. As we advance towards regulatory approval for our product candidates, we may establish a focused commercialization and sales infrastructure suitable for HAE.

Hereditary Angioedema

Disease Overview

HAE is a rare and potentially life-threatening genetic condition. HAE is an autosomal dominant disease, meaning that a defect in only one copy of the gene leads to symptoms and that it occurs at similar rates in both males and females. It is mainly caused by one or more mutations (inherited or spontaneous) in the SERPING1 gene, which codes for the C1-inhibitor protein (C1-INH). Deficiency or malfunction of C1-INH leads to uncontrolled synthesis and activity of plasma kallikrein and unconstrained bradykinin production. Excessive bradykinin production is recognized to be the key mediator of symptoms in patients with HAE and manifests as edema attacks, most commonly in the limbs, face (lips and tongue), intestinal tract, urogenital region, and airways. HAE patients with a deficiency in C1-INH activity are classified as Type 1 or Type 2. Type 1 is the most common form and results in low levels of circulating C1-INH, and Type 2 results in production of a low function protein. An additional form of HAE, called normal C1-INH HAE, can occur in patients with normal levels of C1-INH for a variety of reasons including mutations in genes for Factor XIIa, plasminogen, angiopoietin-1 or kininogen-1. Moreover, bradykinin-induced attacks of angioedema can occur idiopathically in individuals for which a hereditary cause has not yet been identified. Excessive amounts of bradykinin can also be caused by increased circulation of estrogens, reduced C1-INH levels due to underlying diseases, reduced elimination of bradykinin, or through use of medications such as angiotensin-converting enzyme (ACE) inhibitors and tissue plasminogen activator (tPA).

Excessive bradykinin generation and increased risks for edema attacks in HAE may occur during conditions associated with inflammation, infections, ischemia, and allergic reactions. Attacks often lead to discomfort, pain and nausea but can become life-threatening in the case of airway obstruction, with a 30% risk of asphyxiation if the attack remains untreated. The number and severity of attacks vary highly between patients, and the most severely affected patients can experience attacks every few days. Attacks can occur spontaneously although they often are associated with anxiety, stress, minor trauma, surgery, or illnesses. Commonly, patients are alerted to an impending attack by prodromal symptoms which include rash, fatigue, and muscle aches. The severity of attacks is unpredictable and not related to their underlying frequency. Airway swelling is particularly dangerous and can lead to death by asphyxiation. Although rare, at least half of HAE patients have experienced a life-threatening airway swelling attack and airway attacks remain a major cause of mortality in HAE patients. Swelling typically develops over 24 hours and resolves within five days without treatment. Symptoms typically first present in young children and may take 5-10 years (until early adolescence or young adulthood) to be diagnosed. HAE affects 1:50,000 to 1:10,000 individuals globally, or at least 6,600 patients in the U.S. and at least 8,900 patients in the EU.

As a result of the lifelong nature of HAE and the challenges related to the use of many of the injected therapies, patient surveys consistently indicate a desire for an oral therapy. We believe that a safe and effective oral agent has the potential to transform treatment for this disease and become the first-line therapy for both on-demand and prophylaxis. We also believe that opportunities exist for both acute and prophylactic treatments, and we intend to develop drug candidates for both on-demand and prophylactic use with the goal of providing patients with a set of oral options to prevent and treat their disease.

Current Treatments and Their Limitations

There are currently two treatment approaches to the management of HAE: acute (on-demand) treatment of attacks and prevention of attacks with short-or long-term prophylactic therapy.

- *On-Demand Treatment*: The currently approved products for treatment of acute HAE attacks are all injectable products and include C1-INH replacement products such as human plasma-derived C1-INH concentrates (BERINERT, CINRYZE, and CETOR) or recombinant human C1-INH (RUCONEST); the bradykinin B2 receptor antagonist icatibant (FIRAZYR, and available as a generic product); and, the plasma kallikrein inhibitor ecallantide (KALBITOR), which has been known to cause allergic reactions including anaphylaxis and must be administered by a doctor or nurse in a healthcare setting. Human plasma-derived C1-INH concentrate products are isolated from donated human plasma and historically have been impacted by supply shortages. Subcutaneous, or s.c., icatibant is the only available bradykinin B2 receptor antagonist indicated for treatment of acute HAE attacks Type 1 or Type 2 with C1-INH deficiency. In acute HAE attacks, icatibant has been shown to provide a significantly faster onset of relief than placebo (2.0 h versus 19.8 h). Icatibant is recommended as a first-line treatment option for the treatment of acute HAE attacks in patients with HAE.
- *Prophylactic Treatment*: Currently approved prophylactic therapies for HAE include C1-INH replacement products, such as intravenously delivered CINRYZE and subcutaneously delivered HAEGARDA/ BERINERT 2000/3000 (both of which require twice-weekly injections); the monoclonal antibody plasma kallikrein inhibitor lanadelumab-flyo (TAKHZYRO); and the small-molecule plasma kallikrein inhibitor berotralstat (ORLADEYO). Current treatment guidelines recommend against the use of the traditional oral medications for HAE, such as antifibrinolytics (tranexamic acid or epsilon aminocaproic acid) for HAE due to their limited efficacy. Attenuated androgens (e.g., danazol, stanozolol, and oxandrolone) are recommended only as second-line treatments for the prevention of HAE attacks, since there are numerous contraindications, therapeutic class adverse events or

AEs, and overall suboptimal control of HAE in many patients. The use of attenuated androgens is limited by numerous safety issues, including seborrhea, altered libido, depression, fatigue, menstrual abnormalities, and masculinization.

To our knowledge, there is one other angioedema-specific oral medication for on-demand use in clinical development. This kallikrein inhibitor, sebetralstat, is under development by Kalvista and has recently completed Phase 3.

We believe that the properties and mechanism of deucrictibant enable us to develop oral product candidates that will be generally more convenient for patients to take, without sacrificing efficacy for treatment or prevention of angioedema attacks.

Related indications to BK

In addition to Type 1 or Type 2 HAE, bradykinin is also an important mediator for other types of non-histaminergic angioedema, such as: hereditary angioedema with normal C1-INH and acquired angioedema (AAE) due to C1-INH deficiency (AAE-C1INH). Unlike HAE Types 1 and 2, for other BK-mediated angioedema, an unclear pathophysiology and lack of consistent diagnostic criteria have limited the opportunity for clinical investigation and new treatment development. Consequently, there are still no treatments approved for HAE patients with normal C1-INH or AAE-C1INH, who are unresponsive to conventional antihistamine/glucocorticoid treatment and have a high unmet medical need for effective modern therapies. Recently clinical and translational research has made significant progress in non-histaminergic angioedema, similar to Type 1 or 2 HAE. Bradykinin has been shown to be elevated in plasma from non-histaminergic angioedema patients with normal C1-INH (Li et al., Allergy, Asthma & Clinical Immunology 2023) and idiopathic non-mast cell mediated AE (Suffritti J Investig Allergol Clin Immunol 2024). Several clinical reports indicate that icatibant has successfully treated acute attacks in either hereditary angioedema patients with normal C1-INH (Bork et al., Orphanet J Rare Dis. 2020; Bork et al. J Allergy Clin Immunol Pract 2023; Jones et al. World Allergy Organization Journal, 2022; Riedl et al., J Allergy Clin Immunol Pract. 2023), and that deucrictibant successfully treated AAE-C1INH patients (Petersen et al., J Allergy Clin Immunol, 2024). In addition, a recent survey revealed that icatibant was one of the most efficacious on-demand treatments for patients with idiopathic non-mast cell angioedema (Christiansen & Zuraw, Allergy and Asthma Proceedings 2025). All these provide strong rationales to expand the development of deucrictibant to these types of bradykinin-mediated angioedema and address the high unmet medical need.

To our knowledge, one kallikrein inhibitor (lanadelumab-flyo, injected subcutaneously) is in development for hereditary angioedema with normal C1-INH and this inhibitor has recently completed a Phase 3 clinical trial for prophylaxis.

Deucrictibant

Overview

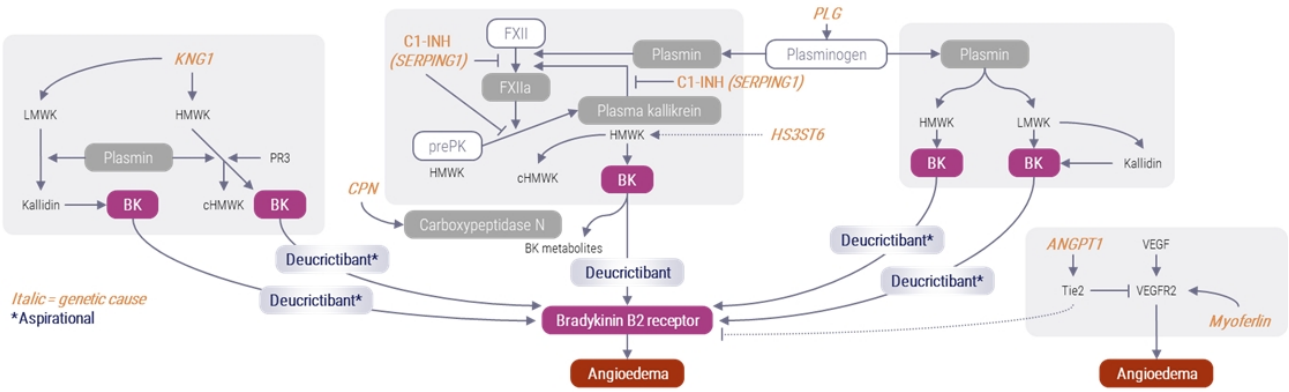
Since the 1990s, many companies have tried but failed to discover oral bradykinin B2 receptor antagonists, as the bradykinin B2 receptor has proved to be a difficult target for the development of orally available antagonists. Historically, compounds targeting the bradykinin B2 receptor with adequate potency have had physicochemical properties inconsistent with oral bioavailability. The bradykinin B2 receptor is a G-protein coupled receptor (GPCR) that binds to the peptide bradykinin in an elongated fashion. It has been challenging to identify a small molecule that can bind in this pocket potently enough to compete with bradykinin while still being small enough with appropriate properties to demonstrate oral bioavailability. Starting with modeled structures of the bradykinin-binding pocket of the bradykinin B2 receptor, we designed and synthesized a novel lead series (a set of molecules with the potential to be further optimized). Through our lead optimization program, we synthesized over 600 compounds to select a small molecule that is designed to fit in the bradykinin-binding pocket at the bradykinin B2 receptor, preventing or halting its signaling activity, while also possessing desirable physicochemical properties and other profiling characteristics.

Bradykinin is the principal mediator of the signs and symptoms that represent acute HAE and other bradykinin-mediated angioedema attacks, acting as a potent and selective agonist of the bradykinin B2 receptor.

In HAE and other bradykinin-mediated angioedema, contact activation triggers increased activity of plasma kallikrein, resulting in excessive breakdown of high-molecular-weight kininogen (HMWK) and increased production of cleaved HMWK (cHMWK) and bradykinin. Excessive bradykinin generation, as in HAE, promotes vascular permeability by activating the bradykinin B2 receptor in vascular endothelium cells, leading to plasma extravasation and subcutaneous or submucosal tissue swelling typical of an angioedema attack.

As the figure below illustrates, treatment with deucrictibant, an orally bioavailable low-molecular weight, potent, competitive and selective antagonist of the human bradykinin B2 receptor, is intended to block and prevent activation of the bradykinin B2 receptor by elevated bradykinin levels and prevent or halt the angioedema process, with reduced or resolved swelling as a consequence. Deucrictibant therefore has the therapeutic potential for both on-demand treatment and long-term prevention of attacks in patients with bradykinin-mediated angioedema.

Deucrictibant combines the preclinical selectivity of bradykinin B2 receptor antagonism with oral bioavailability and acceptable exposure upon a single dose. Deucrictibant is being developed to become the first effective orally administered antagonist of BK activity with therapeutic potential for both acute on-demand treatment and long-term prevention of attacks in patients with HAE and other radykinin-mediated angioedema.

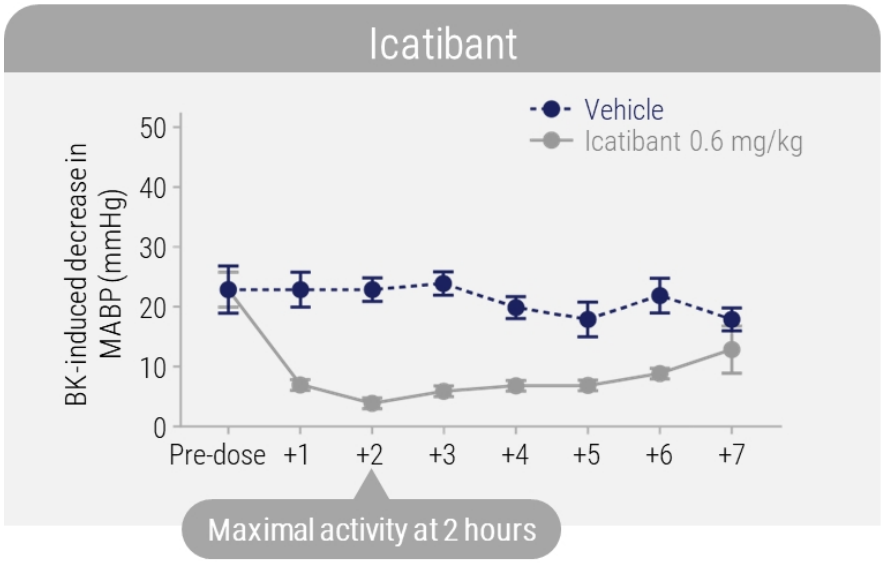


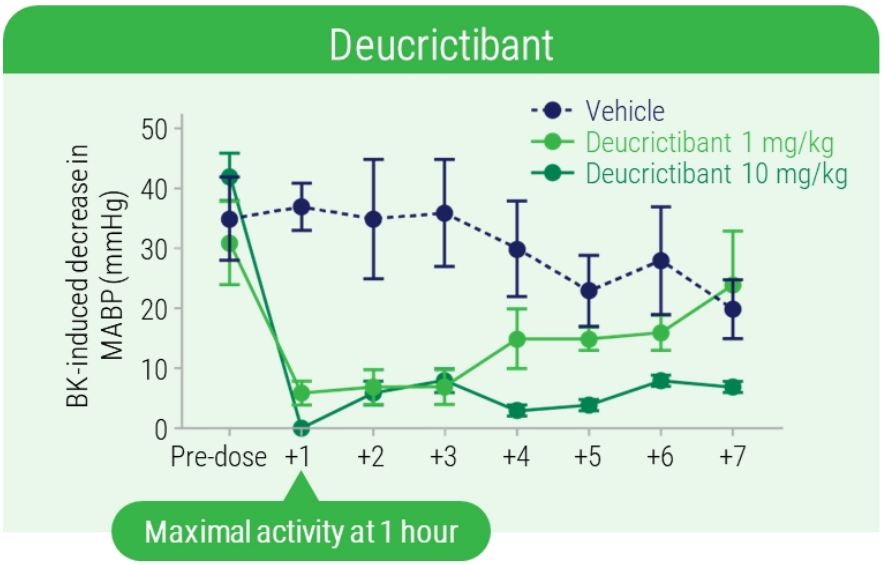
Deucrictibant combines the selectivity of bradykinin B2 receptor antagonism with oral bioavailability and acceptable exposure upon a single dose. Deucrictibant is being developed to become the first effective orally administered antagonist of BK activity with therapeutic potential for both on-demand treatment and long-term prevention of attacks in patients with HAE and other bradykinin-mediated angioedema.

Deucrictibant is an orally bioavailable competitive antagonist of the bradykinin B2 receptor with high affinity and high antagonist potency. Deucrictibant has been observed to be a potent inhibitor *in vitro* as assessed using human recombinant bradykinin B2 receptors (150 pM); *ex vivo* as studied against endogenous bradykinin B2 receptors in a human umbilical vein model (350 pM); and *in vivo* in the human bradykinin-challenge model (170 pM).

Deucrictibant demonstrated over 4000-fold selectivity for the bradykinin B2 receptor when compared to approximately 170 other molecular targets including the bradykinin-B1-receptor. As shown in the graphs below depicting mean arterial blood pressure (MABP) in a bradykinin challenge study in monkeys (back-translated from human), deucrictibant showed clear dose-dependent activity. While differences between human and monkey PK prevent direct extrapolation to human dose, deucrictibant demonstrated longer duration and faster onset of activity than injected icatibant in the same study. However, we have not conducted a head-to-head comparison of icatibant to deucrictibant in a clinical trial but have compared the published data for icatibant to data from our Phase 1 clinical trial of deucrictibant. While we believe this comparison to icatibant to be useful and appropriate, the value of this and other comparisons to icatibant in this Annual Report may be limited because they are not derived from a head-to-head trial, and they are from trials that were conducted under different protocols at different sites and at different times. Without head-to-head data, we will be unable to make comparative claims for our product candidates, if approved.

BK-Challenge in Nonclinical Animal Model





A dose of 0.6 mg/kg sc icatibant was used in monkeys, as PK data indicated that this dose would provide an exposure (Cmax 1,044 ng/mL, AUC 2,155 ng*h/mL) similar to the exposures seen in humans at a therapeutic dose of 30 mg sc (Cmax 979 ng/mL, AUC 2,191 ng*h/mL). The dose was found to effectively antagonize the bradykinin challenge in monkeys up to six hours after dosing, similar to its duration of action in humans. The maximal effect of icatibant in this model was reached at the second time point measured, two hours after dosing. The vehicle in the icatibant study was saline.

Deucrictibant inhibited the bradykinin-induced changes in MABP at all doses tested (0.1, 0.3, 1, 3 and 10 mg/kg given orally). The data show an early onset of activity, as the efficacy was already maximal at the first time point measured, one hour after oral dosing. This is a faster onset of action as compared to icatibant (0.6 mg/kg sc), which was maximally active on the bradykinin-induced changes in MABP at two hours after dosing.

Nonclinical Safety

The conducted nonclinical package for deucrictibant includes secondary pharmacodynamics, safety pharmacology, genotoxicity, reproductive and developmental studies and general toxicity studies up to 6 months in rats and up to 9 months in monkeys. Deucrictibant did not demonstrate any *in vitro* or *in vivo* genotoxicity nor *in vitro* phototoxic potential. No findings considered relevant to humans were observed in GLP (Good Laboratory Practices)-compliant general toxicity studies in rats up to 3-months duration and in cynomolgus monkeys up to 9-months duration at doses up to the maximum tolerated dose in each species. Deucrictibant has not demonstrated any adverse effects on embryo-fetal survival and development in the humanized bradykinin B2 receptor transgenic rat or in the rabbit. Furthermore, male and female fertility studies showed no adverse effects of deucrictibant on gonadal function, mating behavior, and reproductive performance.

Findings were observed in the repeat-dose rat data package that were considered not to be related to bradykinin B2 receptor antagonism. Based on review of these nonclinical findings, in 2022, the FDA put a clinical hold on trials of deucrictibant in the U.S. The FDA requested that Pharvaris conduct an additional long-term rodent toxicology study. Pharvaris aligned with the FDA on the protocol and completed a 6-month rat exploratory study to further investigate the findings and address the clinical holds. Following review of data from a preplanned interim analysis of the ongoing 26-week nonclinical rodent study, the FDA lifted the clinical hold on the IND application for deucrictibant for the on-demand treatment of HAE in June 2023. In January 2024, the FDA lifted the clinical hold on the IND application for deucrictibant for the prophylactic treatment of HAE attacks following review of the full data set from the completed 26-week rodent toxicology study.

Clinical Trial Program

Study Number	Short Description	Design	Status
Phase 1			
C001	Single ascending dose (SAD) and bradykinin challenge/SAD-proof of mechanism (POM)	Randomized, double-blind, placebo-controlled, single ascending dose to assess safety and proof-of-concept through BK-challenge	Completed
C002	SAD extension	Randomized, double-blind, placebo-controlled, single ascending dose to assess safety	Completed
C003	Absorption, metabolism, and excretion (mass balance)	Open-label, single dose 14 C-deucrictibant to characterize the absorption, metabolism, and excretion	Completed
C004	Drug-drug interaction (DDI)—CYP3A4 inhibitor (itraconazole) interaction	Open-label, single-sequence, crossover DDI study	Completed
C005	DDI—CYP interaction (cocktail)	Open-label, single-sequence, crossover DDI study	Completed
C006	Multiple ascending dose (MAD)	Randomized, double-blind, placebo-controlled, multiple ascending doses to assess safety and different doses	Completed
C009	Japanese PK bridging	Double-blind, randomized, single oral dose, two-period crossover comparing pharmacokinetics between Japanese and Caucasian volunteers	Completed
C010	Exploratory XR PK bridging	Open-label, randomized five-period crossover single-dose to assess bioavailability of two different extended-release formulations with and without food	Completed
C012	Hepatic impairment	Open-label, single dose to assess the effect of hepatic impairment on pharmacokinetics	Completed
C013	Renal impairment	Open-label, single dose to assess the effect of renal impairment on pharmacokinetics	Completed
C014	DDI Rabeprazole	Open-label, drug interaction study to investigate the effect of multiple doses of the gastric acid-reducing agent rabeprazole on the single dose pharmacokinetics of extended-release tablet.	Ongoing
C015	Confirmatory XR PK	Open-label, multiple doses to assess PK and safety of extended-release formulation	Completed
C016	DDI CYP3A4	Open-label, single-sequence, drug-drug interaction study to evaluate the effect of multiple oral doses of the moderate CYP3A4 inhibitor verapamil on the single dose PK deucrictibant	Completed
C017	DDI digoxin and rosuvastatin	Open-label, drug interaction study to investigate the effect of the extended-release tablet administered once daily on the pharmacokinetics of the P-gp substrate digoxin and the BCRP substrate rosuvastatin, administered as a drug cocktail	Ongoing
C018	XR Food Effect	Open-label, randomized, two-period, two-way cross-over study to assess the influence of a high-calorie, high-fat meal on the bioavailability of extended-release formulation	Ongoing
C019	XR multi-ethnicity study	Open-label, multiple dose study to compare PK of extended-release formulation between healthy Japanese, Chinese, and Caucasian volunteers	Ongoing
C020	Biovailability study	Open label, randomized, two-period, cross-over single-dose study under fasting condition	Ongoing
C021	XR4 Food Effect	Open-Label, randomized, two-period, cross-over single-dose study in healthy subjects to assess the influence of a high-calorie, high-fat meal on the bioavailability of a 40 mg extended-release (XR) formulation	Ongoing
Phase 2/3			
C201 RAPIDe-1	deucrictibant IR capsule on-demand	Phase 2, randomized, double blind, placebo-controlled, dose ranging study to assess safety and efficacy	Completed
C303 RAPIDe-2	deucrictibant IR capsule on-demand open-label extension	Phase 2/3, Extension Study to evaluate the safety of long-term on-demand treatment with deucrictibant for acute HAE attacks	Ongoing

C301 CHAPTER-1	proof-of-concept deucrictibant prophylaxis and open-label extension	A two-part Phase 2, randomized, double blind, placebo-controlled dose ranging study to Part 1: assess safety and efficacy of prophylactic treatment with deucrictibant and Part 2: evaluate long-term safety and efficacy for prophylactic treatment with deucrictibant	Ongoing
C306 RAPIDe-3	deucrictibant IR capsule on demand	A Phase 3, Randomized, Double-blind, Placebo-controlled, Cross-over Study of Oral Deucrictibant Soft Capsule for On-Demand Treatment of Attacks in Adolescents and Adults with Hereditary Angioedema	Ongoing
C305 CHAPTER-3	deucrictibant XR tablet prophylaxis	A Phase 3, Randomized, Double-blind, Placebo-controlled Study of Orally Administered Deucrictibant Extended-Release Tablet for Prophylaxis to Prevent Angioedema Attacks in Adolescents and Adults with Hereditary Angioedema	Ongoing
C307 CHAPTER-4	deucrictibant XR tablet prophylaxis open-label extension	A Phase 3, Long-term, Open-label Study of Orally Administered Deucrictibant Extended-release Tablet for Prophylaxis to Prevent Angioedema Attacks in Adolescents and Adults with Hereditary Angioedema	Ongoing

PHA121-C001 (SAD and bradykinin challenge / SAD-POM)

Deucrictibant-C001 was a randomized, double-blind, placebo-controlled, single ascending dose and proof-of-concept study to examine the safety, tolerability, PK and PD of orally administered deucrictibant in healthy subjects. A total of 52 subjects received single ascending oral doses of deucrictibant up to 22 mg. The 16 remaining subjects received placebo. No adverse event, or AE, was reported as serious, no premature withdrawals due to AEs occurred and no severe AEs were reported. In addition, no clinically relevant fluctuations of blood pressure linked to deucrictibant groups occurred. The overall incidence of AEs was similar between the placebo and deucrictibant. Treatment-related AEs were reported for three subjects who received deucrictibant (12 or 22 mg), all within the gastrointestinal system and of mild severity: upper abdominal pain, vomiting, and nausea. There were no apparent trends or dose-related changes in hematology, clinical chemistry, vital signs, or ECG.

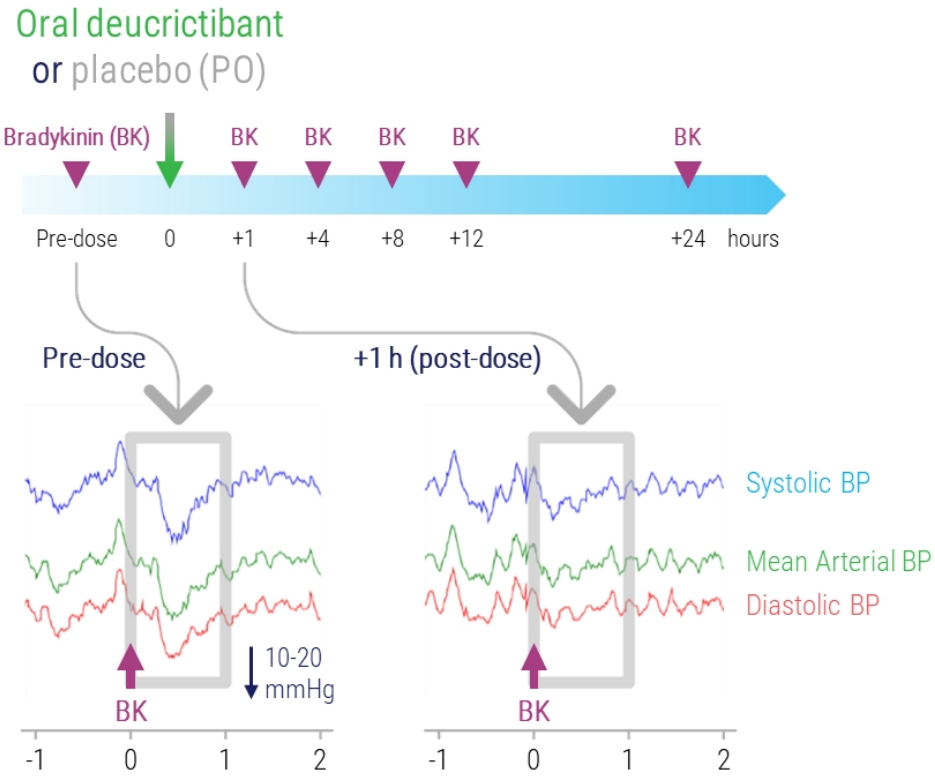
Pharmacokinetics Analysis

Dose proportional PK was observed after single oral administration under fasting condition of deucrictibant in the dose range of 1 mg to 22 mg for Cmax, AUClast and AUCinf. Median tmax in the dose range of 1 mg to 22 mg was between 0.50 hour and 1.00 hour, with comparable ranges of individual values (ranging between 0.25 hour and 1.02 hours). Less than 1% of the dose was excreted unchanged in urine within 72 hours after administration.

Dose (mg)	Cmax (ng/mL)	C0.25h (ng/mL)	C12h (ng/mL)	Tmax (h)	t1/2 (h)
1	11	6	0.5	0.5	3.5
2	20	13	0.8	0.75	4.3
4.5	33	13	1.9	1.0	4.4
12	97	60	5.6	0.5	4.3
22	213	143	8.3	0.75	5.6
22 (high calorie, high-fat meal)	145	48	19.6	3.0	5.3

In this study, a high-calorie, high-fat (HCHF) meal reduced peak exposure and slightly increased overall exposure of deucrictibant: after a 22 mg dose, the mean Cmax of deucrictibant was lower (~32%) while AUCinf was higher (~ 42%) when deucrictibant was administered after a high calorie, high-fat breakfast (fed conditions) compared to administration under fasted conditions. While the median tmax of deucrictibant was delayed by approximately two hours after administration under fed conditions, the plasma concentration for deucrictibant still reached the projected therapeutic levels (EC85, as determined in the bradykinin challenge described below) within 15 minutes. As shown in the table, the concentration of deucrictibant twelve hours post-dosing at 12 mg or 22 mg remained above projected therapeutic levels under both fed and fasted conditions.

Bradykinin Challenge Study



In addition, we also evaluated the PD of deucrictibant in a bradykinin challenge model, which was designed to demonstrate deucrictibant-mediated inhibition of the drop in blood pressure and increase in heart rate resulting from injection of a bradykinin bolus in healthy subjects. The bradykinin challenge is administered at specific intervals after the deucrictibant or placebo dose, and the inhibition of bradykinin-induced hemodynamic effects is a validated surrogate assessment that was used to select the dose in the original development program for icatibant, as reviewed by FDA and EMA. The clinical dose of icatibant established with the bradykinin challenge has demonstrated successful resolution of HAE attacks in randomized clinical trials and over 10 years of data post-approval.

In the bradykinin challenge, we assessed the inhibition of bradykinin effects at single doses of 12 and 22 mg deucrictibant. Bradykinin was injected intravenously before deucrictibant to calibrate each subject's response, and then at 1, 4, 8, 12 and 24 hours after dosing with deucrictibant. We monitored cardiovascular responses at each time point (see figure above). At the same time, blood samples were drawn for PK assessment. Bradykinin injection induced a short-lasting transient change in mean arterial blood pressure, or MABP, heart rate, or HR, and cardiac output. In the presence of deucrictibant, this cardiovascular response was dampened to an extent depending on the plasma concentration of deucrictibant.

We conducted a PK/PD analysis using the same approach as used by FDA in their evaluation of icatibant. The composite EC50 and EC85 values estimated from the combination of each PD response associated with the bradykinin challenge are provided in the table below. Deucrictibant demonstrated higher PD potency based on plasma concentrations (roughly four-fold) published for icatibant. Adjusting for the differences between molecular weight and plasma protein binding, we found that deucrictibant is 24-fold more potent (170 pM) in the bradykinin challenge model than icatibant (4.1 nM) on a molecule-by-molecule basis, consistent with our preclinical *in vitro and ex vivo* measurements.

Composite average	deucrictibant	icatibant
EC50 (ng/mL)	2.4	9.5
EC85 (ng/mL)	13.8	53.8

EC50: concentration at which compound induces a response half of its maximum possible response; EC85: concentration at which a compound induces 85% of its maximum response.

The data also allowed us to compare the projected therapeutic performance of deucrictibant with that of icatibant. However, we have not conducted a head-to-head comparison of icatibant to deucrictibant in a clinical trial but have compared the published data for icatibant to

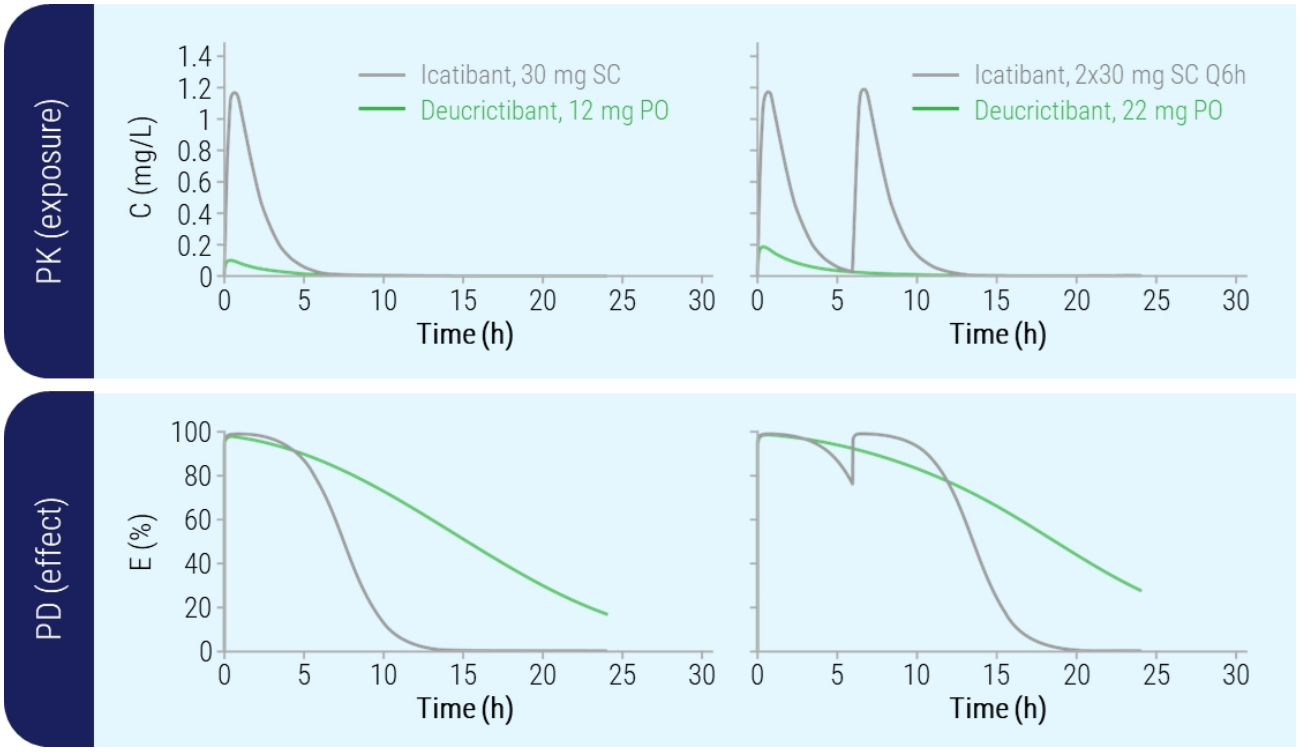
data from our Phase 1 and Phase 2 clinical trial of deucrictibant. While we believe this comparison to icatibant to be useful and appropriate, the value of this and other comparisons to icatibant in this Annual Report may be limited because they are not derived from a head-to-head trial and they are from trials that were conducted under different protocols at different sites and at different times. Without head-to-head data, we will be unable to make comparative claims for our product candidates, if approved. Clinical trials have shown for icatibant that the therapeutic response of icatibant to treat an acute HAE attack wanes approximately 6 hours after dosing, coinciding with the drop in icatibant concentration below therapeutic levels due to the short half-life (1.4 hours) of the drug. More precisely, it was shown that icatibant plasma concentrations with a 75% probability to be above EC50 and a 50% probability to be above EC85 correlate with therapeutic efficacy.

Applying these criteria as exposure targets for deucrictibant leads us to project that due to deucrictibant's longer half-life, we believe deucrictibant will stay above these therapeutic targets for much longer than icatibant. The 12 mg dose of deucrictibant showed rapid absorption and the plasma exposure then stayed above EC50 for 10-12 hours and above the EC85 for 6.5 to 7.5 hours, suggesting that this dose may be at least as effective as a 30 mg s.c. injection of icatibant. A 30 mg s.c. icatibant dose has been documented to effectively treat 93% of acute HAE attacks (Icatibant Outcome Survey, or IOS, study reference).

The table below compares 30 mg of icatibant to 12 mg and 22 mg of deucrictibant based on BK-challenge modeling and simulation.

Response	icatibant 30 mg	deucrictibant 12 mg (oral)	deucrictibant 22 mg (oral)
	Time (h) plasma level above EC50 at a 75% confidence level		
Diastolic blood pressure (DBP)	6.0	11.5	14
MABP	6.0	12	15.5
Heart rate	6.5	10	13
	Time (h) plasma level above EC85 at a 50% confidence level		
DBP	5.5	7.5	10
MABP	5.5	7.0	10
Heart rate	5.5	6.5	9.5

The chart below shows the simulation of PK and PD resulting from single (left) or double (right) doses of icatibant as compared to single doses of deucrictibant at 12 mg (left) or 22 mg (right), using a non-linear mixed-effect model built from published data of icatibant and our bradykinin challenge study. As shown in the bottom row, the modeled PD effect of deucrictibant surpasses that of icatibant at less than half the dose, and equals two 30 mg injections of icatibant with a single oral dose of 22 mg. As demonstrated in a post-commercialization observational study (IOS study reference), a single dose of icatibant was shown to treat 93% of attacks and two doses treated 99% of over 5,000 attacks in the 10 years survey.



In conclusion, deucrictibant was well tolerated when administered orally at the doses tested without any dose-limiting toxicity. Deucrictibant was rapidly absorbed in either fasting or fed conditions and showed dose proportional PK for deucrictibant. The bradykinin challenge demonstrated that deucrictibant potently blocks the effects of bradykinin-induced hemodynamic changes and provided the robust rationale for dose selection in future on-demand and prophylactic HAE trials.

PHA121-C002 (SAD extension)

PHA121-C002 was a randomized, double-blind, placebo-controlled, single ascending dose extension trial designed to examine the safety, tolerability, and PK of single ascending oral doses of 22, 33, and 50 mg of deucrictibant after a standard caloric meal and 40 mg in fasting conditions. A total of 32 subjects received either deucrictibant (24 subjects), or placebo (8 subjects).

The trial results showed that deucrictibant was well tolerated at doses up to 40 mg under fasting and 50 mg under fed conditions. There were no SAEs reported. Treatment-related AEs that were reported as possibly related to deucrictibant were mild nausea (22 mg) (one subject), mild headache (50 mg) (one subject), and moderate headache associated with vomiting (50 mg) (one subject). There were no clinically significant changes in vital signs, laboratory or ECG parameters.

Over the investigated dose range from 22 to 50 mg (factor 2.27 increase) after a standardized breakfast, deucrictibant showed dose-proportional PK with a 2.4-fold increase for mean Cmax and AUC0-24h. Administration of deucrictibant after a standardized breakfast resulted in 40-50% decrease in Cmax without a change in AUCinf as compared to administration under fasting conditions. As a result, C12h and C24h plasma concentration for deucrictibant were higher under fed conditions. These observations support the potential use of this formulation for initial studies in a prophylactic setting by dosing with food.

	22 mg of deucrictibant Fasted	22 mg of deucrictibant HCHF	22 mg of deucrictibant Standard Meal
C12h, ng/mL	8.3	19.6	17.3
C24h, ng/mL	1.1	5.4	2.5
Cmax, ng/mL	213	145	115
AUC0-24h, ng.h/mL	671	966	750
tmax, h	0.25-1.02	2.00-3.00	0.50-4.00
t1/2, h	5.6	5.3	4.3

PHA121-C004 (DDI-CYP3A4 inhibitor, itraconazole, interaction)

Cytochrome P450 3A4 (CYP3A4) plays an important role in the metabolism of deucrictibant. Deucrictibant-C004 was designed as an open-label, single sequence crossover drug-drug interaction trial to evaluate the effect of multiple doses of itraconazole, a potent CYP3A4 inhibitor, at steady-state on the PK of a single dose of deucrictibant in healthy subjects. The primary objective of this study was to determine the effect of multiple doses of the strong CYP3A4 inhibitor itraconazole on the PK of deucrictibant in healthy adult subjects. The secondary objective of this study was to evaluate the safety and tolerability of deucrictibant alone and in combination with multiple doses of the CYP3A4 inhibitor itraconazole in healthy adult subjects. The study has been completed in 13 subjects and deucrictibant was well tolerated with no drug-related adverse events reported. Preliminary analyses show that the exposure of deucrictibant increased when co-administered with itraconazole, as expected from *in vitro* data showing that deucrictibant is a substrate of CYP3A4. Other potential drug-drug interactions will be further assessed by the deucrictibant-C005 cocktail interaction study and in *in vitro* assays recommended by FDA guidance.

PHA121-C006 (MAD)

PHA121-C006 was a randomized, double-blind, placebo-controlled, multiple ascending dose trial to examine the safety, tolerability and PK of deucrictibant in healthy subjects, which demonstrated deucrictibant's pharmacokinetics and tolerability. The trial included 38 subjects and four cohorts, ranging from 12 to 50 mg of healthy subjects who were studied sequentially. Within each cohort, eight subjects received deucrictibant and two subjects received placebo, except for the final cohort with six subjects receiving deucrictibant and two subjects receiving placebo. The trial evaluated multiple ascending doses twice daily for 10 days to establish safety and tolerability and to assess the PK characteristics of deucrictibant after standard caloric meals. Deucrictibant was supplied as an oral solution.

The study showed deucrictibant was well tolerated at all doses studied (including up to the highest dose of 50 mg twice daily (BID)), with approximately dose-proportional exposure. During the study, there have been no SAEs or severe treatment-emergent adverse events, or TEAEs, reported. All reported TEAEs were mild in intensity and resolved completely. There were no clear differences between the different dosing regimens vs. placebo with respect to the total TEAEs and the frequency of TEAEs reported for the different system organ classes. Lab safety, vital signs, and ECG parameters remained well within normal limits in all subjects. The pharmacokinetic profile suggests that therapeutic drug levels of deucrictibant were achieved in day 1 and steady-state plasma concentrations were reached within 72 hours.

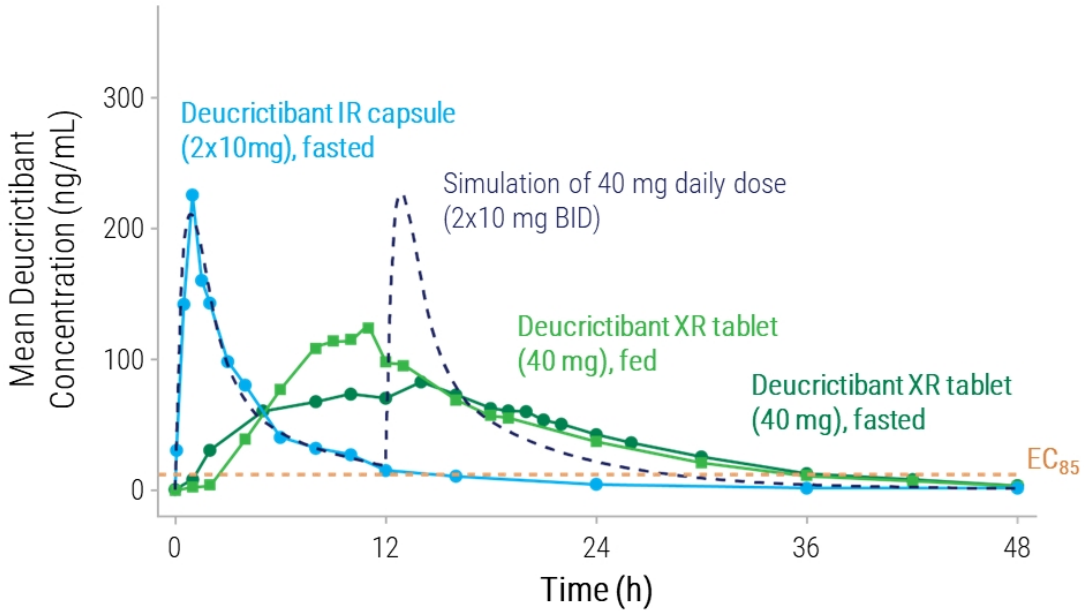
PHA121-C010 (SD)

PHA121-C010 was an open-label randomized five-period crossover single-dose study to assess bioavailability of two different extended-release formulations with and without food, in comparison to a single dose of immediate-release capsules without food. The study included 8 healthy volunteers who received in randomized order a single dose of deucrictibant IR capsules (20 mg, as two 10-mg softgel capsules) without food, a single XR tablet of deucrictibant (20 mg) without food; a single XR tablet of deucrictibant (20 mg) with a high-calorie, high-fat meal; a single XR tablet of deucrictibant (40 mg) without food; and a single XR tablet of deucrictibant (40 mg) with a high-calorie, high-fat meal.

The study showed deucrictibant immediate-release capsules and deucrictibant extended-release tablets were well tolerated. During the study, there were no SAEs or severe treatment-emergent adverse events (TEAEs) reported.

The pharmacokinetic profile observed for deucrictibant confirmed that the softgel capsule formulation under fasting conditions achieved rapid exposure of the deucrictibant active ingredient consistent with previous pharmacokinetic studies using deucrictibant in a solution formulation, rising above clinically relevant exposure (in particular, the EC_{85} determined from the bradykinin challenge, 13.8 ng/mL) within 15 minutes. A single dose of deucrictibant XR tablet (40 mg) under fasted conditions yielded exposure above 13.8 ng/mL by the two-hour timepoint and maintained this exposure for at least an additional 28 hours. The overall exposure was not affected by food. The 24-hour area under the curve (AUC_{24h}) exposure of deucrictibant using deucrictibant XR tablet (40 mg) is similar to that observed in Phase 1 studies with deucrictibant IR capsule dosed 20 mg twice a day with food (one of the doses used in the CHAPTER-1 prophylactic proof-of-concept study).

The observed pharmacokinetic profile of the deucrictibant XR formulation is consistent with a true extended-release formulation designed to provide long-term exposure to deucrictibant. In particular, deucrictibant XR tablets appear to be suitable for once-daily dosing.

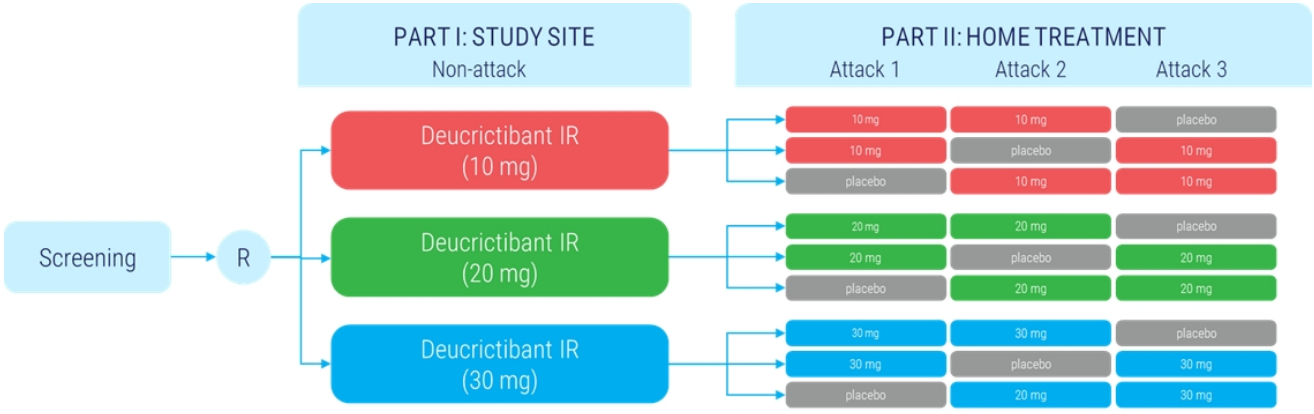


PHA121-C201 (RAPIDe-1 On-Demand)

The availability of an immediate-release softgel capsule formulation provides a good pharmacokinetic profile for on-demand treatment: rapid oral absorption independent of fed status resulting in almost immediate onset of action with longer expected duration of efficacy than subcutaneous injections of icatibant. We have observed in nonclinical animal studies that the deucrictibant softgel capsule provides similar pharmacokinetic profile as the solution formulation we used in Phase 1 trials and have now seen this also in humans from the C010 Phase 1 study.

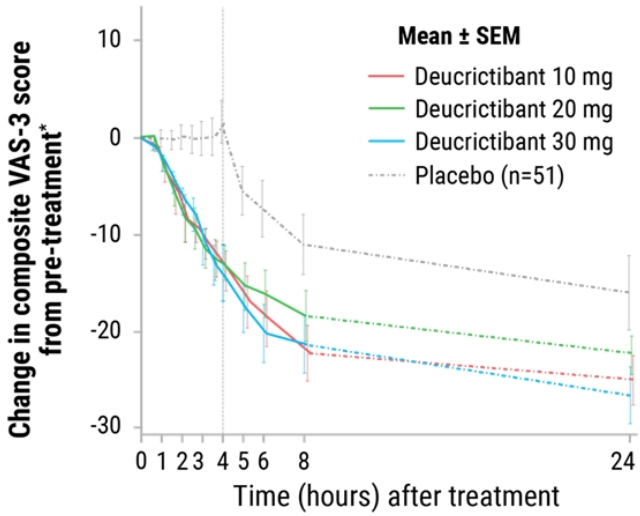
In December 2022, we announced positive top-line data from RAPIDe-1, a Phase 2, double-blind, placebo-controlled, randomized, crossover, dose-ranging study of deucrictibant IR capsule for the on-demand treatment of HAE type 1 and type 2 (HAE-1/2) attacks. The

study, initiated in February 2021, enrolled 74 patients across 13 countries who were randomized into one of three single dose levels of deucrictibant and placebo. The study compared symptom relief during HAE attacks and the safety of each dose of deucrictibant with placebo. In Part I of the study, participants in a non-attack state received the assigned single dose of deucrictibant IR capsule at the study center to assess its pharmacokinetics and safety. In Part II, participants self-administered blinded study drug at home to treat three physician-confirmed HAE attacks with deucrictibant or placebo.



	Deucrictibant IR dose group			
	10 mg (n=22)	20 mg (n=18)	30 mg (n=22)	Total (N=62)
Age (years), mean	42.5	44.5	41.9	42.9
Sex, n (%)				
Male	7 (31.8)	5 (27.8)	8 (36.4)	20 (32.3)
Female	15 (68.2)	13 (72.2)	14 (63.6)	42 (67.7)
Race, n (%)				
White	20 (90.9)	18 (100)	22 (100)	60 (96.8)
Other	2 (9.1)	0	0	2 (3.2)
BMI (kg/m^2), mean	27.5	27.6	27.9	27.7
Time since HAE diagnosis (years), mean	21.11	21.64	23.98	22.28
HAE type, n (%)				
HAE-1	18	15	22	55
HAE-2	4	2	0	6
HAE-1 or HAE-2	0	1	0	1

The primary endpoint of the study is the change of a three-symptom composite (skin pain, skin swelling, abdominal pain) visual analogue scale (VAS-3) score from pre-treatment to four hours post-treatment, as captured electronically using numerically assisted input. The top-line data from 147 attacks collected by 62 participants show that all three dose levels of deucrictibant significantly reduce attack symptoms.



*VAS assessed every 30 minutes up to 4 hours post-treatment, then at 5, 6, 8, 24, 48 hours

	Placebo n=51	Deucrictibant 10 mg n=37	Deucrictibant 20 mg n=28	Deucrictibant 30 mg n=31	Combined deucrictibant n=96
Mean VAS-3 at pre-treatment	27.76	26.16	25.46	29.73	27.11
Change in VAS-3 at 4 hours					
LS mean difference: Deucrictibant – Placebo		-16.75	-15.02	-16.28	-16.08
P value		*P*<0.0001†	*P*<0.0001	*P*<0.0001	

Composite and individual VAS-3, mean symptom complex severity, or MSCS, and treatment outcome score, or TOS, were assessed up to 48-hours post-dose. All key secondary endpoints in the study were met, demonstrating that deucrictibant significantly shortens the time to onset of symptom relief by a ≥30% reduction in VAS-3 score from the pre-treatment score, decreases time to a ≥50% reduction in VAS-3 score from the pre-treatment score, reduces time to almost complete or complete symptom relief by VAS-3, reduces the MSCS score from pre-treatment to four hours post-treatment, and improves the TOS at four hours post-treatment. All other secondary endpoints were met. Participants on deucrictibant also used substantially less rescue medication compared to placebo.

Table of Contents

	Placebo n=51	Deucrictibant 10 mg n=37	Deucrictibant 20 mg n=28	Deucrictibant 30 mg n=31	Combined deucrictibant* N=96
Time to onset of symptom relief by VAS-3 30% reduction†					
Median time in hours (95% CI)	8.0 (7.6, 46.9)	2.1 (1.5, 2.9)	2.7 (1.9, 3.5)	2.5 (1.9, 3.8)	2.4 (2.0, 2.9)
Hazard ratio		3.81	3.08	3.61	
P value		*P*<0.0001§	*P*=0.0021	*P*<0.0001	
Time to VAS-3 50% reduction†					
Median time in hours (95% CI)	22.8 (20.0, 24.1)	3.3 (2.4, 3.9)	4.0 (2.9, 6.0)	4.0 (3.3, 5.8)	3.9 (3.0, 4.8)
Hazard ratio		4.55	3.65	3.87	
P value		*P*<0.0001§	*P*=0.0003	*P*<0.0001	
Time to almost complete or complete symptom relief by VAS†					
Median time in hours (95% CI)	42 (22.0, 48.1)	5.8 (3.6, 7.5)	20 (4.5, 20.0)	20 (6.0, 20.1)	7.5 (5.9, 20.0)
Hazard ratio		5.09	2.25	2.65	
P value		*P*<0.0001§	*P*=0.0127	*P*=0.0001	
Change in MSCS score at 4 hours‡					
LS mean difference: Deucrictibant – Placebo		-0.79	-0.61	-0.39	-0.61
P value		*P*<0.0001§	*P*=0.0008	*P*=0.0291	
TOS at 4 hours‡					
LS mean difference: Deucrictibant – Placebo		64.13	62.69	71.06	66.05
P value		*P*<0.0001§	*P*<0.0001	*P*<0.0001	

*The combined deucrictibant results are based on post-hoc analyses to provide a reference of the result by pooling all three active doses; †Hazard ratios and p-values are based on marginal Cox proportional hazards models; ‡P values are based on mixed-effects models for repeated measures; §Nominal *P* value. Note: N = The number of attacks included in the mITT Analysis Set; *P* values for 20mg and 30mg are based on statistical tests in the pre-specified multiple comparison procedure, other p-values are nominal.
LS mean, least-squares mean; MSCS, mean symptom complex severity; VAS, visual analog scale.

	Placebo	Deucrictibant 10 mg	Deucrictibant 20 mg	Deucrictibant 30 mg	Combined deucrictibant*
Change in MSCS score at 4 hours					
n	40	32	26	27	85
LS mean (95% CI)	-0.29 (-0.51, -0.08)	-1.08 (-1.33, -0.83)	-0.91 (-1.19, -0.62)	-0.68 (-0.95, -0.40)	-0.90 (-1.06, -0.75)
Difference (Deucrictibant – Placebo) *P* value		-0.79 *P*<0.0001*	-0.61 *P*=0.0008	-0.39 *P*=0.0291	-0.61
TOS at 4 hours					
n	40	32	25	28	85
LS mean (95% CI)	-3.62 (-19.68, 12.45)	60.52 (41.74, 79.29)	59.08 (37.58, 80.57)	67.44 (47.15, 87.74)	62.57 (50.95, 74.19)
Difference (Deucrictibant – Placebo) *P* value		64.13 *P*<0.0001*	62.69 *P*<0.0001	71.06 *P*<0.0001	66.05

*Nominal p-value; Note: LS mean, LSMD, CIs, and p-values for MSCS change from pre-treatment/TOS come from mixed-effect models with repeated measures (MMRM). Data after rescue medication use is not included. The combined deucrictibant result is based on post-hoc analysis using similar MMRM with all three active doses combined vs placebo.
CI, confidence interval; LS mean, least-squares mean; LSMD, least-squares mean difference; MSCS, mean symptom complex severity; TOS, treatment outcome score.

	Placebo	Deucrictibant 10 mg	Deucrictibant 20 mg	Deucrictibant 30 mg	Combined Deucrictibant*
Number of attacks	49	36	28	29	93
Attacks achieving "a little better" for all SCs at two consecutive time points - n (%)*	18 (**36.7%**)	32 (88.9%)	25 (89.3%)	27 (93.1%)	84 (**90.3%**)
Median (95% CI) time by KM estimate (hours)	**7.62** (3.95, NE)	1.89 (0.97, 3.97)	2.15 (1.75, 4.00)	1.98 (1.80, 3.87)	**1.98** (1.88, 3.87)
Attacks achieving "a lot better or resolved" for all SCs at any time point – n (%)*	13 (**26.5%**)	30 (83.3%)	23 (82.1%)	25 (86.2%)	78 (**83.9%**)
Median (95% CI) time by KM estimate (hours)	**23.28** (5.78, 47.17)	4.02 (3.93, 5.77)	5.93 (3.90, 8.58)	4.12 (3.92, 7.22)	**5.23** (3.98, 5.78)

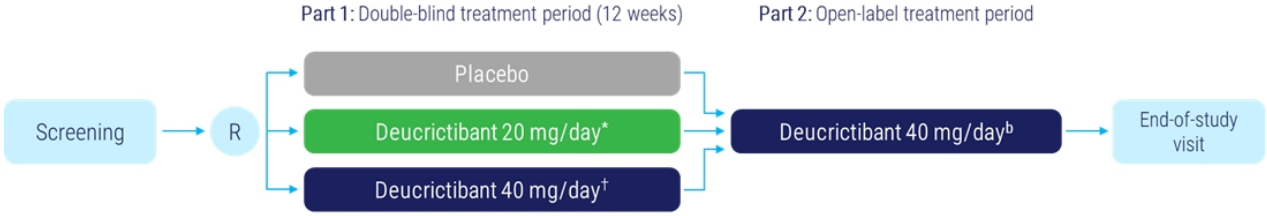
*Within 48-hour assessments.
KM, Kaplan-Meier; NE, not estimable; PRO, patient reported outcome; SC, symptom complex; TOS, treatment outcome score.

Deucrictibant was generally well tolerated with no treatment-related serious adverse events and no adverse events leading to treatment discontinuation. In the non-attack phase, two treatment-related adverse events were experienced by two patients; in the attack treatment phase, three treatment-related adverse events were reported for one attack treated with deucrictibant 30mg (2.8%) and one treatment-related adverse event was reported for one attack treated with placebo (1.9%).

	Part I (Non-Attack)			Part II (Attack 1,2,3)			
	10 mg N=23	20 mg N=24	30 mg N=25	Placebo N=53	10 mg N=38	20 mg N=29	30 mg N=36
Subjects (Part I) or attacks (Part II) with any treatment-related AEs	1 (4.3%)	1 (4.2%)	-	1 (1.9%)	-	-	1 (2.8%)
Headache	-	1 (4.2%)	-	-	-	-	-
Nausea	1 (4.3%)	-	-	-	-	-	1 (2.8%)
Vomiting	-	-	-	-	-	-	1 (2.8%)
Fatigue	-	-	-	-	-	-	1 (2.8%)
Blister	-	-	-	1 (1.9%)	-	-	-

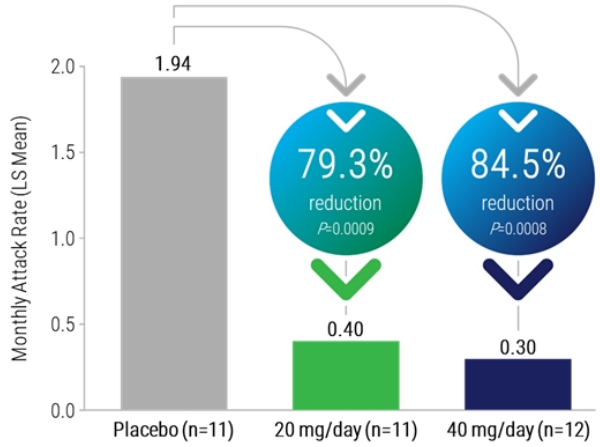
PHA121-C301 (CHAPTER-1 prophylaxis)

PHA022121-C301 is a double-blind, placebo-controlled Phase 2 study evaluating the efficacy as well as the safety and tolerability of deucrictibant for long-term prophylaxis against angioedema attacks in HAE-1/2. In the study, 34 participants were enrolled globally and randomized to receive one of two doses of deucrictibant (20 mg/day or 40 mg/day) or placebo for 12 weeks of treatment. Deucrictibant immediate-release capsule was dosed twice-a-day as a proof-of-concept for the once-daily deucrictibant extended-release tablet, which is the intended formulation for the prophylactic treatment of HAE. The open-label portion of the CHAPTER-1 study is ongoing at the 40 mg/day dose.



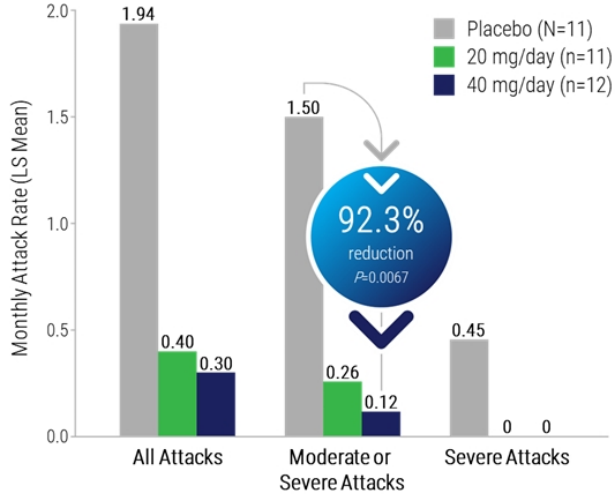
	Placebo n=11	20 mg/day n=11	40 mg/day n=12	All N=34
Age in years – Mean	41.4	38.4	40.8	40.2
Sex: M/F – n	3/8	6/5	4/8	13/21
Race: White – n (%)	11 (100)	11 (100)	12 (100)	34 (100)
BMI (kg/m2) – Mean	26.7	29.5	25.4	27.1
HAE Type – n				
Type 1	10	9	12	31
Type 2	1	2	0	3
Baseline HAE attack rate per month				
Mean	1.9	2.1	2.5	2.2
Median (Min, Max)	1.7 (0.7, 3.7)	1.7 (1.0, 5.3)	1.7 (1.0, 6.7)	1.7(0.7, 6.7)
Randomized baseline HAE attack rate categories – n (%)				
1 to < 2 attacks per 4 weeks	6 (54.5)	7 (63.6)	7 (58.3)	20 (58.8)
2 to < 3 attacks per 4 weeks	3 (27.3)	1 (9.1)	1 (8.3)	5 (14.7)
≥ 3 attacks per 4 weeks	2 (18.2)	3 (27.3)	4 (33.3)	9 (26.5)

The study's primary endpoint measured the time-normalized number of investigator-confirmed HAE attacks during the treatment period. The monthly attack rate was reduced by 84.5% (p=0.0008) compared to placebo in participants who received 40 mg/day deucrictibant. In the analysis of the secondary endpoints, deucrictibant demonstrated clinically meaningful improvement in the severity of attacks (92.3% reduction in occurrence of moderate and severe attacks) and a decrease in the number of attacks treated with on-demand medication (92.6% fewer attacks treated with on-demand medication). Participants on deucrictibant treatment also experienced a meaningful improvement in their quality of life.



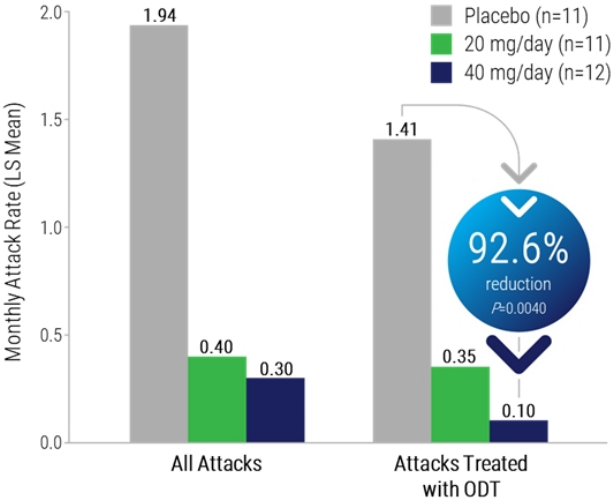
	Placebo n=11	20 mg/day* n=11	40 mg/day† n=12
Monthly attack rate – Median			
Baseline	1.67	1.67	1.74
On study	2.15	0	0.15
Change from baseline	0.33	-1.34	-1.59
% change from baseline	17%	-100%	-96%
Model-based inference			
LS mean	1.94	0.40	0.30
% reduction vs placebo		79.3%	84.5%
P value		0.0009	0.0008

*20 mg/day = deucrictibant immediate-release (IR) capsules 10 mg twice daily; †40 mg/day = deucrictibant IR capsules 20 mg twice daily.
[†]40 mg/day = deucrictibant IR capsules 20 mg twice daily; [‡]Based on time-normalized number of attacks per 4 weeks.



	Placebo n=11	20 mg/day* n=11	40 mg/day† n=12
Monthly attack rate of moderate or severe attacks			
LS mean	1.50	0.26	0.12
% reduction vs placebo		82.8%	92.3%
Nominal *P* value		0.0066	0.0067

*20 mg/day = deucrictibant immediate-release (IR) capsules 10 mg twice daily; †40 mg/day = deucrictibant IR capsules 20 mg twice daily.
†40 mg/day = deucrictibant IR capsules 20 mg twice daily; ‡Based on time-normalized number of attacks per 4 weeks.



	Placebo n=11	20 mg/day* n=11	40 mg/day† n=12
Monthly attack rate of attacks treated with ODT			
LS mean	1.41	0.35	0.10
% reduction vs placebo		75.1%	92.6%
Nominal *P* value		0.0074	0.0040

*20 mg/day = deucrictibant immediate-release (IR) capsules 10 mg twice daily; †40 mg/day = deucrictibant IR capsules 20 mg twice daily.
†40 mg/day = deucrictibant IR capsules 20 mg twice daily; ‡Based on time-normalized number of attacks per 4 weeks.

Throughout 12 weeks of treatment in CHAPTER-1, both dose regimens of deucrictibant (20 mg/day and 40 mg/day) were well-tolerated. There were no serious adverse events, no severe treatment-emergent adverse events, and no adverse events leading to treatment discontinuation.

	Placebo n=11*		20 mg/day* n=11*		40 mg/day† n=12	
	Subjects, n (%)	Number of events	Subjects, n (%)	Number of events	Subjects, n (%)	Number of events
TEAEs	7 (63.6)	16	6 (54.5)	11	7 (58.3)	12
Treatment related TEAEs	1 (9.1)	1	2 (18.2)	2	1 (8.3)	1
Serious TEAEs	0	0	0	0	0	0
Treatment related Serious TEAEs	0	0	0	0	0	0
TEAEs leading to study drug discontinuation	0	0	0	0	0	0
TEAEs leading to withdrawal from study	0	0	0	0	0	0
TEAEs leading to death	0	0	0	0	0	0

Future Development Path

We intend to develop deucrictibant for on-demand and prophylactic indications in parallel using two different product formulations.

On-Demand

The availability of an immediate-release softgel capsule formulation provides a good pharmacokinetic profile for on-demand treatment: rapid oral absorption independent of fed status resulting in almost immediate onset of action with longer expected duration of efficacy than subcutaneous injections of icatibant. We have observed in nonclinical animal studies that administration of deucrictibant in a capsule provides the same pharmacokinetic profile as the solution formulation we used in Phase 1 trials and have now seen this also in humans from the C010 Phase 1 study and in patients from the C201 Phase 2 study.

Based on the positive results of the primary analysis of RAPIDe-1, we have initiated the confirmatory global Phase 3 trial RAPIDe-3 of deucrictibant for the on-demand treatment of HAE attacks. In addition, we also initiated an open-label extension study in the on-demand setting with both RAPIDe-1 and RAPIDe-3 subjects to collect long-time safety and efficacy data.

In March 2024, Pharvaris initiated a global, pivotal, randomized, double-blind-placebo-controlled Phase 3 study of orally administered deucrictibant IR capsule (20 mg) for the on-demand treatment of HAE attacks in adults and adolescents (12 years and older). The company intends to enroll approximately 120 participants. The primary efficacy endpoint is time to onset of symptom relief, as measured by Patient Global Impression of Change (PGI-C) rating of at least “a little better” for two consecutive timepoints within 12 hours post-treatment. Other efficacy endpoints include time to End of Progression (EoP) in attack symptoms, substantial symptom relief, complete attack resolution and proportion of attacks achieving symptom resolution with one dose of deucrictibant as measured by Patient Global Impression of Severity (PGI-S) and by Angioedema Symptom Rating Scale (AMRA).

Prophylaxis Trials

Currently there is no bradykinin B2 receptor antagonist available for HAE prophylaxis. Icatibant has a very short half-life and would require multiple injections each day, making it generally unsuitable for prophylactic use, especially with injection site pain reported for most patients.

Unlike on-demand use, prophylaxis requires maintenance of drug concentration over long periods of time and rapid absorption is unnecessary. In order to project a potential dose for use in prophylactic trials using our projected dose from the bradykinin challenge model (a single dose prevention model), we relied on a similar acute-to-prophylactic extrapolation utilized for products in the plasma kallikrein inhibitor field. Ecallantide is a polypeptide inhibitor of plasma kallikrein used for treatment of attacks. Similar to icatibant, the short half-life of ecallantide makes it generally unsuitable for use in prophylaxis.

Lanadelumab-flyo is a monoclonal antibody with the same target as ecallantide but with higher potency and longer half-life. Lanadelumab-flyo is used for prevention of attacks. Clinical trials and published literature correlate the steady-state concentrations of lanadelumab-flyo (relative to its EC50) to the observed prophylactic control of attacks. Based on the observed potency of deucrictibant in the bradykinin challenge, we believe we can utilize a similar concentration-above-EC50/EC85 approach to predict the required exposure of deucrictibant to control attacks prophylactically.

In addition to the RAPIDe-1 on-demand trial, we also conducted a clinical trial of deucrictibant XR tablets to evaluate the effectiveness and safety profile for prophylaxis with bradykinin B2 receptor-inhibition. In our CHAPTER-1 Phase 2 clinical trial, we aimed to achieve the concentrations desired for prophylactic activity with twice-daily dosing of the deucrictibant IR capsules. The trial included an evaluation of HAE patients randomized to placebo or active doses for a 12-week period for prophylactic treatment and demonstrated that the monthly

attack rate was reduced by 84.5% compared to placebo in patients who received 40 mg/day deucrictibant. Patients on deucrictibant treatment also experienced a statistically and clinically meaningful improvement for all secondary endpoints and their quality of life.

Based on the positive results of the primary analysis of CHAPTER-1, we have initiated the confirmatory global Phase 3 trial CHAPTER-3 for the efficacy and safety evaluation of deucrictibant, as described below, in prophylactic treatment of HAE.

In order to provide a differentiated product featuring more consistent exposure of deucrictibant for the prophylactic setting, we have developed an extended-release, or XR, formulation that features continuous slow release maintaining deucrictibant concentrations above the levels we predict to provide protection against attacks. Deucrictibant has demonstrated properties favorable to the development of XR formulations, and we completed several human pharmacokinetics trials with deucrictibant to enable use of this product candidate in the pivotal prophylactic trial CHAPTER-3. With the results of pharmacokinetic trials with XR formulations, we believe we have identified an extended-release formulation of deucrictibant that enables once-daily dosing in a prophylactic setting.

In December 2024, Pharvaris initiated a global, pivotal, randomized, double-blind, placebo-controlled Phase 3 study of orally administered deucrictibant extended-release tablet for the prophylaxis against angioedema attacks in adults and adolescents (12 years and older) with HAE. The study aims to enroll approximately 81 participants with HAE and randomize them in a 2:1 ratio to receive deucrictibant XR tablet (40 mg/day), which is currently the intended commercial dosage, or placebo, once daily for 24 weeks. The primary endpoint of the study is to evaluate the efficacy of deucrictibant compared to placebo for prophylaxis against angioedema attacks as measured by the time-normalized number of investigator-confirmed HAE attacks during the 24-week treatment period. Other objectives of the study include evaluating additional clinically relevant outcomes, deucrictibant's safety and tolerability, pharmacokinetics and its impact on health-related quality of life measures in the prophylactic setting.

In addition, we also plan to run an open-label extension study, CHAPTER-4, in the prophylactic setting which will include participants from the CHAPTER-1 open-label extension, participants who have completed the randomized Phase 3 study, CHAPTER-3, and novel participants to collect long-time safety and efficacy data.

Intellectual Property

We seek to protect and enhance the proprietary technologies, inventions, product candidates, methods of manufacture and methods of usage of our product candidates, and improvements thereof that are commercially important to the development of our business. We protect our proprietary intellectual property by, among other things, filing patent applications in the United States and internationally covering our proprietary technologies, inventions, product candidates, methods of manufacture and use, and improvements that are important to the development and implementation of our business. We will also seek to rely on regulatory protection afforded by orphan drug designations, inclusion in expedited development and review, data exclusivity, market exclusivity and patent term extensions where available.

As of December 31, 2024, we own three U.S. patents and 134 national/regional patents, including in Australia, India, Indonesia, Japan, Mexico, South Korea, France, Germany, Italy, Netherlands, Spain and United Kingdom, that expire on November 23, 2038 or later, and 92 pending patent applications worldwide, including 8 pending U.S. applications, 84 pending non-U.S. applications, including applications in China, Europe and Japan. The U.S. patents, 91 national/regional patents and 14 of our pending patent applications contain composition-of-matter claims to the deucrictibant small molecule and derivatives thereof; deucrictibant is the active pharmaceutical ingredient (API) in, and therefore extends our patents/patent applications to, our deucrictibant product candidates. Each such patent application can generally be categorized into one of three patent families: (1) those relating to the novel bradykinin B2 receptor antagonists, (2) those relating to the cyclic bradykinin B2 receptor antagonists, and (3) those relating to the new cyclic bradykinin B2 receptor antagonists. 10 of our pending applications contain claims directed to the use of deucrictibant in on- demand treatment of HAE and in prophylaxis for HAE and accordingly extend the patent applications to methods of use of the deucrictibant product candidates. 42 granted national/regional patents and 21 of our pending patent applications contain claims directed to the formulation of our IR product candidate. Two of our applications that are pending in the U.S. and Europe contain claims directed to the crystal form of the API. 45 pending national/regional patent applications are directly or indirectly directed to the formulation of our deucrictibant XR product candidate and its use in chronic or prophylactic treatment of HAE. Not accounting for any patent term adjustment, regulatory extension or terminal disclaimers, and assuming that all annuity and/or maintenance fees are paid timely, these patent applications, if granted, will not expire until November 24, 2038. We also rely upon trade secrets that may be important to the development of our business. Trade secrets are difficult to protect and provide us with only limited protection. There can be no assurance that any of our pending patent applications will be issued or that we will benefit from any patent term extension or favorable adjustment to the term of any patents that may be issued in the future.

The term of individual patents depends upon the legal term for patents in the countries in which they are obtained. In most countries in which we have filed, including the U.S., the patent term is 20 years from the earliest filing date of a non-provisional patent application. In the U.S., a patent's term may be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the USPTO in examining and granting a patent or may be shortened if a patent is terminally disclaimed over an earlier filed patent. The term of a patent that covers a drug or biological product may also be eligible for patent term extension when FDA approval is granted for a portion of the term effectively lost as a result of the FDA regulatory review period, subject to certain limitations and provided statutory and regulatory requirements are met.

Any such patent term extension can be for no more than five years, only one patent per approved product can be extended, the extension cannot extend the total patent term beyond 14 years from approval and only those claims covering the approved drug, a method for using it or a method for manufacturing, it may be extended. We may not receive an extension if we fail to exercise due diligence during the testing phase or regulatory review process, fail to apply within applicable deadlines, fail to apply prior to expiration of relevant patents or otherwise fail to satisfy applicable requirements. Moreover, the length of the extension could be less than we request. In the future, if and when our product candidates receive approval from the FDA or foreign regulatory authorities, we expect to apply for patent term extensions

on issued patents we may obtain in the future covering deucrictibant, depending upon the length of the clinical trials for each product and other factors.

As with other biotechnology and pharmaceutical companies, our ability to establish and maintain our proprietary and intellectual property position for our product candidates will depend on our success in obtaining effective patent claims and enforcing those claims if granted. There can be no assurance that any of our current or future patent applications will result in the issuance of patents or that our future issued patents (if any) will provide meaningful protection of our product candidates or technology. For more information regarding the risks related to our intellectual property, see “ITEM 3. KEY INFORMATION—D. Risk factors—Risks Related to Our Intellectual Property.”

License Agreement

On March 31, 2016, we entered into a license agreement (the "BRAIN License"), and a research agreement with BRAIN to collaborate for the development of an orally available bradykinin B2 receptor antagonist. Pursuant to the BRAIN License, we acquired a worldwide, exclusive license from BRAIN to use (i) a certain proprietary substance class of bradykinin B2 receptor antagonists with the potential of oral activity ("OB2RA"), and (ii) any derivatives, improvements, analogs, isomers, metabolites, or conjugates therefrom (together, the "OB2RA Class"), in each case, for the purpose of developing, manufacturing and marketing compounds on a global basis from the OB2RA Class for the treatment of, among others, hereditary angioedema. Certain rights associated with deucrictibant, IR and XR are subject to the BRAIN License. In consideration for the license, we paid BRAIN a non-refundable up-front payment of approximately €0.3 million.

Under the BRAIN License, we are required to make one-time payments in an aggregate amount of up to €11.7 million upon the achievement of certain development, regulatory, and sales milestones. To date, we have paid an aggregate amount of approximately €2.7 million (approximately €0.3 million up-front plus €2.4 million in milestone payments). Under the BRAIN License, up to €9.0 million in aggregate potential milestone payments remain outstanding. In addition, we will be required to pay low to medium single-digit tiered royalties on direct or indirect net sales of licensed products. The royalties that we are required to pay under this agreement may be reduced on a country-by-country and product-by-product basis if sales of a generic version of a product account for 1% or more of the relevant market.

Our agreement with BRAIN will expire, on a product-by-product basis, upon (i) with respect to a royalty-bearing product, the expiry of the last valid claim of a royalty-bearing patent that claims such royalty-bearing product, and (ii) with respect to a licensed product that is not royalty-bearing, the expiry of the last valid claim of a non-royalty-bearing patent that claims such licensed product. Royalty-bearing patents comprise US Patent No. 10.836,748 and any patent or patent application that shares common priority with such patent. Each of deucrictibant, IR and XR is a royalty-bearing product. Not accounting for any regulatory extension or terminal disclaimers, and assuming that all annuity and/ or maintenance fees are paid timely, the applicable expiration date is November 23, 2038. Either party may terminate the agreement prematurely for cause, in particular, for the other party’s (i) uncured material breach, (ii) bankruptcy or insolvency, or (iii) challenge to the validity or ownership of the intellectual property rights relating to the compounds that form the object of the collaboration with BRAIN. If BRAIN were to (a) terminate the BRAIN License for cause and (b) exercise contractual remedies available to it thereunder, then we could be required to grant to BRAIN an exclusive worldwide license to our intellectual property generated under the collaboration with BRAIN for use in all applications, including HAE. In addition, we could be prevented from competing with BRAIN until five years after the commercial launch of any product containing a compound from the OB2RA Class.

Manufacturing and Supply

We currently have two CDMOs for the production of deucrictibant API. A robust and scalable synthetic route has been established. All raw materials can be purchased from multiple suppliers. We also partner with a leading CDMO for the manufacturing of the on-demand treatment product, deucrictibant IR capsules. Another well-established CDMO produces the prophylactic treatment product, deucrictibant XR tablets. A further CDMO with a global footprint is responsible for packaging and worldwide distribution of Clinical Trial Material.

Sales and Marketing

The Pharvaris team, including its founders, have experience developing and commercializing drug products for rare diseases including HAE specifically. We intend to develop a fully integrated sales and marketing organization ahead of marketing approval for deucrictibant IR or deucrictibant XR. Even though HAE is a competitive market, orphan product companies have demonstrated successful first launches

with excellent preparation and execution. We believe that our products will provide patients with significant new treatment options, and we will evaluate options to optimize the commercial opportunity.

Competition

The biotechnology industry is characterized by rapidly advancing technologies, intense competition and a strong emphasis on intellectual property. We face competition from different sources, including from academic centers as well as from a number of large and specialty biotechnology and pharmaceutical companies.

Currently, there are several licensed therapies for HAE, including the following:

- *FIRAZYR*: The bradykinin BR2 receptor antagonist FIRAZYR (icatibant) is approved by the FDA in the U.S. and by regulators globally for the treatment of acute attacks and is administered by subcutaneous administration. Seven generic forms of icatibant have been approved in the U.S. since July 2019 and more may be approved in the future.
- *C1-INH*: C1-INH replacement therapy is available in the U.S. and globally as an acute therapy (BERINERT, CINRYZE, and CETOR) and as a prophylactic therapy (HAEGARDA/BERINERT 2000/3000 and CINRYZE). These therapies are dosed subcutaneously and intravenously. Recombinant C1-INH (RUCONEST) is also available in the U.S. and in Europe as an acute therapy.
- *Kallikrein Inhibitors*: KALBITOR (ecallantide) is a specific recombinant plasma kallikrein inhibitor that is dosed subcutaneously by healthcare providers in the U.S. to treat acute HAE attacks. TAKHZYRO (lanadelumab-flyo) is a monoclonal antibody approved in the U.S. and a growing number of countries for prophylaxis of HAE attacks and can be self-administered as a subcutaneous injection. ORLADEYO (berotralstat) is a kallikrein inhibitor that was approved in the U.S. in the fourth quarter of 2020 and is dosed orally once daily for the prevention of HAE attacks.
- *Anti-factor XIIa mAb:* ANDEMBRY (garadacimab) is an anti-factor XIIa mAb delivered subcutaneously and approved in Europe, Australia, the UK and Japan for use as a prophylactic treatment.
- *Other Medications*: Prophylactic administration of synthetic attenuated androgens (generically available as danazol or stanozolol) has been utilized to reduce the frequency or severity of attacks. However, long-term use of danazol or stanozolol may result in liver damage, virilization and arterial hypertension. Six-month liver function tests, annual lipid profiles, and biennial hepatic ultrasound are recommended for patients on chronic androgen therapy.

We are also aware of a number of HAE therapies in clinical development. Currently, there is one orally delivered plasma kallikrein inhibitor being developed clinically: Kalvista's sebetralstat (KVD900) for acute treatment. In prophylaxis Ionis is developing donidalorsen, an antisense oligonucleotide inhibitor of prekallikrein for prophylactic treatment, which is delivered subcutaneously. Other products in development are STAR-0215 from Astria, a long-lived monoclonal antibody inhibitor of plasma kallikrein dosed subcutaneously, and a gene therapy – NTLA-2002 from Intellia, using CRISPR technology to knock out the gene for prekallikrein.

Many of our competitors and potential competitors have substantially greater scientific, research and product development capabilities as well as greater financial, manufacturing, commercialization and human resources than we do. In addition, there is intense competition on the clinical trial sites and the enrollment of HAE patients for clinical trials. Many specialized biotechnology firms have formed collaborations with large, established companies to support the research, development and commercialization of products that may be competitive with ours, and many other biotech and pharmaceutical companies are competing for the same potential employees. Accordingly, our competitors may be more successful than we may be in developing, manufacturing, commercializing their products and in achieving widespread market acceptance.

Government regulation and product approval

In each country where we conduct our research and development, manufacture our products and intend to market our product candidates, if approved, we must comply with laws and regulations, including regulations issued by regulatory agencies and by other national or supra-national regulatory authorities, or collectively, the Competent Authorities, as well as industry standards, that govern nearly all aspects of our activities. Among others, the FDA, the EMA and the national Competent Authorities of each Member State of the European Union are the key regulatory agencies that exercise oversight over all aspects of our products.

Our pharmaceutical product candidates are subject to substantial requirements that govern, among other things, their research, development, testing, manufacturing, quality control, approval, safety, efficacy, labelling, storage, record keeping, commercialization, distribution, import and export, post-approval monitoring and reporting, advertising, promotion, reimbursement and pricing. The process of maintaining continued compliance with the regulatory requirements requires the expenditure of substantial amounts of time and money.

The nonclinical and clinical development paths for product candidates are broadly similar in the European Union and the United States.

Nonclinical Studies

Development of the product candidates starts with preclinical studies that enable the first-in-human clinical Phase I trial. The preclinical studies include tests for assessment of primary pharmacodynamics (the mode of action), secondary pharmacodynamics, safety pharmacology and general toxicity. Once in clinical development, additional nonclinical *in vivo* and *in vitro* studies are conducted until adequate proof of safety is established (e.g., animal testing for reproductive and general toxicity and carcinogenicity). The conduct of the nonclinical tests and formulation of the compounds for testing must comply with regulations and requirements set by the Competent Authorities, including compliance with GLP. Acceptance of the nonclinical study packages by regulatory agencies is necessary for the initiation and progression of the product candidate through Phase 1, Phase 2, and Phase 3 clinical trials.

Chemical and Pharmaceutical development

Chemical Development entails the development of the laboratory synthesis of the Drug Substance into a scalable process meeting the requirements of reproducibility, robustness, efficiency, and process safety, to manufacture the Drug Substance in high quality. Laboratory tests are conducted to develop a suitable formulation for clinical use and marketing. Pharmaceutical development includes the development of a formulation of the API, stability testing, and a robust Drug Product manufacturing process. The conduct of Chemical and Pharmaceutical development must comply with regulations and requirements set by the Competent Authorities, including compliance with cGMP.

Clinical Studies

Prior to obtaining approval to commercialize a drug candidate, sponsors typically must demonstrate with substantial evidence from well-controlled clinical trials, and to the satisfaction of the Competent Authorities, that such drug candidates are safe and effective for their intended uses. Clinical trials involve the administration of the investigational product to healthy volunteers or subjects under the supervision of a qualified investigator. Clinical trials must be conducted: (i) in compliance with the requirements of the Competent Authorities; (ii) in compliance with GCP, an international standard meant to protect the rights and health of subjects and to define the roles of clinical trial sponsors, administrators, and monitors; as well as (iii) under protocols detailing the objectives of the trial, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated. The number of clinical studies and trials that will be required for approval varies depending on, e.g., the drug candidate and the disease or condition that the drug candidate is designed to address.

Prior to initiating clinical trials, a request for clinical trial authorization (national Competent Authorities in the European Union) or an IND application in the United States must be submitted to the relevant Competent Authorities. These submissions must be supported by an investigational medicinal product dossier or equivalent as detailed in applicable regulations and guidance documents from the Competent Authorities. Extensive information about the proposed clinical studies, as well as the results of the nonclinical tests, together with manufacturing information and analytical data, are included in these submissions. In the United States, a 30-day waiting period after the submission of an IND is required prior to the commencement of clinical testing in humans. If the FDA has neither commented on nor questioned the IND within this 30-day period, the clinical trial proposed in the IND may begin.

Manufacturing of investigational products is subject to authorization and must be carried out in accordance with cGMP. Furthermore, a clinical trial may only be started after an IRB (United States) or a competent Ethics Committee (European Union) has issued a favorable opinion on the clinical trial application.

During all phases of clinical development, Competent Authorities require extensive monitoring and auditing of all clinical activities, clinical data and clinical trial investigators. Annual progress reports detailing the progress of the clinical trials must be submitted to the Competent Authorities. Important new safety information, that suggests a significant risk for human patients, or any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure, must also be provided to clinical investigators.

The Competent Authorities, sponsor or its data safety monitoring board may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research exposes patients to an unacceptable health risk. Similarly, an IRB or Ethics Committee can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the institutional requirements or if the drug candidate has been associated with unexpected serious harm to patients.

The following section describes specific regulatory regimes and regulations applicable in certain jurisdictions.

United States

U.S. Food and Drug Administration

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FFDCA, and implementing regulations. These laws, govern, among other things, the research, development, testing, manufacture, storage, recordkeeping, approval, labeling, promotion and marketing, distribution, post-marketing monitoring and reporting, sampling, and import and export of drug products. The process of obtaining regulatory approvals and the subsequent compliance with the many statutory and regulatory provisions require the expenditure of substantial time and financial resources. Failure to comply with applicable U.S. requirements may subject a company to a

variety of administrative or judicial sanctions, such as clinical hold, FDA refusal to approve pending regulatory applications, warning or untitled letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, civil penalties, and criminal prosecution.

The FDA Approval Process

Clinical trials to support NDAs for marketing approval are typically conducted in three sequential phases, but the phases may overlap. In Phase 1, the initial introduction of the product candidate is usually into healthy human subjects, and the product candidate is tested to assess metabolism, pharmacokinetics, pharmacological actions, side effects associated with increasing doses, and, if possible, early evidence on effectiveness. Phase 2 usually involves trials in a limited patient population to determine the effectiveness of the product candidate for a particular indication, dosage tolerance, and optimal dosage, and to identify common adverse effects and safety risks. If a product candidate demonstrates evidence of effectiveness and an acceptable safety profile in Phase 2 evaluations, Phase 3 trials are undertaken to obtain additional information about clinical efficacy and safety in a larger number of subjects, typically at geographically dispersed clinical trial sites, to permit the FDA to evaluate the overall benefit-risk relationship of the product candidate and to provide adequate information for the labeling of the product candidate. In most cases, the FDA requires two adequate and well-controlled Phase 3 clinical trials to demonstrate the efficacy of the product candidate. A single Phase 3 trial may be sufficient in certain circumstances.

During the development of a new product candidate, sponsors are given opportunities to meet with the FDA at certain points; specifically, prior to the submission of an IND, at the end of Phase 2 and before an NDA is submitted. Meetings at other times may be requested. These meetings can provide an opportunity for the sponsor to share information about the data gathered to date and for the FDA to provide advice on the next phase of development. Sponsors typically use the meeting at the end of Phase 2 to discuss their Phase 2 clinical results and present their plans for the pivotal Phase 3 clinical trials that they believe will support the approval of the new product candidate.

The results of drug candidate development, nonclinical testing, clinical trials and proposed labeling are submitted to the FDA as part of the NDA. An NDA must include all information regarding and data from pertinent nonclinical and clinical studies, including negative or ambiguous results as well as positive findings, together with detailed information relating to the drug's chemistry, manufacturing and controls. The FDA will accept, as support for an IND or NDA a well-designed, well-conducted, non-IND foreign clinical trial if it was conducted in accordance with GCP and the FDA is able to validate the data from the trial through an on-site inspection, if necessary. Regulatory applications based solely on foreign clinical data meeting these criteria may be approved if the foreign data are applicable to the U.S. population and U.S. medical practice, the trials have been performed by clinical investigators of recognized competence, and the data may be considered valid without the need for an on-site inspection by FDA or, if FDA considers such an inspection to be necessary, FDA is able to validate the data through an on-site inspection or other appropriate means. Failure of an application to meet any of these criteria may result in the application not being approvable based on the foreign data alone. To support marketing approval and authorization, the data submitted must be sufficient in quality and quantity to establish the safety and effectiveness of the investigational drug to the FDA's satisfaction.

The cost of preparing and submitting an NDA is substantial. The submission of most NDAs is additionally subject to a substantial application user fee payment to the FDA, and the manufacturer and/or sponsor under an approved NDA are also subject to certain annual program user fees. The FDA typically increases these fees annually.

The FDA has 60 days from its receipt of an NDA to determine whether it will accept the application for filing based on the agency's threshold determination that the application is sufficiently complete to permit substantive review. The FDA may refuse to file any NDA that it deems incomplete or not properly reviewable at the time of submission and may request additional information. In this event, the NDA must be resubmitted with the additional information and the resubmitted application also is subject to review before the FDA accepts it for filing. Once the FDA accepts the filing, the FDA begins an in-depth review. The FDA has agreed to certain performance goals in the review of NDAs. Under the Prescription Drug User Fee Act, the FDA has a goal of responding to standard review NDAs within ten months from the 60-day filing date. The review process may be extended by the FDA for three additional months to consider certain late-submitted information, or information intended to clarify information already provided in the submission. This late-submitted information is typically requested by the FDA.

The FDA may also refer applications for novel drugs or product candidates that present difficult questions of safety or efficacy, to an FDA Advisory Committee. An Advisory Committee is an outside panel that typically includes clinicians and other experts in the field that will review and evaluate the questions posed by the FDA, and provide recommendations, sometimes including whether the FDA should approve the application. The FDA is not bound by the recommendation of an Advisory Committee, but it generally follows such recommendations.

Before approving an NDA, the FDA will typically inspect one or more clinical study sites to assure compliance with GCP. The FDA may also inspect one or more nonclinical study sites. In addition, the FDA will inspect the facility or the facilities involved in the manufacture of the drug to determine if the facilities, processes and quality are compliant with cGMP. The FDA will not approve an NDA unless compliance with cGMP is satisfactory.

After the FDA evaluates the NDA and the manufacturing facilities, it issues either an approval letter or a complete response letter. A complete response letter indicates that the FDA has completed its review of the NDA, and the agency has determined that it will not approve the application in its present form. A complete response letter generally outlines the deficiencies in the NDA, which may be minor or substantial, and may delineate the requirements needed to successfully progress the NDA to approval. This may require substantial

additional clinical data and/or other significant, expensive, and time-consuming requirements related to clinical studies, nonclinical studies and/or manufacturing. If a complete response letter is issued, the applicant may either resubmit the NDA, addressing the deficiencies identified in the letter, or withdraw the application. The FDA has committed to reviewing resubmissions of the NDA addressing such deficiencies in two or six months, depending on the type of information included. Even if such data is submitted, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval.

An approval letter authorizes commercial marketing of the drug, with specific prescribing information for specific indications. Even if FDA approves the NDA, the approval may be significantly limited to specific indications and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the product. Further, the FDA may require that certain contraindications, warnings or precautions be included in the product labeling. The FDA may impose restrictions and conditions on product distribution, prescribing, or dispensing in the form of a risk evaluation and mitigation strategy, or REMS, or otherwise limit the scope of any approval. REMS can include medication guides, communication plans for healthcare professionals, and elements to assure safe use, or ETASU. ETASU can include, but is not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring, and the use of patient registries. The requirement for a REMS can materially affect the potential market and profitability of the product. In addition, the FDA may require confirmatory post-marketing trials, sometimes referred to as “Phase 4” clinical trials, designed to further assess a product’s safety and effectiveness, and testing and surveillance programs to monitor the safety of approved products that have been commercialized.

Expedited Approval in the U.S.

The FDA has a number of programs that are intended to facilitate and expedite development and review of new drugs to address unmet medical need in the treatment of a serious or life-threatening condition. These are: Fast Track Designation, Breakthrough Therapy Designation, Accelerated Approval and Priority Review Designation.

Fast Track Designation can be requested early in the development process, if evidence of activity in a nonclinical model, a mechanistic rationale or pharmacologic data demonstrates the potential to address an unmet medical need. In the later stages of development, available clinical data should demonstrate the potential to address an unmet medical need. Fast Track Designation provides opportunities for applicants to have frequent interactions with the relevant FDA review teams. In addition, a fast-track product can be eligible for priority review if supported by clinical data at the time of NDA submission. If the FDA determines that a fast-track product may be effective after preliminary evaluation of the NDA, it may consider reviewing portions of a marketing application before the sponsor submits the complete application. Fast Track Designation can be requested after the IND is first submitted but before receiving approval of the NDA. As a practical matter, the FDA should ordinarily receive a Fast Track Designation request no later than the sponsor’s pre-NDA meeting with the agency because many of the features of Fast Track Designation will not apply after that time. The FDA will respond to Fast Track Designation requests within 60 calendar days of receipt of the request.

The FDA’s Breakthrough Therapy Designation is intended to expedite the development and review of drugs which may demonstrate substantial improvement over available therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. A drug that receives Breakthrough Therapy Designation is eligible for all Fast Track Designation features, intensive guidance from FDA on an efficient drug development program, beginning as early as Phase 1, and organizational commitment involving senior managers. Breakthrough Therapy Designation is requested by the manufacturer. A sponsor needs to submit a request to the agency for Breakthrough Therapy Designation, but in some cases the FDA may suggest that the sponsor consider submitting a request after reviewing submitted data and information (including preliminary clinical evidence), the FDA thinks the drug development program may meet the criteria for Breakthrough Therapy Designation; and the remaining drug development program can benefit from the designation. Ideally, a Breakthrough Therapy Designation request should be received by the FDA no later than the End-of-Phase 2 meetings if any of the features of the designation are to be obtained. The FDA will respond to Breakthrough Therapy Designation requests within 60 days of receipt of the request.

Accelerated approval may be granted for a product based upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, or IMM, that is reasonably likely to predict an effect on IMM or other clinical benefit, taking into account the severity, rarity or prevalence of the condition and the availability or lack of alternative treatments. For drugs granted accelerated approval, post-marketing confirmatory trials will be required to verify and describe the anticipated effect on the IMM or other clinical benefit. The accelerated approval pathway has been used primarily in settings in which the disease course is long, and an extended period of time would be required to measure the intended clinical benefit of a drug. Accelerated approval is also potentially useful in acute disease settings where the intended clinical benefit can be demonstrated only in a very large study because the clinical event that would need to be evaluated to demonstrate clinical benefit occurs rarely.

The FDA may withdraw approval of a drug or indication approved under the accelerated approval pathway if e.g., the confirmatory trial fails to verify the predicted clinical benefit, the evidence demonstrates that the product is not shown to be safe and effective under the conditions of use, the applicant fails to conduct the post-approval trials with due diligence or the applicant disseminates false or misleading promotional materials related to the product.

A priority review designation is intended to direct overall attention and resources to the evaluation of an application for a drug that treats, prevents or is used in the diagnosis of a serious condition and if approved would provide a significant improvement in safety or effectiveness. Eligibility for priority review is determined by the FDA at the time of an NDA or efficacy supplement filing. Where an application receives a priority review designation, the FDA’s goal is to take action on the marketing application within six months from the

60-day filing date (as compared to within 10 months under standard review). The FDA determines whether an application qualifies for priority review (versus standard review) for every application it reviews, not just when priority review is requested by the applicant. However, an applicant may expressly request priority review. The FDA will inform the applicant in writing of a priority review designation by day 60 of the review.

Orphan Designation

An orphan drug designation qualifies the manufacturer for certain tax credits and may lead to market exclusivity for seven years following the date of the drug's approval by the FDA. The FDA provides that a drug shall be designated as an orphan drug if its manufacturer can establish that the drug is for a condition that affects fewer than 200,000 individuals in the United States or when there is no reasonable expectation that the cost of developing and making available the drug for the disease or condition will be recovered from sales of the drug in the United States. More than one manufacturer may receive orphan drug designation for the same drug for the same rare disease or condition, but each manufacturer seeking orphan drug designation must file a complete request for designation.

In the United States, a manufacturer may request orphan drug designation of a previously unapproved drug or new orphan indication for a different use for an already marketed drug. In addition, a manufacturer of a drug that is otherwise the same drug as an already approved orphan drug may seek and obtain orphan drug designation for the subsequent drug for the same rare disease or condition if it can present a plausible hypothesis that its drug may be clinically superior to the first drug. FDA may grant the drug orphan exclusivity upon approval, if clinical superiority is demonstrated. Orphan drug exclusivity cannot otherwise be granted for the same drug made by another manufacturer for the same indication during the market exclusivity period unless the original manufacturer consents or the original manufacturer is unable to ensure the availability of sufficient quantities of the drug to meet the needs of persons with the disease or condition for which the drug was designated.

An application for orphan drug designation can be made any time prior to the filing of an application for approval to market the product. The period of orphan exclusivity, if granted, begins on the date that the marketing application is approved. The exclusivity is limited to the indication for which the drug has been approved.

Post-Marketing Requirements

FDA may withdraw approval of an NDA if compliance with regulatory requirements is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product may result in restrictions on the product, product recalls or even complete withdrawal of the product from the market.

After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further FDA review and approval; such changes may require the approval of a new NDA or an NDA supplement. An NDA supplement for a new indication typically requires clinical data similar to that in the original application, and the FDA uses the same procedures and actions in reviewing NDA supplements as it does in reviewing new NDAs. As with new NDAs, the FDA often significantly extends the review process with requests for additional information or clarification. In addition, the FDA may, under some circumstances, require testing and surveillance programs to monitor the effect of approved products that have been commercialized, and the FDA under some circumstances has the power to prevent or limit further commercialization of a product based on the results of these post-marketing programs.

In addition, drug products manufactured or distributed pursuant to the FDA approvals, are subject to additional and continuing regulation by the FDA, including, among other things:

- record-keeping requirements;
- reporting of adverse experiences associated with the product;
- providing the FDA with updated safety and efficacy information;
- distribution of drug samples;
- notifying the FDA and gaining its approval of specified manufacturing or labeling changes;
- drug establishment registration and drug listing requirements; and
- complying with FDA promotion and advertising requirements, which include, among other things, standards for direct-to-consumer advertising, restrictions on promoting products for uses or in patient populations that are not described in the product's approved labeling, limitations on industry-sponsored scientific and educational activities and requirements for promotional activities involving the internet.

Drug manufacturers are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP requirements and other laws. There are strict regulations regarding changes to the manufacturing process, and, depending on the significance of the change, it may require prior FDA approval before it can be implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon drug manufacturers. Drug manufacturers must also satisfy the product tracing, verification and reporting requirements in the Drug Quality and Security Act and have procedures in place to identify and properly handle suspect and illegitimate products. Accordingly, manufacturers must continue to spend

time, money and effort in the area of production, distribution and quality control to maintain compliance with cGMP and other aspects of regulatory compliance.

Sponsors of clinical trials of FDA-regulated products are required to register and disclose certain clinical trial information. Information related to the product, patient population, phase of investigation, trial sites and investigators, and other aspects of the clinical trial is then made public as part of the registration. Sponsors are also obligated to disclose the results of their clinical trials after completion. Disclosure of the results of these trials can be delayed in certain circumstances for up to two years after the date of completion of the trial. Competitors may use this publicly available information to gain knowledge regarding the progress of development programs.

Although rare, the FDA may withdraw approval of an NDA if a company does not comply with its extensive regulatory requirements or if significant safety, efficacy or manufacturing issues arise after the drug reaches the market. More typically, if a company or the FDA discovers previously unknown problems with a drug, including adverse events of unanticipated severity or frequency or issues with manufacturing processes, the FDA may revise the approved labeling to add new safety information; require additional clinical studies to assess new safety risks; or impose distribution or other restrictions under a REMS program. Other potential consequences may include:

- restrictions on the commercialization or manufacturing of the drug, market withdrawals or recalls;
- fines, warning letters or holds on post-approval clinical studies;
- the FDA refusal to approve pending NDAs or supplements to approved NDAs;
- drug seizure or detention, or refusal to permit the import or export of drugs; or
- injunctions or the imposition of civil or criminal penalties.

From time to time, legislation is drafted, introduced and passed in Congress that could significantly change the statutory provisions governing the testing, approval, manufacturing and marketing of products regulated by the FDA. In addition to new legislation, FDA regulations and policies are often revised or interpreted by the agency in ways that may significantly affect our business and product candidates. It is impossible to predict whether further legislative changes will be enacted or whether FDA regulations, guidance, policies or interpretations will be changed or what the effect of such changes, if any, may be.

U.S. Patent Term Restoration

A patent claiming a new product may be eligible for a limited patent term extension under the Hatch-Waxman Act, which permits a patent restoration of up to five years for patent term lost during product development and FDA regulatory review. The restoration period granted on a patent covering a product is typically one-half the time between the effective date of a clinical investigation involving human beings is begun and the submission date of an application, plus the time between the submission date of an application and the ultimate approval date. Patent term restoration cannot be used to extend the remaining term of a patent past a total of 14 years from the product's approval date. Only one patent applicable to an approved product and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended. In addition, the application for the extension must be submitted prior to the expiration of the patent in question. A patent that covers multiple products for which approval is sought can only be extended in connection with one of the approvals. The USPTO reviews and approves the application for any patent term extension or restoration in consultation with the FDA.

Other U.S. Healthcare Laws and Compliance Requirements

In the United States, our activities are potentially subject to regulation by various federal, state and local authorities in addition to the FDA, including but not limited to, the Centers for Medicare and Medicaid Services, or CMS, other divisions of the U.S. Department of Health and Human Services (*e.g., the Office of Inspector General), the U.S. Department of Justice, or DOJ, and individual U.S. Attorney offices within the DOJ, and state and local governments. For example, sales, marketing and scientific/educational grant programs are subject to anti-fraud and abuse provisions of the Social Security Act, the false claims laws, the privacy provisions of HIPAA, transparency reporting laws, and similar state laws, each as amended. Healthcare providers and third-party payors play a primary role in the recommendation and prescription of drug products that are granted marketing approval. Arrangements with providers, consultants, third-party payors and customers are subject to these broadly applicable healthcare laws and regulations that may constrain our business and/or financial arrangements.*

The applicable federal and state healthcare laws and regulations, include, without limitation, the following:

- *The Federal Anti-Kickback Statute* – An intent-based federal criminal statute that prohibits, among other things, any person or entity, from knowingly and willfully offering, paying, soliciting or receiving any remuneration, directly or indirectly, overtly or covertly, 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, recommendation, or arranging of, any item or service for which payment may be made, in whole or in part, by a federal health care program such as Medicare or Medicaid. The term "remuneration" has been interpreted broadly to include anything of value. The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act ("the PPACA"), among other things, amended the intent requirement of the federal Anti-Kickback Statute to clarify that a person or entity need not have actual knowledge of this statute or specific intent to violate it. The 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. A conviction for violation of the Anti-Kickback Statute can result in criminal fines and/or imprisonment and requires mandatory exclusion from participation in federal

health care programs. Exclusion may also be imposed if the government determines that an entity has committed acts that are prohibited by the Anti-Kickback Statute. Although there are a number of statutory exceptions and regulatory safe harbors to the federal Anti-Kickback Statute that protect certain common industry activities from prosecution, the exceptions and safe harbors are drawn narrowly and arrangements may be subject to scrutiny or penalty if they do not fully satisfy all elements of an available exception of safe harbor. The Anti-Kickback Statute safe harbors are the subject of possible regulatory reforms. Any changes to the safe harbors may impact our future contractual and other arrangements with pharmacy benefit managers, group purchasing organizations, third-party payors, wholesalers and distributors, healthcare providers and prescribers, and other entities, as well as our future pricing strategies.

- *The Federal Civil False Claims Act*—Imposes civil penalties, including through civil whistleblower or *qui tam* actions, against individuals or entities for, among other things, knowingly presenting, or causing to be presented, false or fraudulent claims for payment to a federal health care program or knowingly making using or causing to be made or used a false statement or record material to payment of a false claim or avoiding, decreasing or concealing an obligation to pay money to the federal government, with potential liability including mandatory treble damages and significant per-claim penalties, currently set at $11,665 to $22,331 per false claim or statement for penalties assessed after June 19, 2020, with respect to violations occurring after November 2, 2015. Pharmaceutical companies have been investigated and/or subject to government enforcement actions asserting liability under the federal civil False Claims Act in connection with their alleged off-label promotion of drugs, purportedly concealing price concessions in the pricing information submitted to the government for government price reporting purposes (e.g., under the Medicaid Drug Rebate Program), and allegedly providing free product to customers with the expectation that the customers would bill federal health care programs for the product. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal False Claims Act. As a result of a modification made by the Fraud Enforcement and Recovery Act of 2009, a claim includes “any request or demand” for money or property presented to the U.S. government. In addition, manufacturers can be held liable under the federal False Claims Act even when they do not submit claims directly to government payors if they are deemed to “cause” the submission of false or fraudulent claims. There is also the Federal Criminal False Claims Act, which is similar to the Federal Civil False Claims Act and imposes criminal liability on those that make or present a false, fictitious or fraudulent claim to the federal government.
- *The Federal Criminal Statute on False Statements Relating to Health Care Matters*—Makes it a crime to knowingly and willfully falsify, conceal, or cover up a material fact, make any materially false, fictitious, or fraudulent statements or representations, or make or use any materially false writing or document knowing the same to contain any materially false, fictitious, or fraudulent statement or entry in connection with the delivery of or payment for healthcare benefits, items, or services.
- *Criminal Health Care Fraud Statute*—Enacted as part of the HIPAA, makes it a crime to knowingly and willfully execute, or attempt to execute, a scheme or artifice to defraud any health care benefit program or to obtain, by means of false or fraudulent pretenses, representations or promises, any money or property owned by, or under the control or custody of, any healthcare benefit program in connection with the delivery of or payment for healthcare benefits, items or services.
- *The Federal Civil Monetary Penalties Law*—Authorizes the imposition of substantial civil monetary penalties against an entity, such as a pharmaceutical manufacturer, that engages in activities including, among others (1) knowingly presenting, or causing to be presented, a claim for services not provided as claimed or that is otherwise false or fraudulent in any way; (2) arranging for or contracting with an individual or entity that is excluded from participation in federal health care programs to provide items or services reimbursable by a federal health care program; (3) violations of the federal Anti-Kickback Statute; or (4) failing to report and return a known overpayment.
- *HIPAA Health Information Privacy and Security*—HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 ("HITECH"), imposes privacy, security, and breach reporting obligations on certain covered entity healthcare providers, health plans, and healthcare clearinghouse as well as their business associates that perform certain services involving the use or disclosure of individually identifiable health information, including, among other requirements, mandatory contractual terms and technical safeguards to protect the privacy, security and transmission of individually identifiable health information, and require notification to affected individuals and regulatory authorities of certain breaches of security of individually identifiable health information. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in U.S. federal courts to enforce the federal HIPAA laws and seek attorneys’ fees and costs associated with pursuing federal civil actions. In addition, state laws govern the privacy and security of health information in specified circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.
- *The Federal Physician Payments Sunshine Act*—Requires “applicable manufacturers” of drugs, devices, biologics, and medical supplies for which payment is available under Medicare, Medicaid or the State Children’s Health Insurance Program, among others, to track and report annually to the federal government (for disclosure to the public) certain payments and other transfers of value they make to “covered recipients.” The term covered recipients includes U.S.-licensed physicians, teaching hospitals, and, for reports submitted on or after January 1, 2022, physician assistants, nurse practitioners, clinical nurse specialists, certified nurse anesthetists, and certified nurse midwives. Failure to submit required information may result in civil monetary penalties.
- *Analogous State Laws*—There are state law equivalents of the above federal laws, such as the Anti-Kickback Statute and the False Claims Act, which may apply to items and services reimbursed by any third-party payor, including commercial insurers (*i.e.*, so-called “all-payor anti-kickback laws”).

- *State Laws* Regulating *Pharmaceutical Manufacturer Compliance Programs, Drug Price Transparency, and Other Practices*—Some state laws require pharmaceutical companies to implement compliance programs, comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, or to track and report gifts, compensation, or other remuneration to physicians and other healthcare providers. Several U.S. states and localities have enacted legislation requiring pharmaceutical companies to establish marketing compliance programs, file periodic reports, and/or make periodic public disclosures on sales, marketing, pricing, clinical trials, and other activities. Other state laws prohibit certain marketing-related activities including the provision of gifts, meals or other items to certain healthcare providers, and restrict the ability of manufacturers to offer co-pay support to patients for certain prescription drugs. In addition, several recently passed state laws require disclosures related to state agencies and/or commercial purchasers with respect to certain price increases that exceed a certain level as identified in the relevant statutes. Some of these laws and regulations contain ambiguous requirements that government officials have not yet clarified. Given the lack of clarity in the laws and their implementation, our reporting actions could be subject to the penalty provisions of the pertinent federal and state laws and regulations.
- We are also required to satisfy the product tracing, verification and reporting requirements set out in the Drug Quality and Security Act.

We expect that one or more of our products, if approved, may be eligible for coverage under Medicare, the federal health care program that provides health care benefits to the aged and disabled, including coverage for outpatient services and supplies, such as certain drug products, that are medically necessary to treat a beneficiary's health condition. In addition, one or more of our products, if approved, may be covered and reimbursed under other federal health care programs, such as Medicaid and the 340B Drug Pricing Program. The Medicaid Drug Rebate Program requires pharmaceutical manufacturers to enter into and have in effect a national rebate agreement with the Secretary of the Department of Health and Human Services and pay quarterly rebates based on utilization of the manufacturer's drugs under the program as a condition for states to receive federal matching funds for the manufacturer's outpatient drugs furnished to Medicaid patients. Under the 340B Drug Pricing Program, the manufacturer must extend discounts to entities that participate in the program. As part of the requirements to participate in these government programs, many pharmaceutical manufacturers must calculate and report certain price reporting metrics to the government, such as average manufacturer price and best price.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations, guidance, case law or other applicable law. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, individual imprisonment, exclusion from participation in federal health care programs, such as Medicare and Medicaid, disgorgement, reputational harm, additional oversight and reporting obligations pursuant to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with applicable laws and regulations, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to market our products, if approved, and adversely impact our financial results. Although effective compliance programs can mitigate the risk of investigation and prosecution for violations of these laws and regulations, these risks cannot be entirely eliminated. Any action against us for an alleged or suspected violation could cause us to incur significant legal expenses and could divert our management's attention from the operation of our business, even if our defense is successful. If any of the physicians or other healthcare providers or entities with whom we expect to do business is found not to be in compliance with applicable laws, it may be costly to us in terms of money, time and resources, and they may be subject to criminal, civil or administrative sanctions, including exclusions from government-funded healthcare programs.

U.S. Healthcare Reform

In the United States, there have been and continue to be a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability, or the ability of our future collaborators, to effectively sell any drugs for which we, or they, obtain marketing approval. We expect that current laws, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and additional downward pressure on the price that we, or our future collaborators, may receive for any approved drugs. For example, the PPACA substantially changed and continues to impact healthcare financing and delivery by both government payors and private insurers. Among the PPACA provisions of importance to the pharmaceutical industry, in addition to those otherwise described above, 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 statutory minimum rebates a manufacturer must pay under the 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 False Claims Act and the Anti-Kickback Statute, which include, among other things, new government investigative powers and enhanced penalties for non-compliance;
- establishment of the Medicare Part D coverage gap discount program that, as a condition for the manufacturers' outpatient drugs to be covered under Medicare Part D, requires manufacturers to provide a now 70% point-of-sale discount off the negotiated price of applicable brand drugs to eligible beneficiaries during their coverage gap period;

- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals, thereby potentially increasing manufacturers' Medicaid rebate liability;
- expansion of the types of entities eligible for discounts under the Public Health Service pharmaceutical pricing program (*i.e.*, the 340B program);
- reporting of certain financial arrangements between manufacturers of drugs, biologics, devices, and medical supplies and physicians and teaching hospitals under the Physician Payments Sunshine Act;
- a requirement to annually report certain information regarding drug samples that manufacturers and distributors provide to licensed practitioners; and
- creation of the Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

Since its enactment there have been judicial and Congressional challenges to certain aspects of the PPACA to repeal or replace certain aspects of the PPACA.

While Congress has not enacted legislation to comprehensively repeal the PPACA, at least two bills affecting the implementation of the PPACA have been signed into law, including the repeal, effective January 1, 2019, of the tax-based shared responsibility payment imposed by the PPACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year, which is commonly referred to as the "individual mandate." In December 2018, a federal district court in Texas ruled that the PPACA's individual mandate, without the penalty that was repealed effective January 1, 2019, was unconstitutional and could not be severed from the PPACA. As a result, the court ruled the remaining provisions of the PPACA were also invalid. The Fifth Circuit Court of Appeals affirmed the district court's ruling that the individual mandate was unconstitutional, but it remanded the case back to the district court for further analysis of whether the mandate could be severed from the PPACA (i.e., whether the entire PPACA was therefore also unconstitutional). The Supreme Court of the United States granted certiorari on March 2, 2020, heard oral arguments on November 10, 2020, and on June 17, 2021, issued its opinion ruling that Texas and other states that initially challenged the individual mandate did not have standing.

During his tenure, President Trump also signed several Executive Orders, directives, and legislation affecting certain provisions of the PPACA. For example, effective January 1, 2019, the Bipartisan Budget Act of 2018, or the BBA, among other things, further amended portions of the Social Security Act implemented as part of the PPACA to increase from 50% to 70% the point-of-sale discount that pharmaceutical manufacturers who participate in the Medicare Part D Coverage Gap Discount Program must provide to eligible Medicare Part D beneficiaries during the coverage gap phase of the Part D benefit, commonly referred to as the "donut hole," and to reduce standard beneficiary cost sharing in the coverage gap from 30% to 25% in most Medicare Part D plans. Additionally, on December 20, 2019, President Trump signed appropriations legislation for fiscal year 2020 that repealed the PPACA's so-called "Cadillac" tax on certain high-cost employer-sponsored health insurance plans, for tax years beginning after December 31, 2019; the annual fee imposed on certain health insurance providers, for calendar years beginning after December 31, 2020; and the medical device excise tax on non-exempt medical devices, for sales after December 31, 2019. While the Biden administration has repealed or rolled-back certain of the actions taken by the Trump administration, in the future, there may be additional challenges and/or amendments to the PPACA. It remains to be seen precisely what any new legislation will provide, when or if it will be enacted, and what impact it will have on the availability and cost of healthcare items and services, including drug products.

In addition, other legislative changes have been proposed and adopted since the PPACA was enacted. These changes include the Budget Control Act of 2011, which, among other things, led to aggregate reductions to Medicare payments to providers of up to 2% per fiscal year effective April 1, 2013 and, due to subsequent legislation, will stay in effect through 2030 unless additional Congressional action is taken, with the exception of a temporary suspension of the payment reduction from May 1, 2020 through December 31, 2020 enacted as part of the CARES Act. Further, the American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to several types of providers and increased the statute of limitations period for the government to recover overpayments from providers from three to five years. These legislative changes may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used.

Further, there has been heightened governmental scrutiny recently over the manner in which drug manufacturers set prices for their marketed products in the United States. Congress is considering various legislative proposals to further increase transparency around prices and price increases, lower out-of-pocket costs for consumers, and decrease spending on prescription drugs by government programs. On September 13, 2020, President Trump issued an executive order directing the Secretary of Health and Human Services to pursue implementation of two new payment models under which Medicare would test whether paying no more than the "most-favored-nation" price for certain included drugs and biological products covered under Part B and Part D, respectively, would mitigate poor clinical outcomes and increased Medicare expenditures associated with high drug costs. If this executive order is implemented, the "most-favored-nation" price would generally reflect the lowest price, after certain adjustments, for a pharmaceutical product sold in an economically comparable member country of the Organisation for Economic Co-operation and Development. On December 28, 2020, the U.S. District Court for the Northern District of California issued a preliminary injunction halting implementation of the executive order nationwide pending completion of the notice and comment process, and on August 10, 2021, the CMS published a proposed rule that would rescind the "most-favored nation" pricing model for Medicare Part B drugs. However, the U.S. Congress continues to conduct inquiries into the prescription drug industry's pricing practices, and at the state level in the United States, legislatures are also increasingly passing legislation and states are implementing regulations designed to control spending on, and patient out of pocket costs for, drug products. Recently, on August 16, 2022, President Biden signed into law the IRA, which included several measures intended to lower the cost of prescription drugs and limit

out-of-pocket spending, including by requiring drug manufacturers to pay rebates to Medicare if they increase prices faster than inflation for drugs used by Medicare beneficiaries. We cannot be certain what impact, if any, such changes will have on the profitability of any of our drug candidates, if approved for commercial use in the future.

At the state level, legislatures are increasingly passing legislation and states are implementing regulations designed to control spending on, and patient out-of-pocket costs for, drug products. Implementation of cost containment measures or other healthcare reforms that affect the pricing and/or availability of drug products may impact our ability to generate revenue, attain or maintain profitability, or commercialize products for which we may receive regulatory approval in the future.

We expect that these, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and additional downward pressure on the price that we receive for any approved drug. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. 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.

Privacy and Information Security

We may be subject to privacy and data security regulations and legal requirements in the United States and Europe. As we become more dependent on information technologies to conduct our operations, cyber incidents, including deliberate attacks and attempts to gain unauthorized access to computer systems and networks, may increase in frequency and sophistication. Our systems, servers and platforms and those of our service providers may be vulnerable to privacy and information security incidents such as data breaches, viruses or other malicious code, coordinated attacks, data loss, phishing attacks, ransomware, denial of service attacks, or other security or IT incidents caused by threat actors, technological vulnerabilities or human error. If we, or any of our vendors that support our IT or have access to our data, including any third-party vendors that collect, process and store personal data on our behalf, fail to comply with laws requiring the protection of personal information, or fail to safeguard and defend personal information or other critical data assets or IT systems, we may be subject to regulatory enforcement and fines as well as private civil actions. We may be required to expend significant resources in the response, containment, mitigation of cybersecurity incidents as well as in defense against claims that our information security was unreasonable or otherwise violated applicable laws or contractual obligations.

In the United States, numerous federal and state laws and regulations, including federal health information privacy laws, state data breach notification laws, state health information privacy laws and federal and state consumer protection laws (*e.g.*, Section 5 of the Federal Trade Commission Act), that govern the collection, use, disclosure and protection of health-related and other personal information could apply to our operations or the operations of our collaborators.

Domestic laws in this area are complex and developing rapidly. Many state legislatures have adopted legislation relating to privacy, data security and data breaches. Laws in all 50 states require businesses to provide notice to customers whose personally identifiable information has been disclosed as a result of a data breach. The laws are not consistent, and compliance in the event of a widespread data breach is costly. States are also frequently amending existing laws, requiring attention to frequently changing regulatory requirements.

Additionally, the Federal Trade Commission, or FTC, and state attorneys general enforce consumer protection laws that prohibit unfair and deceptive acts and practices, including Section 5 of the FTC Act, which creates standards for the collection, use, dissemination and security of health-related and other personal information. Claims of unfair or deceptive trade practices regarding privacy and security can lead to significant liabilities and consequences, including regulatory investigations, penalties, fines and orders as well as civil claims, which could impact our data practices and operations or cause reputational damage.

Further, HIPAA, as amended by the HITECH, and its implementing regulations, imposes requirements relating to the privacy, security and transmission of individually identifiable health information. Among other things, HITECH makes HIPAA's security standards directly applicable to business associates, independent contractors or agents of covered entities that receive or obtain protected health information in connection with providing a service on behalf of a covered entity.

HITECH also created four new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys' fees and costs associated with pursuing federal civil actions. In addition, state laws govern the privacy and security of health information in specified circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

It is important to note, however, that HIPAA and HITECH only apply directly to "covered entities" (healthcare providers, health insurance plans, and healthcare clearinghouses) and "business associates" (third parties providing services to covered entities). Pharvaris, as a private pharmaceutical company sponsoring clinical research, is itself neither a covered entity nor a business associate within the meaning of these laws and their associated regulations. With that in mind, in respect of HIPAA and HITECH, the risk to Pharvaris primarily lies in the potential lack of compliance by investigators and their service providers may result in the regulators invalidating the sharing of personal health information between investigators and Pharvaris. In other words, the failure of Pharvaris's research partners to comply with these laws could lead to the exclusion of important data from Pharvaris studies.

In addition, state laws in U.S. states, govern the privacy and security of health information in specified circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

We also may be subject to privacy and data security requirements in Europe. Any clinical trial programs we conduct or research collaborations we enter into in the European Economic Area, or EEA, may subject us to European data protection laws, including the EU General Data Protection Regulation 2016/679, or GDPR. We are subject to the GDPR (as implemented by countries in the EEA), which applies extra-territorially and imposes onerous requirements on controllers (e.g., sponsors) and processors (e.g., CROs, laboratories, third-party vendors) of EEA personal data, including, for example: (i) accountability, transparency and accuracy requirements, and enhanced requirements for obtaining valid consent (separate and apart from informed medical consent); (ii) obligations to consider data protection as any new products or services are developed and to limit the amount of personal data processed; (iii) obligations to comply with data protection rights of data subjects; (iv) ensuring that all processors that process personal data on our behalf have adequate protections in place; and (v) reporting of personal data breaches to the supervisory authority without undue delay (and no later than 72 hours). The GDPR also prohibits the international transfer of personal data from the EEA to countries outside of the EEA unless made to a country deemed to have adequate data privacy laws by the European Commission or where a data transfer mechanism with appropriate safeguards has been put in place, such as the standard contractual clauses, or SCCs, and supplementary measures that provide privacy protections additional to those provided under SCCs. Further, the GDPR provides that countries in the EEA may establish their own laws and regulations further restricting the processing of certain personal data, including genetic data, biometric data, and health data. After assessing the severity and frequency of the EEA personal data processing activities we engage in, we appointed an external data protection officer that has expert knowledge of data protection law and practices and assists us with monitoring internal compliance with the GDPR.

Failure to comply with the GDPR requirements could result in regulatory investigations, enforcement notices requiring us to stop or change the way we use personal data and/or fines of up to 20 million Euros or up to 4% of the total worldwide annual turnover of the preceding financial year, whichever is higher, as well as compensation claims for financial or non-financial loss by affected individuals, negative publicity, reputational harm and a potential loss of business and goodwill.

If our operations are found to be in violation of any of the data protection laws described above or any other laws that apply to us, we may be subject to penalties, including, but not limited to, criminal, civil and administrative penalties, damages, fines, disgorgement, individual imprisonment, possible exclusion from participation in government healthcare programs, injunctions, private qui tam actions brought by individual whistleblowers in the name of the government, class action litigation and the curtailment or restructuring of our operations, as well as additional reporting obligations and oversight if we become subject to a corrective action plan or other agreement to resolve allegations of non-compliance with these laws, any of which could adversely affect our ability to operate our business and our results of operations.

The Foreign Corrupt Practices Act

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

Additional Regulation

In addition to the foregoing, state and federal laws regarding environmental protection and hazardous substances, including the Occupational Safety and Health Act, the Resource Conservancy and Recovery Act and the Toxic Substances Control Act, affect our business. These and other laws govern our use, handling and disposal of various biological, chemical and radioactive substances used in, and wastes generated by, our operations. If our operations result in contamination of the environment or expose individuals to hazardous substances, we could be liable for damages and governmental fines. We believe that we are in material compliance with applicable environmental laws and that continued compliance therewith will not have a material adverse effect on our business. We cannot predict, however, how changes in these laws may affect our future operations.

European Union

European Medicines Agency

Marketing approvals under the European Union regulatory system may be obtained through a centralized or national marketing authorization procedures. The EMA and the European Commission administer the centralized authorization procedure. Pursuant to Regulation (EC) No. 726/2004 and Regulation (EC) 1394/2007, as amended, this procedure is compulsory for human medicines containing a new active substance to treat for which the therapeutic indication is the treatment of any of the following diseases: acquired immune deficiency syndrome, cancer, neurodegenerative disorders, diabetes, auto-immune diseases and other immune dysfunctions, viral diseases and all drugs that are designated as orphan drugs pursuant to Regulation (EC) No. 141/2000, as amended. Drugs for other indications may be granted a centralized authorization in accordance with Regulation (EC) No. 726/2004 if the drug contains a new active substance and is of a significant therapeutic, scientific or technical innovation or where the granting of authorization in accordance with Regulation (EC) No. 726/2004 is in the interests of patients or animal health at EU level.

When a centralized authorization is granted, the authorization is automatically valid in all Member States of the European Union and by extension in the European Economic Area, or EEA, Norway, Iceland and Liechtenstein. According to Article 2 of Regulation (EC) No 726/2004, the marketing authorization holder must be established in the EEA. This means for the UK that as of the end of the transition period (end of 2020), a marketing authorization holder currently established in the UK has to have transferred its marketing authorization to

a holder established in the EEA. The transfer of the marketing authorization must be fully completed and implemented by the marketing authorization holder before the end of the transition period. Also, any application for marketing authorizations must be made by applicants established in the EEA. Therefore, applications made by applicants established in the UK will need to change to an applicant established in the EEA.

Under the centralized authorization procedure, the EMA's Committee for Medicinal Products for Human Use, or CHMP, serves as the scientific committee that evaluates applications and renders opinions about the safety, efficacy and quality of human products on behalf of the EMA. The CHMP is composed of experts nominated by the Competent Authority of each European Union Member State, one of which is appointed to act as rapporteur for the coordination of the evaluation with the possible assistance of a further member acting as a co-rapporteur. The CHMP has 210 days to give its opinion to the EMA as to whether a marketing authorization should be granted. This period will be suspended until such time as the supplementary information requested by the CHMP has been provided by the applicant. Likewise, this time-limit will be suspended for the time allowed for the applicant to prepare oral or written explanations. The evaluation process is complex and involves extensive consultation with the Competent Authorities of the Member States of the European Union and a number of experts. It is possible to appeal the opinion within 15 days of receipt of the notification of the opinion. At the end of the re-examination, which lasts up to 60 active days, the CHMP adopts a final opinion. The European Commission usually takes its decision to grant a legally binding authorization within 67 days after obtaining the CHMP decision.

A marketing authorization that has been granted in the European Union may be suspended or withdrawn if ongoing regulatory requirements are not met or if safety problems are identified. Among other things, marketing authorization holders are required to have risk management plans that use risk minimization strategies beyond product labeling to ensure that the benefits of certain prescription drugs outweigh their risks.

Accelerated Assessment Procedures

When an application is submitted for a marketing authorization in the European Union in respect of drugs for human use which is of major interest from the point of view of public health and in particular from the viewpoint of therapeutic innovation, the applicant may request an accelerated assessment procedure pursuant to Article 14 (9) of Regulation (EC) No. 726/2004, as amended. Based on the request, the justifications presented, and the recommendations of the rapporteurs, the CHMP will formulate a decision. Such a decision will be taken without prejudice to the CHMP opinion (positive or negative) on the granting of a marketing authorization. If the CHMP accepts the request, the timeframe for the evaluation will be reduced from the standard 210 days for the centralized procedure to 150 days, but it is possible that the CHMP can revert to the standard time limit for the centralized procedure if it considers that it is no longer appropriate to conduct an accelerated assessment.

Conditional Marketing Authorization and Authorization under Exceptional Circumstances

A conditional marketing authorization is valid for one year, can be renewed annually and may be requested by an applicant or proposed by the CHMP for medicinal products which aim at:

- the treatment, prevention or medical diagnosis of seriously debilitating or life-threatening diseases;
- medicinal products to be used in emergency situations in response to public health threats recognized either by the World Health Organization or by the European Union in the framework of Decision No. 1082/2013/EU (e.g. COVID-19 treatments); or
- medicinal products designated as orphan medicinal products in accordance with Regulation (EC) No. 141/2000, as amended.

A conditional marketing authorization may be requested by an applicant or proposed by the CHMP for medicinal products if all of the following requirements are met:

- the risk-benefit balance of the medicinal product, as defined in Article 1(28a) of Directive 2001/83/EC, as amended, is positive;
- it is likely that the applicant will be in a position to provide comprehensive clinical data;
- unmet medical needs will be fulfilled (no existing satisfactory methods or the medicinal product provides major therapeutic advantage); and
- the benefit to public health of the immediate availability on the market of the medicinal product concerned outweighs the risk inherent in the fact that additional data are still required.

The legal basis for a conditional marketing authorization is Article 14-a of Regulation (EC) No. 726/2004, as amended. The provisions for the granting of such an authorization are further elaborated in Regulation (EC) No. 507/2006. The holder will be required to complete ongoing studies or to conduct new studies within a specified period of time with a view to confirming that the benefit-risk balance is positive. In addition, specific obligations may be imposed in relation to the collection of pharmacovigilance data.

In addition, authorization under exceptional circumstances may be requested when it is not possible to provide comprehensive data on the efficacy and safety under normal conditions of use, because:

- the indications for which the product in question is intended are encountered so rarely that the applicant cannot reasonably be expected to provide comprehensive evidence;
- in the present state of scientific knowledge, comprehensive information cannot be provided; or
- it would be contrary to generally accepted principles of medical ethics to collect such information.

The legal basis for the marketing authorization under exceptional circumstances is Article 14 (8) of Regulation (EC) No. 726/2004, as amended, and the relevant documentation for applications in exceptional circumstances are laid down in Part II of Annex I of Directive 2001/83/EC, as amended. The authorization under exceptional circumstances is granted subject to a requirement for the applicant to meet certain conditions, in particular concerning the safety of the medicinal product, notification to the Competent Authorities of any incident relating to its use, and action to be taken. The renewal of the marketing authorization of a medicinal product under exceptional circumstances follows the same rules as a "normal" marketing authorization. After five years, the marketing authorization will then be renewed under exceptional circumstances for an unlimited period, unless the Competent Authority decides, on justified grounds relating to pharmacovigilance, to proceed with one additional five-year renewal.

Manufacturing and Manufacturers' Authorization

Directive 2003/94/EC, as amended, requires that the manufacturing of investigational medicinal products and approved drugs in the EEA is subject to a separate manufacturing authorization and must be conducted in strict compliance with GMP requirements, which mandate the methods, facilities, and controls used in manufacturing, processing, and packing of drugs to assure their safety and identity. Manufacturers must have at least one Qualified Person, or QP, permanently and continuously at their disposal. Although the ultimate responsibility for the performance of a medicinal product over its lifetime, its safety, quality and efficacy, lies with the marketing authorization holder, the QP is responsible for ensuring that each batch of finished product released onto the market has been manufactured in accordance with GMP, in compliance with EU laws and the specifications set out in the marketing authorization or investigational medicinal product dossier. Certification can only be performed by a QP of the manufacturer and/or importer, which are described in the marketing authorization. GMP requirements are enforced through mandatory registration of facilities and inspections of those facilities. Failure to comply with these requirements could interrupt supply and result in delays, unanticipated costs and lost revenues, and subject the applicant to potential legal or regulatory action, including but not limited to warning letters, suspension of manufacturing, seizure of product, injunctive action or possible civil and criminal penalties.

Commercialization and Promotion

The commercialization and promotion of authorized medicinal products, including industry-sponsored continuing medical education and advertising directed toward the prescribers of drugs, are strictly regulated in the European Union, notably under, among others, Directive 2001/83/EC, as amended, guidance published by the European Commission and the EMA, laws, regulations and guidance set out by the Member States of the European Union and industry wide codes of conduct. The applicable regulatory framework aims to ensure that information provided by holders of marketing authorizations regarding their products is truthful, balanced and accurately reflects the safety and efficacy claims authorized by the EMA or by the Competent Authority of the authorizing Member State. Failure to comply with these requirements can result in adverse publicity, warning letters, corrective advertising and potential civil and criminal penalties. Commercialization and promotion of prescription only medicinal products to consumers or patients (directly or indirectly) is strictly forbidden. Advertising of medicines pre-approval or off-label is also prohibited.

Regulatory Data Protection and Market Exclusivity

In the European Union, all new active substances approved on the basis of a complete independent data package benefit from an 8+2+1 -year data/market exclusivity regime. This regime consists of (i) a regulatory data protection period and market exclusivity period of eight years, (ii) a market exclusivity period of an additional two years after the eight-year period and (iii) an extended market exclusivity period of one year after the 10-year period if, during the first eight years of those 10 years, the marketing authorization holder obtains an approval for one or more new therapeutic indications which, during the scientific evaluation prior to their approval, are determined to bring a significant clinical benefit in comparison with existing therapies. Under the current rules, a third party may reference the nonclinical and clinical data of the original innovator beginning eight years after notification of the grant of the approval in the European Union, but the third party may market a generic version after only 10 or, where applicable, 11 years have lapsed from the notification of the grant of the approval.

Orphan Designation

Medicines that meet the criteria for orphan designation benefit from the incentive of 10 years of market exclusivity once they are approved for commercialization in the European Union. This protects them from market competition with similar medicines with the same indication once they are approved. Market exclusivity is awarded by the European Commission and is specifically linked to one specific orphan designation for which a marketing authorization has been granted. Each orphan designation carries the potential for one market exclusivity for a particular indication. A medicine that has several separate orphan designations for different indications can have several separate market exclusivities if these refer to separate designated conditions. A designated orphan medicinal product shall be removed from the European Union's Community register of orphan medicinal products at the end of the period of market exclusivity.

The period of market exclusivity is extended by two years for medicines that also have complied with an agreed pediatric investigational plan, or PIP. This period may, however, be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for orphan drug designation, including among other things, if the product is sufficiently profitable so that market exclusivity is no longer justified.

Notwithstanding the foregoing, a marketing authorization may be granted, for the same therapeutic indication, to a similar drug if:

- the holder of the marketing authorization for the original orphan drug has given its consent to the second applicant;
- the holder of the marketing authorization for the original orphan drug is unable to supply sufficient quantities of the drug; or
- the second applicant can establish in the application that the second drug, although similar to the orphan drug already authorized, is safer, more effective or otherwise clinically superior.

Regulation (EC) No 847/2000 lays down definitions of the concepts “similar drug” and “clinical superiority.”

In order to be eligible for incentives made available by the European Union and by the Member States to support research into, and the development and availability of, orphan drugs, the medicinal product needs to be designated as an orphan drug pursuant to Regulation (EC)No. 141/2000, as amended. Regulation (EC) No. 141/2000, as amended, states that a medicinal product shall be designated as an orphan medicinal product if its manufacturer can establish:

- that it is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting not more than five in 10,000 persons in the European Union when the application is made or that it is intended for the diagnosis, prevention or treatment of a life-threatening, seriously debilitating or serious and chronic condition in the European Union and that without incentives it is unlikely that the commercialization of the medicinal product in the European Union would generate sufficient return to justify the necessary investment; and
- that there exists no satisfactory method of diagnosis, prevention or treatment of the condition in question that has been authorized in the community or, if such method exists, the medicinal product will be of significant benefit to those affected by that condition.

Small-or Medium-Sized Enterprise Status

In the European Union, manufacturers may benefit from further incentives, including administrative and procedural assistance and fee reductions when they are classified as a small-or medium-sized enterprises, or SME. Within the SMEs, medium enterprises are defined as those which employ between 50 to 249 persons and which have an annual turnover not exceeding €50 million or an annual balance sheet total not exceeding €43 million; a small enterprise is defined as an enterprise which employs between 10 to 49 persons and whose annual turnover or annual balance sheet total does not exceed €10 million; and a microenterprise is defined as an enterprise which employs fewer than 10 persons and whose annual turnover or annual balance sheet total does not exceed €2 million.

Administrative, regulatory and financial support is available to companies assigned the SME status by the EMA, including:

- direct assistance by phone, email, teleconference or through briefing meetings on regulatory aspects of the pharmaceutical legislation;
- fee exemptions and reductions for pre-and post-authorization regulatory procedures, including scientific advice, inspections and pharmaco-vigilance;
- assistance with translations of product information into all official European Union languages;
- inclusion in an online SME register, which is an important source of information on the EU-based SMEs involved in the manufacturing, development or marketing of medicines and promotes partnering and networking between the SMEs;
- guidance on clinical data publication and a free redaction tool license;
- liaison with academic investigators in pediatric-medicine research through the European Network of Pediatric Research at the EMA; and
- workshops and training sessions.

Development of Medicines for Children

Several incentives for the development of medicines for children are available in the European Union:

- medicines that have been authorized across the European Union with the results of PIP studies included in the product information are eligible for an extension of their patent protection by six months even when the studies’ results are negative;
- for orphan medicines, the incentive is an additional two years of market exclusivity;
- scientific advice and protocol assistance at the EMA are free of charge for questions relating to the development of medicines for children; and

- medicines developed specifically for children that are already authorized but are not protected by a patent or supplementary protection certificate, can apply for a pediatric-use marketing authorization, or PUMA, which provides 10 years of market protection.

Pediatric Regulation

On January 26, 2007, the Pediatric Regulation (Regulation (EC) No. 1901/2006 and Regulation (EC) No. 1902/2006) came into force in the European Union. Its objective is to improve the health of children in the European Union by facilitating the development and availability of medicines for children from birth up to 18 years of age, ensuring that medicines for use in children are of high quality, ethically researched and authorized appropriately and improving the availability of information on the use of medicines for children. The aim is to achieve this without subjecting children to unnecessary trials or delaying the authorization of medicines for use in adults. The Pediatric Regulation established the Pediatric Committee, or PDCO, which is responsible for coordinating the EMA's work on medicines for children. The Committee's main role is to determine the studies that companies must carry out on children as part of PIPs. At least an approved PIP needs to be in place before applying for marketing authorization. The PDCO grants deferrals for some medicines, allowing a company to delay development of the medicine in children until there is enough information to demonstrate its effectiveness and safety in adults. The PDCO also grants waivers when development of a medicine in children is not needed or is not appropriate, such as for diseases that only affect the elderly population. When the approved PIP contains studies that need to be performed, the proposed study design and timelines need to be adhered to.

Pharmaceutical Coverage, Pricing and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any product candidates for which we obtain regulatory approval. Countries have different pricing and reimbursement schemes. In the European Union, the United States and markets in other countries, sales of any products for which we receive regulatory approval for commercial sale will depend, in part, on the extent to which third-party payors provide coverage and establish adequate reimbursement levels for such products.

In the European Union, governments influence the price of pharmaceutical products through their pricing and reimbursement rules and control of national health care systems that fund a large part of the cost of those products to consumers. Some jurisdictions operate positive and negative list systems under which products may only be marketed once a reimbursement price has been agreed. To obtain reimbursement or pricing approval, some of these countries may require the completion of clinical trials that compare the cost-effectiveness of a particular product candidate to currently available therapies. Other member states allow companies to fix their own prices for medicines but monitor and control company profits. Special pricing and reimbursement rules may apply to orphan drugs. Inclusion of orphan drugs in reimbursement systems tends to focus on the medical usefulness, need, quality and economic benefits to patients and the healthcare system as for any drug. The downward pressure on health care costs has become very intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, in some countries, cross-border imports from low-priced markets exert a commercial pressure on pricing within a country.

In the United States, third-party payors include federal and state healthcare programs, private managed care providers, health insurers and other organizations. Even if our product candidates are approved, sales of our products will depend, in part, on the extent to which third-party payors provide coverage and establish adequate reimbursement levels for such products. The process for determining whether a third-party payor will provide coverage for a product may be separate from the process for setting the price of a product or for establishing the reimbursement rate that such a payor will pay for the product. Third-party payors may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the FDA-approved products for a particular indication. Third-party payors are increasingly challenging the price, examining the medical necessity and reviewing the cost-effectiveness of medical products, therapies and services, in addition to questioning their safety and efficacy. We may need to conduct expensive pharmaco-economic studies in order to demonstrate the medical necessity and cost-effectiveness of our product candidates, in addition to the costs required to obtain the FDA approvals. Our product candidates may not be considered medically necessary or cost-effective. A payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a product does not assure that other payors will also provide coverage for the product. Adequate third-party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development.

In addition, prices for drugs may be reduced by mandatory discounts or rebates required by federal health care programs (such as the Medicaid Drug Rebate Program and the 340B Drug Pricing Program) or discounts and rebates requested by private payors. In addition, any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States may also impact the pricing of drugs. It is difficult to predict how Medicare coverage and reimbursement policies will be applied to products for which the Company receives marketing approval in the future and coverage and reimbursement under different federal health care programs is not always consistent. Further, private payors often follow the coverage and reimbursement policies established under Medicare. If reimbursement is not available or is available only at limited levels, we may not be able to successfully commercialize our products for which we receive marketing approval.

The containment of healthcare costs also has become a priority of federal, state and foreign governments and the prices of drugs have been a focus in this effort. Governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit a company's revenue generated from the sale of any approved products.

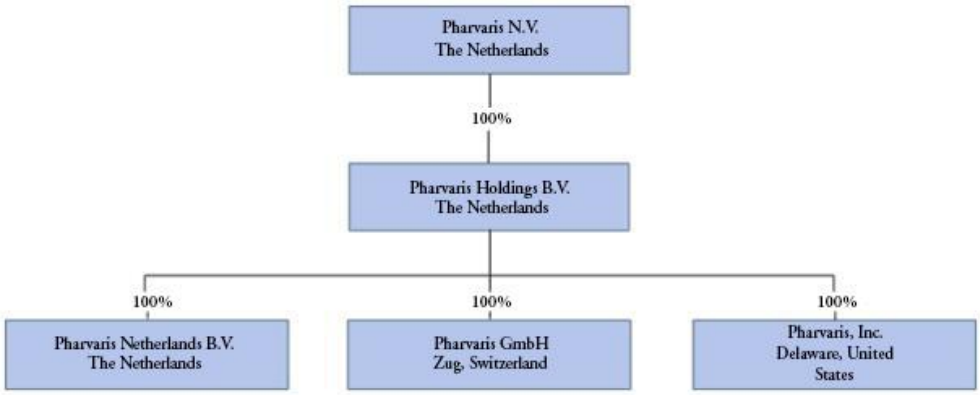
Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which a company or its collaborators receive marketing approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

The marketability of any product candidates for which we receive regulatory approval for commercial sale may suffer if the government and third-party payors fail to provide adequate coverage and reimbursement. In addition, emphasis on managed care in the United States has increased and we expect will continue to increase the pressure on healthcare pricing. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

C. Organizational structure

We were incorporated as a Dutch private company with limited liability (*besloten vennootschap*) and currently exist as a Dutch public company with limited liability (*naamloze vennootschap*) (after the conversion of our legal form in the first quarter of 2021), with operating subsidiaries in the Netherlands, Switzerland and the United States.

The following diagram illustrates our corporate structure:



D. Property, plants and equipment

We have offices in Leiden, the Netherlands, Lexington, Massachusetts (United States) and Zug, Switzerland. Our office space in Leiden measuring approximately 290 square meters is rented through November 30, 2025; our offices in Massachusetts measuring approximately 622 square meters is rented through December 31, 2029 and our office space in Zug measuring approximately 58 square meters is rented on a monthly basis.

ITEM 4A. UNRESOLVED STAFF COMMENTS

Not applicable.

ITEM 5. OPERATING AND FINANCIAL REVIEW AND PROSPECTS

A. Operating results

You should read the following discussion of our financial condition and results of operations in conjunction with the financial statements and the notes included elsewhere in this Annual Report. The following discussion contains forward-looking statements that involve certain risks and uncertainties. Our actual results could differ materially from those discussed in these statements. Factors that could cause or contribute to these differences include those discussed below and elsewhere in this Annual Report, particularly under the "ITEM 3. KEY INFORMATION—D. Risk factors" and "Cautionary Statement Regarding Forward-Looking Statements" sections.

Our audited consolidated financial statements are included elsewhere in this Annual Report. These financial statements are prepared in accordance with the IFRS Accounting Standards (IFRS) as issued by the International Accounting Standards Board (IASB). *As permitted by the rules of the SEC for foreign private issuers, we do not reconcile our financial statements to U.S. GAAP.*

Overview

We are a late-stage biopharmaceutical company focused on the development and commercialization of innovative therapies for rare diseases with significant unmet need, initially focused on angioedema and other bradykinin-mediated diseases. Our first molecule, deucrictibant, is a novel, oral, small-molecule bradykinin B2 receptor antagonist under development for the prevention or treatment of attacks due to bradykinin-mediated angioedema, including hereditary angioedema (HAE) and acquired angioedema due to C1-inhibitor

deficiency (AAE-C1INH). Deucrictibant has the potential to address unmet medical need by improving upon the therapeutic profile of existing medicines and providing patients with quality of life and ease-of-administration that is superior to current standard-of-care. We believe deucrictibant has the potential to provide injectable-like efficacy and placebo-like tolerability with the convenience of an oral therapy for both the prophylactic and on-demand treatment of HAE attacks.

Deucrictibant may address unmet medical needs of people living with HAE by both preventing attacks from occurring, using an extended-release (XR) tablet formulation of deucrictibant, as well as treat the manifestations of HAE attacks, using an immediate-release (IR) capsule formulation of deucrictibant. The XR tablet formulation is designed to maintain therapeutic levels for at least 24 hours and to achieve a steady-state plasma concentration within 72 hours, supporting a once-daily dosing regimen. The IR capsule formulation is designed to rapidly reach therapeutic exposure in order to mitigate HAE attacks symptoms quickly and completely with a single oral dose.

In addition to the differentiation of our individual products, having on-demand and prophylactic products with the same active ingredient enables patients to maintain a trusted active medicine when they change their dosing regimen and delivery mechanism moving from on-demand to prophylactic treatment (or back). This may be particularly valued by children or adolescents who typically begin therapy with on-demand only and gradually move to prophylaxis as attack frequency increases (commonly after puberty).

In our Phase 1 clinical trials to-date, we have observed rapid exposure and predictable linear pharmacokinetics (PK) with and without food. In addition, we observed deucrictibant to be a potent antagonist of the bradykinin B2 receptor, in vitro and in vivo with healthy volunteers.

A Phase 2 placebo-controlled trial evaluating the efficacy and tolerability of deucrictibant IR capsules for the on-demand treatment of attacks in patients with HAE type 1 and 2 (RAPIDe-1) commenced in February 2021 and reported positive topline Phase 2 data in December 2022, demonstrating the clinical efficacy and tolerability of deucrictibant. We believe these positive Phase 2 data support further development of deucrictibant as a potential oral on-demand therapy for HAE attacks. In March 2024, we initiated a global, pivotal, randomized, double-blind-placebo-controlled Phase 3 study, RAPIDe-3, of orally administered deucrictibant IR capsule (20 mg) for the on-demand treatment of HAE attacks in adults and adolescents (12 years and older), and intend to enroll approximately 120 participants. Topline data from RAPIDe-3 is anticipated in the first quarter of 2026.

A Phase 2 placebo-controlled trial evaluating the efficacy and the safety and tolerability of deucrictibant for long-term prophylaxis against angioedema attacks in HAE type 1 and 2 (CHAPTER-1) commenced CHAPTER-1 in 2021 using twice-daily dosing of deucrictibant IR capsules as a proof-of-concept for once-daily deucrictibant XR tablets, and announced positive topline data in December 2023, demonstrating the clinical efficacy and tolerability of deucrictibant. We believe these positive Phase 2 data support further development of deucrictibant as a potential oral prophylactic therapy for HAE attacks. In December 2024, we initiated a global, pivotal, randomized, double-blind, placebo-controlled Phase 3 study, CHAPTER-3, of orally administered deucrictibant extended-release tablet for the prophylaxis against angioedema attacks in adults and adolescents (12 years and older) with HAE. The study aims to enroll approximately 81 participants with HAE and randomize them in a 2:1 ratio to receive deucrictibant XR tablet (40 mg/day), which is currently the intended commercial dosage, or placebo, once daily for 24 weeks. Topline data from CHAPTER-3 is anticipated in the second half of 2026.

In addition, we also are also running open-label extension studies in both on-demand and prophylactic settings to collect long-term safety and efficacy data in HAE patients.

In August 2022, the FDA placed a hold on the clinical trials of deucrictibant in the U.S. based on its review of nonclinical data. The FDA requested that Pharvaris conduct an additional long-term rodent toxicology study and update the Investigator's Brochure. Pharvaris participated in a Type A meeting with the FDA to discuss paths to address the on-demand and prophylactic holds and aligned on a protocol for a 26-week rodent toxicology study. Following review of data from a preplanned interim analysis of the ongoing 26-week nonclinical rodent study, the FDA lifted the clinical hold on the IND application for deucrictibant for the on-demand treatment of HAE in June 2023. In January 2024, the FDA lifted the clinical hold on the IND application for deucrictibant for the prophylactic treatment of HAE attacks following review of the full data set from the completed 26-week rodent toxicology study.

A wide variety of events beyond our control, including natural or man-made disasters, power shortages, fires, extreme weather conditions, pandemics, epidemics or outbreaks of infectious diseases, political instability or other events could disrupt our business or operations or those of our development partners, manufacturers, regulators or other third parties with whom we conduct business now or in the future. These events may cause businesses and government agencies to be shut down, supply chains to be interrupted, slowed, or rendered inoperable, and individuals to become ill, quarantined, or otherwise unable to work and/or travel due to health reasons or governmental restrictions. Additionally, we are exposed to a variety of risks in the ordinary course of our business, including, but not limited to, foreign currency risk and interest rate risk. We regularly assess each of these risks to minimize any adverse effects on our business as a result of those factors. For a detailed discussion, see Note 17 to our consolidated financial statements included elsewhere in this Annual Report.

In addition, the retaliatory measures that have been taken, or could be taken in the future, by the United States, NATO, and other countries with respect to the invasion of Ukraine and the Hamas attack against Israel and the ensuing war have created global security concerns that could result in a regional conflicts and also adversely affect our ability to conduct ongoing and future clinical trials of our product candidates. For example, our RAPIDe-1 and CHAPTER-1 studies include a significant number of patients in Germany, Poland, and Bulgaria, and we have a patient in Israel. A further escalation of the conflict in Ukraine may potentially impact our ability to complete our ongoing and planned clinical trials in these countries on a timely basis, or at all. Clinical trials in these countries could be suspended or

terminated, and we may be prevented from obtaining data on patients already enrolled at affected sites. Any of the foregoing could impede the execution of our clinical development plans.

A discussion of our financial condition and results of operations for the year ended December 31, 2022 can be found in our annual report on form 20-F, filed with the SEC on April 10, 2024.

Financial operations overview

Revenues

We did not record any revenues during the period covered by the historical financial information included in this Annual Report. We do not expect to recognize any revenues before we are able to commercialize our first product.

Research and development expenses

We are focused on the clinical development of deucrictibant. Since our inception, we have devoted substantially all of our resources to research and development efforts relating to the development of deucrictibant and our product candidates IR and XR. We expect that we will continue to incur significant research and development expenses as we seek to complete the clinical development of, and achieve regulatory approval for, our product candidates IR and XR, and in connection with discovery and development of any additional product candidates.

Research and development expenses consist of the following:

- employee benefits expenses, which includes salaries, pensions, share-based compensation expenses, bonus plans and other related costs for research and development staff;
- nonclinical expenses, which include costs of our outsourced discovery and nonclinical development studies;
- clinical expenses, which includes costs of conducting and managing our sponsored clinical trials, including clinical investigator cost, costs of clinical sites, and costs for CROs assisting with our clinical development programs;
- manufacturing expenses, which include costs related to manufacturing of active pharmaceutical ingredients and manufacturing of the products used in our clinical trials and research and development activities;
- costs related to regulatory activities, including collecting data, preparing and submitting filings, communicating with regulatory authorities and reviewing the design and conduct of clinical trials for compliance with applicable requirements;
- costs in connection with investigator-sponsored clinical trials and evaluations;
- advisers' fees, including discovery, nonclinical, clinical, chemistry, manufacturing, and controls-related and other consulting services;
- intellectual property costs, which includes costs associated with obtaining and maintaining patents and other intellectual property; and
- license costs.

We expect that our total research and development expenses will increase in 2025 as we continue to focus on the development of our product candidates IR and XR, as well as explore potential expansion programs. We anticipate that research and development expenses will continue to increase as we continue to progress IR and XR through clinical development.

There is a risk that any clinical development or product discovery program may not result in commercial approval. To the extent that we fail to obtain approval to commercialize our product candidate in a timely manner, we would need to continue to conduct nonclinical studies or clinical trials over a longer period of time, and we anticipate that our research and development expenses may further increase.

Clinical development timelines and associated costs may vary significantly and the successful development of our product candidate is highly uncertain. At this time, we cannot reasonably estimate the nature, timing, and estimated costs of the efforts, including patient recruitment and selection that will be necessary to complete the development of, or the period, if any, in which material net cash inflows may commence from, our product candidates. Moreover, we cannot assure that we will be able to successfully develop or commercialize our product candidates, if approved for marketing. This is due to numerous risks and uncertainties associated with developing drugs. See "ITEM 3. KEY INFORMATION: — D. Risk factors."

Selling and distribution expenses

Historically, we have not incurred any selling and distribution expenses. If our product candidates are approved for registration and marketing, we anticipate incurring substantial selling and distribution expenses in future periods in order to establish an infrastructure for marketing and distribution, obtain supplies of active pharmaceutical ingredients, and manufacture commercial quantities of our product candidate.

General and administrative expenses

We anticipate that we will continue to incur significant general and administrative expenses as we advance our research and development portfolio. General and administrative expenses consist of the following:

- employee benefits, including salaries, pensions, share-based compensation expenses, bonus plans and other related costs for staff and independent contractors in executive and operational functions;
- independent auditors' and advisers' fees, including accounting, tax, legal and other consulting services;
- rental expenses, insurance, facilities and IT expenses and other general expenses relating to our operations; and
- expenses related to the build-out of our commercial organization, including assessments of the HAE market landscape, pricing research and congress attendance.

We anticipate that the continuing development of our business and the expense of maintaining directors' and officers' liability insurance, will contribute to future increase in general and administrative expenses. We also expect that general and administrative expenses will increase in the future as we incur additional costs associated with being a public company in the United States.

Share-based compensation expenses

In 2016, we implemented an Equity Incentive Plan, or the Plan, in order to advance the interests of our shareholders by enhancing our ability to attract, retain and motivate persons who are expected to make important contributions to us and by providing such persons with performance-based incentives that are intended to better align the interests of such persons with those of our shareholders. In order to incentivize our directors and employees, our Board adopted the Pharvaris N.V. 2021 Equity Incentive Plan, or the 2021 Plan, for employees, consultants and directors prior to the completion of our initial public offering. The 2021 Plan became effective upon our conversion from Pharvaris B.V. into Pharvaris N.V., which occurred prior to the consummation of our initial public offering. The 2021 Plan provides for the grant of options, stock appreciation rights, restricted stock, RSUs, performance stock awards, other stock-based awards, performance cash awards and substitute awards.

The fair values of these instruments are recognized as personnel expenses in either research and development expenses or general and administrative expenses.

The share-based payment expense recorded for the years ended December 31, 2024, 2023 and 2022 were €16.2 million, €10.7 million and €11.3 million, respectively.

Comparison of the years ended December 31, 2023 and 2022

A discussion of the financial results for the year ended December 31, 2023 as compared to the year ended December 31, 2022 can be found in the section entitled "Item 5. Operating and Financial Review and Prospects—A. Operating Results— Financial operations overview—Comparison of the years ended December 31, 2023 and 2022" in our annual report on form 20-F, filed with the SEC on April 10, 2024.

Comparison of the years ended December 31, 2024 and 2023

The following table summarizes our loss for the periods indicated:

	For the year ended December 31,			
	2024	2023	Change	%
		(in €)		
Research and development expenses	(98,563,529)	(65,575,030)	(32,988,499)	50 %
General and administrative expenses	(47,124,638)	(31,338,590)	(15,786,048)	50 %
Total operating expenses	**(145,688,167)**	**(96,913,620)**	**(48,774,547)**	**50 %**
Finance income (expense)	13,291,664	(2,912,643)	16,204,307	(556)%
Loss before income tax	**(132,396,503)**	**(99,826,263)**	**(32,570,240)**	**33 %**
Income taxes	(1,825,024)	(1,048,805)	(776,219)	74 %
Loss for the period	**(134,221,527)**	**(100,875,068)**	**(33,346,459)**	**33 %**

Research and development expenses

	For the year ended December 31,			
	2024	2023	Change	%
	(in €)			
Clinical expenses	(55,867,694)	(30,690,293)	(25,177,401)	82%
Personnel expenses	(27,767,184)	(19,132,307)	(8,634,877)	45%
Manufacturing costs	(9,434,537)	(6,500,986)	(2,933,551)	45%
Nonclinical expenses	(3,324,513)	(8,977,187)	5,652,674	(63)%
License costs	(1,592,687)	—	(1,592,687)	0%
Intellectual property costs	(576,914)	(274,257)	(302,657)	110%
Total research and development expenses	**(98,563,529)**	**(65,575,030)**	(32,988,499)	50%

Research and development expenses increased by €33.0 million in 2024, or 50%, from €65.6 million for the year ended December 31, 2023 to €98.6 million for the year ended December 31, 2024. The increase in research and development expenses was mainly driven by an increase in clinical expenses and personnel expenses, offset by a decrease in nonclinical expenses.

For the years ended December 31, 2024 and 2023, clinical expenses were €55.9 million and €30.7 million, respectively. This represents an increase of €25.2 million, or 82%. The increase is primarily due to the initiation of enrollment in the On-Demand Treatment Phase 3 trial, initiation of activities for the prophylaxis Phase 3 trial, and implementation and conduct of the On-Demand Treatment and prophylaxis open-label extension studies.

For the years ended December 31, 2024 and 2023, personnel expenses were €27.8 million and €19.1 million, respectively. This represents an increase of €8.6 million, or 45%. The increase is primarily due to an increase in salary, bonus and benefits expense resulting from hiring additional personnel to handle the expanded clinical development activities. The remaining increase in personnel expenses is driven by share-based compensation expenses due to the new grants made during the period. Share-based compensation expense in the current-year included an amount of €7.9 million of share-based compensation expense versus €4.6 million in the prior-year period.

For the years ended December 31, 2024 and 2023, nonclinical expenses were €3.3 million and €9.0 million, respectively. This represents a decrease of €5.7 million, or 63%. The decrease in nonclinical expenses is primarily due to a decrease in the number and scope of studies conducted in 2024 versus 2023 to lift the deucrictibant clinical hold.

General and Administrative Expenses

	For the year ended December 31,			
	2024	2023	Change	%
	(in €)			
Personnel expenses	(18,883,708)	(13,314,359)	(5,569,349)	42%
Professional fees	(7,757,750)	(4,689,462)	(3,068,288)	65%
Insurance, facilities and office expenses	(6,509,691)	(6,031,513)	(478,178)	8%
Accounting, tax and auditing fees	(4,017,669)	(2,029,554)	(1,988,115)	98%
Travel expenses	(2,129,631)	(1,797,588)	(332,043)	18%
Consulting fees	(858,843)	(602,110)	(256,733)	43%
Other expenses	(6,967,346)	(2,874,004)	(4,093,342)	142%
General and administrative expenses	**(47,124,638)**	**(31,338,590)**	**(15,786,048)**	**50%**

General and administrative expenses increased by €15.8 million, or 50% from €31.3 million for the year ended December 31, 2023 to €47.1 million for the year ended December 31, 2024. The increase in general and administrative expenses was mainly driven by an increase in personnel, professional and other expenses.

For the years ended December 31, 2024 and 2023, personnel expenses were €18.9 million and €13.3 million, respectively. This represents an increase of €5.6 million, or 42%. The increase is primarily due to an increase in salary, bonus and benefits expense resulting from hiring additional employees. The remaining increase in personnel expenses is driven by an increase in share-based compensation expenses due to the new grants made during the period, including equity grants to senior level hires made during the period. Share-based compensation expense in the current-year period included an amount of €8.3 million compared to €6.1 million in the prior-year period.

For the years ended December 31, 2024 and 2023, professional fees were €7.8 million and €4.7 million, respectively. The increase of €3.1 million is primarily due to increased outside legal fees and commercial consulting related to pre-launch activities, including market access.

For the years ended December 31, 2024 and 2023, other expenses were €7.0 million and €2.9 million, respectively. The increase of €4.1 million, is primarily due to an increase in marketing, promotion, conferences and seminars related to pre-launch activities.

Finance income / (expense) - net

Finance income / (expense) - net, for the year ended December 31, 2024 and 2023 were €13.3 million and (€2.9) million, respectively, a change of €16.2 million. The amount mainly relates to unrealized foreign exchange gains of €7.9 million for 2024, compared to a loss of €3.1 million in the prior year which is mostly the result of translating the Company's bank balances held in USD to EUR. Interest income increased from €0.2 million in 2023 to €5.5 million in 2024.

Income taxes

The current period losses for which no deferred tax asset has been recognized, consists of the unrecognized tax effect of losses incurred in Switzerland. Following discussions with the Dutch tax authorities in November 2022, the Company concluded that foreign exchange results should be allocated to the principal Company in Switzerland. As a result, the current losses for Switzerland are partly exacerbated by the allocated foreign exchange results. The Company did not recognize the tax benefit of the losses incurred in previous years.

The Company and its subsidiaries have tax loss carry-forwards as of December 31, 2024 of approximately €449.8 million (2023: €325.0 million, 2022: €182.3 million), that are available for offsetting against future taxable profits of the Companies in which the losses arose. In the Netherlands, profits in a given year can be offset against tax loss carry forwards for an unlimited period of time. The amount of the offset is, however, limited to 50% of taxable income (in excess of €1.0 million). Under Swiss law, losses can be offset against future income or capital gains for seven years.

Critical accounting estimates and judgments

We believe that the following accounting policies involve a high degree of judgment and complexity. Accordingly, these are the policies we believe are the most critical to aid in fully understanding and evaluating our consolidated financial condition and results of our operations. See Note 2 to our consolidated financial statements included elsewhere in this Annual Report for a description of our other material accounting policies. The preparation of our consolidated financial statements in conformity with IFRS requires us to make estimates and judgments that affect the amounts reported in those financial statements and accompanying notes. Although we believe that the estimates we use are reasonable, due to the inherent uncertainty involved in making those estimates, actual results reported in future periods could differ from those estimates.

Share-based Compensation Arrangements

We adopted an equity-settled share-based compensation plan in 2016, pursuant to which certain participants are granted the right to acquire ordinary shares or RSU's of the Company. This plan has been superseded by the 2021 long term incentive plan. The grants made under these plans are accounted for in accordance with the policy as stated in Note 2.15 to our consolidated financial statements included elsewhere in this Annual Report. The total amount to be expensed is determined by reference to the fair value of the options or restricted stock units granted. The fair value of the options is measured at the date of grant using the Black-Scholes formula.

The use of the Black-Scholes formula requires use of certain assumptions relating to the expected option life, the volatility of stock price, the determination of an appropriate risk-free interest rate and expected dividends.

The input used in the measurement of the fair value per option at each grant/measurements date using the Black-Scholes formula (including the related number of options and the fair value of the options) were as follows:

	August 1, 2024	April 15, 2024	April 11, 2024	April 11, 2024	November 15, 2023	April 6, 2023	June 1, 2022	April 1, 2022	January 1, 2022
Number of options	75,000	230,000	70,000	485,000	90,000	846,000	120,000	552,500	70,000
Fair value of the options	€ 11.65	€ 15.41	€ 16.83	€ 16.90	€ 12.27	€ 5.92	€ 11.89	€ 11.50	€ 9.08
Fair value of the ordinary shares	€ 14.43	€ 18.97	€ 20.80	€ 20.80	€ 15.12	€ 7.36	€ 16.88	€ 16.42	€ 12.65
Exercise price	€ 14.43	€ 18.97	€ 20.80	€ 20.80	€ 15.12	€ 7.36	€ 16.88	€ 16.42	€ 12.65
Expected volatility (%)	100 %	100 %	105 %	100 %	100 %	100 %	80 %	80 %	85 %
Expected life (years)	6.1	6.1	5.5	6.1	6.1	6.1	6.1	6.1	6.1
Risk-free interest rate (%)	4.0 %	4.7 %	4.7 %	4.7 %	4.6 %	3.6 %	3.0 %	2.6 %	1.4 %

Expected volatility in 2024 and 2023, was based on the volatility of the Company and comparable peer group companies, while in prior periods expected volatility was based on an evaluation of the historical volatilities of comparable listed biotech-companies only. The expected life is based on Management's best estimate of when the options will be exercised. The risk-free interest rate is based on the yield on US Government bonds depending on whether the exercise price is in euros or in US dollars. The expected dividend yield is zero considering the stage of the Company.

Research and development expenditures

Research and development expenses are currently not capitalized but are expensed because the criteria for capitalization are not met, see Note 2.16 and Note 3 to our consolidated financial statements included elsewhere in this Annual Report. At each balance sheet date, we estimate the level of services performed by the vendors and the associated costs incurred for the services performed. Although we do not expect the estimates to be materially different from amounts actually incurred, the understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and could result in reporting amounts that are too high or too low in any particular period.

B. Liquidity and capital resources

Since inception, we have incurred significant operating losses. We incurred losses of €134.2 million during the year ended December 31, 2024 and €100.9 million during the year ended December 31, 2023. Since inception, we have not generated any revenues or net cash flows from sales. We will not receive any revenues or net cash flows from sales until we successfully develop a product candidate, obtain regulatory approval and successfully commercialize it. There is no assurance that we will be able to do so.

To date, we have relied on the issuance of equity securities and pre-funded warrants to finance our operations and internal growth.

From inception through December 31, 2024, we have raised the following capital:

- issuance of 4,850,000 Common shares raising €0.2 million;
- issuance of 5,242,850 Series A preferred shares raising €14.9 million (net of transaction costs);
- issuance of 3,003,391 Series B-1 preferred shares raising €21.6 million (net of transaction costs);
- issuance of 4,646,756 Series B-2 preferred shares raising €34.2 million (net of transaction costs);
- issuance of 5,826,279 Series C preferred shares raising €67.2 million (net of transaction costs);
- issuance of 9,511,075 ordinary shares raising €146.2 million (net of transaction costs);
- issuance of 593,927 ordinary shares raising €9.3 million (net of transaction costs);
- issuance of 6,951,340 ordinary shares raising €64.1 million (net of transaction costs); and
- issuance of 11,125,000 ordinary shares and 1,375,000 pre-funded warrants raising €261.6 million (net of transaction costs).

On February 5, 2021, the Company became public by listing its ordinary shares on the Nasdaq Stock Exchange. On the same date all Series A preferred shares, Series B and Series C preferred shares were automatically converted to ordinary shares and 9,511,075 ordinary shares were issued. Together with the issuance of new ordinary shares, the par value of each ordinary share was increased from €0.01 to €0.12.

On March 1, 2022, we entered into a sales agreement (the "2022 Sales Agreement") with Leerink Partners LLC (formerly known as SVB Securities LLC), pursuant to which we may sell ordinary shares having an aggregate offering price of up to $75 million from time to time through Leerink Partners. On April 12, 2024, we terminated the 2022 Sales Agreement and entered into a new sales agreement with Leerink Partners, pursuant to which we may sell ordinary shares having an aggregate offering price of up to $175 million from time to time through Leerink Partners (the “2024 Sales Agreement”). In April 2024, we filed a Form F-3 ASR Registration Statement (the “F-3 ASR”) and prospectus with the Securities and Exchange Commission, allowing us to sell an unspecified amount of its securities. The F-3 ASR was supplemented by a prospectus supplement covering an at-the-market program providing for the sales from time to time of up to $175 million of its ordinary shares pursuant to the April 2024 Sales Agreement.

As of December 31, 2024, we have sold a total of 593,927 ordinary shares under the Sales Agreement generating total net proceeds of $9.8 million (€9.3 million), after deducting $0.3 million (€0.3 million), which was payable to Leerink Partners, LLC as commission in respect of such sales. The Company has not sold any securities under the April 2024 Sales Agreement.

In June, 2023, we sold a total of 6,951,340 ordinary shares, par value €0.12 per share, in a private placement at a purchase price of $10.07 per ordinary share. The sale generated total proceeds of $70.0 million (€64.1 million).

During December 2023, we entered into an underwriting agreement with Morgan Stanley & Co. LLC and Leerink Partners LLC as underwriters, pursuant to which we agreed to issue and sell (i) 11,125,000 ordinary shares, par value €0.12 per share and (ii) pre-funded warrants to purchase up to 1,375,000 ordinary shares in an underwritten offering. The Offering closed on December 8, 2023, and we generated net proceeds of $282.0 million (€261.6 million), after deducting bank fees of $18.0 million (€16.7 million). In March 2024, the Company received a partial reimbursement for certain of its expenses in connection with the December 2023 offering which have been accounted for in share premium.

As of December 31, 2024 we held cash and cash equivalents of €280.7 million. Of the cash on hand, €0.1 million relates to guarantees. We do not expect positive operating cash flows in the foreseeable future and remain dependent on additional financing to fund

our research and development expenses, general and administrative expenses and financing costs. We believe that the available cash balances are sufficient to execute our operating plan and strategies and to meet the anticipated working capital requirements and settle all expected liabilities for at least twelve months from the issuance date of the consolidated statements of loss and comprehensive loss. Accordingly, the consolidated statements of loss and comprehensive loss have been prepared on a going concern basis.

We have based our estimate on assumptions that may prove to be wrong, and we may use our available capital resources sooner than we currently expect. For example, we may require additional capital resources due to underestimation of the nature, timing and estimated costs of the efforts that will be necessary to complete the development of our product candidates. We may also need to raise additional funds more quickly if we choose to expand our development activities, our portfolio or if we consider acquisitions. Factors that could influence our future capital requirements and the timing thereof include:

- the progress and cost of our discovery and nonclinical development;
- the progress and cost of our clinical trials, including payments of patient cost, clinical investigator cost and payments to CROs that are assisting with our sponsored clinical trials, and other research and development activities;
- the cost and timing of obtaining regulatory approval to commence further clinical trials;
- the costs associated with any future investigator-sponsored clinical trials;
- the cost of filing, prosecuting, defending and enforcing any patent applications, claims, patents and other intellectual property rights;
- the cost and timing of obtaining sufficient quantities of our product candidates for clinical trials by establishing our contracted and/or own production capacities;
- the costs and expenditures associated with process optimizations and nonclinical and clinical manufacturing;
- the cost and timing to develop suitable formulations and manufacture final product;
- the terms and timing of any collaborative, licensing and other arrangements that we may establish;
- the cost of acquiring or licensing additional products or technologies, if any;
- the cost of preparing for launch and commercialization of our product candidates; and
- the cost of operating as a public company in the United States.

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of public or private equity offerings, debt financings, convertible loans, warrants, collaborations or other means. We may consider raising additional capital to take advantage of favorable market conditions or other strategic considerations even if we have sufficient funds for planned operations.

To the extent that we raise additional funds by issuing and selling equity or equity-linked securities, shareholders will experience dilution. Debt financing, if available, may subject us to financial and other restrictive covenants that limit our ability to engage in activities that we may believe to be in our long-term best interests. Additional financing may not be available on acceptable terms, if at all. Capital may become difficult or impossible to obtain due to poor market or other conditions outside of our control (including wars, regional unrest, pandemics and epidemics). If we are unable to raise additional funds when needed, we may be required to delay, reduce, or terminate some or all of our development programs and clinical trials. We may also be required to sell or license other technologies or our clinical product candidate that we would prefer to develop and commercialize ourselves.

In addition, while we seek to minimize our exposure to third-party losses of our cash and cash equivalents, we hold our balances in a number of large financial institutions. However, these institutions are subject to risk of failure. For example, in March 2023, the Federal Deposit Insurance Corporation was appointed as receiver for Silicon Valley Bank ("SVB"). As of April 7, 2025, none of our cash and cash equivalents are held with SVB. All of our cash and cash equivalents are held with other large financial institutions, and we do not expect further developments with SVB to have a material impact on our cash and cash equivalents balance, expected results of operations, or financial performance for the foreseeable future. However, if there are issues in the wider financial system and if other financial institutions fail, our business and financial condition could be materially affected.

Cash Flows

Comparison for the years ended December 31, 2024 and December 31, 2023

A discussion of our cash flows for the year ended December 31, 2023 as compared to the year ended December 31, 2022 can be found in the section entitled “Item 5. Operating and Financial Review and Prospects—B. Liquidity and Capital Resources—Cash Flows—Comparison of the years ended December 31, 2023 and 2022” in our annual report on form 20-F, filed with the SEC on April 10, 2024.

The following table sets forth our primary sources and uses of our cash and cash equivalents for each of the periods set forth below:

	For the year ended December 31,			
	2024	2023	Change	%
			(in €)	
Net cash flows used in operating activities	(120,130,191)	(93,049,093)	(27,081,098)	29%
Net cash flows used in investing activities	(538,086)	(89,984)	(448,102)	498%
Net cash flows provided by financing activities	2,676,555	325,393,000	(322,716,445)	(99)%
Net (decrease) increase in cash and cash equivalents	**(117,991,722)**	**232,253,923**	**(350,245,645)**	**(151)%**
Cash and cash equivalents at beginning of period	**391,231,637**	**161,837,429**	**229,394,208**	**142%**
Effect of exchange rate changes	7,488,122	(2,859,715)	10,347,837	(362)%
Cash and cash equivalents at end of period	**280,728,037**	**391,231,637**	**(110,503,600)**	**(28)%**

Operating activities

Net cash flows used in operating activities reflect our results for the period adjusted for, among other things, depreciation, unrealized foreign exchange results, share-based compensation arrangements, changes in working capital and accruals.

Net cash flows used in operating activities increased by €27.1 million or 29%, from €93.0 million for the year ended December 31, 2023 to €120.1 million for the year ended December 31, 2024. The increase is primarily due to the increase in research and development expenses, other operating expenses and the growth of our organization.

Investing activities

Net cash flows used in investing activities increased by €0.4 million or 498%, from €0.1 million for the year ended December 31, 2023 to €0.5 million for the year ended December 31, 2024. The increase is due to additional investment in property, plant and equipment to support the growth of the company.

Financing activities

Net cash flows provided by financing activities decreased by €322.7 million from €325.4 million for the year ended December 31, 2023 to €2.7 million for the year ended December 31, 2024. Net cash provided by financing activities in the year ended December 31, 2024 consisted primarily of the gross proceeds related to the pre-funded warrants that were exercised in January 2024 that resulted in the issuance of 1,375,000 ordinary shares.

The net cash provided by financing activities in the year ended December 31, 2023 consisted primarily of the receipt of €342.9 million received from the sale of ordinary shares and pre-funded warrants, offset by transaction costs of €17.3 million and the payment of principal portion of lease liabilities of €0.2 million.

Disclosure of contractual obligations

The Group has entered into research and development commitments amounting to a total of €109.9 million as of December 31, 2024 (2023: €49 million). The amount for research and development commitments does not include potential milestone fees, sublicense fees, royalty fees, licensing maintenance fees, and reimbursement of patent maintenance costs that we may be required to pay under the BRAIN License.

Under the BRAIN License, up to €9.0 million in aggregate potential milestone payments remain outstanding. In addition, we will be required to pay low to medium single-digit tiered royalties on direct or indirect net sales of licensed products. The royalties that we are required to pay under this agreement may be reduced on a country-by-country and product-by-product basis if sales of a generic version of a product account for 1% or more of the relevant market. We have not included such potential obligations because they are contingent upon the occurrence of future events and the timing and likelihood of such potential obligations are not known with certainty. For further information regarding this agreement and amounts that could become payable in the future under this agreement, please see “ITEM 4. INFORMATION ON THE COMPANY -- B. Business Overview-License Agreement.”

Service contracts

The commitments from service contracts mainly result from contracts with nonclinical and clinical CROs and CDMOs.

C. Research and development, patents and licenses, etc.

See “ITEM 4. INFORMATION ON THE COMPANY——B. Business Overview—Intellectual Property.”

D. Trend information

For a discussion of trend information, see “ITEM 5. OPERATING AND FINANCIAL REVIEW AND PROSPECTS.”

E. Critical accounting estimates

Our consolidated financial statements are prepared in conformity with IFRS, as issued by the IASB. In preparing our consolidated financial statements, we make judgements, estimates and assumptions about the application of our accounting policies which affect the reported amounts of assets, liabilities, revenue and expenses. Our critical accounting judgements and sources of estimation uncertainty are described in Note 2.19 to our consolidated financial statements, which are included elsewhere in this Annual Report.

ITEM 6. DIRECTORS, SENIOR MANAGEMENT AND EMPLOYEES

A. Directors and senior management Board of Directors

The following table presents information about our Board and Senior Management as of the date of this Annual Report.

Name	Position	Age	Initial year of appointment	Term
Board				
Berndt Modig	Chief Executive Officer and Executive Director	66	2015	2028
Hans Schikan, Pharm.D.	Non-Executive Director	66	2019	2028
David Meeker, M.D.	Non-Executive Director	70	2021	2025
Robert Glassman, M.D.	Non-Executive Director	61	2021	2025
Viviane Monges	Non-Executive Director	61	2021	2025
Elisabeth Björk, M.D.	Non-Executive Director	63	2021	2026
Senior Management				
Berndt Modig	Chief Executive Officer and Director	66	2015	N/A
Peng Lu, M.D., Ph.D.	Chief Medical Officer	47	2020	N/A
Anne Lesage, Ph.D.	Chief Early Development Officer	64	2015	N/A
Anna Nijdam, MSc RA	Head of Strategic Finance and Principal Accounting Officer	43	2020	N/A
Wim Souverijns, Ph.D.	Chief Commercial Officer	54	2021	N/A
Annick Deschoolmeester	Chief Human Resources Officer	52	2022	N/A
Stefan Abele, Ph.D.	Chief Technical Operations Officer	55	2023	N/A
David Nassif	Chief Financial Officer, Chief Legal Officer	70	2024	N/A

Unless otherwise indicated, the current business address for members of our Board and Senior Management is Pharvaris N.V., Emmy Noetherweg 2, 2333 BK Leiden, the Netherlands.

The following is a brief summary of the business experience of our Board and Senior Management.

Board of Directors

Berndt Modig

Mr. Modig co-founded Pharvaris and has served as Chief Executive Officer since its inception. Mr. Modig is also a director of the Company. Prior to co-founding the Company, Mr. Modig served as Chief Financial Officer of Prosensa Holding N.V., a biopharmaceutical company focusing on novel RNA modulating treatments for rare diseases like Duchenne muscular dystrophy, from March 2010 through its IPO on the Nasdaq in 2013 until its acquisition by BioMarin Pharmaceutical Inc. in January 2015.

From October 2003 to November 2008, Mr. Modig was Chief Financial Officer at Jerini AG through its IPO on the Frankfurt exchange in 2005 and sale to Shire plc in 2008. Jerini developed and launched icatibant for the treatment of HAE, now currently marketed by Takeda Pharmaceuticals under the FIRAZYR brand name. Before Jerini AG, Mr. Modig served as Chief Financial Officer at Surplex AG from 2001 to 2003 and as Finance Director Europe of U.S.-based Hayward Industrial Products Inc. from 1999 to 2001. In previous positions, Mr. Modig was a Partner in the Brussels-based private equity firm Agra Industria from 1994 to 1999 and a Senior Manager in the Financial Services Industry Group of Price Waterhouse LLP in New York from 1991 to 1994. Mr. Modig received a bachelor's degree in business administration, economics and German from the University of Lund, Sweden, and an MBA from INSEAD, Fontainbleau, France.

Hans Schikan, Pharm.D.

Mr. Schikan is a co-founder of the Company and has been a director since August 2019. Mr. Schikan is the former CEO of Prosensa Holding N.V. (Nasdaq: RNA), a biopharmaceutical company focusing on novel RNA modulating treatments for rare diseases including Duchenne muscular dystrophy, from January 2009 through its IPO on the Nasdaq in 2013 until its acquisition by BioMarin Pharmaceutical Inc. in January 2015.

Mr. Schikan was previously at Genzyme, most recently serving as VP for Global Marketing and Strategic Development of Genzyme's product portfolio for rare genetic diseases. He is currently Chairman of the Board Member of Vicore Pharma (STO: VICO) and Microbiotica, and Board Member of Organon N.V. Finally, he is a member of the Top Team of the Dutch Top Sector Life Sciences & Health. Previously, he served on the boards of Sobi (STO: SOBI), Hansa Biopharma (STO: HNSA), Wilson Therapeutics (STO: WTX) (acquired by Alexion), Therachon (acquired by Pfizer), VectivBio (Nasdaq: VECT) (acquired by IronWood), Asceneuron, Complix and InteRNA. Mr. Schikan has a Pharm.D. degree from Utrecht University.

David Meeker, M.D.

Dr. Meeker has been a director since January 2021. Dr. Meeker is the Chairman of the Board of Directors, President and Chief Executive Officer of Rhythm Pharmaceuticals, Inc. Prior to joining Rhythm Pharmaceuticals, Dr. Meeker served as President and Chief Executive Officer of KSQ Therapeutics, Inc. from 2017 to 2020. Prior to joining KSQ, Dr. Meeker worked at Sanofi Genzyme from 2011 to 2017, in a variety of roles, including as President and Chief Executive Officer of Genzyme, a Sanofi Company, as a member of Sanofi's Executive Committee, and as Executive Vice President and Head of Sanofi Genzyme, Sanofi's specialty care unit with responsibility for rare diseases, multiple sclerosis, oncology and immunology franchises. Prior to joining Genzyme, Dr. Meeker was Director of the Pulmonary Critical Care Fellowship at the Cleveland Clinic. Dr. Meeker has served as Chair of Trevi Therapeutics since 2017. He also served as a Director of MyoKardia, Inc. until its acquisition by Bristol Myers Squibb.

Dr. Meeker holds a medical degree from the University of Vermont Medical School and completed the Advanced Management Program at Harvard Business School in 2000.

Robert Glassman, M.D.

Dr. Glassman has been a director since January 2021. Since July 2022, Dr. Glassman served as the Executive Vice President, Search & Evaluation at Enavate Sciences, a $600M private equity fund that is a subsidiary of Patient Square Capital. Dr. Glassman also serves as a board member for Umoja and EluraBio and he is an advisor at Centrexion.

Dr. Glassman is an industry veteran with nearly 30 years of healthcare leadership and investment experience. Most recently, he was a venture partner in public equity at OrbiMed Advisors, returning to the firm after serving as a private equity partner. Previously, he worked as a senior investment banking professional for over seventeen years across Credit Suisse, Merrill Lynch, Bank of America, most recently serving as Vice Chairman of the Global Health Care Investment Banking division at Credit Suisse. Earlier in his career, Dr. Glassman oversaw healthcare investments at Merrill Lynch Global Private Equity and was a consultant within McKinsey & Company's Pharmaceutical and Medical Products practice. Dr. Glassman was a board-certified hematologist-oncologist and remains on the faculty of Weill Cornell as a Clinical Assistant Professor of Medicine. He also spent several years as a basic science investigator at Rockefeller University in the laboratory of Hidesaburo Hanafusa, where he received Howard Hughes Medical Institute and American Cancer Society awards. Dr. Glassman earned his A.B. from Harvard College and an M.D. from Harvard Medical School.

Elisabeth Björk, M.D.

Dr. Björk has been a director since December 2021. Dr. Björk is currently Senior Vice President, Late-stage Development, Cardiovascular, Renal and Metabolism (CVRM), BioPharmaceuticals R&D at AstraZeneca and has led the global development of medicines within this area for over 10 years. Throughout her career at AstraZeneca which began in 2002, she has gained broad drug development experience covering clinical development phase I-IV, large outcomes programs, major global filings and health authority interactions, and commercial strategy/implementation. Dr. Björk is an endocrinologist by training and an associate professor of medicine at Uppsala University, Sweden. She is also a board member of Rocket Pharmaceuticals, Chalmers University of Technology, Vicore Pharma AB and Betula Consulting AB.

Viviane Monges

Ms. Monges has been a director since July 2021 and serves as the Chair of the Audit Committee. She serves as a non-executive director at Ferring Pharmaceuticals, ADC Therapeutics, BioMerieux and Novo Holdings. Prior to these roles, Ms. Monges was Chair of the board of EUROAPI, she held a position as VP of Finance of Nestlé's Business Excellence Division. Prior to that, she served as the Global CFO of the OTC division at Novartis. Ms. Monges also served as CFO of European Pharmaceuticals at Wyeth/Pfizer and as CFO of the Global Pharmaceutical Business unit of Wyeth/Pfizer. She holds an MBA from Ecole Supérieure de Commerce de Paris.

Senior management

Peng Lu, M.D., Ph.D.

Dr. Lu joined the Company in 2020, bringing 15 years of protein therapeutics and small molecule drug development experience, including within rare genetic diseases.

Previously, Dr. Lu served as the Vice President, Global Program Lead for rare diseases at Takeda (via acquisition of Shire). During Dr. Lu's time at Takeda/Shire, she was instrumental in leading project teams that successfully completed two Phase 3 pivotal HAE studies and achieved global approval of TAKHZYRO (lanadelumab-flyo) for the prevention of HAE attacks in the U.S., EU, and the rest of the world. In addition, she has also led the life-cycle management of TAKHZYRO beyond HAE, looking to broaden indications in other plasma-kallikrein-mediated diseases.

Prior to Takeda/Shire, Dr. Lu held roles in clinical development, translational research and clinical pharmacology with increasing levels of responsibility at AbbVie and Roche/Genentech, where she was responsible for the design and implementation of early and late development clinical strategy across a broad range of indications including autoimmune, respiratory, and genetic diseases leading to

multiple approvals. Dr. Lu received her medical degree from Beijing Medical University and Ph.D. from The University of Texas, Austin, in systems biology.

Anne Lesage, Ph.D.

Dr. Anne Lesage is Chief Early Development Officer at Pharvaris. Dr. Lesage is a co-founder of Pharvaris and has led the translational science, preclinical and non-clinical development since its inception. Dr. Lesage has over 30 years' experience in drug discovery, preclinical and early development.

From 1992 until 2010, Dr. Lesage held different leadership positions with increasing responsibility in the neuroscience drug discovery unit at Johnson & Johnson. By 2010, Dr. Lesage served as the biology head of psychiatry.

Dr. Lesage is an inventor on 10 patents and an author of 46 publications. Dr. Lesage founded GrayMatters Consulting in 2010, and advises early and late-stage biotech companies, venture capital organisations, and government agencies and initiatives. In 2013, Dr. Lesage co-founded Kosa Pharma.

Dr. Lesage is trained as a biochemist and holds a Ph.D. in molecular biology. Dr. Lesage studied biochemistry at the University of Ghent, received her Ph.D. in the group of Professor Walter Fiers, and was a post-doctoral fellow in the Child Psychiatry department of Stanford University Medical School and in the CNRS Laboratory of Viral Oncology of Hospital Paul Brousse in Paris.

Anna Nijdam, MSc RA

Ms. Nijdam joined the Company in 2020, with over 12 years' experience in the financial industry as a chartered accountant. From 2008 until 2020, Ms. Nijdam worked in the Assurance Services group at Ernst & Young Accountants LLP in Rotterdam, the Netherlands, where she held various leadership positions, including most recently serving as a Senior Manager. Ms. Nijdam is treasurer at the Entrepreneurs Foundation and previously served as member of the Associations Audit Committee of Hockey Club Rotterdam and as a member of the supervisory board of Access to Seeds foundation. Ms. Nijdam holds a master's in economics from the Erasmus University of Rotterdam and a Register Accountant title (Dutch Certified Public Accountant) from Nivra Nyenrode in the Netherlands.

Wim Souverijns, Ph.D.

Dr. Souverijns joined the Company in July 2021 with over 25 years of experience in pharmaceutical portfolio strategic and operational leadership at ObsEva, Celgene, and Amgen.

Dr. Souverijns joined the Company from his most recent position as the Chief Commercial Officer at ObsEva where he was responsible for the commercialization of its women's health product portfolio. Prior to joining ObsEva, he spent 11 years at Celgene where he contributed to the successful build out of the product portfolio in diverse strategic and operational leadership roles. He developed a broad pharmaceutical background through various international assignments at PwC Consulting and in different market access roles at Amgen, both at the European and global level. Dr. Souverijns holds a degree in bioengineering from the KU Leuven, Belgium, and obtained a Ph.D. from the same institute.

Annick Deschoolmeester

Ms. Deschoolmeester joined Pharvaris in September 2021 and currently serves as the Chief Human Resources Officer with over 25 years of experience in human resources across various industries, including in management consulting and international talent management in the biotech and pharmaceutical industries. Before joining Pharvaris, she served as Global Head of Learning & Talent and as HR Business Leader, Plasma Derived Therapies, with Takeda Pharmaceuticals. Prior to that, Ms. Deschoolmeester developed a broad human resources background, working in human resources leadership roles at European, international, and global levels with companies such as Shire Pharmaceuticals, Allergan, Yahoo, and PricewaterhouseCoopers. She holds a master's degree in Interpreting from the Provincial Hogeschool voor Vertalers & Tolken in Gent, Belgium.

Stefan Abele, Ph.D.

Dr. Abele joined Pharvaris in November 2023 and currently serves as Chief Technical Operations Officer. In this role, he is responsible for all chemistry, manufacturing, and controls (CMC) activities, global supply chain, global project management, patent governance, and IT/Business Information Systems as Pharvaris progresses into late-stage clinical development and preparing for launch. Dr. Abele joined Pharvaris with more than 20 years of experience in process development, end-to-end Active Pharmaceutical Ingredients (API) supply chain, cross-functional CMC activities, GMP manufacturing, global vendor management, and people leadership.

Previously, Dr. Abele served as the Senior Vice President, Chemical Development and Commercial Manufacturing at Idorsia Pharmaceuticals, where he and his team were responsible for the Drug Substance development and manufacturing of QUVIVIQ (daridorexant), PIVLAZ (clazosentan), and aprocitentan. Prior to Idorsia, Dr. Abele worked at Actelion Pharmaceuticals where he established and grew the fully integrated Chemistry Process R&D department. Earlier, he held positions of growing responsibility at

Carbogen-Amcis, including as Head of Production and as a manager of teams in R&D and GMP manufacturing of APIs for global pharma companies. Dr. Abele holds a Diploma in Chemistry from the University of Konstanz and a Ph.D. in Synthetic Organic Chemistry from the ETH Zurich.

David Nassif, J.D.

Mr. Nassif joined Pharvaris in 2024 and currently serves as Chief Financial Officer and Chief Legal Officer, bringing more than 30 years of life sciences industry experience in executive financial management roles in development-stage, commercial-stage, public and private companies.

Mr. Nassif served as Chief Executive Officer, Chief Financial Officer, and Board Member of Sio Gene Therapies, where he was responsible for all finance, accounting, tax, treasury, legal, and SEC compliance and reporting activities until February 2022, when he undertook the liquidation and dissolution of the company. Prior to joining Sio, Mr. Nassif was Executive Vice President and Chief Financial Officer of SteadyMed Therapeutics, where he was instrumental in its acquisition by United Therapeutics in August 2018. From 2011 to 2014, Mr. Nassif served as the President and Chief Financial Officer of Histogen. Previously, he was Executive Vice President and Chief Financial Officer of Zogenix and held several key roles at Amphastar Pharmaceuticals and RealAge Inc. Earlier in his career, Mr. Nassif held various positions with Cypros Pharmaceuticals, where he was instrumental in leading its merger with Ribogene, Inc. to form Questcor Pharmaceuticals, Inc.

He holds a BS in finance and management information systems with honors from the University of Virginia and a JD from the University of Virginia School of Law.

B. Compensation

Compensation and Other Benefits of Members of Our Board

As a foreign private issuer, in accordance with Nasdaq listing requirements, we comply with home country compensation requirements and certain exemptions thereunder rather than complying with Nasdaq compensation requirements. Dutch law does not provide for limitations with respect to the aggregate annual compensation paid to our directors, provided that such compensation is consistent with our compensation policy. Such compensation policy requires approval by our general meeting by a simple majority of votes cast. The Board determines the compensation of individual directors with due observance of the compensation policy. A proposal with respect to compensation schemes in the form of shares or rights to shares in which directors may participate is subject to approval at our general meeting by a simple majority of votes cast. Such a proposal must set out at least the maximum number of shares or rights to subscribe for shares to be granted to the directors and the criteria for granting or amendment.

Our compensation policy authorizes our Board to determine the amount, level, and structure of the compensation packages of our directors at the recommendation of our compensation committee. These compensation packages may consist of a mix of fixed and variable compensation components, including base salary, short-term incentives, long-term incentives, fringe benefits, severance pay and pension arrangements, as determined by our Board.

Disclosure of Compensation of our Board and Senior Management

For so long as we qualify as a foreign private issuer, we are not required to comply with the proxy rules applicable to U.S. domestic companies, including the requirement applicable to emerging growth companies to disclose the compensation of our chief executive officer and other two most highly compensated executive officers on an individual, rather than an aggregate, basis.

The aggregate compensation, including benefits in kind, accrued or paid to members of our Board and Senior Management with respect to the year ended December 31, 2024 for services in all capacities was approximately €16.4 million. For the year ended December 31, 2024, we paid Mr. Modig, our Chief Executive Officer and Executive Director, €1.1 million in compensation and benefits in kind.

The table below shows the aggregate compensation, including benefits in kind, accrued or paid to individual members of the Board for the year ended December 31, 2024 in such capacity.

	Base salary	Total remuneration
Mr. Modig	€ 580,859	€ 1,106,230
Dr. Glassman	—	$ 55,000
Dr. Meeker	—	$ 94,000
Mr. Schikan	—	$ 61,000
Ms. Monges	—	$ 65,000
Dr. Björk	—	$ 45,000

The table below shows the number of options granted to individual members of the Board for the year ended December 31, 2024 in such capacity.

	Number of Options	Exercise Price	Expiration Date
Mr. Modig	150,000	$ 22.31	April 11, 2034
Dr. Glassman	14,000	$ 22.31	April 11, 2034
Dr. Meeker	14,000	$ 22.31	April 11, 2034
Mr. Schikan	14,000	$ 22.31	April 11, 2034
Ms. Monges	14,000	$ 22.31	April 11, 2034
Dr. Björk	14,000	$ 22.31	April 11, 2034

The table below shows the number of RSU's granted to individual members of the Board for the year ended December 31, 2024 in such capacity.

	Number of RSU's
Mr. Modig	50,000
Dr. Glassman	4,667
Dr. Meeker	4,667
Mr. Schikan	4,667
Ms. Monges	4,667
Dr. Björk	4,667

Share Ownership of our Board and Senior Management

The table below sets forth the share ownership of our Board and Senior Management as of April 1, 2025.

	Number of Ordinary Shares [3]	Percentage of Shares Outstanding
Mr. Modig[1]	950,000	1.74 %
Mr. Schikan	400,000	0.73 %
Dr. Lesage[2]	163,969	0.30 %
Dr. Meeker	50,000	0.09 %
Dr. Glassman	—	—
Dr. Björk	—	—
Ms. Monges	—	—
Dr. Lu	—	—
Ms. Nijdam	19,181	0.04 %
Dr. Souverijns	—	—
Ms. Deschoolmeester	30,979	0.06 %
Dr. Abele	—	—
Mr. Nassif	800	0.001 %

[1] Represents ordinary shares held by Schoodic Management B.V., an entity controlled by Mr. Modig.

[2] Represents ordinary shares held by GrayMatters Consulting B.V., an entity controlled by Dr. Lesage.

[3] Each ordinary share carries one vote per share.

Option Ownership of our Board and Senior Management

The table below sets forth the vested and unvested options granted to our Board and Senior Management as of April 1, 2025.

Name	Options	Exercise Price	Percentage of Shares Outstanding	Percentage of Fully Diluted	Expiration Date
Mr. Modig	95,000	€ 2.38	0.17 %	0.16 %	January 1, 2030
Mr. Modig	250,000	€ 16.69	0.46 %	0.43 %	February 5, 2031
Mr. Modig	140,000	€ 16.41	0.26 %	0.24 %	April 1, 2032
Mr. Modig	170,000	€ 7.37	0.31 %	0.29 %	April 6, 2033
Mr. Modig	150,000	€ 20.80	0.28 %	0.26 %	April 11, 2034
Mr. Modig	180,000	€ 14.71	0.33 %	0.31 %	March 12, 2035
Dr. Lesage	16,472	€ 2.38	0.03 %	0.03 %	January 1, 2030
Dr. Lesage	120,000	€ 16.69	0.22 %	0.21 %	February 5, 2031
Dr. Lesage	65,000	€ 16.41	0.12 %	0.11 %	April 1, 2032
Dr. Lesage	100,000	€ 7.37	0.18 %	0.17 %	April 6, 2033
Dr. Lesage	50,000	€ 20.80	0.09 %	0.09 %	April 11, 2034
Dr. Lesage	60,000	€ 14.71	0.11 %	0.10 %	March 12, 2035
Dr. Lu	306,666	€ 2.38	0.56 %	0.53 %	February 3, 2030
Dr. Lu	65,000	€ 16.69	0.12 %	0.11 %	February 5, 2031
Dr. Lu	65,000	€ 16.41	0.12 %	0.11 %	April 1, 2032
Dr. Lu	80,000	€ 7.37	0.15 %	0.14 %	April 6, 2033
Dr. Lu	65,000	€ 20.80	0.12 %	0.11 %	April 11, 2034
Dr. Lu	67,500	€ 14.71	0.12 %	0.12 %	March 12, 2035
Dr. Glassman	23,300	€ 5.94	0.04 %	0.04 %	January 1, 2031
Dr. Glassman	8,000	€ 16.69	0.01 %	0.01 %	February 5, 2031
Dr. Glassman	14,493	€ 16.41	0.03 %	0.02 %	April 1, 2032
Dr. Glassman	21,000	€ 7.37	0.04 %	0.04 %	April 6, 2033
Dr. Glassman	14,000	€ 20.80	0.03 %	0.02 %	April 11, 2034
Dr. Glassman	15,000	€ 14.71	0.03 %	0.03 %	March 12, 2035
Dr. Meeker	80,000	€ 5.94	0.15 %	0.14 %	January 1, 2031
Dr. Meeker	17,500	€ 16.41	0.03 %	0.03 %	April 1, 2032
Dr. Meeker	21,000	€ 7.37	0.04 %	0.04 %	April 6, 2033
Dr. Meeker	14,000	€ 20.80	0.03 %	0.02 %	April 11, 2034
Dr. Meeker	15,000	€ 14.71	0.03 %	0.03 %	March 12, 2035
Ms. Monges	35,000	€ 14.67	0.06 %	0.06 %	July 1, 2031
Ms. Monges	17,500	€ 16.41	0.03 %	0.03 %	April 1, 2032
Ms. Monges	21,000	€ 7.37	0.04 %	0.04 %	April 6, 2033
Ms. Monges	14,000	€ 20.80	0.03 %	0.02 %	April 11, 2034
Ms. Monges	15,000	€ 14.71	0.03 %	0.03 %	March 12, 2035
Dr. Björk	35,000	€ 12.67	0.06 %	0.06 %	January 1, 2032
Dr. Björk	17,500	€ 16.41	0.03 %	0.03 %	April 1, 2032
Dr. Björk	21,000	€ 7.37	0.04 %	0.04 %	April 6, 2033
Dr. Björk	14,000	€ 20.80	0.03 %	0.02 %	April 11, 2034
Dr. Björk	15,000	€ 14.71	0.03 %	0.03 %	March 12, 2035
Dr. Souverijns	115,000	€ 14.67	0.21 %	0.20 %	July 1, 2031
Dr. Souverijns	65,000	€ 16.41	0.12 %	0.11 %	April 1, 2032
Dr. Souverijns	75,000	€ 7.37	0.14 %	0.13 %	April 6, 2033
Dr. Souverijns	45,000	€ 20.80	0.08 %	0.08 %	April 11, 2034
Dr. Souverijns	67,500	€ 14.71	0.12 %	0.12 %	March 12, 2035
Mr. Schikan	35,000	€ 16.69	0.06 %	0.06 %	February 5, 2031
Mr. Schikan	17,500	€ 16.41	0.03 %	0.03 %	April 1, 2032
Mr. Schikan	21,000	€ 7.37	0.04 %	0.04 %	April 6, 2033
Mr. Schikan	14,000	€ 20.80	0.03 %	0.02 %	April 11, 2034
Mr. Schikan	15,000	€ 14.71	0.03 %	0.03 %	March 12, 2035
Ms. Nijdam	30,000	€ 16.69	0.06 %	0.05 %	February 5, 2031
Ms. A. Deschoolmeester	70,000	€ 7.37	0.13 %	0.12 %	April 6, 2033
Ms. A. Deschoolmeester	45,000	€ 20.80	0.08 %	0.08 %	April 11, 2034
Ms. A. Deschoolmeester	60,000	€ 14.71	0.11 %	0.10 %	March 12, 2035
Dr. S Abele	90,000	€ 15.13	0.17 %	0.15 %	November 15, 2033
Dr. S Abele	40,000	€ 20.80	0.07 %	0.07 %	April 11, 2034
Dr. S Abele	60,000	€ 14.71	0.11 %	0.10 %	March 12, 2035
Mr. Nassif	230,000	€ 18.97	0.42 %	0.40 %	April 15, 2034
Mr. Nassif	75,000	€ 20.80	0.14 %	0.13 %	April 11, 2034

The table below sets forth the vested and unvested RSUs granted to our Board and Senior Management as of April 1, 2025.

	Number of RSU's
Mr. Modig	110,000
Dr. Glassman	4,667
Dr. Meeker	4,667
Mr. Schikan	4,667
Ms. Monges	4,667
Dr. Björk	4,667
Dr. Lesage	36,450
Dr. Lu	44,350
Ms. Nijdam	44,416
Dr. Souverijns	37,800
Ms. Deschoolmeester	40,231
Dr. Abele	33,150
Mr. Nassif	109,500

Equity Incentive Plans

2016 Equity Incentive Plan

In 2016, the Company adopted the Pharvaris B.V. 2016 Equity Incentive Plan, or the 2016 Plan, in order to advance the interests of the Company and its stakeholders by enhancing the Company's ability to attract, retain and motivate persons who are expected to make important contributions to the Company and by providing incentives for such persons to exert maximum efforts for the success of the Company and provide a means by which eligible individuals may benefit from increases in the value of the Company's shares. The 2016 Plan was amended and restated in connection with our initial public offering. As of April 1, 2025, there were no shares available for issuance under the 2016 Plan.

The 2016 Plan provided for the grant of options, stock appreciation rights, restricted stock, restricted stock units, or RSUs, performance stock awards, performance cash awards, and other stock-based awards.

In connection with the consummation of our initial public offering, we granted our officers and directors stock options to purchase an aggregate of 873,000 ordinary shares in accordance with the terms of the 2016 Plan and the terms and conditions of award agreements evidencing such grants. The exercise price per share was the initial public offering price per share.

As of April 1, 2025, the total number of options held by the Board and Senior Management and other employees is 3,723,931 with a weighted average exercise price of $10.02 per share.

As of April 1, 2025, the total number of unvested RSUs held by the Board and Senior Management is 338,524.

2021 Equity Incentive Plan

In order to incentivize our directors and employees, our Board adopted the Pharvaris N.V. 2021 Equity Incentive Plan, or the 2021 Plan, for employees, consultants and directors prior to the completion of our initial public offering. The 2021 Plan became effective upon our conversion from Pharvaris B.V. into Pharvaris N.V., which occurred prior to the consummation of our initial public offering. The 2021 Plan provides for the grant of options, stock appreciation rights, restricted stock, RSUs, performance stock awards, other stock-based awards, performance cash awards and substitute awards. The 2021 Plan is intended to help us secure and retain the services of eligible award recipients, provide incentives for such persons to exert maximum efforts for our success and provide a means by which eligible recipients may benefit from increases in the value of our ordinary shares. Subject to adjustment in the event of certain transactions or changes of capitalization in accordance with the 2021 Plan, ordinary shares equal to 9% of the Company's issued share capital as of the date of the consummation of the IPO were initially reserved for issuance pursuant to awards under the 2021 Plan. The total number of ordinary shares reserved for issuance under the 2021 Plan will be increased on January 1 of each calendar year during the term of the 2021 Plan, by the lesser of (i) 4% of the total number of shares outstanding as of the date of increase or (ii) such number of ordinary shares determined by our board of directors.

Employment and Consulting Agreements with Senior Management

We have entered into written employment or service agreements with each member of our Senior Management. See "ITEM 7. MAJOR SHAREHOLDERS AND RELATED PARTY TRANSACTIONS—B. Related party transactions —Agreements and Arrangements with Senior Management" for additional information.

Board Service Contracts

We have entered into service contracts with Dr. Björk, Dr. Glassman, Dr. Meeker, Ms. Monges, and Mr. Schikan that memorialize the terms of their compensation, duties and obligations to the Company. See "ITEM 7. MAJOR SHAREHOLDERS AND RELATED PARTY TRANSACTIONS—B. Related party transactions —Agreements and Arrangements with our Directors" for additional information.

Insurance and Indemnification

Under Dutch law, members of the Board may be held liable for damages in the event of improper or negligent performance of their duties. They may be held jointly and severally liable for damages to the Company and to third parties for infringement of the Articles of Association or of certain provisions of Dutch law. In certain circumstances, they may also incur other specific civil and criminal liabilities.

Members of the Board, Senior Management, certain other of our officers and certain subsidiaries are insured under an insurance policy against damages resulting from their conduct when acting in the capacities as such members or officers.

The Articles of Association provide for an indemnity for current and former members of the Board and such current and former officers and employees of the Company as designated by the Board, collectively, the Indemnified Persons. The Company shall indemnify all Indemnified Persons against any financial losses or damages incurred by such person and any expense reasonably paid or incurred by such person in connection with any threatened, pending or completed suit, claim, action or legal proceedings of a civil, criminal, administrative or other nature, formal or informal, in which such person becomes involved to the extent this relates to his current or former position with the Company and/or a group company and in each case to the extent permitted by applicable law. No indemnification under our Articles of Association shall be given to an Indemnified Person: (a) if a competent court or arbitral tribunal has established, without having (or no longer having) the possibility for appeal, that the acts or omissions of such Indemnified Person that led to the financial losses, damages, expenses, suit, claim, action or legal proceedings are of an unlawful nature (including acts or omissions which are considered to constitute malice, gross negligence, intentional recklessness and/or serious culpability attributable to such Indemnified Person); (b) to the extent that the Indemnified Person's financial losses, damages and expenses are covered under insurance and the relevant insurer has settled, or has provided reimbursement for, these financial losses, damages and expenses (or has irrevocably undertaken to do so); (c) in relation to proceedings brought by such Indemnified Person against the Company, except for proceedings brought to enforce indemnification to which the Indemnified Person is entitled pursuant to the Articles of Association of the Company, any indemnification agreement entered into with such Indemnified Person which has been approved by the Board, or pursuant to insurance taken out by the Company for the benefit of such Indemnified Person; or (d) for any financial losses, damages, or expenses incurred in connection with a settlement of any proceedings effected without the Company's prior consent. Under our Articles of Association, our Board may stipulate additional terms, conditions and restrictions in relation to the indemnification described above.

Dutch Corporate Governance

As a listed Dutch public company with limited liability (*naamloze vennootschap*), we are subject to the DCGC. The DCGC contains principles and best practice provisions on corporate governance that regulate relations between the board of directors and the general meeting and matters in respect of financial reporting, auditors, disclosure, compliance and enforcement standards. The DCGC is based on a "comply or explain" principle. Accordingly, companies must disclose in their annual reports whether they comply with the provisions of the DCGC. If a company subject to the DCGC does not comply with these provisions, that company would be required to give reason for such non-compliance. We do not comply with all best practice provisions of the DCGC. Our main deviations from the DCGC are summarized below, but we cannot exclude the possibility of deviating from additional provisions of the DCGC after the date hereof and including in order to follow market practice or governance practices in the United States.

Under our Articles of Association, directors are to be appointed on the basis of a binding nomination prepared by the Board. This means that the nominee will be appointed to the Board, unless the general meeting removes the binding nature of the nomination (in which case a new nomination will be prepared for a subsequent general meeting). Our Articles of Association provide that the general meeting can only pass such resolution by at least a two-thirds majority of the votes cast, representing more than half of the issued share capital. However, the DCGC recommends that the general meeting can pass such a resolution by simple majority, representing no more than one-third of the issued share capital.

Under the Articles of Association, directors can only be dismissed by the general meeting by simple majority, provided that the Board proposes the dismissal. In other cases, the general meeting can only pass such resolution by a two-thirds majority representing more than half of the issued share capital. The DCGC recommends that the general meeting can pass a resolution to dismiss a director by simple majority, representing no more than one-third of the issued share capital.

The DCGC recommends against providing equity awards as part of the compensation of a non-executive director. However, consistent with U.S. market practice, we have granted equity awards to our non-executive directors.

Our Plan allows us to set the terms and conditions of equity awards granted thereunder. Under the Plan, we may grant ordinary shares that are not subject to a lock-up period of at least five years after the date of grant, and we may grant options without restricting the exercisability of those options during the first three years after the date of grant. In those cases, this would cause additional deviations from the DCGC.

C. Board Practices

Board Structure

The Board is charged with the management of the Company, which includes setting the Company's strategy, subject to the restrictions contained in our Articles of Association. The executive director manages our day-to-day business and operations and implement our strategy. The non-executive directors focus on the supervision of the Company policies, performance of the duties of all directors and our general state of affairs. Subject to certain limitations under Dutch law, the directors may divide their tasks among themselves in or pursuant to internal rules applicable to the Board. Each director has a statutory duty to act in the corporate interest of the Company and its business.

Under Dutch law, the corporate interest extends to the interests of all corporate stakeholders, such as shareholders, creditors, employees, customers and suppliers. The duty to act in the corporate interest of the Company also applies in the event of a proposed sale or break-up of the Company, provided that the circumstances generally dictate how such duty is to be applied and how the respective interests of various groups of stakeholders should be weighed. Any resolution of the Board regarding a material change in our identity or character requires approval of the general meeting.

Our Board is entitled to represent the Company. The power to represent the Company also vests in our Chief Executive Officer, as well as in any other two Executive Directors acting jointly. Any resolution of the Board regarding a material change in our identity or character, as defined under Dutch law, requires approval of our general meeting. The absence of the approval of the general meeting shall result in the relevant resolution being null and void but shall not affect the powers of representation of the Board or of the Executive Directors.

The Board may consist of one or more executive directors and one or more non-executive directors. The Board shall be composed of individuals.

Under our Articles of Association, the directors are appointed by the general meeting upon binding nomination by our Board based on a recommendation of our nomination and corporate governance committee. However, the general meeting may at all times overrule the binding nomination by a resolution adopted by at least a two-thirds majority of the votes cast, provided such majority represents more than half of the issued share capital. If the general meeting overrules the binding nomination, the Board shall make a new nomination.

At a general meeting, a resolution to appoint a director can only be passed in respect of candidates whose names are stated for that purpose in the agenda of that general meeting or in the explanatory notes thereto. Upon the appointment of a person as a director, the general meeting shall determine whether that person is appointed as executive director or as non-executive director.

The general meeting shall at all times be entitled to suspend or dismiss a director. Under our Articles of Association, the general meeting may only adopt a resolution to suspend or dismiss a director by at least a two-thirds majority of the votes cast, provided that such majority represents more than half of the issued share capital, unless the resolution is passed at the proposal of the Board, in which latter case a simple majority of the votes cast is sufficient. If a director is suspended and the general meeting does not resolve to dismiss him or her within three months from the date of such suspension, the suspension shall lapse.

The Board may also suspend, but may not remove, an executive director. The Articles of Association do not contain limitations on the period of a term of appointment nor on the number of consecutive terms, but we will be subject to the Dutch Corporate Governance Code, or DCGC, which provides the following best practice recommendations on the terms for directors' service:

- executive directors should be appointed for a maximum period of four years, without limiting the number of consecutive terms they may serve; and
- non-executive directors should be appointed for two consecutive periods of no more than four years, after which non-executive directors may be reappointed for a maximum of two consecutive periods of no more than two years, provided that of the reasons for any reappointment after an eight-year term of office should be disclosed in the Company's statutory annual Board report.

Board Composition, Diversity and Election of Directors

Our Board is comprised of six members, one of whom is an executive director. The members of our Board do not have a retirement age requirement under our Articles of Association. No family relationships or other arrangements exist among any member of our Board or Senior Management.

Our diversity policy is that we will balance our Board in terms of gender, age, background and nationality as much as reasonably possible while still having our board composed of the best possible candidates overall. It has been and will remain our priority to have the best available specialists on our Board, irrespective of age, background, nationality and gender, who make a balanced panel of directors able to advise and guide our Company to further growth and success for all its stakeholders. This means we require a number of specialties and character traits to be present. Taking into account the aforementioned and the specialist nature of our business, we will actively seek to further improve diversity on our board if and when proposing new appointments to our Board, whilst acknowledging that age, gender and nationality are important, but not the only factors relevant for the ultimate decision to select a board member. The table below provides information as to the gender diversity of our Board. Dutch law prohibits us from gathering and disclosing demographic background data.

Board Diversity Matrix (As of April 1, 2025)				
Country of Principal Executive Offices:	The Netherlands			
Foreign Private Issuer	Yes			
Disclosure Prohibited under Home Country Law	Yes			
Total Number of Directors	6			
	Female	**Male**	**Non-Binary**	**Did Not Disclose Gender**
Part I: Gender Identity				
Directors	2	3	-	1
Part II: Demographic Background				
Underrepresented Individual in Home Country Jurisdiction	-			
LGBTQ+	-			
Did Not Disclose Demographic Background	-			

Corporate Governance Practices

As a "foreign private issuer," as defined by the SEC, we are permitted to follow certain governance practices of the Netherlands instead of those otherwise required under the Nasdaq Stock Market, or Nasdaq, rules for domestic issuers. We intend to take advantage of the following limited exemptions:

- Exemption from filing quarterly reports on Form 10-Q and current reports on Form 8-K disclosing significant events within four days of their occurrence.
- Exemption from Section 16 rules regarding sales of ordinary shares by insiders, which will provide less data in this regard than to shareholders of U.S. companies that are subject to the Exchange Act.
- Exemption from the Nasdaq rules applicable to domestic issuers requiring disclosure within four business days of any determination to grant a waiver of the code of business conduct and ethics to directors and officers.
- Exemption from the requirement that we provide in our bylaws for a generally applicable quorum and that such quorum not be less than one-third of the outstanding voting stock.
- Exemption from the requirement that we solicit proxies and provide proxy statements for all meetings of Shareholders and shall provide copies of such proxy solicitation to Nasdaq.
- Exemption from the requirement for shareholder approval for the issuance of securities in connection with certain events such as the acquisition of shares or assets of another company, the establishment of or amendments to equity-based compensation plans for employees, a change of control of us and certain private placements.

Nasdaq Rule 5615(a)(3) provides that a foreign private issuer may rely on home country corporate governance practices in lieu of certain of the rules in the Nasdaq Rule 5600 Series, Rule 5250(b)(3) and Rule 5250(d).

We intend to take all actions necessary to maintain compliance as a foreign private issuer under the applicable corporate governance requirements of the Sarbanes-Oxley Act, the rules adopted by the SEC and the Nasdaq corporate governance rules and listing standards.

Because we are a foreign private issuer, our directors and senior management are not subject to short-swing profit and insider trading reporting obligations under Section 16 of the Exchange Act. They will, however, be subject to the obligation to report changes in share ownership under Section 13 of the Exchange Act and related SEC rules.

Board Committees

Audit committee

The audit committee, which consists of Mr. Schikan, Ms. Monges and Dr. Glassman, assists the Board in overseeing our accounting and financial reporting processes and the audits of our financial statements. Ms. Monges serves as Chair of the Audit Committee. In addition, the audit committee is responsible for the appointment, compensation, retention and oversight of the work of our independent registered public accounting firm. Our Board has determined that Mr. Schikan, Ms. Monges and Dr. Glassman, satisfy the "independence" requirements set forth in the Nasdaq listing standards and Rule 10A-3 under the Exchange Act. Our Board has determined that Mr. Schikan and Ms. Monges qualify as "audit committee financial experts," as such term is defined in the rules of the SEC.

Compensation committee

The compensation committee, which consists of Dr. Glassman, Dr. Meeker and Mr. Schikan, assists our Board in overseeing compensation for our executive officers and our directors. Mr. Schikan serves as Chairman of the committee. Our Board has determined that Dr. Glassman, Dr. Meeker and Mr. Schikan satisfy the "independence" requirements under the Exchange Act and the Nasdaq listing standards.

Nomination and corporate governance committee

The nomination and corporate governance committee, which consists of Dr. Björk, Dr. Meeker and Ms. Monges, assists our Board in identifying individuals qualified to become members of our Board consistent with criteria established by our Board and in developing our code of conduct.

Dr. Meeker serves as Chairman of the committee. Our Board has determined that Dr. Björk, Dr. Meeker and Ms. Monges satisfy the "independence" requirements under the Exchange Act and the Nasdaq listing standards.

D. Employees

As of December 31, 2024, we had 108 employees. None of our employees are represented by labor unions or covered by collective bargaining agreements. We believe our relations with our employees are good.

The table below sets out the number of employees by main category of activity and geographical location as of December 31, 2024:

Geography	Research and development	General and administrative	Total
Switzerland	28	8	36
The Netherlands	12	11	23
United States	37	12	49
Total	77	31	108

E. Share ownership

See "ITEM 6. DIRECTORS, SENIOR MANAGEMENT AND EMPLOYEES—B. Compensation—Disclosure of Compensation of our Board and Senior Management" and "ITEM 7. MAJOR SHAREHOLDERS AND RELATED PARTY TRANSACTIONS—A. Major shareholders.

F. Disclosure of a registrant's action to recover erroneously awarded compensation

Not applicable.

ITEM 7. MAJOR SHAREHOLDERS AND RELATED PARTY TRANSACTIONS

A. Major shareholders

The following table presents information relating to the beneficial ownership of Pharvaris' ordinary shares as of April 1, 2025, by:

- each person, or group of affiliated persons, known by us to own beneficially 5% or more of our outstanding ordinary shares;
- each member of our Board and Senior Management; and
- all members of our Board and Senior Management as a group.

The number of ordinary shares beneficially owned by each entity, person and member of Pharvaris' Board or Senior Management is determined in accordance with the rules of the SEC, and the information is not necessarily indicative of beneficial ownership for any other purpose. Under such rules, beneficial ownership includes any ordinary shares over which the individual has sole or shared voting power or investment power as well as any ordinary shares that the individual has the right to acquire within 60 days of April 1, 2025 through the exercise of any option, warrant or other right. Except as otherwise indicated, and subject to applicable community property laws, the persons named in the table have sole voting and investment power with respect to all ordinary shares held by that person.

This table is based upon information supplied by our named senior management, directors, and principal shareholders, and Schedules 13D, and 13G filed with the SEC. The percentage of outstanding ordinary shares is computed on the basis of 54,493,142 ordinary shares outstanding as of April 1, 2025. Ordinary shares that a person has the right to acquire within 60 days of April 1, 2025 are deemed outstanding for purposes of computing the percentage ownership of the person holding such rights, but are not deemed outstanding for purposes of computing the percentage ownership of any other person, except with respect to the percentage ownership of all members of

the Board and Senior Management as a group. Unless otherwise indicated below, the address for each beneficial owner is c/o Pharvaris N.V., Emmy Noetherweg 2, 2333 BK Leiden, the Netherlands.

	Ordinary Shares Beneficially Owned	
Name of Beneficial Owner	Number of Shares	Percentage of Class
5% Beneficial Owner:		
General Atlantic PH B.V. (1)	7,531,252	13.85 %
FMR LLC (2)	5,192,894	9.55 %
Entities affiliated with Foresite Capital (3)	4,038,842	7.43 %
Viking Global Opportunities Illiquid Investments Sub-Master LP (4)	3,653,319	6.72 %
EQT Life Sciences (Formerly LSP V Coöperatieve U.A.) (5)	3,556,805	6.54 %
Entities affiliated with venBio Global Strategic Fund III, L.P. (6)	3,547,504	6.52 %
Entities affiliated with Venrock Healthcare Capital Partners III, L.P.(7)	3,220,130	5.92 %
Board and Senior Management:		
Mr. Modig (8)	1,545,626	2.84 %
Dr. Lu (9)	501,038	*%
Mr. Schikan (10)	478,094	*%
Dr. Lesage (11)	420,625	*%
Dr. Souverijns (12)	215,570	*%
Dr. Meeker (13)	123,094	*%
Dr. Glassman (14)	78,094	*%
Ms. Monges (15)	76,636	*%
Dr. Björk (16)	72,261	*%
Ms. Deschoolmeester (17)	79,625	*%
Ms. Nijdam (18)	59,591	*%
Mr. Abele (19)	48,144	*%
Mr. Nassif (20)	80,967	*%
All executive officers and board members as a group		
(13 persons)	3,779,365	6.95 %

* Indicates beneficial ownership of less than 1% of total outstanding ordinary shares.

(1) Represents 7,531,252 ordinary shares held by General Atlantic PH B.V. (“GA PH”), is a wholly owned subsidiary of General Atlantic Coöperatief U.A. (“GA Coop UA”). The members that share beneficial ownership of the shares held by GA PH through GA Coop UA are the following General Atlantic investment funds (the “GA Funds”): General Atlantic Partners (Bermuda) IV, L.P. (“GAP Bermuda IV”), General Atlantic Partners (Bermuda) EU, L.P. (“GAP Bermuda EU”), General Atlantic Partners (Lux) SCSp (“GAP Lux”), General Atlantic Cooperatief, L.P. (“GA Coop LP”), GAP Coinvestments III, LLC (“GAPCO III”), GAP Coinvestments IV, LLC (“GAPCO IV”), GAP Coinvestments V, LLC (“GAPCO V”), and GAP Coinvestments CDA, L.P. (“GAPCO CDA”). The general partner of GAP Lux is General Atlantic GenPar, (Lux) SCSp (“GA GenPar Lux”), and the general partner of GA GenPar Lux is General Atlantic (Lux) S.à r.l. (“GA Lux”). The general partner of GAP Bermuda IV and GAP Bermuda EU and the sole shareholder of GA Lux is General Atlantic GenPar (Bermuda), L.P. (“GenPar Bermuda”). GAP (Bermuda) L.P. (“GAP (Bermuda)”), which is controlled by the Management Committee of GASC MGP, LLC which is being renamed as the Partnership Committee (the “GA Partnership Committee”), effective subject to applicable regulatory approvals, is the general partner of GenPar Bermuda and GA Coop LP. GA LP, which is also controlled by the GA Partnership Committee, is the managing member of GAPCO III, GAPCO IV and GAPCO V and the general partner of GAPCO CDA.GAP (Bermuda),GA LP, GenPar Bermuda, GA Lux, GA GenPar Lux, and the GA Funds, (collectively, the “GA Group”) are a “group” within the meaning of Rule 13d-5 of the Securities Exchange Act of 1934, as amended. The address of GA Coop LP, GAP Bermuda IV, GAP Bermuda EU, GenPar Bermuda, and GAP (Bermuda) is Clarendon House, 2 Church Street, Hamilton HM 11, Bermuda. The address of GA Coop UA is Prinsengracht 769 A, 1017 JZ, Amsterdam, the Netherlands. The address of GAP Lux, GA GenPar Lux and GA Lux is 412F, Route d’Esch, L-1471 Luxembourg. The address of each of GA LP, GAPCO III, GAPCO IV, GAPCO V, and GAPCO CDA is c/o General Atlantic Service Company, L.P., 55 East 52nd Street, 33rd Floor, New York, NY 10055. Each of the members of the GA Partnership Committee disclaims ownership of the shares except to the extent that he has a pecuniary interest therein.

(2) Represents 5,192,894 ordinary shares held by FMR LLC. Abigail P. Johnson is a Director, the Chairman and the Chief Executive Officer of FMR LLC. Members of the Johnson family, including Abigail P. Johnson, are the predominant owners, directly or through trusts, of Series B voting common shares of FMR LLC, representing 49% of the voting power of FMR LLC. The Johnson family group and all other Series B shareholders have entered into a shareholders' voting agreement under which all Series B voting common shares will be voted in accordance with the majority vote of Series B voting common shares. Accordingly, through their ownership of voting common shares and the execution of the shareholders' voting agreement, members of the Johnson family may be deemed, under the Investment Company Act of 1940, to form a controlling group with respect to FMR LLC. Neither FMR LLC nor Abigail P. Johnson has the sole power to vote or direct the voting of the shares owned directly by the various investment companies

registered under the Investment Company Act, or Fidelity Funds, advised by Fidelity Management & Research Company LLC, or FMR Co. LLC, a wholly owned subsidiary of FMR LLC, which power resides with the Fidelity Funds' Boards of Trustees. FMR Co. LLC carries out the voting of the shares under written guidelines established by the Fidelity Funds' Boards of Trustees. The address of FMR LLC is 245 Summer Street, Boston, MA 02210.

(3) Represents 4,038,842 ordinary shares held by Foresite Capital Fund IV, L.P. ("FCF IV"). Foresite Capital Management IV, LLC ("FCM IV"), is the general partner of FCF IV and may be deemed to have sole voting and dispositive power over shares held by FCF IV. James Tananbaum is the sole managing member of FCM IV and may be deemed to have sole voting and dispositive power over shares held by FCF IV. Each of FCM IV and James Tananbaum disclaims beneficial ownership of shares held by FCF IV except to the extent of any pecuniary interest therein. The address of FCF IV, FCM IV, and James Tananbaum is c/o Foresite Capital Management, 900 Larkspur Landing Circle, Suite 150, Larkspur, CA 94939.

(4) Viking Global Opportunities Illiquid Investments Sub-Master LP ("VGOP") has the authority to dispose of and vote the ordinary shares directly owned by it, which power may be exercised by its general partner, Viking Global Opportunities Portfolio GP LLC ("Opportunities Portfolio GP"), and by Viking Global Investors LP ("VGI"), which provides managerial services to VGOP. Viking Global Opportunities Parent GP LLC ("Opportunities Parent") is the general partner of Viking Global Opportunities GP LLC ("Opportunities GP"), which serves as the sole member of Opportunities Portfolio GP and has the authority to dispose of and vote the ordinary shares controlled by Opportunities Portfolio GP, which consists of the ordinary shares directly held by VGOP. O. Andreas Halvorsen, David C. Ott and Rose Shabet, as Executive Committee members of Viking Global Partners LLC (the general partner of VGI and Opportunities GP), have shared authority to direct the voting and disposition of investments beneficially owned by VGI and the Opportunities GP. The business address of VGOP, Opportunities Portfolio GP, Opportunities GP, VGI, O. Andreas Halvorsen, David C. Ott and Rose Shabet is 600 Washington Boulevard, Floor 11, Stamford, CT 06901.

(5) LSP V Coöperatieve U.A. is the record holder of 3,556,805 ordinary shares. LSP V Management B.V. is the sole director of LSP V Coöperatieve U.A. The managing directors of LSP V Management B.V. are Martijn Kleijwegt, Rene Kuijten and Joachim Rothe. As such, LSP V Management B.V., Martijn Kleijwegt, Rene Kuijten and Joachim Rothe may be deemed to beneficially own the ordinary shares held of record by LSP V. Each of Mr. Kleijwegt, Mr. Kuijten and Mr. Rothe disclaims beneficial ownership of such shares. The address of LSP V Coöperatieve U.A. is Johannes Vermeerplein 9, 1071 DV Amsterdam, the Netherlands.

(6) Represents 3,547,504 ordinary shares that are directly held by venBio Global Strategic Fund III, L.P. ("Fund III") and 835,000 ordinary shares that are directly held venBio Global Strategic Fund IV, L.P. ("Fund IV"). As the sole general partner of Fund III, venBio Global Strategic GP III, L.P. ("General Partner III"), may be deemed to beneficially own the shares held by Fund III. As the sole general partner of General Partner III, venBio Global Strategic GP III, Ltd. ("GP Ltd. III"), may be deemed to beneficially own the share held by Fund III. The general partner of Fund IV is venBio Global Strategic GP IV, LLC ("GP LLC IV"), of which each of the directors serves as a member. As members of GP LLC IV, each of the directors may be deemed to beneficially own the Common Shares held by Fund IV. As directors of GP Ltd. III and members of GP LLC IV, each of the Aaron Royston, Robert Adelman and Corey Goodman may be deemed to beneficially own the shares held by Fund III and Fund IV. The address of Fund III, General Partner III, GP Ltd. III, Fund IV, GP LLC IV, Aaron Royston, Robert Adelman and Corey Goodman is c/o venBio Partners, LLC, 1700 Owens Street Suite 595 San Francisco, CA 94158.

(7) Venrock Healthcare Capital Partners III, L.P., VHCP Co-Investment Holdings III, LLC, Venrock Healthcare Capital Partners EG, L.P., VHCP Management III, LLC, VHCP Management EG, LLC, Nimish Shah and Bong Koh are members of a group for the purposes of this filing. Consists of (i) 564,312 shares held by Venrock Healthcare Capital Partners III, L.P.; (ii) 56,444 shares held by VHCP Co-Investment Holdings III, LLC; and (iii) 2,774,850 shares held by Venrock Healthcare Capital Partners EG, L.P. Based on the Schedule 13G/A filed on February 14, 2024 on behalf of Venrock Healthcare Capital Partners III, L.P., a limited partnership organized under the laws of the State of Delaware ("VHCP III LP"), VHCP Co-Investment Holdings III, LLC, a limited liability company organized under the laws of the State of Delaware ("VHCP Co-Investment III"), Venrock Healthcare Capital Partners EG, L.P., a limited partnership organized under the laws of the State of Delaware ("VHCP EG"), VHCP Management III, LLC, a limited liability company organized under the laws of the State of Delaware ("VHCP Management III"), VHCP Management EG, LLC, a limited liability company organized under the laws of the State of Delaware ("VHCP Management EG" and collectively with VHCP III LP, VHCP Co-Investment III, VHCP EG and VHCP Management III, the "Venrock Entities"), Nimish Shah ("Shah") and Bong Koh ("Koh") in respect of the ordinary shares of Pharvaris N.V. VHCP Management III, LLC is the general partner of Venrock Healthcare Capital Partners III, L.P. and the manager of VHCP Co-Investment Holdings III, LLC. VHCP Management EG, LLC is the general partner of Venrock Healthcare Capital Partners EG, L.P. Messrs. Shah and Koh are the voting members of VHCP Management III, LLC and VHCP Management EG, LLC.

(8) Includes 950,000 ordinary shares held by Schoodic Management B.V., an entity controlled by Mr. Modig. Includes 67,085 options and RSU's that vest within 60 days of April 1, 2025. See "ITEM 6. DIRECTORS, SENIOR MANAGEMENT AND EMPLOYEES—B. Compensation—Equity Incentive Plan."

(9) Includes 29,428 options and RSU's that vest within 60 days of April 1, 2025. See "ITEM 6. DIRECTORS, SENIOR MANAGEMENT AND EMPLOYEES—B. Compensation—Equity Incentive Plan."

(10) Includes 20,272 options and RSU's that vest within 60 days of April 1, 2025. See "ITEM 6. DIRECTORS, SENIOR MANAGEMENT AND EMPLOYEES—B. Compensation—Equity Incentive Plan."

(11) Includes 163,969 ordinary shares held by GrayMatters Consulting BVBA, an entity controlled by Dr. Lesage and includes 24,871 options and RSU's that vest within 60 days of April 1, 2025. See “ITEM 6. DIRECTORS, SENIOR MANAGEMENT AND EMPLOYEES—B. Compensation—Equity Incentive Plan.”

(12) Includes 26,820 options and RSU's that vest within 60 days of April 1, 2025. See “ITEM 6. DIRECTORS, SENIOR MANAGEMENT AND EMPLOYEES—B. Compensation—Equity Incentive Plan.”

(13) Includes 20,272 options and RSU's that vest within 60 days of April 1, 2025. See “ITEM 6. DIRECTORS, SENIOR MANAGEMENT AND EMPLOYEES—B. Compensation—Equity Incentive Plan.”

(14) Includes 15,605 options and RSU's that vest within 60 days of April 1, 2025. See “ITEM 6. DIRECTORS, SENIOR MANAGEMENT AND EMPLOYEES—B. Compensation—Equity Incentive Plan.”

(15) Includes 21,731 options and RSU's that vest within 60 days of April 1, 2025. See “ITEM 6. DIRECTORS, SENIOR MANAGEMENT AND EMPLOYEES—B. Compensation—Equity Incentive Plan.”

(16) Includes 21,731 options and RSU's that vest within 60 days of April 1, 2025. See “ITEM 6. DIRECTORS, SENIOR MANAGEMENT AND EMPLOYEES—B. Compensation—Equity Incentive Plan.”

(17) Includes 22,666 options and RSU's that vest within 60 days of April 1, 2025. See “ITEM 6. DIRECTORS, SENIOR MANAGEMENT AND EMPLOYEES—B. Compensation—Equity Incentive Plan.”

(18) Includes 9,054 RSU's that vest within 60 days of April 1, 2025. See “ITEM 6. DIRECTORS, SENIOR MANAGEMENT AND EMPLOYEES—B. Compensation—Equity Incentive Plan.”

(19) Includes 14,394 options and RSU's that vest within 60 days of April 1, 2025. See “ITEM 6. DIRECTORS, SENIOR MANAGEMENT AND EMPLOYEES—B. Compensation—Equity Incentive Plan.”

(20) Includes 800 ordinary shares held and 80,167 options and RSU's that vest within 60 days of April 1, 2025. See “ITEM 6. DIRECTORS, SENIOR MANAGEMENT AND EMPLOYEES—B. Compensation—Equity Incentive Plan."

As of April 1, 2025, approximately 47.8 million of our outstanding ordinary shares are held by at least 10 record holders in the United States, including Cede and Company which is the record holder for 47.8 million ordinary shares. Cede and Company is a specialist United States financial institution that processes transfers of stock certificates on behalf of the Depository Trust Company, or DTC. Cede and Company therefore is the technical shareholder of record for all of our shares that were issued in our initial public offering and are held by DTC participants, as such shareholders do not themselves hold direct property rights in our ordinary shares, but rather have contractual rights in such shares that are part of a chain of contractual rights involving Cede and Company. All ordinary shares carry one voting right. We are not aware of any arrangement that may, at a subsequent date, result in a change of control of our Company.

Significant Changes in Ownership by Major Shareholders

Immediately prior to our initial public offering in February 2021, our principal shareholders were LSP V Coöperatieve U.A. (15.31% ownership), KURMA BIOFUND II (5.68% ownership), entities affiliated with Foresite Capital (15.38% ownership), entities affiliated with Bain Capital Life Sciences Investors, LLC (12.43% ownership), venBio Global Strategic Fund III, L.P (8.50% ownership), entities affiliated with Idinvest Partners S.A. (6.17% ownership), Jens Schneider-Mergener (5.09% ownership), Viking Global Opportunities Illiquid Investments Sub-Master LP (6.03% ownership) and General Atlantic PH B.V. (6.03% ownership).

On February 9, 2021, we completed our initial public offering and listed our ordinary shares on the Nasdaq Global Select Market. In the initial public offering, we sold 9,511,075 ordinary shares, which includes 1,240,575 ordinary shares sold pursuant to the full exercise of the over-allotment option we granted to the underwriters for the offering.

B. Related party transactions

The following is a description of related-party transactions we have entered into since January 1, 2020 with any of the members of the Board, our Senior Management and the holders of more than 5% of our ordinary shares.

Transactions with Our Principal Shareholders

In June 2023, the Company entered into a subscription agreement dated June 16, 2023 relating to the offer and sale of an aggregate of 6,951,340 ordinary shares of the Company, in a private placement to a group of institutional investors, led by General Atlantic and venBio Partners with participation from Bain Capital Life Sciences, Foresite Capital, and Venrock Healthcare Capital Partners, at an offering price of $10.07 per share, for gross proceeds of approximately $70 million before deducting any offering-related expenses. Pursuant to the private offering, General Atlantic PH B.V. purchased 1,986,097 ordinary shares, venBio Global Strategic Fund III, L.P. purchased 1,986,097 ordinary shares, entities affiliated with Bain Capital Life Sciences Investors, LLC purchased 1,688,183 ordinary shares, entities affiliated with Foresite Capital purchased 496,524 ordinary shares and entities affiliated with Venrock Healthcare Capital Partners purchased 794,439 ordinary shares.

In December 2023, the Company entered into an underwriting agreement, dated December 6, 2023, by and among the Company and Morgan Stanley & Co. LLC and Leerink Partners, LLC as the underwriters. As part of this underwritten offer, in addition to purchases of ordinary shares, General Atlantic PH B.V. purchased pre-funded warrants to purchase up to 1,375,000 ordinary shares.

The pre-funded warrants were subsequently exercised in January 2024 for gross exercise proceeds of $0.01 million and resulted in issuance of 1,375,000 ordinary shares.

On February 5, 2024, the Company entered into a registration rights agreement (the "GA Registration Rights Agreement") with General Atlantic PH B.V. relating to the exercised pre-funded warrants to purchase up to 1,375,000 ordinary shares of the Company, which pre-funded warrants were acquired by General Atlantic PH B.V. in December 2023. The GA Registration Rights Agreement contains customary registration rights, including demand registration rights, with respect to the ordinary shares, as well as customary indemnification provisions. A copy of the GA Registration Rights Agreement is filed as an exhibit to this Annual Report.

Agreements and Arrangements with our Directors

We have entered into services agreements with Dr. Meeker, Mr. Schikan, Dr. Glassman, Ms. Monges and Dr. Björk. The service agreements will be terminated, without prior notice, when the non-executive director ceases to be a non-executive director. The Company can also terminate the service agreements with immediate effect for "urgent cause" as defined in Section 7:678 of the Dutch Civil Code. Additionally, both the non-executive director and the Company may terminate the service agreements at any time, subject to a one-month notice period. Each service agreement provides for compensation, including a base compensation, an increase in the base compensation for membership on a committee of the board of directors, and, if considered appropriate by the board of directors and subject to applicable law and the Company's compensation policy, eligibility to participate in the Company's equity incentive plans. The service agreements also provide for the reimbursement of reasonable and necessary expenses incurred by our non-executives in the performance of their duties. The service agreements also contain confidentiality, non-competition and non-solicitation provisions.

Agreements and Arrangements with Senior Management

The Company engages GrayMatters, a management entity for the purpose of providing key management services to the Company. This management entity is considered a related party, as it provides key management services and exercises key management functions. In the 2024, 2023 and 2022 fiscal years, the aggregate amount of expense recognized were €0.2 million, €0.6 million and €0.6 million, respectively.

A new agreement was entered into with GrayMatters, effective December 1, 2023 to November 30, 2027. The agreement provides for daily fixed fees up to a maximum amount per annum and an additional discretionary annual fee with a target based on a percentage of the maximum annual fee determined at the discretion of the Company. The agreement is for a term of four years but may be terminated earlier by either party without notice.

Further, upon a termination of the GrayMatters agreement by the Company without cause, the consultant is entitled to (i) an amount equal to the expected sum of the services fee for the remaining period until the termination date, up to a specified amount, (ii) any unpaid discretionary fee for the prior year, and (iii) a pro rata discretionary fee for the then-current year, subject to approval of the Company.

The GrayMatters Agreement also contains certain restrictive covenants, including a perpetual confidentiality provision and covenants regarding non-solicitation of employees, consultants, independent contractors, suppliers and customers during the term of the agreement and for a period of one year thereafter. In the event a consultant breaches any of these covenants and does not remedy such breach within five business days of receiving written notice, such consultant will be required to pay the Company a lump sum penalty, plus an additional penalty for each day such breach continues.

During 2023 and 2022, Dr. Jochen Knolle received €0.5 million and €0.6 million under his consulting agreement with the Company, while serving as the Company's Chief Scientific Officer ("CSO"). In late 2023, he relinquished the CSO title but remains a consultant.

We have also entered into employment agreements with Mr. Modig (Chief Executive Officer), Dr. Lu (Chief Medical Officer), Ms. Nijdam (Head of Strategic Finance and Principal Accounting Officer),), Dr. Souverijns (Chief Commercial Officer), Ms. Deschoolmeester (Chief Human Resources Officer) Dr. Abele (Chief Technical Operations Officer), and Mr. Nassif (Chief Legal and Financial Officer) (collectively, the "Employment Agreements"). The Employment Agreements generally provide for base salary, discretionary annual bonuses based on a percentage of base salary and eligibility to receive equity awards and to participate in the Company's benefits plans. The Employment Agreements for Mr. Modig, Dr. Lu, Dr. Souverijns, Ms. Deschoolmeester ,Dr. Abele and Mr. Nassif also provide that upon a termination by the Company without Cause or by the member of senior management for Good Reason, or as a result of the individual's death or disability, the member of senior management is entitled to the following (subject to execution of a general release of claims in favor of the Company): (i) 12 months of base salary (ii) with respect to Dr. Lu and Mr. Nassif , for one year after termination, the right to continue health care benefits under COBRA at active employee rates, (iii) any unpaid discretionary bonus for the prior year and (iv) pro rata discretionary bonus for the current year, subject to Board approval. In the case of Mr. Modig, Dr. Souverijns, Ms. Deschoolmeester and Dr. Abele, the severance amount is reduced by (i) any base salary paid during a notice period during which the member of senior management is released from an obligation to work, and/or (ii) the amount of any survivor's or disability annuity payment received for the 12 subsequent months.

The Employment agreements with Mr. Modig, Dr. Lu, Dr. Souverijns, Ms. Deschoolmeester, Dr. Abele and Mr. Nassif also provide that in the event that a notice of termination is served by the Company without Cause, or by the Employee for Good Reason, in each case (i) within one month prior to the consummation of a Change of Control or (ii) within 12 months following the consummation of a Change of

Control, the member of senior management shall be entitled to receive (subject to execution of a general release of claims in favor of the Company): (i) (x) 1.5 times the sum of base salary and bonus target with respect to Mr. Modig, and (y) the sum of the annual base salary and bonus target with respect to Dr. Lu, Dr. Souverijns, Ms. Deschoolmeester, Dr. Abele and Mr. Nassif; (ii) with respect to Dr. Lu and Mr. Nassif, for one year after termination, the right to continue health care benefits under COBRA at active employee rates, (iii) any unpaid discretionary bonus for the prior year and (iv) a pro rata discretionary bonus for the current year, subject to Board approval. In the case of Mr. Modig, Dr. Souverijns, Ms. Deschoolmeester and Dr. Abele, the severance amount is reduced by any base salary paid during a notice period during which the member of senior management is released from an obligation to work.

Clawback Policy

Our Board has adopted a policy relating to recovery of erroneously awarded compensation (a "Clawback Policy") in accordance with the final clawback rules adopted by the SEC, and the listing standards, as set forth in the Nasdaq Listing Rule 5608, to recoup "excess" incentive compensation, if any, earned by current and former executive officers (or any other senior executives or employees who may from time to time be deemed subject to the Clawback Policy by the compensation committee of our Board) during a three year look back period in the event of a financial restatement due to material noncompliance with any financial reporting requirement under the securities laws. Our Clawback Policy shall be administered by the compensation committee of our Board. Our Clawback Policy is filed as Exhibit 97.1 to this Annual Report on Form 20-F for the year ended December 31, 2024.

Indemnification Agreements

We have entered into indemnification agreements with the members of our Board. The indemnification agreements and our Articles of Association require us to indemnify the members of our Board against financial losses or damages or any expense reasonable paid or incurred in connection with any threatened, pending, or completed suit, claim, action or legal proceeding, in each case to the extent permitted by law, subject to certain exceptions.

Directed Share Program

At our request, the underwriters reserved up to 5% of the ordinary shares offered by our prospectus dated February 4, 2021 filed with the SEC on February 8, 2021, for sale at the initial public offering price through a directed share program to certain individuals, including our directors, officers, employees, and certain friends and family members of these persons.

C. Interests of Experts and Counsel

Not applicable.

ITEM 8. FINANCIAL INFORMATION

A. Consolidated statements and other financial information

Financial statements

See "ITEM 18. Financial statements," which contains our audited financial statements prepared in accordance with IFRS.

Legal proceedings

From time to time we are involved in legal proceedings that arise in the ordinary course of business. We believe that the outcome of these proceedings, if determined adversely, will not have a material adverse effect on our financial position. During the period covered by the audited and approved financial statements contained herein, we have not been a party to or paid any damages in connection with litigation that has had a material adverse effect on our financial position. Any future litigation may result in substantial costs and be a distraction to management and our employees. No assurance can be given that future litigation will not have a material adverse effect on our financial position. See "ITEM 3. KEY INFORMATION—D. Risk factors."

Dividends and dividend policy

We have never declared or paid any dividends on our ordinary shares. We expect to retain all earnings, if any, generated by our operations for the development and growth of our business and do not anticipate paying any dividends to our shareholders in the foreseeable future. Under Dutch law, we may only pay dividends and other distributions from our reserves to the extent our shareholders' equity (*eigen vermogen*) exceeds the sum of the paid-up and called-up share capital plus the reserves required to be maintained by Dutch law or our Articles of Association and (if it concerns a distribution of profits) after adoption of our statutory annual accounts by our general meeting from which it appears that such dividend distribution is allowed. Subject to those restrictions, any future determination to pay dividends or other distributions from our reserves will be at the discretion of the Board and will depend upon a number of factors, including our results of operations, earnings, cash flow, financial condition, future prospects, contractual restrictions, capital investment requirements, restrictions imposed by applicable law and other factors considered relevant by the Board.

Under our Articles of Association, our Board may decide that all or part of our profits shown in our adopted statutory annual accounts will be added to our reserves. After reservation of any such profits, any remaining profits will be at the disposal of the general meeting at the proposal of our Board for distribution on our ordinary shares, subject to the applicable restrictions of Dutch law. Our Board is permitted,

subject to certain requirements, and applicable restrictions of Dutch law, to declare interim dividends without the approval of the general meeting. Dividends and other distributions shall be made payable no later than the date determined by the Board. Claims to dividends and other distributions not made within five years from the date that such dividends or distributions became payable will lapse and any such amounts will be considered to have been forfeited to us (*verjaring*).

B. Significant changes

A discussion of the significant changes in our business can be found under "ITEM 4. INFORMATION ON THE COMPANY—A. History and development of the Company."

ITEM 9. THE OFFER AND LISTING

A. Offering and listing details

Not applicable.

B. Plan of distribution

Not applicable.

C. Markets

Our ordinary shares began trading on the Nasdaq Global Select Market under the symbol "PHVS" since February 5, 2021.

D. Selling shareholders

Not applicable.

E. Dilution

Not applicable.

F. Expenses of the issue

Not applicable.

ITEM 10. ADDITIONAL INFORMATION

A. Share capital

Not applicable.

B. Memorandum and Articles of Association

We incorporate by reference into this Annual Report the description of our Articles of Association effective upon the closing of our initial public offering contained in our F-1 registration statement (File No. 333-252157) originally filed with the SEC on January 15, 2021, as amended. Such description sets forth a summary of certain provisions of our Articles of Association as currently in effect.

C. Material contracts

Except as otherwise disclosed in this Annual Report (including the Exhibits), we are not currently, and have not been in the last two years, party to any material contract, other than contracts entered into in the ordinary course of business.

D. Exchange controls

Cash dividends payable on our ordinary shares may be remitted from the Netherlands to non-residents without legal restrictions imposed by the laws of the Netherlands, except that (i) such payments must be reported, if requested, to the Dutch Central Bank for statistical purposes only and (ii) the transfer of funds to jurisdictions subject to general economic sanctions adopted in connection with policies of the United Nations, European Commission or similar measures imposed directly by the Government of the Netherlands may be restricted.

E. Taxation

MATERIAL UNITED STATES FEDERAL INCOME TAX AND DUTCH TAX CONSIDERATIONS

The information presented under the caption "—Material U.S. Federal Income Tax Considerations to U.S. Holders" below is a discussion of material U.S. federal income tax consequences to a U.S. Holder (as defined below) of owning and disposing of our ordinary

shares. The information presented under the caption "—Material Dutch Tax Considerations" is a discussion of the material Dutch tax consequences of owning and disposing of our ordinary shares.

You should consult your tax adviser regarding the applicable tax consequences to you of investing in our ordinary shares under the laws of the United States (federal, state and local), the Netherlands, and any other applicable jurisdiction.

Material U.S. Federal Income Tax Considerations to U.S. Holders

The following is a discussion of the material U.S. federal income tax consequences to the U.S. Holders, as defined below, of owning and disposing of our ordinary shares. It does not describe all tax consequences that may be relevant to a particular person's decision to acquire or dispose of our ordinary shares. This discussion applies only to a U.S. Holder that holds our ordinary shares as capital assets within the meaning of Section 1221 of the Code for U.S. federal income tax purposes, and this discussion applies only to such ordinary shares. This discussion is general in nature and it does not describe all of the U.S. federal income tax consequences that may be relevant in light of the U.S. Holder's particular circumstances, including the potential application of the Medicare contribution tax, estate or gift tax consequences, any tax consequences other than U.S. federal income tax consequences, and tax consequences applicable to U.S. Holders subject to special rules, such as:

- certain financial institutions;
- corporations that accumulate earnings to avoid U.S. federal income tax, or expatriated entities subject to Section 7874 of the Code;
- dealers or traders in securities who use a mark-to-market method of tax accounting;
- persons holding ordinary shares as part of a hedging transaction, straddle, wash sale, conversion transaction or other integrated transaction or persons entering into a constructive sale with respect to the ordinary shares;
- persons whose functional currency for U.S. federal income tax purposes is not the U.S. dollar;
- entities or arrangements classified as partnerships for U.S. federal income tax purposes;
- tax-exempt entities;
- "individual retirement accounts", "Roth IRAs" or other tax-deferred accounts;
- any persons that acquire ordinary shares directly or indirectly in connection with the performance of services;
- persons who are subject to Section 451(b) of the Code;
- persons that own or are deemed to own ten percent or more of our shares (by vote or value);
- S corporations and any investors therein, regulated investment companies, real estate investment trusts, real estate mortgage investment conduits; or
- persons holding ordinary shares in connection with a trade or business conducted outside of the United States.

If an entity that is classified as a partnership for U.S. federal income tax purposes holds ordinary shares, the U.S. federal income tax treatment of a partner will generally depend on the status of the partner and the activities of the partner and the partnership. Partnerships (including entities or arrangements treated as partnerships for U.S. federal income tax purposes) holding ordinary shares and partners in such partnerships should consult their tax advisers as to the particular U.S. federal income tax consequences of owning and disposing of ordinary shares.

This discussion is based on the Code, administrative pronouncements, judicial decisions, final, temporary and proposed Treasury regulations, and the income tax treaty between the Netherlands and the United States, or the Treaty, all as of the date hereof, any of which is subject to change or differing interpretations, possibly with retroactive effect, so as to result in U.S. federal income tax consequences different from those discussed below. We have not sought, and do not expect to seek, any ruling from the U.S. Internal Revenue Service, or the Service, with respect to the statements made and the conclusions reached in the following summary, and there can be no assurance that the Service or a court would agree with our statements and conclusions or that a court would not sustain any challenge by the Service in the event of litigation.

A "U.S. Holder" is a holder who, for U.S. federal income tax purposes, is a beneficial owner of ordinary shares, who is eligible for the benefits of the Treaty and who is:

- an individual who is a citizen or resident in the U.S.;
- a corporation, or other entity taxable as a corporation for U.S. federal income tax purposes, created or organized in or under the laws of the United States, any state therein or the District of Columbia;
- an estate, the income of which is subject to U.S. federal income taxation regardless of its source; or

- a trust if either (1) a court within the U.S. is able to exercise primary jurisdiction over the administration of the trust and one or more U.S. persons have the authority to control all substantial decisions of the trust, or (2) the trust has a valid election in effect under applicable Treasury Regulations to be treated as a U.S. person.

THIS SUMMARY IS FOR GENERAL INFORMATION PURPOSES ONLY, AND IS NOT INTENDED TO BE, AND SHOULD NOT BE CONSTRUED TO BE LEGAL OR TAX ADVICE TO ANY PARTICULAR HOLDER. INVESTORS ARE URGED TO CONSULT THEIR TAX ADVISERS WITH REGARD TO THE APPLICATION OF THE U.S. FEDERAL INCOME TAX LAWS, AS WELL AS THE APPLICATION OF U.S. NON-INCOME TAX LAWS AND THE LAWS OF ANY STATE, LOCAL OR NON-U.S. JURISDICTION, IN LIGHT OF THEIR PARTICULAR SITUATION.

Taxation of Distributions

As discussed above under “Dividends and dividend policy”, we do not expect to make distributions on our ordinary shares in the near future. In the event that we do make distributions of cash or other property, subject to the PFIC rules described below, distributions paid on our ordinary shares will generally be treated as dividends to the extent paid out of our current or accumulated earnings and profits (as determined under U.S. federal income tax principles). Because we do not maintain calculations of our earnings and profits under U.S. federal income tax principles, we expect that distributions generally will be reported to U.S. Holders as dividends. If and for so long as our ordinary shares are listed on the Nasdaq or another established securities market in the United States or if and for so long as we are eligible for benefits under the Treaty, dividends paid to certain non-corporate U.S. Holders may be eligible for taxation as “qualified dividend income” if we are not treated as a PFIC with respect to the U.S. Holder and were not treated as a PFIC with respect to the U.S. Holder in the preceding taxable year, and if certain other requirements are met. Therefore, subject to applicable limitations, dividends paid to certain non-corporate U.S. Holders may be taxable at rates not in excess of the long-term capital gain rate applicable to such U.S. Holders. U.S. Holders should consult their tax advisers regarding the availability of the reduced tax rate on dividends in their particular circumstances. The amount of a dividend will include any amounts withheld by us in respect of Dutch income taxes. Subject to the PFIC rules described below, the amount of the dividend will be treated as foreign-source dividend income to U.S. Holders and will generally not be eligible for the dividends-received deduction generally available to U.S. corporations under the United States Internal Revenue Code.

Subject to the PFIC rules described below, dividends will be included in a U.S. Holder’s income on the date of the U.S. Holder’s receipt of the dividend. The amount of any dividend income paid in euros will be the U.S. dollar amount calculated by reference to the exchange rate in effect on the date of actual or constructive receipt, regardless of whether the payment is in fact converted into U.S. dollars at that time. If the dividend is converted into U.S. dollars on the date of receipt, a U.S. Holder should not be required to recognize foreign currency gain or loss in respect of the dividend income. A U.S. Holder may have foreign currency gain or loss if the dividend is converted into U.S. dollars after the date of receipt.

Subject to applicable limitations, some of which vary depending upon the U.S. Holder’s particular circumstances, Dutch income taxes withheld from dividends on our ordinary shares at a rate not exceeding the rate provided by the Treaty will be creditable against the U.S. Holder’s U.S. federal income tax liability. Dutch taxes withheld in excess of the rate applicable under the Treaty will not be eligible for credit against a U.S. Holder’s U.S. federal income tax liability. The rules governing foreign tax credits are complex, and U.S. Holders should consult their tax advisers regarding the creditability of foreign taxes in their particular circumstances. In lieu of claiming a foreign tax credit, U.S. Holders may, at their election, deduct foreign taxes, including any Dutch income tax, in computing their taxable income, subject to generally applicable limitations under U.S. law. An election to deduct foreign taxes instead of claiming foreign tax credits applies to all foreign taxes paid or accrued in the taxable year.

Sale or Other Disposition of Ordinary Shares

Subject to the PFIC rules described below, gain or loss realized on the sale or other disposition of ordinary shares will be capital gain or loss, and will be long-term capital gain or loss if the U.S. Holder held the ordinary shares for more than one year. The amount of the gain or loss will equal the difference between the U.S. Holder’s tax basis in the ordinary shares disposed of and the amount realized on the disposition, in each case as determined in U.S. dollars. This gain or loss will generally be U.S.-source gain or loss for foreign tax credit purposes. The deductibility of capital losses is subject to various limitations.

Passive Foreign Investment Company Rules

Under the Code, we will be a PFIC for any taxable year in which, after the application of certain “look-through” rules with respect to subsidiaries, either (i) 75% or more of our gross income consists of “passive income,” or (ii) 50% or more of the average quarterly value of our assets consist of assets that produce, or are held for the production of, “passive income.” For purposes of the above calculations, we will be treated as if we hold our proportionate share of the assets of and receive directly our proportionate share of the income of, any other corporation in which we directly or indirectly own at least 25%, by value, of the shares of such corporation. Passive income generally includes dividends, interest, certain non-active rents and royalties and capital gains. Based on the nature of our business, our financial statements, and our expectations about the nature and amount of our income, assets and activities we do not believe we were a PFIC in 2024 and we do not expect to be a PFIC for our current taxable year or in the foreseeable future. In addition, we may, directly or indirectly, hold equity interests in other PFICs, or Lower-tier PFICs. Whether we or any of our subsidiaries will be a PFIC in 2025 or any future year is a factual determination that must be made annually at the close of each taxable year, and, thus, is subject to significant uncertainty, because among other things, a determination of whether a company is a PFIC must be made annually after the end of each taxable year and will depend on the composition of our income and assets and the market value of our assets from time to time. Therefore, we cannot assure you that we will not be a PFIC for the current or any future taxable year. Accordingly, there can be no assurance that we will not be a PFIC in 2025 or any future taxable year. If we are a PFIC for any year during which a U.S. Holder holds or is deemed to hold ordinary shares, we generally would continue to be treated as a PFIC with respect to that U.S. Holder for all succeeding years during which the U.S.

Holder holds or is deemed to hold ordinary shares, even if we ceased to meet the threshold requirements for PFIC status, unless under certain circumstances the U.S. Holder makes a valid deemed sale or deemed dividend election under the applicable Treasury regulations with respect to its ordinary shares.Under certain attribution rules, assuming we are a PFIC, U.S. Holders will be deemed to own their proportionate shares of any Lower-tier PFICs and will be subject to U.S. federal income tax according to the rules described in the following paragraphs on (i) certain distributions by a Lower-tier PFIC and (ii) a disposition of shares of a Lower-tier PFIC, in each case as if the U.S. Holder held such shares directly, even if the U.S. Holder has not received the proceeds of those distributions or dispositions.

Generally, if we were a PFIC for any taxable year during which a U.S. Holder held or is deemed to have held ordinary shares, gain recognized by a U.S. Holder on a sale or other disposition (including certain pledges) of such ordinary shares, or an indirect disposition of shares of a Lower-tier PFIC, would be allocated ratably over the U.S. Holder's holding period for such ordinary shares. The amounts allocated to the taxable year of the sale or other disposition and to any year before we became a PFIC would be taxed as ordinary income. The amount allocated to each other taxable year would be subject to tax at the highest rate in effect for individuals or corporations, as appropriate, for that taxable year, and an interest charge would be imposed on the amount allocated to that taxable year. Further, to the extent that any distribution received by a U.S. Holder with respect to its ordinary shares (or a distribution by a Lower-tier PFIC to its shareholder that is deemed to be received by a U.S. Holder) exceeds 125% of the average of the annual distributions on the ordinary shares received during the preceding three years or the U.S. Holder's holding period, whichever is shorter, that distribution would be subject to taxation in the same manner as gain, described immediately above.

A U.S. Holder can avoid certain of the adverse rules described above by making a mark-to-market election with respect to its ordinary shares, *provided* that the ordinary shares are "marketable." Ordinary shares will be marketable if they are "regularly traded" on a "qualified exchange" or other market within the meaning of applicable Treasury regulations. If a U.S. Holder makes the mark-to-market election, it generally will recognize as ordinary income any excess of the fair market value of the ordinary shares at the end of each taxable year over their adjusted tax basis, and will recognize an ordinary loss in respect of any excess of the adjusted tax basis of the ordinary shares over their fair market value at the end of the taxable year (but only to the extent of the net amount of income previously included as a result of the mark-to-market election). If a U.S. Holder makes the election, the U.S. Holder's tax basis in the ordinary shares will be adjusted to reflect the income or loss amounts recognized. Any gain recognized on the sale or other disposition of ordinary shares, as applicable, in a year when we are a PFIC will be treated as ordinary income and any loss will be treated as an ordinary loss (but only to the extent of the net amount of income previously included as a result of the mark-to-market election). A mark-to-market election generally cannot be made for equity interests in any Lower-tier PFIC unless shares of such Lower-tier PFIC are themselves "marketable." As a result, if a U.S. Holder makes a mark-to-market election with respect to our ordinary shares, the U.S. Holder would nevertheless be subject to the PFIC rules described above with respect to its indirect interest in any Lower-tier PFIC unless the U.S. Holder makes a QEF Election with respect to such Lower-tier PFIC, as discussed below. U.S. Holders should consult their tax advisers regarding the availability and advisability of making a mark-to-market election in their particular circumstances.

In addition, in order to avoid the application of the foregoing rules, a United States person that owns stock in a PFIC for U.S. federal income tax purposes may make a QEF Election with respect to such PFIC, and each PFIC in which the PFIC holds equity interests, if the PFIC provides the information necessary for such election to be made. In order to make such an election, a United States person would be required to make the QEF Election for each PFIC by attaching a separate properly completed IRS Form 8621 for each PFIC to the United States person's timely filed U.S. federal income tax return generally for the first taxable year that the entity is treated as a PFIC with respect to the United States person. A U.S. Holder generally may make a separate election to defer payment of taxes on the undistributed income inclusion under the QEF rules, but if deferred, any such taxes are subject to an interest charge. If a United States person makes a QEF Election with respect to a PFIC, the United States person will be currently taxable on its pro rata share of the PFIC's ordinary earnings and net capital gain (at ordinary income and capital gain rates, respectively) for each taxable year that the entity is classified as a PFIC and will not be required to include such amounts in income when actually distributed by the PFIC. There is no assurance that we will provide information necessary for U.S. Holders to make QEF Elections. If a U.S. Holder makes a QEF Election with respect to us, any distributions paid by us out of our earnings and profits that were previously included in the U.S. Holder's income under the QEF Election will not be taxable to the U.S. Holder. A U.S. Holder will increase its tax basis in its ordinary shares by an amount equal to any income included under the QEF Election and will decrease its tax basis by any amount distributed, if any, on the ordinary shares that is not included in its income. In addition, a U.S. Holder will recognize capital gain or loss on the disposition of ordinary shares in an amount equal to the difference between the amount realized and its adjusted tax basis in our ordinary shares. U.S. Holders should note that if they make QEF Elections with respect to us and Lower-tier PFICs, if any, they may be required to pay U.S. federal income tax with respect to their ordinary shares for any taxable year significantly in excess of any cash distributions, if any, received on the ordinary shares, as applicable, for such taxable year. If we determine that any of our subsidiaries is a Lower-tier PFIC for any taxable year, there is no assurance that we will provide information necessary for U.S. Holders to make a QEF Election with respect to such Lower-tier PFIC. U.S. Holders should consult their tax advisers regarding making QEF Elections in their particular circumstances.

In addition, if we were a PFIC or, with respect to a particular U.S. Holder, were treated as a PFIC for the taxable year in which we paid a dividend or for the prior taxable year, the preferential dividend rates discussed above with respect to dividends paid to certain non-corporate U.S. Holders would not apply.

If a U.S. Holder owns ordinary shares during any year in which we are a PFIC, the U.S. Holder generally must file annual reports, containing such information as the U.S. Treasury may require on IRS Form 8621 (or any successor form) with respect to us, generally with the U.S. Holder's federal income tax return for that year, unless otherwise specified in the instructions with respect to such form.

U.S. Holders should consult their tax advisers concerning our potential PFIC status and the potential application of the PFIC rules. The U.S. federal income tax rules relating to PFICs are very complex. U.S. Holders are strongly urged to consult their tax advisers with respect to the impact of PFIC status on the purchase, ownership and disposition of our ordinary shares, as applicable, the consequences to them of

an investment in a PFIC (and any Lower-tier PFICs), any elections available with respect to the ordinary shares and the IRS information reporting obligations with respect to the purchase, ownership and disposition of ordinary shares of a PFIC.

Information Reporting and Backup Withholding

Payments of dividends and sales proceeds that are made within the United States or through certain U.S.-related financial intermediaries generally are subject to information reporting, and may be subject to backup withholding, unless (i) the U.S. Holder is a corporation or other exempt recipient or (ii) in the case of backup withholding, the U.S. Holder provides a correct taxpayer identification number and certifies that it is not subject to backup withholding.

The amount of any backup withholding from a payment to a U.S. Holder will be allowed as a credit against the U.S. Holder's U.S. federal income tax liability and may entitle it to a refund, *provided* that the required information is timely furnished to the IRS.

Information Reporting With respect to Foreign Financial Assets

Certain U.S. Holders who are individuals and certain entities may be required to report information relating to an interest in our ordinary shares, subject to certain exceptions (including an exception for ordinary shares held in accounts maintained by certain U.S. financial institutions). U.S. Holders should consult their tax advisers regarding whether or not they are obligated to report information relating to their ownership and disposition of ordinary shares.

Material Dutch Tax Considerations

Scope of Discussion

This section only outlines certain material Dutch tax consequences of the acquisition, holding and disposal of our ordinary shares. This section does not purport to describe all possible tax considerations or consequences that may be relevant to a holder or prospective holder of our ordinary shares and does not purport to deal with the tax consequences applicable to all categories of investors, some of which (such as trusts or similar arrangements) may be subject to special rules. In view of its general nature, this section should be treated with corresponding caution.

This section is based on the tax laws of the Netherlands, published regulations thereunder and published authoritative case law, all as in effect on the date hereof, including, for the avoidance of doubt, the tax rates applicable on the date hereof, and all of which are subject to change, possibly with retroactive effect. Any such change may invalidate the contents of this section, which will not be updated to reflect such change. Where this section refers to "the Netherlands" or "Dutch" it refers only to the part of the Kingdom of the Netherlands located in Europe.

THIS SECTION IS INTENDED AS GENERAL INFORMATION ONLY AND IS NOT DUTCH TAX ADVICE OR A COMPLETE DESCRIPTION OF ALL DUTCH TAX CONSEQUENCES RELATING TO THE ACQUISITION, HOLDING AND DISPOSAL OF OUR ORDINARY SHARES. HOLDERS OR PROSPECTIVE HOLDERS OF OUR ORDINARY SHARES SHOULD CONSULT THEIR OWN TAX ADVISERS REGARDING THE DUTCH TAX CONSEQUENCES RELATING TO THE ACQUISITION, HOLDING AND DISPOSAL OF THE ORDINARY SHARES IN LIGHT OF THEIR PARTICULAR CIRCUMSTANCES.

This section does not describe any Dutch tax considerations or consequences arising from the Dutch Minimum Tax Act 2024 (*Wet minimumbelasting 2024*; the Dutch implementation of Directive (EU) 2022/2523 of 14 December 2022 on ensuring a global minimum level of taxation for multinational enterprise groups and large-scale domestic groups in the European Union) which may be relevant for a particular holder.

In addition, please note that this section does not describe the Dutch tax consequences for:

i. a holder of our ordinary shares if such holder has a substantial interest (*aanmerkelijk belang*) or deemed substantial interest (*fictief aanmerkelijk belang*) in us under the Dutch Income Tax Act 2001 (*Wet inkomstenbelasting 2001*). Generally, a holder is considered to hold a substantial interest in such company, if such holder alone or, in the case of an individual together with such holder's partner for Dutch income tax purposes, or any relatives by blood or marriage in the direct line (including foster children), directly or indirectly, holds (i) an interest of 5% or more of the total issued and outstanding capital of that company or of 5% or more of the issued and outstanding capital of a certain class of shares of that company; or (ii) rights to acquire, directly or indirectly, such interest, or (iii) certain profit sharing rights in that company that relate to 5% or more of the company's annual profits or to 5% or more of the company's liquidation proceeds. A deemed substantial interest may arise if a substantial interest (or part thereof) in a company has been disposed of, or is deemed to have been disposed of, on a non-recognition basis;

ii. a holder of our ordinary shares, if the ordinary shares held by such holder qualify or qualified as a participation (*deelneming*) for purposes of the Dutch Corporate Income Tax Act 1969 (*Wet op de vennootschapsbelasting 1969*). Generally, a holder's shareholding of 5% or more in a company's nominal paid-up share capital qualifies as a participation. A holder may also have a participation if such holder does not have a shareholding, or right to acquire, of 5% or more but a related entity (statutorily defined term) has a participation or if the company in which the shares are held is a related entity (statutorily defined term);

iii. a holder of our ordinary shares which is or who is entitled to the dividend withholding tax exemption (*inhoudingsvrijstelling*) with respect to any income (*opbrengst*) derived from the ordinary shares (as defined in Article 4 of the Dutch Dividend Withholding Tax Act 1965 (*Wet op de dividendbelasting*). Generally, a holder of our ordinary shares may be entitled or required to apply, subject to certain other requirements, the dividend withholding tax exemption if it is an entity and holds an interest of 5% or more in our nominal paid-up share capital;

iv. pension funds, investment institutions (*fiscale beleggingsinstellingen*), tax exempt investment institutions (*vrijgestelde beleggingsinstellingen*) (each as defined in the Dutch Corporate Income Tax Act 1969) and other entities that are, in whole or in part, not subject to or exempt from Dutch corporate income tax, entities that have a function comparable to an investment institution or tax exempt investment institution, as well as entities that are exempt from corporate income tax in their country of residence, such country of residence being another state of the European Union, Norway, Liechtenstein, Iceland or any other state with which the Netherlands has agreed to exchange information in line with international standards; and

v. holder of our ordinary shares if such holder is an individual for whom the ordinary shares or any benefit derived from the ordinary shares are a remuneration or deemed to be a remuneration for (employment) activities performed by such holder or certain individuals related to such holders (as defined in the Dutch Income Tax Act 2001).

Withholding Tax on Dividends

Regular Dutch Dividend Withholding Tax

Dividends distributed by us generally are subject to Dutch dividend withholding tax at a rate of 15%. Generally, we are responsible for the withholding of such dividend withholding tax at source; the Dutch dividend withholding tax is for the account of the holder of our ordinary shares.

The expression “dividends distributed” includes, among other things:

- distributions in cash or in kind, deemed and constructive distributions and repayments of paid-in capital not recognized for Dutch dividend withholding tax purposes;
- liquidation proceeds, proceeds from the redemption of our ordinary shares, or proceeds from the repurchase of ordinary shares (other than as temporary portfolio investment; *tijdelijke* belegging) by us or one of our subsidiaries or other affiliated entities, in each case to the extent such proceeds exceed the average paid-in capital of those ordinary shares as recognized for Dutch dividend withholding tax purposes;
- an amount equal to the par value of our ordinary shares issued or an increase of the par value of ordinary shares, to the extent that it does not appear that a contribution, recognized for Dutch dividend withholding tax purposes, has been made or will be made; and
- partial repayment of the paid-in capital, recognized for Dutch dividend withholding tax purposes, if and to the extent that we have net profits (*zuivere winst*), unless (i) the general meeting has resolved in advance to make such repayment and (ii) the par value of the ordinary shares concerned has been reduced by an equal amount by way of an amendment of the Articles of Association. The term “net profits” includes anticipated profits that have yet to be realized.

Corporate legal entities that are resident or deemed to be resident of the Netherlands for Dutch corporate income tax purposes ("Dutch Resident Entities") generally are entitled to an exemption from, or a credit for, any Dutch dividend withholding tax against their Dutch corporate income tax liability. The credit in any given year is, however, limited to the amount of Dutch corporate income tax payable in respect of the relevant year with an indefinite carry forward of any excess amount. Individuals who are resident or deemed to be resident of the Netherlands for Dutch personal income tax purposes ("Dutch Resident Individuals") generally are entitled to a credit for any Dutch dividend withholding tax against their Dutch personal income tax liability and to a refund of any residual Dutch dividend withholding tax. The above generally also applies to holders of our ordinary shares that are neither resident nor deemed to be resident of the Netherlands ("Non-Resident Holders") if the ordinary shares are attributable to a Dutch permanent establishment of such Non-Resident Holder.

A holder of our ordinary shares resident of a country other than the Netherlands may, depending on such holder’s specific circumstances, be entitled to exemptions from, reductions of, or full or partial refunds of, Dutch dividend withholding tax under Dutch national tax legislation, EU law, or treaties for the avoidance of double taxation in effect between the Netherlands and such other country.

Dividend stripping

According to Dutch domestic anti-dividend stripping rules, no credit against Dutch tax, exemption from, reduction, or refund of Dutch dividend withholding tax will be granted if the recipient of the dividends we paid is not considered the beneficial owner (*uiteindelijk gerechtigde*; as described in the Dutch Dividend Withholding Tax Act 1965) of those dividends. This legislation generally targets situations in which a shareholder retains its economic interest in shares but reduces the withholding tax costs on dividends by a transaction with another party. It is not required for these rules to apply that the recipient of the dividends is aware that a dividend stripping transaction took place. The Dutch State Secretary of Finance takes the position that the definition of beneficial ownership introduced by this legislation will also be applied in the context of a double taxation convention. The burden of proof with respect to beneficial ownership of dividends distributed by us rests on the Dutch tax authorities. If, however, a shareholder would receive dividends, including dividends on the ordinary shares, in a calendar year in respect of which an aggregate amount of € 1,000 in Dutch dividend withholding tax would otherwise be due

based on the rate of 15%, the burden of proof with respect to beneficial ownership of such dividends lies with the shareholder. Furthermore, for shares traded on a regulated market, including the ordinary shares, it has been codified that the record date is used when determining the person who is entitled to the dividend.

Conditional Withholding Tax on Dividends

In addition to the regular Dutch dividend withholding tax as described above, a Dutch conditional withholding tax will be imposed on dividends distributed by us to a Related Entity (as defined below), if such Related Entity:

i. is considered to be resident (*gevestigd)* in a jurisdiction that is listed in the yearly updated Dutch Regulation on low-taxing states and non-cooperative jurisdictions for tax purposes (*Regeling laagbelastende staten en niet-coöperatieve rechtsgebieden voor belastingdoeleinden*) (a "Listed Jurisdiction"); or
ii. has a permanent establishment located in a Listed Jurisdiction to which the ordinary shares are attributable; or
iii. holds the ordinary shares with the main purpose or one of the main purposes of avoiding taxation for another person or entity and there is an artificial arrangement or transaction or a series of artificial arrangements or transactions; or
iv. is not considered to be the beneficial owner of the ordinary shares in its jurisdiction of residence because such jurisdiction treats another entity as the beneficial owner of the ordinary shares (a hybrid mismatch); or
v. is not resident in any jurisdiction (also a hybrid mismatch); or
vi. is a reverse hybrid (within the meaning of Article 2(12) of the Dutch Corporate Income Tax Act 1969), if and to the extent (x) there is a participant in the reverse hybrid holding a Qualifying Interest in the reverse hybrid, (y) the jurisdiction of residence of such participant treats the reverse hybrid as transparent for tax purposes and (z) such participant would have been subject to the Dutch conditional withholding tax in respect of dividends distributed by us without the interposition of the reverse hybrid,,

all within the meaning of the Dutch Withholding Tax Act 2021 (*Wet bronbelasting 2021*).

For purposes of this section:

- "Related Entity" means an entity (i) that has a Qualifying Interest in the Company or (ii) in which a third party has a Qualifying Interest if such third party also has a Qualifying Interest in the Company.
- "Qualifying Interest" means a direct or indirectly held interest – either by an entity individually or, if an entity is part of a Qualifying Unity, jointly – that enables such entity or such Qualifying Unity to exercise a definitive influence over another entity's decisions and allows it to determine that other entity's activities (as interpreted by the European Court of Justice in case law on the right of freedom of establishment (*vrijheid van vestiging*)).
- "Qualifying Unity" means entities acting together with the main purpose or one of the main purposes of avoiding Dutch conditional withholding tax at the level of any of those entities (*kwalificerende eenheid*).

The Dutch conditional withholding tax on dividends will be imposed at the highest Dutch corporate income tax rate in effect at the time of the distribution (currently 25.8%). The Dutch conditional withholding tax on dividends will be reduced, but not below zero, by any regular Dutch dividend withholding tax withheld in respect of the same dividend distribution. As such, based on the currently applicable rates, the overall effective tax rate of withholding the regular Dutch dividend withholding tax (as described above) and the Dutch conditional withholding tax on dividends will not exceed the highest corporate income tax rate in effect at the time of the distribution (currently 25.8%).

Taxes on Income and Capital Gains

Dutch Resident Entities

Generally, if the holder of ordinary shares is a Dutch Resident Entity, any income derived or deemed to be derived from the ordinary shares or any capital gains realized on the disposal or deemed disposal of the ordinary shares is subject to Dutch corporate income tax at a rate of 19% with respect to taxable profits up to €200,000 and 25.8% with respect to taxable profits in excess of that amount (rates and brackets for 2025).

Dutch Resident Individuals

If the holder of our ordinary shares is a Dutch Resident Individual, any income derived or deemed to be derived from the ordinary shares or any capital gains realized on the disposal or deemed disposal of the ordinary shares is subject to Dutch personal income tax at the progressive rates (with a maximum of 49.50% in 2025), if:

i. the ordinary shares are attributable to an enterprise from which the holder of ordinary shares derives a share of the profit, whether as an entrepreneur (*ondernemer*) or as a person who has a co-entitlement to the net worth (*medegerechtigd tot het vermogen*) of such enterprise without being a shareholder (as defined in the Dutch Income Tax Act 2001); or

ii. the holder of ordinary shares is considered to perform activities with respect to the ordinary shares that go beyond ordinary asset management (*normaal, actief vermogensbeheer*) or otherwise derives benefits from the ordinary shares that are taxable as benefits from miscellaneous activities (*resultaat uit overige werkzaamheden*).

Taxation of savings and investments

If the above-mentioned conditions (i) and (ii) do not apply to the Dutch Resident Individual, the ordinary shares will be subject to an annual Dutch income tax under the regime for savings and investments (*inkomen uit sparen en beleggen*). Taxation only occurs insofar the Dutch Resident Individual's net investment assets for the year exceed a statutory threshold (*heffingvrij vermoge*n). The net investment assets for the year are the fair market value of the investment assets less the fair market value of the liabilities on January 1 of the relevant calendar year (reference date; *peildatum*). Actual income or capital gains realized in respect of the ordinary shares are in principle not subject to Dutch income tax.

The Dutch Resident Individual's assets and liabilities taxed under this regime, including the ordinary shares, are allocated over the following three categories: (a) bank savings (*banktegoeden*), (b) other investments (*overige bezittingen*), including the ordinary shares, and (c) liabilities (*schulden*). The taxable benefit for the year (*voordeel uit sparen en beleggen*) is equal to the product of (x) the total deemed return divided by the sum of bank savings, other investments and liabilities and (y) the sum of bank savings, other investments and liabilities minus the statutory threshold, and is taxed at a flat rate of 36% (rate for 2025).

The deemed return applicable to the other investments (mentioned under (ii) b) above), including the ordinary shares is set at 5.88% for the calendar year 2025. Transactions in the three-month period before and after January 1 of the relevant calendar year implemented to arbitrate between the deemed return percentages applicable to bank savings, other investments and liabilities will for this purpose be ignored if the holder of ordinary shares cannot sufficiently demonstrate that such transactions are implemented for other than tax reasons.

On June 6 and 14, 2024, the Dutch Supreme Court (*Hoge Raad*) ruled that the current Dutch income tax regime for savings and investments in certain specific circumstances contravenes with Section 1 of the First Protocol to the European Convention on Human Rights in combination with Section 14 of the European Convention on Human Rights (the “Rulings”). This is, in short, the case in the event the deemed return on the investment assets exceeds the actual return realized in respect thereof (calculated in line with the rules set out in the Rulings and successfully demonstrated by the taxpayer). Holders of ordinary shares are advised to consult their own tax advisor to ensure that the tax in respect of the ordinary shares is levied in accordance with the applicable Dutch tax rules at the relevant time. Holders of ordinary shares are advised to consult their own tax advisor to ensure that the tax in respect of the ordinary shares is levied in accordance with the applicable Dutch tax rules at t*he relevant time.*

Non-residents of the Netherlands

A holder of our ordinary shares that is neither a Dutch Resident Entity nor a Dutch Resident Individual will not be subject to Dutch income tax in respect of income derived or deemed to be derived from our ordinary shares or in respect of capital gains realized on the disposal or deemed disposal of the ordinary shares, provided that:

i. such holder does not have an interest in an enterprise or deemed enterprise (as defined in the Dutch Income Tax Act 2001 and the Dutch Corporate Income Tax Act 1969) which, in whole or in part, is either effectively managed in the Netherlands or carried on through a permanent establishment, a deemed permanent establishment or a permanent representative in the Netherlands and to which enterprise or part of an enterprise the ordinary shares are attributable; and

ii. in the event the holder is an individual, such holder does not carry out any activities in the Netherlands with respect to the ordinary shares that go beyond ordinary asset management and does not otherwise derive benefits from the ordinary shares that are taxable as benefits from miscellaneous activities in the Netherlands.

Gift and Inheritance Taxes

Residents of the Netherlands

Gift or inheritance taxes will arise in the Netherlands with respect to a transfer of ordinary shares by way of a gift by, or on the death of, a holder of such ordinary shares who is resident or deemed resident of the Netherlands at the time of the gift or the holder’s death.

Non-residents of the Netherlands

No gift or inheritance taxes will arise in the Netherlands with respect to a transfer of our ordinary shares by way of gift by, or on the death of, a holder of ordinary shares who is neither resident nor deemed to be resident of the Netherlands, unless:

i. in the case of a gift of our ordinary shares by an individual who at the date of the gift was neither resident nor deemed to be resident of the Netherlands, such individual dies within 180 days after the date of the gift, while being resident or deemed to be resident of the Netherlands;

ii. in the case of a gift of our ordinary shares made under a condition precedent, the holder of ordinary shares is resident or deemed to be resident of the Netherlands at the time the condition is fulfilled; or

iii. the transfer is otherwise construed as a gift or inheritance made by, or on behalf of, a person who, at the time of the gift or death, is or is deemed to be resident of the Netherlands.

For purposes of Dutch gift and inheritance taxes, amongst others, a person that holds the Dutch nationality will be deemed to be resident of the Netherlands if such person has been resident in the Netherlands at any time during the ten years preceding the date of the gift or such person’s death. Additionally, for purposes of Dutch gift tax, amongst others, a person not holding the Dutch nationality will be

deemed to be resident of the Netherlands if such person has been resident in the Netherlands at any time during the twelve months preceding the date of the gift. Applicable tax treaties may override deemed residency.

Value Added Tax (VAT)

No Dutch value added tax will be payable by a holder of our ordinary shares in respect of any payment in consideration for the holding or disposal of our ordinary shares.

Other Taxes and Duties

No Dutch documentation taxes (commonly referred to as stamp duties) will be payable by a holder of our ordinary shares in respect of any payment in consideration for the holding or disposal of our ordinary shares.

F. Dividends and paying agents

Not applicable.

G. Statement by experts

Not applicable.

H. Documents on display

We are subject to the informational requirements of the Exchange Act. Accordingly, we are required to file reports and other information with the SEC, including Annual Reports and reports on Form 6-K. The SEC maintains an Internet website that contains reports and other information about issuers, like us, that file electronically with the SEC. The address of that website is www.sec.gov.

I. Subsidiary information

Not applicable.

J. **Annual Report to Security Holders**

If we are required to provide an annual report to security holders in response to the requirements of Form 6-K, we will submit the annual report to security holders in electronic format in accordance with the EDGAR Filer Manual.

ITEM 11. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

We are exposed to a variety of risks in the ordinary course of our business, including, but not limited to, foreign currency risk and interest rate risk. We regularly assess each of these risks to minimize any adverse effects on our business as a result of those factors. For a detailed discussion, see Note 17 to our consolidated financial statements included elsewhere in this Annual Report.

ITEM 12. DESCRIPTION OF SECURITIES OTHER THAN EQUITY SECURITIES

A. Debt securities

Not applicable.

B. Warrants and rights

Not applicable.

C. Other securities

Not applicable.

D. American Depositary Shares

Not applicable.

PART II

ITEM 13. DEFAULTS, DIVIDEND ARREARAGES AND DELINQUENCIES

A. Defaults

No matters to report.

B. Arrears and delinquencies

No matters to report.

ITEM 14. MATERIAL MODIFICATIONS TO THE RIGHTS OF SECURITY HOLDERS AND USE OF PROCEEDS

A Material modifications to instruments

Not applicable.

B. Material modifications to rights

Not applicable.

C. Withdrawal or substitution of assets

Not applicable.

D. Change in trustees or paying agents

Not applicable.

E. Use of Proceeds

Not applicable.

ITEM 15. CONTROLS AND PROCEDURES

A. Disclosure Controls and Procedures

As of December 31, 2024 our management, including our Chief Executive Officer and Chief Financial Officer performed an evaluation of the effectiveness of the design and operation of our disclosure controls and procedures (as defined in Rule 13a-15(e) under the Exchange Act). There are inherent limitations to the effectiveness of any disclosure controls and procedures system, including the possibility of human error and circumventing or overriding them. Even if effective, disclosure controls and procedures can provide only reasonable assurance of achieving their control objectives.

Based on such evaluation, our Chief Executive Officer and Chief Financial Officer concluded that our disclosure controls and procedures were effective as of December 31, 2024.

B. Management's Annual Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over our financial reporting, as defined in Rule 13a-15(f) under the Exchange Act. Internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of our financial reporting and the preparation of our financial statements for external purposes in accordance with IFRS Accounting Standards (IFRS) as issued by International Accounting Standards Board. Internal control over financial reporting includes policies and procedures that (i) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of our assets; (ii) provide reasonable assurance that transactions are recorded as necessary to permit preparation of our financial statements in accordance with IFRS, and that receipts and expenditures are being made only in accordance with authorizations of our management and directors; and (iii) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of our assets that could have a material effect on our financial statements. Our management conducted an assessment of the effectiveness of our internal control over financial reporting based on the criteria set forth in Internal Control - Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission (''COSO''). Based on this assessment, our management concluded that, as of December 31, 2024, our internal control over financial reporting was effective.

C. Attestation Report of the Registered Public Accounting Firm

PricewaterhouseCoopers Accountants N.V., an independent registered public accounting firm, has audited the Company's financial statements for the fiscal year ended December 31, 2024, and has included its attestation report on management's assessment of the effectiveness of the Company's internal control over financial reporting as of December 31, 2024. Their report can be found under "ITEM 18. FINANCIAL STATEMENTS".

D. Changes in Internal Control over Financial Reporting

As previously disclosed, we identified material weaknesses in the design of our internal control over financial reporting across the principles for each component of the COSO framework at the entity level (i.e. control environment, risk assessment, monitoring, information

& communication and control activities) and accordingly, across our business and IT processes. The material weaknesses that we identified related to:

- the lack of consistent and documented risk assessment procedures and control activities related to our financial reporting, among which a sufficient level of (management) review and approval, manual processes, roles and responsibilities, and adequate application and controls over information technology; and
- the lack of maintaining a sufficient complement of personnel commensurate with our accounting and reporting requirements, and able to: (i) design and maintain formal accounting policies, procedures and controls over the fair presentation of our financial statements; (ii) analyze, record and disclose complex accounting matters timely and accurately, including share-based compensation arrangements and other non-routine transactions; (iii) design and maintain controls over the preparation and review of journal entries and financial statements, including maintaining appropriate segregation of duties.

Further, we did not design and maintain effective controls over certain information technology ("IT") general controls for information systems that are relevant to the preparation of its consolidated financial statements. Specifically, we did not design and maintain (a) program change management controls to ensure that IT program and data changes affecting financial IT applications and underlying accounting records are identified, tested, authorized and implemented appropriately, (b) user access controls to ensure appropriate segregation of duties and that adequately restrict user and privileged access to its financial applications and data to appropriate company personnel and (c) testing and approval controls for program development to ensure that new software development is aligned with business and IT requirements.

During the fiscal year ended December 31, 2024, we implemented our material weakness remediation plan that included among others:

- Improving the composition and expertise of accounting and financial reporting personnel;
- Further development, formalization and implementation of risk assessment procedures throughout the organization;
- Implementing a new accounting system, improving the IT general control environment (including program change management controls, user access controls and testing and approval controls for program development), increasing the number of application controls and reducing the manual nature of execution of key controls throughout significant business processes;
- Further development and documentation of scoping our key processes and design of controls in our risk and control frameworks, covering all COSO components and strengthening the controls around analyzing, recording and disclosing complex accounting matters (including share-based compensation arrangements and other non-routine transactions), manual journal entry review and financial statements review;
- Strengthening design and documentation of formal accounting policies and control activities, including sufficient segregation of duties, roles and responsibilities, review and approval procedures;
- Development and implementation of our risk and control framework for IT general controls ensuring key IT risks are mitigated through controls;
- Organizing a series of ongoing trainings and workshops to further educate our personnel, including personnel from the finance department and personnel responsible for performing and reviewing key controls, on key aspects of SOX;
- Implementing a formal SOX testing program, based on which our Management determined effectiveness of the internal control framework per year end.

The enhanced activities noted above have operated for a sufficient period of time in order for our management to conclude, through testing of the design and operational effectiveness of our controls, that the material weaknesses have been remediated as of December 31, 2024.

Except for the changes related to the remediation of the previously identified material weaknesses noted above, there were no changes in our internal control over financial reporting identified in management's evaluation pursuant to Rules 13a-15(d) or 15d-15(d) of the Exchange Act that occurred during the year ended December 31, 2024 that materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

ITEM 16. RESERVED

Not Applicable.

ITEM 16A. AUDIT COMMITTEE FINANCIAL EXPERT

Our Board has determined that Ms. Monges, and Mr. Schikan qualify as "audit committee financial experts," as such term is defined in the rules of the SEC.

ITEM 16B. CODE OF ETHICS

We have adopted a code of ethics applicable to the board of directors and all employees. We have posted a copy of our code of business conduct and ethics on our website at: https://ir.pharvaris.com/corporate-governance/governance-documents. The information on our website is not incorporated by reference into this Annual Report, and you should not consider information contained on our website to be a part of this Annual Report.

ITEM 16C. PRINCIPAL ACCOUNTANT FEES AND SERVICES

A. Audit Fees

Audit fees in 2024 and 2023 amounted to €869,163 and €884,747, respectively, and relate to audit services provided by our principal accountants in 2024 and 2023, respectively, PricewaterhouseCoopers Accountants N.V., in connection with our annual audit, quarterly reviews and review of registration statements and comfort letters for the Company.

B. Audit-Related Fees

None.

C. Tax Fees

None.

D. All Other Fees

None.

E. Audit Committee's Pre-Approval Policies and Procedures

The Audit Committee is responsible for the appointment, replacement, compensation, evaluation and oversight of the work of the independent auditor. As part of this responsibility, the Audit Committee pre-approves all audit and non-audit services performed by the independent auditor in order to assure that they do not impair the auditor's independence from the Company in accordance with the Audit Committee's pre-approval policy.

F. Audit Work Performed by Other Than Principal Accountant if Greater than 50%

Not Applicable.

ITEM 16D. EXEMPTIONS FROM THE LISTING STANDARDS FOR AUDIT COMMITTEES

Not applicable.

ITEM 16E. PURCHASES OF EQUITY SECURITIES BY THE ISSUER AND AFFILIATED PURCHASERS

None.

ITEM 16F. CHANGE IN REGISTRANT'S CERTIFYING ACCOUNTANT

Not applicable.

ITEM 16G. CORPORATE GOVERNANCE

For a description of the significant ways in which our corporate governance practices differ from those required for U.S. companies listed on Nasdaq, see "ITEM 6. DIRECTORS, SENIOR MANAGEMENT AND EMPLOYEES—C. Board Practices—Corporate Governance Practices."

ITEM 16H. MINE SAFETY DISCLOSURE

Not applicable.

ITEM 16I. DISCLOSURE REGARDING FOREIGN JURISDICTIONS THAT PREVENT INSPECTIONS

Not applicable.

ITEM 16J. INSIDER TRADING POLICIES

We have adopted an insider trading policy (the "Insider Trading Policy") that governs the purchase, sale and other dispositions in our securities by our directors, senior management and other covered persons, and which is designed to promote compliance with applicable insider trading laws, rules and regulations, and Nasdaq listing standards. A copy of the Insider Trading Policy is filed as an exhibit to this Annual Report.

ITEM 16K. CYBERSECURITY

We integrate cybersecurity risk management into our overall risk management strategy, reporting to the chief executive officer, executive committee, and board. Our cybersecurity risk management strategy includes conducting regular risk assessments to identify potential cybersecurity threats and working with external cybersecurity experts engaged to assist us in assessing, enhancing, implementing, and monitoring our cybersecurity risk management programs and responding to any incidents

We have adopted and maintain an active cybersecurity strategy, including preventative technology solutions, to assess, identify and manage material risks from cybersecurity threats and respond to cybersecurity incidents. These processes include:

- **System selection**. We use a hybrid cloud strategy, which is designed to deliver secure and reliable information systems while maintaining regulatory compliance, thereby providing operational resilience and agility with critical business processes, systems, and applications available on a continuous basis.
- **System assessment**. Our cybersecurity specialists apply risk assessment, management and mitigation tools, technologies and processes aligned to ISO/IEC 27001. We regularly evaluate our information technology assets, data, systems, and architectures to identify, assess and remediate areas of vulnerability. These evaluations include performing proactive penetration and vulnerability testing and regular maturity assessments against ISO/IEC 27001 controls. Observations noted are considered as part of our risk assessment procedures.
- **System protection**. We deploy a variety of methods of defense such as endpoint security, intrusion detection and prevention, risk-based multi-factor authentication, automatic patch management, email and web filtering, time-of-click URL protection, access management (principle of least privilege) and security monitoring to provide appropriate levels of protection against cybersecurity threats.
- **Threat monitoring**. We actively monitor our systems to prevent and detect any future cybersecurity threats and separately, we monitor cybersecurity threats or incidents committed against other companies as such events become public. We constantly re-evaluate existing risks and vulnerabilities based on their likelihood of being exploited. This allows us to remain current with the latest trends in cybersecurity and make improvements to our strategy to ensure that our defenses consider newly identified and developing areas of cybersecurity threat.
- **Threat response**. We have put in place response procedures for prompt cybersecurity incident identification, reporting and remediation if we are subject to an information system security breach. These include the preparation of detailed response, recovery and business continuity plans in order to minimize the impact of a potential cybersecurity incident. These plans are tested and reviewed on a regular basis to ensure that they adequately capture the potential impact of newly identified and evolving cybersecurity threats.
- **Staff training**. We provide staff with periodic training on cybersecurity risk areas and undertake regular cybersecurity awareness campaigns. The training covers areas such as personal digital footprint, privacy settings, social media, phishing, information security at home and at work, ransomware, password hygiene and business email compromise.
- **Compliance with data protection frameworks**. We closely monitor changes in data protection rules and guidance. This allows us to maintain compliance with applicable laws and to keep ahead of developments and regulatory shifts.
- **Third-party service providers.** We also oversee cybersecurity risks associated with our use of third-party service providers, including restricting access to our systems from non-controlled computers or accounts, evaluation of cybersecurity practices by our third-party service providers, and evaluation of all new hardware or software tools for compliance with our security practices.

Pharvaris has established a cyber risk management program to enhance its capabilities of preventing, detecting and responding to information security threats. The program is overseen by the IT-Manager, who leads a team of dedicated cybersecurity experts and analysts. The team is responsible for developing and implementing the enterprise-wide cybersecurity strategy, vulnerability management, policy, standards, architecture, and processes. The IT-Manager has over 25 years of experience in cybersecurity and consults regularly with the Chief Technical Operations Officer ("CTOO"), who fosters awareness, ownership and alignment among various governance and risk stakeholder groups. The CTOO also ensures effective management and reporting of the dynamic digital threat landscape. The IT-Manager reports to the CTOO and, with the CTOO, provides regular updates to the audit committee of our Board. As of the date of this report, we are not aware of any material risks from cybersecurity threats that have materially affected or are reasonably likely to materially affect the Company, including our business strategy, results of operations, or financial condition.

We describe risks faced by us from identified cybersecurity threats in ITEM 3D, "Risk Factors—General Risk Factors— Our internal computer systems, or those used by our clinical investigators, contractors or consultants, may fail or suffer security breaches".

PART III

ITEM 17. FINANCIAL STATEMENTS

We have responded to Item 18 in lieu of this item.

ITEM 18. FINANCIAL STATEMENTS

Financial Statements are filed as part of this Annual Report, see pages F-1 to F-26 to this Annual Report.

ITEM 19. EXHIBITS

Exhibit No.	Description
1.1	Amended and Restated Articles of Association of Pharvaris N.V. (incorporated herein by reference to Exhibit 3.1 to the Company's Current Report on Form 6-K filed with the SEC on March 6, 2024).
2.1*	Description of Ordinary Shares of the Registrant.
4.1	Form of Indemnification Agreement (incorporated herein by reference to Exhibit 10.1 to the Company's Registration Statement on Form F-1 (File No. 333-252157) filed with the SEC on January 15, 2021).
4.2	Share Subscription Agreement, dated July 26, 2019, between Pharvaris B.V. and certain of its shareholders (incorporated herein by reference to Exhibit 10.2 to the Company's Registration Statement on Form F-1 (File No. 333-252157), as amended, initially filed with the SEC on January 15, 2021).
4.3	Amendment Agreement, dated July 29, 2020, between Pharvaris B.V. and certain of its shareholders (incorporated herein by reference to Exhibit 10.3 to the Company's Registration Statement on Form F-1 (File No. 333-252157), as amended, initially filed with the SEC on January 15, 2021).
4.4	Share Subscription Agreement, dated November 3, 2020, between Pharvaris B.V. and certain of its shareholders (incorporated herein by reference to Exhibit 10.4 to the Company's Registration Statement on Form F-1 (File No. 333-252157), as amended, initially filed with the SEC on January 15, 2021)
4.5	Second Amended and Restated Shareholders Agreement, dated November 5, 2020, between Pharvaris B.V. and its shareholders (incorporated herein by reference to Exhibit 10.5 to the Company's Registration Statement on Form F-1 (File No. 333-252157), as amended, initially filed with the SEC on January 15, 2021).
4.6	License Agreement between Pharvaris B.V. and AnalytiCon Discovery GmbH dated as of March 31, 2016 (incorporated herein by reference to Exhibit 10.6 to the Company's Registration Statement on Form F-1 (File No. 333-252157), as amended, initially filed with the SEC on January 15, 2021) †
4.7	Amendment 1, between Pharvaris Netherlands B.V. and AnalytiCon Discovery GmbH dated as of January 8, 2021, to the License Agreement between Pharvaris B.V. and AnalytiCon Discovery GmbH dated as of March 31, 2016 (incorporated herein by reference to Exhibit 10.7 to the Company's Draft Registration Statement on Form F-1 (File No. 333-252157), as amended, initially filed with the SEC on January 15, 2021).†
4.8	Amendment 2, between Pharvaris Netherlands B.V. and BRAIN Biotech AG dated as of September 20, 2024, to the license Agreement between Pharvaris B.V. and BRAIN Biotech AG (as successor in interest to AnalytiCon Discovery GmbH) dated as of March 31, 2016. ((incorporated herein by reference to Exhibit 99.1 to the Company's Current Report on Form 6-K filed with the SEC on September 23, 2024).†
4.9	Pharvaris N.V. 2021 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.1 to the Company's Registration Statement on Form S-8 (File No. 333-252897) filed with the SEC on February 9, 2021).
4.10	Amended and Restated 2016 Equity Incentive Plan of Pharvaris B.V. (incorporated herein by reference to Exhibit 10.8 to the Company's Registration Statement on Form F-1 (Registration No. 333-252157), as amended, initially filed with the SEC on January 15, 2021).
4.11	Form of Participation Side Letter (incorporated herein by reference to Exhibit 10.10 to the Company's Registration Statement on Form F-1/A (File No. 333-252157), as amended, initially filed with the SEC on January 15, 2021).
4.12	Form of Waiver to Participation Side Letter (incorporated herein by reference to Exhibit 10.11 to the Company's Registration Statement on Form F-1/A (File No. 333-252157), as amended, initially filed with the SEC on January 15, 2021).
4.13	Form of Subscription Agreement (incorporated herein by reference to Exhibit 99.1 to the Company's Current Report on Form 6-K filed with the SEC on June 20, 2023).

4.14	Sales Agreement, dated as of April 12, 2024, between Pharvaris N.V. andLeerink Partners LLC (incorporated herein by reference to Exhibit 1.2 to the Company's Registration Statement on FormF-3ASR (File No. 333-278650), filed with the SEC on April 12, 2024).
4.15	Registration Rights Agreement, dated February 5, 2024 (incorporated herein by reference to Exhibit 99.1 to the Company's Current Report on Form 6-K filed with the SEC on February 7, 2024).
8.1*	List of Subsidiaries.
11.1*	Insider Trading Policy, adopted on 25 November 2024.
12.1*	Certification pursuant to section 302 of the Sarbanes-Oxley Act of 2002.
12.2*	Certification pursuant to section 302 of the Sarbanes-Oxley Act of 2002.
13.1*	Certification pursuant to 18 U.S.C. section 1350, as adopted pursuant to section 906 of the Sarbanes-Oxley Act of 2002.
13.2*	Certification pursuant to 18 U.S.C. section 1350, as adopted pursuant to section 906 of the Sarbanes-Oxley Act of 2002.
15.1*	Consent of PricewaterhouseCoopers Accountants N.V.
97.1*	Pharvaris Clawback Policy, adopted on June 7, 2023 (incorporated herein by reference to Exhibit 97.1 to the Company's Annual Report on Form 20-F filed with the SEC on April 10, 2024).
101.INS	Inline XBRL Instance Document-the instance document does not appear in the Interactive Data File as its XBRL tags are embedded within the Inline XBRL document.
101.SCH	Inline XBRL Taxonomy Extension Schema With Embedded Linkbase Documents.
104	Cover page formatted as Inline XBRL and contained in Exhibit 101.

* Filed herewith.
† Certain information has been excluded from the exhibit because it both (i) is not material and (ii) would likely cause competitive harm to the Company if publicly disclosed.

SIGNATURES

The registrant hereby certifies that it meets all of the requirements for filing on Form 20-F and that it has duly caused and authorized the undersigned to sign this Annual Report on Form 20-F on its behalf.

Pharvaris N.V.
By: /s/ Berndt Modig
Name: Berndt Modig
Title: Chief Executive Officer

Date: April 7, 2025

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

To the board of directors and shareholders of Pharvaris N.V.

Opinions on the Financial Statements and Internal Control over Financial Reporting

We have audited the accompanying consolidated statement of financial position of Pharvaris N.V. and its subsidiaries (the "Company") as of December 31, 2024 and 2023, and the related consolidated statements of loss and comprehensive loss, changes in shareholders' equity, and cash flows for each of the three years in the period ended December 31, 2024, including the related notes (collectively referred to as the "consolidated financial statements"). We also have audited the Company's internal control over financial reporting as of December 31, 2024, based on criteria established in Internal Control - Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO).

In our opinion, the consolidated financial statements referred to above present fairly, in all material respects, the financial position of the Company as of December 31, 2024 and 2023, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2024 in conformity with IFRS Accounting Standards as issued by the International Accounting Standards Board. Also in our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2024, based on criteria established in Internal Control - Integrated Framework (2013) issued by the COSO.

Basis for Opinions

The Company's management is responsible for these consolidated financial statements, for maintaining effective internal control over financial reporting, and for its assessment of the effectiveness of internal control over financial reporting, included in Management's Annual Report on Internal Control over Financial Reporting appearing under Item 15B. Our responsibility is to express opinions on the Company's consolidated financial statements and on the Company's internal control over financial reporting based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audits to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud, and whether effective internal control over financial reporting was maintained in all material respects.

Our audits of the consolidated financial statements included performing procedures to assess the risks of material misstatement of the consolidated financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. Our audit of internal control over financial reporting included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk. Our audits also included performing such other procedures as we considered necessary in the circumstances. We believe that our audits provide a reasonable basis for our opinions.

Definition and Limitations of Internal Control over Financial Reporting

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (i) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (ii) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (iii) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Critical Audit Matters

The critical audit matter communicated below is a matter arising from the current period audit of the consolidated financial statements that was communicated or required to be communicated to the audit committee and that (i) relates to accounts or disclosures that are material to the consolidated financial statements and (ii) involved our especially challenging, subjective, or complex judgments. The communication of critical audit matters does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing a separate opinion on the critical audit matter or on the accounts or disclosures to which it relates.

Research and Development Clinical and Manufacturing Accruals

As described in Notes 2.16 and 16 to the consolidated financial statements, the Company estimates the level of services performed by vendors and the associated cost incurred for the research and development services performed. The Company has recorded €5.2 million and €1.8 million for clinical accrued liabilities and manufacturing accrued liabilities respectively for the estimated research and development costs incurred but not yet billed or paid as of 31 December 2024. These accruals relate to obligations under contracts with clinical research organizations ('CROs'), manufacturers, vendors and consultants.

The principal consideration for our determination that performing procedures relating to research and development clinical and manufacturing accruals is a critical audit matter is the high degree of auditor effort in performing procedures related to the Company's research and development clinical and manufacturing accruals.

Addressing the matter involved performing procedures and evaluating audit evidence in connection with forming our overall opinion on the consolidated financial statements. These procedures included testing the effectiveness of controls relating to management's research and development clinical and manufacturing accruals. These procedures also included, among others, (i) reviewing the Company's contractual agreements with respective clinical research organizations and any related changes to them; (ii) testing management's process for developing the research and development clinical and manufacturing accrual estimate; (iii) evaluating the appropriateness of management's process for developing the estimate; (iv) testing the completeness and accuracy of underlying data used in the process; (v) evaluating the accuracy of the estimated costs incurred for the services which have not been invoiced; and (vi) testing classification of research and development expenses.

/s/ PricewaterhouseCoopers Accountants N.V.
Amsterdam, the Netherlands
April 7, 2025

We have served as the Company's auditor since 2020

Consolidated Statement of Loss and Comprehensive Loss

	Note	Years ended December 31, 2024 €	2023 €	2022 €
Research and development expenses	3	(98,563,529)	(65,575,030)	(57,375,574)
General and administrative expenses	4	(47,124,638)	(31,338,590)	(29,339,034)
Total operating expenses		(145,688,167)	(96,913,620)	(86,714,608)
Finance income (expenses)	6	13,291,664	(2,912,643)	11,061,138
Loss before income tax		(132,396,503)	(99,826,263)	(75,653,470)
Income tax expense	7	(1,825,024)	(1,048,805)	(679,087)
Net Loss		(134,221,527)	(100,875,068)	(76,332,557)
Other comprehensive income / (loss)				
Items that may be reclassified to profit or loss:				
Exchange gain (loss) arising on translation of foreign operations		152,310	(57,874)	17,362
Total comprehensive loss attributable to:				
Equity holders of the Company		(134,069,217)	(100,932,942)	(76,315,195)
Basic and diluted loss per share	19	(2.48)	(2.63)	(2.27)

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

Consolidated Statement of Financial Position

	Notes	As at December 31, 2024 €	As at December 31, 2023 €
Assets			
Non-current assets			
Property, plant and equipment	8	667,000	223,678
Right of use assets	9	813,842	231,893
Deferred tax assets	7	474,347	387,529
Current assets			
Current tax receivable	10	2,486,680	615,538
Receivables	10	457,834	423,486
Other current assets	11	5,747,025	5,580,704
Cash and cash equivalents	12	280,728,037	391,231,637
Total assets		291,374,765	398,694,465
Equity and liabilities			
Equity	13		
Share capital		6,525,539	6,274,833
Share premium		623,641,380	615,811,986
Other reserves		39,711,103	27,894,796
Currency translation reserve		137,726	(14,584)
Accumulated loss		(402,255,007)	(265,918,628)
Total equity		267,760,741	384,048,403
Long term liabilities			
Non-current lease liability	9	639,043	43,564
Current liabilities			
Trade and other payables	14	4,562,900	2,909,725
Accrued liabilities	16	17,588,407	11,067,510
Current lease liability	9	222,427	195,341
Current tax payable		601,247	429,922
Total liabilities		23,614,024	14,646,062
Total equity and liabilities		291,374,765	398,694,465

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

Consolidated Statement of Changes in Shareholders' Equity

	Notes	Share capital	Share premium	Other reserves	Currency translation reserve	Accumulated losses	Total Equity
		€	€	€	€	€	€
Balance at January 1, 2022		3,978,227	278,742,900	9,774,416	25,928	(87,568,401)	204,953,070
Net Loss		—	—	—	—	(76,332,557)	(76,332,557)
Issue of share capital	13	70,572	9,464,901	—	—	—	9,535,473
Transaction costs on issue of shares		—	(307,710)	—	—	—	(307,710)
Tax effect on transaction costs		—	257,734	—	—	—	257,734
Currency translation reserve		—	—	—	17,362	—	17,362
Settlement of share-based payments	18	9,177	1,019,372	(954,157)	—	(287,934)	(213,542)
Share-based payments	18	—	—	11,349,200	—	—	11,349,200
Balance at December 31, 2022		4,057,976	289,177,197	20,169,459	43,290	(164,188,892)	149,259,030
Balance at January 1, 2023		4,057,976	289,177,197	20,169,459	43,290	(164,188,892)	149,259,030
Net Loss		—	—	—	—	(100,875,068)	(100,875,068)
Issue of share capital	13	2,169,859	340,388,989	—	—	—	342,558,848
Transaction costs on issue of shares		—	(17,712,292)	—	—	—	(17,712,292)
Tax effect on transaction costs		—	714,733	—	—	—	714,733
Currency translation reserve		—	—	—	(57,874)	—	(57,874)
Settlement of share-based payments	18	46,998	3,243,359	(2,937,889)	—	(854,668)	(502,200)
Share-based payments	18	—	—	10,663,226	—	—	10,663,226
Balance at December 31, 2023		6,274,833	615,811,986	27,894,796	(14,584)	(265,918,628)	384,048,403
Balance at January 1, 2024		6,274,833	615,811,986	27,894,796	(14,584)	(265,918,628)	384,048,403
Net Loss		—	—	—	—	(134,221,527)	(134,221,527)
Issue of share capital	13	165,000	(165,000)	12,609	—	—	12,609
Transaction costs on issue of shares		—	592,000	—	—	—	592,000
Tax effect on transaction costs		—	851,662	—	—	—	851,662
Currency translation reserve		—	—	—	152,310	—	152,310
Settlement of share-based payments	18	85,706	6,550,732	(4,404,835)	—	(2,114,852)	116,751
Share-based payments	18	—	—	16,208,533	—	—	16,208,533
Balance at December 31, 2024		6,525,539	623,641,380	39,711,103	137,726	(402,255,007)	267,760,741

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

Consolidated Statement of Cash Flows

	Notes	Years ended December 31, 2024 €	2023 €	2022 €
Operating activities				
Loss before tax		(132,396,503)	(99,826,263)	(75,653,470)
Non-cash adjustments to reconcile loss before tax to net cash flows / used in operations:				
Share-based payment expense	5	16,208,533	10,663,226	11,349,200
Depreciation expense	8 & 9	269,562	257,551	152,941
Net foreign exchange (gain) loss		(7,329,038)	2,794,435	(11,100,392)
Finance (income) costs		(5,422,550)	(204,019)	39,254
Changes in working capital:				
(Increase) decrease in receivables		(34,316)	(41,051)	317,612
(Increase) decrease in other current assets		(136,354)	(953,861)	(2,511,076)
Increase (decrease) in trade and other payables		1,653,175	(4,171,990)	3,905,486
Increase (decrease) in accrued liabilities		4,407,453	(695,753)	6,664,878
Income taxes paid		(2,767,247)	(1,108,410)	(182,824)
Received (paid) interest		5,417,094	237,042	(144,243)
Net cash flows used in operating activities		(120,130,191)	(93,049,093)	(67,162,634)
Investing activities				
Purchase of property, plant and equipment	8	(538,086)	(89,984)	(124,296)
Net cash flows used in investing activities		(538,086)	(89,984)	(124,296)
Financing activities				
Proceeds from issue of shares and pre-funded warrants	13	2,244,212	342,911,317	9,609,865
Transaction costs		592,000	(17,297,810)	(839,970)
Payment of principal portion of lease liabilities		(159,657)	(220,507)	(119,527)
Net cash flows provided by financing activities		2,676,555	325,393,000	8,650,368
Net (decrease) increase in cash and cash equivalents		(117,991,722)	232,253,923	(58,636,562)
Cash and cash equivalents at the beginning of the year		391,231,637	161,837,429	209,353,132
Effect of exchange rate changes		7,488,122	(2,859,715)	11,120,859
Cash and cash equivalents at the end of the year	12	280,728,037	391,231,637	161,837,429

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

Notes to the Consolidated Financial Statements

1. Corporate and Group information

This section provides general corporate and group information about Pharvaris N.V. and its subsidiaries.

1.1 Corporate information

The consolidated financial statements of Pharvaris N.V. (the "Company" or "Pharvaris") and its subsidiaries (collectively, "The Group") for the year ended December 31, 2024 were authorized for issue in accordance with a resolution of the directors on April 7, 2025.

Pharvaris N.V. was incorporated on September 30, 2015 and is based in Leiden, the Netherlands. The Company's registered office is located at Emmy Noetherweg 2, Leiden. The Company has been registered at the Chamber of Commerce under file number 64239411.

Pharvaris is a late-stage biopharmaceutical company focused on the development and commercialization of innovative therapies for rare diseases with significant unmet need, initially focused on angioedema and other bradykinin-mediated diseases.

1.2 Group information

Subsidiaries

The consolidated financial statements of the Group include:

Name	Legal seat	Country of incorporation	% of equity interest 2024	% of equity interest 2023
Pharvaris Holdings B.V.	Leiden	The Netherlands	100 %	100 %
Pharvaris Netherlands B.V.	Leiden	The Netherlands	100 %	100 %
Pharvaris, Inc.	Delaware	United States of America	100 %	100 %
Pharvaris GmbH	Zug	Switzerland	100 %	100 %

Pharvaris, Inc. and Pharvaris GmbH were incorporated on January 31, 2020 and March 27, 2020 respectively. Pharvaris, Inc. acts as a service provider to the principal Company of the Group. Pharvaris GmbH is the principal Company of the Group starting April 1, 2020. The principal Company owns the Group's intellectual property and makes the major operating decisions.

The ultimate parent company

The ultimate parent company of the Group is Pharvaris N.V., which is based in the Netherlands.

2. Summary of material accounting policies

2.1 Basis of preparation

The consolidated financial statements of the Group have been prepared in accordance with IFRS Accounting Standards (IFRS) as issued by the International Accounting Standards Board (IASB).

The consolidated financial statements have been prepared on a historical cost basis. Unless otherwise stated, the consolidated financial statements are presented in euro and all values are rounded to the nearest EUR (€), except per share amounts.

2.2 Going concern

Management assessed the Company's ability to fund its operations for a period of at least 12 months after the date of signing these financial statements. Management has not identified significant going concern risks. The financial statements of the Company have been prepared on the basis of the going concern assumption based on its existing funding, taking into account the Company's current cash position and the projected cash flows based on the activities under execution on the basis of Pharvaris' business plan and budget.

2.3 Basis of consolidation

Subsidiaries are entities controlled by the Company. The Company controls an entity when it is exposed to, or has rights to, variable returns from its involvement with the entity and has the ability to affect those returns through its power over the entity. The financial statements of subsidiaries are included in the consolidated financial statements from the date on which control commences until the date on which control ceases. Intra-group balances and transactions are eliminated in the consolidation.

2.4 Segment reporting

Operating segments are identified based on whether the allocation of resources and/ or the assessment of performance of a particular component of Group's activities are regularly reviewed as a separate operating segment by the Executive Committee, or CODM. By these criteria, the activities of Pharvaris are considered to be one segment which comprises the discovery, development and commercialization of oral bradykinin B2 receptor antagonists and the segmental analysis is the same as the analysis for Pharvaris as a

whole. The CODM reviews the consolidated operating results regularly to make decisions about the resources and to assess overall performance.

2.5 Foreign currencies

Items included in the financial statements of each of the group's entities are measured using the currency of the primary economic environment in which the entity operates. The Group's consolidated financial statements are presented in Euro, which is also the functional currency of Pharvaris N.V.

Transactions and balances

Transactions in foreign currencies are initially recorded by the Group's entities at their respective functional currency spot rates at the date the transaction first qualifies for recognition.

Monetary assets and liabilities denominated in foreign currencies are translated at the functional currency spot rates of exchange at the reporting date.

Differences arising on settlement or translation of monetary items are recognized in profit or loss.

Non-monetary items that are measured in terms of historical cost in a foreign currency are translated using the exchange rates at the dates of the initial transactions.

Upon consolidation, the assets and liabilities of foreign operations are translated into euro at the rate of exchange prevailing at the reporting date and their statements of operations are translated at the average exchange rate of the fiscal period. The exchange differences arising on translation for consolidation are recognized directly in other comprehensive income.

2.6 Notes to the cash flow statement

The cash flow statement has been prepared using the indirect method. The cash and cash equivalents disclosed in the cash flow statement comprises of cash at bank.

2.7 Property, Plant and Equipment

Property, plant and equipment comprises office equipment. Property, plant and equipment are stated at historical cost less accumulated depreciation. Historical cost includes expenditure that is directly attributable to the acquisition of the items. Subsequent costs are included in the asset's carrying amount or recognized as a separate asset only when it is probable that future economic benefits associated with the item will flow to the Group and the cost of the item can be measured reliably.

Depreciation on property, plant and equipment is calculated using the straight-line method to allocate their cost over their estimated useful lives, as follows:

- Office equipment 3-5 years

The assets' residual values and useful lives are reviewed, and adjusted if appropriate, at each balance sheet date. An asset's carrying amount is written down immediately to its recoverable amount if the asset's carrying amount is larger than its estimated recoverable amount.

Gains and losses on disposals are determined by comparing proceeds with the carrying amount and are recognized in the consolidated statements of loss and comprehensive loss.

2.8 Financial instruments Recognition and measurement

Financial assets

Initial recognition and measurement

Financial assets are initially measured at fair value plus or minus, for an item not at fair value through profit or loss ("FVTPL") transaction costs that are directly attributable to its acquisition or issue. After the initial measurement, the gains and losses are either recognized in profit and loss, or recognized in other comprehensive income.

The classification of financial assets at initial recognition depends on the financial asset's contractual cash flow characteristics and the Group's business model for managing them. Financial assets are included in Group's consolidated statements of financial position when Pharvaris becomes a party to the contractual provisions of the instrument.

Transaction costs of equity transactions are either accounted for as a deduction from equity, but only to the extent they are incremental costs directly attributable to the equity transaction that otherwise would have been avoided or are deferred on the balance sheet until the equity instrument is recognized. The costs of an equity transaction that is abandoned are recognized as an expense.

Subsequent measurement

Financial assets are subsequently measured at amortized cost. Financial assets at amortized cost are subsequently measured using the effective interest method and are subject to impairment. Gains and losses are recognized in the consolidated statements of loss and comprehensive loss when the asset is derecognized, modified or impaired.

For the year ended December 31, 2024, the Group had the following financial assets to be measured at amortized cost:

- Cash and cash equivalents
- Receivables

Derecognition

Financial assets are derecognized when the rights to receive cash flows from the investments have expired or have been transferred and where the Group has transferred substantially all risks and rewards of ownership.

Financial liabilities

Initial recognition and measurement

All financial liabilities are recognized initially at fair value and, in the case of loans and borrowings and payables, net of directly attributable transaction costs. The Group's financial liabilities include trade payables and accrued liabilities.

Subsequent measurement

After initial recognition, trade payables and accrued liabilities are subsequently measured at amortized cost. Gains and losses are recognized in the consolidated statements of loss and comprehensive loss.

Derecognition

A financial liability is derecognized when the obligation under the liability is discharged or cancelled or is expired.

2.9 Receivables

Receivables are recognized initially at fair value and subsequently measured at amortized cost. If payment of the receivable is postponed under an extended payment deadline, fair value is measured on the basis of the discounted value of the expected payments. When a receivable is uncollectible, it is written off against the allowance account for receivables.

2.10 Cash and cash equivalents

Cash and cash equivalents comprise bank balances.

2.11 Equity

The Group classifies an instrument, or its component parts, on initial recognition as a financial liability or an equity instrument in accordance with the substance of the contractual arrangement and the definitions of a financial liability and an equity instrument.

An instrument is classified as a financial liability when it is either (i) a contractual obligation to deliver cash or another financial asset to another entity or to exchange financial assets or financial liabilities with another entity under conditions that are potentially unfavorable to the Group; or (ii) a contract that will or may be settled in the Group's own equity instruments and is a non-derivative for which the Group is or may be obliged to deliver a variable number of the Group's own equity instruments or a derivative that will or may be settled other than by the exchange of a fixed amount of cash or another financial asset for a fixed number of the Group's own equity instruments. An equity instrument is defined as any contract that evidences a residual interest in the assets of an entity after deducting all of its liabilities. An instrument is an equity instrument only if the issuer has an unconditional right to avoid settlement in cash or another financial asset.

Ordinary shares

Ordinary shares are classified as equity.

Warrants

Pre-funded warrants are classified as equity and are largely paid upfront. The pre-funded warrants can be converted into ordinary shares upon exercise of the warrant, which requires payment of a nominal exercise price to the Company at the time of exercise.

2.12 Trade and other payables

Trade and other payables are obligations to pay for goods or services that have been acquired in the ordinary course of business from suppliers.

Accounts payable are classified as current liabilities if payment is due within one year or less (or in the normal operating cycle of the business if longer).

If not, they are presented as non-current liabilities.

2.13 IFRS 16 Leases

All leases are accounted for by recognizing a right-of-use asset and a lease liability except for:

- leases of low value assets; and
- leases with a duration of 12 months or less.

Lease liabilities are measured at the present value of the contractual payments due to the lessor over the lease term, using the Group's incremental borrowing rate at commencement of the lease.

On initial recognition, the carrying value of the lease liability also includes:

- any penalties payable for terminating the lease, if the term of the lease has been estimated on the basis of termination option being exercised.

Right of use assets are initially measured at the amount of the lease liability, reduced for any lease incentives received, and increased for:

- lease payments made at or before commencement of the lease;
- initial direct costs incurred; and
- the amount of any provision recognized where the Group is contractually required to dismantle, remove or restore the leased asset.

Subsequent to initial measurement lease liabilities increase as a result of interest charged at a constant rate on the balance outstanding and are reduced for lease payments made. Right-of-use assets are amortized on a straight-line basis over the remaining term of the lease.

When the Group revises its estimate of the term of any lease, it adjusts the carrying amount of the lease liability to reflect the payments to be made over the revised term, which are discounted using an updated discount rate.

2.14 Current and deferred income tax

The tax expense for the period comprises current and deferred tax. Tax effects are recognized in the consolidated statements of loss and comprehensive loss.

The current income tax charge is calculated on the basis of the tax laws enacted or substantively enacted at the balance sheet date in the countries where the Company's subsidiaries operate and generate taxable income. Management periodically evaluates positions taken in tax returns with respect to situations in which applicable tax regulation is subject to interpretation. It establishes provisions where appropriate on the basis of amounts expected to be paid to the tax authorities.

Deferred income tax is recognized, using the liability method, on temporary differences arising between the tax basis of assets and liabilities and their carrying amounts in the consolidated financial statements. Deferred income tax is determined using tax rates (and laws) that have been enacted or substantially enacted by the balance sheet date and are expected to apply when the related deferred income tax asset is realized or the deferred income tax liability is settled.

Deferred income tax assets are recognized only to the extent that it is probable that future taxable profit will be available or tax planning opportunities are available to the Company that will create taxable profit in appropriate periods against which the temporary differences and/or tax losses carried forward can be utilized. IAS 12 states that it is 'probable' that there will be sufficient taxable profit if a deductible temporary difference can be offset against a taxable temporary difference (deferred tax liability) relating to the same tax authority and the same taxable entity which will reverse in the same period as the asset, or in a period into which a loss arising from the asset may be carried back or forward.

In allocating the recognition and derecognition of DTAs on losses carried forward within a jurisdiction between equity and profit or loss (considering backward tracing), it is the Company's accounting policy to use a so-called vertical approach instead of a horizontal one to offset results of the current year with carry forward losses of previous years. That means the carry forward losses initially accounted for in profit or loss (equity) are used to offset current year gains accounted for in profit or loss (equity) first insofar available. Any remaining gains accounted for in profit or loss (equity) are offset with losses accounted for in equity (profit or loss) of the same year, and carry forward losses initially accounted for in equity (profit or loss).

Deferred income tax assets and liabilities are offset when there is a legally enforceable right to offset current tax assets against current tax liabilities and when the deferred income tax assets and liabilities relate to income taxes levied by the same taxation authority on either the taxable entity or different taxable entities where there is an intention to settle the balances on a net basis. Deferred tax balances are not discounted.

2.15 Share-based payment

The Company operates an equity-settled share-based compensation plan, under which it receives services as consideration for equity instruments (options or restricted stock units) of the Company. The fair value of these equity instruments granted in exchange for the services received from the participants is recognized as an expense. The total amount to be expensed is determined by reference to the fair value of the options or restricted stock units granted.

Service vesting condition and non-market performance vesting conditions are included in the assumptions about the number of equity instruments that are expected to vest. The total expense is recognized over the vesting period, which is the period over which all of the specified vesting conditions are to be satisfied. The Group recognizes the impact of the revision to previous estimates, if any, in the consolidated statements of loss and comprehensive loss, with a corresponding adjustment to equity. The tax effect of issued restricted stock units is debited to accumulated losses when net settlement is used in order to satisfy the Company's tax withholding obligations.

2.16 Expenses

Research and development expenses

Research activities undertaken with the prospect of gaining new scientific knowledge and understanding are expensed as incurred. Development expenses are capitalized only if the cost involved can be measured reliably, the product or process under development is technically feasible, future economic benefits are probable and the Group has the intention and resources to complete development and use or sell it. Due to the regulatory environment and other types of uncertainty, management has determined that the criteria for capitalizing development costs to intangible assets, as set out in IAS 38, have not been met and therefore the Group has not capitalized any development expenses in 2024 or 2023. See Note 3 for information relating to research and development expenses incurred in the reporting period.

At each balance sheet date, the Group estimates the level of services performed by the vendors and the associated cost incurred for the services performed.

General and administrative expenses

Expenses are recognized in the Group's consolidated statements of loss and comprehensive loss as expenses when incurred.

Personnel expenses

Wages and salaries, social security contributions, paid leave and bonuses, and other employee benefits are recognized in the financial year in which the employee provide the associated services.

The group's pension plans are classified as defined contribution plans, and, accordingly, no pension obligations are recognized in the balance sheet. Costs relating to defined contribution plans are included in the consolidated statements of loss and comprehensive loss in the period in which they are incurred, and outstanding contributions are included in other payables.

2.17 New and amended standards and interpretations

Non-current Liabilities with Covenants (Amendments to IAS 1)

On October 31, 2022, the IASB issued amendments to IAS 1 - Non-current Liabilities with Covenants. The amendment clarifies how conditions with which an entity must comply within twelve months after the reporting period affect the classification of a liability. The amendment is effective for reporting periods beginning on or after January 1, 2024. The amendments do not have a material impact on the Group.

Classification of Liabilities as Current or Non-current (Amendments to IAS 1)

In January 2020, the IASB issued amendments to paragraphs 69 to 76 of IAS 1 to specify the requirements for classifying liabilities as current or non-current. The amendments clarify:

- What is meant by a right to defer settlement
- That a right to defer must exist at the end of the reporting period
- That classification is unaffected by the likelihood that an entity will exercise its deferral right
- That only if an embedded derivative in a convertible liability is itself an equity instrument would the terms of a liability not impact its classification

The amendments are effective for annual reporting periods beginning on or after January 1, 2023 and must be applied retrospectively. The amendments do not have a material impact on the Group.

Lease Liability in a Sale and Leaseback (Amendments to IFRS 16)

On September 22, 2022, the IASB issued amendments to IFRS 16 - Leases. The amendment clarifies how a seller-lessee subsequently measures sale and leaseback transactions that satisfy the requirements in IFRS 15 to be accounted for as a sale. The amendment is effective for reporting periods beginning on or after January 1, 2024. The amendments do not have a material impact on the Group.

2.18 Standards issued but not yet effective

The standards and interpretations that are issued, but not yet effective, up to the date of issuance of the Group's financial statements are disclosed below.

The Group intends to adopt these standards, if applicable, when they become effective.

Amendment to IFRS 9 and IFRS 7 - Classification and Measurement of Financial Instruments

These amendments clarify the requirements for the timing of recognition and derecognition of some financial assets and liabilities, with a new exception for some financial liabilities settled through an electronic cash transfer system; clarify and add further guidance for assessing whether a financial asset meets the solely payments of principal and interest (SPPI) criterion; add new disclosures for certain instruments with contractual terms that can change cash flows (such as some instruments with features linked to the achievement of environment, social and governance (ESG) targets); and make updates to the disclosures for equity instruments designated at Fair Value through Other Comprehensive Income (FVOCI).

The amendment is effective for reporting periods beginning on or after January 1, 2027. The amendments are not expected to have a material impact on the Group.

IFRS 18, Presentation and Disclosure in Financial Statements

This is the new standard on presentation and disclosure in financial statements, with a focus on updates to the statement of profit or loss. The key new concepts introduced in IFRS 18 relate to the structure of the statement of profit or loss; required disclosures in the financial statements for certain profit or loss performance measures that are reported outside an entity's financial statements (that is, management-defined performance measures); and enhanced principles on aggregation and disaggregation which apply to the primary financial statements and notes in general.

The amendment is effective for reporting periods beginning on or after January 1, 2027. The amendments are being assessed by the Group.

2.19 Significant accounting judgements, estimates and assumptions

The preparation of the Group's consolidated financial statements requires management to make judgements, estimates and assumptions that affect the reported amounts of expenses, income, assets and liabilities, and the accompanying disclosures. Uncertainty about these assumptions and estimates could result in outcomes that require a material adjustment to the carrying amount of assets or liabilities affected in future periods.

In the process of applying the Group's accounting policies, management has made various judgements. Those which management has assessed to have the most significant effect on the amounts recognized in the financial statements have been discussed below.

The key assumptions concerning the future and other key sources of estimation uncertainty at the reporting date, that have a significant risk of causing a material adjustment to the carrying amounts of assets and liabilities within the next financial year, are also described in the individual notes. The Group based its assumptions and estimates on parameters available when the consolidated financial statements were prepared. Existing circumstances and assumptions about future developments, however, may change due to market changes or circumstances arising that are beyond the control of the Group. Such changes are reflected in the assumptions when they occur.

Share-based payments

The Group has adopted an equity-settled share-based compensation plan, pursuant to which certain participants are granted the right to acquire ordinary shares of the Company. The grants made under this plan are accounted for in accordance with the policy as stated in Note 2.15. The total amount to be expensed is determined by reference to the fair value of the options or restricted stock units granted. The fair value of the options is measured at the date of grant using the Black-Scholes formula as further explained in Note 18.

The use of the Black-Scholes formula requires use of certain assumptions relating to the expected option life, the volatility of stock price, the determination of an appropriate risk-free interest rate and expected dividends.

Research and development expenses

Research and development expenses are currently not capitalized but are expensed because the criteria for capitalization are not met (Note 2.16 and Note 3). At each balance sheet date, the Group estimates the level of services performed by the vendors and the associated costs incurred for the services performed. Although we do not expect the estimates to be materially different from amounts

actually incurred, the understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and could result in reporting amounts that are too high or too low in any particular period.

3. Research and development expenses

	2024	2023	2022
	€	€	€
Clinical expenses	(55,867,694)	(30,690,293)	(27,653,658)
Personnel expenses (Note 5)	(27,767,184)	(19,132,307)	(13,334,350)
Manufacturing costs	(9,434,537)	(6,500,986)	(11,181,355)
Nonclinical expenses	(3,324,513)	(8,977,187)	(4,853,822)
License costs	(1,592,687)	—	—
Intellectual Property costs	(576,914)	(274,257)	(352,389)
	(98,563,529)	(65,575,030)	(57,375,574)

Development expenses are currently not capitalized but are recorded in the condensed consolidated statements of profit or loss and other comprehensive loss because the recognition criteria for capitalization are not met.

Clinical expenses include costs of conducting and managing our sponsored clinical trials, including clinical investigator cost, costs of clinical sites, and costs for CRO's assisting with our clinical development programs.

Manufacturing expenses include costs related to manufacturing of active pharmaceutical ingredients and manufacturing of the products used in our clinical trials and research and development activities.

Nonclinical expenses include costs of our outsourced discovery, preclinical and nonclinical development studies.

Licensing costs consists of milestone payment reflecting the start of the Phase III study.

4. General and administrative expenses

	2024	2023	2022
	€	€	€
Personnel expenses (Note 5)	(18,883,708)	(13,314,359)	(13,484,996)
Professional fees	(7,757,750)	(4,689,462)	(3,972,771)
Facilities, communication and office expenses	(6,509,691)	(6,031,513)	(6,443,709)
Accounting, tax and auditing fees	(4,017,669)	(2,029,554)	(1,652,995)
Travel expenses	(2,129,631)	(1,797,588)	(1,105,961)
Consulting fees	(858,843)	(602,110)	(898,435)
Other expenses	(6,967,346)	(2,874,004)	(1,780,167)
	(47,124,638)	(31,338,590)	(29,339,034)

In 2022 and 2021 the Group entered into a number of short-term rental arrangements, the expenses are included in "Other expenses".

For the year ended December 31, 2024, depreciation expense of €0.1 million (2023: €0.06 million; 2022: €0.04 million), which relate to property, plant and equipment and leases, is included in the 'Other expenses' line.

5. Personnel expenses

	2024	2023	2022
	€	€	€
Wages and salaries	(25,805,171)	(18,746,645)	(13,408,411)
Pension charges	(1,572,233)	(1,156,028)	(803,460)
Other social security charges	(3,064,955)	(1,880,767)	(1,258,275)
Share-based payments	(16,208,533)	(10,663,226)	(11,349,200)
	(46,650,892)	(32,446,666)	(26,819,346)

The number of staff (in FTEs) employed by the Group at December 31, 2024 was 108 (2023: 82, 2022: 65).

6. Finance income / (expense)

	2024	2023	2022
	€	€	€
Foreign exchange differences	7,869,114	(3,116,662)	11,100,392
Interest income (expense)	5,469,464	224,494	(16,105)
Other finance expenses	(46,914)	(20,475)	(23,149)
	13,291,664	(2,912,643)	11,061,138

The Group reports financial results in Euros. Since bank balances are in Euros, U.S. Dollars and Swiss Francs, changes in the conversion rates of the Dollars and Swiss Francs versus the Euro result in either income or expense over time. Interest income relates to earnings on cash deposits.

7. Income taxes

	2024	2023	2022
	€	€	€
Current income tax expense	(1,033,115)	(473,623)	(757,413)
Deferred tax (charge) benefit	(791,909)	(575,182)	78,326
Income tax benefit / (expense)	(1,825,024)	(1,048,805)	(679,087)

The current tax expenses for the years ended December 31, 2024, 2023 and 2022 relates to the Company's U.S. and Dutch subsidiaries as the result of a cost-plus agreement between the U.S. and Dutch entities and the Group's principal entity in Switzerland resulting in a taxable profit in the U.S. and the Netherlands. For the year ended December 31, 2024, a tax benefit of €0.9 million is additionally directly recognized in equity (2023: €0.7 million; 2022: €0.3 million).

Reconciliation of income tax benefit / (expense) at statutory tax rate and the income tax benefit / (expense) as reported in the consolidated statement of profit or loss and other comprehensive income is as follows:

	2024	2023	2022
	€	€	€
Loss before income tax	(132,396,503)	(99,826,263)	(75,653,470)
Income tax at statutory income tax rate in the Netherlands (2024, 2023 and 2022: 25.8%)	34,158,298	25,755,176	19,518,595
Effect of tax rates in other countries	(17,611,881)	(14,334,369)	(10,823,383)
Recognition (derecognition) of previously unrecognized (recognized) deferred tax assets	762,594	(58,506)	(554,853)
Current period losses for which no deferred tax asset has been recognized	(17,950,456)	(14,771,877)	(9,184,919)
Nondeductible expenses	(1,085,015)	(458,482)	383,153
Prior period adjustments	(98,564)	2,819,253	(17,680)
Income tax benefit / (expense)	(1,825,024)	(1,048,805)	(679,087)

The effective tax rate for 2024 is (1.4)% (2023: (1.1)%; 2022: (0.9)%).

Pharvaris N.V. is the head of the fiscal unity including Pharvaris Netherlands B.V. and Pharvaris Holdings B.V.

The differences in the overseas tax rates are due to the higher tax rate in the USA and the lower tax rate in Switzerland compared to the statutory income tax rate in the Netherlands.

The Current period losses for which no deferred tax asset has been recognized consists of the unrecognized tax effect of losses incurred in Switzerland.

Following discussions with the Dutch tax authorities in November 2022, the Company concluded that foreign exchange results should be allocated to the principal Company in Switzerland. As a result, the current losses for Switzerland are partly offset by the allocated foreign exchange results. The Company did not recognize the tax benefit of the losses incurred in previous years for Switzerland.

The Group has tax loss carry-forwards as of December 31, 2024 of approximately €449.8 million (2023: €325.0 million; 2022: €182.3 million), that are available for offsetting against future taxable profits of the Companies in which the losses arose. A new Dutch tax law came into effect on January 1, 2022. Under the new tax law, profits in a given year can be offset against tax loss carry forwards for an unlimited period of time. The amount of the offset will be limited to 50% of taxable income (in excess of €1.0 million). Under Swiss law, losses can be offset against future income or capital gains for seven years.

Tax loss carry-forwards incurred in current and prior years will expire as follows:

Year	Switzerland € million	Netherlands € million	Tax losses € million
2028	102,287,656	—	102,287,656
2029	86,332,435	—	86,332,435
2030	234,646,383	—	234,646,383
Unlimited	—	26,531,641	26,531,641
Total carry-forward losses	423,266,474	26,531,641	449,798,115

Deferred taxes

Deferred taxes have been recognized to the extent that management concludes that there is sufficient probability as per IAS 12 that there will be future taxable profits available in the foreseeable future against which the unused tax losses and deductible temporary differences can be utilized. Deductible temporary tax differences for which a deferred tax asset of €0.6 million was recognized relate to the personnel bonuses accrual and are expected to revert within 12 months post balance sheet date.

Deferred tax assets relating to losses carried forward have not been recognized, and deferred tax assets on deductible temporary differences in excess of deferred tax liabilities on taxable temporary differences have not been recognized in the consolidated statement of profit and loss and other comprehensive income for the Dutch fiscal unity.

As a result thereof Deferred taxes have been recognized to the extent that management concludes that there is sufficient probability as per IAS 12 that there will be future taxable profits available in the foreseeable future against which the unused tax losses can be utilized.

Movements in deferred tax balances

	R&D expenses	Fixed assets	Non-current provisions and liabilities	Total
Deferred tax assets	€	€	€	€
At January 1, 2024	1,754,773	—	400,200	2,154,973
(Charged)/credited				
- Profit or (loss)	146,740	—	193,381	340,121
- Currency translation differences	—	—	33,257	33,257
At December 31, 2024	1,901,513	—	626,838	2,528,351
Deferred tax liability				
At January 1, 2024	—	(12,671)	(1,754,773)	(1,767,444)
(Charged)/credited				
- Profit or (loss)	—	(133,628)	(146,740)	(280,368)
- Currency translation differences	—	(6,192)	—	(6,192)
At December 31, 2024	—	(152,491)	(1,901,513)	(2,054,004)
Net deferred tax assets at December 31, 2024				474,347

	R&D expenses	Fixed assets	Non-current provisions and liabilities	Total
Deferred tax assets	€	€	€	€
At January 1, 2023	1,792,382	—	301,852	2,094,234
(Charged)/credited				
- Profit or (loss)	(37,609)	—	111,064	73,455
- Currency translation differences	—	—	(12,716)	(12,716)
At December 31, 2023	1,754,773	—	400,200	2,154,973
Deferred tax liability				
At January 1, 2023	—	(42,048)	(1,792,383)	(1,834,431)
(Charged)/credited				
- Profit or (loss)	—	28,489	37,610	66,099
- Currency translation differences	—	888	—	888
At December 31, 2023	—	(12,671)	(1,754,773)	(1,767,444)
Net deferred tax assets at December 31, 2023				387,529

The total unrecognized deferred tax assets from temporary differences amounts to €10.4 million for the year ended December 31, 2024, 2023: €11.0 million, 2022: €8.7 million).

8. Property, plant and equipment

Net book value	Notes	2024 €	2023 €
As of January 1,		223,678	193,474
Additions		538,085	90,051
Depreciation expenses	4	(94,763)	(59,847)
As of December 31,		667,000	223,678

Cumulative depreciation	2024 €	2023 €
As of January 1,	(125,373)	(65,526)
Depreciation	(94,763)	(59,847)
As of December 31,	(220,136)	(125,373)

Cumulative Costs	2024 €	2023 €
As of January 1,	349,051	259,000
Additions	538,085	90,051
As of December 31,	887,136	349,051

During 2024, the Group acquired assets with a cost of €0.5 million (2023: €0.09 million; 2022: €0.1 million). The investments in property, plant and equipment, relate to equipment, tools and installations.

9. Leases

The following table provides information about the Group's right of use assets:

	2024 €	2023 €
As of January 1,	231,893	432,965
Additions / (Disposals)	756,748	(3,302)
Depreciation charges	(174,799)	(197,770)
As of December 31,	813,842	231,893

The following table provides information about the Group's lease liabilities at December 31, 2024:

	2024 €	2023 €
Office leases	(861,470)	(238,905)
Total lease liability	(861,470)	(238,905)
Current Portion	**(222,427)**	**(195,341)**
Non-current Portion	**(639,043)**	**(43,564)**

The following table provides information about the maturities of the Company's lease liabilities at December 31, 2024:

Years ending December 31,	€
Less than 1 year	354,902
1-5 Years	1,006,729
Total lease payments	1,361,631
Less: imputed interest	500,161
Total lease liabilities	861,470
Current lease liabilities	222,427
Long-term lease liabilities	639,043

Office leases consists of (i) a lease that was entered into on December 1, 2022 with an expiration date of November 30, 2025 for offices in Leiden, the Netherlands. The lease has a lease term of three years, and (ii) a new lease agreement entered into on October 16, 2024 with an expiration date of December 31, 2029, for office space in Lexington, Cranberry One Suite 400, United States of America, or the U.S. The lease has a lease term of five years.

On June 30, 2024 a lease related to office space in Lexington, Cranberry One Suite 300, expired.

The average incremental borrowing rate applied to the lease liability related to the Leiden lease was 7.77% during the twelve months ended December 31, 2024 and 2023.

The average incremental borrowing rate applied to the lease liability related to the U.S. lease was 6.39% for the year ended December 31, 2024.

Depreciation expense of €0.2 million, €0.2 million and €0.1 million for the for the years ended December 31, 2024, 2023 and 2022, was incurred and is reflected in general and administrative expenses as determined by the underlying activities.

The total expense related to short-term and low-value leases in 2024 was €0.4 million, (2023: €0.2 million, 2022: €0.3 million) and is included in facility, communication, and office expenses

Cash outflows related to leases during the years ended December 31, 2024, 2023 and 2022 were €0.2 million, €0.2 million and €0.1 million, respectively.

10. Receivables

	2024	2023
	€	€
Current tax receivable	2,486,680	615,538
VAT receivables	457,834	423,486
	2,944,514	1,039,024

11. Other current assets

	2024	2023
	€	€
Prepayments	5,747,025	4,959,889
Other assets	—	620,815
	5,747,025	5,580,704

Prepayments mainly relate to prepaid insurance, prepaid research and development expenses and rent.

Other assets per December 31, 2024 mainly consist of deferred transaction costs related to Group's in-process equity financing (refer to note 13). The Company defers the transaction costs related to any in-process financing. Upon recognition of the equity instruments, the related transaction costs are deducted from share premium.

12. Cash and cash equivalents

	2024	2023
	€	€
Cash and cash equivalents	280,728,037	391,231,637
	280,728,037	391,231,637

The Cash and cash equivalents consist of bank balances and are not subject to any restriction. Of the cash on hand, €0.1 million relates to guarantees.

13. Equity

On December 31, 2024, the Company's authorized share capital amounted to € 14.1 million divided into 117,500,000 ordinary shares, each with a nominal value of (€0.12). (2023 and 2022: authorized share capital amounted to € 14.1 million divided into 58,750,000 ordinary shares and 58,750,000 preferred shares, each with a nominal value of (€0.12).

As of December 31, 2024, the total number of issued and fully paid shares was 54,379,491 (2023: 52,290,212; 2022: 33,816,459).

As of December 31, 2024, the issued share capital totaled €6.5 million (2023: €6.3 million; 2022: €4.1 million).

In March 2022, the Company filed a Form F-3 Registration Statement and prospectus, allowing the Company to sell up to $350 million of its securities, with the Securities and Exchange Commission. This Registration Statement was supplemented by a prospectus supplement covering an at-the-market program providing for the sales from time to time of up to $75 million of its ordinary shares pursuant to a Sales Agreement with SVB Securities LLC.

During June, 2023, the Company entered into a subscription agreement with certain institutional investors relating to the offer and sale of 6,951,340 ordinary shares of the Company, par value €0.12 per share, in a private placement at a purchase price of $10.07 per Ordinary Share. The subscription agreement generated $70.0 million (€64.1 million).

As of December 31, 2023, the Company has sold a total of 593,927 ordinary shares under the Sales Agreement generating total net proceeds of $9.8 million (€9.3 million), after deducting $0.3 million (€0.3 million), which was payable to Leerink Partners, LLC as commission in respect of such sales.

In December, 2023, the Company entered into an underwriting agreement with Morgan Stanley & Co. LLC and Leerink Partners, LLC as underwriters, pursuant to which the Company agreed to issue and sell (i) 11,125,000 ordinary shares, par value €0.12 per share and (ii) pre-funded warrants to purchase up to 1,375,000 ordinary shares in an underwritten offering. The Offering closed on December 8, 2023, and the Company generated net proceeds of $282.0 million (€261.6 million), after deducting bank fees of $18.0 million (€16.7 million).

The Shares were sold in the Offering at the public offering price of $24.00 per share. The Pre-Funded Warrants were sold at a public offering price of $23.99 per Pre-Funded Warrant, which represents the per share public offering price for the common stock less the $0.01 per share exercise price for each such Pre-Funded Warrant. Each Pre-Funded Warrant is exercisable as of December 8, 2023 until fully exercised, subject to an ownership limitation relating to the Hart-Scott-Rodino Antitrust Improvements Act of 1976, as amended, as set forth in the form of Pre-Funded Warrant.

The Pre-funded warrants were subsequently exercised in January 2024 for gross exercise proceeds of $0.01 million and resulted in issuance of 1,375,000 ordinary shares.

In March 2024, the Company received a partial reimbursement for certain of its expenses in connection with the December 2023 offering which have been accounted for in the share premium.

Ordinary shares hold the right to one vote per share.

Issued shares
On February 5, 2021, the Company became public by listing its ordinary shares on the Nasdaq Stock Exchange. On the same date all Preferred shares A, Preferred shares B and Preferred shares C were automatically converted to ordinary shares and 9,511,075 ordinary shares were issued. Together with the issuance of the ordinary shares, the par value of each ordinary share was increased from €0.01 to €0.12.

	2024 Number of shares	2023 Number of shares
Ordinary shares	54,379,491	52,290,212
	54,379,491	52,290,212

No dividend was distributed in 2024, 2023 or 2022.

The following describes the nature and purpose of each reserve within equity:

Share premium

The amount subscribed for share capital in excess of nominal value.

Other reserves

Other reserves consist of share-based payments reserve, which is used to recognize the grant date fair value of options and RSUs issued to employees and consultants over the vesting period.

14. Trade and other payables

	2024 €	2023 €
Trade payables	4,562,900	2,909,725
	4,562,900	2,909,725

15. Financial assets and liabilities fair value

Fair values of cash, receivables, and current liabilities approximate their carrying amounts due to the short-term maturities of these instruments.

16. Accrued liabilities

	2024	2023
	€	€
Consulting, professional and audit liability	729,162	351,064
Clinical accrued liabilities	5,221,572	1,832,590
Manufacturing accrued liabilities	1,767,291	2,079,900
Nonclinical accrued liabilities	445,238	493,907
Personnel related accruals	7,827,392	5,892,087
Other accrued liabilities	1,597,752	417,962
	17,588,407	11,067,510

17. Financial risk management

The Group's principal financial instruments consist of cash and cash equivalents and trade and other trade payables. The financial instruments represent the Group's working capital to serve the Group's day-to-day operations.

The Group is exposed to market risk (including currency risk, interest rate risk and price risk), credit risk and liquidity risk. The Group's management manages each risk as discussed below.

Market risk

Currency risk

The Company is exposed to foreign exchange risk arising from various currency exposures, primarily with respect to the U.S. Dollar and Swiss Franc. The Company received the proceeds from financings in U.S. dollars. The Company seeks to minimize exchange rate risk in cash positions by taking into considerations market conditions and keeping currencies in which it expects to incur the majority of its near future expenses and make related payments from those positions.

For the year ended December 31, 2024, the Group recognized a foreign exchange gain of €7.9 million.(2023: foreign exchange loss of €3.1 million; 2022: foreign exchange gain of €11.1 million). The foreign exchange gain was primarily related to the U.S. dollar cash holding of the Company's subsidiary and the associated strengthening of the U.S. dollar compared to euro during the year.

At December 31, 2024, 2023 and 2022, if the U.S. dollar had weakened / strengthened by 10% against the euro with all other variables held constant, the cash balance would have been €13.5 million, €18.8 million and €6.8 million higher / lower, respectively.

At December 31, 2024, 2023 and 2022, if the CHF had weakened / strengthened by 10% against the euro with all other variables held constant, the cash balance would have been €5.4 million, €7.1 million and €2.0 million higher / lower, respectively.

The Group keeps an amount of $139.8 million, €92.4 million and CHF50.6 million in its bank accounts as of December 31, 2024 (2023: $208.2 million, €131.8 million and CHF65.8 million).

Interest risk

The Group has no borrowings and is therefore not exposed to changes in the interest rates on loans and borrowings. The Group has €280.7 million of cash on the balance sheet at December 31, 2024. The Group is implementing its treasury strategy to monitor the impact of changes in interest rates.

Credit risk

Credit risk arises from cash and other financial assets, including deposits with banks and financial institutions. Cash deposits and investments are placed only with accredited financial institutions. Credit risk is further limited by investing only in liquid instruments. The Group's maximum exposure to credit risk for the components of the statements of financial position on December 31, 2024 and 2023 are the carrying amounts as illustrated in Note 12. There are no financial assets past due date or impaired.

Concentration of Credit Risk

Financial instruments that potentially expose the Group to concentrations of credit risk consist primarily of cash. Cash deposits are placed only with reputable financial institutions with a credit rating of not less than A-(Standard & Poor's). Credit risk is further limited by investing only in liquid instruments. As of December 31, 2024, cash consists of cash deposited with four financial institutions and account balances may exceed insured limits.

Liquidity risk

Liquidity risk is the risk that the Group might encounter difficulties in meeting the obligations associated with its financial liabilities, which are normally settled by delivering cash. The Group's approach to managing liquidity is to ensure, as far as possible, that it will always have sufficient liquidity to meet its liabilities when due.

As of December 31, 2024, the Company has cash and cash equivalents of €280.7 million.

Based on the existing operating plan, anticipated working capital requirements and available capital sources, the Company believes that it can execute on strategy and realize liquidity planning and it is able to settle all expected liabilities for at least twelve months from the issuance date of these consolidated financial statements.

The Company may need additional funding in the future, which could possibly not be available to the Group at all or not at acceptable or favorable terms. This could lead to a situation where the Group would have to delay, reduce, or eliminate some or all of its research and development programs for product candidates, product portfolio expansion or commercialization efforts, which could adversely affect the business prospects, or continuation of operations.

The Group manages liquidity risks by holding appropriate reserves, taking timely action for future funding, as well as by monitoring forecasts and actual cash flows and reconciling the maturity profiles of financial assets and liabilities.

The below table summarizes the maturity profile of the Group's accrued liabilities based on contractual undiscounted payments:

December 31, 2024	Less than 12 months €	1 to 5 years €	Total €
Trade and other payables	4,562,900	—	4,562,900
Accrued liabilities	17,588,407	—	17,588,407
Lease Liabilities	354,902	1,006,729	1,361,631

December 31, 2023	Less than 12 months €	1 to 5 years €	Total €
Trade and other payables	2,909,725	—	2,909,725
Accrued liabilities	11,067,510	—	11,067,510
Lease Liabilities	158,458	96,250	254,708

18. Share-based payments

In 2016, the Group implemented an Equity Incentive Plan, or the Plan, in order to advance the interests of the Company's shareholders by enhancing the Company's ability to attract, retain and motivate persons who are expected to make important contributions to the Company and by providing such persons with performance-based incentives that are intended to better align the interests of such persons with those of the Company's shareholders. This plan has been superseded by the 2021 long term incentive plan.

The main terms and conditions of the separate award agreements entered into under these Plans are provided below.

Stock Option Agreements

On January 1, 2022, a total of 70,000 stock options were granted to members of the board with an exercise price of $14.39 per share with a final exercise date of December 31, 2031 unless forfeited or exercised on an earlier date. 25% of the aggregate number of share options shall vest on December 31, 2022 and thereafter 1/48th of the aggregate number of share options shall vest on each subsequent monthly anniversary of the vesting commencement date until either the option is fully vested or the option holders' continuous service terminates.

On April 1, 2022, a total of 552,500 stock options were granted of which 465,000 were granted to members of key management and 87,500 were granted to members of the board, with an exercise price of $18.14 per share with a final exercise date of March 31, 2031 unless forfeited or exercised on an earlier date. 25% of the aggregate number of share options shall vest on March 31, 2023 and thereafter 1/48th of the aggregate number of share options shall vest on each subsequent monthly anniversary of the vesting commencement date until either the option is fully vested or the option holders' continuous service terminates.

On June 1, 2022, a total of 120,000 stock options were granted to members of key management with an exercise price of $17.98 per share with a final exercise date of May 31, 2031 unless forfeited or exercised on an earlier date. 25% of the aggregate number of share options shall vest on May 31, 2023 and thereafter 1/48th of the aggregate number of share options shall vest on each subsequent monthly anniversary of the vesting commencement date until either the option is fully vested or the option holders' continuous service terminates.

On April 6, 2023, a total of 846,000 stock options were granted of which 571,000 were granted to members of key management and 296,000 were granted to members of the board, with an exercise price of $8.05 per share with a final exercise date of April 6, 2033 unless forfeited or exercised on an earlier date. 25% of the aggregate number of share options shall vest on April 6, 2024 and thereafter 1/48th of the aggregate number of share options shall vest on each subsequent monthly anniversary of the vesting commencement date until either the option is fully vested or the option holders' continuous service terminates.

On November 15, 2023, a total of 90,000 stock options were granted to a member of key management with an exercise price of $16.40 per share with a final exercise date of November 15, 2033 unless forfeited or exercised on an earlier date. 25% of the aggregate number of share options shall vest on November 15, 2024 and thereafter 1/48th of the aggregate number of share options shall vest on each

subsequent monthly anniversary of the vesting commencement date until either the option is fully vested or the option holders' continuous service terminates.

On April 11, 2024, a total of 70,000 stock options were granted to members of the Board of Directors with an exercise price of $22.31 per share with a final exercise date of April 11, 2034, unless forfeited or exercised on an earlier date. 100% of the aggregate number of shares subject to the option shall vest on the 12-month anniversary of the vesting commencement date, subject to the option holder's continuous service.

On April 11, 2024, a total of 485,000 stock options were granted to members of key management with an exercise price of $22.31 per share with a final exercise date of April 11, 2034, unless forfeited or exercised on an earlier date. 25% of the aggregate number of shares subject to the option shall vest on the 12-month anniversary of the vesting commencement date, and thereafter 1/48th of the aggregate number of Shares subject to the option shall vest on each subsequent monthly anniversary of the vesting commencement date, subject to the option holder's continuous service through each applicable vesting date.

On April 15, 2024 a total of 230,000 stock options were granted to a member of key management with an exercise price of $20.15 per share with a final exercise date of April 15, 2034, unless forfeited or exercised on an earlier date. 25% of the aggregate number of shares subject to the option shall vest on the 12-month anniversary of the vesting commencement date, and thereafter 1/48th of the aggregate number of shares subject to the option shall vest on each subsequent monthly anniversary of the vesting commencement date, subject to the option holder's continuous service through each applicable vesting date.

On August 1, 2024 a total of 75,000 stock options were granted to a member of key management with an exercise price of $15.94 per share with a final exercise date of August 1, 2034, unless forfeited or exercised on an earlier date. 25% of the aggregate number of shares subject to the option shall vest on the 12-month anniversary of the vesting commencement date, and thereafter 1/48th of the aggregate number of shares subject to the option shall vest on each subsequent monthly anniversary of the vesting commencement date, subject to the option holder's continuous service through each applicable vesting date.

The share-based payment expenses are recognized over the service period in the consolidated statements of loss and comprehensive loss. The share-based payment expense recorded for the years ended December 31, 2024, 2023 and 2022 that related to Options, amounted to €10.5 million, 6.2 million and €7.6 million, respectively.

The following table illustrates the number and weighted average exercise prices of, and movements in, stock options during the year:

	2024	Weighted average exercise price	2023	Weighted average exercise price	2022	Weighted average exercise price
	Number stock options	€	Number stock options	€	Number stock options	€
Outstanding January 1,	3,830,652	9.46	3,181,538	9.69	2,470,295	9.18
Granted	860,000	19.79	936,000	6.53	742,500	16.12
Exercised	(514,356)	3.41	(241,825)	1.45	(31,257)	2.38
Forfeited	(307,108)	14.79	(45,061)	8.90	—	—
Outstanding December 31,	3,869,188	12.36	3,830,652	9.46	3,181,538	9.69

Out of the total outstanding stock options at December 31, 2024, 2,416,042 stock options were exercisable (2023: 1,919,721, 2022: 1,585,404). The options outstanding at December 31, 2024 had an exercise price in the range of €0.01 to €23.10 (2023: €0.01 to €16.88; 2022: €0.01 to €16.78) and a weighted-average remaining contractual life of 6.1 years (2023: 6.4 years, 2022: 7.5 years).

A total of 514,356 share options were exercised during the period ended December 31, 2024, (2023: 241,825; 2022: 31,257) and had a weighted-average share price of €19.34 (2023: €20.08; 2022: €11.74) at the date of exercise.

Restricted Award Agreements

In 2022 the Company granted a total of 681,588 RSUs to employees with a final vesting date four years later unless forfeited on an earlier date. The RSUs shall vest equally over a four-year period on each of the four anniversaries of the vesting start date until either the RSUs are fully vested or the RSUs holders' continuous service terminates. The fair value of the RSUs granted after the IPO is determined based on the closing share price on the grant date. The weighted-average grant date fair value of the RSUs granted in 2022 amounted to €11.84.

In 2023 the Company granted a total of 528,004 RSUs to employees with a final vesting date four years later unless forfeited on an earlier date. The RSUs shall vest equally over a four-year period on each of the four anniversaries of the vesting start date until either the RSUs are fully vested or the RSUs holders' continuous service terminates. The fair value of the RSUs granted after the IPO is determined based on the closing share price on the grant date. The weighted-average grant date fair value of the RSUs granted in 2023 amounted to €9.52.

In 2024 the Company granted a total of 455,799 RSUs to employees with a final vesting date four years later unless forfeited on an earlier date. The RSUs shall vest equally over a four-year period on each of the four anniversaries of the vesting start date until either the RSUs are fully vested or the RSUs holders' continuous service terminates. The fair value of the RSUs granted after the IPO is determined based on the closing share price on the grant date. The weighted-average grant date fair value of the RSUs granted in 2024 amounted to €19.49.

In 2024 the Company granted 249,650 RSUs to existing and newly joining key Management. The RSUs shall vest over a four-year period, with 25% of the aggregate number of RSUs vesting on the 12-month anniversary of the vesting commencement date, and thereafter 1/48th of the aggregate number of RSUs vesting on each subsequent monthly anniversary of the vesting commencement date, subject to continuous service through each applicable vesting date. The weighted-average grant date fair value of the RSUs granted in 2024 amounted to €19.75.

In 2024 the Company granted 23,335 RSUs to members of the Board of Directors. The RSUs shall vest on the 12-month anniversary of the vesting start date. The weighted-average grant date fair value of the RSUs granted in 2024 amounted to €20.80.

The share-based payment expense recorded for the years ended December 31, 2024, 2023 and 2022 that related to RSUs, amounted to €5.7 million, €4.5 million and €3.8 million, respectively.

The following table illustrates the number of and movements in unvested RSUs during the year:

	2024	2023	2022
	Number RSUs	Number RSUs	Number RSUs
Outstanding January 1,	1,033,814	795,694	259,714
Granted	728,784	528,004	681,588
Vested and settled	(294,238)	(209,671)	(65,846)
Forfeited	(195,570)	(80,213)	(79,762)
Outstanding December 31,	1,272,790	1,033,814	795,694

Fair Value Measurement of the Stock Options

The input used in the measurement of the fair value per option at each grant/measurements date using the Black-Scholes formula (including the related number of options and the fair value of the options) were as follows:

	August 1, 2024	April 15, 2024	April 11, 2024	April 11, 2024	November 15, 2023	April 6, 2023	June 1, 2022	April 1, 2022
Number of options	75,000	230,000	70,000	485,000	90,000	846,000	120,000	552,500
Fair value of the options (€)	€ 11.65	€ 15.41	€ 16.83	€ 16.90	€ 12.27	€ 5.92	€ 11.89	€ 11.50
Fair value of the ordinary shares (€)	€ 14.43	€ 18.97	€ 20.80	€ 20.80	€ 15.12	€ 7.36	€ 16.88	€ 16.42
Exercise price (€)	€ 14.43	€ 18.97	€ 20.80	€ 20.80	€ 15.12	€ 7.36	€ 16.88	€ 16.42
Expected volatility (%)	100 %	100 %	105 %	100 %	100 %	100 %	80 %	80 %
Expected life (years)	6.1	6.1	5.5	6.1	6.1	6.1	6.1	6.1
Risk-free interest rate (%)	4.0 %	4.7 %	4.7 %	4.7 %	4.6 %	3.6 %	3.0 %	2.6 %
Expected dividend yield	—	—	—	—	-	-	-	-

Expected volatility in 2023 and 2024, was based on the volatility of the Company and comparable peer group companies, while in prior periods expected volatility was based on an evaluation of the historical volatilities of comparable listed biotech-companies only. The expected life is based on Management's best estimate of when the options will be exercised. The risk-free interest rate is based on the yield on US Government bonds depending on whether the exercise price is in euros or in US dollars. The expected dividend yield is zero considering the stage of the Company.

Reference is made to Note 5 for allocation of expenses in lines of the consolidated statement of income or loss and other comprehensive income (loss).

19. Basic and diluted loss per share

Basic and diluted loss per share is calculated by dividing the loss attributable to equity holders of the Company by the weighted average number of issued and outstanding ordinary shares as well as pre-funded warrants during the year.

All of the Company's potential dilutive securities have been excluded from the computation of diluted net loss per share attributable to ordinary stockholders as the effect of including them would be antidilutive.

Unvested RSU's and outstanding options are not included in the calculation of diluted earnings per share because they are antidilutive in 2024, 2023 and 2022.

Basic and diluted loss per share

Basic and diluted loss per share

	Year Ended December 31,		
	2024	2023	2022
	€	€	€
Net Loss	(134,221,527)	(100,875,068)	(76,332,557)
Weighted average number of ordinary shares outstanding	54,020,549	38,391,654	33,585,976
Basic and diluted loss per share	(2.48)	(2.63)	(2.27)

20. Related parties

Note 1.2 provides information about the Group's structure, including details of the subsidiaries and the holding company. The following provides the total amount of transactions that have been entered into with related parties for the relevant financial year.

Charité Research Organisation GmbH (Charité CRO)

Dr. Knolle, who served as Chief Scientific Officer and Chief Operating Officer since the Company's inception up to September 30, 2023, was a member of the board of Charité Research Organisation GmbH, or Charité CRO until February 28, 2022. The Company has entered into a service contract with Charité CRO according to which Charité CRO provides services supporting research for the Company. In fiscal years 2023 and 2022, payments to Charité CRO with respect to this service contract amounted to €0.5 million and €0.4 million, respectively.

Key management personnel compensation

	2024	2023	2022
	€	€	€
Short term employee benefits	5,291,290	4,467,603	3,461,860
Post employee benefits	263,873	189,996	148,678
Share-based payments	9,012,222	6,252,492	6,524,726
Total	14,567,385	10,910,091	10,135,264

At 31 December 2024, 2023 and 2022, no short-term employee benefits have been capitalized.

The Group engages a management entity for the purpose of providing key management services and/or strategic advisory services to the Company. This management entity is considered a related party, as it provides key management advisory services and exercises key management functions. The aggregate amount of expense recognized in the consolidated statements of loss and comprehensive loss related to this related party for the 2024, 2023 and 2022 fiscal years were €0.8 million, €0.6 million and €0.6 million, respectively.

During 2023 and 2022, Dr. Jochen Knolle received €0.5 million and €0.6 million under his consulting agreement with the Company, while serving as the Company's Chief Scientific Officer ("CSO"). In late 2023, he relinquished the CSO title but remains a consultant.

At December 31, 2024, 2023 and 2022, the aggregate amounts payable to key management personnel were €1.5 million, €1.4 million and €1.2 million, respectively.

21. Commitments and contingencies

This section provides additional information about items not recognized in the financial statements but could potentially have a significant impact on the Group's financial position and performance.

Service contracts

The Group has entered into research and development commitments in relation to the developments of Group's oral bradykinin B2 receptor antagonist.

The Group's contractual obligations and commitments as of December 31, 2024 amounted to €109.9 million, (December 31, 2023: €49 million) primarily related to research and development activities.

On March 31, 2016, the Company entered into a license agreement (the "BRAIN License") and a research agreement with BRAIN (as successor in interest to AnalytiCon) to collaborate for the development of an orally available bradykinin B2 receptor antagonist. Pursuant to the BRAIN License, the Company acquired a worldwide, exclusive license from BRAIN to use (i) a certain proprietary substance class of bradykinin B2 receptor antagonists with the potential of oral activity ("OB2RA") and (ii) any derivatives, improvements, analogs, isomers, metabolites, or conjugates therefrom (together "OB2RA Class"), in each case, for the purpose of developing, manufacturing and marketing compounds on a global basis from the OB2RA Class for the treatment of, among others, hereditary angioedema. Certain rights associated with deucrictibant, IR and XR are subject to the BRAIN License.

Under the BRAIN License, up to €9.0 million in aggregate potential milestone payments remain outstanding. In addition, the Company will be required to pay BRAIN low to medium single-digit tiered royalties on direct or indirect net sales of licensed products. The royalties that the Company is required to pay BRAIN under this agreement may be reduced on a country-by-country and product-by-product basis if sales of a generic version of a product account for 1% or more of the relevant market.

22. Contingent liabilities and contingent assets

Other than milestones and royalties discussed in Note 21 above, the Group had no contingent liabilities and no contingent assets at December 31, 2024 and 2023.

22. Events after the reporting period

The Company has evaluated subsequent events through April 7, 2025, which is the date the consolidated financial statements were authorized for issuance, and did not identify any significant event after the reporting period that needs to be disclosed.

Signatories to the financial statements

Leiden, April 7, 2025

Pharvaris N.V.
Board of directors

/s/ D. Meeker	/s/ R. Glassman
D. Meeker	R. Glassman
/s/ E. Björk	/s/ B.A.E. Modig
E. Björk	B.A.E. Modig
/s/ V. Monges	/s/ J.G.C.P. Schikan
V. Monges	J.G.C.P. Schikan

Description of Ordinary Shares of the Registrant

As of the date of the Annual Report on Form 20-F of which this Exhibit 2.1 is a part, Pharvaris N.V. (the "**Company"**, "**we**", "**us**" or "**our**") has only one class of securities registered under Section 12 of the Securities Exchange Act of 1934, as amended; our registered ordinary shares.

We are registered with the Trade Register of the Chamber of Commerce (*Kamer van Koophandel*) under number 64239411. Our corporate seat is in Leiden, the Netherlands, and our registered office is also in Leiden, the Netherlands.

The following description of our ordinary shares is a summary and does not purport to be complete. It is subject to and qualified in its entirety by reference to our Articles of Association, which are incorporated by reference as an exhibit to this Annual Report on Form 20-F of which this Exhibit 2.1 is a part.

A. Ordinary Shares

Our ordinary shares shall be in registered form (*op naam*). We may issue share certificates (*aandeelbewijzen*) for registered shares in such form as may be approved by our board of directors, or the Board. Our authorized share capital amounts to €14,100,000, divided into 117,500,000 ordinary shares, each with a nominal value of €0.12.

Under Dutch law, our authorized share capital is the maximum capital that we may issue without amending our Articles of Association.

Our articles of association provide that, for as long as any of our ordinary shares are admitted to trading on Nasdaq, the New York Stock Exchange or on any other regulated stock exchange located in the United States, the laws of the State of New York shall apply to the property law aspects of our ordinary shares reflected in the register administered by our transfer agent, subject to certain overriding exceptions under Dutch law.

The following summarizes the main rights of holders of our ordinary shares:

1. each holder of ordinary shares is entitled to one vote per share on all matters to be voted on by shareholders generally, including the appointment of directors;

2. there are no cumulative voting rights;

3. the holders of our ordinary shares are entitled to dividends and other distributions as may be declared from time to time by us out of funds legally available for that purpose, if any;

4. upon our liquidation or dissolution, the holders of ordinary shares will be entitled to share ratably in the distribution of all of our assets remaining available for distribution after satisfaction of all our liabilities; and

5. the holders of our ordinary shares have preemptive rights in case of share issuances or the grant of rights to subscribe for shares, except if such rights are limited or excluded by the corporate body authorized to do so and except in such cases as provided by Dutch law and our Articles of Association.

B. Shareholders' Register

Pursuant to Dutch law and our Articles of Association, we must keep our shareholders' register accurate and current. The Board keeps our shareholders' register and records names and addresses of all holders of registered shares, showing the date on which the shares were acquired, the date of the acknowledgement by or notification of us as well as the amount paid on each share. The register also includes the names and addresses of those with a right of usufruct (*vruchtgebruik*) on registered shares belonging to another or a pledge (*pandrecht*) in respect of such shares.

C. Corporate Objectives

Pursuant to the Articles of Association, our corporate objectives are:

- to discover, develop and commercialize treatments, including for hereditary angioedema;

- to engage, in any way whatsoever, in trading activities (retail and wholesale), the import, export, purchase, sale and distribution of products, including, but not limited to, pharmaceutical products, and other related

(raw material) products and to render operational and supporting services to its group companies in connection herewith;

- to incorporate, participate in, finance or hold any other interest in and to conduct the management or supervision of other entities, companies, partnerships and businesses;
- to acquire, to manage, to invest, to exploit, to encumber and to dispose of assets and liabilities;
- to furnish guarantees, to provide security, to warrant performance in any other way and to assume liability, whether jointly and severally or otherwise, in respect of obligations of group companies or other parties; and
- to do anything which, in the widest sense, is connected with or may be conducive to the objects described above.

D. Amendment to our Articles of Association

An amendment to our Articles of Association would require a resolution of the general meeting upon proposal by the Board.

E. Limitations on the Rights to Own Ordinary Shares

Our ordinary shares may be issued to individuals, corporations, trusts, estates of deceased individuals, partnerships and unincorporated associations of persons. Our Articles of Association contain no limitation on the rights to own our ordinary shares and no limitation on the rights of nonresidents of the Netherlands or foreign shareholders to hold or exercise voting rights.

F. Limitation on Liability and Indemnification Matters

Under Dutch law, our directors may be held liable for damages in the event of improper or negligent performance of their duties. They may be held jointly and severally liable for damages to the Company and to third parties for infringement of the Articles of Association or of certain provisions of Dutch law. In certain circumstances, they may also incur other specific civil and criminal liabilities. Subject to certain exceptions, our Articles of Association provide for indemnification of our current and former directors (and other current and former officers and employees as designated by our Board). No indemnification under our Articles of Association shall be given to an indemnified person:

- if a competent court or arbitral tribunal has established, without having (or no longer having) the possibility for appeal, that the acts or omissions of such indemnified person that led to the financial losses, damages, expenses, suit, claim, action or legal proceedings as described above are of an unlawful nature (including acts or omissions which are considered to constitute malice, gross negligence, intentional recklessness and/or serious culpability attributable to such indemnified person);
- to the extent that his or her financial losses, damages and expenses are covered under insurance and the relevant insurer has settled, or has provided reimbursement for, these financial losses, damages and expenses (or has irrevocably undertaken to do so);
- in relation to proceedings brought by such indemnified person against the Company, except for proceedings brought to enforce indemnification to which he or she is entitled pursuant to our Articles of Association, pursuant to an agreement between such indemnified person and the Company which has been approved by the Board or pursuant to insurance taken out by the Company for the benefit of such indemnified person; or
- for any financial losses, damages or expenses incurred in connection with a settlement of any proceedings effected without the Company's prior consent.

Under our Articles of Association, our Board may stipulate additional terms, conditions and restrictions in relation to the indemnification described above.

G. Shareholders' Meetings and Consents

General Meeting

General meetings may be held in the Netherlands, in any of the locations specified in our Articles of Association. If and when allowed pursuant to applicable law, those who convene the general meeting may also

decide whether (and if so, under what conditions) the general meeting shall also or exclusively be accessible through the use of electronic means. The annual general meeting must be held within six months of the end of each financial year. Additional extraordinary general meetings may also be held, whenever considered appropriate by the Board, and shall be held within three months after our Board has considered it to be likely that our shareholders' equity (*eigen vermogen*) has decreased to an amount equal to or lower than half of our paid-in and called-up share capital, in order to discuss the measures to be taken if so required.

Pursuant to Dutch law, one or more shareholders or others with meeting rights under Dutch law who jointly represent at least one-tenth of our issued share capital may request us to convene a general meeting, setting out in detail the matters to be discussed. If our Board has not taken the steps necessary to ensure that such meeting can be held within six weeks after the request, the proponent(s) may, on their application, be authorized by the competent Dutch court in preliminary relief proceedings to convene a general meeting. The court shall disallow the application if it does not appear that the proponent(s) has/have previously requested our Board to convene a general meeting and our Board has not taken the necessary steps so that the general meeting could be held within six weeks after the request. The application shall also be disallowed if the proponent(s) has/have not demonstrated to have a reasonable interest in the convening of the general meeting.

General meetings must be convened by an announcement published in a Dutch daily newspaper with national distribution. The notice must state the agenda, the time and place of the meeting, the record date (if any), the procedure for participating in the general meeting by proxy, as well as other information as required by Dutch law. The notice must be given at least 15 calendar days prior to the day of the meeting. The agenda for the annual general meeting shall include, among other things, the adoption of the statutory annual accounts, appropriation of our profits and proposals relating to the composition of the Board, including the filling of any vacancies in the Board. In addition, the agenda shall include such items as have been included therein by the Board.

The agenda shall also include such items requested by one or more shareholders, or others with meeting rights under Dutch law, representing at least 3% of our issued share capital. These requests must be made in writing or by electronic means and received by the Board at least 60 days before the day of the meeting. No resolutions shall be adopted on items other than those that have been included in the agenda.

In accordance with the DCGC, shareholders who have the right to put an item on the agenda for our general meeting or to request the convening of a general meeting shall not exercise such rights until after they have consulted our Board. If exercising such rights may result in a change in our strategy (for example, through the dismissal of one or more of our directors), our Board must be given the opportunity to invoke a reasonable period of up to 180 days to respond to the shareholders' intentions. If invoked, our Board must use such response period for further deliberation and constructive consultation, in any event with the shareholder(s) concerned and exploring alternatives. At the end of the response time, our Board shall report on this consultation and the exploration of alternatives to our general meeting. The response period may be invoked only once for any given general meeting and shall not apply (i) in respect of a matter for which either a response period or a statutory cooling-off period (as discussed below) has been previously invoked or (ii) in situations where a shareholder holds at least 75% of our issued share capital as a consequence of a successful public bid..

Moreover, our Board can invoke a cooling-off period of up to 250 days when shareholders, using their right to have items added to the agenda for a general meeting or their right to request a general meeting, propose an agenda item for our general meeting to dismiss, suspend or appoint one or more directors (or to amend any provision in our Articles of Association dealing with those matters) or when a public offer for our company is made or announced without our support, provided, in each case, that our Board believes that such proposal or offer materially conflicts with the interests of our company and its business. During a cooling-off period, our general meeting cannot dismiss, suspend or appoint directors (or amend the provisions in our Articles of Association dealing with those matters) except at the proposal of our Board.

During a cooling-off period, our Board must gather all relevant information necessary for a careful decision-making process and at least consult with shareholders representing 3% or more of our issued share capital at the time the cooling-off period was invoked, as well as with our Dutch works council (if we or, under certain circumstances, any of our subsidiaries would have one). Formal statements expressed by these stakeholders during such consultations must be published on our website to the extent these stakeholders have approved that publication. Ultimately one week following the last day of the cooling-off period, our Board must publish a report in respect of its policy and conduct of affairs during the cooling-off period on our website. This report must remain available for inspection by shareholders and others with meeting rights under Dutch law at our office and must be tabled for discussion at the next general meeting. Shareholders representing at least 3% of our issued share capital may request the Enterprise Chamber for early termination of the cooling-off period. The Enterprise Chamber must rule in favor of the request if the shareholders can demonstrate that:

- our Board, in light of the circumstances at hand when the cooling-off period was invoked, could not reasonably have concluded that the relevant proposal or hostile offer constituted a material conflict with the interests of our company and its business;

- our Board cannot reasonably believe that a continuation of the cooling-off period would contribute to careful policy-making; or
- other defensive measures, having the same purpose, nature and scope as the cooling-off period, have been activated during the cooling-off period and have not since been terminated or suspended within a reasonable period at the relevant shareholders' request (i.e., no 'stacking' of defensive measures).

The general meeting is presided over by the chairperson of the Board. If no chairperson has been elected or if he or she is not present at the meeting, the general meeting shall be presided over by the vice-chairperson. If no vice-chairperson has been elected or if he or she is not present at the meeting, the general meeting shall be presided over by the chief executive officer. If no vice-chairperson has been elected or if he or she is not present at the meeting, the general meeting shall be presided over by another person designated in accordance with our Articles of Association. Our directors may always attend a general meeting. In these meetings, they have an advisory vote. The chairperson of the meeting may decide at his or her discretion to admit other persons to the meeting..

All shareholders and others with meeting rights under Dutch law are authorized to attend the general meeting, to address the meeting and, in so far as they have such right, to vote pro rata to his or her shareholding. Shareholders may exercise these rights, if they are the holders of shares on the record date, if any, as required by Dutch law, which is currently the 28th day before the day of the general meeting. Under our Articles of Association, shareholders and others with meeting rights under Dutch law must notify us in writing or by electronic means of their identity and intention to attend the general meeting. This notice must be received by us ultimately on the seventh day prior to the general meeting, unless indicated otherwise when such meeting is convened.

Quorum and voting requirements

Each ordinary share confers the right on the holder to cast one vote at the general meeting. Shareholders may vote by proxy. No votes may be cast at a general meeting on shares held by us or our subsidiaries or on shares for which we or our subsidiaries hold depository receipts. Nonetheless, the holders of a right of usufruct (*vruchtgebruik*) and the holders of a right of pledge (*pandrecht*) in respect of shares held by us or our subsidiaries in our share capital are not excluded from the right to vote on such shares, if the right of usufruct (*vruchtgebruik*) or the right of pledge (*pandrecht*) was granted prior to the time such shares were acquired by us or any of our subsidiaries. Neither we nor any of our subsidiaries may cast votes in respect of a share on which we or such subsidiary holds a right of usufruct (*vruchtgebruik*) or a right of pledge (*pandrecht*). Shares which are not entitled to voting rights pursuant to the preceding sentences will not be taken into account for the purpose of determining the number of shareholders that vote and that are present or represented, or the amount of the share capital that is provided or that is represented at a general meeting.

Decisions of the general meeting are taken by a simple majority of votes cast, except where Dutch law or our Articles of Association provide for a qualified majority or unanimity. Subject to any provision of mandatory Dutch law and any higher quorum requirement stipulated by our Articles of Association, if we would be subject to the requirement that our general meeting can only pass resolutions if a certain part of our issued share capital is present or represented at such general meeting under applicable securities laws or listing rules, then such resolutions shall be subject to such quorum as specified by such securities laws or listing rules pursuant to our Articles of Association.

H. Board

Appointment of directors

Under our Articles of Association, the directors are appointed by the general meeting upon binding nomination by our Board, on a recommendation of our nomination and corporate governance committee. However, the general meeting may at all times overrule the binding nomination by a resolution adopted by at least a two-thirds majority of the votes cast, provided such majority represents more than half of the issued share capital. If the general meeting overrules the binding nomination, the Board shall make a new nomination.

At a general meeting, a resolution to appoint a director can only be passed in respect of candidates whose names are stated for that purpose in the agenda of that general meeting or in the explanatory notes thereto. Upon the appointment of a person as a director, the general meeting shall determine whether that person is appointed as executive director or as non-executive director.

Duties and liabilities of directors

The Board is charged with the management of the Company, which includes setting the Company's policies and strategy, subject to the restrictions contained in our Articles of Association. The executive directors manage our day-to-day business and operations and implement our strategy. The non-executive directors focus

on the supervision on the policy and functioning of the performance of the duties of all of our directors and our general state of affairs.

Subject to certain limitations under Dutch law, our directors may divide their tasks among themselves in or pursuant to the internal rules applicable to the Board. Each director has a statutory duty to act in the corporate interest of the Company and its business. Under Dutch law, the corporate interest extends to the interests of all corporate stakeholders, such as shareholders, creditors, employees, customers and suppliers. The duty to act in the corporate interest of the Company also applies in the event of a proposed sale or break-up of the Company, provided that the circumstances generally dictate how such duty is to be applied and how the respective interests of various groups of stakeholders should be weighed. Any resolution of the Board regarding a material change in our identity or character requires approval of the general meeting.

Our Board is entitled to represent our company. The power to represent our company also vests in our chief executive officer individually, as well as in any other two executive directors acting jointly.

I. Dividends and Other Distributions

Amount available for distribution

Under Dutch law, we may only pay dividends and other distributions, from our reserves to the extent our shareholders' equity (*eigen vermogen*) exceeds the sum of the paid-in and called-up share capital plus the reserves we must maintain under Dutch law or by our Articles of Association and (if it concerns a distribution of profits) after adoption of our statutory annual accounts by our general meeting from which it appears that such dividend distribution is allowed.

Our Board may decide that all or part of our profits shown in our adopted statutory annual accounts will be added to our reserves. After reservation of any such profits, any remaining profits will be at the disposal of the general meeting at the proposal of our Board for distribution on our ordinary shares, subject to applicable restrictions of Dutch law.

Our Board is permitted, subject to certain requirements and applicable restrictions of Dutch law, to declare interim dividends without the approval of the general meeting.

Dividends and other distributions shall be made payable no later than a date determined by the Board. Claims to dividends and other distributions not made within five years from the date that such dividends or distributions became payable will lapse and any such amounts will be considered to have been forfeited to us (*verjaring*).

Exchange controls

Under Dutch law, there are no exchange controls applicable to the transfer to persons outside of the Netherlands of dividends or other distributions with respect to, or of the proceeds from the sale of, shares of a Dutch company, subject to applicable restrictions under sanctions and measures, including those concerning export control, pursuant to European Union regulations, the Sanctions Act 1977 (*Sanctiewet 1977*) or other legislation, applicable anti-boycott regulations, applicable anti-money-laundering regulations and similar rules and provided that, under certain circumstances, payments of such dividends or other distributions must be reported to the Dutch Central Bank at their request for statistical purposes. There are no special restrictions in the Articles of Association or Dutch law that limit the right of shareholders who are not citizens or residents of the Netherlands to hold or vote shares.

Squeeze-out procedures

A shareholder who holds at least 95% of our issued share capital for his or her own account, alone or together with group companies, may initiate proceedings against our other shareholders jointly for the transfer of their shares to such shareholder. The proceedings are held before the Enterprise Chamber, and can be instituted by means of a writ of summons served upon each of the other shareholders in accordance with the provisions of the Dutch Code of Civil Procedure (*Wetboek van Burgerlijke Rechtsvordering*). The Enterprise Chamber may grant the claim for squeeze-out in relation to the other shareholders and will determine the price to be paid for the shares, if necessary after appointment of one or three experts who will offer an opinion to the Enterprise Chamber on the value to be paid for the shares of the other shareholders. Once the order to transfer becomes final before the Enterprise Chamber, the person acquiring the shares shall give written notice of the date and place of payment and the price to the holders of the shares to be acquired whose addresses are known to him. Unless the addresses of all of them are known to the acquiring person, such person is required to publish the same in a daily newspaper with a national circulation.

J. Dissolution and Liquidation

Under our Articles of Association, we may be dissolved by a resolution of the general meeting, subject to a proposal of the Board. In the event of a dissolution, the liquidation shall be effected by the Board, unless the general meeting decides otherwise. During liquidation, the provisions of our Articles of Association will remain in force as far as possible. To the extent that any assets remain after payment of all of our liabilities, any remaining assets shall be distributed to our shareholders in proportion to their number of shares.

K. Dutch Financial Reporting Supervision Act

On the basis of the Dutch Financial Reporting Supervision Act (*Wet toezicht financiële verslaggeving*), or the FRSA, the Dutch Authority for the Financial Markets (*Stichting Autoriteit Financiële Markten*), or AFM, supervises the application of financial reporting standards by Dutch companies whose securities are listed on a Dutch or foreign stock exchange.

Pursuant to the FRSA, the AFM has an independent right to (i) request an explanation from us regarding our application of the applicable financial reporting standards if, based on publicly known facts or circumstances, it has reason to doubt that our financial reporting meets such standards and (ii) recommend to us the making available of further explanations. If we do not comply with such a request or recommendation, the AFM may request that the Enterprise Chamber order us to (i) make available further explanations as recommended by the AFM, (ii) provide an explanation of the way we have applied the applicable financial reporting standards to our financial reports or (iii) prepare or restate our financial reports in accordance with the Enterprise Chamber's orders.

L. Comparison of Dutch Corporate Law and U.S. Corporate Law

The following comparison between Dutch corporate law, which applies to us, and Delaware corporation law, the law under which many publicly listed corporations in the United States are incorporated, discusses additional matters not otherwise described in this Exhibit 2.1. Although we believe this summary is materially accurate, the summary is subject to Dutch law, including Book 2 of the Dutch Civil Code and the DCGC and Delaware corporation law, including the Delaware General Corporation Law.

Corporate Governance

Duties of Directors

The Netherlands. We have a one-tier board structure consisting of a board of directors comprising one or more executive directors and one or more non-executive directors. Under Dutch law, our Board is charged with the management of the company, which includes setting the company's policies and strategy, subject to the restrictions contained in our Articles of Association. The executive directors manage our day-to-day business and operations and implement our strategy. The non-executive directors focus on the supervision on the policy and functioning of the performance of the duties of all of our directors and our general state of affairs. Our directors may divide their tasks among themselves in or pursuant to internal rules applicable. Each director has a statutory duty to act in the corporate interest of the Company and its business. Under Dutch law, the corporate interest extends to the interests of all corporate stakeholders, such as shareholders, creditors, employees, customers and suppliers. The duty to act in the corporate interest of the Company also applies in the event of a proposed sale or break-up of the Company, provided that the circumstances generally dictate how such duty is to be applied and how the respective interests of various groups of stakeholders should be weighed.

Our Board is entitled to represent the Company. The power to represent our company also vests in our chief executive officer individually, as well as in any other two executive directors acting jointly.

Any resolution of our Board regarding a material change in our identity or character requires approval of the general meeting. The absence of the approval of the general meeting shall result in the relevant resolution being null and void but shall not affect the powers of representation of the Board or of the executive directors.

Delaware. The board of directors bears the ultimate responsibility for managing the business and affairs of a corporation. In discharging this function, directors of a Delaware corporation owe fiduciary duties of care and loyalty to the corporation and to its stockholders. Delaware courts have decided that the directors of a Delaware corporation are required to exercise informed business judgment in the performance of their duties. Informed business judgment means that the directors have informed themselves of all material information reasonably available to them. The duty of loyalty may be summarized as the duty to act in good faith, not out of self-interest, and in a manner that the director reasonably believes to be in the best interests of the stockholders. Under certain circumstances (such as defensive actions in response to a change of control), Delaware courts may also impose more rigorous standards of conduct upon directors of a Delaware corporation.

Director terms

The Netherlands. The DCGC provides the following best practice recommendations on the terms for tenure of our directors:

- executive directors should be appointed for a maximum period of four years, without limiting the number of consecutive terms executive directors may serve.

- non-executive directors should be appointed for two consecutive periods of no more than four years. Thereafter, non-executive directors may be reappointed for a maximum of two consecutive periods of no more than two years, provided that the reason for any reappointment after an eight-year term of office should be disclosed in the Company's statutory annual report.

The general meeting shall at all times be entitled to suspend or dismiss a director. Under our Articles of Association, the general meeting may only adopt a resolution to suspend or dismiss a director by at least a two-thirds majority of the votes cast, provided that such majority represents more than half of our issued share capital, unless the resolution is passed at the proposal of our Board, in which latter case a simple majority of the votes cast is sufficient. If a director is suspended and the general meeting does not resolve to dismiss him or her within three months from the date of such suspension, the suspension shall lapse.

Delaware. The Delaware General Corporation Law generally provides for a one-year term for directors, but permits directorships to be divided into up to three classes with up to three-year terms, with the years for each class expiring in different years, if permitted by the certificate of incorporation, an initial bylaw or a bylaw adopted by the stockholders. A director elected to serve a term on a "classified" board may not be removed by stockholders without cause. There is no limit in the number of terms a director may serve.

Director vacancies

The Netherlands. Our Board can temporarily fill vacancies in its midst caused by temporary absence or incapacity of directors without requiring a shareholder vote. If all of our directors are absent or incapacitated, our management shall be attributed to the person who most recently ceased to hold office as the chairperson of our Board, provided that if such former chairperson is unwilling or unable to accept that position, our management shall be attributed to the person who most recently ceased to hold office as our chief executive officer. If such former chief executive officer is also unwilling or unable to accept that position, our management shall be attributed to one or more persons whom the general meeting has designated for that purpose. The person(s) charged with our management in this manner may designate one or more persons to be charged with our management instead of, or together with, such person(s).

Under Dutch law, directors are appointed and re-appointed by the general meeting. Under our Articles of Association, directors are appointed by the general meeting upon binding nomination by our Board. However, the general meeting may at all times overrule a binding nomination by a resolution adopted by at least a two-thirds majority of the votes cast, provided such majority represents more than half of the issued share capital. If the general meeting overrules a binding nomination, the Board shall make a new nomination.

Delaware. The Delaware General Corporation Law provides that vacancies and newly created directorships may be filled by a majority of the directors then in office (even though less than a quorum) unless (i) otherwise provided in the certificate of incorporation or bylaws of the corporation or (ii) the certificate of incorporation directs that a particular class of stock is to elect such director, in which case any other directors elected by such class, or a sole remaining director elected by such class, will fill such vacancy.

Conflict-of-interest transactions

The Netherlands. Under Dutch law and our Articles of Association, our directors shall not take part in any discussion or decision-making that involves a subject or transaction in relation to which he or she has a direct or indirect personal conflict of interest with us. Such a conflict of interest would generally arise if the director concerned is unable to serve our interests and the business connected with our Company with the required level of integrity and objectivity due to the existence of the conflicting personal interest. Our Articles of Association provide that if as a result of conflicts of interests no resolution of the Board can be adopted, the resolution may nonetheless be adopted by the Board as if none of the directors had a conflict of interest. In that latter case, each director is entitled to participate in the discussion and decision-making process and to cast a vote.

The DCGC provides the following best practice recommendations in relation to conflicts of interests in respect of directors:

- A director should report any conflict of interest or potential conflict of interest in a transaction that is of material significance to the company and/or to such person to the chairperson of the Board without

delay and should provide all relevant information in that regard, including the relevant information pertaining to his or her spouse, registered partner or other life companion, foster child and relatives by blood or marriage up to the second degree. If the chairperson of the Board has a conflict of interest or potential conflict of interest, he or she should report this to the vice-chairperson of the Board without delay;

- The Board should decide, outside the presence of the director concerned, whether there is a conflict of interest;
- Transactions in which there are conflicts of interest with directors should be agreed on terms that are customary in the market; and
- Decisions to enter into transactions in which there are conflicts of interest with directors that are of material significance to the Company and/or to the relevant directors should require the approval of the Board. Such transactions should be published in our statutory annual report, together with a description of the conflict of interest and a declaration that the relevant best practice provisions of the DCGC have been complied with.

Delaware. Under the Delaware General Corporation Law transactions involving a Delaware corporation and an interested director of that corporation would not be voidable if:

- the material facts as to the director's relationship or interest are disclosed or known to the board of directors and the board in good faith authorizes the transaction by the affirmative vote of a majority of the disinterested directors;
- the material facts are disclosed or known as to the director's relationship or interest and the transaction is specifically approved in good faith by vote of the majority of shares entitled to vote thereon; or
- the transaction is fair to the corporation at the time it is authorized by the board of directors, a committee of the board of directors or the stockholders.

Proxy voting by directors

The Netherlands. An absent director may issue a proxy for a specific board meeting but only to another director in writing or by electronic means.

Delaware. A director of a Delaware corporation may not issue a proxy representing the director's voting rights as a director.

Shareholders Rights

Voting Rights

The Netherlands. In accordance with Dutch law and our Articles of Association, each issued ordinary share confers the right to cast one vote at the general meeting. No votes may be cast at a general meeting on shares held by us or our subsidiaries or on shares for which we or our subsidiaries hold depository receipts. Nonetheless, the holders of a right of usufruct (*vruchtgebruik*) and the holders of a right of pledge (*pandrecht*) in respect of shares held by us or our subsidiaries in our share capital are not excluded from the right to vote on such shares, if the right of usufruct (*vruchtgebruik*) or the right of pledge (*pandrecht*) was granted prior to the time such shares were acquired by us or any of our subsidiaries. Neither we nor any of our subsidiaries may cast votes in respect of a share on which we or such subsidiary holds a right of usufruct (*vruchtgebruik*) or a right of pledge (*pandrecht*). Shares which are not entitled to voting rights pursuant to the preceding sentences will not be taken into account for the purpose of determining the number of shareholders that vote and that are present or represented, or the amount of the share capital that is provided or that is represented at a general meeting.

For each general meeting, the Board may determine that a record date will be applied in order to establish which shareholders are entitled to attend and vote at the general meeting. Such record date shall be the 28th day prior to the day of the general meeting. The record date and the manner in which shareholders can register and exercise their rights will be set out in the notice of the meeting which must be published in a Dutch daily newspaper with national distribution at least 15 calendar days prior to the meeting (and such notice may therefore be published after the record date for such meeting). Under our Articles of Association, shareholders and others with meeting rights under Dutch law must notify us in writing or by electronic means of their identity and intention to attend the general meeting. This notice must be received by us ultimately on the seventh day prior to the general meeting, unless indicated otherwise when such meeting is convened.

Delaware. Under the Delaware General Corporation Law, each stockholder is entitled to one vote per share of stock, unless the certificate of incorporation provides otherwise. In addition, the certificate of incorporation may provide for cumulative voting at all elections of directors of the corporation, or at elections held under specified circumstances. Either the certificate of incorporation or the bylaws may specify the number of

shares and/or the amount of other securities that must be represented at a meeting in order to constitute a quorum, but in no event will a quorum consist of less than one-third of the shares entitled to vote at a meeting.

Stockholders as of the record date for the meeting are entitled to vote at the meeting, and the board of directors may fix a record date that is no more than 60 nor less than 10 days before the date of the meeting, and if no record date is set then the record date is the close of business on the day next preceding the day on which notice is given, or if notice is waived then the record date is the close of business on the day next preceding the day on which the meeting is held. The determination of the stockholders of record entitled to notice or to vote at a meeting of stockholders shall apply to any adjournment of the meeting, but the board of directors may fix a new record date for the adjourned meeting.

Shareholder proposals

The Netherlands. Pursuant to Dutch law, one or more shareholders or others with meeting rights under Dutch law who jointly represent at least one-tenth of our issued share capital may request us to convene a general meeting, setting out in detail the matters to be discussed. If we have not taken the steps necessary to ensure that such meeting can be held within six weeks after the request, the proponent(s) may, on their application, be authorized by the competent Dutch court in preliminary relief proceedings to convene a general meeting. The court shall disallow the application if it does not appear that the proponent(s) has/have previously requested our Board to convene a general meeting and our Board has not taken the necessary steps so that the general meeting could be held within six weeks after the request. The application shall also be disallowed if the proponent(s) has/have not demonstrated to have a reasonable interest in the convening of the general meeting.

The agenda for a general meetings shall also include such items requested by one or more shareholders or others with meeting rights under Dutch law representing at least 3% of our issued share capital,. These requests must be made in writing or by electronic means and received by us at least 60 days before the day of the meeting. No resolutions shall be adopted on items other than those that have been included in the agenda.

In accordance with the Dutch Corporate Governance Code, or DCGC, shareholders who have the right to put an item on the agenda for our general meeting or to request the convening of a general meeting shall not exercise such rights until after they have consulted our Board of directors. If exercising such rights may result in a change in our strategy (for example, through the dismissal of one or more of our directors), our Board must be given the opportunity to invoke a reasonable period of up to 180 days to respond to the shareholders' intentions. If invoked, our Board must use such response period for further deliberation and constructive consultation, in any event with the shareholder(s) concerned and exploring alternatives. At the end of the response time, our Board shall report on this consultation and the exploration of alternatives to our general meeting. The response period may be invoked only once for any given general meeting and shall not apply (i) in respect of a matter for which either a response period or a statutory cooling-off period (as discussed below) has been previously invoked or (ii) in situations where a shareholder holds at least 75% of our issued share capital as a consequence of a successful public bid.

Moreover, our Board can invoke a cooling-off period of up to 250 days when shareholders, using their right to have items added to the agenda for a general meeting or their right to request a general meeting, propose an agenda item for our general meeting to dismiss, suspend or appoint one or more directors (or to amend any provision in the Articles of Association dealing with those matters) or when a public offer for our company is made or announced without our support, provided, in each case, that our Board believes that such proposal or offer materially conflicts with the interests of our company and its business. During a cooling-off period, our general meeting cannot dismiss, suspend or appoint directors (or amend the provisions in the Articles of Association dealing with those matters) except at the proposal of our Board.

During a cooling-off period, our Board must gather all relevant information necessary for a careful decision-making process and at least consult with shareholders representing 3% or more of our issued share capital at the time the cooling-off period was invoked, as well as with our Dutch works council (if we or, under certain circumstances, any of our subsidiaries would have one). Formal statements expressed by these stakeholders during such consultations must be published on our website to the extent these stakeholders have approved that publication. Ultimately one week following the last day of the cooling-off period, our Board must publish a report in respect of its policy and conduct of affairs during the cooling-off period on our website. This report must remain available for inspection by shareholders and others with meeting rights under Dutch law at our office and must be tabled for discussion at the next general meeting. Shareholders representing at least 3% of our issued share capital may request the Enterprise Chamber of the Amsterdam Court of Appeal, or the Enterprise Chamber (*Ondernemingskamer*) for early termination of the cooling-off period. The Enterprise Chamber must rule in favor of the request if the shareholders can demonstrate that:

- our Board, in light of the circumstances at hand when the cooling-off period was invoked, could not reasonably have concluded that the relevant proposal or hostile offer constituted a material conflict with the interests of our company and its business;

- our Board cannot reasonably believe that a continuation of the cooling-off period would contribute to careful policy-making; or other defensive measures, having the same purpose, nature and scope as the cooling-off period, have been activated during the cooling-off period and have not since been terminated or suspended within a reasonable period at the relevant shareholders' request (i.e., no 'stacking' of defensive measures).

Delaware. Delaware law does not specifically grant stockholders the right to bring business before an annual or special meeting. Delaware law provides that stockholders have the right to put any proposal before the annual meeting of stockholders, so long as it complies with the notice provisions in the corporation's governing documents. In addition, if a Delaware corporation is subject to the SEC's proxy rules, a stockholder who satisfies certain specified criteria with respect to the amount and length of ownership of the corporation's securities, such stockholder may be eligible to have its proposal included in the corporation's proxy statement for consideration by all of the corporation's shareholders.

Action by written consent

The Netherlands. Under Dutch law, shareholders' resolutions may be adopted in writing without holding a meeting of shareholders, provided that (i) the Articles of Association allow such action by written consent, (ii) the Company has not issued bearer shares or, with its cooperation, depository receipts for shares in its capital, and (iii) the resolution is adopted unanimously by all shareholders that are entitled to vote. Although our Articles of Association allow for shareholders' resolutions to be adopted in writing, the requirement of unanimity renders the adoption of shareholder resolutions without holding a meeting not feasible for us as a publicly traded Company.

Delaware. Although permitted by Delaware law, publicly listed companies do not typically permit stockholders of a corporation to take action by written consent.

Appraisal rights

The Netherlands. Subject to certain exceptions, Dutch law does not recognize the concept of appraisal or dissenters' rights. However, Dutch law does provide for squeeze-out procedures as described under "Dividends and Other Distributions—Squeeze-out procedures." Also, Dutch law provides for cash exit rights in certain situations for dissenting shareholders of a company organized under Dutch law entering into certain types of mergers. In those situations, a dissenting shareholder may file a claim with the Dutch company for compensation. Such compensation shall then be determined by one or more independent experts. The shares of such shareholder that are subject to such claim will cease to exist as of the moment of entry into effect of the merger.

Delaware. The Delaware General Corporation Law provides for stockholder appraisal rights, or the right to demand payment in cash of the judicially determined fair value of the stockholder's shares, in connection with certain mergers and consolidations.

Shareholder suits

The Netherlands. In the event a third-party is liable to a Dutch company, only the Company itself can bring a civil action against that party. The individual shareholders do not have the right to bring an action on behalf of the Company. Only in the event that the cause for the liability of a third-party to the Company also constitutes a tortious act directly against a shareholder does that shareholder have an individual right of action against such third-party in its own name. Dutch law provides for the possibility to initiate such actions collectively, in which a foundation or an association can act as a class representative and has standing to commence proceedings and claim damages if certain criteria are met. The court will first determine if those criteria are met. If so, the case will go forward as a class action on the merits after a period allowing class members to opt out from the case has lapsed. All members of the class who are residents of the Netherlands and who did not opt-out will be bound to the outcome of the case. Residents of other countries must actively opt in in order to be able to benefit from the class action. The defendant is not required to file defenses on the merits prior to the merits phase having commenced. It is possible for the parties to reach a settlement during the merits phase. Such a settlement can be approved by the court, which approval will then bind the members of the class, subject to a second opt-out. This new regime applies to claims brought after January 1, 2020 and which relate to certain events that occurred prior to that date. For other matters, the old Dutch class actions regime will apply. Under the old regime, no monetary damages can be sought. Also, a judgment rendered under the old regime will not always bind all individual class members. Even though Dutch law does not provide for derivative suits, our directors and officers can still be subject to liability under U.S. securities laws.

Our Articles of Association provide that the sole and exclusive forum for any complaint asserting a cause of action arising under the U.S. Securities Act of 1933, as amended, to the fullest extent permitted by applicable law, shall be the U.S. federal district courts.

Delaware. Under the Delaware General Corporation Law, a stockholder may bring a derivative action on behalf of the corporation to enforce the rights of the corporation. An individual also may commence a class action suit on behalf of himself and other similarly situated stockholders where the requirements for maintaining a class action under Delaware law have been met. A person may institute and maintain such a suit only if that person was a stockholder at the time of the transaction which is the subject of the suit. In addition, under Delaware case law, the plaintiff normally must be a stockholder at the time of the transaction that is the subject of the suit and throughout the duration of the derivative suit. Delaware law also requires that the derivative plaintiff make a demand on the directors of the corporation to assert the corporate claim before the suit may be prosecuted by the derivative plaintiff in court, unless such a demand would be futile.

Repurchase of shares

The Netherlands. Under Dutch law, when issuing shares, a public company such as ours may not subscribe for newly issued shares in its own capital. Such company may, however, subject to certain restrictions of Dutch law and its Articles of Association, acquire shares in its own capital. A listed public company such as ours may acquire fully paid shares in its own capital at any time for no valuable consideration. Furthermore, subject to certain provisions of Dutch law and its Articles of Association, such company may repurchase fully paid shares in its own capital if (i) the company's shareholders' equity (*eigen vermogen*) less the payment required to make the acquisition does not fall below the sum of paid-in and called-up share capital plus any reserves required by Dutch law or its Articles of Association and (ii) the aggregate nominal value of shares of the company which the company acquires, holds or on which the company holds a pledge (*pandrecht*) or which are held by a subsidiary of the company, would not exceed 50% of its then-current issued share capital. Such company may only acquire its own shares if its general meeting has granted the Board the authority to effect such acquisitions.

An acquisition by us of ordinary shares in our capital for a consideration must be authorized by our general meeting. Such authorization may be granted for a maximum period of 18 months and must specify the number of ordinary shares that may be acquired, the manner in which ordinary shares may be acquired and the price limits within which ordinary shares may be acquired. The actual acquisition may only be effected pursuant to a resolution of our Board. On June 28, 2024, our general meeting adopted a resolution pursuant to which our Board is authorized, for a period of 18 months following June 28, 2024 to cause the repurchase of ordinary shares (or depositary receipts for ordinary shares) by us of up to 10% of our issued share capital, for a price per share not exceeding 110% of the average market price of our ordinary shares on Nasdaq (such average market price being the average of the closing prices on each of the five consecutive trading days preceding the date the acquisition is agreed upon by us). These shares may be used to deliver shares underlying awards granted pursuant to our equity-based compensation plans.

No authorization of the general meeting is required if fully paid ordinary shares are acquired by us with the intention of transferring such ordinary shares to our employees under an applicable employee stock purchase plan.

Delaware. Under the Delaware General Corporation Law, a corporation may generally purchase or redeem its own shares unless the capital of the corporation is impaired or the purchase or redemption would cause an impairment of the capital of the corporation. A Delaware corporation may, however, purchase or redeem out of capital any of its own shares which are entitled upon any distribution of its assets to a preference over another class or series of its stock, or if no shares entitled to such a preference are outstanding, any of its own shares, if such shares will be retired upon acquisition and the capital of the corporation will be reduced in accordance with specified limitations.

Anti-Takeover provisions

The Netherlands. Under Dutch law, various protective measures are possible and permissible within the boundaries set by Dutch law and Dutch case law.

In this respect, certain provisions of our Articles of Association may make it more difficult for a third-party to acquire control of us or effect a change in the composition of our Board. These include:

- a provision that our directors can only be appointed on the basis of a binding nomination prepared by our Board, which can only be overruled by the general meeting by a resolution adopted by a two-thirds majority of the votes cast, representing more than half of our issued share capital (in which case the Board shall make a new nomination);

- a provision that our directors may only be dismissed by the general meeting by a two-thirds majority of the votes cast representing more than half of our issued share capital, unless the dismissal is proposed by our Board in which latter case a simple majority of the votes cast would be sufficient;
- a provision which allows the most recent (former) chairman of our Board or our most recent (former) chief executive officer to be charged with our management if all of our directors are absent or incapacitated; and
- requirements that certain matters, including an amendment of our Articles of Association, may only be resolved upon by our general meeting if proposed by our Board.

Dutch law also allows for staggered multi-year terms of our directors, as a result of which only part of our directors may be subject to appointment or re-appointment in any given year.

Furthermore, our Board may, under certain circumstances invoke a reasonable period of up to 180 days to respond to certain shareholder proposals or a statutory cooling-off period of up to 250 days to respond to certain shareholder proposals or a hostile bid. See above under "Shareholder Proposals."

Delaware. In addition to other aspects of Delaware law governing fiduciary duties of directors during a potential takeover, the Delaware General Corporation Law also contains provisions that protect Delaware companies from hostile takeovers and from actions following the takeover by prohibiting some transactions once an acquirer has gained a significant holding in the corporation.

Section 203 of the Delaware General Corporation Law prohibits "business combinations," including mergers, sales and leases of assets, issuances of securities and similar transactions with an "interested stockholder" (which could include a shareholder that beneficially owns 15% or more of a corporation's voting stock) for a period of three years following the time that such person becomes an interested stockholder, unless:

- prior to such time the board of directors of the corporation approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder;
- after the completion of the transaction in which the person becomes an interested stockholder, the interested stockholder holds at least 85% of the voting stock of the corporation not including shares owned by persons who are directors and officers of interested stockholders and shares owned by specified employee benefit plans; or
- after the person becomes an interested stockholder, the business combination is approved by the board of directors of the corporation and holders of at least 66.67% of the outstanding voting stock, excluding shares held by the interested stockholder.

A Delaware corporation may elect not to be governed by Section 203 by a provision contained in the original certificate of incorporation of the corporation or an amendment to the original certificate of incorporation or to the bylaws of the Company, which amendment must be approved by a majority of the shares entitled to vote and may not be further amended by the board of directors of the corporation. In most cases, such an amendment is not effective until 12 months following its adoption.

Inspection of books and records

The Netherlands. The Board must provide the general meeting all information that it requires, unless this would be contrary to an overriding interest of our Company. If the Board invokes such an overriding interest, it must give reasons.

Delaware. Under the Delaware General Corporation Law, any stockholder may inspect for any proper purpose certain of the corporation's books and records during the corporation's usual hours of business.

Dismissal of Directors

The Netherlands. Under our Articles of Association, our directors can only be dismissed by the general meeting by simple majority, provided that our Board proposes the dismissal. In other cases, the general meeting can only pass such resolution by a two-thirds majority representing more than half of the issued share capital. The DCGC recommends that the general meeting can pass a resolution to dismiss a director by simple majority, representing no more than one-third of the issued share capital.

Delaware. Under the Delaware General Corporation Law, any director or the entire board of directors may be removed, with or without cause, by the holders of a majority of the shares then entitled to vote at an election of

directors, except (i) unless the certificate of incorporation provides otherwise, in the case of a corporation whose board is classified, stockholders may effect such removal only for cause, or (ii) in the case of a corporation having cumulative voting, if less than the entire board is to be removed, no director may be removed without cause if the votes cast against such director's removal would be sufficient to elect such director if then cumulatively voted at an election of the entire board of directors, or, if there are classes of directors, at an election of the class of directors of which he is a part.

Issuance of Shares

The Netherlands. Under Dutch law, a company's general meeting is the corporate body authorized to resolve on the issuance of shares and the granting of rights to subscribe for shares. The general meeting can delegate such authority to another corporate body of the company, such as the Board, for a period not exceeding five years; this authorization may only be extended from time to time for a maximum period of five years.

On June 28, 2024, our general meeting adopted a resolution pursuant to which our Board is authorized, for a period of five years following June 28, 2024, to issue shares or grant rights to subscribe for shares up to our authorized share capital from time to time. We may not subscribe for our own shares on issue.

Delaware. The issuance of shares requires the board of directors to adopt a resolution or resolutions, authorizing the issuance, pursuant to authority expressly vested in the board of directors by the provisions of the Company's certificate of incorporation.

Pre-emptive rights

The Netherlands. Under Dutch law, in the event of an issuance of ordinary shares, each shareholder will have a pro rata preemptive right in proportion to the aggregate nominal value of the ordinary shares held by such holder (with the exception of ordinary shares to be issued to employees or ordinary shares issued against a contribution other than in cash or pursuant to the exercise of a previously acquired right to subscribe for shares). Under our Articles of Association, the preemptive rights in respect of newly issued ordinary shares may be restricted or excluded by a resolution of the general meeting upon proposal of the Board.

Another corporate body may restrict or exclude the preemptive rights in respect of newly issued ordinary shares if it has been designated as the authorized body to do so by the general meeting. Such designation can be granted for a period not exceeding five years. A resolution of the general meeting to restrict or exclude the preemptive rights or to designate another corporate body as the authorized body to do so requires a majority of not less than two-thirds of the votes cast, if less than one-half of our issued share capital is represented at the meeting.

On June 28, 2024, our general meeting authorized our Board, for a period of five years following June 28, 2024, to limit or exclude preemptive rights in relation to an issuance of shares or a grant of rights to subscribe for shares that the Board is authorized to resolve upon. See above under "—Issuance of Shares."

Delaware. Under the Delaware General Corporation Law, stockholders have no preemptive rights to subscribe for additional issues of stock or to any security convertible into such stock unless, and to the extent that, such rights are expressly provided for in the certificate of incorporation.

Dividends

The Netherlands. Under Dutch law, we may only pay dividends and other distributions from our reserves to the extent our shareholders' equity (*eigen vermogen*) exceeds the sum of our paid-in and called-up share capital plus the reserves we must maintain under Dutch law or our Articles of Association and (if it concerns a distribution of profits) after adoption of our statutory annual accounts by our general meeting from which it appears that such dividend distribution is allowed. Subject to those restrictions, any future determination to pay dividends or other distributions from our reserves will be at the discretion of our Board and will depend upon a number of factors, including our results of operations, financial condition, future prospects, contractual restrictions, restrictions imposed by applicable law and other factors we deem relevant. See "Dividend Policy."

Under our Articles of Association, our Board may decide that all or part of the profits shown in our adopted statutory annual accounts will be added to our reserves. After reservation of any such profits, any remaining profits will be at the disposal of the general meeting at the proposal of our Board for distribution on our ordinary shares, subject to applicable restrictions of Dutch law. Our Board is permitted, subject to certain requirements and applicable restrictions of Dutch law, to declare interim dividends without the approval of our general meeting.

Dividends and other distributions shall be made payable no later than a date determined by the Board. Claims to dividends and other distributions not made within five years from the date that such dividends or

distributions became payable will lapse and any such amounts will be considered to have been forfeited to us (*verjaring*).

Delaware. Under the Delaware General Corporation Law, subject to any restrictions contained in the corporation's certificate of incorporation, a Delaware corporation may pay dividends out of its surplus (the excess of net assets over capital), or in case there is no surplus, out of its net profits for the fiscal year in which the dividend is declared and/or the preceding fiscal year (provided that the amount of the capital of the corporation is not less than the aggregate amount of the capital represented by the issued and outstanding stock of all classes having a preference upon the distribution of assets). Dividends may be paid in the form of shares of the corporation's capital stock, property or cash.

Shareholder vote on Certain Reorganizations

The Netherlands. Under Dutch law, the general meeting must approve resolutions of the Board relating to a significant change in the identity or the character of the Company or the business of the Company, which includes:

- a transfer of the business or virtually the entire business to a third-party;
- the entry into or termination of a long-term cooperation of the Company or a subsidiary with another legal entity or company or as a fully liable partner in a limited partnership or general partnership, if such cooperation or termination is of a far-reaching significance for the Company; and
- the acquisition or divestment by the Company or a subsidiary of a participating interest in the capital of a company having a value of at least one-third of the amount of its assets according to its balance sheet and explanatory notes or, if the Company prepares a consolidated balance sheet, according to its consolidated balance sheet and explanatory notes in the last adopted annual accounts of the Company.

The absence of such approval shall result in the relevant resolution being null and void but shall not affect the powers of representation of the Board or of the executive directors.

Delaware. Under the Delaware General Corporation Law, the vote of a majority of the outstanding shares of capital stock entitled to vote thereon generally is necessary to approve a merger or consolidation or the sale of all or substantially all of the assets of a corporation. The Delaware General Corporation Law permits a corporation to include in its certificate of incorporation a provision requiring for any corporate action the vote of a larger portion of the stock or of any class or series of stock than would otherwise be required.

Under the Delaware General Corporation Law, no vote of the stockholders of a surviving corporation to a merger is needed, however, unless required by the certificate of incorporation, if (i) the agreement of merger does not amend in any respect the certificate of incorporation of the surviving corporation, (ii) the shares of stock of the surviving corporation are not changed in the merger, and (iii) the number of shares of common stock of the surviving corporation into which any other shares, securities or obligations to be issued in the merger may be converted does not exceed 20% of the surviving corporation's common stock outstanding immediately prior to the effective date of the merger. In addition, stockholders may not be entitled to vote in certain mergers with other corporations that own 90% or more of the outstanding shares of each class of stock of such corporation, but the stockholders will be entitled to appraisal rights.

Remuneration of Directors

The Netherlands. Dutch law does not provide for limitations with respect to the aggregate annual compensation paid to our directors, provided that such compensation is consistent with our compensation policy. Our compensation policy has been adopted by the general meeting with effect from February 5, 2021. Changes to such compensation policy will require a vote of our general meeting by simple majority of votes cast. Our Board determines the remuneration of individual directors with due observance of the compensation policy. A proposal with respect to remuneration schemes in the form of shares or rights to shares in which directors may participate is subject to approval by our general meeting by simple majority of votes cast. Such a proposal must set out at least the maximum number of shares or rights to subscribe for shares to be granted to our directors and the criteria for granting or amendment.

Delaware. Under the Delaware General Corporation Law, the stockholders do not generally have the right to approve the compensation policy for directors or the senior management of the corporation, although certain aspects of executive compensation may be subject to stockholder vote due to the provisions of U.S. federal securities and tax law, as well as exchange requirements.

Exhibit 8.1

Subsidiaries of Pharvaris N.V.

Subsidiary	Jurisdiction
Pharvaris Holdings B.V.	The Netherlands
Pharvaris Netherlands B.V.	The Netherlands
Pharvaris GmbH	Zug, Switzerland
Pharvaris, Inc.	Delaware, United States of America

INSIDER TRADING POLICY PHARVARIS N.V.

ARTICLE 1 INTRODUCTION

This document sets out the Company's insider trading policy.

ARTICLE 2 DEFINITIONS AND INTERPRETATION

2.1 In this policy the following definitions shall apply:

Article An article of this policy.

Board The Company's board of directors.

CEO The Company's chief executive officer.

Chairman The chairman of the Board.

Company Pharvaris N.V.

Company Group The Company and its Subsidiaries collectively or, where the context so requires, any of them individually.

Company Security A security, derivative or other financial instrument issued by or relating to the Company, including:

a. Shares;

b. depository receipts for Shares;

c. options, futures, swaps, forward rate agreements and other derivative contracts relating to Shares; and

d. debt instruments of the Company.

Compliance Officer The Company's Chief Legal Officer ("CLO") unless designated otherwise by the Board.

Director A member of the Board of any company in the Company Group.

Insider Any Director, any employees with the title of vice president or higher, investor relations employees that assist with

earnings releases, finance, accounting and legal department employees that directly assist with preparing SEC filings, any employees on the Company's disclosure committee, and any persons designated by the Compliance Officer as being subject to these procedures.

NASDAQ The NASDAQ Stock Market.

Share A share in the Company's capital, irrespective of its class.

Subsidiary A subsidiary of the Company within the meaning of Section 2:24a of the Dutch Civil Code.

Trading Window After the close of trading on the second business day following an earnings release by the Company with respect to the preceding financial period until the day that is fourteen calendar days prior to the close of the then current financial quarter.

2.2 References to "**transactions**" in Company Securities include sales, purchases or other acts consisting of or aimed at acquiring or disposing of such Company Securities (either directly or indirectly and for one's own account or the account of another person), but exclude the grant or exercise of options for, or other rights to acquire, Company Securities under any equity or incentive plan established by the Company (provided that subsequent transactions in Company Securities acquired pursuant to the exercise of such options or rights shall be subject to this policy).

2.3 References to statutory provisions are to those provisions as they are in force from time to time.

2.4 Terms that are defined in the singular have a corresponding meaning in the plural.

2.5 Words denoting a gender include each other gender.

2.6 Except as otherwise required by law, the terms "written" and "in writing" include the use of electronic means of communication.

ARTICLE 3
DEFINITION OF MATERIAL INFORMATION AND PROHIBITIONS

3.1 Material Information: Information is considered "material" if a reasonable investor would consider that information important in making a decision to buy, hold or sell securities. Any information that could be expected to affect a company's stock price, whether it is positive or negative, should be considered material. There is no bright-line standard for assessing materiality; rather, materiality is based on an assessment of all of the facts and circumstances and is often evaluated by enforcement authorities with the benefit of hindsight. While it is not possible to define all categories of material information, some examples of information that ordinarily would be regarded as material are:

- Pre-clinical or clinical trial results (positive or negative);
- Regulatory feedback;
- Financial results or guidance;
- Pre-clinical, clinical and regulatory timeline guidance;
- A pending or proposed merger, acquisition or tender offer;
- A pending or proposed acquisition or disposition of a significant asset (including intellectual property);
- A pending or proposed collaboration or joint venture;
- A change in senior management;
- A Company restructuring;
- Significant related party transactions;
- An offering of Company Securities;
- Bank borrowings or other financing transactions out of the ordinary course;
- A change in auditors or notification that the auditor's reports may no longer be relied upon;
- Pending or threatened significant litigation, or the resolution of such litigation;
- Impending bankruptcy or the existence of severe liquidity problems; and
- Significant cybersecurity incidents.

If you are unsure whether information is material, you should either consult the Chief Legal Officer before making any decision to disclose such information (other than to persons who need to know it) or to trade in or recommend securities to which that information relates or assume that the information is material.

3.2 Without prejudice to the relevant restrictions and prohibitions under applicable law

concerning insider trading and market manipulation, Insiders are prohibited from:

a. directly or indirectly conducting or recommending a transaction in Company Securities when the Insider has knowledge of Material Nonpublic Information ("MNPI"), subject to the exceptions provided for by applicable law, including if it concerns a transaction conducted in discharge of an enforceable obligation that already existed at the time the Insider became acquainted with such MNPI (and in those cases only with the prior written approval of the Compliance Officer);

b. engaging in hedging transactions, including transactions involving options, puts, calls, prepaid variable forward contracts, equity swaps, collars and exchange funds or other derivatives, that are designed to hedge or speculate on any change in the market value of Company Securities;

c. selling Company Securities within six months after having purchased such Company Securities;

d. purchasing or writing options on Company Securities or short-selling Company Securities; and

e. pledging Company Securities, including by purchasing Company Securities on margin or holding Company Securities in a margin account.

3.3 Each Insider shall provide his full cooperation to the Compliance Officer in any inquiry in relation to such Insider as referred to in Article 7.3, including by providing (or instructing and authorizing his bank, investment manager, broker or other institution where his securities account(s) is/are being administered to provide) the Compliance Officer with any information as may reasonably be requested by the Compliance Officer.

3.4 Each Insider shall take note of, and shall comply with, the requirements under applicable law concerning the notification and disclosure of his actual and deemed shareholdings (or other voting and economic interests) in the Company, net and gross short positions in relation to the Company, and transactions conducted in Company Securities. If any Insider is in doubt as to his notification and disclosure obligations in this respect, he should consult the Compliance Officer.3.5 Insiders are also prohibited from directly or indirectly conducting or recommending a transaction in the securities of another company or corporation, if the Insider learns in the course of his position with the Company Group material non-public information, or otherwise confidential information, about such other company or corporation that is likely to affect the value of those securities.

3.5 Each Insider is responsible for ensuring that its family members who reside with such Insider (including a spouse, a child, a child away at college, stepchildren, grandchildren, parents, stepparents, grandparents, siblings and in-laws), anyone else who lives in such Insider's household, and any family members who do not live in such Insider's household but whose transactions in Company Securities are directed by such Insider or are subject to such Insider's influence or control complies with the terms of this policy. Each Insider is responsible for the transactions of these other persons and therefore should make them aware of the need to confer with such Insider before they trade in Company Securities.

ARTICLE 4 TRADING WINDOW

4.1 Subject to Articles 3.1 and 5.1, transactions by Insiders in Company Securities are only permitted:

a. during a Trading Window; or

b. outside a Trading Window for reasons of exceptional personal hardship and subject to prior review by the Compliance Officer, provided that, if the Compliance Officer wishes to trade outside a Trading Window, such trade shall be subject to prior review by the CEO.

4.2 At times the Company may determine that Insiders are not permitted to conduct transactions in Company Securities even during a Trading Window. No reasons may be provided, and the closing of a Trading Window itself may constitute MNPI that should not be communicated.

4.3 The restrictions in this Article 4 do not apply to:

a. transactions in Company Securities conducted by Insiders pursuant to a pre- arranged plan under Article 6;

b. the acceptance of Company Securities under an equity or incentive plan established by the Company; and

c. the exercise of options for or the exercise of similar rights to Company Securities under an equity or incentive plan established by the Company, provided there is no sale of Company Securities in connection with such exercise, including sales to cover the exercise price or taxes.

ARTICLE 5 PRE-CLEARANCE

5.1 All transactions in Company Securities (including the creation or modification of a pre- arranged trading plan) by Insiders must be pre-cleared by the Compliance Officer. Preclearance requests should be submitted at least two trading days in advance of the proposed transaction. If the Compliance Officer wishes to execute such a transaction, this shall be subject to pre-clearance by the CEO. Pre-cleared transactions not initiated with a broker within ten trading days shall again require pre-clearance under the previous sentence.

5.2 Pre-clearance under Article 5.1 may be delayed or denied at the discretion of the Compliance Officer or the CEO, as applicable, without providing any reason for such decision.

5.3 Notwithstanding the pre-clearance process under this Article 5, it is each Insider's

responsibility to determine whether he is in possession of Inside Information, and neither an open Trading Window nor pre-clearance of a transaction absolves the Insider from the general prohibition of trading on MNPI.

ARTICLE 6
PRE-ARRANGED TRADING PLAN

6.1 Performing transactions in Company Securities under a pre-arranged trading plan is not deemed a violation of this policy, even if the Insider is in possession of MNPI at the time such a transaction is executed under such plan, provided that such plan meets the following conditions:

a. the Insider must enter into a binding contract or written plan with a licensed brokerage firm or other fiduciary that holds discretionary authority over the plan;

b. the plan specifies the amount, price and date on which Company Securities are to be purchased or sold (or a formula for making such determinations);

c. the plan is established (or modified) at a time when the Insider does not possess Inside Information and a Trading Window is open;

d. the plan prohibits the Insider from later asserting any influence over any person who exercises discretion as to how, when or whether to effect the transactions under such plan;

e. the plan allows for the cancellation of a transaction and/or suspension of the plan upon notice and request by the Company to the Insider if the proposed transaction fails to comply with applicable laws or would create material adverse consequences for the Company;

f. the plan may be terminated by the Insider at any time subject to prior consultation with the Compliance Officer or, if the Insider is the Compliance Officer, the CEO;

g. the plan and any modifications thereof are approved by the Compliance Officer or, if the Insider is the Compliance Officer, the CEO, which approval may be delayed or denied at his sole discretion without providing any reason for such decision; and

h. the first transaction under the plan occurs after a waiting period of 30 calendar days.

6.2 Transactions in Company Securities by an Insider pursuant to an approved pre-arranged trading plan as described in Article 6.1 will not require pre-clearance under Article 5 at the time of the transaction. Notwithstanding any pre-clearance of a trading plan, neither the Company, nor the Directors or other officers of the Company assume liability for the consequences of any transaction made pursuant to such plan.

ARTICLE 7 COMPLIANCE OFFICER

7.1 The Compliance Officer shall be appointed and dismissed by the Board. Until such time that the Board has appointed a Compliance Officer, or in the event of a vacancy in this office, the CLO shall fulfill the duties and responsibilities of the Compliance Officer and shall exercise such powers as are conferred upon the Compliance Officer pursuant to this policy and such other powers as the Board may confer on the Compliance Officer from time to time.

7.2 The Compliance Officer shall have the duties and powers conferred on him by this policy and such other duties and powers as the Board may confer on him from time to time.

7.3 The Compliance Officer may hold an inquiry, or procure an inquiry to be held, into the transactions in Company Securities conducted by, at the instruction of, or for the benefit

of any Insider. The Compliance Officer shall report the outcome of such an inquiry in writing to the CEO (or to the Chairman, if such inquiry concerns the CEO). The CEO (or the Chairman, if the inquiry concerns the CEO) shall report his findings and conclusions concerning the inquiry in writing to the Insider concerned.

ARTICLE 8 AMENDMENTS AND DEVIATIONS

Pursuant to a resolution to that effect, the Board may amend or supplement this policy, subject to ongoing compliance with applicable law and NASDAQ requirements.

ARTICLE 9 GOVERNING LAW AND JURISDICTION

This policy shall be governed by and shall be construed in accordance with the laws of the Netherlands. Any dispute arising in connection with this policy shall be submitted to the exclusive jurisdiction of the competent court in Amsterdam, the Netherlands.

Exhibit 12.1

CERTIFICATION OF THE PRINCIPAL EXECUTIVE OFFICER PURSUANT TO EXCHANGE ACT RULE 13A-14(A) OR 15D-14(A) AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Berndt Modig, certify that:

1. I have reviewed this annual report on Form 20-F of Pharvaris N.V.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the company as of, and for, the periods presented in this report;

4. The company's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the company and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the company, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the company's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the company's internal control over financial reporting that occurred during the period covered by the annual report that has materially affected, or is reasonably likely to materially affect, the company's internal control over financial reporting;

5. The company's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the company's auditors and the

audit committee of the company's board of directors (or persons performing the equivalent functions):

(a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the company's ability to record, process, summarize and report financial information; and

(b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the company's internal control over financial reporting.

Date: April 7, 2025

By: /s/ Berndt Modig
Name: Berndt Modig
Title: Director and Chief Executive Officer

Exhibit 12.2

CERTIFICATION OF THE PRINCIPAL FINANCIAL OFFICER PURSUANT TO EXCHANGE ACT RULE 13A-14(A) OR 15D-14(A) AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, David Nassif, certify that:

1. I have reviewed this annual report on Form 20-F of Pharvaris N.V.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the company as of, and for, the periods presented in this report;

4. The company's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the company and have:Pharvaris N.V. (the

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the company, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the company's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the company's internal control over financial reporting that occurred during the period covered by the annual report that has materially affected, or is reasonably likely to materially affect, the company's internal control over financial reporting;

5. The company's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the company's auditors and the audit committee of the company's board of directors (or persons performing the equivalent functions):

(a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the company's ability to record, process, summarize and report financial information; and

(b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the company's internal control over financial reporting.

Date: April 7, 2025

By: /s/ David Nassif
Name: David Nassif
Title: Chief Financial Officer

Exhibit 13.1

Certification by the Principal Executive Officer
Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002

In connection with the Annual Report of Pharvaris N.V. (the "Company") on Form 20-F for the fiscal year ended December 31, 2024 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Berndt Modig, Chief Executive Officer of the Company, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to my knowledge:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: April 7, 2025

By: /s/ Berndt Modig
Name: Berndt Modig
Title: Director and Chief Executive Officer

Exhibit 13.2

Certification by the Principal Financial Officer
Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002

In connection with the Annual Report of Pharvaris N.V. (the "Company") on Form 20-F for the fiscal year ended December 31, 2023 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, David Nassif, Chief Financial Officer of the Company, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to my knowledge:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: April 7, 2025

By: /s/ David Nassif
Name: David Nassif
Title: Chief Financial Officer

Exhibit 15.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in the Registration Statements on Form S-8 (No. 333-252897) and Form F-3 (Nos 333-273757 and 333-277705 and 333-278650) of Pharvaris N.V. of our report dated April 7, 2025 relating to the financial statements, which appears in this Form 20-F.

/s/ PricewaterhouseCoopers Accountants N.V.

Amsterdam, The Netherlands
April 7, 2025

Exhibit 97.1

PURPOSE

CLAWBACK POLICY PHARVARIS N.V.

Pharvaris N.V. (the "Company") believes that it is in the best interests of the Company and its shareholders to create and maintain a culture that emphasizes integrity and accountability and that reinforces the Company's pay-for-performance compensation philosophy. The Company's Board of Directors (the "Board") has therefore adopted this policy which provides for the recoupment of certain executive compensation in the event that the Company is required to prepare an accounting restatement of its financial statements due to material noncompliance with any financial reporting requirement under the federal securities laws (this "Policy"). This Policy is designed to comply with Section 10D of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), the rules promulgated thereunder, and the listing standards of the national securities exchange on which the Company's securities are listed.

ADMINISTRATION

This Policy shall be administered by the Compensation Committee of the Board (the "Compensation Committee"). Any determinations made by the Compensation Committee shall be final and binding on all affected individuals.

COVERED EXECUTIVES

This Policy applies to the Company's current and former executive officers (as determined by the Compensation Committee in accordance with Section 10D of the Exchange Act, the rules promulgated thereunder, and the listing standards of the national securities exchange on which the Company's securities are listed) and such other senior executives or employees who may from time to time be deemed subject to this Policy by the Compensation Committee (collectively, the "Covered Executives"). This Policy shall be binding and enforceable against all Covered Executives.

RECOUPMENT; ACCOUNTING RESTATEMENT

In the event that the Company is required to prepare an accounting restatement of its financial statements due to the Company's material noncompliance with any financial reporting requirement under the securities laws, including (i) any required accounting restatement to correct an error in previously issued financial statements that is material to the previously issued financial statements, or (ii) that would result in a material misstatement if the error were corrected in the current period or left uncorrected in the current period (each an "Accounting Restatement"), the Compensation Committee will reasonably promptly require reimbursement or forfeiture of the Overpayment (as defined below) received by any Covered Executive (x) after beginning service as a Covered Executive, (y) who served as a Covered Executive at any time during the performance period for such Incentive-Based Compensation, and (z) during the three (3) completed fiscal years immediately preceding the date on which the Company is required to prepare an Accounting Restatement and any transition period (that results from a change in the Company's fiscal year) within or immediately following those three (3) completed fiscal years. Notwithstanding the

foregoing, this Policy shall only apply to Incentive-Based Compensation received on or after June 9, 2023.

INCENTIVE-BASED COMPENSATION

For purposes of this Policy, "Incentive-Based Compensation" means any compensation that is granted, earned, or vested based wholly or in part upon the attainment of a financial reporting measures, including, but not limited to: (i) non-equity incentive plan awards that are earned solely or in part by satisfying a financial reporting measure performance goal; (ii) bonuses paid from a bonus pool, where the size of the pool is determined solely or in part by satisfying a financial reporting measure performance goal; (iii) other cash awards based on satisfaction of a financial reporting measure performance goal; (iv) restricted stock, restricted stock units, stock options, stock appreciation rights, and performance share units that are granted or vest solely or in part based on satisfaction of a financial reporting measure performance goal; and (v) proceeds from the sale of shares acquired through an incentive plan that were granted or vested solely or in part based on satisfaction of a financial reporting measure performance goal.

Compensation that would not be considered Incentive-Based Compensation includes, but is not limited to: (a) salaries; (b) bonuses paid solely based on satisfaction of subjective standards, such as demonstrating leadership, and/or completion of a specified employment period; (c) non- equity incentive plan awards earned solely based on satisfaction of strategic or operational measures; (d) wholly time-based equity awards; and (e) discretionary bonuses or other compensation that is not paid from a bonus pool that is determined by satisfying a financial reporting measure performance goal.

A financial reporting measure is: (i) any measure that is determined and presented in accordance with the accounting principles used in preparing financial statements, or any measure derived wholly or in part from such measure, such as revenues, EBITDA, or net income and (ii) stock price and total shareholder return. Financial reporting measures include, but are not limited to: revenues; net income; operating income; profitability of one or more reportable segments; financial ratios (e.g., accounts receivable turnover and inventory turnover rates); net assets or net asset value per share; earnings before interest, taxes, depreciation and amortization; funds from operations and adjusted funds from operations; liquidity measures (e.g., working capital, operating cash flow); return measures (e.g., return on invested capital, return on assets); earnings measures (e.g., earnings per share); sales per square foot or same store sales, where sales is subject to an accounting restatement; revenue per user, or average revenue per user, where revenue is subject to an accounting restatement; cost per employee, where cost is subject to an accounting restatement; any of such financial reporting measures relative to a peer group, where the Company's financial reporting measure is subject to an accounting restatement; and tax basis income.

OVERPAYMENT: AMOUNT SUBJECT TO RECOVERY

The amount to be recovered will be the amount of Incentive-Based Compensation received that exceeds the amount of Incentive-Based Compensation that otherwise would have been received had it been determined based on the restated amounts, and must be computed without regard to any taxes paid (the "Overpayment"). Incentive-Based Compensation is deemed received in the Company's fiscal period during which the financial reporting measure specified in the

incentive-based compensation award is attained, even if the vesting, payment or grant of the incentive-based compensation occurs after the end of that period.

For Incentive-Based Compensation based on stock price or total shareholder return, where the amount of erroneously awarded compensation is not subject to mathematical recalculation directly from the information in the Accounting Restatement, the amount must be based on a reasonable estimate of the effect of the Accounting Restatement on the stock price or total shareholder return upon which the Incentive-Based Compensation was received; and the Company must maintain documentation of the determination of that reasonable estimate and provide such documentation to the exchange on which the Company's securities are listed.

METHOD OF RECOUPMENT

The Compensation Committee will determine, in its sole discretion, the method or methods for recouping any Overpayment hereunder which may include, without limitation:

- requiring reimbursement of cash Incentive-Based Compensation previously paid;
- seeking recovery of any gain realized on the vesting, exercise, settlement, sale, transfer, or other disposition of any equity-based awards granted as Incentive-Based Compensation;
- offsetting any or all of the Overpayment from any compensation otherwise owed by the Company to the Covered Executive;
- cancelling outstanding vested or unvested equity awards; and/or
- taking any other remedial and recovery action permitted by law, as determined by the Compensation Committee.

LIMITATION ON RECOVERY; NO ADDITIONAL PAYMENTS

The right to recovery will be limited to Overpayments received during the three (3) years prior to the date on which the Company is required to prepare an Accounting Restatement and any transition period (that results from a change in the Company's fiscal year) within or immediately following those three (3) completed fiscal years. In no event shall the Company be required to award Covered Executives an additional payment if the restated or accurate financial results would have resulted in a higher Incentive-Based Compensation payment.

NO INDEMNIFICATION

The Company shall not indemnify any Covered Executives against the loss of any incorrectly awarded Incentive-Based Compensation.

INTERPRETATION

The Compensation Committee is authorized to interpret and construe this Policy and to make all determinations necessary, appropriate, or advisable for the administration of this Policy. It is intended that this Policy be interpreted in a manner that is consistent with the requirements of Section 10D of the Exchange Act and the applicable rules or standards adopted by the Securities

and Exchange Commission or any national securities exchange on which the Company's securities are listed.

EFFECTIVE DATE

This Policy shall be effective as of the date it is adopted by the Board (the "Effective Date") and shall apply to Incentive-Based Compensation (including Incentive-Based Compensation granted pursuant to arrangements existing prior to the Effective Date).

AMENDMENT; TERMINATION

The Board may amend this Policy from time to time in its discretion. The Board may terminate this Policy at any time.

OTHER RECOUPMENT RIGHTS

The Board intends that this Policy will be applied to the fullest extent of the law. The Compensation Committee may require that any employment or service agreement, cash-based bonus plan or program, equity award agreement, or similar agreement entered into on or after the adoption of this Policy shall, as a condition to the grant of any benefit thereunder, require a Covered Executive to agree to abide by the terms of this Policy. Any right of recoupment under this Policy is in addition to, and not in lieu of, any other remedies or rights of recoupment that may be available to the Company pursuant to the terms of any similar policy in any employment agreement, equity award agreement, cash-based bonus plan or program, or similar agreement and any other legal remedies available to the Company.

IMPRACTICABILITY

The Compensation Committee shall recover any Overpayment in accordance with this Policy except to the extent that the Compensation Committee determines such recovery would be impracticable because:

(A)The direct expense paid to a third party to assist in enforcing this Policy would exceed the amount to be recovered;

(B)Recovery would violate home country law of the Company where that law was adopted prior to November 28, 2022; or

(C)Recovery would likely cause an otherwise tax-qualified retirement plan, under which benefits are broadly available to employees of the Company, to fail to meet the requirements of 26
U.S.C. 401(a)(13) or 26 U.S.C. 411(a) and regulations thereunder.

SUCCESSORS

This Policy shall be binding and enforceable against all Covered Executives and their beneficiaries, heirs, executors, administrators or other legal representatives.